PEM GUIDES

PEDIATRIC EMERGENCY MEDICINE

VERSION 10.0 (2023)

NYU Langone Health

INTRODUCTION

WELCOME: PEM GUIDES 10.0

PEM (Pediatric Emergency Medicine) Guides was developed as an online, point of care resource for the residents and medical students who work with us in our pediatric emergency departments.

PEM Guides are not intended to be a definitive resource but were developed to provide the caregiver with a concise answer to the question:

> "How do I take care of my pediatric patient in the emergency department?

PEM Guides focus on the essential diagnostic, treatment and disposition decisions. Critical information is summarized in easy to read tables.

The PEM Guides iBook is updated annually as new evidence and recommendations become available. Version 10.0 (2023) includes 10 new PEM Guides as well as revisions of 30 existing chapters in the past year. Since version 1.0 we have added 95 new chapters (total 235 chapters) and completed over 268 chapter revisions.

MANDATORY DISCLAIMER
The information provided in this ebook does not represent specific practice guidelines that are endorsed by the faculty of the division of pediatric emergency medicine and should not be interpreted as the standard of care at our institutions. In addition, some of the information is specific to our institutions and will need to be adapted to your setting.

The approach to the clinical care of every patient must be individualized. Clinical decision-making is a dynamic process and options presented in our PEM Guides may not reflect all possible solutions or the best possible solution for your patient as diagnosis and management decisions evolve.

DISCLOSURE
The editor and authors of PEM Guides have no conflicts of interest with any of the medications or devices discussed.

CONTACT US
PEM Guides is a work in progress. We will be adding additional topics and revising our content annually. Your feedback is essential to our success. If you would like to contribute in any way please let us know.

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REVISION HISTORY

2023 UPDATES (VERSION 10.0)

NEW PEM GUIDES

PEM Guide: Gastroenterology: Clostridium Difficile: Michael Mojica, MD
PEM Guide: Gastroenterology: Gastritis: Matthew Paik, MD
PEM Guide: Gastroenterology: Umbilical Disorders: Didier Murillo-Parra, MD
PEM Guide: Infections: Cat Scratch Disease: Alexandra Van Oyen, MD
PEM Guide: Infections: Poliomyelitis: Michael Mojica, MD
PEM Guide: Orthopedics: Hand Fractures: Nicholas Delacruz, MD
PEM Guide: Orthopedics: Slipped Capital Femoral Epiphysis: Michael Mojica, MD
PEM Guide: Respiratory: Parapneumonic Effusions: Michael Mojica, MD
PEM Guide: Respiratory: Point of Care Lung Ultrasound: Alexandra Van Oyen, MD
PEM Guide: Surgery: Meckel's Diverticulum: Michael Mojica, MD

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PEM Guide: Rheumatology: Multisystem Infammatory Syndrome in Children (MIS-C)

PEM Guide: Resuscitation: Brief Resolved Unexplained Events
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PEM Guide: Trauma: Chest Trauma: Primary Survey
PEM Guide: Trauma: Concussions
PEM Guide: Trauma: Dental and Oral Trauma
PEM Guide: Trauma: Skull Fractures

2022 UPDATES (VERSION 9.0)

NEW PEM GUIDES

PEM Guide: Airway Procedures: Post Intubation Sedation/Paralysis: Michael Mojica, MD
PEM Guide: Cardiology: Heart Transplant: Ellen Duncan, MD, PhD et al.
PEM Guide: Cardiology: Ductal Dependent Cardiac Lesions: Michael Mojica, MD
PEM Guide: Child Protection: Sudden Infant Death: Evan Yanni, MD
PEM Guide: Gastroenterology: Cholelithiasis and Cholecystitis: Alexa Goldfarb, DO
PEM Guide: Gastroenterology: Constipation: Arielle Grossman, MD
PEM Guide: Gastroenterology: Gallbladder POC Ultrasound: Adriana Manikian, MD
PEM Guide: Infections: Mycoplasma Pneumoniae: Giovanna Varuzza Baye MD
PEM Guide: Respiratory: Allergic Conjunctivitis and Rhinitis: N Barney, MD, Y Silber, MD
PEM Guide: Obstetrics-Gynecology: Precipitous Vaginal Delivery: Elise Perlman, MD
PEM Guide: Psychiatry: Eating Disorders: Jennifer Grad, MD
PEM Guide: Rheumatology: MIS-C: Michael Mojica, MD
PEM Guide: Trauma: Skull Fractures: Michael Mojica, MD

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2021 UPDATES (VERSION 8.0)

NEW PEM GUIDES

PEM Guide: Endocrine-Metabolic: Hypokalemia: Michael Mojica, MD
PEM Guide: Environmental Injuries: Frostbite: Michael Mojica, MD
PEM Guide: Gastroenterology: Gastrostomy Tube Complications: Michael Mojica, MD
PEM Guide: GI: Inflammatory Bowel Disease: Arielle Grossman MD, Melanie Greifer, MD
PEM Guide: Gastroenterology: Upper Gastrointestinal Hemorrhage: Michael Mojica, MD
PEM Guide: Hematology-Oncology: Leukemia: Ellen Duncan, MD, PhD
PEM Guide: Hematology-Oncology: Tumor Lysis Syndrome: Elise Perlman, MD
PEM Guide: Infections: Enteroviral Infections: Ellen Duncan, MD, PhD
PEM Guide: Respiratory: Spontaneous Pneumothorax: Michael Mojica, MD
PEM Guide: Resuscitation: Vasoactive Medication for Shock: Michael Mojica, MD
PEM Guide: Rheumatology: Neonatal Lupus: Michael Mojica, MD
PEM Guide: Trauma: Facial Fractures: Ellen Duncan, MD, PhD

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PEM Guide: Airway Procedures: Endotracheal Intubation
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PEM Guide: Resuscitation: PALS Update 2020: Post-resuscitation Care
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PEM Guide: Vascular Access: Umbilical Vein Catheterization

2020 UPDATES (VERSION 7.0)

CHAPTER REORGANIZATION

The shock chapters have been moved to their respective sections. Arrhythmias: An Overview and Cardiogenic Shock have been moved to the Cardiology section. Neurogenic shock has been moved to the trauma section and is joined by a new PEM Guide on Hemorrhagic Shock. Shock: An overview and Hypovolemic shock remain in the resuscitation section. Three chapters have been moved from the Head and Neck Infection section. Bacterial tracheitis and croup have been moved to the respiratory section. Infectious mononucleosis has been moved to the Infection section.

NEW PEM GUIDES

PEM Guide: Cardiology: Myocarditis: Luv Makadia, MD
PEM Guide: Dermatology: Benign Newborn Rashes: Ellen Duncan, MD, PhD
PEM Guide: Endocrine-Metabolic: Congenital Adrenal Hyperplasia: Michael Mojica, M.D.
PEM Guide: Environmental: Marine Envenomations: Invertebrates: Mariju Baluyot, MD
PEM Guide: Environmental: Marine Envenomations: Vertebrates: Mariju Baluyot, MD
PEM Guide: Environmental: Marine Toxic Ingestions: Mariju Baluyot: Mariju Baluyot, MD
PEM Guide: GU-Renal: Balanitis: Ellen Duncan, MD, PhD
PEM Guide: GU-Renal: Phimosis and Paraphimosis: Ellen Duncan, MD, PhD
PEM Guide: Hematology-Oncology: Immune Thrombocytopenia: Ellen Duncan, MD, PhD
PEM Guide: Infections: Rocky Mountain Spotted Fever: Michael Mojica, MD
PEM Guide: Neurology: Breath Holding Spells: Ellen Duncan, MD, PhD
PEM Guide: Rheumatology: Acute Rheumatic Fever: Luv Makadia, MD
PEM Guide: Surgery: Hirschsprung's Disease: Michael Mojica, MD
PEM Guide: Toxicology: Lithium: Sasha Gifford, MD
PEM Guide: Trauma: Hemorrhagic Shock: Michael Mojica, MD
PEM Guide: Trauma: Thoracolumbar Spine Injuries: Michael Mojica, MD

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PEM Guide: Administrative Issues: Medico-Legal Issues
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PEM Guide: Vascular Access: Ultrasound Guided Peripheral IV

2019 UPDATES (VERSION 6.0)

CHAPTER REORGANIZATION

The addition of over 40 new chapters since the first version has resulted in a few sections with a large numbers of topics. The chapters have been reorganized to improve navigability .

Orthopedic chapters have been removed from the Trauma section into a separate Orthopedics section.

Infection chapters have been moved to their respective sections. For example, the Pneumonia chapter has been moved to the Respiratory section and the Meningitis chapter has been moved to the Neurology section. A new Head and Neck Infections section has been added.

The procedure chapters have been moved to their respective sections. For example, the Pericardiocentesis chapter has been moved to the Cardiology section and Laceration Repair chapter has been moved to the Trauma section. Three new Procedure Sections have been added: Airway Procedures, Painful Procedures and Vascular Access

NEW PEM GUIDES

PEM Guide: Dermatology: Approach to Rashes - Joe Bennett MD, Chris Caspers, MD
PEM Guide: Dermatology: Febrile Rashes - Joe Bennett MD
PEM Guide: Endocrine-Metabolic: Rhabdomyolysis - Ellen Duncan, MD, PhD
PEM Guide: Genitourinary-Renal: Renal Stones - Michael Mojica, MD
PEM Guide: Head and Neck Infections: Infectious Mononucleosis - Michael Mojica, MD
PEM Guide: Infections: Acute Otitis Externa - Roshni Patel, MD
PEM Guide: Infections: Mastoiditis - Evan Yanni, MD
PEM Guide: Infections: Measles - Shweta Iyer, MD
PEM Guide: OB-GYN: Ovarian Torsion - Nisha Narayanan, MD
PEM Guide: Resuscitation: Circulation: Cardiogenic Shock - Michael Mojica, MD
PEM Guide: Resuscitation: Healthy Newborn - John Park, MD

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PEM Guide: Airway Procedures: Difficult Airway
PEM Guide: Airway Procedures: Noninvasive Ventilation
PEM Guide: Cardiology: Hypertensive Emergencies
PEM Guide: Endocrine-Metabolic: Inborn Errors of Metabolism
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2018 UPDATES (VERSION 5.0)

NEW PEM GUIDES

PEM Guide: Cardiology: Pericarditis - Thomas Kennedy, M.D.
PEM Guide; Endocrine-Metabolic: Hyponatremia - Ellen Duncan, M.D., PhD.
PEM Guide: Gastroenterology: Gastroenteritis - Michael Mojica, M.D.
PEM Guide: Gastroenterology: Pancreatitis: Roshni Patel, M.D., Joseph Levy, M.D.
PEM Guide: Infections: Bacterial Tracheitis - Michael Mojica, M.D.
PEM Guide: Infections: Conjunctivitis - Elise Perlman, M.D.
PEM Guide: Infections: Pertussis - Michael Mojica, M.D.
PEM Guide: Obstetrics & Gynecology: Vaginal Discharge - Sabina Kahn, M.D.
PEM Guide: Procedures: Analgesia - Lauren Vrablik, M.D., Kelsey Fawcett, M.D.
PEM Guide: Procedures: Capnography - Guillermo De Angulo, M.D.
PEM Guide: Procedures: Peritonsillar Abscess - Ellen Duncan, M.D., PhD.
PEM Guide: Resuscitation: Critically Ill Infant - Michael Mojica, M.D.
PEM Guide: Rheumatology: Systemic Lupus Erythematosus - Roshni Patel, M.D.
PEM Guide: Toxicology: Cholinergics - Elise Perlman, M.D.
PEM Guide: Toxicology: Serotonergic Agents - MaryAnn Mansour, M.D.
PEM Guide: Trauma: Elbow Dislocations - Svetlana Dani, M.D.

REVISIONS

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PEM Guide: Environmental Injuries: Airway Foreign Bodies
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PEM Guide: Trauma: Knee Injuries

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NEW PEM GUIDES

PEM Guide: Environmental Injuries: High Altitude Illness - Shweta Iyer, M.D.
PEM Guide: GU-Renal: Post-infectious Glomerulonephritis - Ellen Duncan, M.D. PhD.
PEM Guide: OB-GYN: Abnormal Uterine Bleeding - Amanda Schneider, M.D.
PEM Guide: Resuscitation: Brief Resolved Unexplained Events - Nicole Gerber, M.D.
PEM Guide: Resuscitation: Circulation: Neurogenic Shock - Michael Mojica, M.D.
PEM Guide: Toxicology: Methemoglobinemia - Chelsea Kadish, M.D.
PEM Guide: Trauma: Acromioclavicular Joint Separation - Stephanie Kramer, D.O.
PEM Guide: Trauma: Clavicle Fractures - Stephanie Kramer, D.O.
PEM Guide: Trauma: Rotator Cuff Tears & Impingement - Stephanie Kramer, D.O.

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PEM Guide: Environmental Injuries: Submersion Injury
PEM Guide: Hematology Oncology: Febrile Oncology Patient
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PEM Guide: Rheumatology: Henoch Schonlein Purpura
PEM Guide: Trauma: Concussion

MARCH 2016 UPDATES (VERSION 2.0)

NEW PEM GUIDES

PEM Guide: Hematology/Oncology: Hyperbilirubinemia - Michael Mojica, M.D.
PEM Guide: Resuscitation: Circulation: Hypovolemic Shock - Michael Mojica, M.D.

REVISIONS

PEM Guide: Child Protection: Child Abuse and Neglect*
PEM Guide: Environmental Injuries: Airway Foreign Bodies
PEM Guide: Environmental Injuries: Spider and Snake Bites**
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PEM Guide: Trauma: Ankle Injuries

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The authors are faculty and fellows of the division of pediatric emergency medicine as well as emergency medicine and pediatric residents at NYU School of Medicine. The authors are listed in each chapter's table of contents as well as at the beginning of each topic that they wrote.

About the Editor

Michael Mojica, MD is an associate professor of pediatrics and emergency medicine and director of education for the Division of Pediatric Emergency Medicine, as well as the former director of the pediatric emergency medicine fellowship program. His is a member of the Institute for Innovation in Medical Education at NYU School of Medicine and is involved in educating medical students, residents, fellows, faculty and nurses.

Dr. Mojica is the developer and editor of PEM Guides. This site has served as our syllabus site for medical students and residents with the goal of providing concise topic reviews to be used at the point of care.

He is interested in teaching evidence based clinical practice, biostatistics and research design and in educating the next generation of teachers how to teach. He is interested in the use of high fidelity simulation for teaching resuscitation leadership and communication skills. He has completed simulation training with the Institute for Medical Simulation and has completed TEAMSTEPPS master training.

Produced by the Institute for Innovations in Medical Education

ADMINISTRATIVE ISSUES

1. Disaster Preparedness	Dennis Heon, MD
2. Emergency Medical Services	Jessica Foltin, MD
3. Medico-Legal Issues	Michael Tunik, MD
4. Transport	Jessica Foltin, MD

DISASTER PREPAREDNESS

INTRODUCTION (DENNIS HEON, M.D. 5/2020)
A Mass Casualty Incident (MCI) (AKA Multiple Casualty Incident) is an emergency situation usually involving 5 or more patients at once, or any number of patients that create a situation that is beyond responders' immediate ability to manage. Examples include: a school bus collision on a highway; an urban high-rise fire; a train/airplane accident and a terrorist attack. A disaster is an MCI situation overwhelms local resources. Disasters can either be natural events (flood, hurricane, earthquake) or man-made (9/11 Word Trade Center attack, Chernobyl nuclear reactor fire).

CHEMICAL, BIOLOGICAL, RADIOLOGICAL, NUCLEAR, EXPLOSIVES (CBRBE)	
Chemical	Sarin (Tokyo subway)
Biological	Anthrax (New York City)
Radiological	Radiologic dispersal device (RDD). A "dirty bomb" is a conventional explosive device that disperses radioactive material
Nuclear	Fission device: Improvised, purchased, or stolen (Hiroshima)
Explosives	High-yield explosive detonation (Oklahoma City)

DISASTER PREPAREDNESS FOR CHILDREN
Disaster preparedness includes:
1. Preparation, planning and equipping for events (Before).
2 Federal, state and regional response to the event (During).
3. Mitigation: Decreasing secondary damage. Address psychological component (After).

PEDIATRIC RISK FACTORS	
↑ Skin to Body mass ratio	↑ Risk for hypothermia after decontamination ↑ Dermal absorption of toxins
↓ Skin keratinization	↑ Dermal damage, ↑ dermal absorption
↑ Minute Ventilation to Body mass	↑ Increase absorption of aerosolized toxins
↓ Height	↑ Exposure to dense chemical agents near ground
↓ Less fluid reserve	↑ Risk of dehydration post GI losses
↑ Rapidly dividing cells, ↑ Lifespan	↑ Cancer risk from radiation exposure

EMERGENCY MEDICAL SYSTEMS TRIAGE
During a mass casualty event the goal of triage is for the "greater good", to maximize the survival of the greatest number of victims and not necessarily focusing on each victim. There are a number of triage algorithms. The START algorithm (Simple Triage and Rapid Treatment) is intended for adult patients. The JumpSTART algorithm was developed in parallel to the START algorithm to address the needs of children in a multi-casualty incident. Its objectives are:
1. To optimize the primary triage of injured children in the MCI setting
2. To enhance the effectiveness of resource allocation for all MCI victims
3. To reduce the emotional burden on triage personnel who may have to make rapid life-or-death decisions about injured children in chaotic circumstances

A combined algorithm including elements of both START and JumpSTART is also available so that triage to be based on a single algorithm (See Appendix for Algorithms).

Patients are triaged into one of 4 categories: **GREEN** (Minor), **YELLOW** (Delayed), **RED** (Immediate) and **BLACK** (Deceased). The primary distinction between JumpSTART and START is in the assessment of breathing. An adult who remains apneic after positioning the airway is triaged as **BLACK** (Deceased). A child who remains apneic after positioning the airway is triaged based on the presence of a pulse and their response to 5 rescue breaths. If the child does not have a pulse or if they have a pulse but remain apneic after 5 rescue breaths, they are triaged as **BLACK** (Deceased). If the child has a pulse and begins breathing spontaneously after 5 rescue breaths, then they are triaged as **RED** (Immediate).

DECONTAMINATION

Patients requiring decontamination may not be brought into the hospital without decontamination under any circumstances, and may need to wait outside regardless of condition until the decontamination staff is appropriately protected.

DECONTAMINATION
DECONTAMINATION GOALS
Prevent further absorption of toxins
Prevent secondary exposure in hospital personnel
PEDIATRIC CONSIDERATIONS
Warmer water temperature to prevent hypothermia
Lower pressure to prevent dermal damage
Families should remain together

PERSONAL PROTECTIVE EQUIPMENT

PAPR (POWERED AIR PURIFYING RESPIRATOR) SPLASH SUIT

N95 MASK GOGGLES SPLASH SUIT

N95 MASK GOGGLES TRAUMA GOWN

Properly fitted N95 and N100 masks block particles over 0.3 microns (Anthrax powder: 1-5microns, droplets from a patient's breath: 1-15 microns).

MANAGEMENT

In general, keep families together. The exception is a red triaged parent with a green triaged child. Children will require more assistance with shower decontamination and are at greater risk of hypothermia due to their greater surface area to body mass ratio.

Patient tracking can be difficult. Unaccompanied children should have an ID band and pictures of their face and the entire child. Report can be made to a database aimed at re-connecting parents and their child. Accompanied children should have ID bands with the name and date of birth of both the parent and child. Pediatric safe area(s) in hospital should be designated and utilized.

CHEMICAL

Most solids agents are irritants. They are generally not absorbed through the skin and contamination can be blocked by particle mask and gloves. Liquid agents can be absorbed through the skin. Heavy-duty gloves and splash suits are required. If it is volatile (like Sarin gas) inhalation risk is a possibility and chemical filter masks are required. An aerosolized agent is the mist form of a liquid. If it is absorbable or volatile the same issues apply as to non-aerosolized liquids. A vapor is a gaseous phase of a material that is normally a liquid.

CHEMICAL WEAPON CATEGORIES	
Pulmonary agents	Chlorine (yellow/green), phosgene (newly mown hay)
Blood agents	Cyanide compounds (bitter almonds)
Vesicants (blister agents)	Sulfur mustard (yellow/brown, onions, garlic), Lewisite
Nerve agents	Cholinergic Agents: Sarin, Soman, Tabun, VX
Incapacitating agents	Anticholinergic agents

Most chemicals of interest are heavier than air and stay close to the ground. This increases the risk to shorter children. They may be deployed by an explosive device that causes little or no structural damage

For chemical exposures the risk assessment entails: identification of the agent and the extent, route and duration of exposure. Agent specific management options can be obtained through The Local Poison Center (1-800-222-1222).

VESICANTS (AKA BLISTERING AGENTS): Vesicants are cellular poisons that injure rapidly reproducing/dividing cells. Eye involvement includes conjunctival inflammation, corneal damage and severe lid edema. Skin lesions begin are areas of erythema and progress to blister formation. Respiratory symptoms may include a productive cough and dyspnea. Treatment is decontamination and supportive care

NERVE AGENTS	
Mechanism	CNS, nicotinic and muscarinic systems
Symptoms	CNS: Alerted mental status, ataxia, seizures, central apnea, coma
	Muscarinic: DUMBELS SLUDGE “killer B’s (see table below)
	Nicotinic: Muscle fasciculations, flaccid paralysis
Treatment	Decontamination to prevent further absorption
	Supportive care, benzodiazepines for seizures
	Atropine: Antimuscarinic effects
	Pralidoxime: Reactivates acetylcholinesterase
See PEM Guide: Toxicology: Cholinergics	

CHOLINERGIC TOXIDROME			
D	Diarrhea	S	Salivation
U	Urination	L	Lacrimation (tearing)
M	Miosis/muscle weakness	U	Urination
B*	Bronchorrhea, bronchospasm	D	Defecation or Diarrhea
B*	Bradycardia	G	Gastrointestinal Distress
E	Emesis	E	Emesis (vomiting)
L	Lacrimation	*Killer B's: Bradycardia, bronchorrhea, bronchospasm	
L	Lethargy		
S	Salivation/sweating		

CHOLINERGIC TOXICITY: ANTIDOTES		
	ATROPINE	PRALIDOXIME (2 PAM)*
Mechanism	Competitively blocks central and peripheral muscarinic receptors	Reactivates acetylcholinesterase by releasing toxin
Indication	Improve muscarinic symptoms of organophosphate and carbamate toxicity	Improve muscarinic and nicotinic symptoms of organophosphate and carbamate toxicity Neuromuscular weakness or significant Atropine requirement
Dosing	0.05 mg/kg IM or 0.02 mg/kg IV Toddler: 0.5 mg, Child: 1.0 mg, > 40 kg: 1-2 mg (mild-moderate) > 40 kg: 3-5 mg (severe) No maximum dose Very large doses may be required. Double dose Q3-5 minutes PRN Titrate dose to reverse bronchorhea, bronchospasm, and respiratory distress.	Administer immediately with Organophosphates to prevent permanent inactivation ("aging") Adult: 1-2 grams IV Child: 20-40 mg/kg IV (max 2gms) over 15-30 minutes If severe initiate an infusion of: Adults: 250-500 mg/hour Children: 10-20 mg/kg/hour
Adverse Reactions	Signs of anticholinergic toxicity if too large a dose is given (hot, dry, flushed skin, tachycardia, urinary retention, mydriasis, CNS agitation, tachycardia)	Transient dizziness, blurred vision, elevated diastolic BP. Rapid IV admin may result in cardiac/ respiratory arrest due to muscle rigidity and laryngospasm

CYANIDE	
Mechanism	Mitochondrial toxin → cellular anoxia Binds/inhibits cytochrome oxidase → anaerobic metabolism → anion gap metabolic acidosis (lactic acid)
Symptoms	Low concentration: Headache, light headedness, nausea, ataxia
	Classic symptoms: headache, anxiety, respiratory distress, abdominal pain, vomiting, cheery red skin, bitter almond odor Progress to: loss of consciousness seizures, CV collapse, CVarrest
Treatment	Supportive Care, correction of metabolic acidosis, seizure control
	Hydroxocobalamin (cyanokit): Binds CN → converted to cyanocobalamin and excreted in urine
See PEM Guide: Toxicology: Cyanide	

CYANIDE ANTIDOTE: HYDROXOCOBALAMIN	
Mechanism	Chelation: The central cobalt atom binds cyanide Hydroxocobalamin + CN → Cyanocobalamin (Vitamin B12) Rapidly enters the mitochondria Safer, faster, though not always readily available, higher cost
Indications	Suspected cyanide toxicity
Dosing	Adult: 70 mg/kg (max 5 grams) IV over 30 min (may push in an arrest) May repeat to max 15 grams. Subsequent doses given over 6-8 hours
	Pediatric: 70 mg/kg (max 5 grams), subsequent dose 35 mg/kg
	Do not give at same site or time of thiosulfate. Thiosulfate binds to Hydroxocobalamin rendering it inactive
Adverse events	Dark red skin, mucous membranes and urine (hours-day) Allergic reactions, local reaction at the infusion site, lymphopenia Interfere with subsequent laboratory testing, particularly colorimetric testing (AST, bilirubin, creatine, magnesium, iron)

NUCLEAR

The lethal dose at which 50% of patients are expected to survive is approximately 400 REM. Below 100 REM patients are generally expected to survive and above 800 REM they are very unlikely to survive. For comparison, the background radiation exposure is 0.2 REM/year, A chest XRAY is 0.003 REM and a cardiac catheterization is 45 REM

A “dirty bomb” is a conventional explosive device that disperses radioactive material. Radioactive contamination refers to external contamination on patients’ clothing and skin that can be washed off. Patients with inhaled or ingested “internal” contamination and patients exposed to radiation do not pose a danger to caregivers. For example, a patient who gets a chest x-ray is not “contaminated” and would not need a decontamination shower. The goals of decontamination are to reduce the incorporation of external radiation into the body and prevent contamination of the hospital. The decontamination team should wear regular gloves, goggles and gown to prevent contamination from getting onto your skin and an N95 mask to protects from radioactive dust. It is safe to care for the patient in the ED after decontamination.

If a patient with radioactive contamination arrives at the hospital, hospital security activates a “lock-down” procedure. Arriving patients are directed to the outdoor decontamination showers and the hospital radiation safety officer is paged. A portable Geiger counter is available in the disaster closet in the ambulance bay.

ACUTE RADIATION SYNDROME
Acute exposure to whole body radiation of 1 Gy (100 rad)
Lower doses are not expected to cause clinically apparent ARS
Whole body dose: 4.5Gy: 50% mortality, >10 Gy: 100% mortality
All forms of ionization radiation cause internal tissue damage
Ingestion, inhalation or transfer through a wound
Organs with rapidly dividing cells (GI tract, bone marrow) are most susceptible

ACUTE RADIATION SYNDROME: PHASES	
Prodromal phase (0-2 days)	Nausea, vomiting, diarrhea, fatigue, headache
Latent phase (2-20 days)	Improvement, asymptomatic
Final phase (21-60 days	Begins with infection, anemia and bleeding Followed by uncontrollable diarrhea, hypovolemia, electrolyte disturbances Progress to altered mental status, cerebral edema and cardiovascular collapse

IODINE: Radioactive iodine is a product of nuclear fission of uranium. Potassium iodide is indicated for nuclear explosions and nuclear reactor incidents. It saturates iodine binding sites and prevents the uptake of radioactive iodine. It should be given as soon as possible. It is given with 12 hours of exposure and has been demonstrated to prevent the development of thyroid cancer years later. A single dose provides 24 hours protection. It does not affect acute radiation sickness. Potassium iodide It is not indicated for “dirty bombs” (traditional explosive devices mixed with radioactive material)

POTASSIUM IODINE DOSING	
Adults/Adolescents	130 mg (1 tablet) daily for 10 days
Children 3-12 years	65 mg (1/2 tablet) daily for 10 days
1 month-3 years	32.5 mg (1/4 tablet daily for 10 days
Birth-1 month	16.25 mg (1/8 tablet) daily for 10 days
Do not ingest 'Tincture of Iodine‘. It is toxic	

BIOLOGIC

In a biological attack the event may be unnoticed initially and symptom onset can be delayed for hours to days. Exposure may be via and aerosol, food or water contamination of dermally,

Unfortunately, many biologic agents present with nonspecific symptoms. Bio-terrorism should be suspected for unusual syndromes (e.g. influenza out of flu season), unexpected geography (e.g. plague in NYC) or abnormal clusters (pets, humans, neighborhoods). The toxins (Botulism, Staph enterotoxin B, Ricin) are not contagious.

Decontamination is only required if they had agents sprayed on them the day of presentation. The patient should be isolated. Droplet precautions are recommended for plague. Airborne precautions are recommended for small pox and viral hemorrhagic fevers. The caregivers should wear the appropriate level of personal protective equipment.

ACUTE ONSET OF FLU-LIKE SYMPTOMS
Inhalational Anthrax
Pneumonic Plague*
Q-Fever
Brucellosis
Smallpox*
Tularemia
Viral Hemorrhagic fevers*
*Contagious: transmitted from person to person through the air after symptom onset

ANTHRAX	
Cause	Bacillus anthracis, gram (+) rod, spores
Exposure	Spores introduced sub-dermally from infected animal or animal product
Symptoms	Cutaneous: Most common, exposed areas (face, neck, arms, hands) Painless papule → Enlarge with central vesicle/bullae → Painless necrotic ulcer (DDx: Ecthyma, brown, recluse spider bite) +/- Systemic symptoms: Fever, malaise, headache
	Inhalational: Toxin release in thoracic lymph node → Hemorrhagic necrosis, mediastinitis Prodromal phase: Nonspecific, myalgias, fever, malaise, 4-5 days Fulminant phase: Catastrophic illness, death within a few days CXR: widened mediastinum, +/- pleural effusion
Treatment	Inhalational: Standard precautions: cannot be spread by droplet, contact
	Cutaneous: Contact Precautions
	Ciprofloxacin, Doxycycline, most effective in prodromal phase

PLAGUE	
Cause	Yersenia pestis, Gram (-) rod-shaped, coccobacillus
Exposure	Zoonic infections of domestic and wild animals
	Transmitted by fleas
Symptoms	Bubonic: Sudden onset fever, chills, headache, weakness Lymphadenitis: Intense pain/swelling, inguinal, axillary, cervical Buboes are painful/tender without fluctuance
	Pneumonic: Fever, cough, myalgias, rapid progression to hemoptysis, respiratory failure, bleeding diathesis (DIC), circulatory collapse
	Other: Septicemic, pharyngeal, meningeal plague
Treatment	Usually fatal if not treated early: Streptomycin, Gentamicin, Doxycycline, Prophylaxis of contacts with Doxycycline

BIOTERRORISM ASSOCIATED BOTULISM	
Cause	Toxin produced by Clostridium Botulinum
Exposure	Inhalation of aerosolized toxin
Symptoms	Neurologic: Acute symmetric descending flaccid paralysis, bulbar palsies Diplopia, dysarthria, dysphonia, dysphagia +/- absent gag reflex No change in mental status
Treatment	Standard precautions: Cannot be spread by droplet or contact

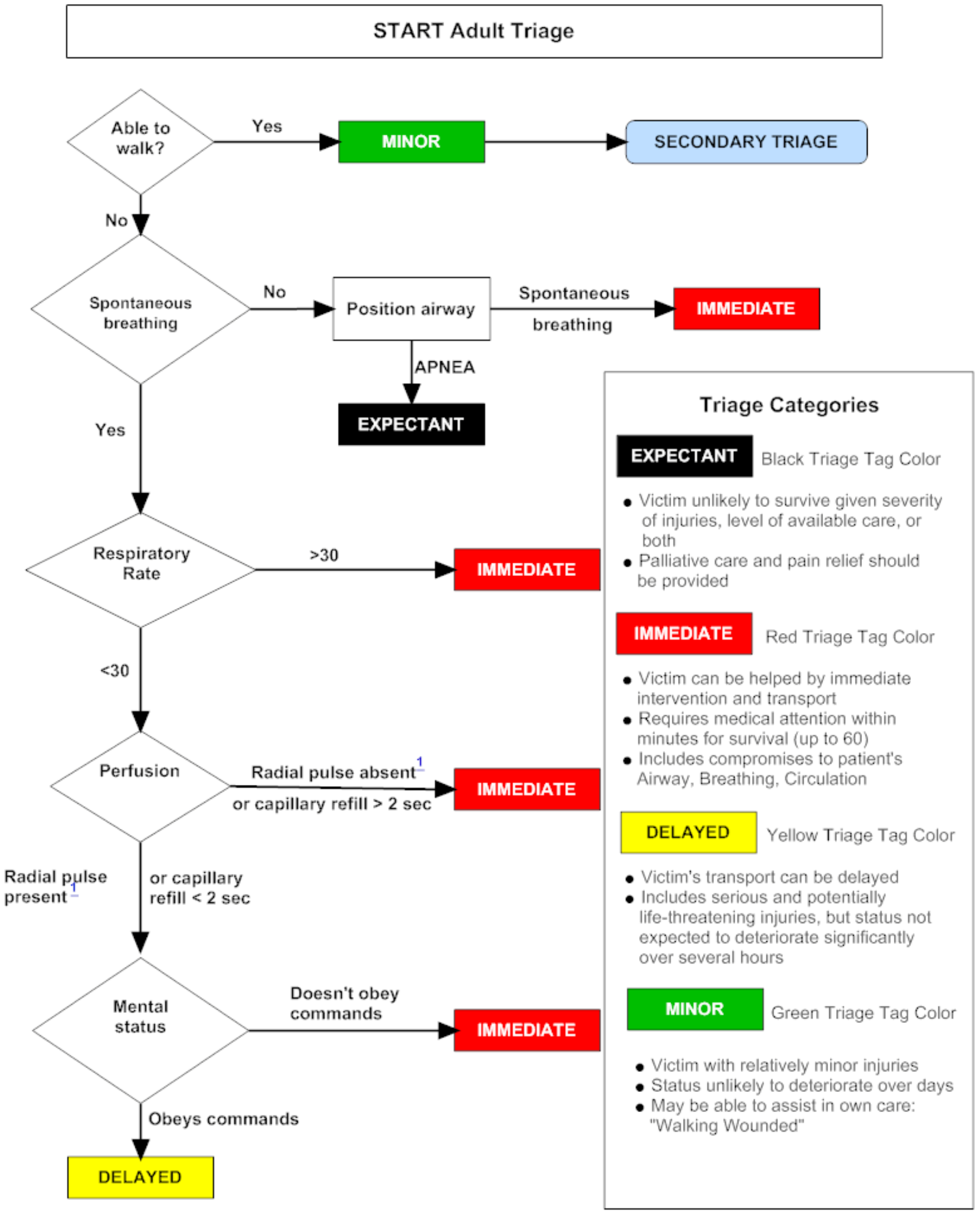
SMALL POX	
Cause	Variola virus
Exposure	Spread only through humans via respiratory viral shedding
	High mortality rate
Symptoms	Malaise, fever, vomiting, headache, 15% with delirium
	After 2-3 days develops skin lesions Macules → Papules → Pustular vesicles Appears on face, centrifugal distribution, develops synchronously (Varicella appears on the trunk and develops asynchronously)
Treatment	Isolation, supportive care Contacts should be quarantined for 17 days

STAPHYLOCOCCAL ENTEROTOXIN B	
Cause	Weaponized version of one of the toxins responsible for food poisoning
	Super antigen: stimulates cytokine release and inflammation
Exposure	Can be administered in food water or as an aerosol
Symptoms	Flu-like illness: Sudden onset fever, chills, headache, myalgias and nonproductive cough
	Additional symptoms depend on route of exposure
	CXR may be negative
Treatment	Supportive Care Only

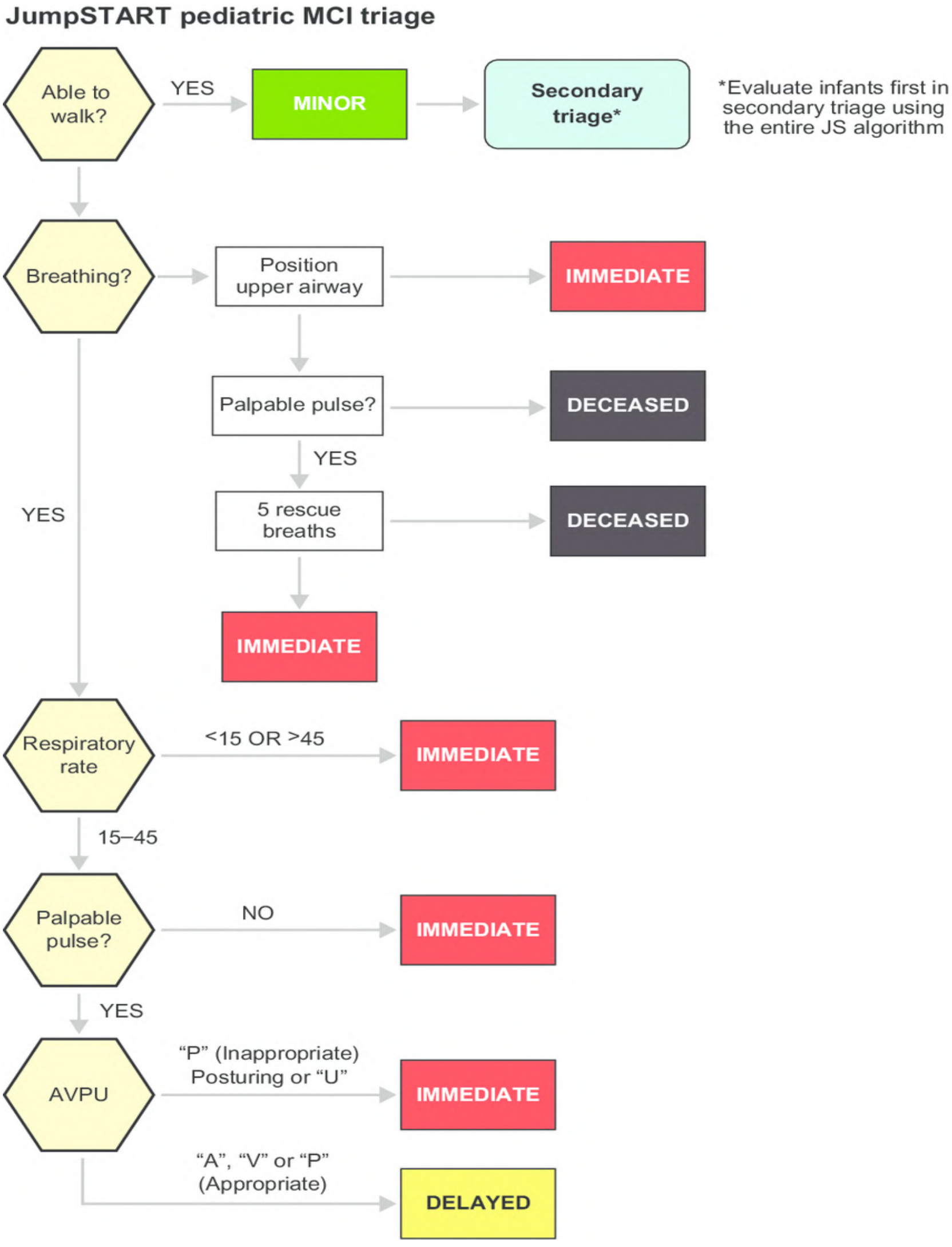
TULAREMIA	
Cause	Zoonic infection with Francisella Tularensis (gram (-) coccobacillus)
Exposure	Contact with infected animals (e.g. rabbits)
	Contaminated food/water, airborne spread or vectors (ticks, fleas, lice)
Symptoms	Rapid onset of nonspecific symptoms: fever, malaise
	6 major clinical forms: Ulcero-glandular, glandular, oculo-glandular pharyngeal, pneumonic, typhoidal
Treatment	Streptomycin, Gentamicin, Doxycycline, Ciprofloxacin

POST-EXPOSURE PROPHYLAXIS	
Anthrax	Doxycycline or Ciprofloxacin
Plague	Doxycycline or Ciprofloxacin
Q-fever	Doxycycline
Brucellosis	Doxycycline (& Rifampin or Streptomycin)
Smallpox	Vaccine within 4 days
None available for Equine encephalitis, VHF or toxins	

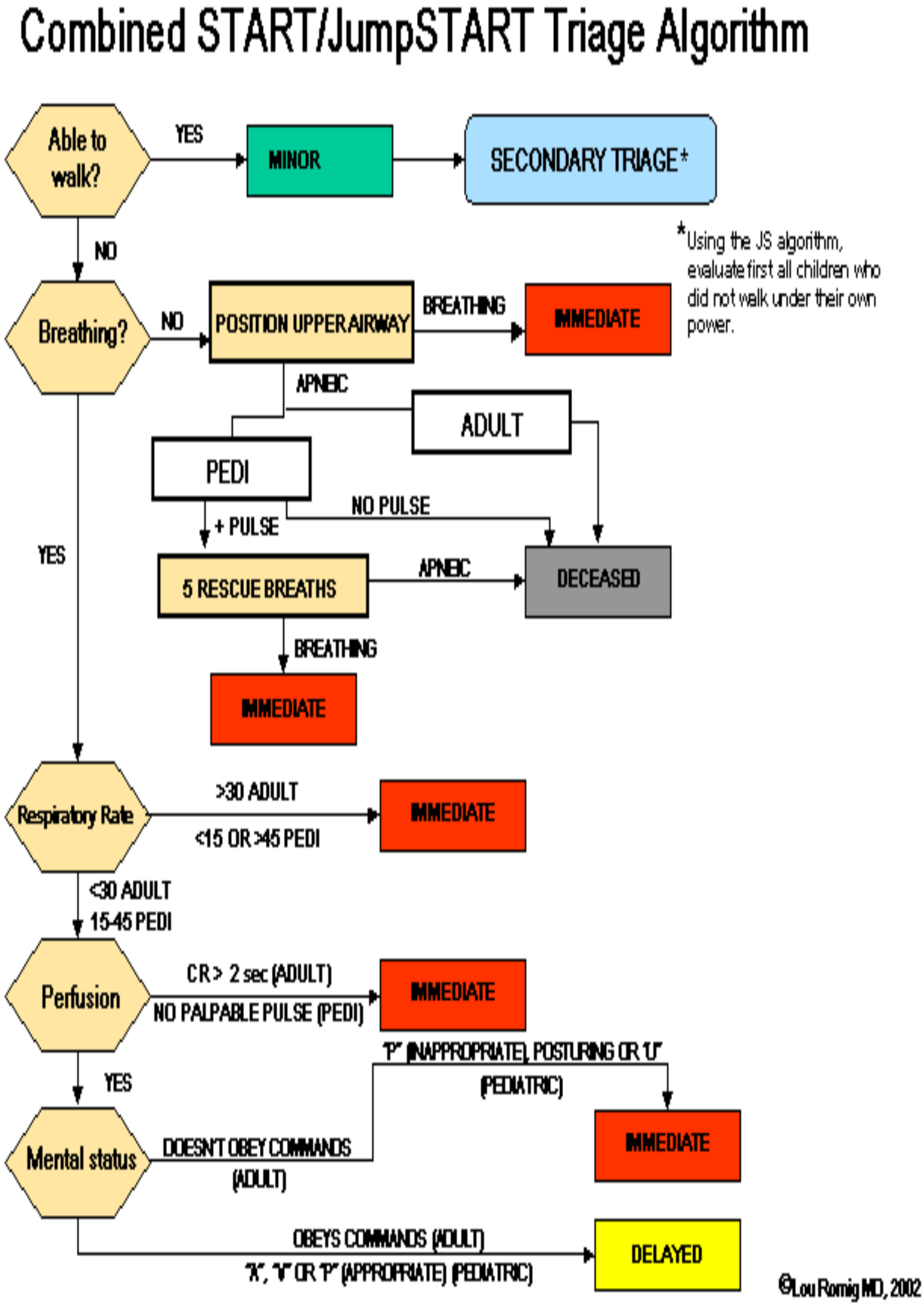
APPENDIX: START TRIAGE ALGORITHM (ADOLESCENTS, ADULTS)



APPENDIX: JUMPSTART TRIAGE ALGORITHM (CHILDREN)



APPENDIX: COMBINED START/JUMPSTART TRIAGE ALGORITHM



EMERGENCY MEDICAL SERVICES

INTRODUCTION (JESSICA FOLTIN, M.D. 9/2016)
Emergency Medical Services (EMS) is a system for the provision of emergent pre-hospital medical care. 50% of pediatric calls are related to trauma and the other 50% to medical issues. The etiology of mortality is governed by age and geographic location. The EMS system is typically activated by a call to 911 and dispatch will send appropriately trained personnel to the scene). Enhanced 911 systems will provide the location of the patient to the dispatcher. On scene medical care is provided, and the patient is transported to an appropriate emergency facility. Care is transferred to hospital personnel on Emergency Department arrival. See: PEM Guide: Administrative Issues: Disaster Preparedness, PEM Guide: Administrative Issues: Transport

Emergency Medical Services for Children is an focusing on issues for the prehospital and in hospital treatment of pediatric patients. EMSC is a national initiative designed to reduce child and youth disability and death due to severe illness and injury. Medical personnel, parents and volunteers, community groups and businesses, and national organizations and foundations all contribute to the effort. A federal grant program (HRSA, MCHB, NHTSA) supports state and local action.

TRAINING: The National Highway Transportation and Safety Administration (NHTSA) has developed the National Standard Curriculum (NSC) for the training of pre-hospital providers. They recognize 4 categories of responders: Certified First Responders (CFRs), Emergency Medical Technicians Basic (EMT-B), Emergency Medical Technician Intermediate (EMT-I) and Emergency Medical Technicians Paramedic (EMT-P). The scope of practice at each level is clearly defined.

Training and scope of practice is determined at the state and regional level. A provider at a given level in one state or region may or may not perform some of the skills as a provider at the same level in another state or region. In some states, such as Connecticut, paramedics are licensed medical professionals. In most states, EMTs and paramedics are certified, with renewal requirements on a 2 to 3 year cycle.

SPECIALTY CENTERS: Defined as designated centers for the care of specific populations. Standards for certification must be met. These include pediatric and adult trauma, pediatric (emergency department, PICU, neonatal, trauma), burns, stoke, cardiac and hyperbaric centers. Bellevue hospital is also designated as a hand/reimplantation center and spinal cord injury center. Jacobi Hospital is a certified snake bite center and hyperbaric center for NYC. Cornell and Harlem hospital are designated burn centers in NYC.

TIERED DISPATCH: In many systems first responders (1st tier) are the initial providers (FDNY in NYC). EMT-Basics (2nd tier) are next on scene and are followed by paramedics (3rd tier) if needed.

SCOPE OF PRACTICE

CERTIFIED FIRST RESPONDER (CFR): CFRs are usually the lowest level of training in any given EMS system. CFRs complete a 48-hour course, which includes CPR, first aid, spinal stabilization, and oxygen delivery. In some states, CFRs can perform defibrillation using an automated external defibrillator (AED). For example, in New York City, fire fighters are additionally trained to the CFR-Defibrillation level.

EMERGENCY MEDICAL TECHNICIAN BASIC (EMT-BASIC): a pre-hospital provider who has completed at minimum an approximately 150-hour course. EMTs are Basic Life Support (BLS) providers, and in addition to the skills possessed by CFRs, are capable of more complex immobilization and stabilization techniques, basic airway management (OPA/NPA, suction), and can assist in or perform the administration of certain medications. In most locations, EMTs are the minimum-trained personnel required to provide care on ambulances

SCOPE OF PRACTICE: EMT-BASIC
Open airway, provide bag-valve mask ventilation, (not endotracheal intubation)
Cardiopulmonary resuscitation
IV Access
Automated External Defibrillator (AED) use (EMT-D) (no EGK reading, defibrillation)
Fundamental extrication, stabilize spine, splint
Control hemorrhage
Fundamental burn, ingestion management
Fundamental newborn delivery
Oral glucose admin
Assist patients with patient medications, Epinephrine-Pen, Nitroglycerin, bronchodilators

EMERGENCY MEDICAL TECHNICIAN INTERMEDIATE (EMT-I): EMT-I's perform all EMT skills and add advanced airway management (endotracheal intubation), IV fluid administration, and some additional medications (depending on area).

SCOPE OF PRACTICE: EMT- INTERMEDIATE
EMT-Basic Skill Set
Orotracheal intubation without medications
Administer nebulizer
Intravenous and intraosseous access
Fundamental rhythm interpretation
Level 1 Trauma transport

EMERGENCY MEDICAL TECHNICIAN PARAMEDIC (EMT-P): Completing up to 1200 (or more) hours of training, paramedics perform all of the previous skills, and are educated in advanced assessment, trauma management, pharmacology, cardiology, and other skills. Most are ACLS and PALS providers.

SCOPE OF PRACTICE: EMT-P (PARAMEDIC)	
EMT Basic and EMT Intermediate Skill Set	Chest decompression
Advanced Triage	Advanced newborn resuscitation
Nasotracheal intubation	Advanced burn and ingestion management
Orotracheal Intubation with medications	Comprehensive medication administration
Surgical Airway	Transcutaneous pacing
Advanced rhythm interpretation	Intravenous and central venous line infusions
Manual defibrillation, synchronized cardioversion	

OVERSIGHT

ON-LINE MEDICAL CONTROL (DIRECT): A physician who is certified to provides direct orders to a pre-hospital provider, either by radio or telephone. In many circumstances, medical direction has provided standing orders for a list of potential emergencies, with medical control options to be exercised only after consulting in real-time with a designated physician. In many systems on-line medical control is hospital based. In NYC it is centralized through the Fire Department of New York (FDNY) bureau of Emergency Medical Services.

OFF LINE MEDICAL CONTROL (INDIRECT): Policies, procedures and standardized protocols that a medical director has set up in advance (standing orders). Quality assurance and improvement are also included.

PROTOCOLS: standardized approach to frequent patient care issues (e.g., chest pain, seizures, pediatric asthma, etc.)

ADDITIONAL ISSUES

CONSENT: A minor is a person who is under the age of 18. Minors cannot make medical decisions for themselves. They can neither give consent to nor refuse treatment or transportation to a hospital. Exceptions are made for emancipated minors and mature minors. Emancipated minors are less than 18 years of age who can provide consent for themselves. Examples include: married (past or present), high school graduates, pregnant or are a parent, self-employed, serving in the armed forces or living independently (are self sufficient). Mature minors are older than 14 years are declared to be mature minors by a state superior court. They must demonstrate competence to refuse and not be on psychiatric hold.

As a general rule, the provider should always act in the best interest of the patient. This includes situation where the parents do not wish transport. The emergency exception rule allows prehospital personnel to presume consent and provide treatment to minors if the following conditions are met:
1. An emergency condition that puts the child's like or health in jeopardy
2. Unavailability or inability of the legal guardian to provide consent
3. The delay in treatment is unsafe and can not be readily obtained
4. Only administer emergency treatment for conditions that are an immediate threat
Signing "against medical advice" is not appropriate for minors with a life threatening condition

INFANTS: Infants that do not require resuscitation may be transferred in a rear-facing car seat

MEDICO-LEGAL ISSUES: Care provided while on duty is not subject to good Samaritan laws. Prehospital providers are subject to malpractice claims under tort law. Care provided should be carefully documented and is protected by HIPAA (The Health Insurance Portability and Accountability Act: 1996). Prehospital providers should not perform interventions that are not within their scope of practice.

CHILD ABUSE AND NEGLECT: In most states, EMS providers are mandated reporters. Suspicion of child abuse and neglect must be reported to the receiving hospital staff and reported to the appropriate state agency, independent of the hospital's obligations to report.

END OF LIFE CARE: Prehospital care providers may occasionally be called for a patient with an advanced directive, such as a Do Not Resuscitate (DNR) order, in place. The legal guardian may rescind that order an any time and providers are obligated to resuscitate the patient at the legal guardian's request even if a DNR order is in place.

LAW ENFORCEMENT OFFICERS: Law enforcement officers can act *in loco parentis* in the absence of a parent or legal guardian. In NYC a police officer must accompany a minor if transport to the emergency department is required.

MEDICO-LEGAL ISSUES

INTRODUCTION (MICHAEL TUNIK, M.D5. 3/2023)
Medico-legal issues are often encountered in the emergency department. Some of the more common situations are defined below. Most laws applicable to emergency medicine are state laws. The specifics of laws differ from state to state so it is important to be aware of the law in the state that you practice in. Federal statutes that apply most to an ED include the Emergency Medical Treatment and Labor Act (EMTALA) and the Health Insurance Portability and Accountability Act (HIPAA). For child protection legal issues See: PEM Guide: Child Protection: Child Abuse and Neglect, PEM Guide; Child Protection: Sexual Abuse and Assault.

AGAINST MEDICAL ADVICE (AMA): Competent adults can refuse treatment and sign out AMA.

AMA: DOCUMENTATION REQUIREMENTS:
1. Parental competence
2. Options discussed, include results of refusal or leaving AMA
3. Parent signature
4. Parents reaction to discussion documented

All patients should be given appropriate therapy (prescriptions, follow-up and advised that they may return at any time and appropriate discharge instruction. Do not let your own anger or frustration get in the way of the best medical care you can deliver in the circumstances. If a competent adult leaving or refusing care for a child puts the child in imminent risk of death or disability or if child abuse is suspected then child protection laws can remove parental guardianship in best interest of the child.

COMPETENCE: Competence is the ability to understand one's condition, treatment options and consequences of decisions. Intoxicated or psychiatrically impaired adults are not competent. Documentation and possibly consultation with psychiatry may be required. Most minors are not considered competent to make decisions, with some exceptions.

DUTY TO TREAT: The physician has a duty to treat all in the ED, unless a competent adult in an informed fashion refuses the treatment for the child.

EMTALA (Emergency Medical Transport and Active Labor Act): EMTALA is a federal statute that grants every individual the right to emergency care. Patients in Emergency Department must receive a medical screening exam, and stabilization/treatment for any emergency medical condition, and transfer to a facility capable of ongoing care/stabilization if sending hospital is not capable.

An emergency medical condition is a condition "manifesting itself by acute symptoms of sufficient severity, including severe pain, psychiatric disturbances, or symptoms of substance abuse, such that absence of immediate medical attention could reasonably be expected to result in:
a. Placing the health of the individual in serious jeopardy
b. Serious dysfunction of any bodily organ or part"

The condition of the patient as well as the risks and potential benefit of the transfer must be documented and patient must consent to the transfer.

EMTALA: APPROPRIATE TRANSFER CIRCUMSTANCES	
1	Patient is stable and specialty services are not available at the transferring facility
2	An individual or patient’s caregiver requests to be transferred and accepts the documented risks
3	The risk of transfer is outweighed by the expected benefits of the care that can be provided at the receiving institution.

EMTALA: TRANSFERRING INSTITUTIONS RESPONSIBILITIES	
1	Stabilize the patient to the fullest extent of its capabilities until transfer complete
2	Confirm the capability and capacity of the receiving facility and identify and accepting physician
3	Provide copies or relevant documentation
4	Determine the level of personnel necessary to accompany patients during transfer. Considering the patient condition, foreseeable complications and urgency of the transport

If a transfer to a facility that can provide a higher level of care is required, the receiving facility must agree to accept the transfer.

HIPPA: (Health Insurance Portability and Accountability Act) mandates that all possible care be taken to ensure the confidentiality of a patient's medical records.

Consent is not required for disclosure of personal health information for purposes of treatment, payment, and health care operations. Patient's consent is also not required for communication between consultants when threats to patient of public safety are involved, such as suicidal or homicidal ideation, certain instances of abuse and neglect, and certain issues involving law enforcement.

GOOD SAMARITAN LAWS: Protects physician from threat of malpractice if:
1. Assistance rendered for free
2. An emergency exists
3. Out of the physician’s area of usual practice
4. Physician has no preexisting duty to treat
5. Care must be in good faith and no gross negligence committed

MANDATED REPORTING: Physicians or hospitals failing to report may be subject to prosecution.

MANDATED REPORTING
Child abuse/neglect
Animal bites
Burns
Gunshot wounds
Deaths
Poisoning
Vaccine injuries
Certain communicable diseases

MEDICAL MALPRACTICE:

ELEMENTS OF MEDICAL MALPRACTICE	
Duty	The physician must have a duty to treat
Breach of Duty	Breach the duty to treat (through failing to meet the community “standard of medical care” or what a reasonable physician practicing in a similar setting would have done)
Damages	The patient suffer an adverse outcome
Causation	The adverse outcome is a result of the breach of duty to treat

Approximately half of suits for pediatric patients occur in those less than 2 years of age and a diagnostic error are most commonly encountered

MALPRACTICE: HIGH RISK DIAGNOSES
Meningitis
Fracture
Appendicitis
Testicular torsion
Wound foreign bodies

MALPRACTICE CONDITIONS
Improper performance of procedures
Failure to supervise staff
Failure to consult
Failure to admit
Medication errors

The best defense against malpractice litigation is good medical care, good communications and clear documentation of history, physical, labs, consults, assessment and plan, including follow-up visits and discharge instructions. Most cases settle out of course but approximately 10% will reach a jury trial.

PARENTAL RIGHTS TO CONSENT AND HAVE CHILD TREATED: The only exceptions of the parental right to consent to treatment is the right of state to intervene on behalf of child when the child has been placed at risk. In most states, the age at which a patient can consent for or refuse medical care is 18.

PRESUMED CONSENT: Even if parents are not available or patient is unconscious, they are presumed to give consent for life or limb saving emergency treatment.

PARENTAL CONSENT NOT REQUIRED
Sexually transmitted infections including HIV
Pregnancy and termination of pregnancy
Contraceptive Services
Drug, alcohol abuse services

RIGHTS OF MINORS: Minors have no rights to consent with some limited exceptions.
Many states have laws allowing older minors to consent for themselves, however age limits and scope of treatments vary. Many states have special minor consent laws for sexually transmitted infection, substance abuse and pregnancy with no age limits.

Emancipated minors are minors less than 18 years of age who can provide consent for themselves. Mature minors may consent to some procedures in some states under common law. Most states consider a mature minor to be over 14 years or age. Risk of treating a minor even in states without statutes are minimal. It is always best to do what is in patient's best interest if parental consent is required.

EXAMPLES OF EMANCIPATED MINORS
Married (past or present)
High school graduate
Pregnant or are parents
Self-employed
Serving in the armed forces
Living Independently (self-sufficient)

TELEPHONE ADVICE: Telephone advice from the emergency department is risky. There is usually not an established relationship with the patient, the history is often limited and a physical examination is not possible. Phone advice should be limited to: poisonings, life threatening emergencies, patients who have just left the ED and to assist patients access to care. All patients should be told to come to the ED.

ARRESTED YOUTH: Consent is required before providing medical care unless a life-threatening condition is present. If the legal guardian is unreachable then an officer may consent for the patient's care "in loco parentis" (in place of parents). This does not require formal legal approval. An arrested youth and their legal guarding can refuse care for non-emergent conditions. If the treating physician believes that refusal may affect the child's health, then a court order is required.

END OF LIFE CARE ISSUES

State-specific laws recognize the autonomy of mature minors to consent for medical care for specific conditions. This includes sexual assault, sexually transmitted infections and pregnancy. The mature minor with a terminal illness will benefit from an advance directive specifying a surrogate decision-maker if decisional capacity is lost, as well as a POLST, that specifies patient preferences with a medical order. A portable medical order/POLST can be used in pediatric patients in most states. 28 states have explicit laws allowing use of POLST in pediatric populations. Palliative care consultation can facilitate decision making at the end of life

PALLIATIVE CARE
Assessment and management of patient symptoms
Assessment of caregivers and their needed supports
Multi-specialty care coordination
Goals of care that center around family decision-making
Attention to functional, physical, psychological, and spiritual needs
Overall improvement in the quality of life for the child and family

POLST: PORTABLE MEDICAL ORDER: SPECIFIES …
Desired treatment: Cardiopulmonary resuscitation versus “do not resuscitate”
Preference for full intensive care unit–level care vs limited care
Short-duration interventions for reversible conditions vs comfort-focused care only
Transport to hospital vs remaining in home or hospice setting
Artificial nutrition consent vs refusal
By name all present during the discussion/completion of the document
Describes decisional capacity of the patient
Includes signatures from the physician and patient
Previously named for “Physician Orders for Life-Sustaining Treatment”

ADVANCED DIRECTIVE
Not a physician order
Designates: End-of-life wishes
Designates: A surrogate decision-maker when a patient loses decisional capacity
May include: Values/beliefs, enjoyed activities, treatment goals, and end-of-life wishes

DURABLE POWER OF ATTORNEY
A legal document governed by state-specific laws
Specifies a surrogate who will make health care decisions once the physician certifies the patient is unable to do so
Does not stipulate specific treatments
In the event of recovery of decisional capacity, surrogate no longer has legal authority

LIVING WILL
Another advance directive
Specifies preferences for end-of-life care
Written without required guidance from a physician or attorney
No power after death.

PEDIATRIC TRANSPORT

INTRODUCTION (JESSICA FOLTIN, M.D. 1/2023)
Transport involves the transfer of a patient from one location to another. The three main types of transport are based on the initial and final settings involved and include: inter-hospital (moving a patient from hospital A to hospital B), pre-hospital transport (patients who are not currently in a hospital who are transported to a hospital) and intra-hospital transport (patients moving from one area to another within the same hospital). This PEM Guide will focus on issues common to both inter-hospital and pre-hospital transports. See also: PEM Guide: Administrative Issues: Emergency Medical Service

MODE OF TRANSPORT

The majority of inter-hospital and pre-hospital transport occurs via ground transport, or ambulance. However, in specific situations involving a great physical distance, or unusual terrain, an air transport may be required. Air transports are by fixed wing airplanes and rotary wing helicopters. The cabins of fixed wing airplanes may be pressurized or not.

Ambulance and helicopter transports have the benefit of door-to-door service. The major limitation of fixed wing transports is that they are required to land at an airport and necessitate an additional ground transport to the hospital. Helicopter transports usually can cover a 150-mile service area and can cover that distance in 1-1½ hours. The appropriateness of air transports is governed by environmental factors. Air transports should not put transport personnel at risk.

MODE OF TRANSPORT CONSIDERATIONS
Patient status, underlying disease process
Skill level of the providers
Distance of the nearest appropriate facility
Local emergency medical system resources
Safety of the method of travel, including weather conditions
Ground traffic

GROUND: Ground transport It is generally always available, of lower cost and requires only 2 patient transfers. Traffic and weather condition can impede ground transport and advance life support capability may not be available. Helicopter or fixed wing transport may be considered based if the patient condition, or distance from the receiving facility is too far for ground transport.

HELICOPTER: Helicopter transport may save time if ground transport time is greater than 20-30 minutes and the distance is less than 150 miles. In addition, helicopter transport will limit the number of transfers when compared to fix wing transport if the patient is picked up at the scene of an accident and flown to the arriving hospital's helipad. Helicopter transport may also be the only mode able to reach inaccessible remote areas. Helicopter transfer requires space to land, has limited cabin capacity, there is no cabin pressurization and is limited by extreme weather conditions. Lack of cabin pressurization can exacerbate conditions with trapped air (e.g., pneumothorax, bowel obstruction).

FIXED WING: Fixed wing transport is rapid, can cover longer distances than a helicopter, has adequate cabin space, has a pressurized cabin and can fly around poor weather conditions. Fixed wing transport is expensive and requires multiple transfers. For example, fixed wing transport would require ground transport to the airport, transfer to the plane and then transfer to ground transport at the target airport and transfer to the receiving hospital. Fixed wing transport is typically recommended for distances of over 150 miles.

PHYSIOLOGY

Boyle's law governs the relationship between the pressure, volume and temperature of a gas. There is an inverse relationship between pressure and volume (if temperature is held constant). As an aircraft ascends pressures decreases and volume increases. Helicopters can only climb to an altitude of a few thousand feet, and gas expansion is approximately 10-15%. At 8,000 feet, which is the effective cabin pressure for pressurized aircraft at 35,000-40,000 feet, gas expansion may be as much as 30%,

Boyle's law should be considered prior to transport of patients with closed air collections such as a closed pneumothorax, intestinal obstruction, or the presence of cuffed endotracheal tubes. Patients with a pneumothorax should have a chest tube placed prior to transport and the patency of the chest tube should be repeatedly assessed during transport. Orogastric or nasogastric tubes should be strongly considered in infants and children who have gastrointestinal obstruction.

Scuba divers are at risk of decompression sickness if they ascend rapidly or dive within 24 hours of a flight. For those with decompression sickness, ground transportation is preferred to prevent further injury by air bubble expansion. Expansion of air can occur in the joints (the bends), the lungs (the chokes), along the tracts of peripheral nerves (paresthesias) and in the central nervous system (paralysis, weakness, ischemic stroke) If air transfer is required to a hyperbaric center, then a flight to an altitude of less than 1,000 feet is recommended.

Dalton's Law, states that the total pressure of a gas is the sum of the partial pressure, may impact gas exchange as altitude increases. Air is less dense (i.e. has a lower partial pressure) at higher altitudes. The partial pressure of oxygen decreases, less air exchange occurs across the alveolar membrane and oxygen saturation will decrease. At 8,000 feet, which is the effective cabin pressure for pressurized aircraft at 35,000-40,000 feet the oxygen saturation of a healthy patient at approximately 93%. Methods to address these issues include optimal oxygenation prior to departure on transport, and close monitoring of patient respiratory status. A higher fraction of inspired oxygen may be required to maintain oxygen saturation at greater than 95%. Hypoxemia must be monitored by the use of continuous pulse oximetry and by adjusting the fractional inspired oxygen concentration.

Maintain temperature and humidity is to avoid hypothermia and dehydration. Hypoxia can worsen with extreme temperatures. Warmed intravenous fluids and humidified oxygen may be required.

Transporter personnel should be aware of the multiple physiologic stressors of flight. These may include nausea, dizziness, blurry vision, paresthesias and an increased sensation of body heat. Hypoxemia is of particular concern because it may impair clinical judgment. The effects of hypoxemia increase as altitude increases and physical activity increases (increased oxygen demand). Giddiness or laughing is often the first symptoms. Barotrauma can occur to the ears, sinuses, teeth, extremities and gastrointestinal tract.

TRANSPORT TEAMS

Those performing the transport vary with the type of transport. Inter-hospital transfer is typically conducted by designated transfer teams. Pre-hospital transfers are conducted primarily by emergency medical services personnel and intra-hospital transports are conducted by varying hospital personnel depending on the clinical status of the patient. See also: PEM Guide: Administrative Issues: Emergency Medicine Services.

Pre-hospital transports and inter-hospital transports are generally categorized in terms of the training of the transport personnel. Advanced Life Support (ALS) units are staffed by paramedics (EMT-P) who generally receive 450–1,100 training hours, though with a relatively small percentage dedicated to pediatrics. Paramedics are credentialed to intubate, place intravenous and intraosseous catheters, and administer intravenous medications.

Basic life support ambulances are staffed by Emergency Medical Technicians (EMT's). EMT's receive approximately 110 hours of training, including approximately 2 hours in pediatrics. Basic Life Support ambulance staff are credentialed to administer CPR, and are allowed to open the airway and provide assisted ventilation (via Bag-Valve-Mask), and administer oxygen. They can also stabilize the cervical spine with application of a cervical collar, interpret vital signs and utilize an AED (Automated External Defibrillator).

Pediatric inter-facility transport teams often rely on advanced practice nurses as primary care provider with or without physicians. In one study, RN's successfully performed all advanced airway maneuvers that were required by patients receiving inter-hospital transport. Pediatric Transport Teams have been shown to provide enhanced care, and improve outcome, particularly when a dedicated pediatric transport team functions within a setting of a regional critical care outreach program.

TRANSPORT PROCESS

In general, patients are transferred to a higher level of care. For example, a patient with an intracranial injury may be transferred to a facility with a neurosurgeon. A critically ill pediatric patient may be transferred to a pediatric trauma center or a facility with a pediatric intensive care unit. Patients should be stabilized to the degree possible prior to a transport. This may include airway stabilization and intravascular rehydration and administration of pressure stabilizing medications. Procedures or studies such as CT scans in a trauma patient may be performed but should not delay transfer if they cannot be managed at the sending facility.

Parental or guardian consent is required of all pediatric patients requiring inter-hospital transport. The risks and benefits of transport must be discussed with the family in advance. For an unstable patient, any hospital is a better place to be than the back of an ambulance. When to transfer the patient may be a difficult decision.

Medical responsibility for the patient during inter-hospital transport is complex and is shared by both the sending and the receiving hospital. As the patient leaves the sending hospital and physically approaches the receiving hospital in the ambulance, the receiving hospital assumes an increasing level of responsibility. Existing inter-hospital transport agreements facilitate the transport process.

EMTALA (EMERGENCY MEDICINE TREATMENT AND LABOR ACT)

EMTALA is a federal law enacted in 1986 to protect the rights of patients presenting for emergency care. In is often referred to as the "anti-dumping law". The intent of the law was to prevent the transfer of patients based simply on their ability to pay. All physicians caring for patients in the emergency department should be familiar with the law in order to prevent significant financial and administrative penalties as well as patient harm.

Patients in Emergency Department must receive a medical screening exam (MSE), and stabilization/ treatment for any emergency medical condition (EMC), and transfer to a facility capable of ongoing care and stabilization if sending hospital is not capable. Responsibility occurs when an individual or anyone on behalf of the patients come to the emergency department and request an examination or treatment.

The purpose of the medical screening exam is to determine if an emergency medical condition exists. If an emergency medicine condition does not exist (see definition below) then EMTALA does not apply. The law does not specify whether a physician, nurse, or other healthcare provider must perform the MSE. The health care finance administration (HCFA) requires the screening exam be done by "qualified medical personnel" as designated by a hospital's governing body. Triage by a nurse does not constitute a MSE. There are two components to a MSE. The examination must be "reasonably calculated to identify critical medical conditions," and the "exact same level of screening must be uniformly provided to all patients who present with substantially similar complaints."

An emergency medical condition is defined as "a condition manifesting itself by acute symptoms of sufficient severity (including severe pain) such that the absence of immediate medical attention could reasonably be expected to result in placing the individual's health [or the health of an unborn child] in serious jeopardy, serious impairment to bodily functions, or serious dysfunction of bodily organs."
If the patient is unstable, then the hospital may not transfer the patient unless a physician certifies the medical benefits expected from the transfer outweigh the risks Transfer of unstable patients must be "appropriate" under the law, such that:

1. The transferring hospital must provide ongoing care within it's capability until transfer to minimize transfer risks
2. Provide copies of medical records
3. Must confirm that the receiving facility has space and qualified personnel to treat the condition and has agreed to accept the transfer, and
4. The transfer must be made with qualified personnel and appropriate medical equipment.
5. Consent for transfer must be obtained

AIRWAY PROCEDURES

1. Capnography	Guillermo De Angulo M.D., MSc
2. Cricothyrotomy	Eric Weinberg, MD
3. Difficult Airway	Dennis Heon, MD
4. Endotracheal Intubation	Adriana Manikian, MD
5. Mechanical Ventilation	Michael Mojica, MD
6. Non-invasive Ventilation	Michael Mojica, MD
7. Post-Intubation Sedation/Paralysis	Michael Mojica, MD
8. Rapid Sequence Intubation	Michael Mojica, MD

CAPNOGRAPHY

INTRODUCTION (GUILLERMO, DE ANGULO, M.D., MSc., 4/2018)
Capnography is the measurement of the partial pressure of carbon dioxide (CO_2) in exhaled breaths by non-invasive means. While pulse oximetry provides information regarding oxygenation, capnography provides a real time assessment of ventilation, perfusion and metabolism. However, capnography is not as accurate as blood gas analysis of PCO_2.

CO_2 is a metabolic by-product. Measurement of CO_2 allow for an assessment of how much CO_2 is being produced at the cellular level (metabolic rate), how effective the vascular system is at transporting CO_2 to the heart (perfusion) and subsequently to the lungs and how effective CO_2 is being eliminated by the lungs (ventilation). Capnography is particularly helpful in those receiving supplemental oxygen for which oxygen saturation may remain normal despite hypoventilation.

Capnography should always be interpreted in conjunction with other physiologic parameters such as the patient's respiratory rate, oxygen saturation, blood pressure and physical examination.

DEFINITIONS	
Capnogram	The wave form of CO_2 during the respiratory cycle
Capnography	Graphical display of CO_2 level over time
Capnometer	The device that performs the measurement and displays the results
Capnometry	The measurement and numeric display of ETCO2
End Tidal CO_2	Partial pressure of CO_2 at the end of expiration (end of tidal volume)
$PaCO_2$	Partial pressure of CO_2 in arterial blood (normal 35-45)

TECHNOLOGY
CO_2 monitors use the absorption of infrared radiation wavelength 4.3 microns by CO_2 molecules within exhaled breaths in order to calculate the CO_2 concentration.

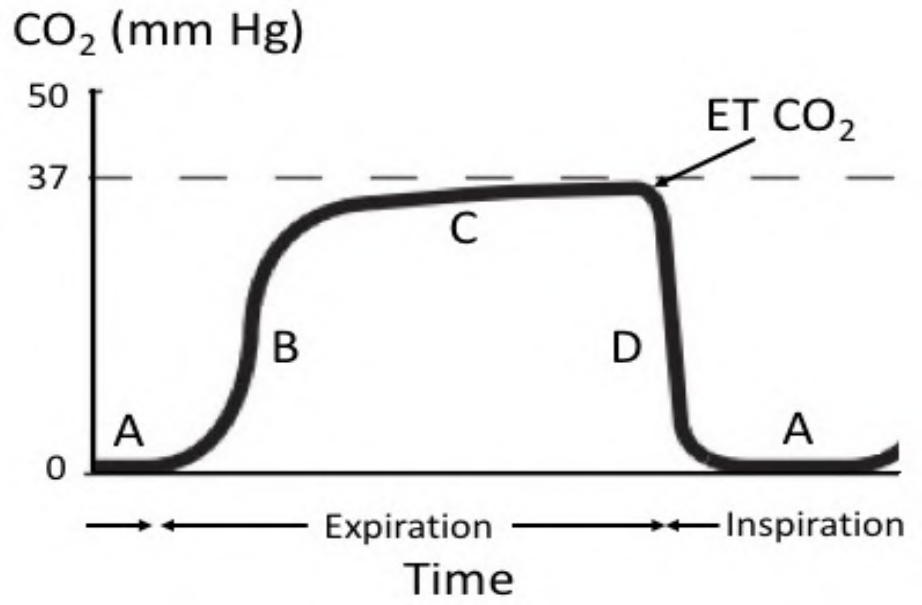
The monitors used can be designed using mainstream or side-stream configurations.
The mainstream configured devices measure CO_2 levels directly from the airway by having the sensor connected directly into the breathing circuit. Side-stream configured devices measure CO_2 levels by siphoning a small amount from the breath via cannula to the capnometer sensor. Side-stream devices can be used for intubated and non-intubated patients.

In addition, the CO_2 monitoring devices can be classified as quantitative or qualitative. Quantitative devices measure the numeric level of end tidal carbon dioxide ($ETCO_2$) while qualitative devices report ranges of value. An example of a qualitative device is the colorimetric CO_2 detector that is used to confirm endotracheal intubation. The device uses a pH sensitive filter that changes color from purple to yellow in the presence of CO_2 concentration greater than 15 mmHg.

PHYSIOLOGY: THE CAPNOGRAM

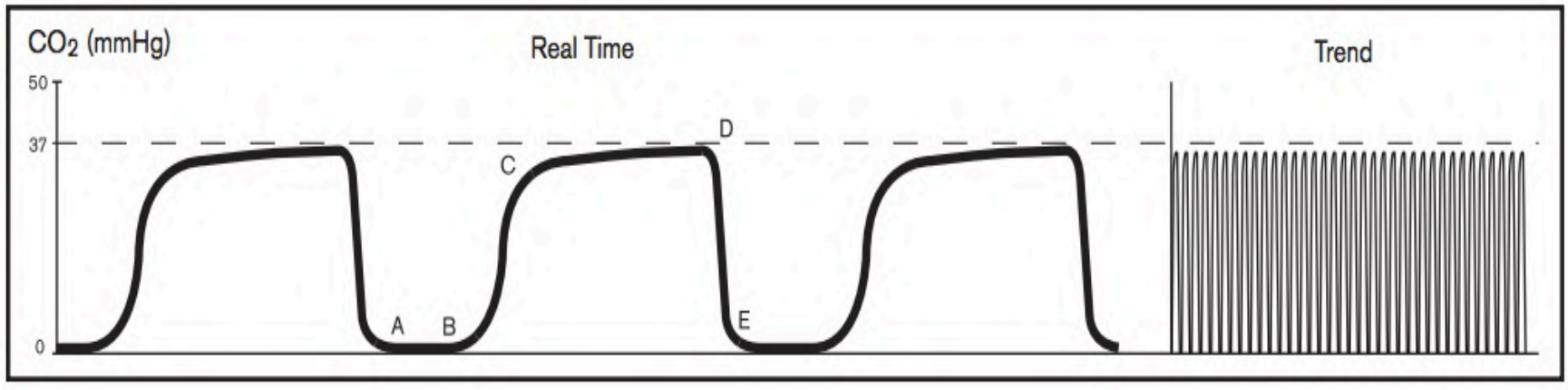
The capnogram illustrate changes in CO_2 during the respiratory cycle.

1. Ventilation: Amplitude of capnogram
2. Respiratory rate: Number of cycles/minute
3. Airway status: Obstruction
4. Metabolic rate: ↑ rate → ↑ CO_2 production
5. Perfusion: ↓ cardiac output → ↓ CO_2 to lungs
6. The shape of the capnogram can indicate certain conditions such as bronchospasm.

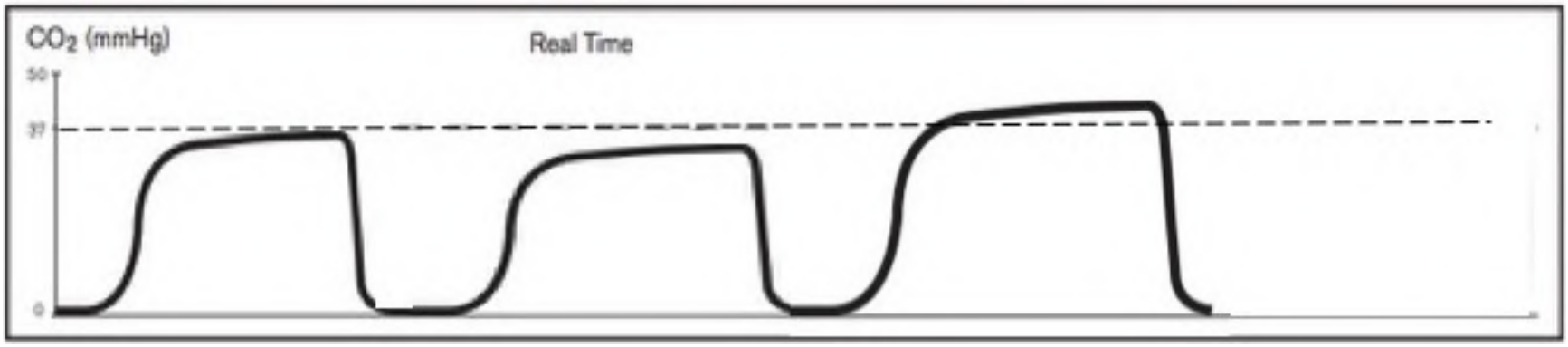


CAPNOGRAM: CHANGES IN CO_2 DURING THE RESPIRATORY CYCLE		
PHASE	NAME	PHYSIOLOGY
I or A	Baseline	Beginning of exhalation of dead space air (no CO_2)
II or B	Ascending	Exhalation of mixed dead space and alveolar air (mixed CO_2)
III or C	Plateau	Exhalation of alveolar air (pure CO2) End of phase = $ETCO_2$
IV or D	Descending	Start of inhalation. Return to baseline (no CO_2)

NORMAL VENTILATORY PATTERNS



NORMAL	
SpO_2	Normal
$ETCO_2$	Normal
Capnogram Amplitude	Normal
Capnogram Duration	Normal
Respiratory Rate	Normal



NORMAL: PHYSIOLOGIC VARIABILITY	
SpO_2	Normal
$ETCO_2$	Normal
Capnogram Amplitude	Normal with minor variability from breath to breath
Capnogram Duration	Normal with minor variability from breath to breath
Respiratory Rate	Normal

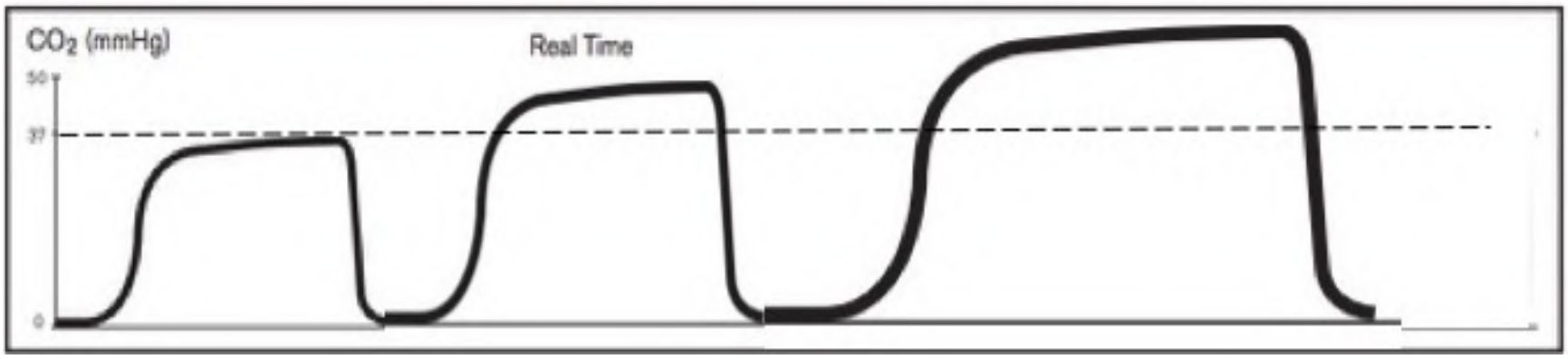
DIFFERENTIAL DIAGNOSIS: CHANGE IN $ETCO_2$		
	INCREASE $ETCO_2$	DECREASE $ETCO_2$
Cellular	↑ metabolic rate e.g. fever ↑ muscle activity e.g. shivering	Decrease metabolic rate Decreased muscle activity Hypothermia, hypovolemia
Cardiac	Increased cardiac output during resuscitation	Decreased cardiac output/arrest Pulmonary embolism
Pulmonary	Decreased minute ventilation e.g. Decrease respiratory rate e.g. Decrease tidal volume	Increased minute ventilation e.g. Increase respiratory rate e.g. Increase tidal volume

CLINICAL APPLICATIONS

PROCEDURAL SEDATION AND ANALGESIA

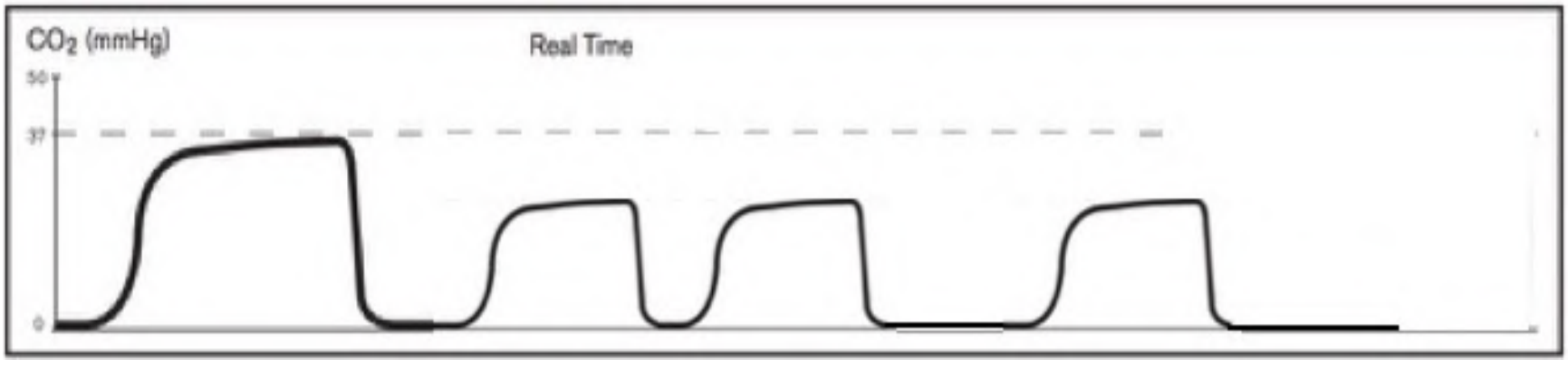
Capnography has the capability to assess the patient's airway, breathing and perfusion. A normal waveform signifies a patent airway with air movement, while a normal $ETCO_2$ level signifies adequate perfusion. Furthermore, by providing continuous data, it is possible to establish a patient's baseline status and then track changes over time. Numerous studies have shown that capnography has the ability to demonstrate respiratory complications associated with procedural sedation prior to clinical manifestations (Burton, Acad Emerg Med 2006, PubMed ID: 16569750), Soto, Anesth Analg 2004, PubMed ID: 15271710, Krauss, Ann Emerg Med 2016, PubMed ID: 27553482). It is because of these capabilities that capnography should be one of the parameters monitored during procedural sedation and analgesia. The medications used for procedural sedation and cause distinct ventilatory patterns.

BRADYPNEIC HYPOVENTILATION: Bradypneic ventilation is typically seen with opioid medications. There is a decrease in respiratory rate with an increase in expiratory time and an increase in $ETCO_2$ level. This leads to a capnogram with a waveform with a high CO2 (increased amplitude) and long duration (wide). With bradypneic hypoventilation, the $ETCO_2$ will increase until respiratory failure or apnea occurs.



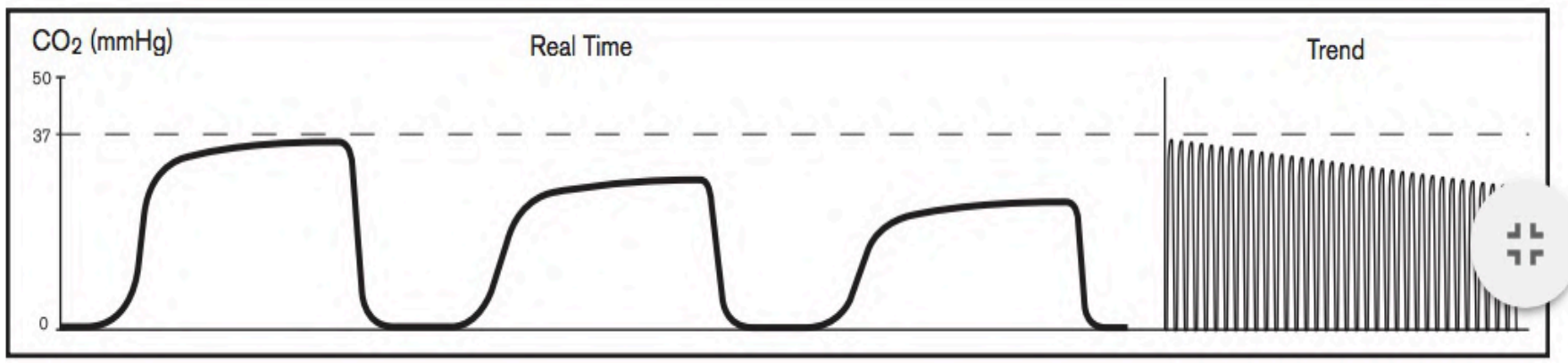
BRADYPNEIC HYPOVENTILATION	
SPO_2	Normal or Decreased
$ETCO_2$	Increased
CAPNOGRAM AMPLITUDE	Increased
CAPNOGRAM DURATION	Increased
RESPIRATORY RATE	Decreased

HYPOPNEIC HYPOVENTILATION: Hypopneic hypoventilation is typically seen with sedative-hypnotic medications. There is a decrease in the tidal volume causing an increase in the proportion of exhaled dead space air (fraction = dead space volume/ tidal volume). As the fraction increases there is a decrease in the $PaCO_2$ due to the mix of dead and alveolar air during exhalation. The clinical course of hypopneic hypoventilation is variable. I can remaining stable or progress to the development of periodic breathing to central apnea.



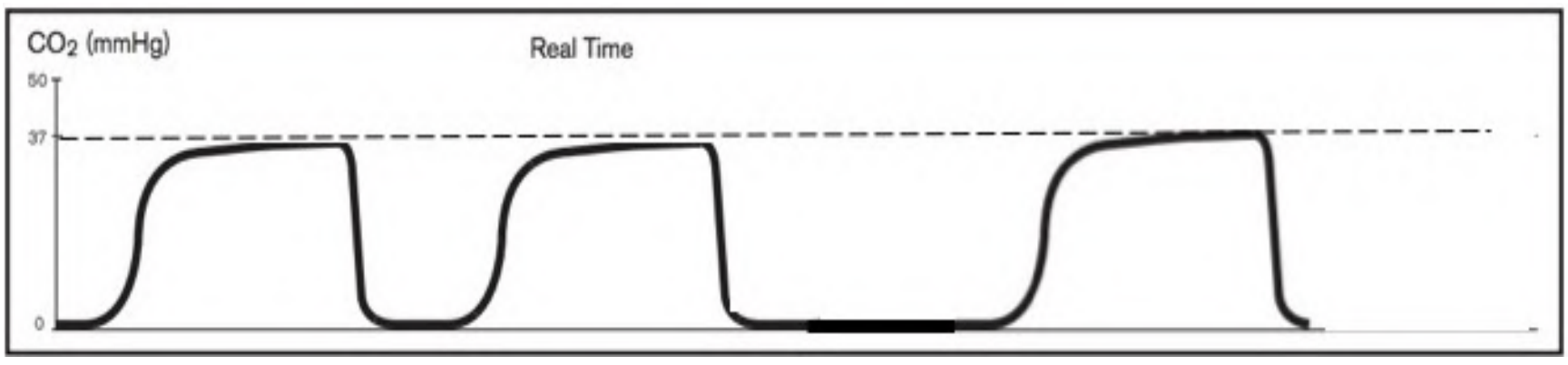
HYPOPNEIC HYPOVENTILATION	
SPO_2	Normal / Decreased
$ETCO_2$	Decreased
CAPNOGRAM AMPLITUDE	Decreased
CAPNOGRAM DURATION	Decreased
RESPIRATORY RATE	Decreased

HYPERVENTILATION: The effect of hyperventilation on the capnogram will depend on the metabolic rate. In a patient with a normal metabolic rate who increased their respiratory rate the ETCO2 will decrease (image below). In a patient with an increased metabolic rate (increased CO2 production e.g. fever, DKA) who increased their respiratory rate the ETCO2 will remain the same or increase.



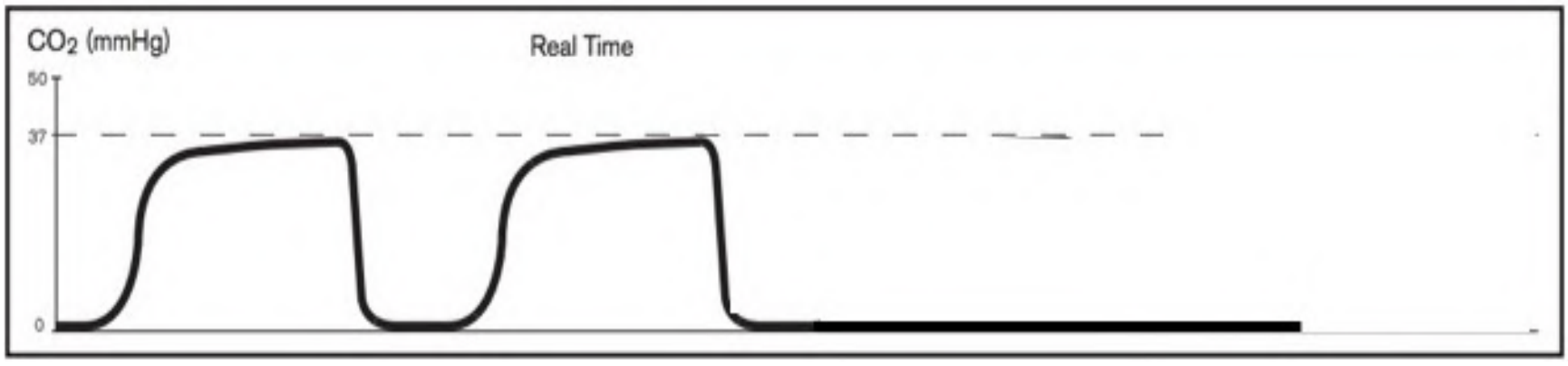
HYPERVENTILATION:	
SPO_2	Normal
$ETCO_2$	Decreased: Normal metabolism Normal or Increased: ↑ metabolism (e.g. fever, DKA)
CAPNOGRAM AMPLITUDE	Decreased: Normal metabolism (RR > metabolic need) Normal or Increased: ↑ metabolism (e.g. fever, DKA)
CAPNOGRAM DURATION	Normal
RESPIRATORY RATE	Increased

PERIODIC BREATHING: This ventilatory pattern is composed of alternating breaths with brief apneic pauses. This occurs most frequently with deep sedation and it can either be self-resolving or progress to central apnea.



PERIODIC BREATHING	
SPO_2	Normal (Decreased if severe)
$ETCO_2$	Normal (Increased if severe)
CAPNOGRAM AMPLITUDE	Normal (Increased if severe)
CAPNOGRAM DURATION	Normal
RESPIRATORY RATE	Decreased
OTHER	Apneic pauses

APNEA: Due to the continuous feedback this can be diagnosed almost immediately. Central apnea can be diagnosed with loss of capnogram, cessation of chest wall movement and absence of breath sounds.

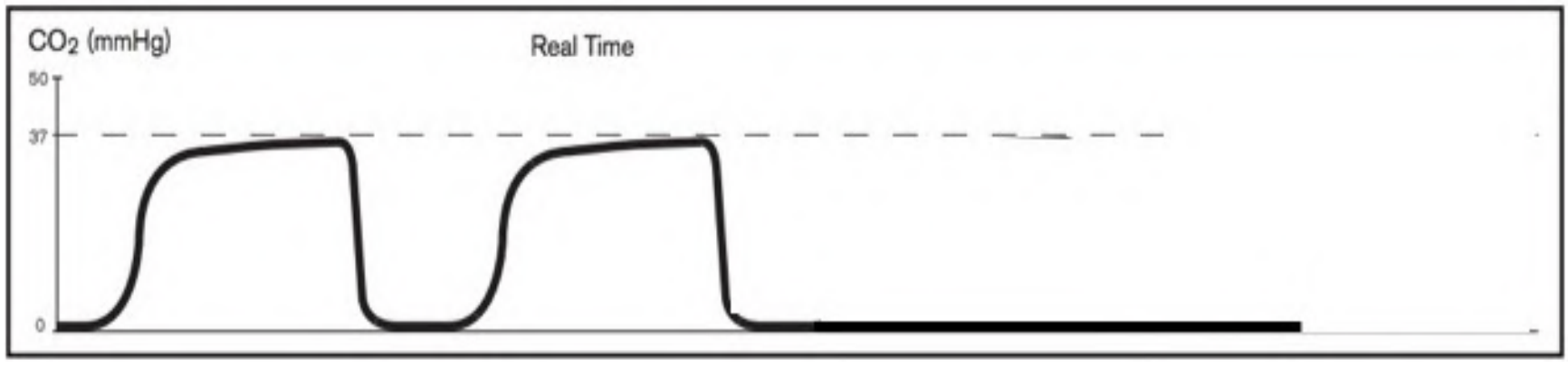


APNEA	
SPO_2	Decreased
$ETCO_2$	Zero
CAPNOGRAM AMPLITUDE	Absent
CAPNOGRAM DURATION	Absent
RESPIRATORY RATE	Zero
OTHER	Not relieved by airway maneuvers No breath sounds or chest wall movement Chest rise with bag-valve-mask ventilation

UPPER AIRWAY OBSTRUCTION/LARYNGOSPASM

OBSTRUCTION: Partial upper airway obstruction is clinically diagnosed by the presence of noisy breathing or stridor. It can be relieved by airway realignment maneuvers. Complete obstruction is diagnosed by the complete loss of waveform in the setting of chest wall movement, absence of noisy breathing or stridor and no breath sounds on auscultation. The presence or absence of chest wall movement is used to distinguished apnea from upper airway obstruction.

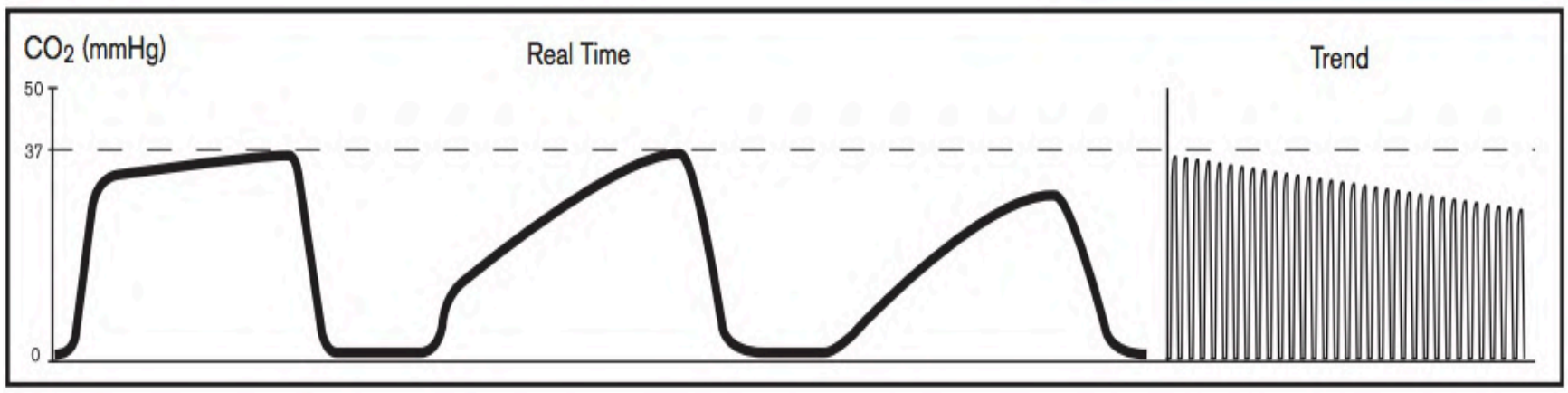
LARYNGOSPASM: Partial laryngospasm is clinically diagnosed by noisy breathing that is not relieved by airway realignment maneuvers. Complete laryngospasm is diagnosed by complete loss of waveform with chest wall movement, absence of noisy breathing/stridor, no response to airway realignment maneuvers and no breath sounds on auscultation. Complete upper airway obstruction and complete laryngospasm have capnograms that appear like apnea.



UPPER AIRWAY OBSTRUCTION/LARYNGOSPASM	
SPO_2	Normal (Decreased if complete
$ETCO_2$	Variable (partial), Absent (complete)
CAPNOGRAM AMPLITUDE	Variable (partial), Absent (complete)
CAPNOGRAM DURATION	Variable (partial), Absent (complete)
RESPIRATORY RATE	Variable (partial), Absent (complete)
OTHER	Partial/Complete obstruction: Relieved by airway maneuvers

DIFFERENTIAL DIAGNOSIS: COMPLETE LOSS OF WAVEFORM[1]			
	APNEA	COMPLETE UPPER AIRWAY OBSTRUCTION	COMPLETE LARYNGOSPASM
Noisy breathing, stridor[2]	NO	NO	NO
Breath sounds	NO	NO	NO
Chest wall motion	NO	YES	YES
Improved by Airway maneuvers	NO	YES	NO
Chest Rise with BVM	YES	YES	NO
1. Can also be seen in cardiopulmonary arrest and with equipment malfunction 2. Present in partial upper airway obstruction or partial laryngospasm			

BRONCHOSPASM: Lower airway obstruction leads to a curved ascending phase and an up-sloping plateau (shark fin pattern). This can also been seen in obstructive lung disease such as asthma or bronchiolitis. Because of air trapping and variable areas of ventilation and perfusion there is a less acute risk of CO_2 (lower amplitude of phase 2 and gradual increase in phase 3) and a longer duration (prolonged expiratory phase).



BRONCHOSPASM	
SPO_2	Normal or Decreased if severe
$ETCO_2$	Normal or Decreased or Increased
CAPNOGRAM SHAPE	Up-sloping (“shark fin” shaped)
CAPNOGRAM AMPLITUDE	Normal or Decreased or Increased
CAPNOGRAM DURATION	Increased (prolonged respiratory phase)
RESPIRATORY RATE	Normal / Decreased / Increased
OTHER	Wheezing

VERIFICATION OF ENDOTRACHEAL TUBE PLACEMENT

Misplacement of the endotracheal tube can have catastrophic consequences. Thus it is imperative to confirm endotracheal tube placement immediately post insertion. While direct visualization of passage beyond the cords is the best confirmation, capnography has been used to verify adequate endotracheal intubation.

Multiple studies for qualitative and quantitative capnography have shown a sensitivity and specificity of 100% for endotracheal intubation placement confirmation. In adult patients with a palpable pulse quantitative capnography had a sensitivity of 100% (137/137). However the sensitivity decreased to 72% (76/103) in cardiac arrest patients (MacLeod, Ann Emerg Med 1991, PubMed ID: 1899985).

A colorimetric $ETCO_2$ detector using a pH sensitive filter can be used to determine appropriate tracheal intubation by changing color from purple (poor) to yellow (mellow) in the presence of CO_2. A CO_2 concentration of 15 mmHg is needed to induce color change, with values between 3 and 14 causing a partial color change. With esophageal intubation, there is no CO_2, and therefore no color change though a patient who recently ingested a carbonated beverage may have a false positive change to yellow with an esophageal intubation. A right mainstem intubation will also cause a color change. This illustrates the importance of secondary confirmation with auscultation.

With capnography, a normal waveform with all four phases indicates a tracheal intubation, while a flat waveform generally indicates an esophageal intubation. However, in prolong cardiac arrest, complete distal airway obstruction, endotracheal tube obstruction or malfunction of the monitor a flat waveform can be present.

MANAGEMENT OF CARDIAC ARREST

$ETCO_2$ measurements have been shown to reflect cardiac output during cardiopulmonary resuscitation. The $ETCO_2$ will increase as the effectiveness of CPR improves leading to improved perfusion. With return of spontaneous circulation there is an increase in cardiac output, perfusion and $ETCO_2$ levels as accumulated CO_2 is exhaled. A rise in end tidal CO_2 can be an early indicator of ROSC (Paiva, Resuscitation 2018, PubMed ID: 29217394).

While initial levels of $ETCO_2$ levels have not been shown to predict outcome of resuscitation, numerous studies have shown a correlation between the height of $ETCO_2$ level and return of spontaneous circulation (ROSC). Levels of 10 mmHg during resuscitation have been shown to be a good predictor of ROSC, with a higher level being a stronger predictor of ROSC. Initial levels less than 10 mmHg do not predictor futility of resuscitation and should not be used to determine the utility of continuing resuscitation. However, levels less than 10 mmHg after 20 minutes of resuscitation have shown a 0.5% likelihood of ROSC (Sheak, Resuscitation 2015, PubMed ID: 25643651). While further studies are needed to determine the prognostic use of $ETCO_2$ levels during CPR, particularly in pediatric patients, levels can be used to monitor cardiac output, possible return of ROSC, and used a possible predictor of ROSC during the late portions of resuscitation.

AHA PALS: CONTINUOUS END TIDAL CO_2 MONITORING (2015)
End tidal CO_2 will be normal in right mainstem bronchus intubations
End tidal CO_2 correlates with increased cardiac output
End tidal CO_2 < 10-15 mm may indicate ineffective compressions in adults
An abrupt rise in $ETCO_2$ is often seen prior to return of spontaneous circulation (ROSC)
Epinephrine will result in a decrease CO_2 for 1-2 minutes after administration due to reduction in pulmonary blood flow (vasoconstriction)
AHA: PALS: Circulation 2015: PubMed ID: 26472999

CRICOTHYROTOMY

INTRODUCTION (ERIC WEINBERG, M.D., 4/2021)
There are multiple techniques that may be used to perform a cricothyrotomy. These include: needle cricothyrotomy, percutaneous cricothyrotomy, cricothyrotomy using the Seldinger technique and surgical cricothyrotomy without or without the use of a bougie. The choice of technique is based on the patient's age, equipment available and user experience. Cricothyrotomy should be performed by those with the most experience and may require urgent surgical consultation if time permits.

CRICOTHYROTOMY TECHNIQUE COMPARISON				
TECHNIQUE	OXYGENATION	VENTILATION	DIFFICULTY	AGE
Needle	Yes	No	Low	Any
Percutaneous	Yes	Yes	Moderate	> 1 year
Seldinger[1]	Yes	Yes	High	?
Surgical[2]	Yes	Yes	Highest	> 10 years[3]

1. The Seldinger technique is not designed for pediatrics. Use at physician discretion
2. The surgical technique can be performed with or without a bougie and with a tracheal or an endotracheal tube
3. The age at which surgical cricothyrotomy is safe is not well established. The risk of laryngeal injury is higher in patients <10-12 years of age

The following PEM Guides provide additional review of advance airway management.
PEM Guide: Resuscitation: Airway
PEM Guide: Airway Procedures: Endotracheal Intubation
PEM Guide: Airway Procedures: Difficult Airway

DISCLOSURE
The authors do not have a financial interest in any of the products discussed. The equipment discussed is not an endorsement of a specific product and solely represents what is available at our institutions.

INDICATIONS
Inability to provide positive pressure ventilation with a bag-valve-mask or laryngeal mask airway or to perform endotracheal intubation in a patient requiring both oxygenation and ventilation (Difficult Airway = "Can't intubate and Can't ventilate" scenario). For example, complete airway obstruction in child due to: trauma, bleeding, foreign body or edema (anaphylaxis, infection (croup), smoke inhalation).

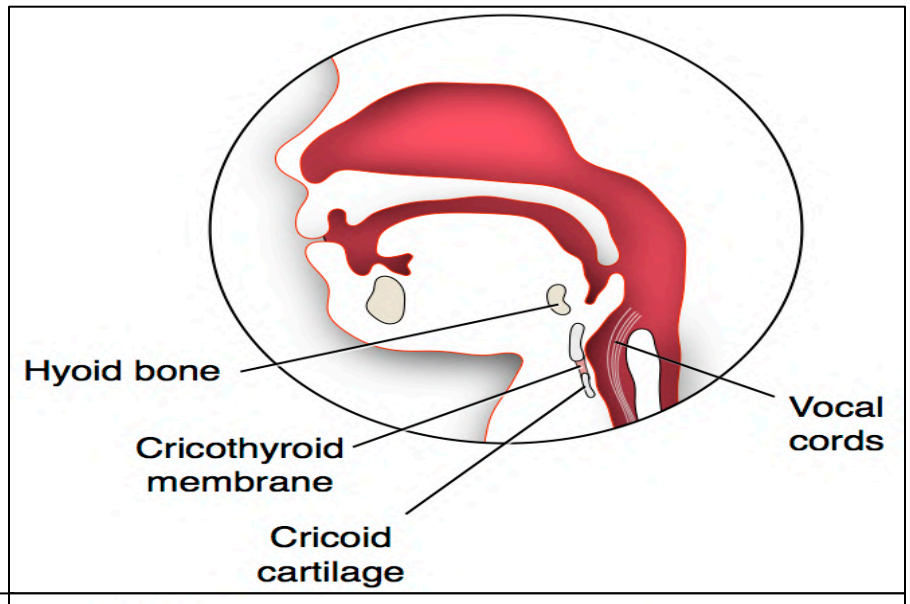
CONTRAINDICATIONS
Laryngeal or tracheal injury is an absolute contraindication to cricothyrotomy. Anatomic abnormalities of the neck are a relative contraindication

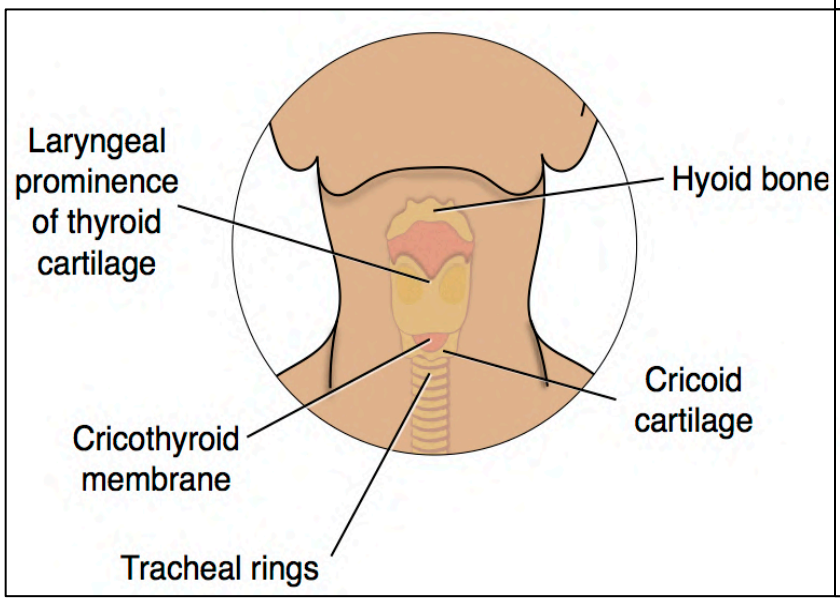
COMPLICATIONS
Complications of cricothyrotomy include hemorrhage (cricothyroid artery over the superior membrane, recurrent laryngeal nerve injury (run parallel to the lateral margins of the thyroid cartilage), crepitus and perforation of the posterior tracheal wall or esophagus

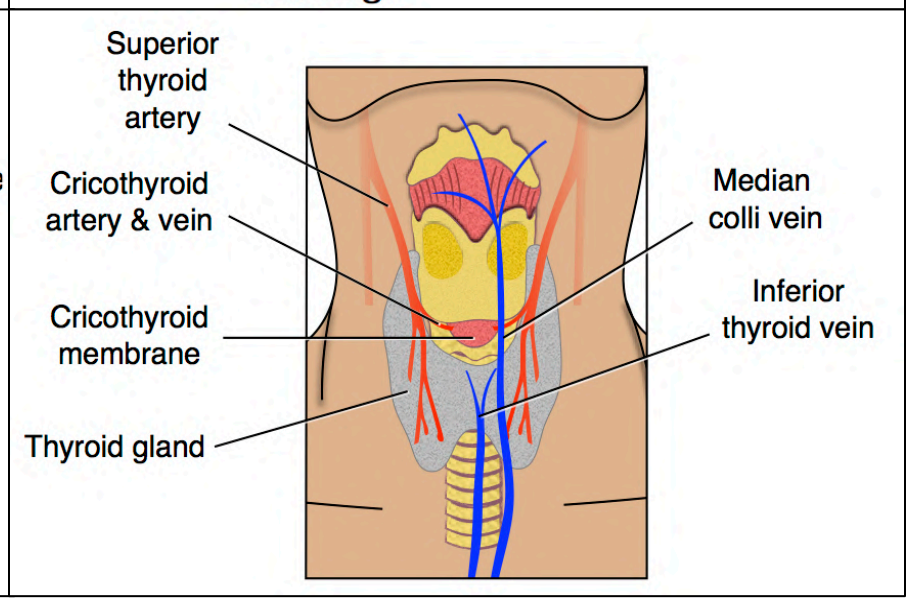
ANATOMIC LANDMARKS

The cricothyroid membrane is bordered by the thyroid cartilage superiorly and the cricoid cartilage inferiorly.

The cricothyroid artery is located at the top of the cricoid membrane at the inferior border of the thyroid cartilage. Damage to the artery should be avoided







IDENTIFICATION OF THE CRICOTHYROID MEMBRANE	
1	Extend head to better visualize the anatomy (if c-spine injury is not a concern)
2	Follow tracheal rings superiorly to cricoid cartilage.
3	Locate cricothyroid membrane immediately superior to cricoid cartilage
4	Use universal precautions and sterile technique to prep the skin with Betadine
5	Stabilize trachea with non-dominant hand
6	Provide skin tension with thumb/middle finger of non-dominant hand
7	Palpate lower cricothyroid membrane with index finger of non-dominant hand
Steps 1-7 for each procedure is to prepare and identify the cricothyroid membrane	

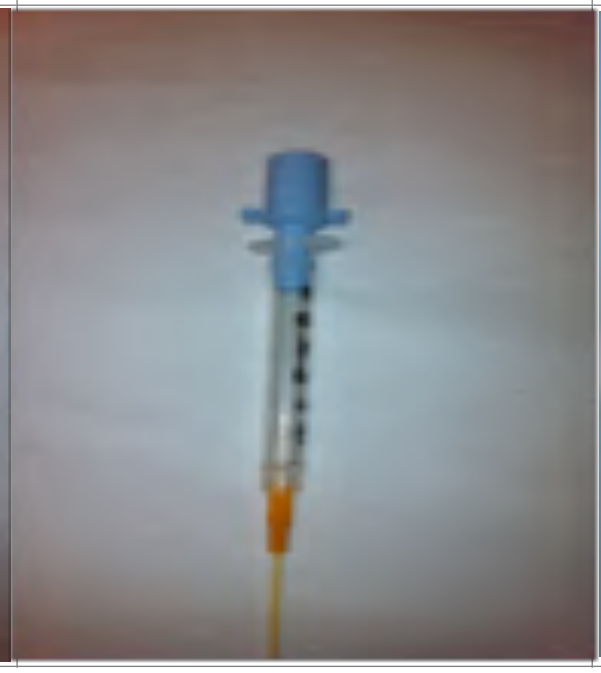
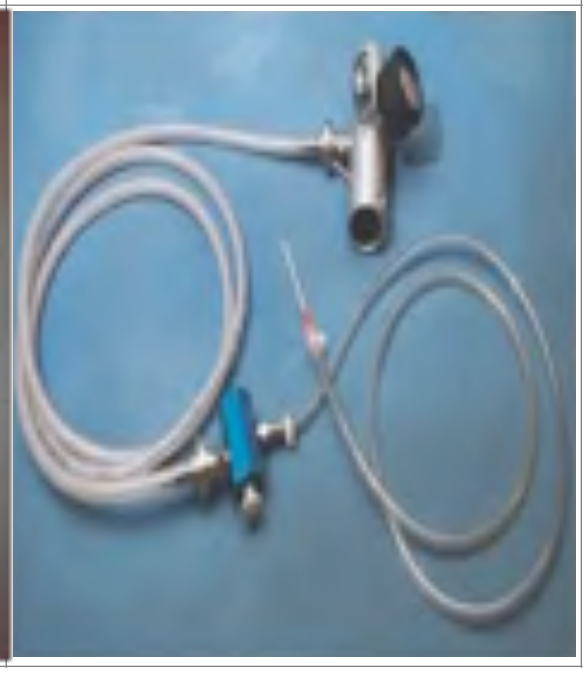
CRICOTHYROTOMY PROCEDURE PEARLS
Overall rates of surgical cricothyrotomy are declining because of better airway skills training, additional rescue airway techniques and anesthesia consultant availability
The most common indications for cricothyrotomy are facial fractures, blood/vomitus in airway, traumatic obstruction and failed intubation
The majority of PEM physicians have not done a cricothyrotomy in the clinical setting so advanced preparation and regular practice are essential
The recommended safe age for surgical cricothyrotomy is not well established. Most recommend > 5-12 years old
The Seldinger technique is comparable the classic surgical technique in speed, and may have lower complication rates

NEEDLE CRICOTHYROTOMY

Needle cricothyrotomy is the simplest of the techniques yet provides only for oxygenation and not ventilation. A device used to provide oxygen through the catheter should be prepared in advance. This is the only technique recommended for patients less than a year of age. Animal models and retrospective human data shows needle cricothyrotomy reverses hypoxia with tolerable hypercapnia for up to 30 min, using either low flow oxygen, high flow oxygen, or a self-inflating bag

NEEDLE CRICOTHYROTOMY: EQUIPMENT	
1	Universal precautions, drape, antiseptic (e.g. Betadine or Chlorhexidine)
2	1% Lidocaine with Epinephrine if awake and time permits
3	6 ml syringe filled with saline (will see bubbles syringe when trachea entered)
4	Catheter: Infant/Child: 16-18-gauge, Adult: 12-16 gauge Catheter needs to be able to connect to a syringe. Modern safety catheters cannot be connected directly to a syringe. Needles from central venous line kits or commercial kits can be required. Alternatively, a modern safety catheter without a syringe may be used
5	Oxygen connector device (See table below) a. Commercial trans-tracheal jet ventilator device b. 7.5 ET tube connector, 3 ml syringe +/- 3-way stopcock, c. 3.0 ET tube connector, meconium aspirator +/- 3-way stopcock,
6	High pressure oxygen: Infant/child 10-12 liters/min, Adult: 15 liters/min

NEEDLE CRICOTHYROTOMY: PROCEDURE	
1	Extend head to better visualize the anatomy (if c-spine injury is not a concern)
2	Follow tracheal rings superiorly to cricoid cartilage.
3	Locate cricothyroid membrane immediately superior to cricoid cartilage
4	Use universal precautions and, sterile technique, prep the skin with Betadine orChlorhexidine
5	Stabilize trachea with non-dominant hand
6	Provide skin tension with thumb/middle finger of non-dominant hand
7	Palpate lower cricothyroid membrane with index finger of non-dominant hand
8	Enter cricothyroid membrane with needle at inferior/central aspect
9	Direct needle caudally at 30-45 degrees
10	Advance needle while applying negative pressure on the syringe plunger
11	When bubbles or air is seen, advance catheter off needle into trachea
12	Attach connector device (see table below)
13	Connect oxygen tubing to: ET tube connector via meconium aspirator OR Directly if using 3-way stopcock OR To commercial jet ventilation device
14	Provide oxygen at 12-15 liters/min
15	Ventilate; I:E ratio 1:4, RR 10-12, complete airway obstruction, I:E 1:8, RR 5-6
	Control ventilation via thumb over meconium aspirator, or 3-way stopcock
	May have to push on chest to expire air otherwise pressure will increase
16	Secure with suture or tracheal tie

NEEDLE CRICOTHYROTOMY: CONNECTOR DEVICES		
Meconium Aspirator ET adapter 3.0 mm ID Angiocatheter: 16-18G infant/child 12-16G adult Connects to O_2 tubing	ET adapter 7.5 mm ID 3 cc syringe (no plunger) 3-way stopcock Angiocath: 16-18G infant/child, 12-16G adult Connects to Bag-valve-mask	Commerical jet ventilation device
		

VIDEO LINK: NEEDLE CRICOTHYROTOMY

PERCUTANEOUS CRICOTHYROTOMY

PERCUTANEOUS CRICOTHYROTOMY: EQUIPMENT	
1	Universal precautions, drape, antiseptic
2	1% Lidocaine with Epinephrine if awake and time permits
3	Pediatric: 2.0 mm for 10-35 kg (or 1-11 years) Adult: 4.0 mm for > 35 kg (or > 11 years)
4	High pressure oxygen: 10-12 L/min infant, 15 L/min adult

Flexible tubing connector

Padded Strap

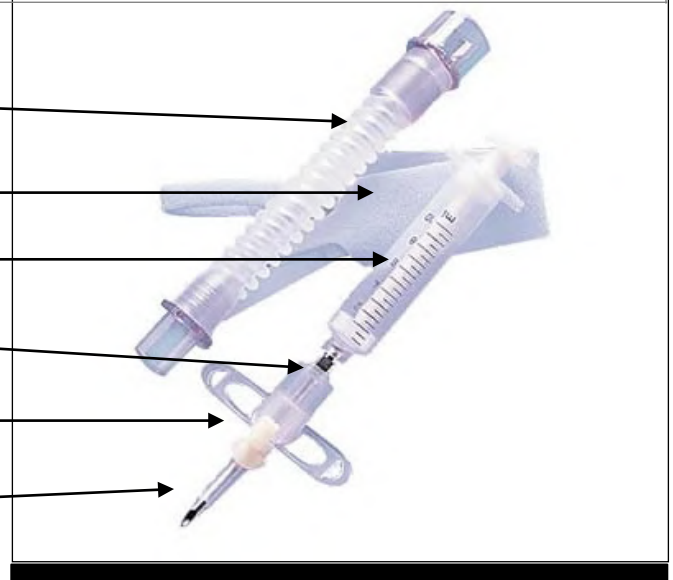
Syringe

Cricothyroid cannula with 15mm connector

Safety Stopper (Prevents damage to posterior tracheal wall)

Conical cricothyrotomy needle

VIDEO LINK: PERCUTANEOUS CRICOTHYROTOMY

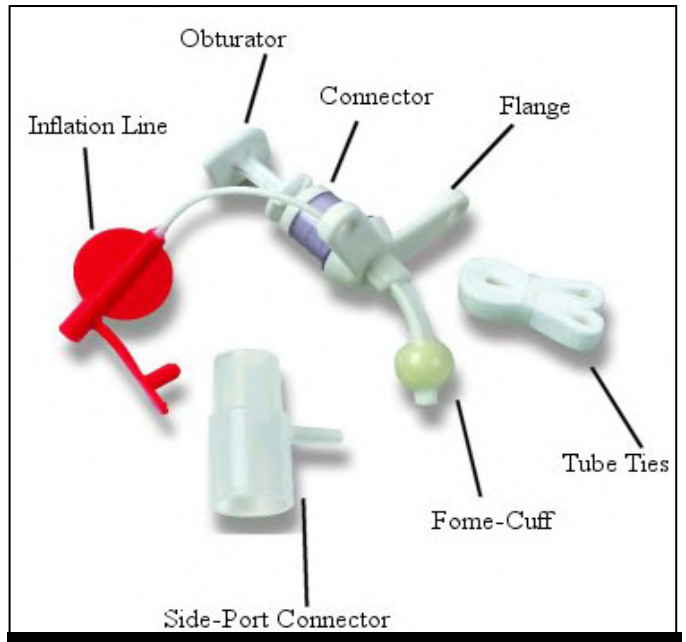


RUSCH QUICKTRACH

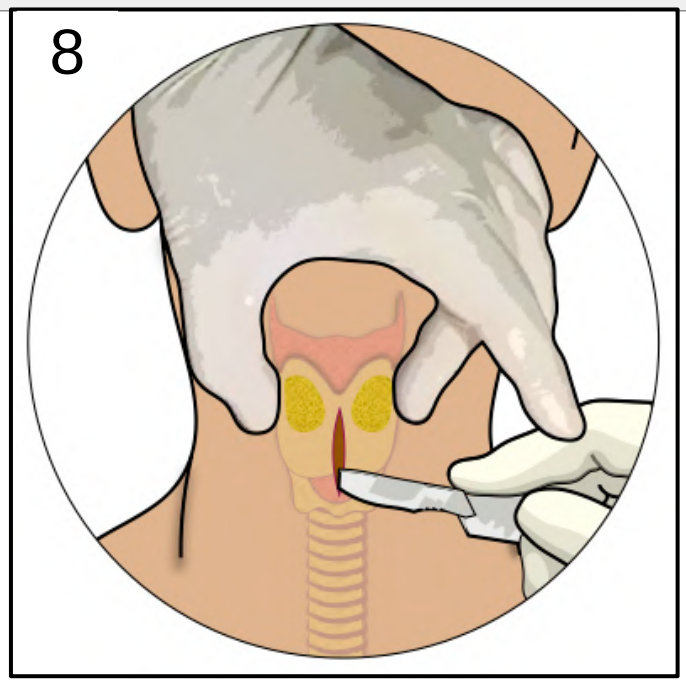
PERCUTANEOUS CRICOTHYROTOMY: PROCEDURE	
1	Extend to head to better visualize the anatomy (if neck trauma is not a concern)
2	Utilize universal precautions and sterile technique,
3	Follow tracheal rings superiorly to cricoid cartilage
4	Locate cricothyroid membrane located immediately superior to cricoid cartilage.
5	Stabilize trachea with non-dominant hand
6	Provide skin tension with thumb/middle finger on non-dominant hand
7	Palpate cricothyroid membrane with index finger
8	Enter cricothyroid membrane in its inferior/central aspect
9	Direct needle caudally at 90 degrees to skin
10	Advance needle while applying negative pressure on syringe
11	When bubbles seen, advance catheter off needle into trachea at a 45-degree angle
12	When safety stopper reaches skin stop advancing the needle
13	Remove the safety stopper
14	Hold the needle in place while advancing the catheter until the flange is on the skin
15	Remove the cricothyrotomy needle
16	Attach flexible connector tube to the cricothyrotomy catheter
17	Attach bag-valve-mask to flexible tube connector
18	Attached padded strap to flange of cricothyrotomy catheter to secure

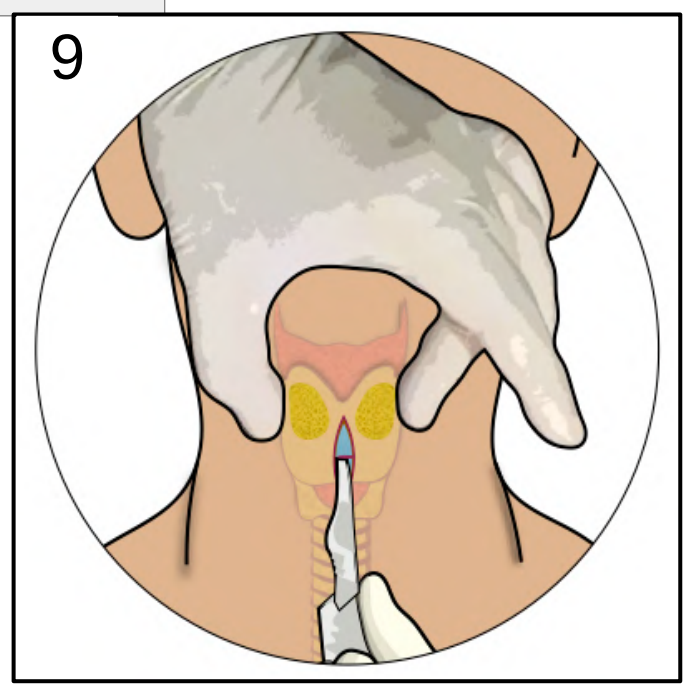
SURGICAL CRICOTHYROTOMY

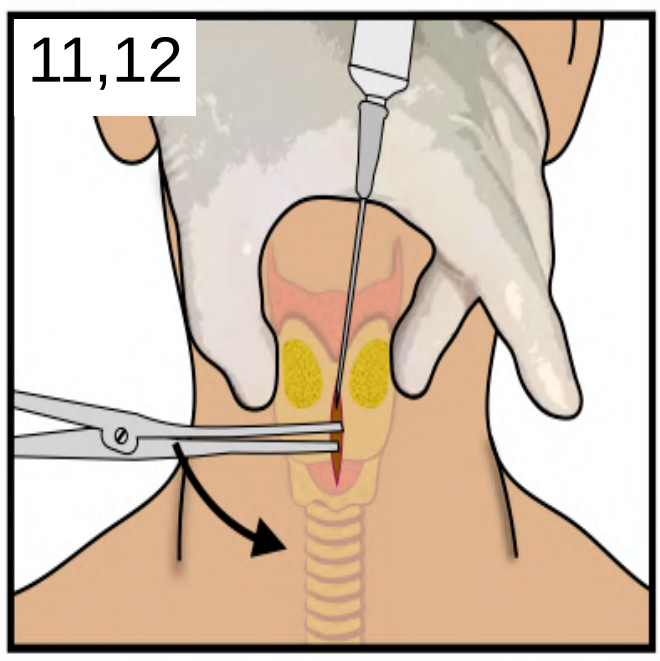
SURGICAL CRICOTHYROTOMY EQUIPMENT
Universal precautions, drape, antiseptic
1% Lidocaine with Epinephrine if awake
Suction catheter
Number 11 scalpel
Trousseau dilator
Tracheal hook
10ml syringe (for balloon)
Tracheostomy tube Internal Diameter = ((Age(years)/4) + 4))
Obturator (inner tube)
Inner cannula for tracheostomy tube
Tie/Suture
Alternative: Commercial cricothyrotomy kits

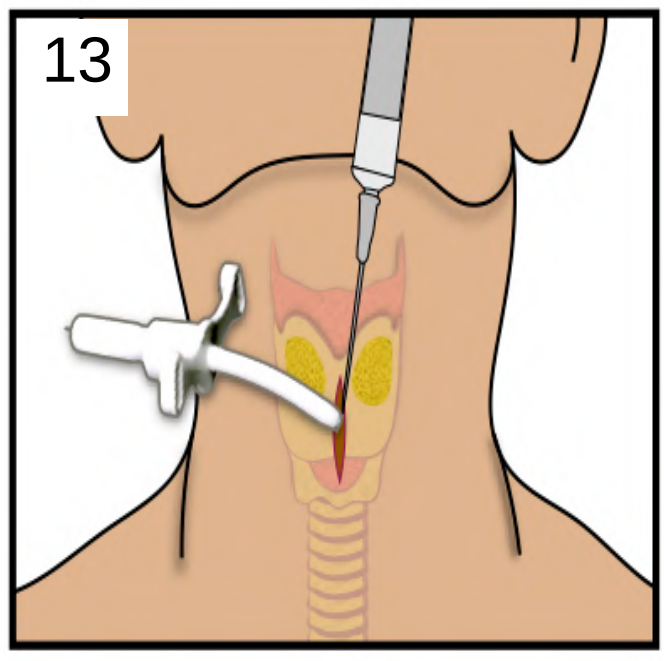


TRACHEOSTOMY TUBE









SURGICAL CRICOTHYROTOMY: PROCEDURE	
1a	Extend to head to better visualize the anatomy (if neck trauma is not a concern)
1b	Stand by the stretcher with your non-dominant hand towards the patient's head
2	Utilize universal precautions and sterile technique
3	Follow tracheal rings superiorly to cricoid cartilage
4	Locate cricothyroid membrane located immediately superior to cricoid cartilage.
5	Stabilize trachea with non-dominant hand
6	Provide skin tension with thumb/middle finger on non-dominant hand
7	Palpate cricothyroid membrane with index finger
8	Incise skin VERTICALLY in midline 3-5cm. Avoids lateral recurrent laryngeal n
9	Incise cricothyroid membrane HORIZONTALLY. Minimize the depth of the incision to avoid penetration of the posterior trachea and esophagus
10	Aim caudally to avoid vocal cords.
11	Insert tracheal hook, remove the scalpel and provide upward traction
12	Insert dilator, enlarge vertically, then rotate horizontally (or use back of scalpel)
13	Insert tracheostomy tube (if unable, tube can be placed of a bougie)
14	Remove hook and dilator
15	Remove obturator (tracheostomy tube stylet)
16	Insert inner cannula and inflate balloon (an ET tube is more difficult to secure)
17	Secure with suture or tracheal tie

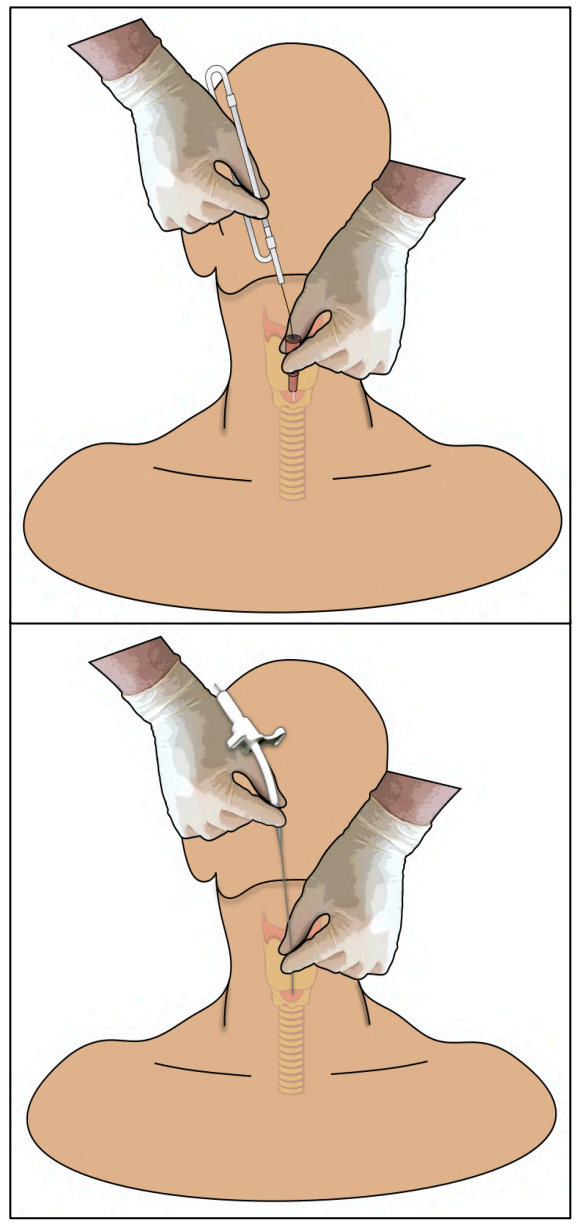
VIDEO LINK: SURGICAL CRICOTHYROTOMY

CRICOTHYROTOMY USING THE SELDINGER TECHNIQUE

The Seldinger technique combines elements of the needle technique and surgical technique.

MELKER EMERGENCY CRICOTHYROTOMY SETS (COOK MEDICAL)	
SELDINGER SETS	SURGICAL SETS
ID 3.5 mm, length 3.8 cm (uncuffed)	
ID 4.0 mm, length 4.2 cm (uncuffed)	
ID 5.0 mm, length 9.0 cm (cuffed)*	ID 5.0 mm, length 9.0 cm (cuffed)*
ID 6.0 mm, length 7.5 cm (uncuffed)	
*Universal set includes equipment for both Seldinger and Surgical techniques	

SELDINGER TECHNIQUE: PROCEDURE	
1	Universal precautions, sterile technique
2	Follow tracheal rings superiorly to cricoid cartilage
3	Locate cricothyroid membrane superior to cricoid cartilage
4	Attach 6ml saline filled syringe to IV catheter
5	Stabilize trachea with non-dominant hand
6	Provide skin tension with thumb/middle finger
7	Palpate cricothyroid membrane with index finger
8	Enter the cricothyroid membrane in inferior/central aspect
9	Direct needle caudally at 30-45 degrees
10	Advance needle while applying negative pressure on syringe
11	When bubbles seen, advance catheter off of the needle and into the trachea
12	Thread guide wire through catheter then remove catheter
13	Make 1cm incision with scalpel at entrance point of guide wire
14	Thread cricothyrotomy kit catheter and dilator through incision
15	Do not let go of the guide wire
16	Remove dilator and guide wire
17	Secure with suture or tracheal tie



VIDEO LINK: SELDINGER TECHNIQUE CRICOTHYROTOMY

APPENDIX: PEDIATRIC TRACHEOSTOMY TUBE SIZES

PEDIATRIC TRACHEOSTOMY TUBE SIZE					
Age	Shiley	Holinger	Portex	Bivona	Berdeen
Premature	00	00	3.0	2.5-3.0	---
Newborn	0	0	3.0	3.0-3.5	3.5
0-6 months	0-1	1-2	3.5	3.5-4.0	3.5-4.0
6-12 months	1-2	2-3	4.0	4.0-4.5	4.0-4.5
12-24 months	3	3	4.5	4.5-5.0	5.0
3-6 years	4	4	5.0	5.0	5.0
7-10 years	4	5	5.0	5.0-6.0	6.0
10-12 years	6	6	6.0	6.0-7.0	6.0
12-14 years	6	6	7.0	7.0	7.0

DIFFICULT AIRWAY

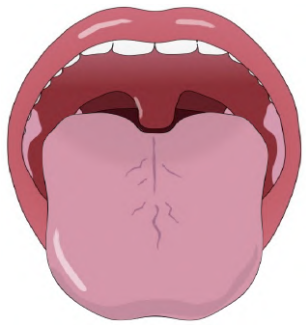
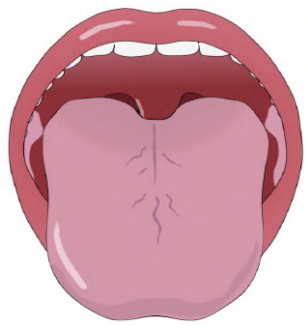
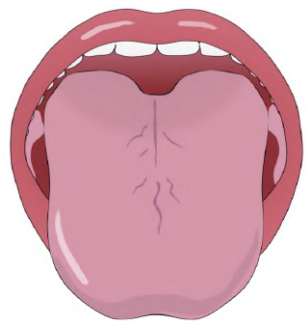
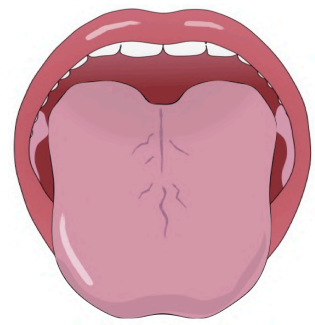
INTRODUCTION (DENNIS HEON, M.D., 2/2022)
The focus of this PEM Guide is on the pediatric difficult airway and presumes familiarity with the pediatric airway procedures. (PEM Guide: Resuscitation: Pediatric Airway, PEM Guide: Airway Procedures: Endotracheal intubation, PEM Guide; Airway Procedures: Rapid sequence intubation). Proper patient positioning and proper equipment sizing are vital to a successful intubation attempt. The incidence of a difficult pediatric airway is approximately 0.5–1% and most of these can be predicted.

CLINICAL ASSESSMENT

There are several common mnemonics used to help predict difficult airway situations. While these are taken from adult literature, many parts are still applicable to the pediatric population. The problem with the mnemonics is that the parameters cannot always be adequately assessed in the emergency department. For example, the Mallampati score requires an alert, cooperative patient that is sitting upright. The majority of the patients requiring intubation in the ED are trauma patients who requiring cervical spine immobilization. Neck stiffness, neck mobility and the 3-3-2 rule can not be assessed in these patients.

PROCEDURE	MNEMONIC
Difficult BVM VENTILATION	MOANS
Difficult DIRECT LARYNGOSCOPY	LEMON
Difficult EXTRA GLOTTIC DEVICE	RODS
Difficult CRICOTHYROTOMY	SMART

DIFFICULT BAG-VALVE-MASK VENTILATION: MOANS	
M	**MASK SEAL**: Improper seal may arise from an operator with small hands (may require both hands to make appropriate seal and a second person to squeeze bag), severe lower facial trauma, or beards in adolescents. Some authors include Mallampati scores of 3 or 4 as another predictor of difficult to BVM ventilate. (LEMON below for Mallampati score)
O	**OBESITY**: Obese children will have decreased diaphragmatic excursion due to increased resistance from abdominal contents as well as overcoming the weight of the chest wall. They may also have redundant soft tissues that can impede airflow. **OBSTRUCTION:** Obstruction can occur from infectious causes such as epiglottitis, retropharyngeal abscess, peritonsillar abscess, Ludwig's angina or from foreign bodies or airway trauma
	OBSTRUCTION: Obstruction can occur from infectious causes such as epiglottitis, retropharyngeal abscess, peritonsillar abscess, Ludwig's angina or from foreign bodies or airway trauma
A	**AGE**: This is not typically a problem in the pediatric population except in certain neuromuscular diseases where one loses muscle tone in the upper airway.
N	**NO TEETH**: Not a problem in most children as facial tone sufficient to create a good mask seal.
S	**STIFF**: Children who require high-pressures from illnesses that decrease lung compliance such as asthma, ARDS, or severe pneumonias.
	SNORING: Snoring in children is another sign of redundant soft tissues. Sleep apnea is a likely predictor of difficult airways.

DIFFICULT DIRECT LARYNGOSCOPY: LEMON				
L	**LOOK** (quick first impression): Predictive features include small mandible, large tongue, large teeth, and short neck.			
E	**EVALUATE 3:3:2 RULE:** (NOTE: must use child's fingers, not yours) Should be able to insert 3 fingers vertically oriented into the mouth Should be able to place 3 fingers under chin between mentum and hyoid bone Should be able to place 2 fingers between thyroid notch and hyoid bone. Last measurement is often not met in young children and indicates an anterior placed larynx.			
M	**MALLAMPATI SCORE:** Class 4 failure rates approach 10% in some studies. Most children cannot perform the test properly. Patient is sitting, opens mouth as wide as possible and protrudes tongue as far as possible without phonating. If patient is supine and you use a tongue blade to look into posterior pharynx, many experts believe this result is just as valid.			
				
	M1 Anterior Pillars Posterior Pillars Fauces Uvula Soft Palate	**M2** Posterior Pillars Fauces Uvula Soft Palate	**M3** Uvula (base only) Soft Palate	**M4**
O	**OBESITY**: Obese children will have decreased diaphragmatic excursion due to increased resistance from abdominal contents as well as overcoming the weight of the chest wall. They may also have redundant soft tissues that can impede airflow.			
	OBSTRUCTION: Obstruction can occur from infectious causes such as epiglottitis or peritonsillar abscess, or from foreign bodies or airway trauma			
N	**NECK MOBILITY**: Cervical spine collars for trauma patients limit neck extension and may make direct laryngoscopy more difficult. Intrinsic causes such as cervical spinal fusion can make direct laryngoscopy impossible.			

DIFFICULT EXTRA GLOTTIC DEVICE: RODS	
R	**RESTRICTED MOUTH OPENING:** Some rescue devices require more space to insert than a traditional laryngoscope.
O	**OBESITY:** Obese children will have decreased diaphragmatic excursion due to increased resistance from abdominal contents as well as overcoming the weight of the chest wall. They may also have redundant soft tissues that can impede airflow.
	OBSTRUCTION: Obstruction can occur from infectious causes such as epiglottitis or peritonsillar abscess, or foreign bodies and airway trauma
D	**DISTORTED OR DISRUPTED ANATOMY**: Epiglottitis, retropharyngeal abscess, cleft palate, or expanding hematoma from neck trauma.
S	**STIFF**: Children who require high pressures from illnesses that decrease lung compliance such as asthma, ARDS, or severe pneumonias.
	SNORING: Snoring in children is a sign of redundant soft tissues. Sleep apnea is a predictor of difficult airways.

DIFFICULT CRICOTHYROTOMY: SMART	
S	**SURGERY:** Recent or remote in neck region. In recent surgery, bleeding and edema are more likely to impede visualization or distort location of structures. Remote surgery may have firm scar tissue and distorted anatomy.
M	**MASS:** Neck mass distort landmarks and make procedure more challenging.
A	**ACCESS**: Extraneous devices: Trauma cervical collar or halo neck brace Patient anatomy; Short neck, redundant neck tissue Patient illnesses; Edema, soft tissue infections, subcutaneous emphysema
R	**RADIATION**: Rare in children but may distort anatomy from scar formation.
T	**TUMOR**: Also rare in children but may make neck access challenging.

DIFFICULT AIRWAY APPROACH

The algorithm below assumes that airway protection or positive pressure ventilation is required. Non-invasive techniques such as CPAP and BIPAP may be an option in some cases. (See PEM Guide: Airway Procedures: Non-invasive Ventilation). The most important aspect of the algorithm is to call for help early if a difficult airway is anticipated or encountered. There are 3 difficult airway situations: Can't ventilate/Can't intubate, Can ventilate/Can't intubate and Can't ventilate/Can intubate. The indications and use of specific rescue devices as reviewed in detail below.

CAN'T VENTILATE, CAN'T INTUBATE

This is the most dangerous situation. The most experienced provider available may attempt endotracheal intubation using video laryngoscopy (e.g. Glidescope). A Bougie may allow passage of an endotracheal tube with only a view of the epiglottis or partial view of vocal cords. If bag-valve mask ventilation, ventilation with an extra glottic airway (e.g. LMA) and endotracheal intubation using direct or video laryngoscopy are unsuccessful the patient may require a cricothyrotomy (PEM Guide: Airway Procedures: Cricothyrotomy)

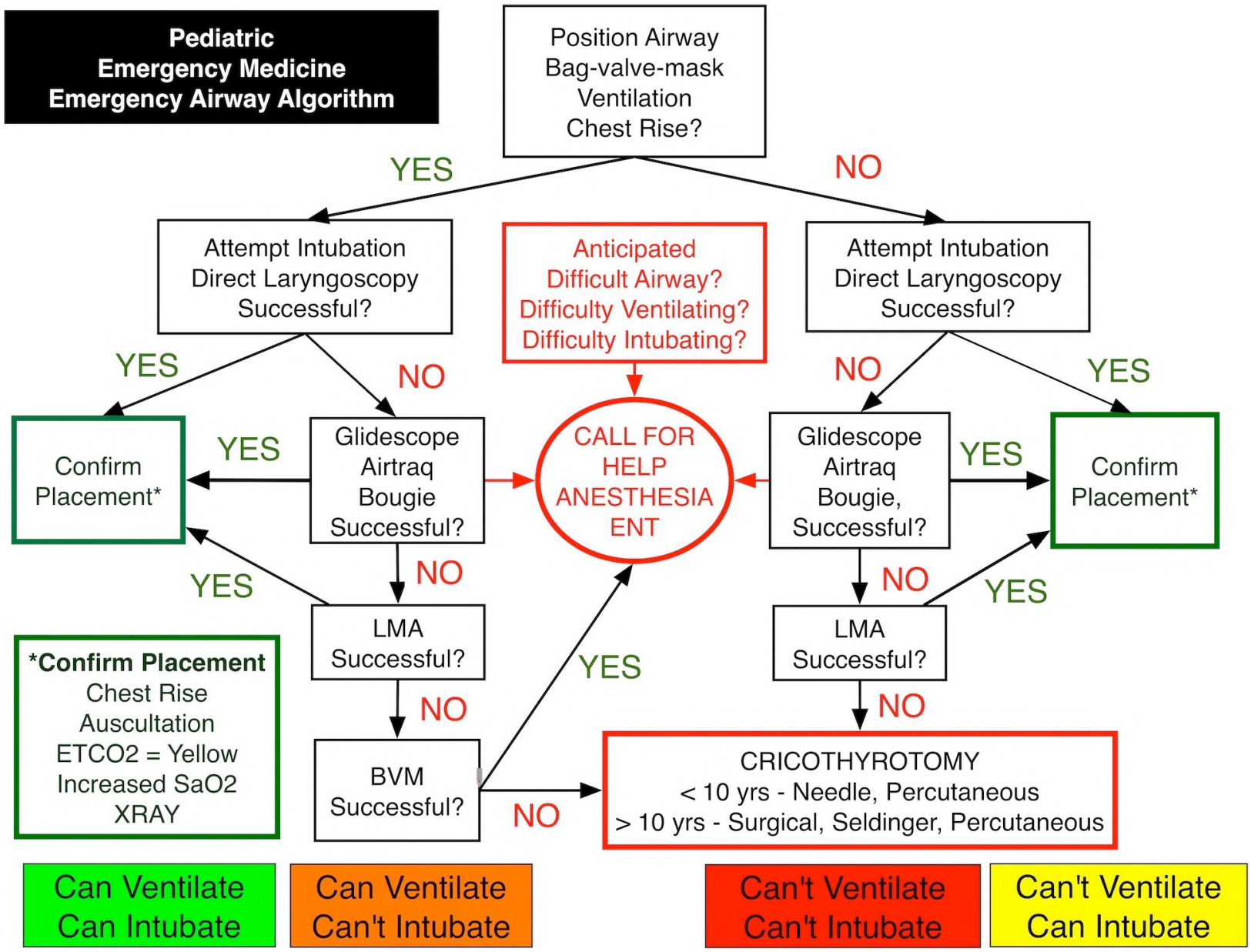
CAN VENTILATE, CAN'T INTUBATE

In this situation, ventilation may be successful with a bag-valve-mask or an extra glottic airway but intubation with direct or video laryngoscopy is unsuccessful. An extra-glottic airway is not a definitive airway in a patient with upper airway obstruction. Further supraglottic, glottic or subglottic swelling may make ventilation impossible. Upper airway obstruction may occur due to: trauma, laryngotracheal bronchitis (croup), epiglottitis, bacterial tracheitis, smoke inhalation, extrinsic masses and anaphylaxis.

There are several rescue devices that may help you secure an airway in this situation. If the problem is lack of proper visualization, use of a video laryngoscope such as the Glidescope can improve the view of the vocal cords. A Bougie may allow passage of an endotracheal tube with only a view of the epiglottis or partial view of vocal cords. A fiber optic scope or an intubating LMA can also be used if available.

CAN'T VENTILATE, CAN INTUBATE

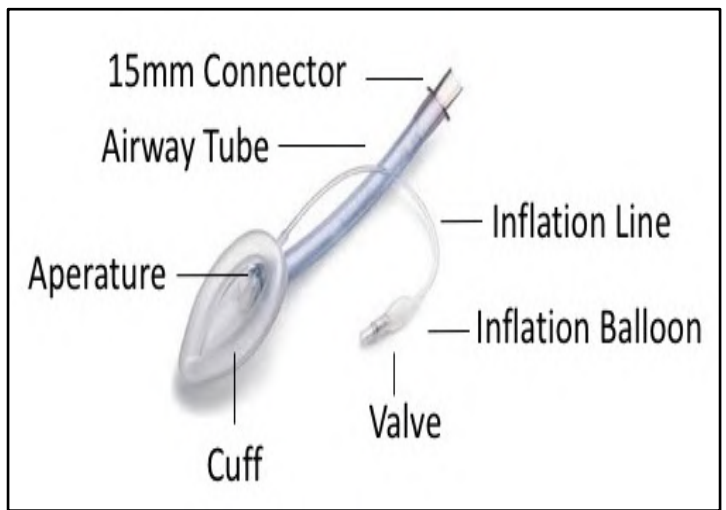
This is the least dangerous of the difficult airway scenarios. If endotracheal intubation with direct laryngoscopy is successful, then airway protection and a means to provide oxygenation and positive pressure ventilation are available. If intubation with direct laryngoscopy is unsuccessful than the use of a video laryngoscope (Glide Scope) or optical laryngoscope (Airtraq) may be attempted.



RESCUE DEVICES

Only those devices available in the pediatric ED's at Bellevue and NYU are reviewed. The authors have no financial interests in any of the products discussed. Videos links demonstrating the use of each device are included below for each device.

LARYNGEAL MASK AIRWAYS (LMA and I-GEL): These are extra-glottic devices that will allow ventilation and oxygenation without passing a tube through the vocal cords. They also limit gastric distention when compared to bag-valve mask ventilation. The laryngeal mask airways are inflated after they are placed. The i-Gel airways do not require inflation and mold to the airway. The patients weight determines the correct size used. The supraglottic airways are lubricated prior to insertion into the mouth.



LMA

Advantages include the ability to ventilate even when unable to pass an endotracheal tube. It is possible to intubate through some LMA devices.

There are several disadvantages. Since the device is extra glottic, there is a risk of glottic closure or complete airway obstruction distal to the device that makes ventilation impossible. It is also difficult to generate high airway pressures using these devices due to large air leaks. Finally, they are easily displaced with patient movement.

LARYNGEAL MASK AIRWAY: SELECTION		
SIZE	WEIGHT (KG)	INFLATION*
1	0-5	4 ml
1.5	5-10	7 ml
2	10-20	10 ml
2.5	20-30	14 ml
3	30-50	20 ml
4	50-70	30 ml
5	70-100	40 ml
*Maximum Inflation (ml)		

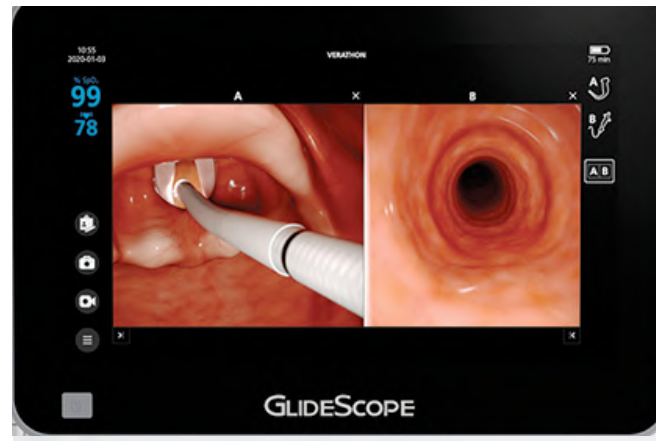
I-GEL LARYNGEAL MASK AIRWAY: SELECTION							
COLOR	Pink	Blue	Grey	Clear	Yellow	Green	Orange
DESCRIPTION	Neonate	Infant	Small Pediatric	Large Pediatric	Small Adult	Medium Adult	Large Adult
SIZE	1	1.5	2	2.5	3	4	5
WEIGHT (KG)	2-5	5-12	10-25	25-35	30-60	50-90	≥ 90
NYU: Sizes 1-3 available. Use regular LMA if size 4 or 5 required							

LARYNGEAL MASK AIRWAY PROCEDURE	
Inflate/Deflate the cuff	Inflate the cuff to insure the absence of air leaks. Then deflate by pressing the LMA aperture side down against a firm, flat surface. Ensure the leading edge is wrinkle free. The primary goal is to ensure that the tip of the LMA does not fold over or trap the epiglottis which can prevent a good seal. Some recommend partially inflating the cuff prior to insertion
Lubricate	Lubricate the back to the LMA (not the side of the aperture)
Position head	Slight head flexion (not extreme sniffing position) facilitates passage
Open the mouth	Open the mouth by grasping the chin and the tongue with the non-insertion hand. This will facilitate passage and avoid damage to the lips and chin.
Hold the LMA	Hold the LMA like a pen with the index finger of the dominant hand at the junction of the LMA tube and cuff.
Advance the LMA	Hold the cushion firmly to the palate as you advance it. This will prevent the tip of the cushion from folding over and trapping the epiglottis. Advance gently in the midline until resistance is felt at the level of the upper esophageal sphincter overlying the larynx.
Trouble shooting	If the LMA does not advance either the anterior or posterior side may be obstructed. The anterior side is typically obstructed by the tongue. A tongue blade may be used to pull the tongue away from the LMA. The posterior side is typically obstructed if the tip of the cuff folds over. Insert the index finger of the insertion hand to manually uncurl the tip. If these are not successful, withdraw and then reinsert the LMA.
Inflate the cuff	While the cuff is inflated, the tip of the LMA the tube will rise anteriorly slightly out of the mouth and the larynx
Assess ventilation	Assess ventilation immediately to determine the positioning and seal of the cuff. Inability to ventilate may be due to: 1. The cuff is insufficiently inflated 2. The cuff tip and/or epiglottis are folder over obstructing the larynx 3. Cuff is twisted behind the tongue and not making good contact If adding more air to the cuff doesn't result in ventilation then deflate the cuff, pull the LMA back 1-2 cm and re-advance, inflate and attempt ventilation again. If this does not result in ventilation the tube should be removed and inserted again or a differ size LMA should be used.

VIDEO LINK: PEDIATRIC LMA

VIDEO LINK: I-GEL LMA

GLIDESCOPE: GlideScope is a video-based laryngoscopy system that improves visualization of the vocal cords. The GlideScope video laryngoscopes have a hyper-angulated blade. This is purported to improve visualization and reduce the lift pressure necessary. Miller and Macintosh blades are also available. There are three video batons sizes.



GLIDESCOPE ADVANTAGES
Provides improved airway visualization compared to DL
No need to align the oral, pharyngeal and tracheal axes
The procedure can be visualized by all providers present
Magnifies the view of the airway

GLIDESCOPE: SIZE SELECTION		
GVL*	WEIGHT	VIDEO BATON SIZE
Miller S0	3-5 kg	1-2 (Pediatric)
Miller S1	6-11 kg	1-2 (Pediatric)
Hyper-angulated 1	1.5-3.8 kg	1-2 (Pediatric)
Hyper-angulated 2	1.8-10 kg	1-2 (Pediatric)
Hyper-angulated 2.5	10-28 kg	1-2 (Pediatric)
Hyper-angulated 3	≥ 10 kg	3-4 (Adult)
Hyper-angulated 4	≥ 40 kg	3-4 (Adult)
Macintosh S3	≥ 10 kg	3-4 (Adult)
Macintosh S4	≥ 40 kg	3-4 (Adult)
Glidescope Rigid Stylet: Small (ET 3.0-4.0), Medium (ET 4.5-5.5), Large (ET ≥ 6.0)		

GLIDESCOPE TROUBLE SHOOTING: The view can be obscured due to camera fogging or by secretions. Allow the Glidescope to warm up prior to use if possible. Aggressive suctioning should be able to clear the view.

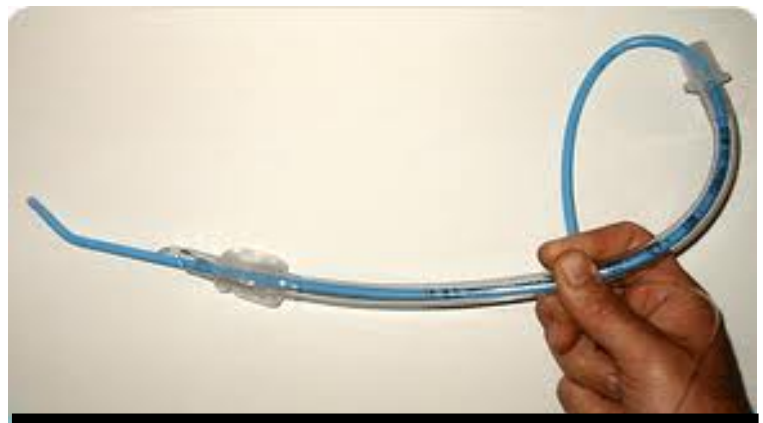
While the GlideScope hyper-angulated blades improve airway visualization, passage of the endotracheal tube may be more difficult compared to directly laryngoscopy. If the tip of the GlideScope is too close to the cords (the airway image fills the entire screen), the airway will be anterior and tube placement will be difficult. While counter-intuitive, pull up and back on the GlideScope handle to increase the distance from the cords and pass the tube.

When inserting the endotracheal tube into the patient’s mouth, if you hit any structures, you tend to lose a little bend. If you lose the bend, the tube will not go anterior enough to enter the vocal cords. Finally, when the tube is at the opening of vocal cords you may have trouble advancing it. If this occurs, slightly withdraw the stylet as the extreme bend causes the tube to want to continue to go anteriorly as opposed to down the trachea.

GLIDESCOPE PROCEDURE		
0	Positioning	Place a towel/sheet under shoulders of an infant or young child. The head and neck are in a more neutral position than the extreme “sniffing” position required for direct laryngoscopy. There is no need to align the oral, pharyngeal and tracheal axes.
1	Look DOWN	Introduce the Glidescope in the midline. Advance to the tip of the tongue and lift slightly. Do not lift the epiglottis. This may improve visualization of the glottis but make endotracheal tube passage more difficult.
2	Look UP	Visualize the Glottis: Center glottis in the top 1/3 of the screen. Advance or withdraw Glidescope slightly to optimize the glottic image. Lift the mandible slightly
3	Look DOWN	Introduce the endotracheal tube to the right side of the mouth. Advance the ET tube beyond the tonsillar pillars Glidescope Stylet: Small (ET 3.0-4.0), Medium (ET 4.5-5.5), Large (ET ≥ 6.0)
4	Look UP	Visualize intubation. If difficulty advancing use cricoid pressure to move glottis down or rotate 90 clockwise and then advance tube through the vocal cords. Partially retract the stylet and then complete advancement the tube.

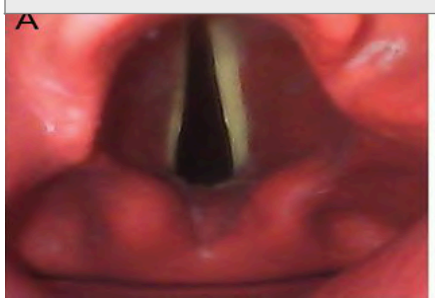
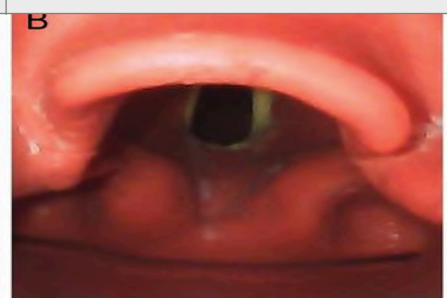
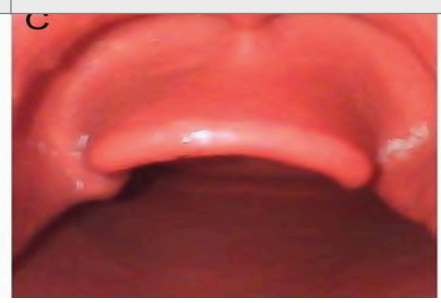
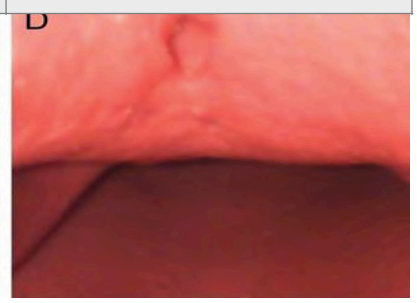
VIDEO LINK: PEDIATRIC GLIDESCOPE

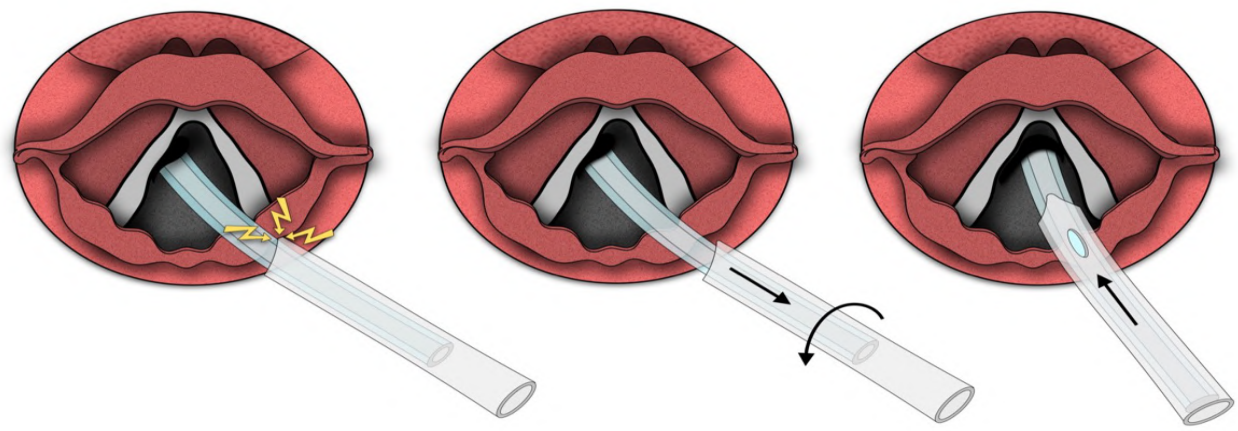
BOUGIE is an endotracheal tube introducer. It is low-tech device that is a rigid stylet with a bend at one end. It does not obscure the airway view to the degree that an ET tube does. The upward angle of the tip (30 degrees) facilitates passage into the trachea. The bend allows the Bougie to angle upwards into the trachea even when there is poor visualization of the true vocal cords such as with Cormack–Lehane class 3 or 4 airways (see below). This makes it useful for the anterior airways in pediatric patients. It can also be use to exchange endotracheal



BOUGIE

ADULT BOUGIE	Accommodates endotracheal tubes ≥ 6.0 mm ID
PEDIATRIC BOUGIE	Accommodates endotracheal tubes 4.0-6.0 mm ID

CORMACK LEHANE CLASSIFICATION			
I	II	III	IV
			

BOUGIE PROCEDURE	
Preparation	Prepare the endotracheal tube. The endotracheal tube can be preloaded over the Bougie or can be loaded by an assistance after the Bougie is inserted. Measure the distance to the mid-trachea prior to placement
Insert the Bougie	The Bougie can be inserted if only the posterior arytenoid cartilage is seen or blindly if the glottic open is not visualized. The tip of the Bougie is oriented upward and care is taken to avoid rotation of the tube as it is inserted. If a blinded technique is used, then correct insertion can be determined as the anterior tip of the Bougie “clicks” across the anterior tracheal rings. Alternatively, it can be advanced to the mid trachea. The Bougie is semi-rigid and can cause significant anatomic damage if forced.
Advance the endotracheal tube	Do not remove the laryngoscope until tube passage is completed. If the ET tube gets caught on the glottis, pull back an few centimeters, rotate the tube 90° degrees counter-clockwise and advance the tube (see image below). This orients the bevel posteriorly.
Rotation of the ET Tube 90 Degrees Counter-Clockwise to Facilitate Passage	
Remove the Bougie	The bougie should be removed gently to avoid pulling the ET tube out.

VIDEO LINK: BOUGIE

CRICOTHYROTOMY

In a patient who: requires ventilation or airway protection, fails non-invasive techniques such as continuous positive airway pressure (CPAP) and fail attempts at both ventilation and intubation (can’t ventilate, can’t intubate scenario) a cricothyrotomy may be required. There are a number of techniques available. These include: needle cricothyrotomy, percutaneous cricothyrotomy, cricothyrotomy using a Seldinger technique and surgical cricothyrotomy. The patient’s age, equipment available, the users experience and the clinical scenario will govern the choice of technique. (See: PEM Guide: Airway Procedures: Cricothyrotomy)

See: PEM Guide: Airway Procedures: Mechanical Ventilation
PEM Guide: Airway Procedures: Post Intubation Sedation and Paralysis

ENDOTRACHEAL INTUBATION

INTRODUCTION (ADRIANA MANIKIAN, M.D., 5/2020)
There are many anatomic differences between the pediatric and adult airway. These differences impact the approach to endotracheal intubation in the child. With the exception of the strength required to visualize the airway in the adult, every pediatric anatomic difference make endotracheal intubation with direct laryngoscopy more difficult than in the adult. By 8-12 years of age the airway assumes adult characteristics. This PEM Guide reviews the approach to endotracheal intubation using direct laryngoscopy. See: PEM Guide: Procedure: Difficult Airway for a description of video intubation and intubation using a bougie.

PEDIATRIC AIRWAY: ANATOMIC DIFFERENCES
Large occiput: Leads to head flexion in supine position
Hypertrophied tonsils and adenoids
Smaller airway cavity and relatively larger tongue
The airway is more cephalad (Level of C2-3 as compared to C4-5 in adults)
The airway is more anterior (Smaller distance between the mandible and airway)
Larger, omega shaped epiglottis
Cricoid cartilage is narrowest portion, creating a cylindrical shaped larynx

INTUBATION INDICATIONS
Cardio-pulmonary arrest
Respiratory failure
Coma, head trauma: protection of airway, unstable airway from facial trauma
Increased ICP with actual or impending herniation for hyperventilation
Functional/anatomical airway obstruction: Croup, smoke inhalation, anaphylaxis
Delivery of endotracheal medications

INTUBATION COMPLICATIONS
Hypoxemia/bradycardia
Pneumothorax: Excessive positive pressure, e.g. right mainstem bronchus, asthma
Vomiting and aspiration
Fracture/dislodgment of teeth
Laceration of gums/lips
Laryngeal trauma
Esophageal intubation

EQUIPMENT SELECTION
Laryngoscope handle/blades Miller (straight) or McIntosh (curved) sizes 0-3
Endotracheal tubes (ETT) sizes 2.5- 8 with stylet, cuffed and uncuffed
Suction equipment: Yankauer, ETT suction catheters
Colorimetric or quantitative end-tidal CO_2 monitor: infant and adult sizes
Tape, adhesive solution to secure ETT
Patient monitoring devices: cardiopulmonary monitor and pulse oximeter
Rescue airway equipment (LMA, needle or surgical airway) should be available

LARYNGOSCOPE SELECTION

DIRECT LARYNGOSCOPY: Miller (straight) blades are more suitable for visualizing the vocal cords of infants and young children. They are generally recommended for children less than 2 years. They have a slim profile and do not obstruct the visual field as infants have relatively smaller buccal cavity and larger tongue. The tip of the Miller blade lifts the floppy and large epiglottis of young children and moves it effectively out of the way. It provides better visualization of the vocal cords as they are located more anterior and cephalad.

McIntosh (curved) blades should be used in older children (usually older than 8 years). The tip of the blade rests in the vallecula of the tongue and when lifted, lifts the epiglottis as well, thus opening the view to the vocal cords.

LARYNGOSCOPE BLADE SIZE	
Premie / Newborn	Miller 0
Infant – 2 years	Miller 1
2 – 8 years	Miller or McIntosh 2
> 8 years	McIntosh or Miller 3

VIDEO LARYNGOSCOPE: Video laryngoscopy (VL) offers several advantages to direct laryngoscopy (DL). Video laryngoscopy can improve airway visualization, decrease the risk of infection transmission and allow a second viewer to provide advice and support. A Cochrane metanalysis, including 12 randomized clinical trials and 803 children concluded that video laryngoscopy was associated with higher rate of intubation failure and a longer time to intubation (Abdelgadir, Cochrane DSR 2017, PubMed ID: 28539007). However, the evidence was graded as low quality. A study including 625 pediatric patients intubated in the ED from the National Emergency Airway Registry (NEAR) of 25 international academic and community ED's found a higher first pass success rate for video laryngoscopy after adjusting for a number of difficult airway predictors in a regression model (aOR: 1.8, 95% CI 1.0, 3.1) and in a propensity score adjusted model (aOR: 1.8, 95% CI (1.1, 3.3) (Kaji, Acad Emerg Med. 2020, PubMed ID: 31617640). There were no statistically significant differences in overall adverse events or any of the individual adverse events (aOR: 0.8, 95% CI (0.4, 1.4).

GLIDESCOPE: SIZE SELECTION		
GVL*	WEIGHT (KG)	VIDEO BATON SIZE
0	< 1.5	1-2 (Pediatric)
1	1.5 – 3.6	1-2 (Pediatric)
2	1.8 – 10	1-2 (Pediatric)
2.5	10 - 28	1-2 (Pediatric)
3	10 – Adult	3-4 (Adult)
4	40 – Morbidly obese	3-4 (Adult)
ET Tube ≥ 6.0mm: Use Glidescope Rigid Stylet ET Tube < 6.0 mm: Use Stylet with 60-90 degree turn at end (Glidescope shaped)		

ENDOTRACHEAL TUBE (ETT) SELECTION

The American heart association states that both cuffed and uncuffed endotracheal tubes are acceptable for intubating infants and children. Cuffed endotracheal tubes may decrease the risk of aspiration. If cuffed endotracheal tubes are used, cuff inflation pressure should be monitored and limited according to manufacturer's instruction (usually less than 20 to 25 cm H_2O).

In certain circumstances (e.g. poor lung compliance, high airway resistance, or a large glottic air leak) a cuffed endotracheal tube may be preferable to an uncuffed tube. In one study the use of cuffed tubes did not result in an increase in post extubation stridor but did decrease the proportion requiring endotracheal tube replacement secondary to air leaks when compared to uncuffed tubes (Weiss, Brit J Anesth 2009, PubMed ID: 19887533).

ENDOTRACHEAL TUBE SELECTION		
	UNCUFFED	CUFFED
Infant (< 1 year)	3.5	3.0
1-2 years	4.0	3.5
> 2 years	(Age(years)/4) + 4	(Age(years)/4) + 3.5
Size = Internal Diameter in millimeters		

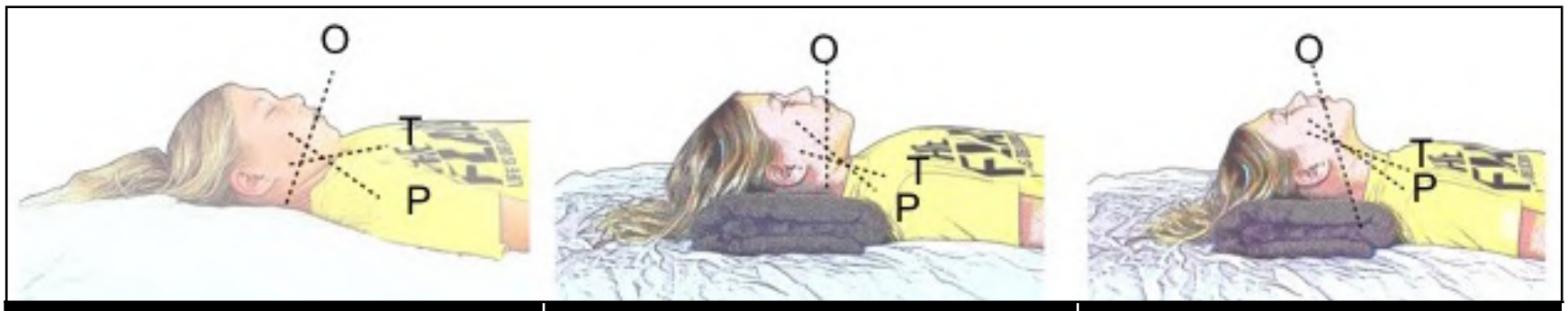
INSERTION DEPTH: Depth of insertion from the lip (cm) = 3 x ID of ETT (mm). These are estimates. There should always be 0.5 size smaller/larger tube available. Uncuffed tubes have a vocal cord mark, which when passed through the vocal cords would indicate placement of the ETT in the proper position above the carina. Cuffed tubes should be advance until the cuff is just beyond the vocal cords.

CUFFED TUBE INFLATION: Cuffs should be inflated before insertion to test cuff, then deflated, & inserted. Cuff Pressure should be < 20 mm cm H2O when measured.

CUFFED TUBE INFLATION VOLUME		
SIZE	SOFT	FULL
3.0	1 ml	2 ml
3.5	1 ml	2 ml
4.0	1 ml	2 ml
4.5	1 ml	2 ml
5.0	1 ml	2 ml
5.5	1.5 ml	2 ml
6.0	4 ml	7 ml
6.5	5 ml	8 ml
7.0	5 ml	10 ml

PATIENT POSITIONING

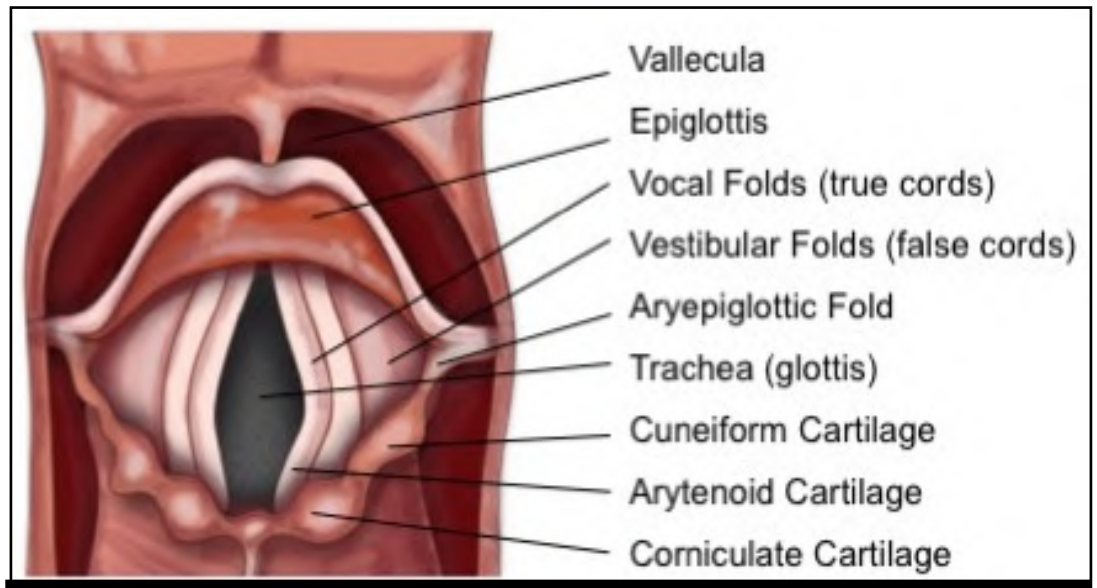
Alignment of the oral, pharyngeal and tracheal axes improves identification of anatomic landmarks and facilitates passage of the endotracheal tube. First elevate the head 8-10 cm with slight neck flexion. This aligns to pharyngeal and tracheal axes. Next, tilt the head backward resulting in atlanto-occipital extension (contraindicated in suspected cervical spine injury). This brings the oral axis in alignment with the pharyngeal and tracheal axes. Adjust the height of the bed upward until the patient's head is at the level of the incubator's lower sternum. This aligns the visual axis.



A	B	C
Oral (O) Pharyngeal (P) Tracheal (T) Axes	Elevate Head Flex Neck at the junction with the Thorax	Extend Head at the junction with the Neck

LANDMARK IDENTIFICATION

Visualization of anatomic landmarks is essential for successful endotracheal tube passage. Visualization can be improved by selection of an appropriately size laryngoscope blade and optimizing patient and intubator positioning. In pediatric patients who have a more cephalad and anterior airway visualization can be improved by the BURP maneuver of the thyroid cartilage (Backward, Upward, Rightward, Pressure).



AIRWAY ANATOMY

INTUBATION PROCEDURE: OVERVIEW	
1	Position the patient at optimal height
2	Position the airway aligning the oral, pharyngeal and tracheal axes
3	Control the tongue with the laryngoscope
4	Control the epiglottis with the laryngoscope
5	Identify airway anatomic landmarks
6	Pass the endotracheal tube through the vocal cords
7	Confirm correct endotracheal tube location
8	Secure the endotracheal tube

INTUBATION TECHNIQUE (DIRECT LARYNGOSCOPY)	
1	Align the oral, pharyngeal and tracheal axes. Infants should be in sniffing position (a roll under shoulders will provide neutral position and account for the large occiput).
2	Insert the laryngoscope blade from the right side of the mouth with a sweeping motion to move the tongue towards the midline and allow for direct visualization of the vocal cords and provide a channel for passage of the ETT. Avoid levering of the laryngoscope to present trauma to the upper gums or teeth
3	Once vocal cords are visualized, insert the ETT from the right side of the mouth (not through the barrel of the blade) until you see the tip and then the vocal cord mark or cuff pass through the vocal cords – an assistant may provide cricoid pressure to move the glottis into view for infants and to pull the right corner of the mouth down to facilitate passage of the ETT
4	Remove laryngoscope, then stylet, inflate the cuff and attempt ventilation
5	Confirm appropriate placement of the ETT:
	a. Water vapor in the ETT during exhalation
	b. Equal breath sounds over both lung fields in the axillae
	c. No audible breath sounds over upper abdomen (stomach)
	d. Symmetric bilateral chest wall rise
	e. Colorimetric change in End-tidal CO_2 detector – purple (no CO_2) to yellow CO2 may be absent in cardiopulmonary arrest despite correct ETT location
	f. Sustained improvement in O_2 saturation
	g. Chest radiograph
6	Secure ETT with a tape or a commercially available device.
7	Placement of appropriate size oral airway to avoid biting the ETT
See PEM Guide: Airway Procedures: Difficult Airway for alternative techniques	

VIDEO LINK: PEDIATRIC INTUBATION

See: PEM Guide: Airway Procedures: Mechanical Ventilation
PEM Guide: Airway Procedures: Post-intubation Sedation and Paralysis

COMPLICATIONS

Sudden deterioration in the intubated patient can occur from a variety of causes. The mnemonic DOPE aids in considering possible etiologies.

COMPLICATIONS IN THE INTUBATED PATIENT		
D	Dislodgment	Mainstem bronchus or esophagus
O	Obstruction	Secretions, blood, foreign body, vomitus, kinking of ETT
P	Pneumothorax	Decreased or absent breath sounds over the affected lung fields
E	Equipment	Failure of ventilator, power supply, oxygen supply, etc

ASSESSMENT FOR POST INTUBATION COMPLICATIONS
Disconnect from the ventilator and manually ventilate
Evaluate the following parameters
1. Observe chest rise: Present?, Symmetrical?
2. Observe tracheal location: Midline?, Deviated?
3. Auscultate over both axilla and over the stomach: Present?, Absent?
4. Attach $ETCO_2$ detector: Color change?
5. Observe tube for kinks, suction tube: Tube patent?
6. Observe tube location via direct laryngoscopy: Pass through cords?

IDENTIFICATION AND MANAGEMENT OF POST INTUBATION COMPLICATIONS	
DISLODGMENT: RIGHT MAIN-STEM BRONCHUS	Decreased breath sounds on left and good breath sounds on right without signs of tension pneumothorax
	Pull tube back in 0.5 cm increments until breath sounds are equal
DISLODGMENT: ESOPHAGEAL	No chest rise, no breath sounds, no $ETC0_2$ detected or tube seen in esophagus on direct laryngoscopy
	Remove tube. Provide bag valve mass ventilations. Prepare to re-intubate
OBSTRUCTION	If no air is entering tube observe for kinks
	Straighten kinks. Suction tube
PNEUMOTHORAX (TENSION)	One side of chest is hyper-resonant with decreased breath sounds and trachea is deviated to the contralateral side
	Perform needle thoracentesis, Place Chest tube
EQUIPMENT FAILURE	Ventilator disconnected. Can provide effective Bag-Valve-Mask ventilation
	Identify and correct ventilator problem

MECHANICAL VENTILATION

INTRODUCTION (MICHAEL MOJICA, M.D. 7/2015)
This PEM Guide reviews mechanical ventilation (positive pressure ventilation) in the intubated patient (endotracheal tube or laryngeal mask airway) and emphasizes the initial settings in the emergency department. (See also PEM Guide: Noninvasive Ventilation for a discussion of ventilation in the non-intubated patient). There is no one best method of mechanical ventilation and the approach needs to be individualized to the patient and clinical situation.

INDICATIONS
Respiratory failure (hypoxia and hypoventilation) due to:
1. Increased lower airway resistance/obstruction: Asthma
2. Decreased airway compliance: Pneumonia, ARDS
3. Disordered control of breathing; Sedation, drug overdose, head trauma
4. Upper airway obstruction: Anaphylaxis, croup, smoke inhalation
Airway protection: Altered mental status, head trauma
Decrease work of breathing, decrease oxygen utilization: Sepsis
Hyperventilation for actual/impending herniation: Increased intracranial pressure
Delivery of endotracheal medications if alternatives routes are unavailable

COMPLICATIONS
Barotrauma e.g. pneumothorax
Ventilator induced lung injury
Ventilator associated pneumonia
Decreased cardiac output: ↑ intrathoracic pressure → ↓ Right heart venous return

PROCEDURE GOALS
1. Airway protection
2. Oxygenation
3. Ventilation: Maintain normal PCO_2 and pH
4. Avoid barotrauma: Ventilator associated lung injury, pneumothorax

VENTILATOR MODES
Ventilator modes are defined by:
1. How the ventilator initiates a breath,
2. How the breath is delivered,
3. When the breath is terminated.
With volume control methods the breath is terminated based on the set tidal volume and the peak inspiratory pressure is variable. Pressure control methods are typically used in infants less than 10 kg and have a lower potential for lung injury. With pressure control methods the breath is terminated based on the set peak inspiratory pressure and the tidal volume is variable. Common ventilator modes are discussed below. There are a number of alternative modes that can be used in specific circumstances with the aim of mitigating complications of ventilation.

COMMON VENTILATOR MODES	
CMV	Controlled Mechanical Ventilation
AC	Assist Controlled Ventilation
SIMV	Synchronized Intermittent Mandatory Ventilation
PS	Pressure Support Ventilation

CONTROLLED MECHANICAL VENTILATION (CMV): CMV delivers only ventilator breaths. It is used in the sedated and paralyzed patient without spontaneous breathing.

ASSIST CONTROL VENTILATION (AC): In AC ventilation breaths can be triggered by the ventilator or the patient. If the patient does not breath for a period of time based on the set respiratory rate the ventilator delivers a breath based on the set tidal volume (control). If the patient does breathe, the ventilator delivers a full tidal volume breath (assist). The advantages of AC ventilation are that it lowers the work of breathing, every breath is supported and minute ventilation is assured. The disadvantage is the potential for breath stacking (with resulting barotrauma) and hyperventilation.

SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION (SIMV): SIMV is similar to AC ventilation in that breaths can be triggered by the ventilator or the patient. It delivers a mandatory minimum number of ventilator breaths per minute synchronized to the patient's effort. It differs from AC ventilation in that the patient breaths are not assisted. The tidal volume is determined by the patient's efforts and lung mechanics. This allows the patient to exercise respiratory muscles but may increase the work of breathing, increase oxygen utilization and lead to respiratory muscle fatigue.

PRESSURE SUPPORT VENTILATION (PSV): PSV is used to facilitate spontaneous breathing. When used alone it does not provide any ventilator breaths. Instead, all patient breaths are partially assisted during inspiration decreasing their work of breathing. PSV may be used for weaning a patient from the ventilator. PSV can also be added to SIMV to provide inspiratory assistance to the patient's breaths.

	CMV	AC	SIMV	PS	SIMV+PS
Ventilator Breath	Full Tidal Volume	Full Tidal Volume	Full Tidal Volume	None	Full Tidal Volume
Patient Breath	None	Full Assist	No Assist	Partial Assist	Partial Assist
CMV, AC, SIMV and SIMV+PS are the same if patient is not spontaneously breathing AC, SIMV and PS differ in the amount of assistance provided for patient breaths					

VENTILATOR SETTINGS

To determine appropriate ventilators settings, it is essential to understand how the ventilator defines and manages the respiratory cycle.

VENTILATOR CYCLE
Inspiration initiation trigger
Air flow
Inspiration termination trigger
Expiration that is typically passive

Initiation triggers can be patient effort or ventilator initiated based on time (respiratory rate). Termination triggers are based on set tidal volume (Volume Controlled) or peak inspiratory pressure (Pressure Controlled). Ventilator settings will differ based on the underlying pathophysiology. For example, those with acute lung injury benefit from a lower tidal volume. Settings provided in the table below and in the appendix are those generally applicable to patients with normal lung function. Patients with abnormal lung function (e.g. lower airway obstruction due to asthma) and patients hyperventilating to compensate for severe metabolic acidosis (e.g. diabetic ketoacidosis) are discussed separately. Initial ventilator settings are just the beginning of the process and adjustments will be required. (See Appendix: Ventilator Settings).

VENTILATOR SETTINGS: NORMAL LUNGS			
	INFANT	CHILD	ADOLESCENT/ADULT
Control Method	Pressure	Volume	Volume
RR (BPM)	30	20	12
TV (ml)	8-10	8-10	8-10
PIP (cm H_2O)	20	20	20
PEEP (cm H_2O)	4-5	4-5	4-5
PS (cm H_2O)	5-10	5-10	5-10

DIFFICULT VENTILATION: HYPERPNEA WITH NORMAL LUNGS

Patient with tachypnea compensating for a metabolic acidosis (e.g. diabetic ketoacidosis, salicylate ingestion, organic acidurias) require ventilation at a greater than normal minute ventilation. This is achieved with a higher respiratory rate. Ventilating these patients at a normal minute ventilation will result in a worsening acidosis and could precipitate cardiopulmonary arrest.

DIFFICULT VENTILATION: ABNORMAL LUNGS

1. INCREASED AIRWAY RESISTANCE

Causes of increased airway resistance include bronchospasm, mucosal edema, mucous plugging and intraluminal debris (e.g. asthma) and extrinsic compression (e.g. pleural effusion, hemothorax)
In the intubated asthma patient, the respiratory rate should be slow enough and the expiratory time long enough to allow for complete passive exhalation. Otherwise, air will be trapped in the alveoli at the end of expiration (auto-peep). The next ventilated breath will add to the existing air and result in barotrauma. The patient's respiratory rate and length of expiration prior to intubation can be used as a guide to initial respiratory rate and inspiratory to expiratory ratio. Alternative ventilator modes include pressure regulated volume control (PRVC) which combines the advantages of both pressure controlled and volume controlled ventilation while limiting the disadvantages of each.

ASTHMA VENTILATIONS GOALS
Reverse hypoxemia (increase O_2 delivery)
Relieve respiratory muscle fatigue (decrease O_2 utilization)
Maintain minute ventilation at acceptable $PC0_2$ (permissive hypercapnia) and pH
Avoid ventilator induced barotrauma: pneumothorax, pneumomediastinum

VENTILATOR SETTING: STATUS ASTHMATICUS	
NIPPV with BiPAP	Inspiratory PAP: Start 8-10 cm H_2O, Typical 8-16 cm H_2O Expiratory PAP: Start 2-4 cm H_2O, Typical 4-8 cm H_2O
Endotracheal Intubation	Mode: SIMV, (CMV if paralyzed) FiO_2: Titrate to O_2 saturation ≥ 94% RR: 8-10 breaths/minute (RR is adjusted to ensure complete exhalation) TV: 5-7 ml/kg Peak inspiratory pressure (PIP) < 40 cm H_2O Inspiratory time I:E ratio > 1:2 or Inspiratory Time 1 – 1.5 sec PEEP: controversial, 0 in paralyzed patient,

2. DECREASED AIRWAY COMPLIANCE

Causes of decreased airway compliance include pneumonia, pulmonary edema, submersion injury, pulmonary contusion and acute respiratory distress syndrome (ARDS). High frequency oscillatory ventilation (HFOV) and high frequency jet ventilation (HFJV) delivers very low tidal volumes at very high respiratory rates. Both inspiration and expiration are active. These modes provide for better oxygenation than ventilation and can decrease the risk of lung injury.

APPENDIX: ACUTE DETERIORATION IN THE VENTILATED PATIENT

Agitation in the intubated patient should not be considered due to inadequate sedation until other more serious causes are considered. This include complications outlined by the mnemonic D*O*P*E (Displaced, Obstructed, Pneumothorax and Equipment) as well as ventilator/patient asynchrony due to inappropriate ventilator settings.

COMPLICATIONS IN THE INTUBATED PATIENT		
D	Dislodgment	Mainstem bronchus or esophagus
O	Obstruction	Secretions, blood, foreign body, vomitus, kinking of ETT
P	Pneumothorax	Decreased/Absent breath sounds over the affected lung fields
E	Equipment	Failure of ventilator, power supply, oxygen supply, etc.

ASSESSMENT FOR POST INTUBATION COMPLICATIONS
Disconnect from the ventilator and manually ventilate
Evaluate the following parameters
1. Observe chest rise: Present?, Symmetrical?
2. Observe tracheal location: Midline?, Deviated to what side?
3. Auscultate over both axilla and over the stomach: Present? , Absent?
4. Attach $ETCO_2$ detector: Color change?
5. Observe tube for kinks, suction tube: Tube patent?
6. Observe tube location via direct laryngoscopy: Pass through cords?

IDENTIFICATION AND MANAGEMENT OF POST INTUBATION COMPLICATIONS	
Dislodgment: Right main-stem bronchus	Decreased breath sounds on left and good breath sounds on right without signs of tension pneumothorax
	Pull tube back in 0.5 cm increments until breath sounds are equal
Dislodgment: Esophageal	No chest rise, no breath sounds, no $ETC0_2$ detected or tube seen in esophagus on direct laryngoscopy
	Remove tube. Provide bag valve mass ventilations. Prepare to re-intubate
Obstruction	If no air is entering tube observe for kinks
	Straighten kinks. Suction tube
Pneumothorax (Tension)	One side of chest is hyper-resonant with decreased breath sounds and trachea is deviated to the contralateral side
	Perform needle thoracentesis, Place Chest tube
Equipment Failure	Ventilator disconnected. Can provide effective Bag-Valve-Mask ventilation
	Identify and correct ventilator problem

APPENDIX: INITIAL VENTILATOR SETTINGS

VENTILATOR SETTINGS	
Control Method	Pressure Control: Set the peak inspiratory pressure (PIP) Delivers a variable tidal volume necessary to achieve set PIP Tidal volume depends on I time, lung compliance, airway resistance Minute ventilation is not assured Allows for effective tidal volume at lower PIP (lung protective) Typically used in children < 1 year of age (< 10 kg)
	Volume Control: Set the tidal volume (TV) Delivers a variable PIP to achieve the set tidal volume Higher PIP and risk of lung injury than with pressure control ventilation
Modes	CMV (Controlled Mechanical Ventilation): no spontaneous breaths
	AC (Assist Control): assists full set TV patient spontaneous breaths
	SIMV (Synchronized Intermittent Mechanical Ventilation) Allows unassisted spontaneous breaths between ventilator breaths Can be used with or without pressure support (PS)
	PS (Pressure Support Ventilation). No ventilator-initiated breaths. Inspiratory assistance for patient breaths Used independently in the spontaneously breathing patient or with SIMV
MV	Minute Ventilation (ml/min) = Tidal Volume x Respiratory Rate Set TV and RR to maintain normal PCO_2 and pH
TV	Tidal volume: Typically, 8-10 ml/kg (lower if significant lung disease) A high tidal volume decrease preload and increases risk of barotrauma
RR	Respiratory Rate: Inversely related to age Neonates, 40 bpm, Infant: 30 bpm Child: 20 bpm, Adolescent/Adult: 12 bpm Higher in patients compensating for metabolic acidosis (e.g. DKA)
PIP	Peak inspiratory pressure = PEEP + Pressure above PEEP (ΔP) Normal lungs 18-22 cm, Moderate disease 23-27 cm, Severe 28-35 cm
PEEP	Positive end expiratory pressure: mitigates alveolar collapse Typically, 5 cm H_2O Higher in atelectasis, abdominal distention, severe lung injury High peep can decrease preload and increase barotrauma risk
PS	Pressure Support: Assists inspiration in a spontaneously breathing patient. Used alone in PS mode or with SIMV Start 10 cc H_2O
I:E Ratio	I:E Ratio typically 1:2 or 1:3 I:E Longer in patients with lower airway obstruction (e.g. asthma) Inspiratory/Expiratory ratio (I/E ratio) = IT/ET Cycle time = Inspiratory Time (IT) + Expiratory Time (ET) e.g. a RR of 10 bpm corresponds to a cycle time 6 seconds At a 1:E ratio of 1:2 inspiration will be 2 seconds and expiration 4 seconds
FiO_2	Fraction of Inspired Oxygen (%) Start high and titrate down to achieve O_2 saturation of ≥ 94%

NONINVASIVE VENTILATION

INTRODUCTION (MICHAEL MOJICA M.D., 11/2022)
Noninvasive positive pressure ventilation (NPPV or NIPPV) is defined as the delivery of pressurized, oxygen enriched gas to the airway via the nose and/or oropharynx without an invasive device such as an endotracheal intubation, a tracheostomy or a laryngeal mask airway. Pressure can be delivery continuously or at varying levels (e.g. different inspiratory and expiratory pressures).

Noninvasive ventilation can avoid or reduce the complications of endotracheal intubation such as airway trauma (vocal cord dysfunction and subglottic stenosis), barotrauma (pneumothorax) and infectious complications such as ventilator-associated pneumonia. It does not require paralysis and can obviate the need for sedation.

Meta-analysis of randomized clinical trials in adults with acute respiratory failure due to cardiogenic pulmonary edema and COPD have demonstrated a decreased need for endotracheal intubation; decrease length of stay and improved mortality. Large, well-controlled trials in pediatric causes of acute respiratory failure in the emergency department setting are lacking. There have been limited pediatric studies demonstrating a benefit in acute respiratory failure due to pneumonia, bronchiolitis, asthma and acute chest syndrome in patients with sickle cell disease.

PHYSIOLOGY
An increase in mean airway pressure recruits atelectatic alveoli improving alveolar gas exchange (increasing oxygen delivery) and decrease the work of breathing (reducing oxygen utilization). In addition, increased airway pressure can help maintain airway patency with lower airway obstruction. High oxygen flow rate contribute to nitrogen and CO_2 washout and provide an oxygen reservoir.

PATIENT SELECTION
Patients are selected based on: the cause of respiratory distress/failure, the likelihood of the reversibility of the cause, their mental status and their ability to tolerate/cooperate with specific non-invasive ventilation devices. Contraindications are included in the patient selection algorithm (See Appendix).

Mental status, vomiting, heart rate, blood pressure, oxygen saturation and end tidal CO_2 should be monitored closely. An upright position should be maintained if possible. This limits atelectasis from a supine position, allows for a jaw thrust position to limit occlusion of the hypopharynx and prevents passive regurgitation.

Evidence of improvement may include a decreasing respiratory rate and work of breathing, increase in oxygen saturation, decrease in end tidal CO_2 and increased lung volumes on chest XRAY or aeration on examination. Patients without improvement or a worsening progression of illness may require invasive ventilation such as endotracheal intubation or a laryngeal mask airway.

EQUIPMENT: Noninvasive ventilation can be delivered through specific devices or with traditional ventilators. Traditional ventilators have the benefit of finer control of oxygen delivery; better identification of air leaks and separates circuits for inspiration and expiration, which limit CO_2 rebreathing.

INTERFACES: A variety of interfaces are available. Nasal masks are better tolerated, are less claustrophobic and allow the patient to speak, expectorate and vomit. The primary problem with nasal prongs and masks is that opening of the mouth open the circuit and reduces the pressure administered. Some nasal masks include chinstraps to prevent air leaks through the mouth. A pacifier may be used in infants and young toddlers to keep the mouth closed. Face masks, full face masks and hoods or helmets prevent interruption of the closed circuit and therefore have greater efficacy at delivering the desired pressure. However, they must be removed to speak, expectorate or vomit. In addition, they may induce claustrophobia and may require sedation due to increased anxiety and poor compliance.

NONINVASIVE VENTILATION INTERFACES
Nasal prongs
Nasal masks
Face masks: Covering the mouth and nose
Full face masks: Covering mouth, nose and eyes
Hoods or helmet devices: Covering the entire head

SETTINGS: There is little data to guide initial settings, the rate of escalation or weaning. There is also limited data to determine when to move from one form of invasive ventilation to another. Frequent re-assessment and setting alteration is required to achieve the desired effect.

MODES OF NONINVASIVE VENTILATION: We will review the three modes of noninvasive ventilation in the order of increasing ventilatory support. They differ in terms of interfaces available and whether they provide continuous or varying pressures.

HHFNC	Humidified High Flow Nasal Cannula
CPAP	Continuous Positive Airway Pressure
BPAP	Bi-level Positive Airway Pressure

MODE SUMMARY				
	PATIENT	FLOW	INTERFACE	AEROSOL
HHFNC	Infant	Continuous	Nasal prongs	No*
CPAP	Infant	Continuous	Nasal prongs, Nasal/Face mask	No*
BPAP	OlderChild	Bi-Level	Nasal/Face mask	Yes
*Can be delivered by separate face mask				

HFNC: HUMIDIFIED HIGH FLOW NASAL CANNULA

Warm (35-37 C) and humidified nasal oxygen is better-tolerated than normal wall oxygen. The positive end expiratory pressure generated high flow rates can open the soft palate by separating it from the posterior pharyngeal wall. It also provides an oxygen reservoir in the nasopharynx and promotes CO2 washout. HFNC is considered less invasive than CPAP, easier to set up and better tolerated. However CPAP has a valve that prevents reverse flow of oxygen and water and more consistently provides a stable pressure.

The primary problem with the nasal prongs and masks used for HFNC is that opening of the mouth open the circuit and reduces the pressure administered. Some nasal masks include chinstraps to prevent air leaks through the mouth. A pacifier may be used in infants and young toddlers to keep the mouth closed. In general, those comfortable on low for rates can be fed orally as long as feeding does not result in an increase in the degree of respiratory distress though this approach is controversial.

An Australian randomized clinical trial including 200 children younger than 2 years of age with moderate bronchiolitis admitted to the hospital found no difference in the primary outcome of time to weaning off oxygen between the High-Flow Warm Humidified Oxygen (HFWHO) group (20 hours) and Low Flow (≤ 2 liters/minute) group (24 hours) (Kepreotes, Lancet. 2017, PubMed ID: 28161016). The authors considered a 12-hour difference to be clinically significant. However, there was a statistically significant difference in the proportion who remained free from treatment failure within 24 hours of admission (HFWHO: 90%, Standard Therapy: 60%, 95% CI (50, 70%). Hazard Ratio 0.3, 95% CI (0.2, 0.6). In addition, 20 of the 32 patients who deteriorated on standard therapy and then trialed on HFWHO were successfully rescued and did not require transfer to the ICU or more invasive therapy.

A multicenter (17 regional and tertiary care hospital in New Zealand and Australia), randomized clinical trial including 1,472 infants younger than 1 year of age admitted for bronchiolitis requiring supplemental oxygen treatment failure occurred 12% in the HFNC group an 23% in the standard therapy group (Risk difference: 11%, 95% CI (7, 15%). The authors considered a 5% reduction to be clinically significant in their power analysis. 100% of the escalations in care that occurred in the standard therapy group were started on HFNC and 61% responded (Franklin, NEJM 2018, PubMed ID: 29562151).

HHFNC SETTINGS
Infants: Start at 1-2 liters/kg/min
Increase as needed and tolerated
Older children and Adults: Up to 40 liters/min

CPAP: CONTINUOUS POSITIVE AIRWAY PRESSURE

CPAP delivers a constant level of pressure support (inspiratory and expiratory) without regard to the respiratory cycle. It may be delivered through a variety of interfaces. A full face-mask is typically used in older children and adults. Short bi-nasal prongs are preferred in neonates and infants due to the difficulty of maintaining an adequate face-mask fit and seal. In general, CPAP is utilized initially in those with more significant respiratory distress or in those failing high flow nasal cannula.

A multicenter clinical trial in English Pediatric ICUs randomized 600 patients patients requiring non-invasive ventilation to high flow nasal cannula (HFNC) with flow rates determined by weight or continuous positive airway pressure (CPAP)(Ramnarayan, JAMA, 2022, PubMed ID: 35997738). The median time to liberation from respiratory support in the HFNC group was 52.9 hours, 95% CI (46.0, 60.9 hours) compared to 47.9 hours, 95% CI (40.5, 55.7 hours) in the CPAP group. The adjusted hazard ratio for time to liberation from support for HFNC compared to CPAP was 1.03 with a 1-sided 97.5% CI of 0.86 to infinity. This met the pre-specified definition of non-inferiority of a hazard ratio of 0.75 in both the intention to treat and per protocol analyses. A hazard ratio of 0.75 corresponds to a maximally clinically acceptable difference in median time of 16 hours of additional respiratory support. In the subgroup analyses, HFNC was also non-inferior to CPAP in time to liberation from respiratory support in the subgroup of patients with bronchiolitis (Figure 2, Hazard Ratio: 0.96, 95% CI (0.76, 1.23)).

In the intention to treat analysis of the secondary outcomes, there was a statistically significant longer length of PICU stay in the CPAP group (Adjusted Mean Difference: -3.0 days, 95% CI (0.86, 1.22 days) and a higher rate of sedative use in the CPAP group (Risk Difference: -9.3% (-17.1, -1.5%). The number of patients with at least one adverse event was statistically higher in the CPAP group (Risk Difference: 5.5%, 95% CI (0.4, 10.8%)). The most common adverse event was nasal trauma (CPAP 6.5%, HFNC 2.0%).

CPAP SETTINGS
Pressure is usually started at 5 cm H_20 Increased by 1 cm H_20 as needed and tolerated Typical levels are 5-10 cm H_20 with a maximum of 15 cm H_20

BPAP/BiPAP/BIPAP: BILEVEL POSITIVE AIRWAY PRESSURE

(The terms BiPAP or BIPAP are often used interchangeably but refer to specific commercial products) BPAP provides two levels of positive airway pressure: inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). IPAP mechanically assists the patient's inspiratory efforts. It increases tidal volume and increases CO_2 elimination. IPAP can be triggered by the patient's inspiration (S mode: Spontaneous) or at a back up rate if the patient does not breath (S/T mode: Spontaneous and Timed). EPAP serves a function similar to PEEP. It recruits alveoli and improves oxygenation Supplemental oxygen and aerosols may be delivered with BPAP.

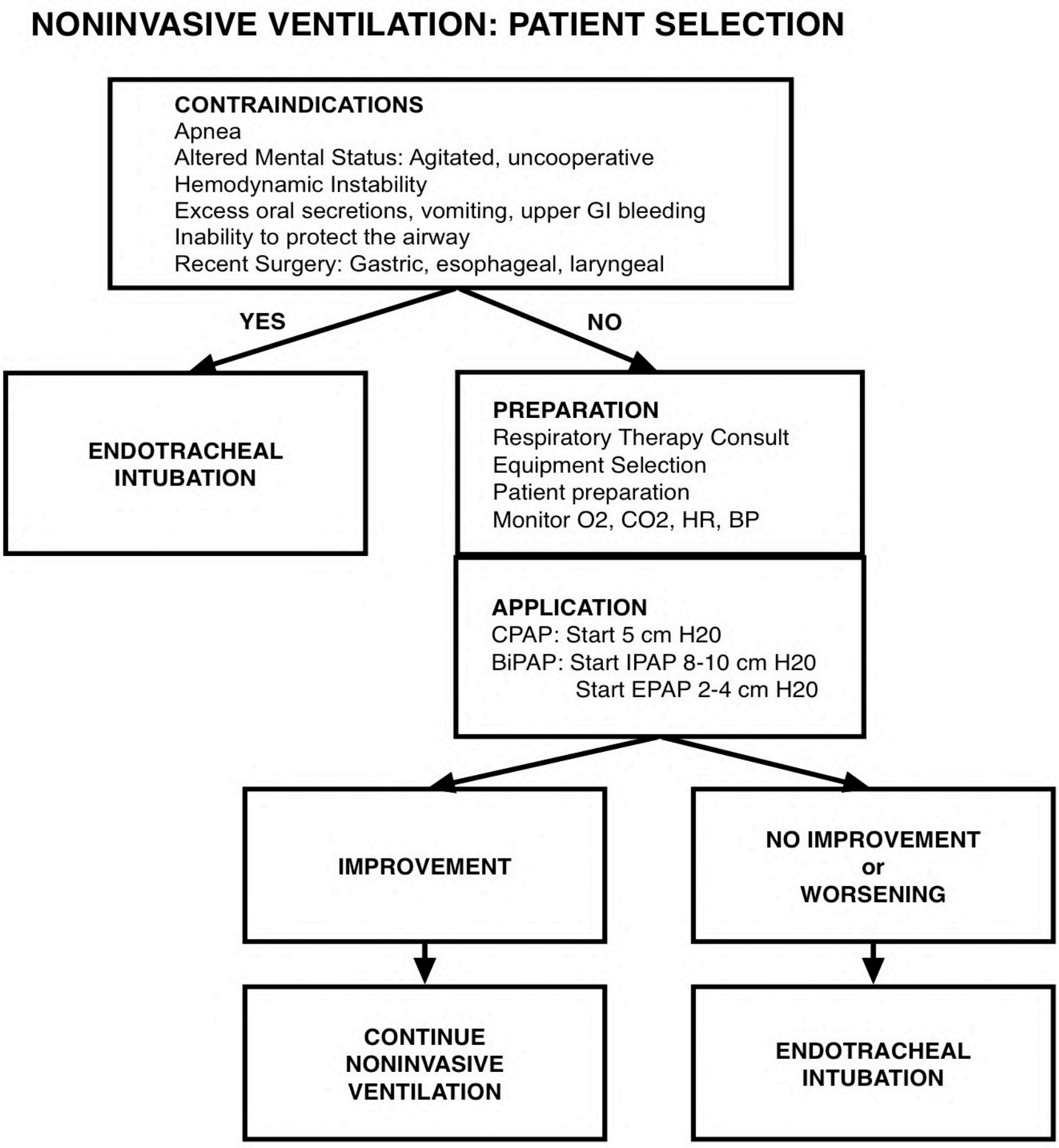
BPAP is most effective when there is patient-device synchrony. This requires an alert and cooperative patient. Adequate coaching and a gradual increase in pressure may decrease anxiety and increase cooperation.

A proper mask fitting is essential as air leaks reduce effectiveness. There is a balance between reducing air leaks and reducing excess pressure on the face that can cause anxiety and skin breakdown. A nasal mask induces less anxiety and claustrophobia and the patient can speak but air can escape form an opened mouth. A face-mask is preferred in the critically ill patient.

Sedation with a low dose of a benzodiazepine may be required. Low dose Ketamine (0.5 mg/kg bolus) followed by a continuous infusion of 0.25 mg/kg/hour will provide sedation and bronchodilation in the patient with asthma.

BPAP SETTINGS
Start IPAP at 8-10cm H_2O. Increase as needed to decrease work of breathing. 10-16 cm of H_20 is sufficient in most cases but levels as high as 20-25cm H_20 may be required. Pressure > 25 cm H_20 cause gastric dissension
Start EPAP at 2-4 cm H_20 Increase to 5-10 cm H_20 as needed
Pressure support (PS) is the difference between IPAP and EPAP (PS = IPAP – EPAP). IPAP should exceed EPAP by > 2 cm H_20 to ensure flow

APPENDIX: NONINVASIVE VENTILATION: PATIENT SELECTION



POST-INTUBATION SEDATION AND PARALYSIS

INTRODUCTION: (MICHAEL MOJICA, MD, 8/2021)
Patients requiring endotracheal intubation in the emergency department will likely require post-intubation sedation and sometimes post-intubation paralysis as part of their ongoing care. This PEM Guide focuses on ED management and assumes that correct endotracheal intubation has been confirmed and that appropriate mechanical ventilation has been initiated. See: PEM Guides: Airway Procedures: Rapid Sequence Intubation, Endotracheal Intubation, Difficult Airway, Mechanical Ventilation.

SEDATION

Sedative selection is situation-dependent. For example, a sedative with anticonvulsant properties may be preferred in the patient with status epilepticus such as a benzodiazepine or propofol. A patient with bronchospasm may benefit from the bronchodilator properties of Ketamine. A patient requiring frequent neurologic assessments will benefit from a short acting sedative.

Selection of a post-intubation sedative will often parallel sedative selection for rapid sequence intubation. It is also helpful to select a sedative in accordance with pediatric ICU preferences and policies. The lack of high-quality, comparative evidence leads to significant variability in clinical practice. Recommendations are based primarily on observational data and consensus expert opinion. Sedative dosing must be individualized, and titration will be required to maintain the patient at the targeted level of sedation without either under- or over-sedation. A sedation scale, such as the Richmond Agitation Sedation Scale (RASS)(See Appendix), should be used to monitor sedation depth.

CLINICAL EFFECTS OF SEDATIVES AND ANALGESICS				
	Analgesia	Sedation	Amnesia	Anxiolysis
Dexmedetomidine (Precedex)	X	X		X
Fentanyl (Sublimaze)	X	X		
Midazolam (Versed)		X	X	X
Ketamine (Ketalar)	X	X	X	
Propofol (Diprivan)		X	X	

POST-INTUBATION SEDATIVE SELECTION	
1st Line	NYU/Bellevue: Dexmedetomidine (Precedex) AND Fentanyl (Sublimaze)
	A bolus dose of an opioid (Fentanyl) or benzodiazepine (Midazolam or Lorazepam) is often required as a bridge until Dexmedetomidine takes effect. Dexmedetomidine should not be bolused due to concern for hemodynamic compromise
Asthma	Ketamine
Shock	?Ketamine: Potential hypotension if catecholamine depleted
Status Epilepticus	Antiepileptics: Midazolam, Propofol
Head Trauma	Propofol: Short half-life allows frequent neurologic assessment

SEDATION AND ANALGESIA: MECHANICALLY VENTILATED PATIENT				
		< 40 kg AND < 18 years	40 kg OR 18 years	Comments
Dexmed-etomidine[a] (Precedex)	Bolus1	No bolus!	No bolus!	Do not bolus! Intermittent hypotension bradycardia,
	Infusion	0.5 mcg/kg/hour	0.2-0.5 mcg/kg/hour	
	Bolus2	No bolus!	No bolus!	
	Titrate Infusion	↑↓ 0.2-0.3 mcg/kg/hour Q30 min	↑↓ 0.1-0.2 mcg/kg/hour Q30 min	
	Max	2 mcg/kg/hour	1.5 mcg/kg/hour	
Fentanyl[b] (Sublimaze)	Bolus1	0.5-1.0 mcg/kg	50-100 mcg	Preferred 1st Line opioid. Little hemodynamic compromise.
	Infusion	0.5-1.0 mcg/kg/hour	25-50 mcg//hour	
	Bolus2	Same as hourly	25-100 mcg	
	Titrate Infusion	↑↓ 0.2-0.3 mcg/kg/hour Q30 min	↑↓ 25-50 mcg//hour Q30 min	
	Max	5 mcg/kg/hour	300 mcg/hour	
Ketamine[a,c] (Ketalar)	Bolus1	1.0-1.5 mg/kg	1.0-1.5 mg/kg	Bronchodilator Adverse events: HTN, HR, sialorrhea, Potential BP if catecholamine depleted
	Infusion	0.3-0.5 mg/kg/hour	0.5 mg/kg/hour	
	Bolus2	Same as hourly rate	Same as hourly rate	
	Titrate Infusion	↑↓ 0.2-0.3 mg/kg/hour Q60 min	↑↓ 0.1-0.2 mg/kg/hour Q60 min	
	Max	2 mg/kg/hour	2 mg/kg/hour	
Midazolam (Versed)	Bolus1	0.1 mg/kg	2-4 mg	Prolonged use renal/hepatic dysfunction. Less hypotension than Dexmedetomidine and Propofol
	Infusion	0.05 mg/kg/hour	1 mg/hour	
	Bolus2	Same as hourly rate	Same as hourly rate	
	Titrate Infusion	↑↓ 0.03-0.05 mg/kg/hour Q30 min	↑↓ 1-2 mg 1-2 mg/hour Q30 min	
	Max	0.2 mg/kg/hour	12 mg/hour	
Propofol[a] (Diprivan)	Bolus1	0.5-1.0 mg/kg	0.5-1.0 mg/kg	No analgesia Monitor for Propofol infusion syndrome with prolonged use
	Infusion	50 mcg/kg/min	10-20 mcg/kg/min	
	Bolus2	0.5-1.0 mg/kg	10-20 mg	
	Titrate Infusion	↑↓ 25 mcg/kg/min Q5 min	↑↓ 5-10 mcg/kg/min Q5 min	
	Max	200 mcg/kg/min	75 mcg/kg/min	

Bolus1: Given as a bolus as the infusion is being prepared and before it is started
Bolus2: Given after infusion started as needed for under-sedation
"Same as hourly infusion rate": If infusion rate is 0.2 mg/kg/hour then 2nd bolus = 0.2 mg/kg
Titrate: Up for under-sedated, Down for over-sedated based on target RASS score

a. WEB LINK: MDCALC: Ideal Body Weight (Use ideal BW unless actual BW < Ideal BW)
b. Other opioids are not included as tolerance is unlikely to develop in the ED timeframe
c. Potential hypotension: (-) Inotropy > (+) Sympathomimetic activity if catecholamine depleted

NEUROMUSCULAR BLOCKADE

Neuromuscular blockade can be a useful adjunct to sedation and analgesia. It is essential to ensure adequate sedation (e.g., RASS score -3 to -5) prior to initiation of neuromuscular blockade, as the adequacy of sedation cannot be assessed after neuromuscular block has been initiated. The degree of neuromuscular blockade should be monitored with clinical assessments and train-of-four or tetanic peripheral nerve stimulation. Due to concerns for long term consequences, (e.g. polyneuromyopathy) prolonged use of neuromuscular blockade has decreased. Neuromuscular blockade should be discontinued as quickly as possible to avoid long-term consequences.

BENEFITS OF NEUROMUSCULAR BLOCKADE
Reduced oxygen consumption in shock and respiratory failure
Facilitate ventilation in patients with high peak airway pressures (ARDS)
Reduce the risk of barotrauma (Asthma) and ventilator-induced lung injury
Reduce the risk of extubation
Reduce patient-ventilator asynchrony
Avoid spikes in blood pressure in patients with increased intracranial pressure
Treat therapeutic hypothermia-induced shivering

NEUROMUSCULAR BLOCKADE: MECHANICALLY VENTILATED PATIENT				
		< 40 kg AND < 18 years	40 kg OR 18 years	Comments
Rocuronium[a] (Zemurion or Esmuron)	Bolus1	0.6-1.2 mg/kg	0.6-1.2 mg/kg	↑ Duration in hepatic insufficiency
	Infusion	0.5 mg/kg/hour	0.5 mg/kg/hour	
	Bolus2	0.6-1.2 mg/kg	0.6-1.2 mg/kg	
	Titrate Infusion	↑↓ 0.25 mg/kg/hour Q30 minutes	↑↓ 0.25 mg/kg/hour Q30 minutes	
	Max	1 mg/kg/hour	1 mg/kg/hour	
Vecuronium[a] (Norcuron)	Bolus1	0.1 mg/kg	0.1 mg/kg	↑ Duration in renal insufficiency
	Infusion	0.05 mg/kg/hour	0.05 mg/kg/hour	
	Bolus2	0.05-0.1 mg/kg	0.05-0.1 mg/kg	
	Titrate Infusion	↑↓ 0.5 mg/kg/hour Q30 minutes	↑↓ 0.5 mg/kg/hour Q30 minutes	
	Max	0.15 mg/kg/hour	0.15 mg/kg/hour	
Cisatracurium[a] (Nimbex)	Bolus1	0.1-0.2 mg/kg	0.1-0.2 mg/kg	Clearance is independent of renal and hepatic function
	Infusion	0.06 mg/kg/hour	0.06 mg/kg/hour	
	Bolus2	0.1-0.2 mg/kg	0.1-0.2 mg/kg	
	Titrate Infusion	↑↓ 0.03 mg/kg/hour Q30-60 minutes	↑↓ 0.03 mg/kg/hour Q30-60 minutes	
	Max	0.6 mg/kg/hour	0.6 mg/kg/hour	
Bolus1: Given as infusion is being prepared and before it is started Bolus2: Given after infusion started as needed for under-paralyzed Titrate: Up for under-paralyzed, Down for over-paralyzed				
a. Use ideal BW unless actual BW < Ideal BW (WEB LINK: MDCALC: IDEAL BODY WEIGHT).				

APPENDIX: RICHMOND SEDATION SCORE

RICHMOND AGITATION SEDATION SCALE (RASS)		
4	Combative	Overtly combative, violent, immediate danger to staff
3	Very Agitated	Pulls or remove tubes or catheters; aggressive
2	Agitated	Frequent non-purposeful movements, fights ventilator
1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and Calm	Alert and Calm
-1	Drowsy	Sustained awakening (≥ 10 seconds) to voice
-2	Light Sedation	Briefly awakes (< 10 seconds) with eye contact to voice
-3	Moderate Sedation	Movement or eye opening to voice but no eye contact
-4	Deep Sedation	No response to voice but movement or eye opening to physical stimulation
-5	Cannot be Aroused	No response to voice or physical stimulation
WEB LINK: MDCALC: RASS SCALE		

SEDATION DEPTH		
	RASS	Non-procedural sedative doses required
Under-Sedation	> Target RASS Goal	> 3 in 6 hours
Ideal Sedation	= Target RASS Goal	1-3 in 6 hours
Over-Sedation	< Target RASS Goal	0 in 24 hours

RAPID SEQUENCE INTUBATION

INTRODUCTION (MICHAEL MOJICA M.D., 4/2018)
Rapid sequence intubation (RSI) is defined as the use of a sedative and a paralytic to facilitate endotracheal intubation through muscle relaxation and improved airway visualization. RSI also reduces the potential side effects of intubation.

PROCEDURE OVERVIEW (7 P'S)	
1. Preparation	1A: Patient Selection: Directed history and physical (AMPLE)
	1B: Equipment selection and preparation
	Medication selection and preparation
2. Pre-oxygenation	High flow oxygen via nasal cannula and face mask if spontaneously breathing, Bag-Valve-Mask ventilation if not
3. Pretreatment	Premedication and sedative delivery
4. Paralysis	Depolarizing or Non-depolarizing muscle relaxant
5. Positioning	"Sniffing" position (if no c-spine injury concerns)
6. Placement with proof	Endotracheal intubation
	Confirmation of Endotracheal tube placement
7. Post intubation	Maintenance ventilation, sedation, paralysis

1A. PREPARATION: PATIENT SELECTION

A directed history and physical examination should be performed. The aim is to answer the following questions:

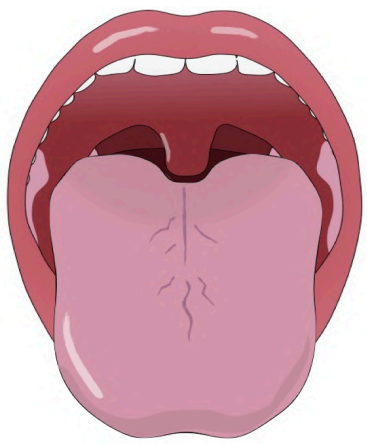
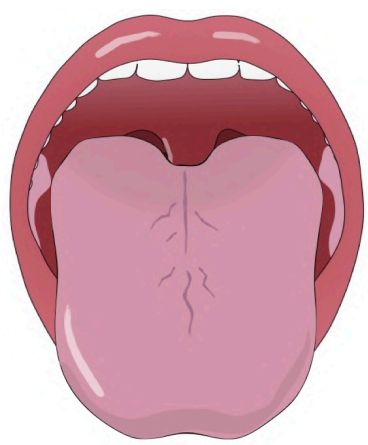
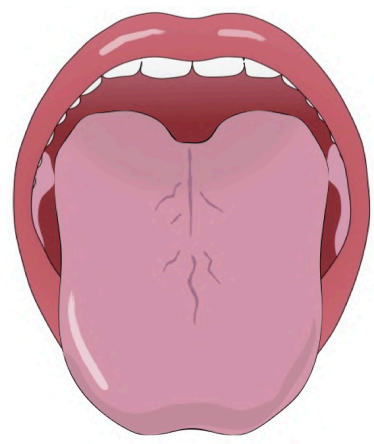
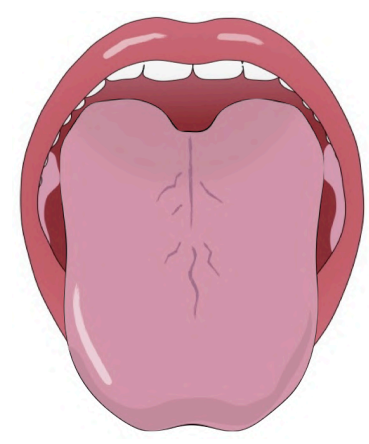
- Is there an indication for intubation?
- Is there an indication for rapid sequence intubation?
- Are there any contraindications?
  - Is this patient going to be difficult to ventilate?
  - Is this patient going to be difficult to intubate?
- What are my difficult airway options?

DIRECTED HISTORY: AMPLE	
Allergies	Egg and/or soy allergy may preclude Propofol use
Medications	Medications metabolized by the cytochrome P450 enzyme pathway, (e.g. anticonvulsants and psychotropic medications) May interfere with pharmacokinetics of some sedatives
Past Medical History	Relevant hospitalizations Prior sedation or anesthesia-related adverse events Patient/family history of anesthesia complications
Last meal	Timing, contents (liquids, solids)
Existing Medical Status	Conditions predisposing to airway obstruction, pulmonary compromise Pregnancy status Vital signs

AMERICAN SOCIETY OF ANESTHESIOLOGISTS (ASA) CLASSIFICATION	
I	A normal, healthy patient
II	Mild systemic disease (no functional limitation)
III	Moderate or severe systemic disease that limits activity but is not incapacitating
IV	An incapacitating systemic disease that is a constant threat to life
V	A moribund patient, not expected to survive 24 hours with/without the procedure

PHYSICAL EXAMINATION: The focus of the head and neck exam is to determine the likelihood of a difficult ventilation or intubation. This includes the oral cavity (fracture, instability, obstruction, foreign body) and neck (mass, swelling, trauma, limited mobility). Abnormalities in vital signs such as hypotension may limit medication selection.

The Mallampati classification is used to predict the ease of intubation. A high Mallampati Score (3 or above) is associated with a more difficult intubation. The score is determined with patient sitting up with their jaw thrust forward, tongue protruded and without phonation. The score is of limited use, as it can't be obtained in the two most common indications for emergency intubation: head trauma and status epilepticus.

MALLAMPATI SCORE			
			
1	2	3	4
Anterior Pillars Posterior Pillars Fauces Uvula Soft Palate	Posterior Pillars Fauces Uvula Soft Palate	Uvula (Base only) Soft Palate	

INDICATIONS
Head trauma: Suspected increased intracranial pressure
Aspiration risk: Full stomach, pregnant, altered mental status
Suspected cervical spine injury
Respiratory failure
Inadequate muscle relaxation: Awake, seizures
An agitated, combative patient requiring further evaluation (e.g. CT) or treatment

CONTRAINDICATIONS
RSI should not be used in patients that have difficult airway access, as the patients will be paralyzed and unable to ventilate themselves if intubation is unsuccessful.
Known allergy to any of the intended agents (pre-medications, sedatives, paralytics)
In patients that are unconscious and have no muscle tone, RSI may not be necessary, particularly in the situation of cardiopulmonary arrest.

HIGH RISK PATIENTS		
↓ Lung compliance	Barotrauma: Pneumothorax/mediastinum	Asthma
Metabolic acidosis	Worsening acidosis Cardiopulmonary arrest	DKA, Salicylate
Shock	Cardiopulmonary arrest	Hypotension

1B. PREPARATION: EQUIPMENT SELECTION

EQUIPMENT: “SOAPME” MNEMONIC		
S	Suction	A variety of types should be available including a tonsillar tip and different sized tracheal suction catheters
O	Oxygen	Pre-oxygenating the patient with 100% O_2 will increase the amount of time available for the clinician to intubate the patient before hypoxemia develops (i.e. Safe Apnea)
A	Airway	Age appropriate equipment of such as; laryngoscope handles and blades, endotracheal tubes, stylets, oral airways, and ventilation bags should be readily available. Rescue equipment should be available: Laryngeal mask airways, video laryngoscopes, cricothyrotomy equipment, bougie.
P	Pharmacology	The common medications used in RSI will be discussed below. Ideally, medications should be drawn up and ready to use. A weight based dosing system should be available to reduce the potential for errors and speed administration
ME	Monitoring Equipment	A cardiac monitor and pulse oximeter are mandatory when performing RSI. Frequent blood pressure checks should also be performed. Once the tube is in place, secondary confirmation with a capnometer (qualitative or quantitative) for end tidal CO_2 measurement should be obtained.

2. PRE-OXYGENATION

Pre-oxygenation with 100% $Fi0_2$ will result in 95% nitrogen washout within 2 min. (operating room data). This provides on oxygen reserve of 3-4 minutes of apnea without hypoxia. This is marginally effective in the patient who is ill prior to intubation. It also precludes the need for bag-valve-mask ventilation.

Warm (35-37 C) and humidified high flow nasal oxygen (HHFNC) is better tolerated than non-humidified oxygen. It can open the soft palate separating it from the posterior pharyngeal wall and provide an oxygen reservoir in the nasopharynx. When used in conjunction with a non-rebreather face-mask (both a 15 liters/min in adults) it can increase the fraction of inspired oxygen (FiO_2) to 100%.

NASAL CANULA OXYGEN	
INFANTS	Start at 2-4 liters/minute, increase to 8 liters/minute.
ADULTS	Start at 15 liters/minute increase to 40 liters/minute.

3. PRETREATMENT: PREMEDICATION AND SEDATIVE SELECTION

The purpose of pretreatment is to avoid physiologic responses to intubation and the potential adverse effects of sedatives and paralytics. This may include the use of targeted predications such as Lidocaine or Atropine.

Patients who are in shock and in particular those who are hypotensive are at risk of cardiopulmonary arrest with positive pressure ventilation. Increased intrathoracic pressure decreases preload and subsequently decreases cardiac output. If possible, intubation should be deferred until after fluid resuscitation or initiation of vasoactive infusions as indicated based on the type of shock.

3A. PREMEDICATIONS

LIDOCAINE	
Class	Local airway anesthetic
Benefits	Blunts cough reflex, blunts increases in HR, BP May blunt increase in intracranial pressure
Indications	Head trauma
Dose	1.5 - 3.0 mg/kg, 3 minutes prior to paralytic if possible
Comment	Used traditionally in head trauma though effect on intracranial pressure in conjunction with other neuro-protective medications such as Etomidate is unclear.

ATROPINE	
Class	Anticholinergic
Benefits	Decreases airway secretions Mitigates bradycardia
Adverse Effects	Tachycardia
Indications	< 1 year 1-5 years if receiving Succinylcholine
Dose	0.01-0.02 mg/kg IV
Comment	Atropine is no longer recommended as a routine premedication in children (AHA 2015). It may be considered if there is a high risk of bradycardia (e.g. Succinylcholine use)). A minimum dose of 0.1 mg is also no longer recommended.

3B: SEDATIVE SELECTION

SEDATIVE SELECTION			
SEDATIVE	HEAD TRAUMA	CARDIOVASCULAR DEPRESSION	MISCELLANEOUS
Etomidate	YES	YES	NO: Septic shock
Ketamine	YES	YES	YES: Asthma
Propofol	YES	NO	YES: Seizure

KETAMINE	
Class	Phencyclidine derivative, dissociative agent
Pharmacology	Onset: 1-2 minutes Duration: 10-30 minutes
Benefits	Rapid onset, amnestic, analgesic Sympathomimetic activity, bronchodilation
Adverse Effects	Laryngospasm (reversed with a paralytic) Increased airway secretions (Pre-medicate with Atropine) Increased ICP but overall effect may be neuro-protective Exacerbates psychosis
Indications	Status asthmaticus Mild hypovolemic shock
Contraindications	Catecholamine depletion: The unopposed direct negative inotropic effects of ketamine may lead to cardio-vascular compromise in patients with shock
Dose	1-2 mg/kg IV
Comment	Previously thought to increase intra-ocular and intracranial pressure but recently found evidence to the contrary

PROPOFOL	
Class	Sedative-hypnotic
Pharmacology	Onset: 30-60 seconds Duration: 10-15 minutes
Benefits	Titratable, decreases ICP
Adverse Effects	Cardiovascular depression resulting in hypotension Apnea (not an issue in RSI), Medical acidosis in children with prolonged use
Indications	Precise controlled sedation
Contraindications	Hypotension (optimize volume status prior) < 6 months of age associated with a high rate of complications Egg/Soy allergies are no longer considered a contraindication)
Dose	<u>Adults</u> Initial dose: 0.5-1.0 mg/kg Subsequent doses: 0.25-0.5 mg/kg Q1-3 minutes to effect Infusion: 100-150 µg/kg/minute (0.1-0.15 mg/kg/min) <u>Children</u> Initial dose: 1.5–2.0 mg/kg Subsequent doses: 0.5-1.0 mg/kg Q1-3 minutes to effect Infusion: 250 µg/kg/minute (0.25 mg/kg/min)
Class	Sedative-hypnotic

ETOMIDATE	
Class	Imidazole sedative hypnotic
Pharmacology	Onset: 1 minute Duration: 3-12 minutes
Benefits	Cardiovascular stability, decreases ICP
Adverse Effects	Transient cortisol depression, myoclonic activity
Indications	Head trauma
Contraindications	Adrenal insufficiency, chronic steroid use PALS recommends to avoid use in septic shock
Dose	0.3-0.4 mg/kg
Comment	Reduces cortisol production but clinical significance with a single dose for rapid sequence intubation is unclear

4. PARALYSIS

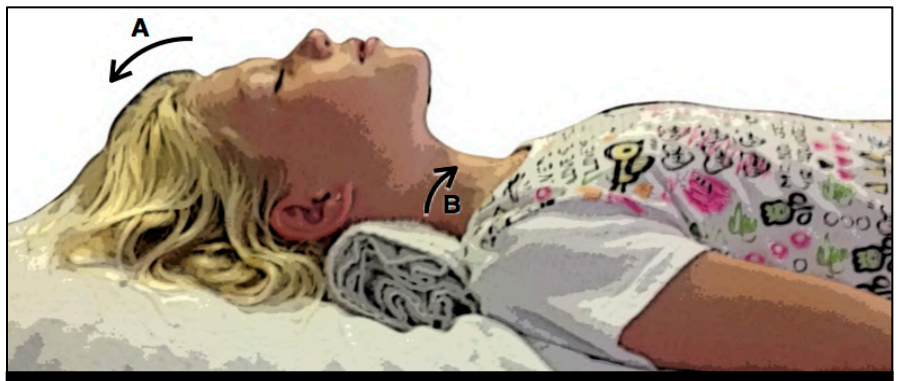
There are two very commonly used paralytic drugs: Succinylcholine, a depolarizing muscle relaxant, and Rocuronium, a non-depolarizing agent. Vecuronium (0.1 – 0.2 mg/kg) may be substituted for Rocuronium at some institutions.

SUCCINYLCHOLINE	
Class	Depolarizing muscle relaxant
Pharmacology	Onset: 30-60 seconds Duration: 10-15 minutes
Benefits	Short onset and duration
Adverse Effects	Nicotinic Effects: Muscle fasciculations (minimal < 5 years) May increase ICP, IOP, hyperkalemia Muscarinic effects: Increases secretions, bradycardia, cardiovascular depression, dysrhythmias Malignant hypothermia (1:15:000), Rx Dantrolene
Contraindications	Cholinesterase deficiency, muscular dystrophy Family history malignant hyperthermia Hyperkalemia, late crush injuries, burns (not initial presentation) Relative contraindications: Increased ICP, IOP
Dose	Infant: 2.0 mg/kg Child/Adult: 1.0 mg/kg

ROCURONIUM	
Class	Non-depolarizing muscle relaxant
Pharmacology	Onset: 40-60 seconds Duration 60-90 minutes
Benefits	Short onset and duration
Dose	0.6-1.0 mg/kg IV

5. POSITIONING

The sniffing position allows for optimal visualization of the glottic opening. It is achieved by elevating the patient's head and extending the head at the atlanto-occipital joint. Positioning of the neck should not be used in patients at risk for cervical spine injury.



AIRWAY POSITIONING

6. PLACEMENT WITH PROOF

Endotracheal intubation (See: PEM Guide: Airway Procedures: Endotracheal Intubation)

CRICOID PRESSURE (SELLICK MANEUVER): Evidence shows that cricoid pressure does not occlude the esophagus (90% slip to side) and may worsen airway visualization. It is no longer routinely recommended by American Heart Association. However, it may improve visualization of the anterior pediatric airway.

CONFIRMATION OF ENDOTRACHEAL TUBE PLACEMENT
Direct visualization of tube passing through cords
Auscultation of both lung fields and over stomach
End-tidal CO_2 monitor: Colorimetric or continuous
Chest XRAY

7. POST INTUBATION

Post intubation care includes the provision of maintenance ventilation (See: PEM Guide: Procedures: Mechanical Ventilation) and both maintenance sedation and paralysis ((See: PEM Guide: Airway Procedures: Post-intubation Sedation and Paralysis). Repeat boluses of the initial sedative and paralytic may be administered but the patient will eventually require continuous infusions of sedatives and possibly paralytics.

RESCUE AIRWAY PROCEDURES: If attempts at bag valve mask ventilation and endotracheal intubation fail, additional techniques could be utilized to provide a definitive airway. These techniques include the supraglottic airways such as the laryngeal mask airway, fiberoptic intubation, the use of video laryngoscopy or intubation with a bougie (See: PEM Guide: Airway Procedures: Difficult Airway). If unsuccessful, cricothyroidotomy may be required (See: PEM Guide: Airway Procedures: Cricothyrotomy). Equipment and personnel trained in these techniques should be readily available if rapid sequence intubation is to be attempted.

CARDIOLOGY

1. Arrhythmias: An Overview	Michael Mojica, MD
2. Cardiac Pacing for Bradycardia	Michael Mojica, MD
3. Cardiogenic Shock	Michael Mojica, MD
4. Cyanotic Congenital Heart Disease	Kelly Cleary, MD
5. Ductal Dependent Cardiac Lesions	Michael Mojica, MD
6. EKG Interpretation	Michael Mojica, MD
7. Heart Transplant	Ellen Duncan MD, PhD, Arin Teymouri, MD Rebecca Rogoff, NP, Rakesh Singh, MD
8. Hypertensive Emergencies	Nicole Gerber, MD
9. Myocarditis	Luv Makadia, MD
10. Pericardiocentesis	Eric Weinberg, MD
11. Pericarditis	Thomas Kennedy, MD
12. Supraventricular Tachycardia	Rachel Kowalsky, MD, MPH
13. Tetralogy of Fallot Spells	Adriana Manikian, MD
14. Ventricular Arrhythmias	Rachel Kowalsky, MD, MPH

ARRHYTHMIAS: AN OVERVIEW

INTRODUCTION (MICHAEL MOJICA, M.D., 10/2020)
The term “arrhythmia” technically refers to an absence of heart rate or rhythm. Asystole is the only true “arrhythmia”. Arrhythmia is often used in place of the term “dysrhythmia” which indicates an abnormality of the heart rate or rhythm. Arrhythmias can be classified in a number of ways. They can be classified by their location of origin (atrial, ventricular), their effect on the circulatory system (cardiopulmonary compromise or stable) and by their rate (bradycardia, tachycardia). The American Heart Association classifies rhythms as bradycardias, tachycardias and cardiac arrest rhythms.

Tachyarrhythmias limit the time for ventricular filling and decreased stroke volume and cardiac output. (Cardiac Output = Heart Rate x Stroke Volume). Children have higher heart rates and limited ability to increase contractility and stroke volume. Bradycardia can significantly decrease cardiac output in child. Ventricular fibrillation represents disordered electrical activity that does not result in effective stroke volume.

COMMON ARRHYTHMIAS		
	PEDIATRIC	ADULT
CARDIAC ARREST	Sinus Bradycardia Asystole	Ventricular Fibrillation Ventricular Tachycardia
BRADYCARDIA	Sinus Bradycardia	Heart Blocks
TACHYCARDIA	Supraventricular Tachycardia	Atrial Fibrillation

CLINICAL ASSESSMENT
Older children, adolescents and adults can present with altered mental status, shortness of breath, syncope, seizure, chest pain or palpitations. Infants cannot verbalize symptoms and may present late in their course of illness with non-specific symptoms such as: poor feeding, sweating when feeding, cyanosis/pallor, respiratory distress (pulmonary edema), irritability and vomiting. The diagnosis of an arrhythmia in the young infant or child not presenting in arrest requires a high index of suspicion.

In clinically evaluating any arrhythmia, it is helpful to start with the following questions:
1. Is a pulse present or absent?
2. Is there cardiopulmonary compromise? (hypotension, shock, altered mental status)

A complete assessment of both central and peripheral circulation should take place with emphasis on signs that represent congestive heart failure such as: rales on lung auscultation, hepatomegaly and jugular venous distention (rare in young children)

HYPOTENSION	
AGE	SYSTOLIC BP (mm/Hg)
0-28 days	< 60
1month – 1 year	< 70
1 – 10 years	< 70 + 2 x (age in years)
> 10 years	< 90

HEART RATE			
AGE	AWAKE	MEAN	SLEEPING
< 3 months	85-205	140	80-160
3mo – 2 years	100-190	130	75-160
2 -10 years	60-140	80	60-90
> 10 years	60-100	75	50-90

ASSESSMENT OF CIRCULATORY STATUS	
Central Circulation	Mental Status
	Blood Pressure
	Central Pulse Rate and Quality
	Signs of CHF – Rales, Hepatomegaly
Peripheral Circulation	Skin Color
	Skin Temperature
	Peripheral Pulse Rate and Quality
	Capillary Refill

EKG INTERPRETATION

A full 12 lead EKG should be obtained when a rhythm strip on a monitor or a patient's clinical condition is suggestive of an arrhythmia. The EKG needs to be interpreted in conjunction with the patient's condition. For example, a narrow complex at 70 BPM can be normal sinus rhythm in an adult, sinus bradycardia in an infant and pulse electrical activity in a pulseless patient. (See PEM Guide: Cardiology: EKG Interpretation)

EKG INTERPRETATION: RHYTHM ANALYSIS	
Rate: ventricular and atrial	
Pattern: regular, regularly irregular, irregularly irregular	
QRS width: narrow, wide, QTc	
P wave: morphology, axis, PR interval	
P:QRS Ratio	
	P = QRS, normal PR interval = Sinus
	P = QRS, prolonged PR = 1st degree block
	P > QRS = 2nd/3rd blocks, atrial fibrillation, atrial flutter
	P < QRS = Ventricular ectopy

MANAGEMENT

The effect of the arrhythmia on the circulatory system will dictate the urgency of treatment and therapeutic options. Precipitating factors should be identified and treated appropriately. Cardioversion can be achieved with either electrical or pharmacologic approaches. High quality chest compressions are a priority for those in cardiac arrest.

ARRHYTHMIA MANAGEMENT OVERVIEW		
CLASS	TYPE	TREATMENT OPTIONS
TACHY CARDIA	Sinus tachycardia	Treat underlying cause
		Fever, pain, anxiety, hypoxia, shock
	Supraventricular tachycardia	Vagal Maneuvers
		Adenosine
		Synchronized cardioversion
		Amiodarone
		Overdrive pacing
	Ventricular tachycardia with pulse	Adenosine (regular & monomorphic)
		Amiodarone *or* Procainamide
		Synchronized cardioversion
BRADY CARDIA	Sinus bradycardia	O2, ventilation
		Chest compression for HR < 60
		Epinephrine (respiratory etiology)
		Atropine (cardiac etiology)
		Pacing
ARREST	Asystole and PEA	Compressions, O_2, Ventilation
		Epinephrine
		Underlying causes: H’s & T’s
	Ventricular fibrillation or Ventricular tachycardia without pulse	Compressions, O_2, Ventilation
		Defibrillation
		Epinephrine
		Amiodarone
		Lidocaine
		Magnesium (for Torsades)

CARDIAC ARREST: ASYSTOLE, PULSELESS ELECTRICAL ACTIVITY (PEA)

PEDIATRIC CARDIAC ARREST ALGORITHM: ASYSTOLE, PEA
Basic Life Support: High quality CPR, O_2, attach monitor
Epinephrine within 5 minutes of CPR and then every 3-5 minutes until ROSC Intravenous/Intraosseous: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/ml Epinephrine, Adult 1 mg Endotracheal: 0.1 mg/kg = 0.1 ml/kg of 1.0 mg/kg Epinephrine, Adult 2.5 mg
Vasopressin is no longer recommended in adults (2015)
Consider and treat underlying causes (H's and T's)

CARDIAC ARREST: VFIB (VF), VTACH WITHOUT A PULSE (pVT)

PEDIATRIC CARDIAC ARREST ALGORITHM: VF, pVT	
Basic Life Support: High quality CPR, O_2, attach monitor and defibrillator	
Defibrillation: 2 Joules/kg → 4 J/kg → 4 J/kg (To maximum of 10 J/kg or adult dose) Use an initial dose of 2-4 J/kg, consider 2 J/kg for ease of teaching Adult: Biphasic (manufacturers suggested) or 120-200J, Monophasic at 360J)	
No stacked shocks: Single shock followed by compressions (start with compressions)	
Continue CPR: 2-minute cycles with ventilations, then pulse and rhythm assessment	
Medications: Give during chest compressions	
Epinephrine	Within 5 min of chest compressions, repeat Q3-5 minutes until ROSC IV/IO: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/kg Epinephrine, Adult 1.0mg ETT: 0.1 mg/kg = 0/1 ml/kg of 1.0 mg/ml Epinephrine, Adult 2.5 mg
Amiodarone OR Lidocaine is an acceptable antiarrhythmic agent for shock-refractory pediatric ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT)	
Lidocaine	1 mg/kg IV, repeat Q5-10min, If successful → 20-50 mcg/kg/min
Amiodarone	5 mg/kg IV/IO push. Repeat x 2 to total of 15 mg/kg Maximum single dose: Adult 1st dose = 300 mg, 2nd dose = 150 mg
Magnesium Sulfate	Indicated for Torsade de points (a type of polymorphic VT) 25-50 mg/kg, Maximum dose: 2 grams
See: PEM Guide: Cardiology: Ventricular Arrhythmias	

REVERSIBLE CAUSES (H'S AND T'S)	
Hypovolemia	Tension pneumothorax
Hypoxia	Tamponade, cardiac
Hydrogen ion (acidosis)	Toxins
Hypoglycemia	Thrombosis, pulmonary
Hypo/hyperkalemia	Thrombosis, cardiac
Hypothermia	Trauma

WEB LINK: PEDIATRIC CARDIAC ARREST ALGORITHM (AHA 2020)
WEB LINK: ADULT CARDIAC ARREST ALGORITHM (AHA 2020)

NARROW COMPLEX TACHYCARDIA WITH A PULSE

Evaluate the QRS duration. Narrow: ≤ 0.09 sec, Wide: > 0.09 sec. Narrow-complex tachycardias primarily include sinus tachycardia and supraventricular tachycardia. If sinus tachycardia is present, identify and intervene based on the underlying cause (shock, fever, pain etc.). Wide complex tachycardias with a pulse include ventricular tachycardia and supraventricular tachycardia with aberrant conduction. See: PEM Guide: Cardiology: Supraventricular Tachycardai

NARROW COMPLEX TACHYCARDIAS (QRS ≤ 0.09 SECONDS)		
	SINUS TACHYCARDIA	SUPRAVENTRICULAR TACHYCARDIA
History: Infants	Dehydration, hypovolemia, Fever, Pain, Stress Medications, Ingestions	Non-specific vague history Irritability, sleepiness Poor feeding, Decreased activity
History: Child	Fever, Pain, Stress Medications / Ingestions	Sudden onset, Palpitations Chest discomfort, Anxiety
Onset	Warm-up and cool-down	Abrupt onset, termination
P waves	Present/normal	Absent/abnormal
R-R (HR)	Variable	Not variable
Infants HR	< 220 beats/min	> 220 beats/min
Child HR	< 180 beats/min	>180 beats/min

NARROW COMPLEX (QRS ≤ 0.9 SEC): SUPRAVENTRICULAR TACHYCARDIA	
ALL PATIENTS	
Maintain airway, ventilation PRN, IV/IO access, 12 lead ECG, monitor/defibrillator Assess for cardiopulmonary Compromise: Altered mental status, shock, hypotension?	
CARDIOPULMONARY COMPROMISE: NO	
Vagal Maneuvers	Infants: ice to face without occluding airway Child: Unilateral carotid massage or Valsalva
IV Access Adenosine	Deliver centrally via a 3-way stopcock followed by rapid flush 0.1 mg/kg (max 6 mg), repeat as needed 0.2 mg/kg (max 12 mg)
Expert consultation	Cardiology consult prior to additional medications (see below) if vagal maneuvers and Adenosine unsuccessful and remains stable
CARDIOPULMONARY COMPROMISE: YES	
IV Access Adenosine	Do not delay cardioversion if IV access not readily available Deliver centrally via a 3-way stopcock followed by rapid flush 0.1 mg/kg (max 6 mg), repeat as needed 0.2 mg/kg (max 12 mg)
Synchronized Cardioversion	0.5 Joules/Kg ® 1.0 J/Kg ® 2 J/Kg (Adult: 50-100 Joules) Sedate if needed as does not delay cardioversion
Expert consultation	Cardiology consult prior to additional medications (see below) if vagal maneuver, Adenosine and cardioversion are unsuccessful
CONTINUED ON NEXT PAGE	

ADDITIONAL MEDICATIONS: Expert consultation advised prior to use	
Consider Amiodarone OR Procainamide (not both, both prolong QRS, QTc)	
Amiodarone	Child: 5 mg/kg IV/IO over 30-60 min. Repeat x 2 to a total of 15 mg/kg Adult: 1st dose = 300 mg, 2nd dose = 150 mg)
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes, monitor QRS duration Adult: 20 mg/min infusion to max dose of 17 mg/kg
Verapamil	Child: 0.1-0.3 mg/kg > 2 years (Not in < 2 years. May cause myocardial depression, BP and arrest) Adult: 1st dose 5 mg, 2nd dose 10 mg)
See: PEM Guide: Cardiology: Supraventricular Tachycardia	

WIDE COMPLEX TACHYCARDIA (QRS > 0.09 SECONDS) WITH A PULSE

WIDE COMPLEX TACHYCARDIA (QRS > 0.09 SECONDS) WITH A PULSE	
ALL PATIENTS	
Maintain airway, ventilation PRN, IV/IO access, 12 lead ECG, monitor/defibrillator Assess for cardiovascular compromise: Altered mental status, shock, hypotension? a. Ventricular Tachycardia with a pulse (VT) b. Wide-complex Supraventricular Tachycardia (SVT with aberrant conduction)	
CARDIOVASCULAR COMPROMISE: YES	
Synchronized Cardioversion: 0.5-1.0 Joules/Kg ® 2 Joules /Kg (Adult 100 Joules)	
CARDIOVASCULAR COMPROMISE: NO	
Expert consultation prior to antiarrhythmic No pediatric evidence for specific antiarrhythmic in wide complex tachycardia Antiarrhythmics complications may occur in cardiomyopathy, WPW, prolonged QT Do not give both Amiodarone and Procainamide. Both increase QRS, QTc	
Adenosine	Consider adenosine if rhythm is regular and monomorphic. Adenosine: 0.1 mg/kg (max 6 mg) then 0.2 mg/kg (max 12 mg) Distinguish between wide complex SVT and Ventricular Tachycardia
Amiodarone	Child: 5 mg/kg IV/IO over 30-60 minutes. Repeat x 2 to total 15 mg/kg Adult: 1st dose = 300 mg, 2nd dose = 150 mg
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes, monitor QRS width Adult: 20 mg/min infusion to max dose of 17 mg/kg
See: PEM Guide: Cardiology: Ventricular Arrhythmias	

WEB LINK: PEDIATRIC TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

BRADYCARDIA WITH A PULSE

Bradycardia is defined as a heart rate lower than the lower limit for age. It results from intrinsic dysfunction or injury or external effects to the conduction system. Infants and young children are particularly at risk from bradycardia as their cardiac output is driven to a greater degree by heart rate than contractility. As a result, they have little contractile reserve when compared to older children and adults. They present with nonspecific symptoms such a poor feeding or lethargy. In contrast, older children and adolescents may present with fatigue, syncope, dizziness or exercise intolerance.
See: PEM Guide: Cardiology: Cardiac Pacing for Bradycardia

PEDIATRIC BRADYCARDIA WITH A PULSE AND POOR PERFUSION
ALL PATIENTS
Assess for cardiopulmonary Compromise: Hypotension, altered mental status, shock?
CARDIOPULMONARY COMPROMISE: NO
Support ABC's, O_2, observe, 12-lead EKG, Identify and treat underlying causes
CARDIOPULMONARY COMPROMISE: YES
Maintain airway, O_2, ventilate PRN, cardiac monitor: rhythm, BP, O_2 saturation Identify and treat underlying causes
CHEST COMPRESSIONS: HR < 60, poor perfusion despite adequate O_2, ventilation Pulse check every 2 minutes. Move to cardiac arrest algorithm if becomes pulseless
EPINEPHRINE: Asphyxial, repeat Q3-5 minutes IV/IO: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/ml Epinephrine, Adult 1.0 mg Endotracheal: 0.1 mg/kg = 0.1 ml/kg of 1.0 mg/kg Epinephrine, Adult 2.5 mg
ATROPINE: Increased vagal tone or primary AV block. Repeat once. IV/IO: 0.02 mg/kg, ET: 0.04-0.6 mg/kg, Max dose 0.5 mg, Min dose 0.1 mg Minimum Atropine dose of 0.1 mg is still recommended for bradycardia
TRANS-THORACIC PACING: Indicated for complete heart block or sinus node dysfunction that is unresponsive to ventilation, oxygenation, chest compressions and medications. Not indicated for post arrest hypoxic/ischemic myocardial insult or respiratory failure. See also: PEM Guide: Procedures: Cardiac Pacing for Bradycardia

BRADYCARDIA: RHYTHM CLASSIFICATION	
Sinus	Normal PR interval, heart rate below normal for age (P=QRS)
Sinus arrest	Irregular or no P waves, junctional or ventricular escape rhythm
First degree	Prolonged PR interval follow by QRS complex (P=QRS)
Second degree	All p waves do not conduct to ventricles (P>QRS)
	Mobitz I (Wenckebach): Progressive increase in the PR interval, last p wave not conducted (may be physiologic if asymptomatic) Typically associated with AV node dysfunction
	Mobitz II: Non-conducting P wave without PR interval prolongation or progressive lengthening of PR interval. Pathologic until proven otherwise. Risk of progressing to third degree block. Typically associated with dysfunction distal to the His bundle
Third degree	Atrial and ventricular rate are independent (AV dissociation). Junction/ventricular escape rhythm slower intrinsic rate (P>QRS)

BRADYCARDIA: DIFFERENTIAL DIAGNOSIS	
Inflammation: Viral, autoimmune	Medications
Myocarditis*, Pericarditis*	HTN: Clonidine*, Beta blockers*
Lyme*, acute rheumatic fever*	Ca^{++} channel blockers*
Bacterial endocarditis, syphilis	Rhythm: Amiodarone, Digital, Adenosine
Myocardial infarct/ischemia	Other: Cholinergic agents*
Collagen vascular disease	Increased vagal tone
SLE*, neonatal SLE*, dermatomyositis	Breath holding*, cough
Congenital heart disease	Esophageal/Oral stimulation: intubation*
ASD, AV Canal*, VSD, TGV*, PS*	Increased intracranial pressure*
Congenital conduction abnormality	Cardiac surgery: Atrial
Prolonged QT, WPW	Electrolytes: Hyperkalemia*
Respiratory failure*: Hypoxia, acidosis	Hypothermia*
*Discussed in detail in a separate PEM Guide	

WEB LINK: PEDIATRIC BRADYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT BRADYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

APPENDIX: CARDIOVERSION AND DEFIBRILLATION

INTRODUCTION
Use of a defibrillator can be life-saving. However, a number of steps are required in order to use it both effectively and safely.
It is important to be familiar with whichever brand of defibrillator is available at sites that you will be working.
Think of the use of the defibrillator as hitting the electrical reset switch (as opposed to the pharmacologic reset switch). Essentially it stops whatever bad rhythm is currently happening with the hope that a normal rhythm will restart
No stacked shocks. Shock → CPR x 2 minutes → Shock → CPR x 2 minutes
Give medications during CPR (no pause): Epinephrine, Amiodarone, Lidocaine

PROCEDURE: DEFIBRILLATION/CARDIOVERSION	
Sedation	Consider sedation and analgesia in an awake, cardio-vascularly stable patient
Modes	SYNCHRONIZED CARDIOVERSION: SVT, VT with pulse, atrial fibrillation, atrial flutter
	DEFIBRILLATION: VF, pVT
	MONITOR: Including use of the paddles for a “quick look”
	PACEMAKER
	AED: Some defibrillators may be used as an AED as well
Energy level: Defibrillation	Child: 2 → 4 → 8 Joules/kg Adult: Biphasic: manufacturer recommendation or 120-200 Joules, Monophasic 360 Joules Biphasic at least as effective as monophasic and less harmful
Energy level: Synchronized Cardioversion	Child: 0.5 → 1.0 → 2.0 Joules/kg Adult: SVT: 50-100 Joules, ↑ PRN, VT with a pulse monomorphic: 100 Joules
Paddle/Pad Size	Pediatric paddles < 10 kg (must remove adults paddles first)
Interface material	“Electrode” gel, paste, pads. No ultrasound gel or alcohol pads
Paddle/Pad Location	The heart goes between the paddles/pads 1. Sternum and apex OR 2. Anterior and posterior
Safety	“I’m clear, you are clear, we are all clear” The airway person is usually last to leave.
Charge	If using paddles, it is safer to charge while paddles are on the patient’s chest to avoid discharging them by accident on the way to the patient. Use of pads avoids this concern.
Discharge	Discharge can be initiated from the defibrillator or the paddles. Discharge is immediate for defibrillation but may require a second to attain synchronization with cardioversion
Re-evaluate	Both the patient and the monitor

APPENDIX: PALS ANTIARRHYTHMIC MEDICATIONS (2020)

PALS MEDICATIONS (2020)			
	DOSE	INDICATIONS	COMMENT
Adenosine	0.1 mg/kg IV/IO (max 6mg) Repeat PRN 0.2mg/kg IV/IO(max 12mg)	SVT, Wide complex tachycardia with pulse monomorphic	Monitor EKG Rapid IV Push with 3-way stopcock
Amiodarone	5 mg/kg IV/IO Repeat x 2 to total of 15 mg/kg Max 1st dose: 300 mg Max 2nd dose: 150 mg	VF, pVT IV/IO: Push VT, SVT IV/IO: Over 20-60 minutes	Monitor QRS Don't give with Procainamide
Atropine	0.02 mg/kg IV/IO 0.04-0.06 mg/kg ET Repeat PRN x 1 Max 0.5 mg, Min 0.1 mg	Bradycardia related to heart block or increased vagal tone	May need higher doses with organophosphate poisoning
Calcium (10%) Chloride OR Calcium (10%) Gluconate	20 mg/kg IV/IO Ca^{++} Chloride: 0.2 ml/kg Ca^{++} Gluconate: 0.6 ml/kg Slow infusion	Hypocalcemia Hyperkalemia Hypermagnesemia Ca^{++} channel blocker overdose	Ca Chloride: Arrest +/- Central line: Ca Gluconate: Non-arrest +/ Peripheral
Epinephrine	0.01 mg/kg IV/IO 0.1 ml/kg of 0.1 mg/ml Max: 1 mg IV/IO 0.1 mg/kg ET 0.1 ml/kg of 1 mg/ml Max: 2.5 mg ET	Asystole Bradycardia Pulseless Electrical Activity Ventricular Fibrillation Ventricular Tachycardia without a pulse	IV/IO preferred May repeat every 3-5 minutes Do not give with HCO_3 in same line
Glucose	0.5-1.0 grams/kg IV/IO Newborn: D10 5-10 ml/kg Child: D25 2-4 ml/kg Adult: D50 1-2 ml/kg	Hypoglycemia	
Lidocaine	1 mg/kg IV 20-50 mcg/kg/min IV	VF, pVT	Repeat bolus Q5-10min
Magnesium Sulfate	20-50 mg/kg over 12-20 min IV/ IO. Max: 2 grams	Torsade de point Polymorphic VT	
Naloxone	< 20 kg: 0.1 mg/kg IV/IO > 20 kg: 2 mg IV/IO	Opiate overdose Clonidine toxicity	Incremental dosing if chronic user
Procainamide	Child: 15 mg/kg IV/IO Infuse over 20-60 minutes Adult: 20 mg/min infusion to max dose of 17 mg/kg	VT with pulse	Monitor QRS Don't give with Amiodarone
NaBicarbonate	1 meq/kg IV/IO slowly	Tricyclic overdose	
Verapamil	0.1-0.3 mg/kg Max 1st 5 mg, 2nd 10 mg	SVT	Not < 2yrs without Expert consultation

CARDIAC PACING FOR BRADYCARDIA

INTRODUCTION (MICHAEL MOJICA, M.D., 11/2020)
Transcutaneous cardiac pacing is a safe and rapid method when initiated with modern defibrillators that include a pacing function. This PEM Guide will focus on the use of emergency transcutaneous cardiac pacing for pediatric patients with bradycardia due to heart blocks or abnormal sinus node function.

Bradycardia is defined as a heart rate lower than the lower limit for age. It results from intrinsic dysfunction or injury or external effects on the conduction system. The parasympathetic nervous system (e.g. vagus nerve) decreases the pacing rate of the sinoatrial (SA) node and atrioventricular (AV) node conduction. The sympathetic nervous system increases the SA node pacing rate.

Infants and young children are particularly at risk from bradycardia as cardiac output is driven to a greater degree by heart rate than contractility. They have little contractile reserve when compared to older children and adults. They present with nonspecific symptoms such a poor feeding or lethargy. In contrast, older children and adolescents may present with fatigue, syncope, dizziness or exercise intolerance.

Transcutaneous cardiac pacing is indicated when bradycardia results in poor perfusion or shock and interventions specified in the American Heart Association Pediatric Bradycardia Algorithm are unsuccessful. These interventions include: oxygenation, ventilation, chest compressions for a heart rate of less the 60 beats per minute, Epinephrine and Atropine. (See Appendix B). Other therapeutic options may also exist in specific circumstances. (See: PEM Guide: Toxicology: Antihypertensive Toxicity, PEM Guide: Toxicology: Cholinergics).

BRADYCARDIA: DIFFERENTIAL DIAGNOSIS	
ATRIOVENTRICULAR NODE DYSFUNCTION	SINOATRIAL NODE DYSFUNCTION
Inflammation: Viral, autoimmune	Respiratory failure*: Hypoxia, acidosis
Myocarditis*, Pericarditis*	Increased vagal tone
Lyme*, acute rheumatic fever*	Breath holding*, cough
Bacterial endocarditis, syphilis	Esophageal/Oral stimulation: Intubation*
Myocardial infarct/ischemia	Increased intracranial pressure*
Collagen vascular disease	Hypothermia*
SLE*, neonatal SLE*, dermatomyositis	Electrolytes: ↑↓ K+*, ↓ Mg++, ↑↓ Ca++, ↓ glucose
Congenital heart disease	Post-Op: Arterial switch for TGA
ASD, AV Canal*, VSD, TGV*, PS*	MEDICATIONS
Congenital conduction abnormality	AntiHTN*: Clonidine, Beta/Ca++ chanel blockers
Prolonged QT*, WPW*	AntiRhythm: Amiodarone, Digoxin, Adenosine
Post-op: MV/AV repair/replacement, VSD repair	Other: Cholinergics (Organophosphates)*, Opioids*
AV canal repair	
*Discussed in detail in a separate PEM Guide	

DIAGNOSIS

BRADYCARDIA: RHYTHM CLASSIFICATION	
Sinus bradycardia	Normal PR interval* follow by QRS complex (P=QRS), ↓ heart rate for age
Sinus arrest	Irregular or no P waves, junctional or ventricular escape rhythm
First degree heart block	Prolonged PR interval* follow by QRS complex (P=QRS)
Second degree heart block	All p waves do not conduct to ventricles (P>QRS)
	Mobitz I (Wenckebach): Progressive increase in the PR interval*, the last p wave is not conducted. (may be physiologic if asymptomatic) Typically associated with AV node dysfunction
	Mobitz II: Non-conducting P wave without PR interval prolongation or progressive lengthening of PR interval* (pathologic until proven otherwise, risk of progressing to third degree block) Typically associated with dysfunction distal to the HIS bundle
Third degree heart block	Atrial and ventricular rate are independent (AV dissociation), junction or ventricular escape rhythm have slower intrinsic rate than the atria (P>QRS)
*The PR interval must be adjusted for age and heart rate (see table below)	

NORMAL PEDIATRIC HEART RATES			
AGE	AWAKE	MEAN	SLEEPING
< 3 months	85-205	140	80-160
3 months – 2 years	100-190	130	75-160
2 -10 years	60-140	80	60-90
> 10 years	60-100	75	50-90

PR INTERVAL BY AGE AND HEART RATE: MEAN (UPPER LIMIT OF NORMAL)								
	0-1mo	1-6mo	6mo-1yr	1-3yr	3-8yr	8-12yr	12-16yr	Adult
> 60						0.16 (0.18)	0.16 (0.19)	0.17 (0.21)
60-80					0.15 (0.17)	0.15 (0.17)	0.15 (0.18)	0.16 (0.21)
80-120	0.10 (0.12)				0.14 (0.16)	0.15 (0.16)	0.15 (0.17)	0.15 (0.20)
100-120	0.10 (0.12)			(0.15)	0.13 (0.16)	0.14 (0.15)	0.15 (0.16)	0.15 (0.19)
120-140	0.10 (0.11)	0.11 (0.14)	0.11 (0.14)	0.12 (0.14)	0.13 (0.15)	0.14 (0.15)		0.15 (0.18)
140-160	0.09 (0.11)	0.10 (0.13)	0.11 (0.13)	0.11 (0.14)	0.12 (0.14)			(0.17)
160-180	0.10 (0.11)	0.10 (0.12)	0.10 (0.12)	0.10 (0.12)				
> 180	0.09	0.09 (0.11)	0.10 (0.11)					

MANAGEMENT

PEDIATRIC BRADYCARDIA WITH A PULSE AND POOR PERFUSION
ALL PATIENTS
Assess for cardiopulmonary Compromise: Hypotension, altered mental status, shock?
CARDIOPULMONARY COMPROMISE: NO
Support ABC's, O_2, observe, 12-lead EKG, Identify and treat underlying causes
CARDIOPULMONARY COMPROMISE: YES
Maintain airway, O_2, ventilate PRN, cardiac monitor: rhythm, BP, O_2 saturation Identify and treat underlying causes
CHEST COMPRESSIONS: HR < 60, poor perfusion despite adequate O_2, ventilation Pulse check every 2 minutes. Move to cardiac arrest algorithm if becomes pulseless
EPINEPHRINE: Asphyxial, repeat Q3-5 minutes IV/IO: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/ml Epinephrine, Adult 1.0 mg Endotracheal: 0.1 mg/kg = 0.1 ml/kg of 1.0 mg/kg Epinephrine, Adult 2.5 mg
ATROPINE: Increased vagal tone or primary AV block. Repeat once. IV/IO: 0.02 mg/kg, ET: 0.04-0.6 mg/kg, Maximum dose 0.5 mg, Minimum dose 0.1 mg Note: Minimum Atropine dose of 0.1 mg is still recommended for bradycardia Atropine is rarely effective in 3rd degree (complete) AV block
TRANS-THORACIC PACING: Indicated for hemodynamically unstable complete heart block or sinus node dysfunction that is unresponsive to ventilation, oxygenation, chest compressions and medications. Not indicated for post arrest hypoxic/ischemic myocardial insult or respiratory failure.

WEB LINK: PEDIATRIC BRADYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT BRADYCARDIA WITH A PULSE ALGOROTHM (AHA 2020)

CARDIAC PACING

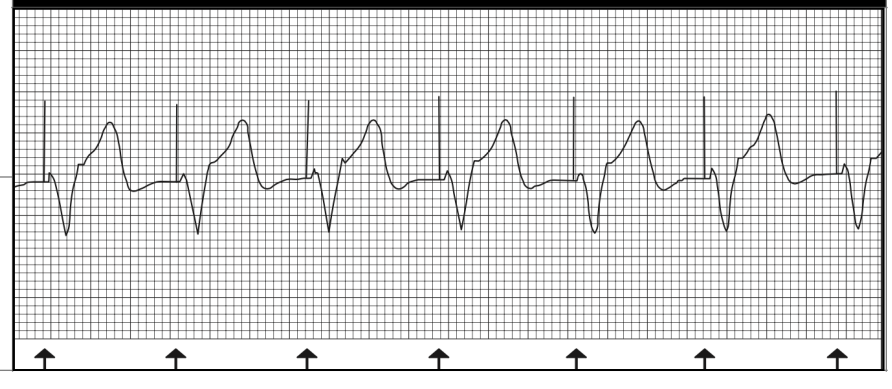
APPROACH
Transcutaneous (focus of this PEM Guide)
Transvenous (right heart)
Transesophageal (behind the heart)

INDICATIONS
1. Refractory bradycardia: Sinus node dysfunction, atrioventricular heart blocks
2. Refractory tachyarrhythmias: Overdrive pacing eg SVT (not discussed in this PEM Guide)

COMPLICATIONS
The primary complications of transcutaneous pacing are pain and skin erythema/burns at the point of contact. Pretreatment with benzodiazepines is indicated in conscious patients. The energy levels used for pacing have not been shown to produce significant myocardial injury or to induce ventricular fibrillation.

EQUIPMENT
Defibrillator/Pacer
Pacing pads

PROCEDURE OVERVIEW		
1	SEDATE	Sedate if indicated and time permits
2	ATTACH	Attach the pacing pads
3	SET MODE	Set the pacing mode
4	SET RATE	Set the pacing rate
5	SET OUTPUT	Set the pacer output
6	ADJUST OUTPUT	Adjust output until electrical and mechanical capture occur

PROCEDURE: TRANSTHORACIC PACING			
1	Sedate if indicated: Pretreatment with benzodiazepines in conscious patients		
2	Attach Pacing Pads: Pads placed so that the heart is between the pads		
	ANTERIOR-POSTERIOR		**ANTERIOR-LATERAL**
	ANTERIOR		ANTERIOR
	Left anterior chest between Xiphoid and nipple. Upper edge of pad below nipple line		Left chest Mid-axillary line Intercostal space 4
	POSTERIOR		LATERAL
	Posterior chest beneath the scapula and lateral to spine		Right chest Sub-clavicular area
3	Set the Pacing Mode: Demand versus Fixed. In general, start with demand mode		
	a	Demand mode (synchronous): paces if patient heart rate is below set rate.	
	b	Fixed mode: Continues at set rate regardless of patient's heart rate	
4	Set the Pacing Rate: Generally faster than underlying intrinsic rate		
	a	Adolescents and adults: 80-100 beats/minute	
5	Set the Output		
	a	Average adult requires 60-100 mA for unstable bradycardias	
6	Adjust the Output: Two options: Start high/titrate down or start low/titrate up		
	a	Start high and come down until capture is lost and then increase to the lowest level at which capture is obtained	
	b	Start low and increase every 10 seconds until capture obtained	
	c	Transthoracic pacing involves only the ventricles. Electrical capture of the ventricles is indicated by a pacer spike (indicated by the up arrows) followed by a wide ventricular complex	**ELECTRICAL CAPTURE** 
	d	Mechanical capture is indicated by a palpable pulse with each QRS complex at the rate set on the pacer.	

BARRIERS TO EFFECTIVE PACING
Increased distance or mass between pacer pads and heart
Barrel chest: Chronic lung disease such as bronchopulmonary dysplasia
Pericardial effusion
Pleural effusion
Pneumothorax
Breasts (female), musculature (male)
Severe acidemia

CARDIOGENIC SHOCK

INTRODUCTION (MICHAEL MOJICA, MD, 7/2020)
Cardiogenic shock is defined as inadequate perfusion due to decreased cardiac output.
It can be classified as compensated (deficient peripheral perfusion) or hypotensive (deficient peripheral and central perfusion). The term heart failure is used in a different manner. Compensated heart failure is defined by symptom absence or the presence of readily manageable symptoms. Decompensated heart failure occurs when there is an acute onset or exacerbation of chronic heart failure requiring urgent management. The term high output cardiogenic shock is used to define an increased cardiac output that is insufficient metabolic and perfusion needs typically in response to distributive shock (septic, anaphylactic, neurogenic).

Cardiogenic shock is rarer in children than adults where the primary etiology of heart failure is ischemic heart disease. Cardiogenic shock in children may result from congenital heart disease (#1) or acquired cardiac diseases including cardiomyopathy, myocarditis, rheumatic fever and ischemic heart disease (e.g. Kawasaki disease).

CAUSES OF PEDIATRIC CARDIOGENIC SHOCK	
Congenital heart disease (structural)	Volume Overload: Ventricular septal defect, endocardial cushion defect, patent ductus arteriosus* Pressure Overload: Coarctation of the aorta, aortic or pulmonic stenosis Complex: Hypoplastic left heart, unbalanced AV canal Ischemic: Anomalous left coronary artery off the pulmonary artery
Cardiomyopathy	Primary: Hypertrophic, dilatated, restrictive, noncompaction
Cardiomyopathy (secondary)	Infectious: Myocarditis*, endocarditis (valve disease) Inflammatory: Rheumatic fever* (carditis, valve disease), Kawasaki disease* (Coronary artery aneurysm → Ischemia) Toxic: Anthracyclines (e.g. Adriamycin, Daunorubicin)
Arrhythmias	Tachyarrhythmias*, Bradyarrhythmias* (particularly in infants)
Extracardiac	Metabolic: Mitochondrial, glycogen & lysosomal storage disorders
	Obstruction: Cardiac tamponade*, pulmonary embolism*
	High Output: Severe anemia, arteriovenous malformations, distributive shock (septic*, neurogenic*, anaphylactic*)
	Hematologic: Iron overload in those requiring transfusions
*Discussed in greater detail in a separate PEM Guide	

PHYSIOLOGY
Cardiac output is the product of stroke volume and heart rate. Cardiac output falls secondary to a decrease in stroke volume (“pump failure”) or impaired rhythm generation (dysrhythmias). Stroke volume is the difference been end-diastolic ventricular volume and end-systolic ventricular volume and is governed by a number of factors. An increase in venous return (preload), ventricular relaxation (lusitropy) and myocardial contractility lead to an increase in stroke volume. In contrast, a decrease in vascular resistance (afterload) leads to an increase in stroke volume.

Bradycardia results in a decreased cardiac output. Infants and young children have less contractile reserve than adults. In the face of bradycardia, children cannot compensate by increasing stroke volume. Tachyarrhythmias result in insufficient time for ventricular filling and a decrease in stroke volume and subsequently a decrease in cardiac output.

CLINICAL MANIFESTATIONS

Misdiagnosis is common. There is considerable overlap with the presentation of common conditions such as asthma, pneumonia, bronchiolitis and gastroenteritis. Patients often require multiple visits to make the initial diagnosis. Maintain a high index of suspicion as a delay in diagnosis may be life-threatening. Cardiogenic shock should be considered in any child in shock who worsens with fluid resuscitation or is persistently tachycardic without a clear etiology.

The diagnosis of cardiogenic shock can be made on the basis of symptoms and physical exam findings as well as by laboratory and imaging studies. However, these findings are neither sensitive nor specific. A point of care ultrasound can be used to support the diagnosis of cardiogenic shock. Cardiology consultation with complete echocardiography provides confirmatory evidence of heart failure. Biopsy may be required to determine the specific etiology of heart failure (e.g. myocarditis vs a non-inflammatory cardiomyopathy) but is seldom performed in pediatrics.

Heart failure results in an accumulation of fluids before reaching the ventricle (downstream effect). Left heart failure results in the accumulation of fluid in the lungs (pulmonary edema). Right heart failure results in systemic fluid accumulation. Biventricular failure results in signs and symptoms of both right and left heart failure. Heart failure results in inadequate systemic tissue perfusion (upstream effect).

Signs and symptoms can be categorized as cardiac, respiratory and gastrointestinal. Symptoms of pulmonary edema from left heart failure include shortness of breath, cough and frothy pink tinged sputum. Physical examination may reveal rales, rhonchi and wheezing as well as tachypnea and increased work of breathing. Respiratory symptoms are exacerbated in the supine position. Exam findings of right heart failure may include jugular venous distention (rare in infants), hepatomegaly, ascites and peripheral edema. A gallop rhythm and a heart murmur may or may not be present.

A decrease in cardiac output can result in signs of inadequate peripheral perfusion (cool, pale/mottled extremities, weak distal pulses and prolonged capillary refill) and central perfusion (hypotension, weak central pulses, altered mental status). Signs and symptoms in young infants are often non-specific. A prior history of syncope may be present. A family history of early heart disease and/or sudden unexplained death should be elicited.

SIGNS AND SYMPTOMS OF CARDIAC FAILURE		
SYMPTOMS: INFANTS	SYMPTOMS: CHILDREN	EXAM
Poor feeding	Chest pain	Pallor, cyanosis
Irritability	Palpitations	Diaphoresis
Cough	Cough, frothy, pink sputum	Tachypnea, ↑ Resp effort
Failure to thrive	Shortness of breath	Rales, rhonchi, wheezes
Vomiting	Vomiting, nausea	Hepatomegaly
Oliguria	Fatigue, ↓ Exercise tolerance	Ascites, peripheral edema

IMAGING

XRAY: A chest XRAY may demonstrate increased pulmonary vascular markings in the setting of pulmonary edema. An enlarged cardiothymic silhouette may be a sign of both cardiomegaly and pericardial effusion. However, the heart size may be normal in acute heart failure due to myocarditis.

ULTRASOUND: A limited point of care cardiac ultrasound can help to distinguish between cardiomegaly and pericardial effusion. Dilation of the atria and ventricles and decreased contractility may be seen. A dilated inferior vena cava with poor collapsibility is a sign of right heart failure. B lines on lung ultrasound are consistent with pulmonary edema. A complete cardiac ultrasound will provide a definite assessment of structural anatomy, chamber sizes and pressures and function (normal LV ejection fraction > 60%).

EKG: EKG findings are nonspecific and many children may have normal EKG's.

EKG FINDINGS* IN CARDIOGENIC SHOCK	
COMMON	RARE
Sinus tachycardia	Atrioventricular blocks
Atrial hypertrophy: P wave Morphology	Decreased voltages
Ventricular hypertrophy: Voltage, Axis	Bundle branch blocks
Strain: Wide QRS-T wave angle (>90°)	QT interval prolongation
Focal or diffuse ST elevations	
T wave inversions	
*See PEM Guide: Cardiology: EKG Interpretation	

LABORATORY STUDIES

Myocyte damage will increase cardiac enzymes such as CPK (Isozyme CPK-MB) and Troponin. Troponin may be elevated in ischemic or inflammatory etiologies such as myocarditis but are frequently normal in non-inflammatory/ischemic cardiomyopathy. B-type natriuretic peptide (BNP) and N-Terminal-Pro-BNP (NT-Pro-BNP) are produced by the myocardium in response to strain. Unlike cardiac enzymes, the natriuretic peptides are also elevated in non-ischemia, non-inflammatory causes of heart failure. Data on the cutoffs and utility of natriuretic peptides and cardiac enzymes is limited in children. BNP should be use as an adjunctive marker and not a sole marker of heart failure in children.

Elevated white blood cell count and acute phase reactants (ESR, CRP) may be present in myocarditis. End-organ function (BUN/Creatine, LFT's, Coagulation profile, Lactate) should be assessed as markers for perfusion.

MANAGEMENT

The goal of therapy is to increase tissue oxygen delivery. Tissue oxygen delivery (DaO_2) is the product of arterial oxygen content (CaO_2) and cardiac output (CO). Therefore, tissue oxygen delivery can be increased by interventions targeted to <u>increase</u> cardiac output (↑ Preload, ↑ Lusitropy, ↑ Contractility, ↓ Afterload) and <u>increase</u> arterial oxygen content (supplemental oxygen, blood transfusion). Tissue oxygen delivery can also be relatively increased by <u>decreasing</u> oxygen utilization. Patients in cardiogenic shock are often also in respiratory distress. Intubation with sedation and paralysis can decrease oxygen utilization by decreasing respiratory effort. Control of seizures, fever and pain also reduce oxygen utilization (See Appendix A).

FLUIDS: Fluid resuscitation is not a primary intervention for cardiogenic shock. Fluid resuscitation can increase preload and increase contractility due to the Starling effect. A recommended fluid bolus in cardiogenic shock is 5-10 ml/kg over 10-20 minutes or longer. Care should be taken to avoid over-hydration. The patient's lung sounds (rales of pulmonary edema) and hepatomegaly should be monitored continuously.

DIURETICS: Loop diuretic therapy (e.g. Furosemide 1-2 mg/kg) is recommended for patients with compensated heart failure with signs of fluid overload without signs of shock to reduce afterload. The patient should be monitored closely for hypotension.

VASOACTIVE MEDICATION SELECTION

In patients in cardiogenic shock, selection of vasoactive medications with inotropic (↑ Contractility) and/or vasodilator (↓ Afterload) properties is prioritized. There are no large clinical trials on vasoactive agent selection in pediatrics. Most data is extrapolated from animal or adult studies or from pediatric patients with congenital heart disease immediately post-cardiac surgery. In addition, selection is complicated by

the variety of causes of heart failure in pediatrics compared to primarily ischemic heart failure in adults. As a result, there is no consensus on the selection of vasoactive infusions for a given clinical situation. (See also: Pediatric Cardiac Intensive Care Society Guidelines (Tume, Pediatr Crit Care Med 2016, PubMed ID: 26945325). See also PEM Guide: Resuscitation: Vasoactive Medications for Shock.

Patients with cardiac shock with and without hypotension are managed with vasoactive medications. In patients in cardiogenic shock without hypotension, inodilators (↑ CO, ↓ SVR), such as Dobutamine and Milrinone are often recommended. In patients with cardiogenic shock with hypotension, the inodilators should not be used as they may worsen hypotension. Low dose Epinephrine (0.05-0.3 mcg/kg/min ((↑ CO > ↑ SVR) is often recommended. At higher Epinephrine doses (> 0.3 mcg/kg/min), vasoconstriction predominates and increased afterload can reduce cardiac output. Dobutamine or Milrinone can be added as hypotension resolves on Epinephrine.

1. ADRENERGIC AGONISTS: The term adrenergic refers to receptors that respond to Epinephrine (Adrenaline), Norepinephrine (Noradrenalin) and Dopamine.

DOBUTAMINE: Dobutamine is synthetic catecholamine and an “inodilator”. Predominant activity is at the $beta_1$ receptor increasing stroke volume more than heart rate and increasing cardiac output. It has weak $beta_2$ and $alpha_1$ activity. $Beta_2$ activity results in vasodilation and decreased afterload, further improving stroke volume and cardiac output.

The effect on blood pressure is variable. If the heart has already maximally responded by increasing stroke volume and heart, hypotension can occur due to vasodilation. However, If Dobutamine can increase stroke volume and heart rate, as well as reduce afterload, then it can increase blood pressure.

Dobutamine is primarily indicated in cardiogenic shock but should be used with caution, if at all, in hypotensive patients. Effects are similar to Milrinone but with a higher rate of tachycardia and dysrhythmias and a lower rate of hypotension

EPINEPHRINE: Epinephrine has potent $beta_1$ and moderate $beta_2$ and $alpha_1$ activity. Epinephrine’s response is dose dependent. At low doses, the $beta_1$ activity predominates increasing cardiac output. $Alpha_1$ (vasoconstriction) and $beta_2$ (vasodilation) have offsetting effects on systemic vascular resistance at low doses. At high doses, $alpha_1$ activity (vasoconstriction) predominates increasing systemic vascular resistance. Splanchnic vasoconstriction is more common with Epinephrine than with Norepinephrine or Dopamine. See Appendix: Push Dose Epinephrine

Epinephrine is the first line agent for anaphylactic shock (it also stabilizes mast cells). In adults, it is a second line agent for septic shock after Norepinephrine. In pediatrics, it is the first line agent for hypotensive, cold septic shock. Low-dose Epinephrine has some alpha activity (↑ SVR) and it will tend to prevent hypotension in cardiogenic shock when compared to Dobutamine and Milrinone which are inodilators (↑ CO, ↓ SVR).

2. PHOSPHODIESTERASE INHIBITORS: PDE inhibitors, such as Milrinone, are inodilators. The primary inotropic effect is due to an increase in intracellular cyclic AMP leading to an increase in intracellular calcium and increased contractility. In addition, lusitropy (ventricular relaxation) increases the time for ventricular filling and increases stroke volume. These effects are independent of adrenergic receptors making it an effective option for those on beta blockers. Vasodilation (secondary) is a result of inhibition of vascular phosphodiesterase. The effect on blood pressure is variable. If the heart has already maximally responded by increasing stroke volume and heart rate, hypotension can occur due to vasodilation. However, if it can increase stroke volume and heart rate, as well as reduce afterload, then it can increase blood pressure.

Milrinone is primarily indicated in cardiogenic shock but should be used with caution, if at all, in hypotensive patients. Effects are similar to Dobutamine with a lower rate of tachycardia and dysrhythmias but with a higher rate of hypotension.

3. OTHER AGENTS: Nitric oxide donors, such as Nitroprusside and Nitroglycerin that cause vasodilation, have been shown to significantly increase stroke volume and cardiac output in adults. Dopamine or Epinephrine can be used in conjunction with Nitroprusside to avoid hypotension. Pediatric data is limited.

CARDIOGENIC SHOCK: VASOACTIVE AGENT SELECTION	
Heart failure without shock	Loop diuretic
Cardiogenic Shock: Compensated	Dobutamine or Milrinone
Cardiogenic Shock: Hypotensive	Epinephrine (low dose)

MEDICATION: CLASSIFICATION			
Class	Medication	Action	Shock Indication
Inodilators	Dobutamine	$Beta_1 > Beta_2$	Cardiogenic Compensated
	Milrinone	↑ cAMP	Cardiogenic Compensated
Inopressors	Epinephrine	Low: $Beta_1 > Alpha_1$ High: $Alpha_1 > Beta_1$	Cardiogenic (Low BP)
	Norepinephrine	$Alpha_1 > Beta_1$	Cardiogenic (Low BP)?
	Dopamine	Dop → $Beta_1$ → $Alpha_1$	Cardiogenic (?)

CARDIOGENIC SHOCK: VASOACTIVE AGENT DOSING	
Dopamine	Low: 3-5 mcg/kg/min (“Renal” dose): 1° dopaminergic activity Moderate: 5-10 mcg/kg/min: 1° $Beta_1$ activity (↑ CO) High: 10-20 mcg/kg/min: 1° $Alpha_1$ activity (↑ SVR)
Dobutamine	2-20 mcg/kg/min
Milrinone	0.25-0.75 mcg/kg/min (start 0.25, titrate up as needed)
Epinephrine	Low: 0.05-0.3 mcg/kg/min: 1° $Beta_1$ activity (↑ CO) High: > 0.3 mcg/kg/min 1° $Alpha_1$ activity (↑ SVR)

ADVERSE EVENTS

Tachyarrhythmias are a potential adverse event of catecholamine administration. Tachyarrhythmias are more likely in those with cardiogenic shock due to ischemia or inflammation (carditis). Amiodarone (5 mg/kg) should be readily available. Amiodarone is a cardiac depressant and should be administered slowly (at least over 30 minutes and potentially longer). If bolus Epinephrine is required in the arresting patient, avoid giving regular arrest dosing. Instead give diluted Epinephrine (1 ml of 1:10,000 Epinephrine diluted in 9 ml of normal saline). 1 milliliter boluses of this diluted solution can be slowly titrated to desired blood pressure. See Appendix: Push Dose Epinephrine

POSITIVE PRESSURE VENTILATION: Intubation should be avoided if possible. The risk of cardiac arrest, particularly in the hemodynamically unstable patient, is high. Initiate vasoactive infusions to support cardiac output prior to rapid sequence intubation or have them readily available.

There are both positive and negative effects of positive pressure ventilation and administration of sedatives and paralytics. ET intubation and positive pressure ventilation promote alveolar recruitment and improves lung compliance. Paralysis eliminates metabolic activity and oxygen consumption associated with increased respiratory effort.

The cardiac effects of positive pressure ventilation differ on the right and left heart. These effects are primarily related to changes in the gradient between intrathoracic and intra-abdominal pressure (See Appendix). Positive pressure ventilation can decrease right heart cardiac output by decreasing systemic venous return and increase left heart cardiac output by increasing the pressure gradient from intrathoracic pressure to intra-abdominal pressure.

Sedative administration can result in vasodilation with a decrease in blood pressure as well as a decrease in heart rate. A decrease in heart rate can significantly reduce cardiac output as pediatric cardiac output is primarily driven by heart rate and not stroke volume. Propofol should be avoided and benzodiazepines should be administered in lower than typical doses. Potential sedatives include Etomidate, Fentanyl and Ketamine. Ketamine causes catecholamine release and has intrinsic sympathomimetic activity. However, Ketamine is a negative inotrope in the catecholamine depleted patient. Atropine should be considered as a premedication to rapid sequence intubation to avoid a significant decrease in heart rate.

MECHANICAL CIRCULATORY SUPPORT: Mechanical support techniques include ECMO and ventricular assist devices. These are indicated for patients who fail medical treatment. Referral to a center with these capabilities should be considered early in those with persistent hypotensive cardiogenic shock

APPENDIX: TARGETING THERAPY TO PHYSIOLOGY

SHOCK: Inadequate perfusion (oxygen and glucose delivery, metabolic acid removal)

THERAPY OPTIONS
A. Decrease oxygen utilization
B. Increase oxygen delivery
   1. Increase oxygen content
   2. Increase cardiac output

A. DECREASE OXYGEN UTILIZATION
1. Early intubation, sedation and paralysis: Decreases work of breathing and accumulation of metabolic acids
2. Treat fever
3. Treat seizures
4. Treat pain, anxiety

B. INCREASE OXYGEN DELIVERY (DaO_2)

DaO_2 = CaO_2 (Arterial oxygen content) x CO (Cardiac output)

= (Hb x 1.36 x $Sa0_2$) + (0.003 x $Pa0_2$) x SV* (Stroke Volume) x HR

1. Preload (Increase)
2. Contractility (Increase)
3. Lusitropy (Increase)
4. Afterload (Decrease)

TARGETED THERAPY OPTIONS: CARDIOGENIC SHOCK		
1	↑ Hemoglobin	Transfuse for Hemoglobin < 7 mg/dl (primary determinant of O_2 carrying capacity)
2	↑ SaO_2, PaO_2	Supplemental oxygen, ventilation PRN
3	↑ Preload	Fluid resuscitation: 5-10 ml/kg slowly to avoid fluid overload
4	↑ Contractility	Inotrope, correct metabolic abnormalities (acidosis, hypoglycemia, hypocalcemia, hyperkalemia)
5	↑, ↓ Heart rate	Not targeted to increase cardiac output unless bradyarrhythmia or tachyarrhythmia
6	↓ Afterload	Vasodilator (cardiogenic shock)

*Stroke Volume = Ventricular End-Diastolic Volume - Ventricular End-Systolic Volume
SV = VEDV - VESV

↑ Preload → ↑ VEDV → ↑ SV → ↑ CO
↑ Lusitropy → ↑ VEDV → ↑ SV → ↑ CO
↑ Inotropy → ↓ VESV → ↑ SV → ↑ CO
↓ Afterload → ↓ VESV → ↑ SV → ↑ CO

APPENDIX: CARDIAC EFFECTS OF (+) PRESSURE VENTILATION

The effect positive pressure ventilation differs on the right and left hearts (See below). There is a pressure gradient between the thoracic and abdominal cavities (Abdominal pressure – Intrathoracic pressure). Positive pressure ventilation increases intrathoracic pressure.

NORMAL VENTILATION
Negative Pressure Ventilation: Inspiration (diaphragm contracts)
→ ↓ Inter-thoracic pressure (ITP)
→ ↑ Intra-abdominal pressure (as diaphragm descends)
→ ↑ Pressure gradient (Abdominal >> Thoracic)
→ ↑ Systemic venous return (Preload)
→ ↑ Right ventricle end-diastolic volume (RVEDV)
→ ↑ Right ventricle stroke volume (SV = RVEDV – RVESV)
→ ↑ Right heart cardiac output

RIGHT HEART EFFECTS

Positive Pressure Ventilation:
→ ↑ Inter-thoracic pressure (ITP)
→ ↓ Pressure gradient (Abdominal > Thoracic)
→ ↓ Systemic venous return (Preload)
→ ↓ Right ventricle end-diastolic volume (RVEDV)
→ ↓ Right ventricle stroke volume (SV = RVEDV – RVESV)
→ ↓ Right heart cardiac output

LEFT HEART EFFECTS

Positive Pressure Ventilation
→ ↑ Inter-thoracic pressure (ITP)
→ ↓ Aorta Transmural pressure = Pressure Aorta – Intrathoracic Pressure
→ ↑ Left heart cardiac output

→ ↑ Inter-thoracic pressure (ITP)
→ ↑ Afterload
→ ↑ LVEDV
→ ↓ Left ventricle stroke volume (SV = RVEDV – RVESV)
→ ↓ Right heart cardiac output

→ ↓ Right heart cardiac output (= LV preload)
→ ↓ Left ventricle end-diastolic volume (RVEDV)
→ ↓ Left ventricle stroke volume (SV = RVEDV – RVESV)
→ ↓ Left heart cardiac output

APPENDIX: PUSH-DOSE PRESSORS: EPINEPHRINE

PUSH DOSE PRESSORS	
Definition	Small bolus doses of vasoactive agents to support blood pressure
History	Used anesthesiologists in the OR for many years
	Recently, more common in the ED and ICU settings
Indications	Bridge the time until a vasoactive infusion is available
	Expected short lived ↓ BP: e.g. after RSI, during procedural sedation
Adverse Events	Incorrect preparation → ↓ dose (ineffective),↑ dose (adverse events)
	Must label syringes appropriately to avoid dosing errors
Pediatric Dose	Weight base concentration: 1 mcg/kg/ml and dosed in 1 ml aliquots
Adult Dose	Standard Concentration: 10 mcg/ml and dosed in 1 ml aliquots
Other	Norepinephrine and Phenylephrine can also be used in push doses

EPINEPHRINE DOSING: NEW CONCENTRATIONS				
	CONCENTRATION		PEDIATRIC DOSING	
Route	Old	New	mg/kg	mL/kg
Intravenous	1:10,000	0.1 mg/mL	0.01	0.1
Intramuscular	1:1,000	1 mg/mL	0.01	0.01

PUSH-DOSE EPINEPHRINE: STANDARD PREPARATION (ADULT)	
Epinephrine (0.1 mg/ml)	Code Dose: 1 mg = 100 mcg = 10 ml
Normal Saline	9 ml Normal Saline
Preparation	1 ml of Epinephrine (0.1 mg/ml) + 9 ml of NS = 10 ml
Concentration	0.01 mg/ml (10 mcg/ml)
Dosing	0.5-2 ml (5-20 mcg) Q2-4 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION (PEDIATRICS)	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 10 mcg/kg = 0.1 ml/kg
Normal Saline	Normal Saline to total 10 ml
Preparation	0.1 ml/kg + NS to total 10 ml
Concentration	0.01 mg/kg/ml = 1 mcg/kg/ml
Dose	1 ml Q2 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION: 20 KG CHILD	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 0.2 mg, 10 mcg/kg = 200 mcg 0.1 ml/kg = 2 ml
Preparation	2 ml of Epinephrine (0.1 mg/ml) + 8 ml of NS = 10 ml
Preparation (concentration)	200 mcg/10 ml = 20 mcg/ml = 1 mcg/kg/ml
Dosing	1 ml (20 mcg or 1 mcg/kg) Q2 minutes PRN
Infusion Comparison	0.5-1.0 mcg/kg/min (10-20 mcg/min) Push-dose: 1 ml = 20 mcg (1/10th code dose) Equals: 0.5 mcg/kg/min x 2 min, 1.0 mcg/kg/min x 1 min

APPENDIX: HEART FALURE MANAGEMENT PARADIGM

ASSESSMENT		CONGESTION	
		NO	YES
HYPO-PERFUSION	NO	WARM	WARM
		DRY	WET
	YES	COLD	COLD
		DRY	WET

CELL: Top Row = Perfusion (Warm or Cold), Bottom Row = Congestion (Wet or Dry)
1. Hypo-perfusion: Altered mental status, ↓ BP, ↑ HR, poor distal perfusion (cool, mottled extremities, ↓ distal pulses, ↑ capillary refill).
2a. Congestion: RV Failure: JVD, hepatomegaly, ascites, peripheral edema
2b. Congestion: LV Failure: ↑ HR, ↑ RR, ↑ work of breathing, rales (pulmonary edema)

MANAGEMENT		PULMONARY CONGESTION	
		NO	YES
HYPO-PERFUSION	NO	Monitor	Diuretics ± PPV
	YES	Inotrope ± Pressor Gentle Fluids	Inotrope ± Pressor PPV

GOALS: Tissue oxygen delivery (DaO_2) is the product of arterial oxygen content (CaO_2) and cardiac output (CO). Tissue oxygen delivery can be increased by interventions targeted to <u>increase</u> cardiac output (↑ Preload, ↑ Lusitropy, ↑ Contractility, ↓ Afterload) and <u>increase</u> arterial oxygen content (supplemental oxygen, blood transfusion). Tissue oxygen delivery can also be increased relatively by <u>decreasing</u> oxygen utilization through sedation, paralysis and mechanical ventilation.

APPENDIX: PEDIATRIC MEAN ARTERIAL PRESSURE: 1-10 YEARS

PEDIATRIC MEAN ARTERIAL PRESSURE (BASED ON PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
1	5th	30	35	33	37	34	37	36	39	37	40
	50th	49	53	52	54	53	55	54	57	56	58
	95th	69	71	70	72	72	73	73	74	74	76
2	5th	35	39	38	41	39	42	40	42	41	44
	50th	54	57	56	58	57	59	59	60	60	62
	95th	73	75	75	76	76	77	77	78	79	80
3	5th	39	42	41	44	42	44	44	46	45	47
	50th	58	60	60	61	61	62	62	64	64	65
	95th	77	78	78	79	80	80	81	81	82	83
4	5th	42	45	43	46	46	47	47	47	48	49
	50th	61	63	63	65	64	65	66	65	67	67
	95th	79	80	82	82	83	83	84	84	86	85
5	5th	45	46	47	48	49	49	49	50	51	52
	50th	63	64	66	66	67	67	68	68	69	69
	95th	82	82	84	83	85	85	87	86	88	87
6	5th	47	49	49	50	50	51	52	52	53	54
	50th	66	66	67	68	69	69	70	67	71	71
	95th	84	84	86	85	87	86	88	87	90	89
7	5th	51	50	50	51	52	52	53	53	54	55
	50th	67	68	69	69	70	70	72	71	73	72
	95th	83	85	88	87	89	88	90	89	92	90
8	5th	50	52	53	52	54	54	55	55	56	56
	50th	69	70	71	70	72	71	73	72	75	74
	95th	87	81	89	88	91	89	92	90	93	91
9	5th	51	53	53	54	55	55	56	56	58	57
	50th	70	71	72	71	73	73	75	74	76	75
	95th	88	89	91	89	92	90	93	91	94	93
10	5th	52	54	55	55	56	56	56	57	59	59
	50th	71	72	73	73	75	74	75	75	77	76
	95th	90	90	92	90	93	92	94	93	96	94

Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40
Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55

CONTINUED ON NEXT PAGE →

APPENDIX: PEDIATRIC MEAN ARTERIAL PRESSURE: 11-17 YEARS

PEDIATRIC MEAN ARTERIAL PRESSURE (BASED ON PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
11	5th	54	55	57	56	57	57	58	59	59	60
	50th	72	73	74	74	75	75	76	76	78	78
	95th	91	91	92	92	94	93	95	94	96	95
12	5th	54	57	57	58	58	58	60	60	61	61
	50th	73	75	75	75	77	76	78	78	79	79
	95th	92	92	94	93	95	94	96	95	98	97
13	5th	56	58	57	59	59	60	60	61	61	62
	50th	75	76	76	77	77	78	79	71	80	80
	95th	93	94	95	94	96	95	97	97	99	98
14	5th	59	60	59	60	61	61	62	62	63	64
	50th	75	77	78	78	79	79	80	80	82	81
	95th	91	95	96	96	97	97	99	98	100	99
15	5th	58	61	61	61	62	62	63	63	64	64
	50th	77	78	79	79	80	80	82	81	83	82
	95th	96	91	98	97	99	98	100	99	102	100
16	5th	90	61	62	62	63	63	65	63	66	66
	50th	79	79	81	90	82	81	83	82	85	84
	95th	98	96	99	98	101	99	102	100	104	101
17	5th	63	61	63	62	65	63	67	65	69	66
	50th	81	79	83	80	84	81	85	82	87	84
	95th	100	96	102	98	103	99	104	100	106	101
Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40 Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55											

Haque IU, Zaritsky AL.
Analysis of the Evidence for The Lower Limit of Systolic and Mean Arterial Pressure in Children
Pediatr Crit Care Med. 2007 Mar;8(2):138-44., PubMed ID: 17273118

CYANOTIC CONGENITAL HEART

INTRODUCTION (KELLY CLEARY, M.D. 8/2013)

Congenital heart disease (CHD) is the most common congenital disorder affecting about 1 out of every 115 live births. Of these, approximately 15% are disorders that present with cyanosis in the neonatal period. Cyanosis occurs when the level of deoxygenated hemoglobin in blood exceeds 3-5 gm/dl. In the neonatal period, it is often difficult to differentiate cyanosis that originates from a cardiac etiology compared to a non-cardiac etiology. Prompt recognition is crucial for early emergency intervention.

CYANOTIC HEART LESIONS: THE “5 T’S +”		
T	Transposition of the Great Arteries (TGA)	Mixing Lesion
T	Tetralogy of Fallot (TOF)	R to L Shunt
T	Truncus Arteriosus (TA)	Mixing Lesion
T	Total Anomalous Pulmonary Venous Return (TAPVR)	Mixing Lesion
T	Tricuspid Atresia (TA), Epstein’s anomaly	R to L Shunt
+	Double Outlet Right Ventricle (DORV)	Mixing Lesion
+	Pulmonary Atresia/Stenosis (PA/PS)	R to L Shunt

HISTORY: INCREASED RISK OF CONGENITAL HEART DISEASE
Maternal diabetes +/- obesity
Smoking in first trimester
Congenital heart block (mother with Lupus)
CMV, HSV, Rubella, Coxsackie maternal infection
Phenytoin, Fosphenytoin, Lithium
Assisted reproductive technology
1st degree relative with congenital heart disease

CLINICAL EVALUATION

VITAL SIGNS	
Heart Rate	Tachycardia
Blood pressure	BP gradient may exist between upper and lower extremities (coarctation, interrupted aortic arch) Infant may be hypotensive (shock)
Respiratory	Varying degrees of respiratory distress Mild tachypnea to severe respiratory distress
O_2 saturation	Low saturation with cyanotic lesions Differential cyanosis (upper half of the body is non-cyanotic and the lower half is cyanotic, or vice versa)

DIFFERENTIAL DIAGNOSIS: CRITICALLY ILL INFANT		
T	Trauma	Consider intentional trauma
H	Heart disease	Congenital heart disease, arrhythmias
E	Endocrine	Congenital adrenal hyperplasia
M	Metabolic	Hypoxia, hypoglycemia
I	Inborn errors	Acidosis, hyperammonemia
S	Sepsis	Bacterial, viral
F	Formula (Na)	Hypo/hypernatremia
I	Intestinal	Malrotation
T	Toxicants	Methemoglobinemia
S	Seizures	Primary, secondary

DIFFERENTIAL DIAGNOSIS: CYANOSIS	
Airway	Obstruction: choanal atresia, laryngomalacia, Pierre Robin
Pulmonary	Internal: Transient tachypnea of the newborn, respiratory distress syndrome, pneumonia, aspiration, atelectasis, pulmonary hemorrhage, hypoplasia or edema
	External: Pneumothorax, hemothorax, diaphragmatic hernia, pleural effusion
Cardiac	R-L Shunts: TET, Tricuspid atresia (TA), Ebstein's anomaly, PA/PS Mixing Lesions: Truncus arteriosus, TAPVR, TGV, DORV
	Shock: Hypoplastic left heart, critical aortic stenosis, critical coarctation
Neurology	Central Nervous System: Asphyxia, sedation (maternal drugs), intraventricular hemorrhage, seizure, meningitis, encephalitis
	Neuromuscular disease: Neonatal myasthenia, phrenic nerve injury
Shock	Any cause of shock: Sepsis, hypothermia, hypoglycemia
Hematology	Methemoglobinemia, polycythemia

Cyanotic congenital heart disease should be considered in any neonate or infant that presents critically ill as well as those with cyanosis. Elements of the history, vital signs, physical exam and ancillary testing will aid in the diagnosis.

PHYSICAL EXAMINATION

PHYSICAL EXAM FINDINGS
Cyanosis
Murmur
Poor perfusion
Hepatomegaly
Crackles/rales on lung auscultation
Weakened pulses

EVALUATION

Initial work-up should include a chest XRAY (CXR), EKG, arterial blood gas (ABG), pulse oximetry, CBC, and echocardiogram. Often a sepsis work-up is done since the presenting features of neonatal sepsis may mimic those of CHD. On chest XRAY, careful attention should be given to heart size and shape, pulmonary vascular markings and the location of the aortic arch. Echocardiography will provide definitive diagnosis of CHD.

XRAY AND EKG FINDINGS				
LESION	CXR HEART	CXR VASCULARITY	EKG	DUCTAL DEPENDENT*
TOF	Boot shaped	Decreased	RAD/RVH	YES (possibly)
TGA	Egg-on-a-string	Increased	RAD/RVH	YES (possibly)
TAPVR	Snowman	Increased	RAD/RVH	NO
TA (truncus)		Increased	RAD/RVH	NO
TA (tricuspid)		Decreased	LAD/LVH	YES (always)
*Whether or not a lesion is ductal dependent depends on the presence of other lesions (communication between chambers). For example, transposition of the great vessels is not ductal dependent if there is a large atrial or ventricular septal defect.				

EKG: The EKG in the infant with cardiac disease may be normal or suggestive of atrial or ventricular enlargement, though some lesions are associated with specific EKG patterns. The normal neonatal EKG has a right axis deviation (QRS +90 to+180) and right ventricular hypertrophy. The EKG of patients with Tricuspid atresia and Epstein's Anomaly will demonstrate pathognomonic superior axis (0-90 degree). Cardiac lesions with a small right ventricle, such as tricuspid atresia will show signs of left axis deviation, right atrial enlargement (tall peaked P waves in lead II) and left ventricular hypertrophy.

HYPEROXIA TEST: The hyperoxia test is used to help distinguish between cardiac and non-cardiac causes of cyanosis. Neonates with cyanotic congenital heart disease typically do not have a significant increase in the PaO_2 with administration of 100% oxygen. The PaO_2 in patients with pulmonary disease usually increases significantly because V-Q mismatches are overcome by oxygen administration. This test is performed by measuring the arterial oxygen tension in the right radial artery (pre-ductal) while administering room air and then comparing this to the arterial oxygen tension while administering high levels of inspired oxygen (100%) for 10 minutes. A significant increase in the systemic arterial oxygen saturation or PaO_2 (above 150 mmHg) suggests pulmonary disease as an etiology. The pre-ductal oxygen tension while breathing 100% oxygen rarely exceeds 150 mmHg in patients with cardiac lesions.

HYPEROXIA TEST: RESPONSE TO SUPPLEMENTAL OXYGEN	
Normal	Increased PaO_2
Methemoglobinemia	Increased PaO_2, no change in SaO_2
Pulmonary disease	Some increased $Pa0_2$
Cyanotic Congenital Heart	No increase $Pa0_2$ or SaO_2

MANAGEMENT

Assess and manage airway, breathing and circulation. Consider early intubation and support with inotropes (Dopamine, Dobutamine) as needed.

PROSTAGLANDIN E1: If there is clinical suspicion for a ductal-dependent cardiac lesion, prostaglandin E1 (PGE1) should be used immediately to maintain a patent ductus arteriosus. The initial dose is 0.05 – 0.1 mcg/kg/min. Complications of PGE1 are listed below. The clinician should be prepared to intubate and support hemodynamics after its administration. Patients being transported to an outside institution should be intubated prior to transport.

PGE1 COMPLICATIONS
Hypotension
Tachycardia, bradycardia
Apnea
Seizure
Hyperthermia
Rash, skin flushing
Thrombocytopenia

ANTIBIOTICS: Infants with cyanotic cardiac lesions often present in extremis with cyanosis, left ventricular dysfunction and tachypnea after the ductus closes. Given that these symptoms mimic neonatal sepsis; these infants are often empirically started on broad-spectrum antibiotics.

APPENDIX: SPECIFIC CYANOTIC HEART LESIONS

TRANSPOSITION OF THE GREAT ARTERIES (TGA): This is the most common congenital cyanotic lesion diagnosed in the newborn period, affecting approximately 5% of patients with congenital heart defects. (Tetralogy of Fallot is the most common overall, but is usually diagnosed later). In TGA, the aorta arises from the morphologic right ventricle and the pulmonary artery arises from the left ventricle. With normal cardiac anatomy, pulmonary and systemic circulations run in series; with TGA, two parallel systems without connection exist. The clinical scenario that results is severe hypoxemia secondary to deoxygenated venous blood traversing through the right atria and right ventricle just to be returned to the systemic system deoxygenated. It is incompatible with life if a connection between the pulmonary and systemic systems is not present.

Cyanosis, with or without a murmur are the most common presenting clinical findings. An electrocardiogram shows right axis deviation and right ventricular hypertrophy (RVH), which is typical of a newborn EKG. Chest X-ray may show increased pulmonary vascular markings as well as an “egg on a string” pattern (narrow mediastinum due to a small thymus and anterior/posterior positioning of the great vessels as opposed to the usual right/left positioning of the vessels). Echocardiography can provide a definitive diagnosis. Immediate stabilization is provided by PGE1 administration. If inadequate oxygenation or acidosis persists despite PGE1, a balloon atrial septostomy (Rashkind procedure) is indicated. Definitive treatment is an arterial switch procedure with re-implantation of the coronary arteries.)

TRUNCUS ARTERIOSUS (TA) is a non-ductal dependent cardiac lesion in which one great vessel emerges from the heart; the aorta, pulmonary arteries and coronary arteries all originate a single vessel. The vessel has combined output from the left and right ventricles. Symptomatology is dependent on the amount of pulmonary blood flow (PBF); the greater the PBF, the greater the degree of congestive heart failure (CHF) that develops. CXR findings include increased pulmonary vascular markings and cardiomegaly. Initial emergent treatment includes management of CHF. Definitive treatment is closure of the VSD, separating the pulmonary arteries from the trunk and creating a conduit to the right ventricle (Rastelli procedure).

TOTAL ANOMALOUS PULMONARY VENOUS RETURN (TAPVR): There are four types of TAPVR defined by the connection of the pulmonary veins (see table below). In all lesions, the pulmonary veins do not connect to the left atrium. A right to left shunt is necessary for survival to distribute oxygenated blood to the body. The degree of cyanosis is dependent upon the degree of mixing as well as obstruction of the pulmonary veins.

In TAPVR, an EKG will likely show RVH and RAH. The CXR will show increased pulmonary vascular markings, and in cases of supracardiac TAPVR may have a “snowman” or “figure of 8” appearance. This is caused by a dilated superior vena cava (SVC) and vertical vein (formed by the pulmonary veins joining together).

TOTAL ANOMALOUS PULMONARY VENOUS RETURN	
SUBTYPE	PULMONARY VEIN CONNECTION
Supracardiac	Superior vena cava
Cardiac	Right atrium
Infracardiac	Portal vein → hepatic vein → inferior vena cava
Mixed	Combination of the above

TETRALOGY OF FALLOT (TOF): This is the most common cyanotic heart lesion when considering all groups. Clinical presentation is dependent on the severity of the pulmonary outflow obstruction. “Pink TETS”, those with mild ventricular outflow obstruction tract obstruction, may present with CHF due to pulmonary over-circulation. However, as the degree of pulmonary stenosis increases, the pulmonary blood flow decreases, and the degree of cyanosis increases.

TETRALOGY OF FALLOT	
1	Right Ventricular Outflow Tract obstruction
2	Ventricular Septal Defect
3	Right Ventricular Hypertrophy
4	Overriding aorta

A loud systolic ejection murmur may be detected (due to right ventricular outflow tract (RVOT) obstruction) at the left sternal border. The second heart sound may be diminished as the aorta overrides the pulmonary artery. EKG may show nonspecific RVH. CXR may show decreased pulmonary vascular markings and a “boot shaped” heart due to an absent or decreased pulmonary artery segment.

Treatment of TOF initially includes PGE1 if the patient is cyanotic and pulmonary blood flow is ductal dependent. Surgical intervention includes initial modified Blalock-Taussig shunt (Gortex conduit connecting the subclavian artery to a branch pulmonary artery). Definitive treatment includes repair of the RVOT obstruction with augmentation and/or repair of the pulmonic stenosis and closure of the VSD.

Patients may develop cyanotic or hypoxic spells, which consist of sudden onset of increased cyanosis, excessive crying, hypoxemia, acidosis, dyspnea, syncope, rarely seizures, and occasionally death if untreated. (See: PEM Guide: Cardiology: Tetralogy of Fallot Spells). During these “Tet” spells, there is increased right-to-left shunting due to obstructed pulmonary outflow tract and/or decreased systemic vascular resistance.

Treatment of TET spells include increasing pulmonary blood flow by:
1. Increase systemic venous resistance (SVR) to increase systemic venous return: Knee-chest position, squatting, intravenous fluids and Phenylephrine increase SVR
2. Decrease pulmonary vascular resistance (PVR): Calming the infant and sedation with Morphine or Ketamine decreases PVR.
3. Reduce the degree of right ventricular outflow tract (RVOT) obstruction: Propranolol reduces heart rate, relaxes the RVOT

Severe cases may require abdominal aorta compression and emergent Blalock-Taussig shunt placement, Sodium bicarbonate may be required to correct acidosis.

TRICUSPID ATRESIA (TA): No communication is present between the right atrium and ventricle resulting in a hypoplastic right ventricle. A patent foramen ovale or ASD is necessary for survival. Severe cyanosis is the rule. EKG will show pathognomonic superior axis (0 to -90 degree), Right atrial and left atrial enlargement, and left ventricular hypertrophy. Initial management includes prostaglandin, balloon septostomy (Rashkind procedure) or an emergency by a Blalock Taussig shunt.

EBSTEIN ANOMALY: This lesion is referred to as “atrialization” of the right ventricle. There is inferior displacement of the tricuspid valve. In its most severe form, the tricuspid leaflets may extend into the right ventricular outflow tract. Chest X-ray shows a large right atrium and massive cardiomegaly (due to atrial enlargement), and EKG may show right bundle branch block, large P waves, and sometimes first degree atrio-ventricular block or Wolf-Parkinson-White syndrome. Treatment is usually palliative. Cyanosis from the right-to left atrial shunting typically improves as PVR decreases in the neonatal period.

PULMONARY ATRESIA: With this lesion, pulmonary blood flow is a ductal dependent; depending on blood flow from the aorta to the pulmonary artery through a patent ductus arteriosus (PDA). Initial treatment includes stabilization with PGE-1. Definitive treatment includes opening the pulmonary valve via cardiac catheterization or surgical repair to create a right ventricular to pulmonary artery connection.

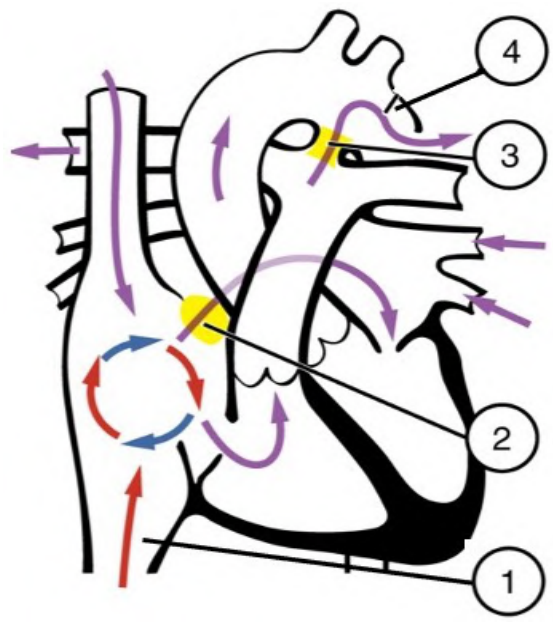
DOUBLE OUTLET RIGHT VENTRICLE: Both the pulmonary artery and aorta arises from the right ventricle. DORV always includes a VSD. Children with this lesion often present in CHF. DORV is treated surgically.

DUCTAL DEPENDENT CARDIAC LESIONS

INTRODUCTION: (MICHAEL MOJICA, MD, 8/2021)
Congenital heart disease is the most common congenital abnormality occurring in approximately 1% of births. Critical congenital heart disease is defined as requiring an operative or catheter intervention within the first year of life and represents approximately one-quarter of congenital heart disease. Ductal dependent cardiac lesions are those that are dependent on a patent ductus arteriosus for pulmonary (e.g. pulmonary atresia) or systemic blood flow (e.g. critical aortic stenosis) or as a connection between independent circulations (e.g. transposition of the great vessels). Congenital heart disease may be identified by fetal echocardiography or in the newborn nursery based on exam findings and oxygen saturation screening. Those that leave the nursery without a diagnosis are at high risk of mortality.

ANATOMY

In utero, the ductus arteriosus connects the pulmonary artery to the descending aorta. It allows blood flow from the right ventricle to bypass the fluid filled and high resistance lungs and enter the systemic circulation. The placenta takes the place of the lungs in providing for oxygenation and exchange of carbon dioxide.



At birth, decreasing pulmonary vascular resistance and oxygenation stimulate closure of the ductus arteriosus. The time to physiologic ductal closure due of smooth muscle contraction is typically 1-2 days in full-term neonates. Anatomic closure of the ductus arteriosus due to fibrosis occurs over a few weeks resulting in the ligamentum arteriosus. Ductal closure can occur later in preterm infants and in those with ductal dependent cardiac lesions. The interval between physiologic and anatomic closure of the ductus arteriosus allows prostaglandin to reopen the closed duct.

1. Oxygenated blood from the placental mixes with deoxygenated blood from the upper body in the RA
2. Mixed blood: RA → Foramen Ovale → LA → LV
3. Mixed blood: RA → RV → Ductus Arteriosus → Aorta
4. Mixed blood: Head and body → Placenta

DUCTAL DEPENDENT CARDIAC LESIONS
RIGHT-SIDED LESIONS: Ductal dependent pulmonary blood flow (Left to Right)
Pulmonary Atresia (PA)
Critical pulmonary stenosis (PS)
Tricuspid Atresia (TA): Depends on VSD, pulmonary outflow tract obstruction size
Tetralogy of Fallot (TET) with severe right ventricular outflow tract obstruction
LEFT SIDED LESIONS: Ductal dependent systemic blood flow (Right to Left)
Coarctation of the aorta, interrupted aortic arch
Critical Aortic stenosis (AS)
Hypoplastic left heart syndrome
RIGHT/LEFT SIDED CIRCULATION SEPARATED: Ductus dependent connection
Transposition of the great arteries (TGA) without a large VSD or ASD

PHYSIOLOGY

Both right-sided and left-sided cardiac lesions can be ductal dependent. However, not all right-sided or left-sided congenital heart lesions are ductal dependent. In addition, some congenital heart lesions are conditionally ductal dependent. Whether or not a lesion is ductal dependent can be determined by the presence of other communication between chambers. For example, transposition of the great vessels is not ductal dependent if an ASD or VSD is present. In fact, emergency treatment for a ductal dependent TGV is the creation of an ASD through a catheter placed in the foramen ovale (balloon atrial septostomy) prior to definitive operative repair.

Both right-sided and left-sided ductal dependent cardiac lesions result in some degree of obstruction to flow. Right-sided cardiac lesions, such as pulmonic atresia, require a patent ductus arteriosus for pulmonary blood flow from the systemic circulation and typically present with cyanosis. Left-sided cardiac lesions, such as critical aortic stenosis, require a patent ductus arteriosus for systemic blood flow from the pulmonary circulation and typically present with cardiogenic shock.

CLINICAL PRESENTATION

Symptoms of cardiac disease in neonates are often non-specific and include decreased or slow feeding often associated with sweating and signs of respiratory distress. Neonates with a ductal dependent cardiac lesion present acutely when the duct closes and are often critically ill. A ductal dependent cardiac lesion should be suspected in all critical ill children less than 1-2 weeks of age though this timeframe may be prolonged for premature neonates and specific cardiac lesions.

DIFFERENTIAL DIAGNOSIS: CRITICALLY ILL INFANT		
T	Trauma	Consider intentional trauma
H	Heart disease	Congenital heart disease, arrhythmias
E	Endocrine	Congenital adrenal hyperplasia
M	Metabolic	Hypoxia, hypoglycemia
I	Inborn errors	Acidosis, hyperammonemia
S	Sepsis	Bacterial, viral
F	Formula (Na)	Hypo/hypernatremia
I	Intestinal	Malrotation
T	Toxicants	Methemoglobinemia
S	Seizures	Primary, secondary

Color changes may be due to congenital heart disease but hematologic (e.g. severe anemia) and toxicologic (e.g. methemoglobinemia) causes should also be considered. More specific findings for cardiac disease include hepatomegaly and pulmonary edema due to heart failure and difference in pre-ductal and post-ductal oxygen saturation and pulses/blood pressure.

RIGHT-SIDED LESIONS: The right-sided ductal dependent lesions typically present acutely with cyanosis. Currently, newborns are screened for cyanotic congenital heart disease after 24 hours of age in the newborn nursery. Oxygen saturation is measured in the right hand (pre-ductal) and either foot (post-ductal). A failed screen is an oxygen saturation < 90% in the right hand or foot on the initial screen, an oxygen saturation < 95% in the right hand or foot on three measurement separated by 1 hour or a differential of greater than 3% between the right hand and foot on three measures separated by 1 hour.

LEFT-SIDED LESIONS: Left sided lesions typically present acutely with signs of congestive heart failure such as trouble feeding, breathing, sweating, irritability, rales, hepatomegaly due to left heart output obstruction (e.g. critical aortic stenosis) and signs of shock such as hypotension, weak or absent pulses, signs of poor distal perfusion due to decreased or obstructed systemic blood flow (e.g. coarctation of the aortic arch). Prior to ductal closure the neonate will have some degree of cyanosis because the systemic circulation is being provided by pulmonary artery blood that has not been oxygenated. After ductal closure, neonates will appear grey.

EVALUATION

Initial work-up should include pulse oximetry, assessment of pulses and blood pressure. CBC, chest XRAY and EKG. Pediatric cardiology should be consulted as soon as a cardiac etiology is suspected. Echocardiography will provide definitive diagnosis of congenital heart disease. 4-extremity blood pressures should be obtained in the setting of poor distal perfusion and the hyperoxia test should be performed in the setting of cyanosis. The potential for sepsis should be acknowledged for all critical ill neonates.

HYPEROXIA TEST: The hyperoxia test is used to help distinguish between cardiac and non-cardiac causes of cyanosis and specifically to identify cyanotic congenital heart disease. However, the hyperoxia test does not distinguish between ductal dependent and non-ductal dependent cyanotic congenital heart disease and does not identify ductal dependent left-sided lesions.

This test is performed by measuring the oxygen saturation in the right hand (pre-ductal) while administering room air and then comparing this to the oxygen saturation while administering high levels of inspired oxygen (100%) for 10 minutes. may have a mildly increased oxygen saturation but the PaO2 is less than 150 mmHg. For this reason, oxygen saturations alone should not be used if oxygen saturation is in the 90s. A significant increase in the systemic arterial oxygen saturation or PaO_2 suggests a pulmonary etiology.

HYPEROXIA TEST: RESPONSE TO SUPPLEMENTAL OXYGEN		
	PaO_2	SaO_2
Normal	Increased	Increased
Methemoglobinemia	Increased	No increase
Pulmonary disease	Some increase	Some increase
Cyanotic Congenital Heart	No increase	No increase

4-EXTREMITY BLOOD PRESSURES: Traditionally, four extremity blood pressure are used to identify aortic defects (coarctation, interrupted aortic arch). However, it does not distinguish between ductal-dependent and non-ductal dependent aortic arch lesions.

Normally, blood pressure is higher in the lower extremities than in the upper extremities. Right upper extremity blood pressure that is higher than the lower extremity blood pressure by more than 10mm Hg is suggestive of an aortic arch lesion. However, there is significant variability and 4 extremity blood pressure has poor sensitivity and specificity in identifying aortic arch lesions. The presence of a left sided heart lesion should be corroborated by absent or decreased femoral artery pulses with poor systemic perfusion and signs of congestive heart failure (pulmonary edema and hepatomegaly). The left upper extremity blood pressure may be the same as the right upper extremity if coarctation occurs after the origin of the left subclavian artery or lower than the right upper extremity if the coarctation occurs before the origin of the left subclavian artery.

CHEST XRAY: On chest XRAY, careful attention should be paid to heart size and shape and to pulmonary vascular markings. Decrease pulmonary vascular markings can be seen in right-sided lesions and increased pulmonary vascular markings (pulmonary edema) can be seen in left-sided lesions. Increased heart size is associated with some obstructive lesions. Some heart lesions are associated with characteristic heart shapes (e.g. the boot shaped heart of Tetralogy of Fallot). Small heart sizes can be seen with hypoplastic left or right ventricles.

EKG: The neonatal EKG has a right axis deviation (QRS axis: 1st week: 60-180, 1-3 weeks: 45-160) as a result of right ventricular dominance in the fetal circulation. Evidence of ventricular hypertrophy may be present. The EKG of patients with Tricuspid atresia with hypoplastic right ventricles will demonstrate pathognomonic superior (left) axis (-30 to -90 degrees).

MANAGEMENT

Assess and manage airway, breathing and circulation. Consider early intubation but be prepared for hemodynamic compromised with the use of sedatives and positive pressure ventilation, Support the circulation with inotropes (low dose Epinephrine and Milrinone) as required. Identification of the specific cardiac lesion is not required to initiate treatment with prostaglandin. Often a sepsis work-up is initiated since the presenting features of neonatal sepsis may mimic those of congenital heart disease. However, fluid resuscitation may worsen cardiac disease and the neonate should be assessed frequently for signs of fluid overload.

OXYGEN: Oxygen administration may worsen ductal dependent lesions by promoting closure of the ductus. Oxygen also causes pulmonary vasodilation which can increase left to right flow for left-sided cardiac lesions. Left-sided cardiac lesions can develop worsening congestive heart failure and decreased systemic blood flow with oxygen administration. If a left-sided ductal dependent lesion is suspected, the patient should me managed on room air if possible though some oxygen may be required with very low oxygen saturations (<80%)

PROSTAGLANDIN E1: Endogenous, gestational prostaglandins assist in maintaining ductal patency in utero. If there is clinical suspicion for a ductal-dependent cardiac lesion, prostaglandin E1 (PGE1) should be used immediately to open and maintain a patent ductus arteriosus. Complications of PGE1 are listed below. The clinician should be prepared to intubate and support hemodynamics after its administration. Patients being transported to an outside institution should be intubated prior to transport.

PROSTAGLANDIN (ALPROSTADIL: PGE1)
DOSING
0.05-0.1 mcg/kg/min (maximum: 0.4 mcg/kg/min)
COMPLICATIONS
Hypotension
Tachycardia, bradycardia
Apnea
Seizure
Hyperthermia
Rash, skin flushing
Thrombocytopenia

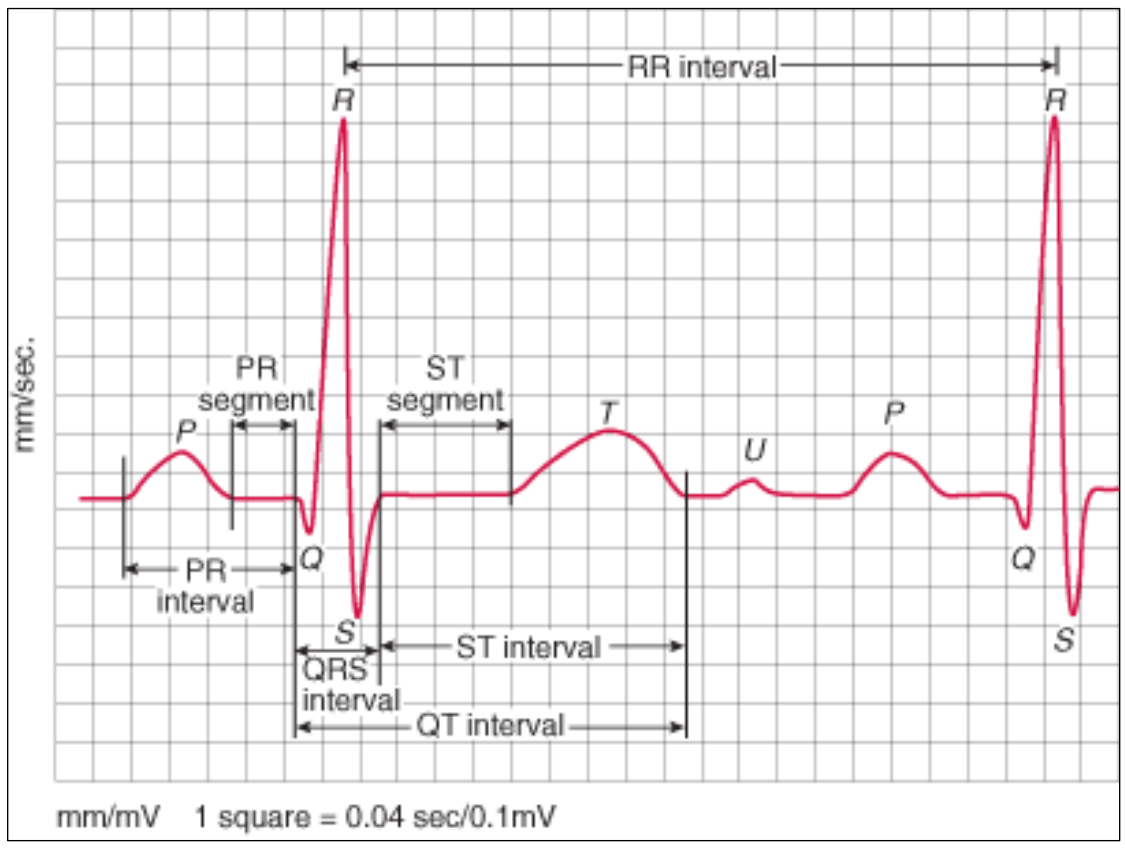
EKG INTERPRETATION

INTRODUCTION (MICHAEL MOJICA, M.D. 2/2020)
The interpretation of pediatric EKGs is a complex procedure that requires a systematic approach. This task is made more complex by changes in pediatric cardiovascular physiology and anatomy that occur as the child ages. Neonates are right ventricular dominant. The change from right to left ventricular dominance with age (by 3-4yrs) results in changes in the QRS axis and age specific voltage changes. In addition, neonate and infant cardiac output is determined primarily by heart rate (compared to stroke volume determined in older children and adults). The decrease in heart rate over times results in age specific norms for interval measurements.

USING THE WORK SHEET
The attached worksheet provides a systematic approach to pediatric EKG interpretation. It has been divided into four sections: dysrhythmia, heart size, ischemia/infarction and miscellaneous findings. It is intended as an aide to diagnosis. Determine the normal values for the patients age and compare them to those found on the EKG. Management of EKG abnormalities is not discussed. Definitive EKG interpretation by a pediatric cardiologist should be obtained in the cardiovascularly symptomatic patient and for any abnormal or uncertain findings on the EKG.

CLINICAL APPROACH	
1	Patient’s age
2	History: Chief complaint, HPI, PMHx, family Hx (cardiac disease, sudden death)
3	Physical: Complete including vital signs, focused cardiovascular, pulmonary exam
4	Presumptive differential diagnosis
5	Indication for EKG?
6	EKG Interpretation: Determine normal values for age and patient values
7	Consultation with Pediatric Cardiology
8	Management and disposition planning

EKG INDICATIONS
Abnormal cardiac exam
Altered mental status
Cardiac arrest
Chest pain
Drug exposure
Electrical injuries/burns
Electrolyte abnormalities
Palpitations
Seizure
Shock
Suspected dysrhythmia
Syncope



EKG STANDARDS

Standard Voltage	10 mm/mV
Standard Speed	25 mm/sec
1 small box (vertical)	1 mm
1 large box (vertical)	5 mm
1 small box (horizontal)	0.04 sec or 40 msec
1 large box (horizontal)	0.2 sec or 200 msec
1500 small boxes (horizontal)	1 minute
300 large boxes (horizontal)	1 minute

PEDIATRIC EKG NORMAL VALUES

Age	HR (bpm)	QRS axis (degrees)	QRS Interval (seconds)	R in V1 (mm)	S in V1 (mm)	R in V6 (mm)	S in V6 (mm)
1st week	90–160	60–180	0.03–0.08	5–26	0–23	0–12	0–10
1–3 weeks	100–180	45–160	0.03–0.08	3–21	0–16	2–16	0–10
1–2 months	120–180	30–135	0.03–0.08	3–18	0–15	5–21	0–10
3–5 months	105–185	0–135	0.03–0.08	3–20	0–15	6–22	0–10
6–11 month	110–170	0–135	0.03–0.08	2–20	0.5–20	6–23	0–7
1–2 years	90–165	0–110	0.03–0.08	2–18	0.5–21	6–23	0–7
3–4 years	70–140	0–110	0.04–0.08	1–18	0.5–21	4–24	0–5
5–7 years	65–140	0–110	0.04–0.08	0.5–14	0.5–24	4–26	0–4
8–11 years	60–130	-15–110	0.04–0.09	0–14	0.5–25	4–25	0–4
12–15 year	65–130	-15–110	0.04–0.09	0–14	0.5–21	4–25	0–4
>16 years	50–120	-15–110	0.05–0.10	0–14	0.5–23	4–21	0–4

R/S RATIO: MEAN (LOWER LIMIT - UPPER LIMIT)

	0-1mo	1-6mo	6mo-1yr	1-3yr	3-8yr	8-12yr	12-16yr	Adult
V1	1.5 (0.5-19)	1.5 (0.3-S=0)	1.2 (0.3-6)	0.8 (0.5-4)	0.65 (0.1-2)	0.5 (0.15-1)	0.3 (0.1-1)	0.3 (0-1)
V6	2 (0.1-S=0)	4 (1.5-S=0)	6 (2-S=0)	20 (3-S=0)	20 (2.5-S=0)	20 (4-S=0)	10 (2.5-S=0)	9 (2.5-S=0)

PR INTERVAL BY AGE AND HEART RATE: MEAN (UPPER LIMIT OF NORMAL)

	0-1 mo	1-6 mo	6 mo-1 yr	1-3 yr	3-8y r	8-12 yr	12-16 yr	Adult
< 60						0.16 (0.18)	0.16 (0.19)	0.17 (0.21)
60-80					0.15 (0.17)	0.15 (0.17)	0.15 (0.18)	0.16 (0.21)
80-120	0.10 (0.12)				0.14 (0.16)	0.15 (0.16)	0.15 (0.17)	0.15 (0.20)
100-120	0.10 (0.12)			(0.15)	0.13 (0.16)	0.14 (0.15)	0.15 (0.16)	0.15 (0.19)
120-140	0.10 (0.11)	0.11 (0.14)	0.11 (0.14)	0.12 (0.14)	0.13 (0.15)	0.14 (0.15)		0.15 (0.18)
140-160	0.09 (0.11)	0.10 (0.13)	0.11 (0.13)	0.11 (0.14)	0.12 (0.14)			(0.17)
160-180	0.10 (0.11)	0.10 (0.12)	0.10 (0.12)	0.10 (0.12)				
> 180	0.09	0.09 (0.11)	0.10 (0.11)					

RHYTHM						
PARAMETER		NL	PT	INTERPRETATION		
Ventricular Rate				☐ Normal for Age ☐ Bradycardia: ↓ for Age ☐ Tachycardia: ↑ for Age	= 1500/(# small boxes (R – R)) If irregular = # complexes on rhythm strip x 6	
Regularity				☐ Normal: Regular ☐ Regularly Irregular: ☐ Sinus Arrhythmia, ☐ Other ☐ Irregularly Irregular: ☐ Atrial fibrillation, ☐ Other		
QRS Complex	QRS Interval			☐ Normal: Narrow (Supraventricular: Origin above AV node0) ☐ Abnormal: Wide ☐ Ventricular rhythms ☐ Bundle Branch Blocks (see QRS morphology) ☐ Abnormal: “pseudo wide’, delta wave appears to ↑ QRS duration ☐ Wolf Parkinson White (aberrant conduction short PR)		
	Morphology			☐ Normal (includes rsR′, V1,V2, with a normal QRS duration) ☐ Abnormal ☐ Ventricular Ectopy: PVC’s (see P > QRS below) ☐ Ventricular Fibrillation ☐ Ventricular Tachycardia: Monomorphic ☐ Ventricular Tachycardia: Polymorphic (Torsades) ☐ Bundle Branch Blocks ☐ RBBB: RAD, Wide QRS, V1, V2 . RSR′, ‘V5,V6, I. ‘Slurred’ S ☐ LBBB: LAD, Wide QRS V5, V6, I. ‘Blunted’, Pos QRS, Inverted T V1-V3. Absence of Q waves I, V5, V6		
	QTc Interval = ___QT____ √ RR Interval			☐ < 490 (< 6 mo) ☐ < 440 (men) ☐ < 460 (women)	Long: ↓Ca, carditis, head injury, congenital, meds	Short: ↑Ca, Digoxin, congenital
P Wave	PR Interval			☐ Normal ☐ Prolonged: Heart blocks, MI, carditis, Dig, ↑ K+, Epstein’s, ASD ☐ Shortened: Pre-excitation (WPW w/delta), glycogen storage disease ☐ Variable (wandering atrial pacemaker, Wenckebach (Mobitz 1)		
	P Wave Axis			☐ Normal (0-90 degrees): Upright I, AVF = Sinus rhythm ☐ Abnormal (≠ 0-90 degrees): Non-Sinus rhythm		
	P Morphology			☐ Normal: Unifocal, (duration < 90 msec, height < 3 mm) ☐ Abnormal ☐ Multifocal: ☐ Wandering Atrial Pacer ☐ Multifocal Atrial Tachy ☐ Atrial Fibrillation ☐ Atrial Flutter ☐ Right Atrial Enlargement: Peaked (< 1yr ≥ 3mm. > 1yr > 2.5mm ☐ Left Atrial Enlargement Wide (>100 msec), bimodal		
P:QRS Ratio (# P Waves:# QRS)				☐ P:QRS Ratio = 1:1, with a normal PR Interval ☐ Normal Sinus Rhythm ☐ Sinus Bradycardia ☐ Sinus Tachycardia ☐ Supraventricular Tachycardia (if p waves present) ☐ Atrial Fibrillation with 1:1 Conduction ☐ Atrial Flutter with 1:1 Conduction		
				☐ P:QRS Ratio = 1:1, with a prolonged PR interval = 1° Heart Block		
				☐ P > QRS ☐ 2° Heart Block ☐ Mobitz 1(Wenckebach): Dropped QRS, progressive ↑ PR ☐ Mobitz 2: Dropped QRS without progressive ↑ PR ☐ 3° Heart Block: Separate P wave & QRS progression, fixed P-P ☐ Atrial Fibrillation (without 1:1 conduction) ☐ Atrial Flutter (without 1:1 conduction)		
				☐ P < QRS: Ventricular Ectopy (PVC’s) Morphology ☐ Unifocal ☐ Multifocal Pattern ☐ Couplets ☐ Runs of ≥ 3 ☐ Bigeminy ☐ Trigeminy		

HEART SIZE

PARAMETER		NL	PT	INTERPRETATION
QRS Axis				☐ Normal: Axis between lower and upper limits ☐ Right Axis Deviation: > Upper Limit = RVH, RBBB ☐ Left Axis Deviation: < Lower Limit: LBBB ☐ Superior Axis (-30 to -120), AV Canal, Tricuspid Atresia
Atria	Right Atrial Enlargement			☐ Normal ☐ Peaked P waves (< 1 year ≥ 3 mm, > 1year, > 2.5 mm)
	Left Atrial Enlargement			☐ Normal ☐ Wide (> 80 msec < 1yr, > 100 msec > 1 year), bimodal P waves
Ventricular Enlargement				
Ventricles Measure LL. UL. PT R V1 S V1 R V6 S V6 R/S VI R/S V6 LL: Lower Limit of Normal UL; Upper Limit of Normal PT: Patient	Right Ventricular Hypertrophy			☐ Right Axis Deviation: Axis > Upper Limit (See QRS Axis) ☐ Voltage Criteria ☐ R V1 > Upper Limit of Normal ☐ S V6 > Upper Limit of Normal ☐ R/S ratio V1 > Upper Limit of Normal ☐ R/S ratio V6 < 1 mm (after 1 month) ☐ Other criteria ☐ Upright T V1 (3 days – 6 years) ☐ Q waves V1. qR or qRs pattern ☐ QRS-T angle = QRS axis – T wave axis (> 90° = heart strain)
	Left Ventricular Hypertrophy			☐ Left Axis Deviation: Axis < Lower Limit (See QRS Axis) ☐ Voltage Criteria ☐ S V1 > Upper Limit of Normal ☐ R V6 > Upper Limit of Normal ☐ R/S ratio V1 < Lower Limit of Normal ☐ Other criteria ☐ Q ≥ 4mm in V5-6 +/- Tall T ☐ QRS-T angle = QRS axis – T wave axis (> 90° = heart strain)

ISCHEMIA, INFARCTION, INFLAMMATION

PARAMETER	NL	PT	INTERPRETATION
Q Waves			☐ Normal: II, III, AVF, V5-6 ☐ Duration < 0.4 msec, ☐ Ht < 5 mm limb, <2-3 mm precordial ☐ Abnormal: present V1-2 or exceeds duration, height criteria
ST Segments			☐ Normal: Isoelectric, limb leads +/- 1mm, precordial leads +/- 2mm ☐ Early repolarization (adolescent, young adults) typically V2-5 ☐ J point elevation, concave ST segment elevation, upright T ☐ J point and ST depression with up-sloping ST ☐ Abnormal: ☐ ↑or ↓ > 5mm limb, > 2-3mm precordial ☐ Down sloping ST with biphasic inverted T ☐ Convex ST elevation (“Tomb stones”) = STEMI ☐ Brugada: V1-3 with J point elevation, down sloping ST, ↓ T
T Waves			☐ Normal ☐ Negative T waves V1, AVR (right sided leads) ☐ Juvenile Repolarization: ↓ T waves V1-V4, ↑ by 8-12 years ☐ Abnormal ☐ Peaked: LVH, hyperkalemia, early repolarization ☐ Flattened: Pericarditis/myocarditis, hypokalemia, hypothyroid ☐ Inverted: Ischemia, newborns, increased ICP

MISCELLANEOUS EKG FINDINGS

PROCESS	Nl	ABNORMAL FINDINGS
Hyperkalemia	☐	☐ Peaked T waves, ↑ PR interval, ↑ QRS → Sinusoidal wave, Vent fibrillation
Hypokalemia	☐	☐ PVC’s, U waves, flat or diphasic T waves, ↓ST seg, late →↑ PR, SA block
U waves	☐	☐ Deflection after T wave, normal < 1/3 height of T waves, > 1/3 height = ↓ K+
Osborne J Wave	☐	☐ Hypothermia: J point elevation, “hump” where QRS and ST segment join
Pulmonary Emb	☐	☐ ↓ T V1-2, $S_1Q_3T_3$ pattern, +/- RBBB, ↑ ST and T wave inversion, RV strain
Pericarditis	☐	☐ Diffuse, concave ↑ST, ↓ST V1, AVR, ↓ PR except V1, AVR), T wave variable

SUMMARY

Rhythm	☐	☐ Abnormal (describe):
Heart Size	☐	☐ Abnormal (describe):
Ischemia/Infarct	☐	☐ Abnormal (describe):
Miscellaneous	☐	☐ Abnormal (describe):
INTERPRETATION:		

APPENDIX: APPROACH TO ARRHYTHMIAS

An approach to identifying an abnormal rhythm is provided in the check list above. It in involves an assessment of rate, pattern, QRS (width, morphology, QTc), P wave (PR interval. P wave axis, morphology) and the P:QRS ratio.

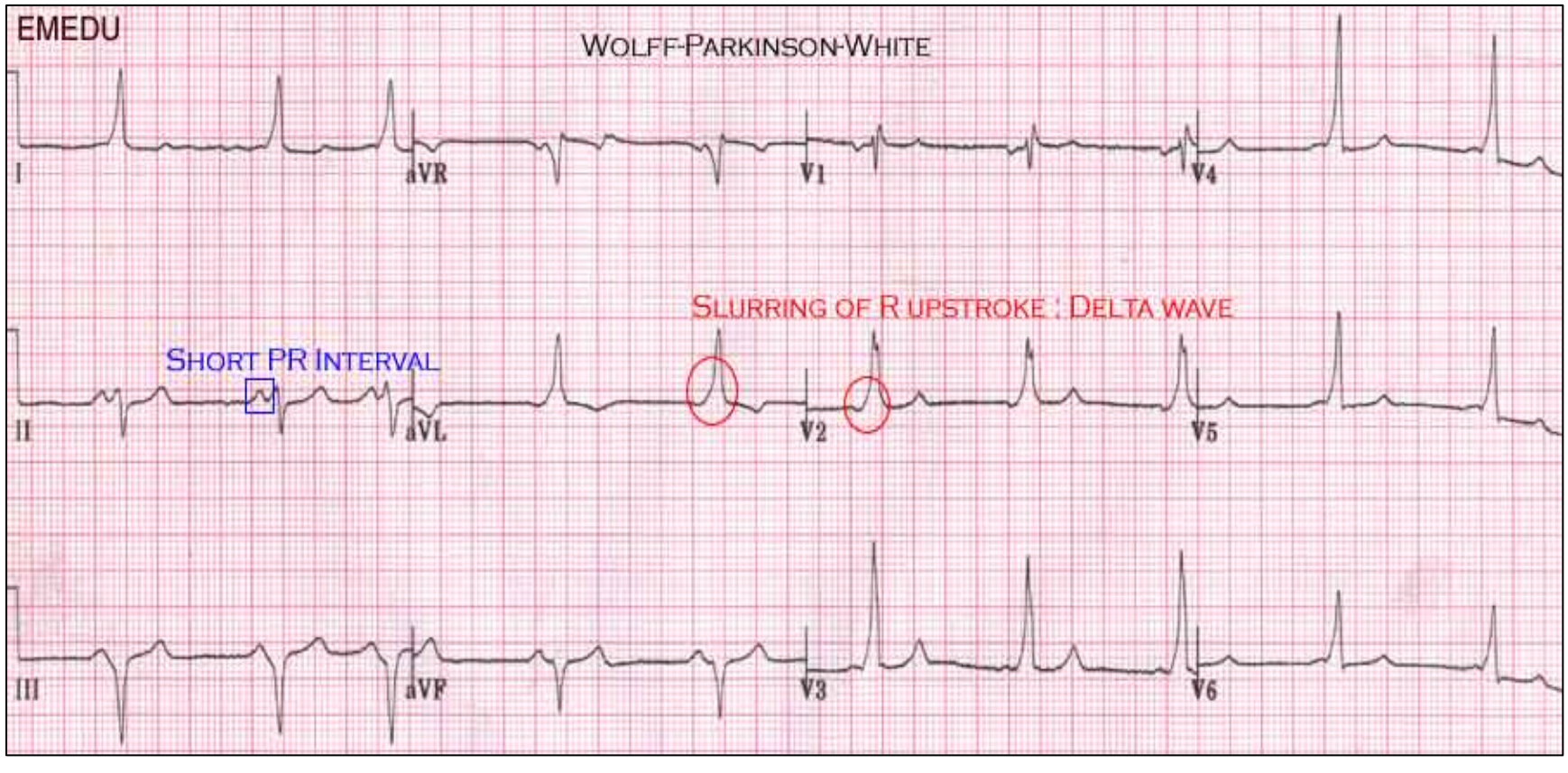
Many arrhythmias will be identified by this approach or have a characteristic pattern (e.g. Ventricular tachycardia). Some arrhythmias may have terminated prior to presentation and have subtle EKG findings suggesting a risk for an arrhythmia. For example, a prolonged QT interval may be suggestive of a ventricular arrhythmias.

See:
PEM Guide: Cardiology: Arrhythmias: An Overview
PEM Guide: Cardiology: Cardiac Pacing for Bradycardia
PEM Guide: Cardiology: Supraventricular Tachycardia
PEM Guide: Cardiology: Ventricular Arrhythmias

SYNDROMES LEADING TO ARRHYTHMIAS	
SYNDROME	EKG FINDING
1. Wolff-Parkinson-White	Short PR, delta wave (Lead II), pseudo-wide QRS
2. Brugada Syndrome	Elevation of the J point, coved-type ST segment, inverted T wave in V1 and V2.
3. Hypertrophic Cardiomyopathy	LVH, LAD, prominent Q waves (septal hypertrophy) deep ↓ T wave (inferior and lateral leads)
4. Arrhythmogenic RV dysplasia	Epsilon wave V1-4, QRS > 110 msec, ↓ T V1-3

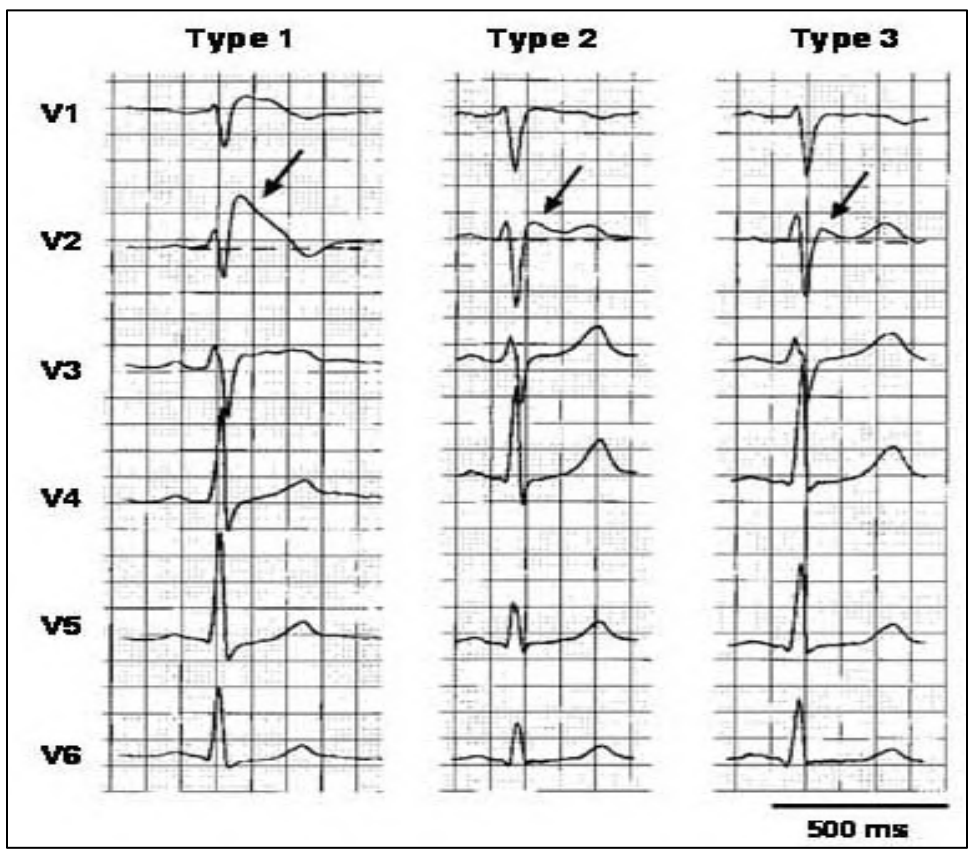
1. **WPW SYNDROME (WOLFF-PARKINSON WHITE)** is a type of supraventricular tachycardia (SVT). EKG changes suggestive of WPW include a shortened PR interval and a slurring of the R wave upstroke (delta wave). A “pseudo-wide” QRS can also be found due to the delta wave.

WEB LINK: LITF EKG LIBRARY: WPW



2. BRUGADA SYNDROME
Sodium channel defect leading to ventricular tachycardia.

WEB LINK: LITF EKG LIBRARY: BRUGADA



BRUGADA

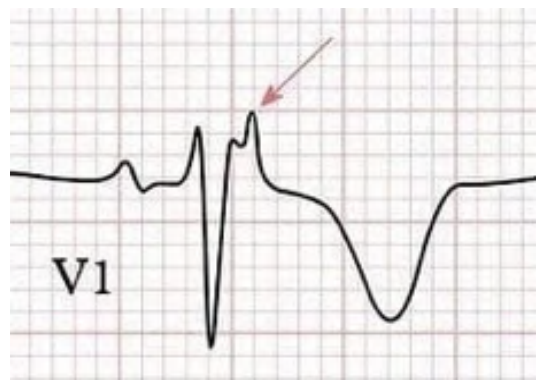
Type 1:
1. Pronounced elevation of the J point,
2. A coved-type ST segment,
3. Inverted T wave in V1 and V2.
(Type 1 pattern is diagnostic of Brugada)

Type 2:
Saddleback ST-segment elevated by > 1 mm

Type 3:
ST segment is elevated < 1 mm

3. ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA (ARVD): An inherited disorder characterized by fibrosis and fatty replacement of the right ventricle leading to ventricular dysrhythmias. An epsilon wave is most specific (seen in 30%). Visualization of epsilon waves can be enhanced with the use of Fontaine leads (RA→Manubrium, LA→Xiphoid, LL→V4).

WEB LINK: LITFL EKG LIBRARY: ARVD

EKG CHARACTERISTICS: ARVD	
Epsilon wave: Small (+) deflection in end of QRS V1-4	
T wave inversion in V1-V3	
S wave upstroke > 55 msec in V1-V3	
QRS width > 110 msec in V1-V3	
Ventricular tachycardia with LBBB morphology (RV)	
*Also seen in posterior or RV MI, sarcoidosis	
	EPSILON WAVE

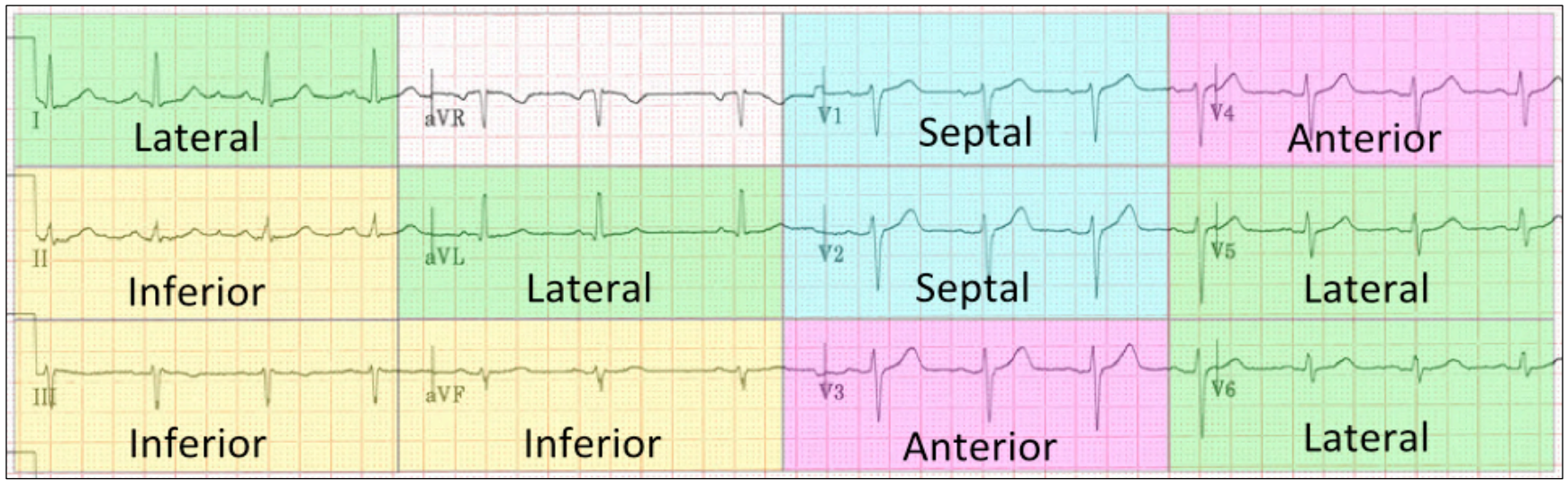
4. HYPERTROPHIC CARDIOMYOPATHY (HCM) is an autosomal dominant disorder that results in asymmetric hypertrophy of the left ventricle, which causes subaortic stenosis impeding left ventricular outflow. HCM patients are also at risk for a variety of atrial and ventricular dysrhythmias. EKG changes may include sign of left ventricular hypertrophy, left axis deviation, prominent Q waves (due to septal hypertrophy) and deep T wave inversions in the inferior or lateral leads.

WEB LINK: LITF EKG LIBRARY: HCM

APPENDIX: CHEST PAIN: ST SEGMENT CHANGES

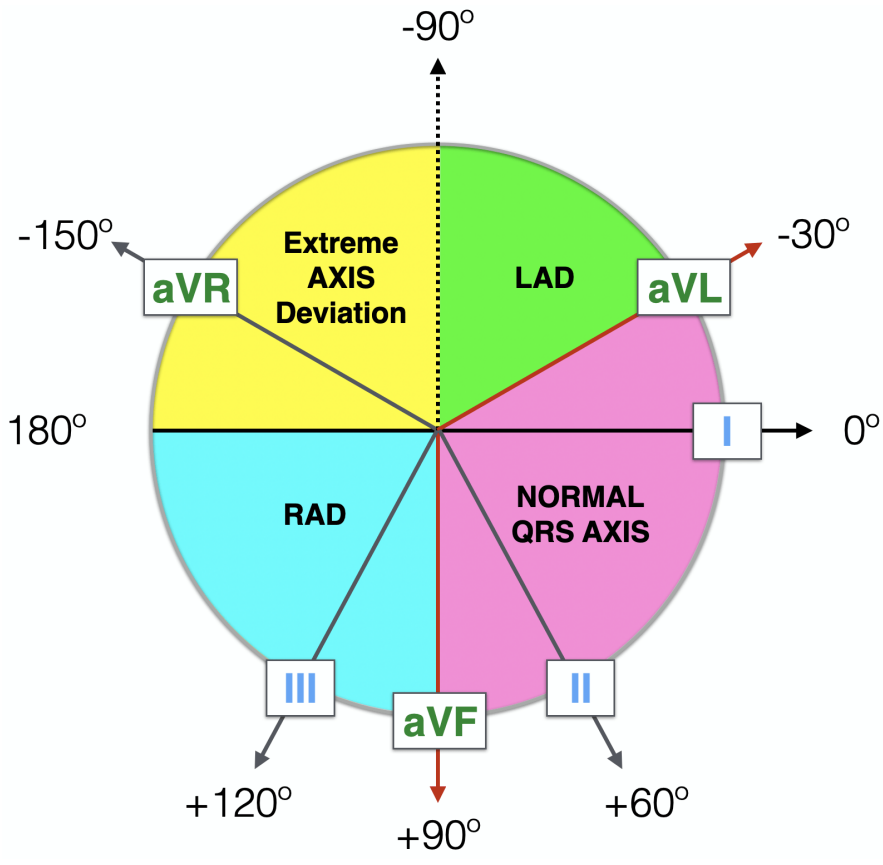
See: PEM Guide: Cardiology: Pericarditis

ST SEGMENT ELEVATION: COMPARISON OF COMMON CAUSES			
	Pericarditis	ST Elevation Myocardial Infarction	Benign Early Repolarization
J Point Elevation	No	No	Yes
J Point Notching	No	No	Yes
Leads Involved	Diffuse	Coronary distribution[3]	Precordial (V2-5)
ST Elevation Type[1]	Concave	Convex, concave, horizontal	Concave
ST:T Wave Ratio	> 0.25	N/A	< 0.25
PR Depression[1]	Yes	No	No
Change Over Time	Yes (days)	Yes (hours)	No
ST Elevation III:II	Lead III < Lead II	Lead III > Lead II	
Reciprocal Changes[2]	No	Yes	No
T Waves	Normal T wave amplitude	+/- T wave inversions	Tall T waves in QRS direction minor asymmetry
1. ST elevation and PR depression are measured relative to the TP segment 2. AVR and VI are right sided leads. Not counted as reciprocal ST depression 3. Septal (V1-2), Ant (V3-4), Lat (I, AVL, V5-6), Infer (II, III, AVF), RV (V1, AVR)			



RECIPROCAL CHANGES		
SITE	FACING	RECIPROCAL
SEPTAL	V1, V2	None
ANTERIOR	V3, V4	None
ANTEROSEPTAL	V1, V2, V3, V4	None
LATERAL	I, AVL, V5, V6	II, III, AVF
ANTEROLATERAL	I, AVL, V3, V4, V5, V6	II, III, AVF
INFERIOR	II, III, AVF	I, AVL

APPENDIX: AXIS DEVIATION



HEART TRANSPLANT

INTRODUCTION (ELLEN DUNCAN, MD, PHD; ARIN TEYMOURI, MD; REBECCA ROGOFF, NP; RAKESH SINGH, MD, 4/2022).
The first pediatric heart transplant took place in 1967; currently, about 600 are performed annually, and there have been many technological advances since the first transplant. The median survival is approximately 25 years. Because of the increasing prevalence, providers working in pediatric emergency departments should familiarize themselves with potential post-transplant complications. Every heart transplant patient seen in the ED should be discussed with the cardiology team as soon as possible.

POST-TRANSPLANT COMPLICATIONS	
1	Rejection
2	Infections
3	Cardiac allograft vasculopathy (CAV)
4	Cardiac dysrhythmias
5	Malignancy and post-transplant lymphoproliferative disease (PTLV)
6	Side effects of immunosuppressive medication regimens

1. REJECTION

INTRODUCTION: Rejection is one of the most common complications after transplantation. Rejection often occurs during the first year, though it can happen after that time. It is the leading cause of death in the first 5 years after transplantation and second leading cause of death within the 1 year (#1 graft failure). There are two different types of rejection, acute cellular and antibody mediated, which are differentiated based on endo-myocardial biopsy. The risk of rejection has decreased with the advancement of immunosuppressive medications, but it remains a significant concern

CLINICAL MANIFESTATIONS: Symptoms of rejection vary by age. Whereas infants may have nonspecific symptoms, older children have symptoms more classically seen in heart failure. Patients may also have vague symptoms such as abdominal pain and vomiting. Notably, symptoms may be mild or absent in a significant number of patients with rejection. Fever and other symptoms of rejection may be mistaken for infection.

CLINICAL MANIFESTATIONS OF REJECTION		
SYMPTOMS: INFANTS	SYMPTOMS: CHILDREN	PHYSICAL EXAM
Poor feeding	Shortness of breath	Tachycardia
Lethargy	Peripheral edema	S3 gallop
Irritability	Palpitations	Jugular venous distention
	Syncope	New murmur
	Exercise intolerance	Hepatomegaly
	Abdominal pain, nausea, vomiting, diarrhea	Poor perfusion (shock)

ANCILLARY TESTING: Laboratory and radiographic studies can be helpful in evaluating patients with suspected rejection.

ANCILLARY FINDINGS		
LABORATORY	IMAGING	EKG
BNP (may be normal or at baseline) BNP more useful	CXR: Nonspecific, Cardiomegaly Pleural effusion Pulmonary edema	Sinus tachycardia
Troponin (may be normal)		Atrial or ventricular dysrhythmias
Low tacrolimus trough levels may indicate medication noncompliance		Low-voltage QRS complexes
	Echo: ventricular systolic dysfunction, valvar regurgitation, pericardial effusion	ST-T wave changes

MANAGEMENT: As patients with rejection are at risk for sudden cardiopulmonary arrest, treatment should be initiated as soon as possible in consultation with the cardiology, cardiac critical care, and heart transplant teams.

Initial treatment includes: a STAT echocardiogram, two peripheral intravenous lines, NPO status, and type and screen. Patients in extremis should receive hemodynamic and respiratory support as needed. This may include initiation of CPAP/BiPAP, inotropes such as Epinephrine or Milrinone, judicious fluid boluses). ECMO consult is warranted in patients with severe ventricular dysfunction or cardiorespiratory instability (tachycardia, hypotension, mental status changes, requires intubation). For patients that experience cardiac arrest, atropine should be avoided as a code medication given the denervated heart (give epinephrine per protocol). See PEM Guide: Cardiology: Cardiogenic Shock

Subsequent treatment in the cardiac ICU may include high-dose methylprednisolone (10mg/kg/dose IV q12h for 3 days), antithymocyte globulin (ATG), intravenous immune globulin (IVIG), and monoclonal antibodies such as rituximab and plasmapheresis.

2. INFECTIONS

INTRODUCTION: Post-transplant immunosuppression to prevent allograft rejection significantly increases the risk of infection. For this reason, post-cardiac transplant patients are often maintained on antibiotic and/or antiviral regimens, especially in the first 6 months after transplant. This typically includes prophylaxis against oropharyngeal candidiasis (Nystatin), *Pneumocystis jirovecii* pneumonia (Trimethoprim/Sulfamethoxazole), and CMV (Valganciclovir).

Post-transplant infections include nosocomial infections (donor or recipient), activation of latent infections, opportunistic infections, and community acquired infections. While nosocomial and surgical site infections are common in the first month, opportunistic and community acquired infections predominate after that time.

CLINICAL MANIFESTATIONS: Fever is the most cost common ED presenting complaint. Any post-transplant patient with a fever should be evaluated for infection, though not all patients will mount a fever. Typical signs and symptoms may be absent in the immunocompromised state.

The most commonly encountered infections are pneumonia and other respiratory tract infections, as well as gastrointestinal infections. CMV is the most common viral infection and can present on a spectrum from upper respiratory infection to disseminated disease (pneumonitis, hepatitis, meningoencephalitis). The severity of disease is proportional to the degree of immunosuppression.

POST-TRANSPLANTATION INFECTIONS				
Type	Organism	Time	Treatment	Notes
Bacterial	*Staphylococcus* spp.	Early post-transplant		
	Pseudomonas spp.	Early post-transplant		
	Enterobacter cloacae	Early post-transplant		
	Streptococcus pneumoniae	One year post-transplant		immune response to pneumococcal vaccine
Viral	Cytomegalovirus (CMV)	Peak 6-8 weeks post-transplant	Prophylaxis: Valganciclovir, Duration: 3-6 months	Associated with acute rejection and coronary allograft graft vasculopathy
	Epstein-Barr virus (EBV)			Post-transplant lymphoproliferative disease (PTLD)
	Herpes Simplex Virus (HSV)		Acyclovir	Primary infection or reactivation
	Varicella zoster virus (VZV)			Primary infection or reactivation
	Influenza virus			
Fungal (rare)	*Pneumocystis jirovecii*		Prophylaxis: Trimethoprim/ Sulfamethoxazole Duration: 3-6 months	1% of transplant recipients Pneumonitis, hilar adenitis
	Candida spp.		Prophylaxis: Nystatin	
	Aspergillus			

ANCILLARY TESTING Work up for potential infection comprises bloodwork, including cultures of blood and urine as well as other sites (e.g. stool, CSF, central lines) as clinically indicated. Chest radiography can help evaluate for pneumonia and hilar adenopathy (infection vs lymphoproliferative disease).

MANAGEMENT: Typical childhood infections such as acute otitis media may be treated on an outpatient basis. Patients with more severe infections and fever without a source will require admission. Empiric and targeted antibiotics and antiviral coverage should be discussed with pediatric infectious disease. Patients on steroid therapy should receive stress-dose steroids given the risk of adrenal insufficiency.

3. CARDIAC ALLOGRAFT VASCULOPATHY (CAV)

INTRODUCTION: CAV is a common late post-transplant complication affecting approximately one-third of patients in the first 10 years post-transplant. It is an accelerated form of coronary artery disease due to fibrous intimal hyperplasia resulting in loss of proximal or distal coronary vessels.

CLINICAL MANIFESTATIONS: CAV manifests as systolic and/or diastolic dysfunction with subsequent graft failure. Symptoms of myocardial ischemia may also be present.

MANAGEMENT: CAV is managed through a combination of m-TOR inhibitors (Sirolimus, Everolimus) as well as aspirin, beta blockers, and statins. Coronary stent placement may also be useful.

4. CARDIAC DYSRHYTHMIAS

INTRODUCTION: Post-transplant patients may have a variety of different dysrhythmias, most commonly atrial dysrhythmias such as ectopic atrial tachycardia, intra-atrial reentrant tachycardia, atrial flutter, and atrial fibrillation. Presence of a dysrhythmia may indicate rejection or CAV.

MANAGEMENT: Medical management includes Amiodarone, beta-blockers, and Digoxin. Use caution with Adenosine for SVT given risk for prolonged heart block (start with 25% of recommended dose). Transplanted hearts are denervated, and vagal maneuvers and Adenosine may be ineffective or have a paradoxical response.

5. MALIGNANCY AND POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE

INTRODUCTION: Post-transplant oncologic complications are comparatively uncommon, and the majority of patients who develop oncologic complications develop post-transplant lymphoproliferative disease (PTLD). PTLD is generally related to Epstein-Barr infection (EBV), and is characterized by abnormal B cell proliferation. PTLD has protean manifestations, from benign lymphoid hyperplasia to aggressive lymphoma, especially in the GI or pulmonary systems.

MANAGEMENT: Management generally consists of reduction in the immunosuppressive regimen, but this can lead to increases in other complications such as rejection.

6. SIDE EFFECTS OF IMMUNOSUPPRESSIVE MEDICATION REGIMENS

INTRODUCTION: Post-transplant immunosuppressive medication regimens include numerous drugs, whose common side effects are listed in the below. Drug-drug interactions can occur between immunosuppressive medications and other medications such as antibiotics and anticonvulsants. For example, macrolides and azole antifungals can increase calcineurin inhibitor levels significantly, leading to toxicity. Alternatively, anti-epileptics (Phenytoin, Phenobarbital, Carbamazepine) and antibiotics (Cephalosporins, Sulfonamides, Rifampin, Isoniazid) increase calcineurin inhibitor clearance, leading to an increased risk of rejection.

MANAGEMENT: Consultation with the heart transplant team and pharmacy is essential, as is monitoring immunosuppressant levels. NSAIDs should be avoided given the risk of renal toxicity in patients on calcineurin inhibitors (Acetaminophen is ok).

IMMUNOSUPPRESSIVE MEDICATION ADVERSE EVENTS		
MEDICATION CLASS	EXAMPLES	SIDE EFFECTS
Calcineurin Inhibitors	Cyclosporine Tacrolimus (Prograf)	Hypertension Renal dysfunction Diabetes mellitus, Electrolyte: ↑ Glucose, ↑ K, ↓ Mg Neurotoxicity: HA, tremor, seizure, encephalopathy Lymphoproliferative disorder
Antiproliferative Agents	Mycophenolate mofetil Azathioprine (Cellcept)	Hypertension Bone marrow suppression GI side effects (MM)
mTOR (Mechanistic Target of Rapamycin) receptor inhibitors	Sirolimus (Rapamune) Everolimus (Afinitor)	Hypertension Bone marrow suppression, Mucosal irritation
Corticosteroids		Hypertension ↑ Glucose GI bleeding Cushingoid changes Mood changes including psychosis
Antilymphocyte Antibodies	Anti-thymocyte gamma Globulin (polyclonal)	Fever, serum sickness, anaphylaxis, anemia, platelets
	OKT3, IL-2 receptor antibody (monoclonal)	IL2: Rare anaphylaxis OKT3 (1st 3 days): HA, aseptic meningitis, encephalopathy, seizure, nausea, vomiting, diarrhea, pulmonary edema

HYPERTENSIVE EMERGENCIES

INTRODUCTION (NICOLE GERBER, M.D. 9/2018)
Hypertension is relatively rare in the pediatric population, with a prevalence of 1-2%. Severe hypertension is a potentially life-threatening medical emergency. Stage II hypertension is also known as hypertensive crisis. Hypertensive crisis is classified as hypertensive urgency, without associated evidence of end organ damage, and hypertensive emergency, with associated with evidence of end organ damage. While hypertensive urgencies are less severe, they can rapidly progress to hypertensive emergencies. Below are definitions of hypertension and potential etiologies in the pediatric population.

BLOOD PRESSURE CATEGORIES AND STAGES		
	1-13 years	≥ 13 years
Normal BP	< 90th percentile	< 120/< 80 mm Hg
Elevated BP	≥ 90th to < 95th percentile OR 120/80 mm Hg to < 95th percentile[1]	120/<80 to 129/<80 mm Hg
Stage I HTN	≥ 95th to < 95th percentile + 12 OR 130/80 to 138/89 mm Hg[1]	130/80 to 139/89 mm Hg
Stage II HTN	≥ 95th percentile + 12 mm Hg OR ≥ 140/90 mm Hg[1]	≥ 140/90 mm Hg
1. Whichever is lower See Appendix for blood pressure percentiles by age and sex		

HYPERTENSIVE CRISES	
Hypertensive Urgency	Stage II HTN without evidence of target organ injury
Hypertensive Emergency	Stage II HTN with evidence of target organ injury

Blood pressure should be obtained from the right arm at heart level. The cuff should be 40% of arm circumference and located midway between the acromion and the olecranon. A too large cuff can result in a falsely low BP. A too small cuff may result in a falsely high BP.

Hypertension obtained by an automatic oscillometric device should be repeated with auscultation and a sphygmomanometer. Four extremity BP's can be used to determine if coarctation of the aorta is the etiology of hypertension. Right upper extremity BP will be greater than BP in left upper extremity and both legs if the coarctation occurs proximal to the left subclavian artery. BP will be greater in both upper extremities than in the legs if the coarctation occurs distal to the left subclavian artery.

ETIOLOGY
There is an extensive differential diagnosis of causes of pediatric hypertensive. In general, the likelihood of primary hypertension increases directly proportion to age. The younger the age and the higher the blood pressure the greater the likelihood that there is a secondary cause of hypertension. Primary hypertension is the most commonly seen in children over age 6 years. It is associated with obesity and a family history of hypertension. Primary hypertension is most commonly systolic. In contrast, secondary hypertension is most commonly diastolic. Renal parenchymal and vascular disease is the most likely cause of secondary hypertension in pediatric patients.

DIFFERENTIAL DIAGNOSIS: SECONDARY HYPERTENSION	
RENAL	MEDICATIONS (continued)
Congenital dysplastic kidneys	Vitamin D intoxication
Polycystic kidney disease	Cocaine
Hydronephrosis	Alcohol
Renal artery stenosis	Lead, thallium, mercury toxicity
Renal vein thrombosis	Discontinuation of anti-hypertensives
Glomerulonephritis	CENTRAL NERVOUS SYSTEM
Acute tubular necrosis	Intracranial hemorrhage
Hemolytic-uremic syndrome (HUS)	Increased intracranial pressure
Obstructive uropathy	Autonomic dysfunction
Pyelonephritis with renal scarring	AUTOIMMUNE
CARDIOVASCULAR	Lupus
Coarctation of the aorta	Polyarteritis nodosa
Arteritis: Takayasu	Rheumatoid arthritis
Kawasaki	Goodpasture’s disease
Henoch-Schonlein purpura (HSP)	Wegner’s granulomatosis
ENDOCRINE	ONCOLOGY
Cushing syndrome	Pheochromocytoma
Hyperthyroidism	Wilms tumor
Hyperparathyroidism	Brain tumors
Congenital adrenal hyperplasia (CAH)	GENETIC
Hyperaldosteronism	Gordon syndrome
MEDICATIONS	Liddle syndrome
Corticosteroids	Turner syndrome
Decongestants	William syndrome
NSAIDS	Friedreich ataxia
Tacrolimus	Von Hippel-Lindau syndrome
Cyclosporine	Neurofibromatosis
Erythropoietin	Multiple endocrine neoplasia (MEN)
Amphetamines	OTHER
Oral contraceptives	Pregnancy (pre-eclampsia)
Anabolic steroids	Umbilical artery catheterization
Phencyclidine (PCP)	

COMPLICATIONS	
CNS	Altered mental status, hypertensive encephalopathy, stroke (hemorrhagic, ischemic, PRES (Posterior reversible encephalopathy syndrome), seizures
EYE	Retinal hemorrhage/exudates
CARDIAC	Cardiac: Ischemia, myocardial ischemia or infarction, acute left ventricular dysfunction, acute pulmonary edema, aortic dissection
OTHER	Acute renal failure

CLINICAL PRESENTATION

Hypertensive emergencies present with signs of end organ damage. Symptoms may be subtle and non-specific in a child. Patients with an acute onset of hypertension are generally more symptomatic than those with a sub-acute or chronic onset of hypertension. Hypertensive encephalopathy is the most common complication in pediatrics. Hypertension results in endothelial damage which leads to cerebral edema and failure of cerebral auto-regulation.

SYMPTOMS OF END ORGAN DAMAGE	
CNS	Headache, nausea, vomiting (particularly in the morning), ataxia, mental status changes, seizures
EYE	Visual changes
RENAL	Renal insufficiency: Flank pain, hematuria
CARDIAC	Congestive heart failure: Shortness of breath chest pain, chest pain, diaphoresis

PHYSICAL EXAMINATION FINDINGS	
FINDING	CAUSE
Edema	Congestive heart failure, renal failure
Thyromegaly, exophthalmos	Hyperthyroidism
Decreased femoral pulses	Coarctation of the aorta
Abdominal mass	Renal structural anomalies, Wilms tumor, neuroblastoma
Sympathomimetic toxidrome	Tachycardia, sweating, mydriasis, agitation. Cocaine, amphetamines
Fundoscopy	Papilledema, retinal hemorrhage, exudates

EVALUATION

Evaluation should always initially include repeating the blood pressure with a manual blood pressure cuff of the appropriate size. Once confirmed, evaluation should include a combination of laboratory testing and imaging based on the most likely etiology.

LABORATORY EVALUATION	
URINE	Urinalysis: Occult renal disease, chronic UTIs
	Urine steroid levels
	Urine pregnancy test (pre-eclampsia)
	Urine toxicology screen (sympathomimetics e.g. cocaine)
BLOOD	Renal function: BUN, Creatinine
	Electrolytes (Na, K, Ca, HCO_3) for endocrine/genetic causes
	CBC: Anemia as a sign of chronic disease
	Plasma renin activity
	Plasma steroid levels
	Plasma metanephrines
	Thyroid function tests

RADIOGRAPHIC EVALUATION	
MODALITY	FINDING
Head CT	Evidence of increased ICP
Renal/Bladder Ultrasound	Kidney anatomy
Echocardiogram	Signs of CHF, cardiac obstructive lesions
Renal arteriogram	If high suspicion for renal artery stenosis

MANAGEMENT

Patients with signs and symptoms of end organ damage should be rapidly assessed for the likely etiology of the hypertension and treated promptly. The primary goal of therapy is to lower the mean arterial BP by ¼ of the planned reduction over 8-12 hours, ¼ over the next 8-12 hours and ½ over the next 24 hours. Reduce slowly to preserve cerebral auto-regulation.

MEAN ARTERIAL PRESSURE	= 1/3 systolic BP + 2/3 diastolic BP

There is no single best choice for an antihypertensive in all cases of hypertension. Pediatric medication data is limited to case series or is extrapolated from adult randomized clinical trials. Medication should be selected based on: the proposed etiology, the side effect profile and the severity of symptoms.

CAUTION: Patients with hypertension secondary to increased intracranial pressure should not be treated with antihypertensives. The goal of therapy in the setting of increased intracranial pressure is to maintain cerebral perfusion pressure. A decrease in blood pressure may result in cerebral ischemia and/or herniation.

HYPERTENSIVE EMERGENCY: APPROACH TO ASSESSMENT & MANAGEMENT
Confirm hypertension: Correct cuff size, auscultation with sphygmomanometer
Rapidly assess for signs and symptoms of end organ damage
Rapidly assess for the likely etiology
Exclude cases for which a reduction in BP may be harmful (e.g. Increased ICP)
Cardiac Monitor: BP, HR q15 minutes
Monitor for loss of pupillary reflex, which indicates retinal ischemia
Have a second IV for bolus fluid administration in case of precipitous decrease in BP
Antihypertensive Medications (see medication section for details below)
Labetalol: Unless beta blocker contraindicated (asthma, CHF)
Nicardipine: 2nd line unless Labetalol contraindication
Sodium Nitroprusside: Most rapidly acting
Additional/alternate therapies
Sympathomimetic (cocaine, amphetamine): Benzodiazepine, Phentolamine
Renal failure: Diuretics, hemodialysis
Severe pain: Analgesics
Neonate with coarctation of the aorta: Prostaglandin E1
Pre-eclampsia: Labetalol, Mg, delivery prevents progression, fetal complications

APPENDIX: ANTIHYPERTENSIVES

CAUTION: Patients with hypertension secondary to increased intracranial pressure should not be treated with antihypertensives. The goal of therapy in the setting of increased intracranial pressure is to maintain cerebral perfusion pressure. A decrease in blood pressure may result in cerebral ischemia and/or herniation.

LABETALOL	
Mechanism	Alpha and Beta-blocker: Lowers peripheral resistance with little or no effect on cardiac output
Pharmacology	3-5-hour half-life, not as easy to titrate
Indication	First line in those without a contraindication of beta blockers
Adverse Effects	May mask hypoglycemia symptoms
Contraindications	Left ventricular failure: Negative inotropic and dromotropic effects, bradycardia
	Asthma, other chronic lung disease e.g. bronchopulmonary dysplasia
	Diabetes
	Cocaine, amphetamine: beta blocker leads to unopposed alpha Adrenergic effect: Increased BP. MI
Dosing	Infusion: 0.2-0.3 mg/kg/hour
	Bolus: 0.2 - 1 mg/kg (max 40 mg)

SODIUM NITROPRUSSIDE	
Mechanism	Direct arteriolar and venous smooth muscle dilator
Pharmacology	Short half-life, continuous infusion only, easily titratable Protect from light to avoid degradation
Indications	Good for severe CHF with severe hypertension
Adverse Effects	Tachyphylaxis, cyanide toxicity (metabolized by erythrocytes to cyanide which is converted to thiocyanate in the liver and excreted by the kidneys.)
Contraindication	Renal failure, hepatic failure, pregnancy
Dosing	0.3–0.5 mcg/kg/min (max 8 mcg/kg/min, most respond by 3 mcg/kg/min)

NICARDIPINE	
Mechanism	Dihydropyridine calcium channel blocker. Selective vasodilation of cerebral and coronary vessels.
Pharmacology	Onset of action within a few minutes, half-life 10-15 minutes Little effect on HR, contractility (unlike other Ca++ channel blockers)
Indication	Sodium Nitroprusside or Labetalol are contraindicated
Adverse Effects	May cause increased intracranial pressure
Dosing	0.5–1.0 mcg/kg/min Increase q15-30 min to a max of 3.0 mcg/kg/min

ESMOLOL	
Mechanism	Cardio-selective B1 blocker
Pharmacology	Very short acting
Indication	May be useful with congenital heart disease
Adverse Effects	Beta blocker contraindications: Asthma, congestive heart failure
Dosing	Load with 100-500 mcg/kg, then infusion of 50-300 mcg/kg/min

HYDRALAZINE	
Mechanism	Arterial vasodilator
Pharmacology	Onset in 5-30 minutes, duration 4-12 hours (Slower onset then Labetalol and Nicardipine, longer duration)
Indication	Mostly been replaced by new medications
Adverse Effects	Flushing, tachycardia, hypotension, lupus-like syndrome
Dose	0.1-0.5 mg/kg/dose to a maximum of 20 mg IV q4-6 hours

FENOLDOPAM	
Mechanism	Selective dopamine agonist: Vasodilation of the renal, coronary, cerebral and splanchnic vasculature
Indication	Used as an alternative to conventional therapy Less potent. Not recommended for initial treatment Little pediatric experience
Adverse Effects	Reflex tachycardia, increased intracranial and intraocular pressure
Dose	0.1-0.2 mcg/kg/min, increase Q15 min to max 0.8 mcg/kg/min

PHENTOLAMINE	
Mechanism	Alpha blocker
Indication	Excess circulating catecholamines: Cocaine, pseudoephedrine, pheochromocytoma
Adverse Effects	Reflex tachycardia and cardiac arrhythmias
Dose	0.1 mg/kg, max 5 mg

APPENDIX: NORMAL BLOOD PRESSURE: BOYS 1-9 YEARS

BLOOD PRESSURE BY AGE AND HEIGHT PERCENTILE: BOYS 1-9 YEARS

		Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile or Measured Height							Height percentile or Measured Height						
Yr	BP%	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
1	Ht in	30.4	30.8	32.6	32.4	33.3	34.1	34.6	30.4	30.8	31.6	32.4	33.3	34.1	34.6
	Ht cm	77.2	78.3	80.2	82.4	84.6	86.7	87.9	77.2	78.3	80.2	82.4	84.6	86.7	87.9
	50th	85	85	85	86	87	88	88	40	40	40	41	41	42	42
	90th	98	99	99	100	100	101	101	52	52	53	53	54	54	54
	95th	102	102	103	103	104	105	105	54	54	55	55	56	57	57
	95th+12	114	114	115	115	116	117	117	66	66	67	67	68	69	69
2	Ht in	33.9	34.4	35.3	36.3	37.3	38.2	38.8	33.9	34.4	35.3	36.3	37.3	38.2	38.8
	Ht cm	86.1	87.4	89.6	92.1	94.7	97.1	98.5	86.1	87.4	89.6	92.1	94.7	97.1	98.5
	50th	87	87	88	89	89	90	91	43	43	44	44	45	46	46
	90th	100	101	101	102	103	103	104	55	55	56	56	57	58	58
	95th	104	105	105	106	107	107	108	57	58	58	59	60	61	61
	95th+12	116	117	117	118	119	119	120	69	70	70	71	72	73	73
3	Ht in	36.4	37	37.9	39	40.1	41.1	41.7	36.4	37	37.9	39	40.1	41.1	41.7
	Ht cm	92.5	93.9	96.3	99	101.8	104.3	105.8	92.5	93.9	96.3	99	101.8	104.3	105.8
	50th	88	89	89	90	91	92	92	45	46	46	47	48	49	49
	90th	101	102	102	103	104	105	105	58	58	59	59	60	61	61
	95th	106	106	107	107	108	109	109	60	61	61	62	63	64	64
	95th+12	118	118	119	119	120	121	121	72	73	73	74	75	76	76
4	Ht in	38.8	39.4	40.5	41.7	42.9	43.9	44.5	38.8	39.4	40.5	41.7	42.9	43.9	44.5
	Ht cm	98.5	100.2	102.9	105.9	108.9	111.5	113.3	98.5	100.2	102.9	105.9	108.9	111.5	113.2
	50th	90	90	91	92	93	94	94	48	49	49	50	51	52	52
	90th	102	103	104	105	105	106	107	60	61	62	62	63	64	64
	95th	107	107	108	108	109	110	110	63	64	65	66	67	67	68
	95th+12	119	119	120	120	121	122	122	75	76	77	78	79	79	80
5	Ht in	41.1	41.8	43.0	44.3	45.5	46.7	47.4	41.1	41.8	43.0	44.3	45.5	46.7	47.4
	Ht cm	104.4	106.2	109.1	112.4	115.7	118.6	120.3	104.4	106.2	109.1	112.4	115.7	118.6	120.3
	50th	91	92	93	94	95	96	96	51	51	52	53	54	55	55
	90th	103	104	105	106	107	108	108	63	64	65	65	66	67	67
	95th	107	108	109	109	110	111	112	66	67	68	69	70	70	71
	95th+12	119	120	121	121	122	123	124	78	79	80	81	82	82	83
6	Ht in	43.4	44.2	45.4	46.8	48.2	49.3	50.2	43.4	44.2	45.4	46.8	48.2	49.4	50.2
	Ht cm	110.3	112.2	115.3	118.9	122.4	125.6	127.5	110.3	112.2	115.3	118.9	122.4	125.6	127.5
	50th	93	93	94	95	96	97	98	54	54	55	56	57	57	58
	90th	105	105	106	107	109	110	110	66	66	67	68	68	69	69
	95th	108	109	110	111	112	113	114	69	70	70	71	72	72	73
	95th+12	120	121	122	123	124	125	126	81	82	82	83	84	84	85
7	Ht in	45.7	46.5	47.8	49.3	50.8	52.1	52.9	45.7	46.5	47.8	49.3	50.8	52.1	52.9
	Ht cm	116.1	118	121.4	1251	128.9	132.4	134.5	116.1	118	121.4	125.1	128.9	132.4	134.5
	50th	94	94	95	97	98	98	99	56	56	57	58	58	59	59
	90th	106	107	108	109	110	111	111	68	68	69	70	70	71	71
	95th	110	110	111	112	114	115	116	71	71	72	73	73	74	74
	95th+12	122	122	123	124	126	127	128	83	83	84	85	85	86	86
8	Ht in	47.8	48.6	50	51.6	53.2	54.6	55.5	47.8	48.6	50	51.6	53.2	54.6	55.5
	Ht cm	121.4	123.5	1278	131	135.1	138.8	141	121.4	123.5	127	131	135.1	138.8	141
	50th	95	96	97	98	99	99	100	57	57	58	59	59	60	60
	90th	107	108	109	110	11	112	112	69	70	70	71	72	72	73
	95th	111	112	112	114	115	116	117	72	73	73	74	75	75	75
	95th+12	123	124	124	126	127	128	129	84	85	85	86	87	87	87
9	Ht in	49.6	50.5	52	53.7	55.4	56.9	57.9	49.6	50.5	52	53.7	55.4	56.9	57.9
	Ht cm	126	128.3	132.1	136.3	140.7	144.7	147.1	126	128.3	132.1	136.3	`140.7	144.7	147.1
	50th	96	97	98	99	100	101	101	57	58	59	60	61	62	62
	90th	107	108	109	110	112	113	114	70	71	72	73	74	74	74
	95th	112	112	113	115	116	118	119	74	74	75	76	86	77	77
	95th+12	124	124	125	127	128	130	131	86	86	87	88	88	89	89

APPENDIX: NORMAL BLOOD PRESSURE: BOYS 10-17 YEARS

BLOOD PRESSURE BY AGE AND HEIGHT PERCENTILE: BOYS 10-17 YEARS

		Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile or Measured Height							Height percentile or Measured Height						
Yr	BP%	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
	Ht in	51.3	52.2	53.8	55.6	57.4	59.1	60.1	51.3	52.2	53.8	55.6	57.4	59.1	60.1
	Ht cm	130.2	132.7	136.7	141.9	145.9	150.1	152.7	130.2	132.7	136.7	141.3	145.9	150.1	152.7
	50th	97	98	99	100	101	102	103	59	60	61	62	63	63	64
	90th	108	109	111	112	113	115	116	72	73	74	74	75	75	76
	95th	112	113	114	116	118	120	121	76	76	77	77	78	78	78
	95th+12	124	125	126	128	130	132	133	88	88	89	89	90	90	90
11	Ht in	53	54	55.7	57.6	59.6	61.3	62.4	53	54	55.7	57.6	59.6	61.3	62.4
	Ht cm	134.7	137.3	141.4	146.4	151.3	155.8	158.6	134.7	137.3	141.5	146.4	151.3	155.3	158.6
	50th	99	99	101	102	103	104	106	61	61	62	63	63	63	63
	90th	110	111	112	114	116	117	118	74	74	75	75	75	76	76
	95th	114	114	116	118	120	123	124	77	78	78	78	78	78	78
	95th+12	126	126	128	130	132	135	136	89	90	90	90	90	90	90
12	Ht in	55.2	56.3	58.1	60.1	62.2	64	65.2	55.2	56.3	58.1	60.1	62.2	64	65.2
	Ht cm	140.3	143	147.5	152.7	157.9	162.6	165.5	140.3	143	147.5	152.7	157.9	162.6	165.5
	50th	101	101	102	104	106	108	109	61	62	62	62	62	63	63
	90th	113	114	115	117	119	121	122	75	75	75	75	75	76	76
	95th	116	117	118	121	124	126	128	78	78	78	78	78	79	79
	95th+12	128	129	130	133	136	138	140	90	90	90	90	90	91	91
13	Ht in	57.9	59.1	61	63.1	65.2	67.1	68.3	57.9	59.1	61	63.1	65.2	67.1	68.3
	Ht cm	147	150	154.9	160.3	165.7	170.5	173.4	147	150	154.9	160.3	165.7	170.5	173.4
	50th	103	104	105	108	110	111	112	61	60	61	62	63	64	65
	90th	115	116	118	121	124	126	126	74	74	74	75	76	77	77
	95th	119	120	122	125	128	130	131	78	78	78	78	80	81	81
	95th+12	131	132	134	137	140	142	143	90	90	90	90	92	93	93
14	Ht in	60.6	61.8	63.8	65.9	68.0	69.8	70.9	60.6	61.8	63.8	65.9	68.0	69.8	70.9
	Ht cm	153.8	156.9	162	167.5	172.7	177.4	180.1	153.8	156.9	162	167.5	172.7	177.4	180.1
	50th	105	106	109	111	112	113	113	60	60	62	64	65	66	67
	90th	119	120	123	126	127	128	129	74	74	75	77	78	79	80
	95th	123	125	127	130	132	133	134	77	78	79	81	82	83	84
	95th+12	135	137	139	142	144	145	146	89	90	91	93	94	95	96
15	Ht in	62.6	63.8	65.7	67.8	69.8	71,5	72.5	62.6	63.8	65.7	67.8	69.8	71,5	72.5
	Ht cm	159	162	166.9	172.2	177.2	181.6	184.2	159	162	166.9	172.2	177.2	181.6	184.2
	50th	108	110	112	113	114	114	61	62	62	64	65	66	67	68
	90th	123	124	126	128	129	130	130	75	76	78	79	80	81	81
	95th	127	129	131	132	134	135	135	78	79	81	83	84	85	85
	95th+12	139	141	143	144	146	147	147	90	91	93	95	96	97	97
16	Ht in	63.8	64.9	66.8	68.8	70.7	72.2	73.4	63.8	64.9	66.8	68.8	70.7	72.2	73.4
	Ht cm	162.1	165	169.6	174.6	179.5	183.8	186.4	162.1	165	169.6	174.6	179.5	183.8	186.4
	50th	111	112	114	115	115	116	116	63	64	66	67	68	69	69
	90th	126	127	128	129	131	131	132	77	78	79	80	81	82	82
	95th	130	131	133	134	135	136	137	80	81	83	84	85	86	86
	95th+12	142	143	145	146	147	148	149	92	93	95	96	97	98	98
17	Ht in	64.5	65.5	67.3	69.2	71.1	72.8	73.8	64.5	65.5	67.3	69.2	71.1	72.8	73.8
	Ht cm	163.8	166.5	170.9	175.8	180.7	184.9	187.5	163.8	166.5	170.9	175.8	180.7	184.9	187.5
	50th	114	115	116	117	117	118	118	65	66	67	68	69	70	70
	90th	128	129	130	131	132	133	134	78	79	80	81	82	82	83
	95th	132	133	134	135	137	138	138	81	82	84	85	86	86	87
	95th+12	144	145	146	147	149	150	150	93	94	96	97	98	98	99

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APPENDIX: NORMAL BLOOD PRESSURE: GIRLS 1-9 YEARS

BLOOD PRESSURE BY AGE AND HEIGHT PERCENTILE: GIRLS 1-9 YEARS

		Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile or Measured Height							Height percentile or Measured Height						
Yr	BP%	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
1	Ht in	29.7	30.2	30.9	31.8	32.7	33.4	33.9	29.7	30.2	30.9	31.8	32.7	33.4	33.9
	Ht cm	75.4	76.6	78.6	80.8	83	84.9	86.1	75.4	76.6	78.6	80.8	83	84.9	86.1
	50th	84	85	86	86	87	88	88	41	42	42	43	44	45	46
	90th	98	99	99	100	101	102	102	54	55	56	56	57	58	58
	95th	101	102	102	103	104	105	105	59	59	60	60	61	62	62
	95th+12	113	114	114	115	116	117	117	71	71	72	72	73	74	74
2	Ht in	33.4	34	34.9	35.9	36.9	37.8	38.4	33.4	34	34.9	35.9	36.9	37.8	38.4
	Ht cm	84.9	86.3	88.6	91.1	93.7	96	97.4	84.9	86.3	88.6	91.1	93.7	96	97.4
	50th	87	87	88	89	90	91	91	45	56	47	48	49	50	51
	90th	101	101	102	103	104	105	106	58	58	59	60	61	62	62
	95th	104	105	106	106	107	108	109	62	63	63	64	65	66	66
	95th+12	116	117	118	118	119	120	121	74	75	75	76	77	78	78
3	Ht in	35.8	36.4	37.3	38.4	39.6	40.6	41.2	35.8	36.4	37.3	38.4	39.6	40.6	41.2
	Ht cm	91	92.4	94.9	97.6	100.5	103.1	104.6	91	92.4	94.9	97.6	100.5	103.1	104.6
	50th	88	89	89	90	91	92	93	48	48	49	50	51	53	53
	90th	102	103	104	104	105	106	107	60	61	61	62	63	64	65
	95th	106	106	107	108	109	110	110	64	65	65	68	67	68	69
	95th+12	118	118	119	120	121	122	122	76	77	77	78	79	80	81
4	Ht in	38.3	38.9	39.9	41.1	42.4	43.5	44.2	38.3	38.9	39.9	41.1	42.4	43.5	44.2
	Ht cm	97.2	98.8	101.4	104.5	107.6	110.5	112.2	97.2	98.8	101.4	104.5	107.6	110.5	112.2
	50th	89	90	91	92	93	94	94	50	51	51	53	54	55	55
	90th	103	104	105	106	107	108	108	62	63	64	65	66	67	67
	95th	107	108	109	109	110	11	112	66	67	68	69	70	70	71
	95th+12	119	120	121	121	122	123	124	78	79	80	81	82	82	83
5	Ht in	40.8	41.5	42.6	43.9	45.2	46.5	47.3	40.8	41.5	42.6	43.9	45.2	46.5	47.3
	Ht cm	103.6	105.3	108.2	111.5	114.9	118.1	120	103.6	105.3	108.2	111.5	114.9	118.1	120
	50th	90	91	92	93	94	95	96	52	52	53	55	56	57	57
	90th	104	105	106	107	108	109	110	64	65	66	67	68	69	70
	95th	108	109	109	110	111	112	113	68	69	70	71	72	73	73
	95th+12	120	121	121	122	123	124	125	80	81	82	83	84	85	85
6	Ht in	43.3	44	45.2	46.6	48.1	49.4	50.3	43.3	44	45.2	46.6	48.1	49.4	50.3
	Ht cm	110	111.8	114.9	118.4	122.1	125.6	127.7	110	111.8	114.9	118.4	122.1	125.6	127.7
	50th	92	92	93	94	96	97	97	54	54	55	56	57	58	59
	90th	105	106	107	108	109	110	111	67	67	68	69	70	71	71
	95th	109	109	110	111	112	113	114	70	71	72	72	73	74	74
	95th+12	121	121	122	123	124	125	126	82	83	84	84	85	86	86
7	Ht in	45.6	46.4	47.7	49.2	50.7	52.1	53	45.6	46.4	47.7	49.2	50.7	52.1	53
	Ht cm	115.9	117.8	121.1	124.9	128.8	132.5	134.7	115.9	117.8	121.1	124.9	128.8	132.5	134.7
	50th	92	93	94	95	97	98	99	55	55	56	57	58	59	60
	90th	106	106	107	109	110	111	112	68	68	69	70	71	72	72
	95th	109	110	111	112	113	114	115	72	72	73	73	74	74	75
	95th+12	121	122	123	124	125	126	127	84	84	85	85	86	86	87
8	Ht in	47.6	48.4	49.8	51.4	53	54.5	55.5	47.6	48.4	49.8	51.4	53	54.5	55.5
	Ht cm	121	123	126.5	130.6	134.7	138.5	140.9	121	123	126.5	130.6	134.7	138.5	140.9
	50th	93	94	95	97	98	99	100	56	56	57	59	60	61	61
	90th	107	107	108	110	111	112	113	69	70	71	72	72	73	73
	95th	110	111	112	113	115	116	117	72	73	74	74	75	75	75
	95th+12	122	123	124	125	127	128	129	84	85	86	86	87	87	87
9	Ht in	49.3	50.2	51.7	53.4	55.1	56.7	57.7	49.3	50.2	51.7	53.4	55.1	56.7	57.7
	Ht cm	125.3	127.6	131.3	135.6	140.1	144.1	146.6	125.3	127.6	131.3	135.6	140.1	144.1	146.6
	50th	95	95	97	98	99	100	101	57	58	59	60	60	61	61
	90th	108	108	109	111	112	113	114	71	71	72	73	73	73	73
	95th	112	112	113	114	116	117	118	74	74	75	75	75	75	75
	95th+12	124	124	125	128	128	129	130	86	86	87	87	87	87	87

APPENDIX: NORMAL BLOOD PRESSURE: GIRLS 10-17 YEARS

BLOOD PRESSURE BY AGE AND HEIGHT PERCENTILE: GIRLS 10-17 YEARS

		Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile or Measured Height							Height percentile or Measured Height						
Yr	BP%	5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
10	Ht in	51.1	52	53.7	55.5	57.4	59.1	60.2	51.1	52	53.7	55.5	57.4	59.1	60.2
	Ht cm	129.7	132.2	136.3	141	145.8	150.2	152.8	129.7	132.2	136.3	141	145.8	150.2	152.8
	50th	96	97	98	99	101	102	103	58	59	59	60	61	61	62
	90th	109	110	111	112	113	115	116	72	73	73	73	73	73	73
	95th	113	114	114	116	117	119	120	75	75	76	76	76	76	76
	95th+12	125	126	126	128	129	131	132	87	87	88	88	88	88	88
11	Ht in	53.4	54.5	56.2	58.2	60.2	61.9	63	53.4	54.5	56.2	58.2	60.2	61.9	63
	Ht cm	135.6	138.3	142.8	147.8	152.8	157.3	160	135.6	138.3	142.8	147.8	152.8	157.3	160
	50th	98	99	101	102	104	105	106	60	60	60	61	62	63	64
	90th	111	112	113	114	116	118	120	74	74	74	74	74	75	75
	95th	115	116	117	118	120	123	124	76	77	77	77	77	77	77
	95th+12	127	128	129	130	132	135	136	88	89	89	89	89	89	89
12	Ht in	56.2	57.3	59	60.9	62.8	64.5	65.5	56.2	57.3	59	60.9	62.8	64.5	65.5
	Ht cm	142.8	145.5	149.9	154.8	159.6	163.8	166.4	142.8	145.5	149.9	154.8	159.6	163.8	166.4
	50th	102	102	104	105	107	108	108	61	61	61	62	64	65	65
	90th	114	115	116	118	120	122	122	75	75	75	75	76	76	76
	95th	118	119	120	122	124	125	126	78	78	78	78	79	79	79
	95th+12	130	131	132	134	136	137	138	90	90	90	90	91	91	91
13	Ht in	58.3	59.3	60.9	62.7	64.5	66.1	67	58.3	59.3	60.9	62.7	64.5	66.1	67
	Ht cm	148.1	150.6	154.7	159.2	163.7	167.8	170.2	148.1	150.6	154.7	159.2	163.7	167.8	170.2
	50th	104	105	106	107	108	108	109	62	62	63	64	65	65	66
	90th	116	117	119	121	122	123	123	75	75	75	76	76	76	76
	95th	121	122	123	124	126	126	127	79	79	79	79	80	80	81
	95th+12	133	134	135	136	138	138	139	91	91	91	91	92	92	93
14	Ht in	59.3	60.2	61.8	63.5	65.2	66.8	67.7	59.3	60.2	61.8	63.5	65.2	66.8	67.7
	Ht cm	150.6	153	156.9	161.3	165.7	169.7	172.1	150.6	153	156.9	161.3	165.7	169.7	172.1
	50th	105	106	107	108	109	109	109	63	63	64	65	66	66	66
	90th	118	118	120	122	123	123	123	76	76	76	76	77	77	77
	95th	123	123	124	125	126	127	127	80	80	80	80	81	81	82
	95th+12	135	135	136	137	138	139	139	92	92	92	92	93	93	94
15	Ht in	59.7	60.6	62.2	63.9	65.6	67.2	68.1	59.7	60.6	62.2	63.9	65.6	67.2	68.1
	Ht cm	151.7	154	157.9	162.3	166.7	170.6	173	151.7	154	157.9	162.3	166.7	170.6	173
	50th	105	106	107	108	109	109	109	64	64	64	65	66	67	67
	90th	118	119	121	122	123	123	124	76	76	76	77	77	78	78
	95th	124	124	125	126	127	127	128	80	80	80	81	82	82	82
	95th+12	136	136	137	138	139	139	140	92	92	92	93	94	94	94
16	Ht in	59.9	60.8	62.4	64.1	65.8	67.3	68.3	59.9	60.8	62.4	64.1	65.8	67.3	68.3
	Ht cm	152.1	154.5	158.4	162.8	167.1	171.1	173.4	152.1	154.5	158.4	162.8	167.1	171.1	173.4
	50th	106	107	108	109	109	110	110	64	64	65	66	66	67	67
	90th	119	120	122	123	124	124	124	76	76	76	77	78	78	78
	95th	124	125	125	127	127	128	128	80	80	80	81	82	82	82
	95th+12	136	137	137	139	139	140	140	92	92	92	93	94	94	94
17	Ht in	60.0	60.9	62.5	64.2	65.9	67.4	68.4	60.0	60.9	62.5	64.2	65.9	67.4	68.4
	Ht cm	152.4	154.7	158.7	163.0	167.4	171.3	173.7	152.4	154.7	158.7	163.0	167.4	171.3	173.7
	50th	107	108	109	110	110	110	111	64	64	65	66	66	66	67
	90th	120	121	123	124	124	125	125	76	76	77	77	78	78	78
	95th	125	125	126	127	128	128	128	80	80	80	81	82	82	82
	95th+12	137	137	138	139	140	140	140	92	92	92	93	94	94	94

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MYOCARDITIS

INTRODUCTION (LUV MAKADIA, M.D., 4/2020)
Myocarditis is an inflammatory disease of the myocardium. It can be caused by infections, autoimmune diseases and direct drug toxicity and drug hypersensitivity reactions. Viral etiologies are most frequently identified in the pediatric population. The annual incidence of pediatric myocarditis is approximately 1 in 100,000. The true incidence is likely higher due to subclinical disease and those who die prior to a definitive diagnosis. See: PEM Guide: Cardiology: Cardiogenic Shock

The myocardium, or heart muscle, is thick layer of striated muscle tissue that lies in between the epicardium and the endocardium. Inflammation of the myocardium can reduce contractility with decreased cardiac output (heart failure/cardiogenic shock) as well as precipitate life-threatening arrhythmias such as ventricular arrhythmias and complete heart block. Reduced mechanical and electrical function can lead to cardiopulmonary arrest.

ETIOLOGY (EXAMPLES)	
Infectious	
Viral	Enterovirus (e.g. Coxsackie B), adenovirus, parvovirus B19, Epstein-Barr virus, cytomegalovirus, and human herpes virus 6
Bacterial	Chlamydia, Clostridium, Gonococcus, Haemophilus, Mycoplasma, Pneumococcus, Staphylococcus, Streptococcus, Borrelia (Lyme)
Fungal	Actinomycetes, Aspergillus, Candida, Histoplasma
Parasitic	Entamoeba, Trypanosoma (Chagas), Echinococcus, Toxoplasma
Non-infectious	
Toxins	Alcohol, anthracyclines, carbon monoxide, catecholamines, cocaine, cyclophosphamide, heavy metals
Hypersensitivity	Antibiotics, diuretics, insect bites, lithium, tetanus toxoid
Systemic disorders	Celiac, collagen-vascular, Wegener's, inflammatory bowel disease, Kawasaki[1], sarcoidosis, thyrotoxicosis, acute rheumatic fever[2].
Radiation	Radiation therapy for oncologic disease
1. See: PEM Guide: Rheumatology: Kawasaki Disease 2. See: PEM Guide: Rheumatology: Acute Rheumatic Fever	

CLINICAL MANIFESTATIONS
The distribution of myocarditis is bimodal with peaks in infancy and adolescence. Approximately 2/3 are missed at initial presentation due to non-specific signs and symptoms and the lack of sensitive and specific diagnostic testing.

Signs and symptoms can be categorized as those relating to upstream effects (poor cardiac output leading to inadequate perfusion) and downstream effects (accumulation of fluids in the lungs (LV failure) and body (RV failure). Signs of hemodynamic instability such as hypotension, weak pulses, and altered mental status may also be present. Rarely, a patient may present with a sudden cardiac arrest.

HISTORY: Presenting complaints are highly variable. In general, infants and young children present with respiratory and/or gastrointestinal signs and symptoms while older children and adolescents present with cardiac signs and symptoms. Many will report a recent viral illness prodrome. Some patients may have subclinical disease and have no to minimal complaints (Canter, Circulation 2014, PubMed ID: 24396015).

SYMPTOMS	
Viral Prodrome	Respiratory ± gastrointestinal symptoms, fever, malaise, myalgias
Heart failure	Dyspnea, exercise intolerance, syncope, chest pain
Arrhythmia, heart block	Syncope, dizziness, lightheadedness, palpitations, exercise intolerance, fatigue, weakness

PHYSICAL EXAMINATION: Sinus tachycardia is the most common presenting rhythm. Tachycardia may be out or proportion to fever (↑ 10 beats/minute for each 1 degree Celsius above normal). Extreme tachycardia can be seen with tachyarrhythmias. In contrast, bradycardia is associated with heart block. An S3 or S4 heart sound (gallop rhythm) may be present (SOUND FILE: GALLOP RHYTHM). A systolic murmur of mitral or tricuspid insufficiency may be present if the ventricles are significantly dilated. A friction rub may be heard in myopericarditis (SOUND FILE: FRICTION RUB),

The respiratory exam will show tachypnea with increased work of breathing as well as lung sounds indicative of pulmonary edema. (SOUND FILE: PULMONARY EDEMA). Hepatomegaly or peripheral edema may be present in right heart failure.

COMMON SIGNS AND SYMPTOMS AT PRESENTATION	
Chest pain	45%
Viral prodrome	41%
Respiratory distress	28%
Gastrointestinal symptoms	27%
Hepatomegaly	27%
Gallop rhythm	20%
Poor perfusion/diminished extremity pulses	16%
Single center, n=150 (Butts, Pediatr Cardiol 2017, PubMed ID: 28536746)	

DIAGNOSTIC TESTING

LABORATORY: Non-specific markers of inflammation such as the total WBC, CRP and ESR may be elevated but normal levels do not exclude the diagnosis of myocarditis. This is also true of more cardiac specific biomarkers such as troponin and brain natriuretic peptide (BNP). An elevated Troponin indicates myocardial injury and is present in the majority of patients with myocarditis. However, a negative troponin does not exclude the diagnosis of myocarditis and the degree of troponin elevation does not correlate with disease severity. BNP may help in distinguishing a respiratory (normal BNP) from a cardiac (↑ BNP) etiology of respiratory signs and symptoms. Obtain a serum Lactate level as a general marker of perfusion and a basic metabolic panel (kidney) and liver function tests to assess end-organ perfusion.

Viral studies may help identify the etiology. However, viral panels may be falsely positive due to common viral prevalence or falsely negative because myocarditis can develop much after the initial infection.

EKG/ECHO: EKG and diagnostic imaging can help establish the diagnosis and assess disease severity. However, a normal EKG does not exclude myocarditis. Point of care ultrasound can be used at the bedside to assess cardiac contractility, chamber sizes and the presence of a pericardial effusion.

EKG/IMAGING FINDINGS	
EKG	Nonspecific: ↑ or ↓ ST-segments, T wave flattening or inversion, ↓ QRS voltages, abnormal axis, ventricular or atrial enlargement, ↓ QRS voltages
	Rhythm: Sinus tachycardia is the most common rhythm Others: Ventricular or atrial premature beats, supraventricular or ventricular arrhythmias and heart block (any degree)
Chest XRAY	Heart: Cardiomegaly: Cardiac:Thoracic ratio (AP view): >0.6 (neonates), >0.55 (infants), >0.5 (children) Lungs: Pulmonary vasculature congestion, pleural effusion
Echo-cardiograph (structure and function)	Decreased ventricular function (↓ Ejection or shortening fraction) Adults: EF preserved (≥ 50%), borderline (41-49%), reduced (40%) Changes in chamber size (ventricular, atrial enlargement) Segmental wall motion abnormalities (may mimic ischemia) Mitral/tricuspid regurgitation (due to dilation) Pericardial effusion

BIOPSY: Traditionally, endo-myocardial biopsy (EMB) is considered the gold standard. Histopathologic diagnosis is made by standard light microscopy according to the Dallas criteria: “an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic damage associated with coronary heart disease.” Infiltrates may be mononuclear, neutrophilic, or eosinophilic (Aretz, Am J Cardiovasc Pathol 1987, PubMed ID: 3455232). Biopsy is invasive requiring cardiac catheterization. Limitations include procedure complications (pneumothorax, hemothorax, arrhythmia, perforation, death), limited diagnostic accuracy and inconsistent interpretation. New techniques may improve diagnostic accuracy. EMB is not often performed in pediatric patients.

CARDIAC MR: Given the limitations of biopsy, diagnosis is more commonly made clinically with or without cardiac MR (CMR). CMR can identify ventricular ejection fraction, and size, wall thickness and tissue injury/inflammation (edema, hyperemia, fibrosis) and can distinguish between myocarditis and ischemia.

CLINICAL DIAGNOSIS: MYOCARDITIS
Prodromal infectious illness within the past few weeks
Signs and symptoms of cardiac dysfunction
EKG: Signs of acute myocardial injury or arrhythmia
Elevated Troponin, BNP
ECHO: Ventricular function (↓ Ejection fraction) in a structurally normal heart

DIFFERENTIAL DIAGNOSIS

The differential of myocarditis is extensive and includes conditions that may present with acute heart failure and/or respiratory distress. Myocarditis is difficult to distinguish from common febrile respiratory illnesses such as bronchiolitis, pneumonia and asthma (with fever) requiring a high index of suspicion.

DIFFERENTIAL DIAGNOSIS	
Structural Heart disease	ALCAPA, severe valvular heart disease (e.g. critical aortic stenosis). Can be identified by echocardiogram.
Cardiomyopathy	Type: Hypertrophic, restrictive, arrhythmogenic right ventricular Myocarditis is more likely to have an acute onset, a recent viral illness and to recover heart function over time. Myocarditis is less likely to have significant ventricular dilation.
Sepsis	May present similarly to fulminant myocarditis. Echo in sepsis typically demonstrates normal contractility a small inferior vena cava (IVC is distended in right heart failure)
Kawasaki Disease	Persistent fevers, bilateral bulbar conjunctivitis, oral mucosa and peripheral extremity changes, rash, cervical lymphadenopathy Typically with mild cardiac involvement
Primary Arrhythmias	In primary arrhythmia, ventricular dysfunction should resolve with successful management of the arrhythmia.
Respiratory Illness	Myocarditis is more likely with an abnormal cardiac exam (gallop rhythm, tachycardia out of proportion to fever), hepatomegaly, elevated Troponin and BNP, chest XRAY with cardiomegaly, EKG (ST-T wave changes, arrhythmias), ECHO (poor ejection fraction) and clinical deterioration with intravenous fluids.

MANAGEMENT

All patients with suspected myocarditis should have a pediatric cardiology consult and continuous cardiorespiratory monitoring. Initial management is guided by symptom severity. Supportive care includes efforts to improve tissue oxygenation, support cardiac output and treat arrhythmias. See: PEM Guide: Cardiology: Cardiogenic Shock, See Appendix: Heart Failure Management Paradigm.

MILD: For patients that have mild symptoms, oral diuretics, angiotensin converting enzyme (ACE) inhibitors (reduce afterload) and supplemental oxygen is provided as needed

MODERATE TO SEVERE: For more severe cases with decompensated heart failure and/or cardiogenic shock, more aggressive management will be required. This may include intravenous diuretics (e.g. Furosemide) and intravenous inotropes, preferably with afterload reduction (Milrinone, Dopamine (low dose), Dobutamine). Vasopressors (Norepinephrine, Epinephrine) may be required for persistent hypotension and signs of organ failure unresponsive to inotropes. Mechanical ventilation and/or mechanical circulatory support may be required.

INTRAVENOUS FLUIDS: It is important to be carefully titrate fluid resuscitation. Those with a fluid deficit may require gentle volume expansion (e.g. 10 ml/kg over 1 hours with continuous monitoring for signs of fluid overload). Excess fluids can worsen pulmonary congestion. Those with signs of fluid overload may require fluid restriction and diuretics.

ARRHYTHMIA MANAGEMENT: Arrhythmia management should follow American Heart Association Guidelines (See: PEM Guide: Cardiology: Arrhythmias: An Overview). Most antiarrhythmics depress cardiac function, cause vasodilation, or may have proarrhythmic effects. Supraventricular or ventricular tachycardia with a pulse and hemodynamic compromise should be immediately electrically cardioverted. Cardiac pacing may be required for complete heart block (See: PEM Guide: Cardiology: Cardiac Pacing for Bradycardia).

POSITIVE PRESSURE VENTILATION: Positive pressure ventilation (PPV) can have both positive and negative consequences. PPV decreases metabolic activity by decreasing the work of breathing. PPV increases intrathoracic pressure. This increased the pressure gradient between the thoracic and abdominal cavities. This improves left ventricular cardiac output. However, the gradient can decrease venous return to the right heart. The patients hemodynamic status should be maximized with inotrope infusions and push-dose pressures should be available at the bedside prior to sedation, paralysis and endotracheal intubation. PPV can be non-invasive (CPAP, BiPAP) or invasive (intubation). There is considerable evidence on the efficacy of non-invasive ventilation in adult heart failure but very limited pediatric data.

MECHANICAL CIRCULATORY SUPPORT: Mechanical circulatory support is indicated if pharmacologic support fails (persistent elevated lactate, signs of end organ failure) or if there is severe cardiogenic shock. Extracorporeal membrane oxygenation (ECMO) supports both cardiac and respiratory function. Ventricular assist devices (VAD) only supports cardiac function. The goal is to temporarily provide circulatory support while the heart regains function or serve as a bridge to cardiac transplantation.

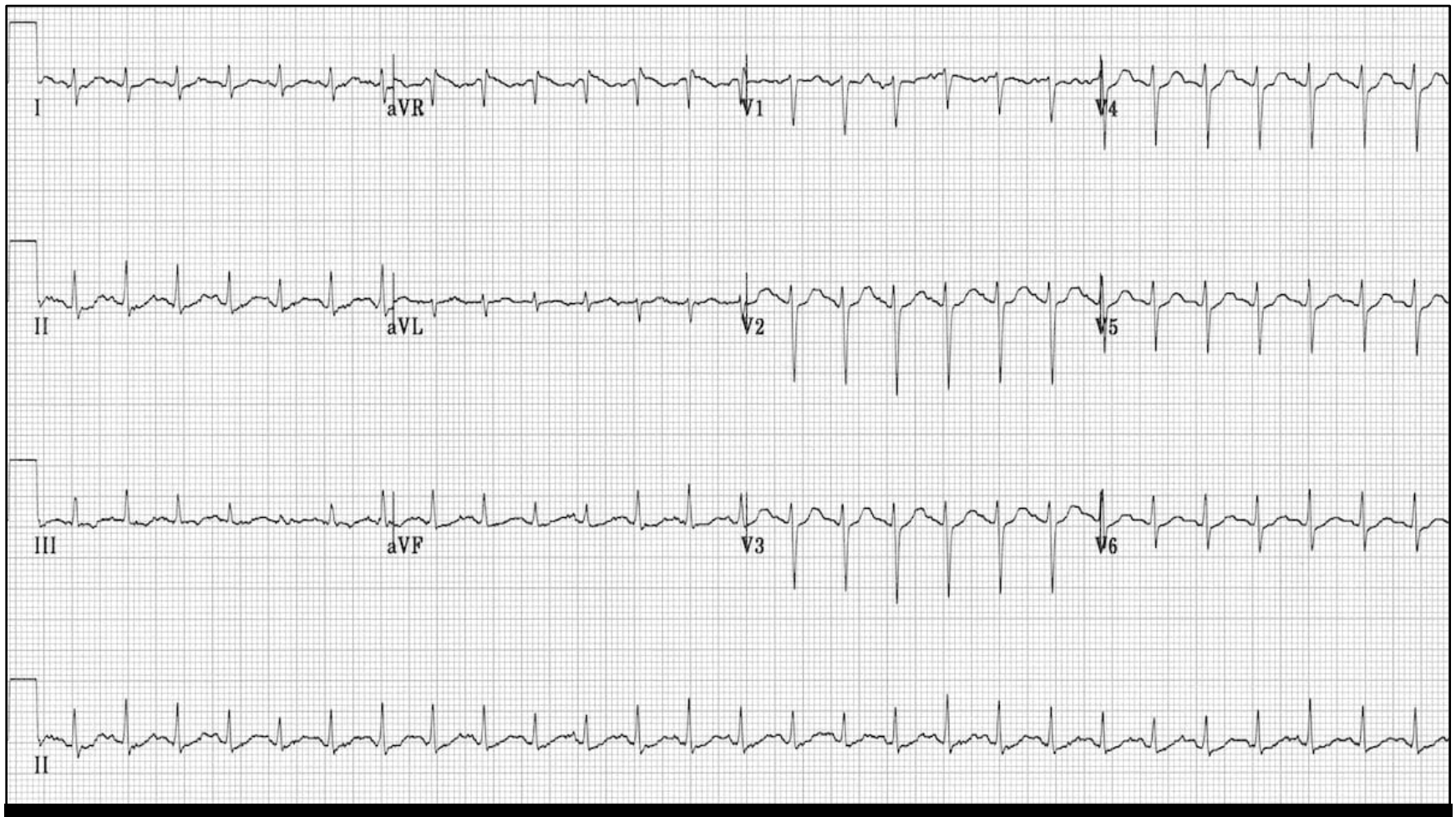
IMMUNO-MODULATORY THERAPY: Data is limited and inconclusive on the utility of immuno-modulatory therapy. Many academic centers use high dose immune globulin (IVIG: 2 grams/kg over 24 hours) for acute myocarditis. Glucocorticoids are typically reserved for autoimmune causes of myocarditis without clear evidence of their efficacy.

ANTIMICROBIALS: Viral infections with effective antiviral therapy include: CMV, HSV, influenza and HIV. Identified bacterial, fungal and parasitic infections should be treated appropriately in consultation with pediatric infectious disease.

DISPOSITION

The majority of pediatric patients with myocarditis require ongoing monitoring in a pediatric ICU setting. Prognosis is good compared to heart failure due to cardiomyopathy. Most resolved without sequelae with supportive care within 2-4 weeks. A subset develops dilated cardiomyopathy.

APPENDIX: EKG: PEDIATRIC MYOCARDITIS



FINDINGS: SINUS TACHYCARDIA (FOR AN ADOLESCENT), NON-SPECIFIC ST SEGMENT CHANGES

WEB LINK: LITFL ECG LIBRARY: MYOCARDITIS

APPENDIX: HEART FALURE MANAGEMENT PARADIGM

ASSESSMENT		CONGESTION	
		NO	YES
HYPO-PERFUSION	NO	WARM	WARM
		DRY	WET
	YES	COLD	COLD
		DRY	WET
CELL: Top Row = Perfusion (Warm or Cold), Bottom Row = Congestion (Wet or Dry) 1. Hypo-perfusion: Altered mental status, ↓ BP, ↑ HR, poor distal perfusion (cool, mottled extremities, ↓ distal pulses, ↑ capillary refill). 2a. Congestion: RV Failure: JVD, hepatomegaly, ascites, peripheral edema 2b. Congestion: LV Failure: ↑ HR, ↑ RR, ↑ work of breathing, rales (pulmonary edema)			

MANAGEMENT		PULMONARY CONGESTION	
		NO	YES
HYPO-PERFUSION	NO	Monitor	Diuretics ± PPV
	YES	Inotrope ± Pressor Gentle Fluids	Inotrope ± Pressor PPV

GOALS: Tissue oxygen delivery (DaO_2) is the product of arterial oxygen content (CaO_2) and cardiac output (CO). Tissue oxygen delivery can be increased by interventions targeted to increase cardiac output (↑ Preload, ↑ Lusitropy, ↑ Contractility, ↓ Afterload) and increase arterial oxygen content (supplemental oxygen, blood transfusion). Tissue oxygen delivery can also be increased relatively by decreasing oxygen utilization through sedation, paralysis and mechanical ventilation (Tume, Pediatr Crit Care Med 2016, PubMed ID: 26945325).

CARDIOGENIC SHOCK: VASOACTIVE AGENT SELECTION	
Heart failure without shock	Loop diuretic
Cardiogenic Shock: Compensated	Dopamine (low dose) or Milrinone
Cardiogenic Shock: Hypotensive	Epinephrine (low dose), Milrinone as BP allows

CARDIOGENIC SHOCK: MEDICATION DOSING	
Furosemide	1-2 mg/kg IV
Dopamine	5-10 mcg/kg/min IV (vasoconstriction at higher doses)
Dobutamine	2-20 mcg/kg/min IV
Milrinone	0.25-1.0 mcg/kg/min IV (start at 0.25, titrate up as needed)
Epinephrine	0.03-0.3 mcg/kg/min IV (refractory hypotensive)

PERICARDIOCENTESIS

INTRODUCTION (ERIC WEINBERG M.D., 9/2015)
Pericardiocentesis can be a life preserving procedure in the setting a cardiac tamponade. As fluid accumulates in the pericardial space the ability of the heart to fill during diastole and contract during systole is compromised. The rapidity of the fluid accumulation determines the degree of cardiac impairment. If fluid accumulates rapidly over a few hours as little as a few hundred milliliters can result in tamponade physiology while if it accumulates over days to weeks it may require 1-2 liters. Sources of fluid accumulation include: trauma, aortic dissection, central venous line placement, cancer, post-pericardiotomy syndrome and infections (TB, viral, bacterial).

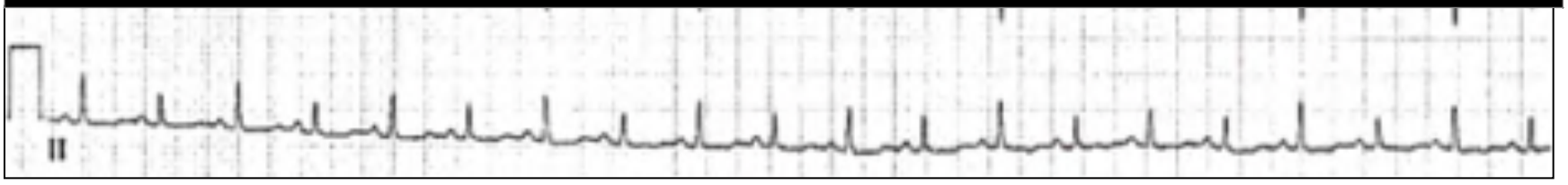
CLINICAL MANIFESTATIONS

Beck's triad may be seen in the setting of cardiac tamponade. The triad includes: hypotension (decreased cardiac output), distended neck veins (impaired venous return) and distant or muffled heard sounds (pericardial fluid collection dampens heart sounds). Unfortunately, the complete Beck's triad is only seen in approximately 1/3 of cases.

A narrow pulse pressure may also be seen. Diastolic pressure rises to compensate for a fall in systolic pressure. Pulses may be weak. Pulsus paradoxus is a late sign of cardiac tamponade. It is defined as a drop in blood pressure on inspiration that's greater than 10 mm Hg.

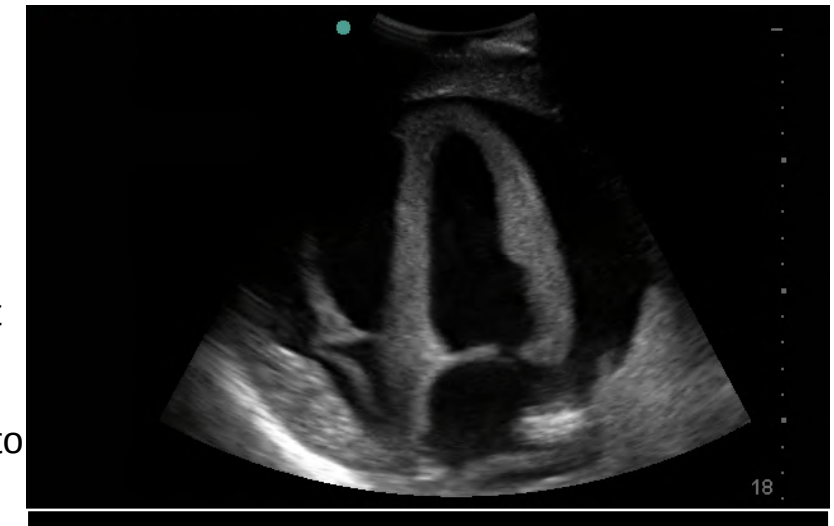
EKG: EKG findings include: decreased voltages, tachycardia and electrical alternans. Electrical alternans is defined as consecutive, normally conducted QRS complexes alternating in height. This is a result of the heart swinging back in the pericardial sac in large pericardial effusion.

ELECTRICAL ALTERNANS



CHEST XRAY: A chest XRAY may demonstrate an enlarged cardiothymic silhouette. The differential diagnosis of an enlarged cardiothymic silhouette includes a pericardial fluid collection as well as cardiomegaly.

ECHOCARDIOGRAPHY: Bedside echocardiography can be used to identify a pleural fluid collection, contractility and signs of pericardial tamponade. The apical four chamber view is the most difficult to obtain but is best to assess chamber size. The ultrasound is placed in the 5th intercostal space in the midclavicular line or at the point of maximal impulse with the marker dot to right. This view can be improved with the patient in the left lateral decubitus position. Normally the right ventricle is approximately 2/3 of the size of the left ventricle and intraventricular septum should be bow into the right ventricle.



PERICARDIAL FLUID COLLECTION

ECHOCARDIOGRAM FINDINGS IN CARDIAC TAMPONADE
A large pericardial effusion
Diastolic collapse of the right atrium and ventricle
Distended inferior vena cava without respiratory variation

PROCEDURE PERICARDIOCENTESIS

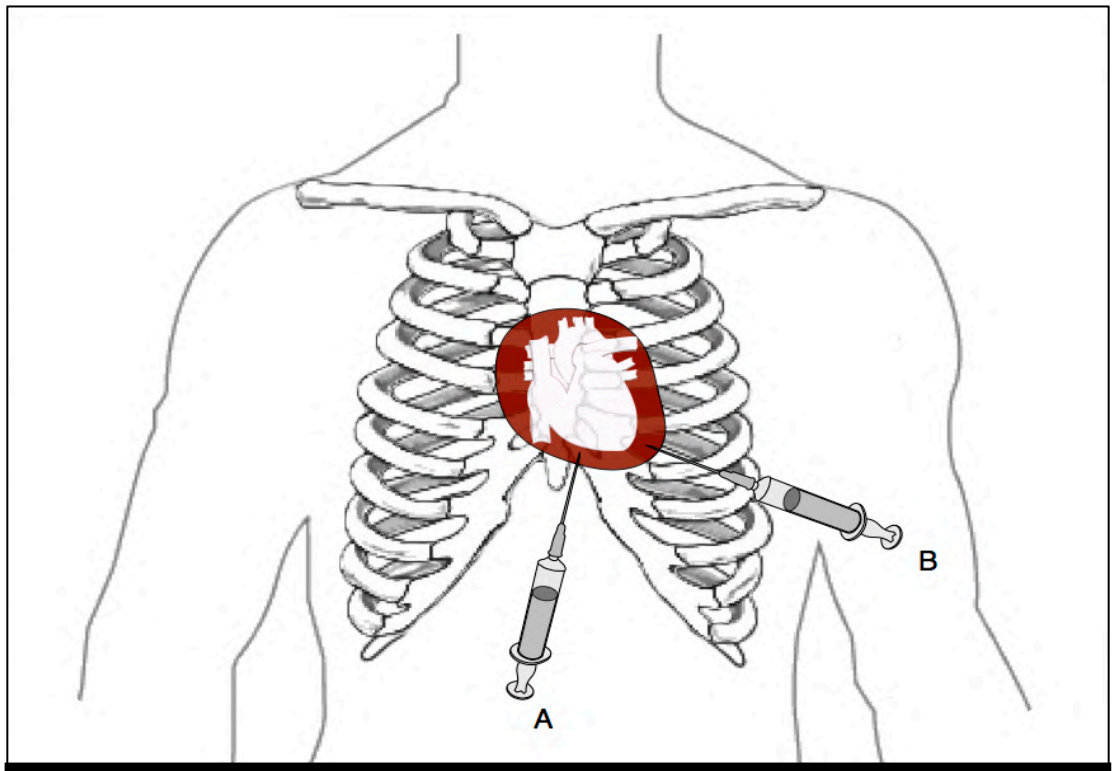
INDICATIONS
Therapeutic: Cardiac tamponade (suspected or confirmed)
Diagnostic: Establish etiology of pericardial effusion

CONTRAINDICATIONS
Relative = Aortic dissection, bleeding diathesis, traumatic tamponade (surgical approach recommended

ANATOMIC LANDMARKS

A: Inferior and lateral to Xiphoid process

B: Left sterno-costal margin between 5th and 6th ribs



PERICARDIOCENTESIS: ANATOMIC LANDMARKS

EQUIPMENT	
1	Universal precautions with drape and Betadine
2	1% Lidocaine with Epinephrine
3	10 ml and 60 ml syringe
4	11 blade scalpel
5	18G spinal needle (~10 cm long)
6	Ultrasound machine with probe cover
7	Alligator clip for connection to V1 lead (optional)

PROCEDURE: SUBCOSTAL APPROACH	
1	Universal precautions/sterile technique/Betadine
2	Locate pericardial effusion using ultrasound
3	Infiltrate subcutaneous tissue with Lidocaine and Epinephrine several millimeters inferior and lateral to xiphoid process (patient's left side).
4	Advance puncture needle posteriorly below costal margin
5	Then direct needle cephalad, less shallow, toward L shoulder WITH CAUTION
6	Aspirate fluid
7	Secure needle to skin, attach to 3-way stopcock for intermittent drainage
8	Can inject agitated saline to confirm position on ultrasound

PROCEDURE: PARASTERNAL APPROACH	
1	Universal precautions/sterile technique/Betadine
2	Locate pericardial effusion using ultrasound
3	Infiltrate tissue with Lidocaine 1cm lateral to sternal edge, superior to 6th rib
4	Direct needle toward aortic valve under ultrasound guidance, WITH CAUTION
5	Aspirate fluid
6	Secure needle to skin, attach to 3-way stopcock for intermittent drainage
7	Can inject agitated saline to confirm position on ultrasound

VIDEO LINK: ULTRASOUND GUIDED PERICARDIOCENTESIS

PROCEDURE PEARLS
Percutaneous approach is recommended for tamponade in the setting of unstable vital signs or with large recurrent pericardial effusions
Open surgical approach is preferred in patients with traumatic hemopericardium, purulent pericarditis, and aortic dissection
EKG monitoring of needle does not protect against myocardial injury
Ultrasound-guided pericardiocentesis is as effective as fluoroscopy guided pericardiocentesis
Fluid should be drained in <1,000 ml intervals to avoid right ventricular dilatation

PERICARDITIS

INTRODUCTION (THOMAS KENNEDY, M.D., 4/2018)
The pericardium is a double-walled sac enclosing the heart and parts of the ascending aorta, pulmonary trunk, and venae cavae. It is composed of a serous visceral layer and a fibrous parietal layer between which there is a small amount of pericardial fluid.

A retrospective case series evaluated the etiology of chest pain in 4,288 patients ≤ 18 years old without a history of cardiovascular disease who presented to pediatric emergency departments (Drossner, Amer J EM 2011, PubMed ID: 20627219). 24 (0.6%) were determined to have chest pain of cardiac origin. Of those with a cardiac etiology of chest pain, 6 (25%) were diagnosed with pericarditis (Adler, European Heart J 2015, PubMed ID: 26320112).

PERICARDITIS DEFINITIONS	
Acute (≥ 2 of 4 criteria)	1. Chest pain (> 85-90% cases) 2. Pericardial friction rub (≤ 33% cases) 3. New widespread ST elevation or PR depression on ECG (60% cases) 4. Pericardial effusion (60% cases)
Incessant	> 4-6 weeks and < 3 months
Chronic	> 3 months
Recurrent	Recurrence of pericarditis after a documented first episode and a symptom-free interval of 4-6 weeks or longer

The etiology of pericarditis can be divided into idiopathic, infectious, and non-infectious categories. In developed countries, idiopathic pericarditis accounts for 40-90% of cases and is assumed to be viral in etiology. Viral pathogens are the most commonly identified infectious etiology. Bacterial (purulent) pericarditis is caused by either direct invasion from adjacent structures, frequently the lungs, or hematogenous spread. Staphylococcus aureus is the most common pathogen in developed countries while Mycobacterium tuberculosis is most common in endemic regions.

PERICARDITIS: ETIOLOGY (EXAMPLES)	
INFECTIOUS	
Viral	Adenovirus, enterovirus (e.g., coxsackie), influenza
Bacterial	B. burgdorferi, M. tuberculosis, S. aureus, S. pneumoniae
Fungal	Actinomyces, Histoplasma capsulatum
Parasitic	Echinococcus, Toxoplasma gondii
NON-INFECTIOUS	
Auto-immune	Systemic lupus erythematosus
Auto-inflammatory	Familial Mediterranean fever
Iatrogenic	Radiation therapy, drug-induced (e.g., Isoniazid, Cyclosporine)
Metabolic	Myxedema, uremia
Neoplastic	Primary and metastatic
Post-injury	Post-pericardiotomy, post-traumatic, post-myocardial infarction

Constrictive pericarditis is a late complication of pericarditis in which a thickened, adherent pericardium develops from scarring that restricts ventricular filling. The risk depends on the etiology of pericarditis: bacterial pericarditis has the highest risk (20-30%), immune-mediated and neoplastic cases have an intermediate risk (2-5%), viral and idiopathic cases have the lowest risk (< 1%).

CLINICAL MANIFESTATIONS

HISTORY: Pediatric patients with pericarditis commonly present with chest pain, fever, and vomiting. The chest pain is often described as sharp or stabbing, worse with inspiration and lying flat, and improved by sitting or leaning forward. It may radiate to the scapular ridge. Palpitations, shortness of breath, and myalgias may be present.

Review past medical and family history for autoimmune diseases, immunosuppressive conditions, malignancies, renal diseases, and thyroid diseases. Review surgical history to determine if the patient has had a cardiac operation. Document recent and current medications with particular attention to the use of immunosuppressive drugs. Lastly, obtain a travel history.

PHYSICAL EXAMINATION: In addition to fever, vital signs may reveal sinus tachycardia and tachypnea. In the setting of cardiac tamponade, a narrow pulse pressure or pulsus paradoxus, defined as a fall in systolic blood pressure > 10 mmHg during inspiration, may be present.

Physical examination findings may include a pericardial friction rub in the presence of a small pericardial effusion or muffled heart sounds if there is a large effusion. A friction rub is considered pathognomonic for pericarditis and is heard best at the left lower sternal border while the patient is leaning forward. Large effusions are more common with bacterial infections and uremia. Tamponade is characterized by Beck’s triad of jugular venous distention, muffled heart sounds, and hypotension. Constrictive pericarditis typically presents with signs of right-sided heart failure, such as jugular venous distention, hepatomegaly, and dependent edema.

LABORATORY TESTING

In all patients with suspected pericarditis, obtain a complete blood count with a differential, CRP and/or ESR, and a troponin. Elevation of inflammatory markers is a common and supportive finding in pericarditis. Additionally, trending these values may be helpful in determining the efficacy of therapy and when it can be discontinued. A significant leukocytosis should raise concern for bacterial pericarditis while leukopenia or anemia may suggest the presence of an autoimmune disorder. Troponin elevation indicates concomitant myocardial involvement (myopericarditis or perimyocarditis).

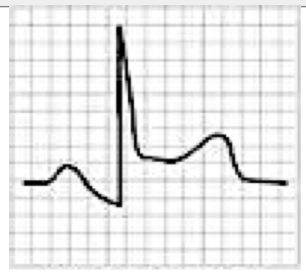
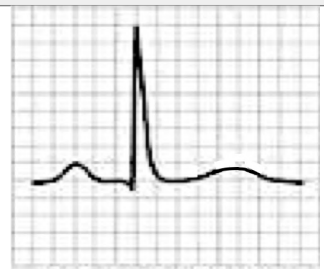
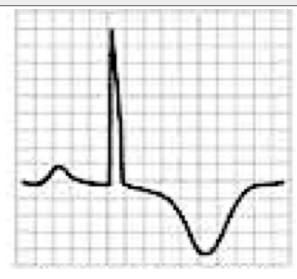
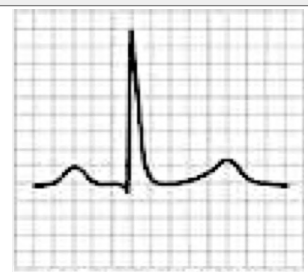
If the diagnosis of pericarditis is confirmed and there is no reason to suspect a specific cause other than a viral infection, further laboratory testing may be unnecessary. If pericardiocentesis is performed, send the pericardial fluid for analysis including cell count and differential, glucose, protein, lactate dehydrogenase, Gram stain, bacterial and viral cultures, cytological evaluation, and PCR for specific pathogens.

ELECTROCARDIOGRAM (ECG)

ECG findings typically progress through 4 stages. However, less than 50% of patients progress through each of the 4 stages and progression may not follow this pattern. The most important distinction is between pericarditis and ST-segment elevation myocardial infarction (STEMI). Patients with convex ST-segment elevations, reciprocal ST-segment depressions, or rapid changes are more likely to have a STEMI.

Diffuse low-voltage QRS and electrical alternans may be seen with a large pericardial effusion. Electrical alternans is an alternating QRS voltage due to the movement of the heart within the pericardial fluid. A normal ECG does not exclude pericarditis given the changes that occur over time.

WEB LINK: LIFE IN THE FAST LANE: EKG LIBRARY: ST SEGMENTS

EKG STAGES: PERICARDITIS				
	STAGE I	STAGE II	STAGE III	STAGE IV
				
PR	Depression	Normal	Normal	Normal
ST	Concave Elevation	Normal	Normal	Normal
T wave	Normal	Flattened	Deep Inverted	Normal or Remain Inverted
AVR and VI are right sided leads. Will see PR elevation and ST depression in Stage I				

ST SEGMENT ELEVATION: DIFFERENTIAL DIAGNOSIS*	
ST elevation myocardial infarction	Left ventricular hypertrophy
Coronary vasospasm	Brugada syndrome
Pericarditis	Ventricular aneurysm
Benign early repolarization	Increased intracranial pressure
Left bundle branch block	Ventricular paced rhythm

DIAGNOSTIC IMAGING

ST SEGMENT ELEVATION: COMPARISON OF COMMON CAUSES			
	Pericarditis	ST Elevation Myocardial Infarction	Benign Early Repolarization
J Point Elevation	No	No	Yes
J Point Notching	No	No	Yes
Leads Involved	Diffuse	Coronary distribution[3]	Precordial V2-5
ST Elevation Type[1]	Concave	Convex, concave, horizontal	Concave
ST:T-wave Ratio	> 0.25	N/A	< 0.25
PR Depression[1]	Yes	No	No
Change Over Time	Yes (days)	Yes (hours)	No
ST Elevation III:II	Lead III < Lead II	Lead III > Lead II	
Reciprocal Changes[2]	No	Yes	No
T-waves	Normal T-wave amplitude	+/- T-wave inversions	Tall T-waves in QRS direction minor asymmetry
1. ST elevation and PR depression are measured relative to the TP segment 2. AVR and VI are right sided leads. Not counted as reciprocal ST depression 3. Septal (V1-2), Ant (V3-4), Lat (I, AVL, V5-6), Infer (II, III, AVF), RV (V1, AVR)			

CHEST XRAY: Obtain chest radiographs for all patients. The cardiac silhouette appears enlarged, described as the water bottle sign, if a pericardial effusion > 200-300 mL is present. Calcifications appearing as curvilinear densities at the extreme margins of the cardiac silhouette, described as an egg shell appearance, may be seen in constrictive pericarditis. Lastly, associated mediastinal enlargement and pulmonary pathology, such as pneumonia or pulmonary congestion, may be identified.

ECHOCARDIOGRAM: Perform a focused cardiac ultrasound (FoCUS) study to evaluate cardiac function and to assess for the presence of a pericardial effusion that may require immediate drainage. Order a formal echocardiogram as well. Notably, the absence of abnormalities on echocardiography does not exclude the diagnosis. Wall motion abnormalities are suggestive of STEMI.

ADVANCED IMAGING: For equivocal cases, consider the use of cardiac magnetic resonance imaging (preferred) or cardiac computed tomography.

MANAGEMENT

PERICARDIOCENTESIS: The first priority in management is to determine if tamponade physiology is present. Hemodynamic compromise is related to the acuity of pericardial fluid accumulation with rapid accumulation resulting in greater compromise. If present, rapid intravenous fluid administration can be lifesaving until pericardiocentesis is performed. An increase in preload increases stroke volume and thereby increases cardiac output.

Cardiac tamponade is an indication for performing emergent pericardiocentesis in the emergency department (See: PEM Guide: Cardiology: Pericardiocentesis). In contrast, elective pericardiocentesis in a more controlled setting is indicated for suspected bacterial pericarditis, suspected malignant pericarditis, and large pericardial effusions (diastolic echo-free space > 20 mm in width) present for more than 3 months. The most common acute complication of this procedure is myocardial puncture. The complication rate can be reduced by the use of ultrasound for procedural guidance.

MEDICATIONS: The goal of initial medical treatment is reduction of pericardial inflammation. Nonsteroidal anti-inflammatory drugs (NSAIDs) are accepted as first-line treatment in viral and idiopathic pericarditis. Ibuprofen is the most commonly used NSAID. The weight-based dose is 10 mg/kg up to 600 mg every 6 hours. Naproxen or indomethacin are alternatives. The usual treatment course is 1-2 weeks, although this varies based on clinical response. Use proton pump inhibitors with NSAIDs for gastrointestinal protection. If a specific cause other than a viral infection is identified, then tailor therapy for that condition (e.g., antibiotics for a bacterial infection).

The adult literature supports the use of colchicine in addition to NSAIDs as first-line treatment for acute pericarditis. Evidence suggests that colchicine use decreases the rate of recurrent pericarditis. The recommended weight-based dose is 0.5 mg daily for patients < 70 kg and 0.5 mg twice daily for patients ≥ 70 kg. The usual treatment course is 3 months, although this varies based on clinical response. A systematic review of the pediatric literature in 2016 concluded that there is not enough evidence to support or discourage the use of colchicine for pediatric pericarditis (Alabed, Arch Dis Child 2016, PubMed ID: 27083755). Early consultation with a pediatric cardiologist for guidance is warranted.

Corticosteroids are reserved for pericarditis refractory to initial treatment, pericarditis caused by autoimmune diseases, and uremic pericarditis. Evidence demonstrates that their use increases the risk of recurrent pericarditis.

ADDITIONAL THERAPIES: Bacterial pericarditis requires pericardiocentesis with continuous drainage of pericardial pus by placement of an indwelling catheter, antibiotic therapy, and the use of intrapericardial fibrinolytic agents as needed. In some cases, surgical consultation is necessary to perform a pericardial window or pericardiectomy. Partial or complete pericardiectomy is recommended for constrictive pericarditis.

DISPOSITION

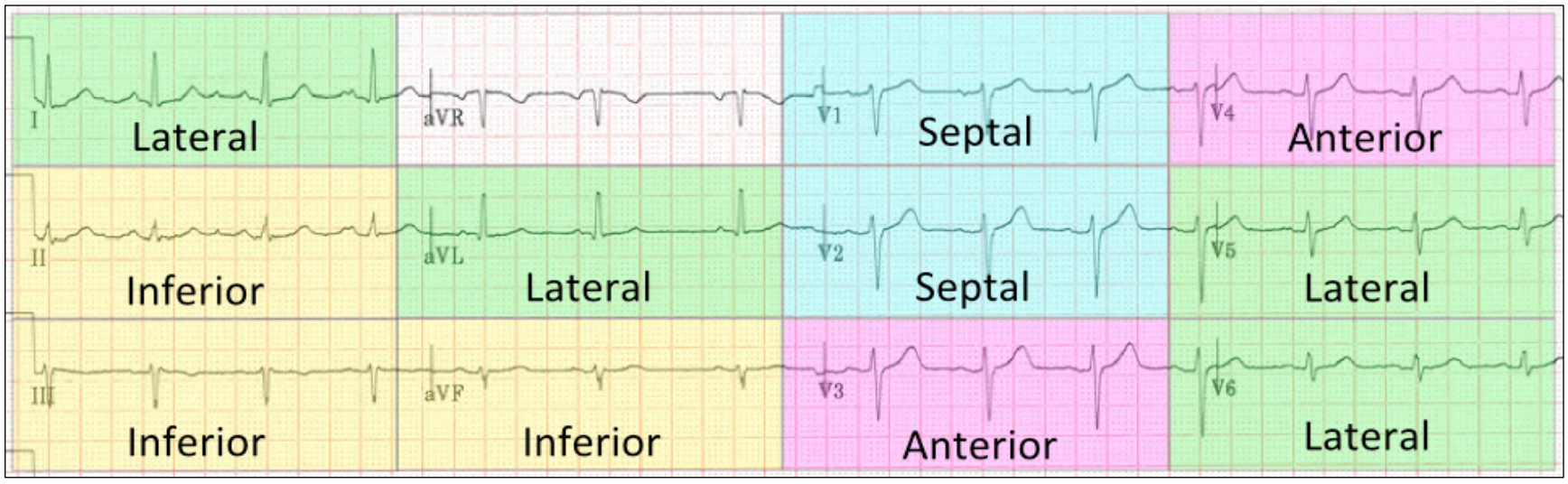
There are criteria published in the adult literature that identify low-risk patients who may be safely discharged home from the emergency department and managed on an outpatient basis. In a study of 300 patients, 85% met low-risk criteria and were managed as outpatients. 13% managed as outpatients required subsequent admission with no major complications (Imazio, J Amer Coll Cardiology 2004, PubMed ID: 15028364).

However, these criteria have not been validated in the pediatric population. Pediatric cardiology should be involved in the disposition decision for pediatric patients. In general, patients with evidence of myocardial involvement (troponin elevation), a large pericardial effusion, or hemodynamic instability should be admitted to a monitored setting.

ADULT LOW-RISK PERICARDITIS CRITERIA
Not a subacute onset
No fever
No immunosuppression
No trauma
No myopericarditis
No large pericardial effusion
No cardiac tamponade
No anticoagulant therapy

APPENDIX: MYOCARDIAL INFARCTION

CORONARY ARTERY DISTRIBUTIONS



RECIPROCAL CHANGES		
SITE	FACING	RECIPROCAL
SEPTAL	V1, V2	None
ANTERIOR	V3, V4	None
ANTEROSEPTAL	V1, V2, V3, V4	None
LATERAL	I, AVL, V5, V6	II, III, AVF
ANTEROLATERAL	I, AVL, V3, V4, V5, V6	II, III, AVF
INFERIOR	II, III, AVF	I, AVL

SUPRAVENTRICULAR TACHYCARDIA

INTRODUCTION (RACHEL KOWALSKY, M.D., MPH, 11/2020)
The term supraventricular tachycardia describes any narrow complex tachycardia that originates in the atria (See Table below). A narrow complex tachycardia is defined by a QRS duration of less than or equal to 0.09 seconds (90 milliseconds) and a ventricular rate of greater than 100 beats/minute (in adults). See: PEM Guide: Cardiology: Arrhythmias: An Overview, PEM Guide: Resuscitation: PALS Update 2020: Advanced Life Support

SUPRAVENTRICULAR TACHYCARDIAS	
Sinus Tachycardia	Atrial Fibrillation
AV Node Reentrant Tachycardia (AVNRT)	Atrial Flutter
AV Reentrant Tachycardia (AVRT)	Ectopic Atrial Tachycardia
Multifocal Atrial Tachycardia	Junctional Tachycardia
All SVTs have a narrow QRS complex with the exception of antidromic AVRT	

Atrioventricular Nodal Reentrant Tachycardia (AVNRT) is a narrow complex tachycardia with the reentrant loop within the AV node. In AVNRT the heart rate is typically greater than 220 beats/min in infants and young children and greater than 180 beats/min in adolescents and adults.

AVNRT should be distinguished from Atrioventricular reentrant tachycardia (AVRT). In AVRT, the reentrant loop is through an accessory pathway (AKA bypass tract or aberrant conduction). AVRT conduction can be further classified as orthodromic (95%) or antidromic (5%). The conduction pathway taken is dependent on the responsiveness of the AV node. If the AV node is in an excitable state, a premature atrial beat travels anterograde down the AV node and retrograde through the accessory pathway (orthodromic). Anterograde conduction through the AV node results in a narrow QRS complex. If the AV node is in a refractory state, a premature atrial beat travels anterograde down the accessory pathway and retrograde through the AV node (antidromic). Anterograde conduction through the accessory pathway results in a wide QRS complex.

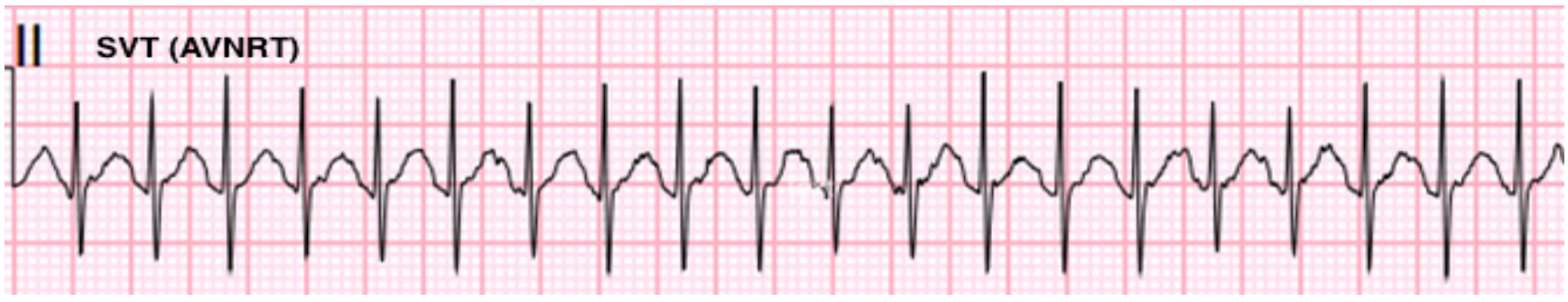
PATHOPHYSIOLOGY
Tachycardia reduces the time for ventricular filling thus reducing stroke volume. This results in a decrease in cardiac output. In addition, tachycardia increases myocardial oxygen consumption and decreases the length of diastole decreasing coronary perfusion.

CLINICAL MANIFESTATIONS
Infants typically present with nonspecific symptoms such as poor feeding (decreased PO intake, longer time to feed, sweating during feeding), irritability and tachypnea. Nonspecific symptoms result in delayed identification and infants often present with signs of cardiogenic shock. Older patients may present with an acute onset of palpitations, dizziness, syncope or chest pain. The physical exam may demonstrate signs of fluid overload such as pulmonary edema, hepatomegaly and ascites. Jugular venous distention is difficult to identify in young children.

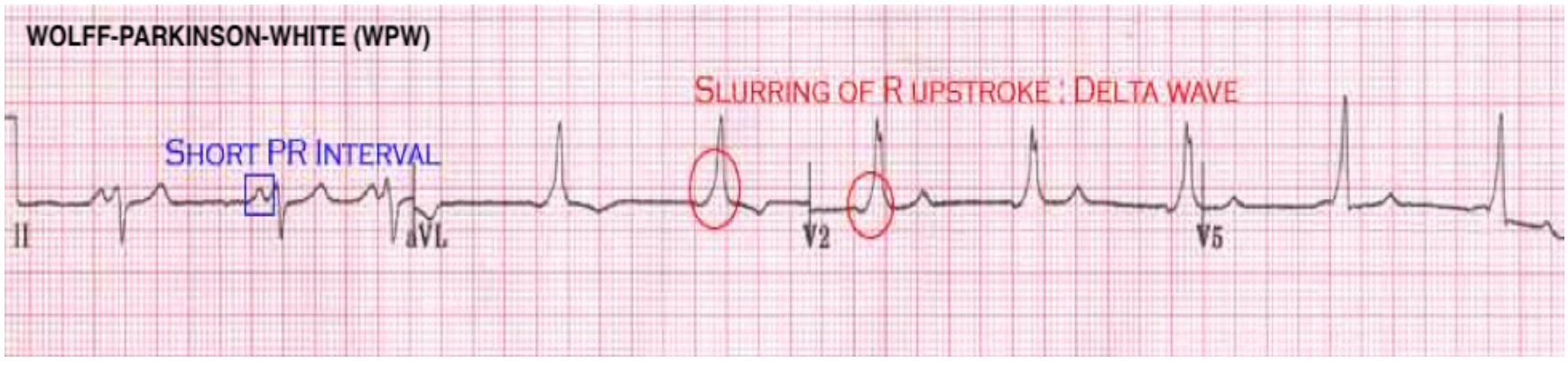
DIAGNOSIS

The diagnosis and management of SVT is illustrated by the American Heart Association Pediatric Tachycardia with a Pulse and Poor Perfusion Algorithm (2015). The first step in the algorithm is the evaluation of the QRS duration in order to distinguish between narrow (e.g. SVT. Sinus Tachycardia, etc.) and wide complex tachycardias (Ventricular Tachycardia, Antidromic AVRT, Bundle Branch Blocks). A narrow complex tachycardia is defined as a QRS duration less than or equal to 0.09 seconds (90 milliseconds). It is important to distinguish between the most common narrow complex tachycardias in pediatric patients: AVNRT and Sinus Tachycardia (see table below) Atrial fibrillation and atrial flutter are rare in pediatric patients without congenital heart disease.

COMPARISON: SINUS TACHYCARDIA VS SVT (AVNRT)		
	SINUS TACHYCARDIA	SUPRAVENTRICULAR TACHYCARDIA (AVNRT)
History: Infants	Dehydration, hypovolemia, Fever, Pain, Stress Medications, Ingestions	Non-specific vague history Irritability, sleepiness Poor feeding, Decreased activity
History: Child	Fever, Pain, Stress Medications, Ingestions	Sudden onset, Palpitations Chest discomfort, Anxiety
Onset	Warm-up and cool-down	Abrupt onset and termination
P waves	Present and Normal	Absent or Abnormal
R-R (HR)	Variable (irregular)	Not variable (regular)
Infants HR	< 220 beats/min	> 220 beats/min
Child HR	< 180 beats/min	>180 beats/min



WPW SYNDROME (WOLFF-PARKINSON WHITE) is an AVRT (has an accessory pathway). The EKG demonstrates evidence of pre-excitation. Conduction through the accessory pathway bypasses the AV node resulting in a shortened PR interval and a slurring of the R wave upstroke (Delta wave). A “pseudo-wide” QRS can also be found due to the delta wave. Orthodromic conduction does not demonstrate evidence of pre-excitation (RESOURCE LINK: LITF EKG)



MANAGEMENT

Support airway and breathing as needed and provide supplemental oxygen. Obtain intravenous access and consider an analgesic and/or sedative if the cardiopulmonary status permits. Initiate continuous cardio-pulmonary monitoring. Obtain a 12-lead EKG and run a continuous rhythm strip during interventions. Managements options include mechanical maneuvers, pharmacologic cardioversion and electrical cardioversion. Selection among these options is based on the patient's cardiovascular status and the availability of intravenous access. Cardiopulmonary compromise is defined as hypotension, signs of shock or altered mental status.

SUPRAVENTRICULAR TACHYCARDIA: MANAGEMENT OVERVIEW	
ALL PATIENTS	
Maintain airway, ventilation PRN, IV/IO access, 12 lead ECG, monitor/defibrillator Assess for cardiopulmonary Compromise: Altered mental status, shock, hypotension?	
CARDIOPULMONARY COMPROMISE: NO	
Vagal Maneuvers	Infants: ice to face without occluding airway Child: Unilateral carotid massage or Valsalva
IV Access Adenosine	Deliver centrally via a 3-way stopcock followed by rapid flush 0.1 mg/kg (max 6 mg), repeat as needed 0.2 mg/kg (max 12 mg)
Expert consultation	Cardiology consult prior to additional medications (see below) if vagal maneuvers and Adenosine unsuccessful and remains stable
CARDIOPULMONARY COMPROMISE: YES	
IV Access Adenosine	Do not delay cardioversion if IV access not readily available Deliver centrally via a 3-way stopcock followed by rapid flush 0.1 mg/kg (max 6 mg), repeat as needed 0.2 mg/kg (max 12 mg)
Synchronized Cardioversion	0.5 Joules/Kg →1.0 J/Kg → 2.0 J/Kg (Adult: 50-100 Joules) Sedate if needed as does not delay cardioversion
Expert consultation	Cardiology consult prior to additional medications (see below) if vagal maneuver, Adenosine and cardioversion are unsuccessful
ADDITIONAL MEDICATIONS: Expert consultation advised prior to use	
Consider Amiodarone OR Procainamide (not both, both prolong QRS, QTc)	
Amiodarone	Child: 5 mg/kg IV/IO over 30-60 min. Repeat x 2 to a total of 15 mg/kg Adult: 1st dose = 300 mg, 2nd dose = 150 mg)
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes, monitor QRS duration Adult: 20 mg/min infusion to max dose of 17 mg/kg
Verapamil	Child: 0.1-0.3 mg/kg > 2 years (Not in < 2 years. May cause myocardial depression, BP and arrest) Adult: 1st dose 5 mg, 2nd dose 10 mg)
See also: PEM Guide: Cardiology: Supraventricular Tachycardia	

WEB LINK: PEDIATRIC TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

HEMODYNAMICALLY STABLE SVT

VAGAL MANEUVERS
VAGAL MANEUVERS
Diving reflex: Apply a bag filled with ice water to the forehead, eyes and bridge of the nose for 10-15 seconds (without obstructing the nares or mouth)
Unilateral carotid massage (not bilateral)
Eye globe pressure is contraindicated due to the risk of retinal detachment
VALSALVA
Forced expiration against closed glottis: Bear down, blow through a straw
MODIFIED VALSALVA
Sitting patient blows into a sphygmomanometer at pressure of 40 mmHg for 15 seconds or blows into a 10 ml syringe until just moving the plunger
Then lie back in the Trendelenburg position with legs elevated.
Multicenter, RCT (n=428, adults with SVT. Conversion: Modified Valsalva: 43% vs Standard Valsalva 17% (NNT = 3)
Appelboam, REVERT Trial, Lancet 2015, PubMed ID: 26314489). VIDEO LINK: MODIFIED VALSALVA PROCEDURE

ADENOSINE
Adenosine: 0.1 mg/kg (Adult 6 mg) then repeat as needed at 0.2 mg/kg (Adult 12 mg)
Push Adenosine fast, follow immediately with 5-10 ml rapid NS flush. Due to its short half-life it is recommended that adenosine be administered rapidly through a stopcock system so that a flush can be administered immediately. If needed, IO line can be used.
If a response is not seen within 20 seconds, the Adenosine did not work
Many patients feel an impending sense of doom as if they are going to die when treated with Adenosine. It is important to warn them that they may feel this prior to administration.
May serve a diagnostic if not therapeutic purpose. Adenosine causes transient AV-block and may unmask Atrial flutter or Atrial fibrillation with 1:1 conduction

ADENOSINE REFRACTORY STABLE SVT
Consider synchronized cardioversion, alternative medications or overdrive pacing in consultation with pediatric cardiology if the above interventions are unsuccessful and the patients remain hemodynamically stable. If time permits sedation and/or analgesia should be provided prior to cardioversion.
Consider Amiodarone OR Procainamide (Not both. Both increase QRS duration)
Amiodarone: 5 mg/kg IV/IO over 20-60 minutes (Adult 1st dose = 300 mg) Repeat x 2 to a total of 15 mg/kg (Adult 2nd dose = 150 mg)
Procainamide: Child 15 mg/kg IV/IO over 30-60 minutes, monitor QRS width Adult 20 mg/min infusion to max dose of 17 mg/kg
Verapamil: Do not given in patents less than 2 years of age without expert consultation. It may cause myocardial depression, hypotension and arrest Verapamil: 0.1-0.3 mg/kg > 2 years (1st dose max 5 mg, 2nd dose max 10 mg) Avoid in WPW → ↑ accessory pathway conduction → ↑ ventricular fibrillation

HEMODYNAMICALLY UNSTABLE SVT

Consider medication options if intravenous access can be rapidly obtained. Consider an analgesic and/or sedative for an awake patient. If clinical status does not permit intravenous access and medical conversion, perform electrical conversion with synchronized cardioversion: 0.5 Joules/Kg → 1.0 J/Kg → 2 J/Kg (Adult 50-100 J)

MANAGEMENT: WIDE COMPLEX (SVT WITH ABERRANT CONDUCTION)

A wide QRS complex is consider ventricular tachycardia until proven otherwise.
Antidromic conduction in SVRT (e.g. WPW) occurs in 5-10% of SVT. This results in a wide QRS complex. If the wide complex tachycardia is monomorphic and regular, Adenosine may be considered. Adenosine slows conduction through the AV nodes and can differentiate between SVT and ventricular tachycardia. Otherwise Amiodarone or Procainamide should be administered or synchronized cardioversion should be attempted. Wide complex SVT can also be seen in those with a rate related or preexisting bundle branch block. See: PEM Guide: Cardiology: Ventricular Tachycardias

APPENDIX: SUPRAVENTRICULAR TACHYCARDIAS MEDICATIONS

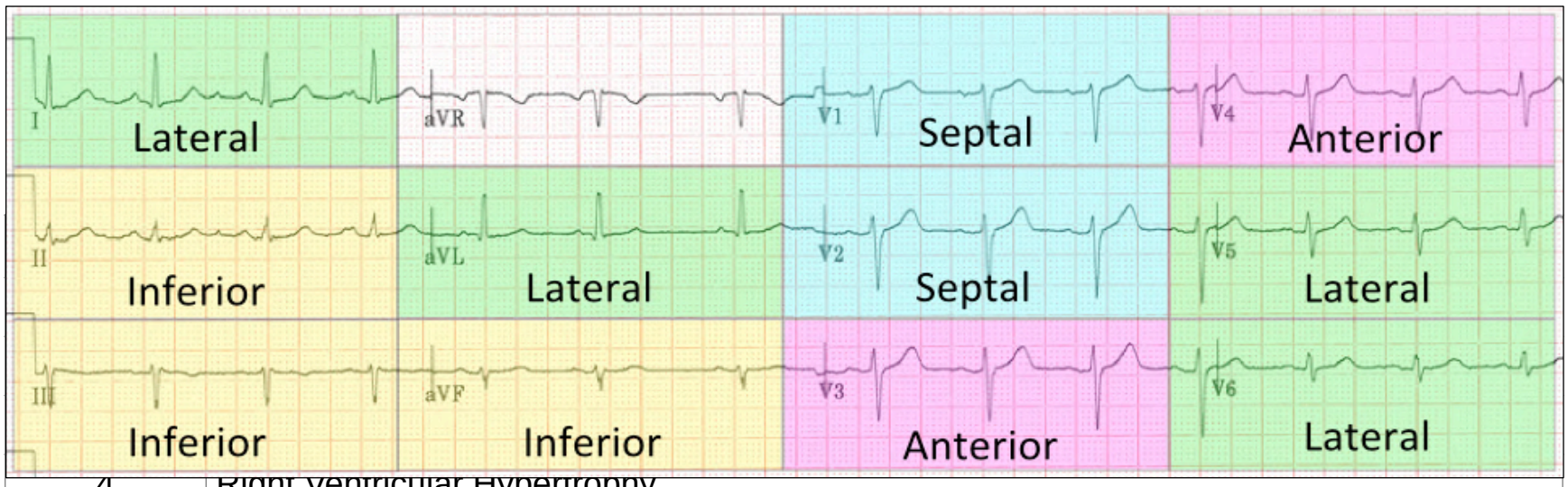
MEDICATION SELECTION FOR SUPRAVENTRICULAR TACHYCARDIAS			
MEDICATION	BOLUS	INFUSION	COMMENTS
Adenosine	0.1 mg/kg (Adult 6 mg) 0.2 mg/kg (Adult 12 mg)	None	Rapidly push and flush with stopcock system
Amiodarone	5 mg/kg over 20-60 min Repeat x 2 to a total dose of 15 mg/kg Adult 1st dose = 300 mg Adult 2nd dose = 150 mg	5-10 mg/kg/day	Do not give with Procainamide
Digoxin	5 mcg/kg (infants) 10 mcg/kg (children)	None	Contraindicated > 1yr with pre-excitation (WPW)
Esmolol	100-500 mcg/kg over 1 min	200 mcg/kg/min	
Procainamide	15 mg/kg over 30-60min Max 100 mg/dose Adult 20 mg/min infusion to max dose of 17 mg/kg	20-80 mcg/kg/min	Do not give with Amiodarone Monitor QRS width
Verapamil	0.1 – 0.03 mg/kg Over 2 minutes Max 1st 5mg, 2nd 10mg	1-7 mcg/kg/min	Contraindicated < 2 years

APPENDIX: DEFIBRILLATOR USE

INTRODUCTION
Use of a defibrillator can be life-saving. However, a number of steps are required in order to use it effectively and safely.
It is important to become familiar with whichever brand of defibrillator is available at sites that you will be working.
Think of the use of the defibrillator as hitting the electrical reset switch (as opposed to the pharmacologic reset switch). Essentially it stops whatever bad rhythm is currently happening with the hope that a normal rhythm will restart
No stacked shocks. Shock → CPR x 2 minutes → Shock → CPR x 2 minutes
Give medications during CPR (no pause): Epinephrine, Amiodarone, Lidocaine

PROCEDURE: DEFIBRILLATION/CARDIOVERSION	
Sedation	Consider sedation and analgesia in an awake, cardiovascularly stable patient
Modes	1. Cardioversion: (synchronized): Supraventricular tachycardia, Ventricular tachycardia with pulse, atrial fibrillation/flutter
	2. Defibrillation: Ventricular fibrillation and tachycardia without a pulse
	3. Monitor: (including use of the paddles for a “quick look”)
	4. Pacemaker: Cardiovascularly unstable heart blocks
	5. AED: Some defibrillators may be used as an AED as well
Energy level: Defibrillation	Child: 2 → 4 → 8 Joules/kg Adult: Biphasic: manufacturer recommendation or 120-200 Joules, Monophasic 360 Joules (Biphasic at least as effective as monophasic and less harmful)
Energy level: Synchronized Cardioversion	Child: 0.5 →1.0 → 2.0 Joules/kg Adult: SVT: 50-100 Joules, ↑ PRN, VT with a pulse, regular and monomorphic: 100 Joules
Paddle/Pad Size	Pediatric paddles < 10 kg (must remove adults paddles first)
Interface material	“Electrode” gel, paste, pads. No ultrasound gel or alcohol pads
Paddle/Pad Location	The heart goes between the paddles/pads 1. Sternum and apex OR 2. Anterior and posterior
Safety	“I’m clear, you are clear, we are all clear” The airway person is usually the last to leave.
Charge	If using paddles, it is safer to charge while paddles are on the patient’s chest to avoid discharging them by accident on the way to the patient. Use of pads avoids this concern.
Discharge	Discharge can be initiated from the defibrillator or the paddles. Discharge is immediate for defibrillation but may require a second to attain synchronization with cardioversion Discharge takes longer for synchronized cardioversion
Re-evaluate	Both the patient and the monitor

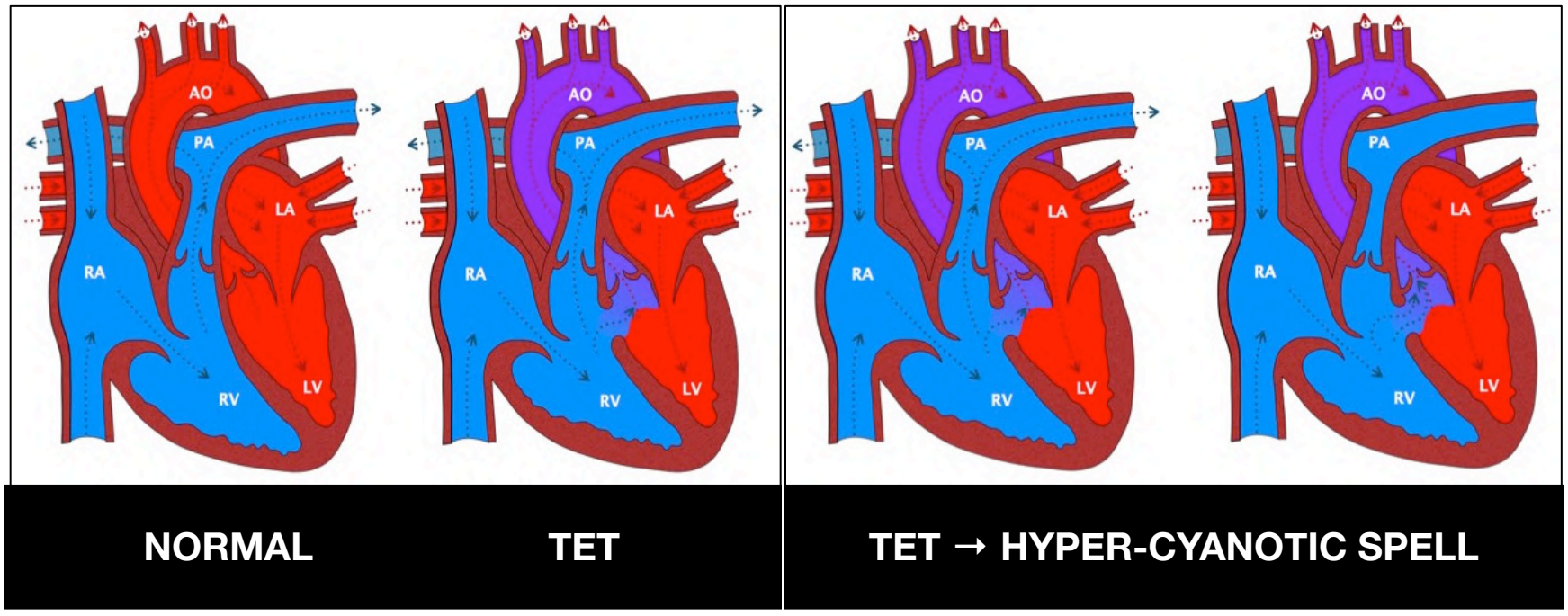
TETRALOGY OF FALLOT SPELLS



4	Right Ventricular Hypertrophy

INTRODUCTION (ADRIANA MANIKIAN, MD, 9/2019)
Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart lesion (See: PEM Guide: Cardiology: Cyanotic Congenital Heart Disease). The large VSD and overriding aorta result in complete mixing of the pulmonary and systemic circulations. Right ventricular outflow tract (RVOT) obstruction results in right to left shunting of blood and pulmonary under circulation.

HYPER-CYANOTIC SPELL
A hyper-cyanotic spell in TOF is a sudden exacerbation of existing cyanosis and is a true emergency. The pathophysiology is poorly understood. It appears to be due to up-regulation of the beta-receptors in the RVOT which are more numerous than in other parts of the myocardium in these children. The end result is an increase in RVOT obstruction which results in an increase in left to right shunting and an increase in cyanosis.



TET Spells typically develops in infants 2-3-month of age. TET spells can occur in both “pink” and cyanotic TOF patients. They typically occurs in the morning after feeding, bowel movement or bathing when systemic vascular resistance (SVR) is low or during periods of acute agitation (such as during invasive procedures) that are thought to increase RVOT obstruction. Presenting signs are irritability, persistent crying and worsening cyanosis or a sudden onset of cyanosis. If left untreated, TET spell may result in hypoxic seizures, stroke and death.

CLINICAL FINDINGS

The clinical presentation is dependent on the severity of the pulmonary outflow obstruction. The primary clinical manifestation of tetralogy of Fallot is cyanosis. In contrast, “pink” TETS, those with normal or increased pulmonary blood flow, present in congestive heart failure due to pulmonary over circulation.

Neonates with significant RVOT obstruction depend on a patent ductus arteriosus for pulmonary blood flow (Left to Right). When the ductus closes, they can present with cyanosis and require prostaglandin. Neonate with significant RVOT obstruction may require a surgical systemic to pulmonary shunt (e.g. Blalock-Taussig shunt) prior to definitive repair around 1 year of age.

Hypoxia in TOF is due to R-to-L shunting through a large ventricular septal defect (VSD) that equalizes right and left ventricular pressures. Complete venous mixing in these patients usually sustains oxygen saturation at around 70-80%. The degree of shunting depends on the balance between pulmonary vascular resistance (PVR), the degree of right ventricular outflow tract (RVOT) obstruction and systemic vascular resistance (SVR). Any condition that increases the PVR or increases RVOT obstruction, such as pneumonia, bronchiolitis or a hyper-cyanotic spell will result in increased shunting R-to-L through the VSD. Similarly, any condition that decreases SVR such as dehydration, will also result in increased R-to-L shunting.

A loud systolic ejection murmur may be detected at the left sternal border in TOF due to right ventricular outflow tract (RVOT) obstruction. The absence of a murmur in a patient in distress may represent complete RVOT obstruction. The large, unrestrictive VSD is not the source of the murmur. The second heart sound may be diminished as the aorta overrides the pulmonary artery. The absence of a murmur in a patient with a systemic to pulmonary shunt is indicative of shunt blockage.

An EKG may show nonspecific right ventricular hypertrophy (Appendix). A chest XRAY may show decreased pulmonary vascular markings and a “boot shaped” heart due to an absent or decreased pulmonary artery segment (Appendix).

MANAGEMENT

Treatment of TOF in the neonate includes PGE1 if the patient is cyanotic and pulmonary blood flow is ductal dependent. Surgical intervention may include a modified Blalock-Taussig shunt (Gortex conduit connecting of the subclavian artery to a branch pulmonary artery). Definitive treatment typically occurs around 1 year of age and includes repair of the RVOT obstruction with augmentation and or repair of the pulmonic stenosis and closure of the VSD.

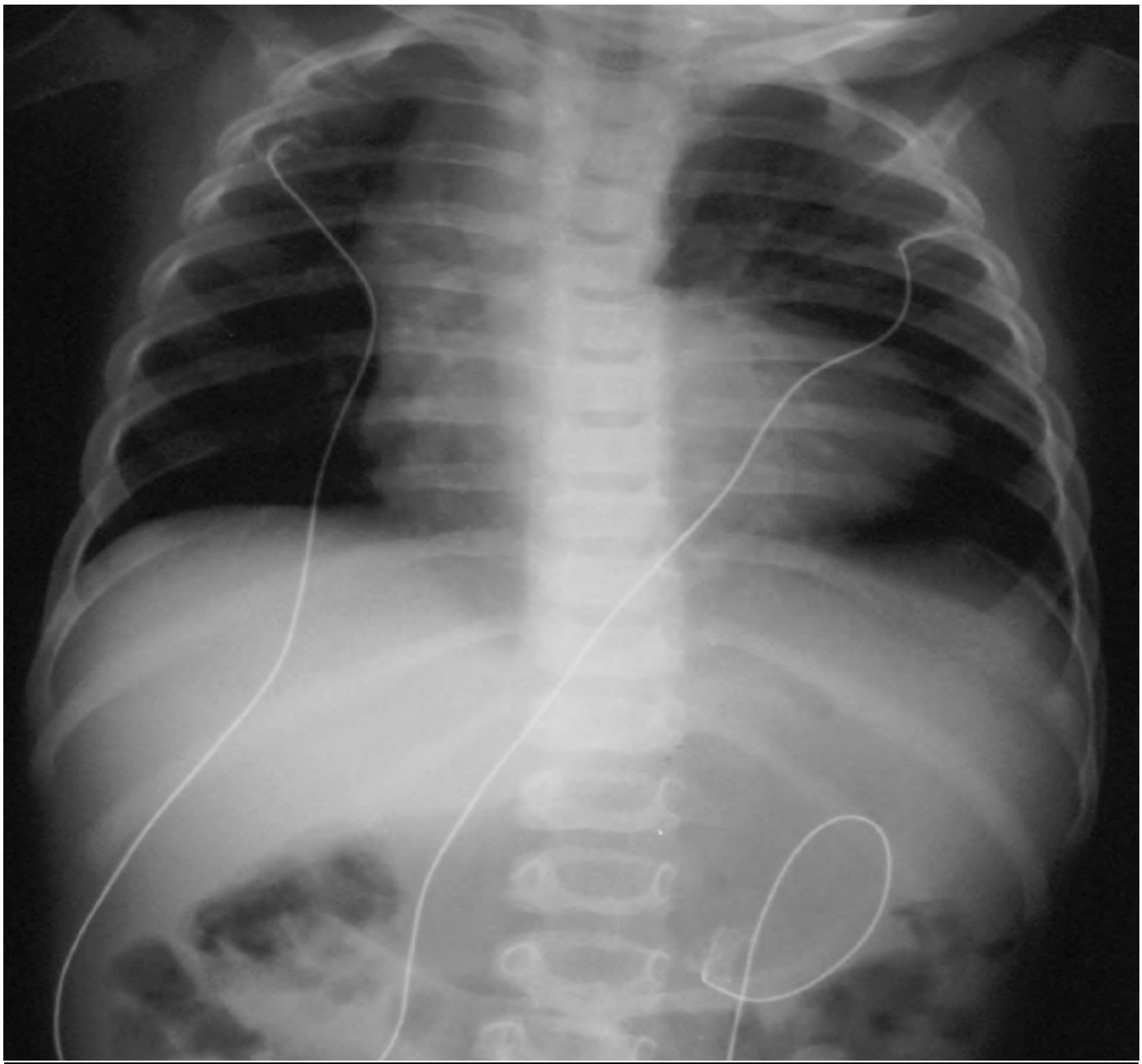
Avoid agitating the infant with procedures such as blood drawing. Try to keep the child in a position of comfort with the parents. Cardiology should be consulted early in the management of these patients, since the patient may require more intensive therapy and possibly emergent surgery if the spell cannot be aborted. Severe cases may require abdominal aorta compression and an emergent Blalock-Taussig shunt. Sodium bicarbonate may be required to correct acidosis.

Those with suspected Blalock-Taussig shunt blockage require urgent cardiology and cardiothoracic surgery consultation and possible anticoagulation with tissue plasminogen activator and heparin and emergency operative repair if anticoagulation is not successful.

GENERAL MANAGEMENT	
↑ SVR	Knee-chest position, squatting, IV fluids, vasoconstrictors
↓ PVR	Calming, sedation
↓ RVOT Obstruction	Beta blockers
Surgery	Emergent systemic to pulmonary shunt

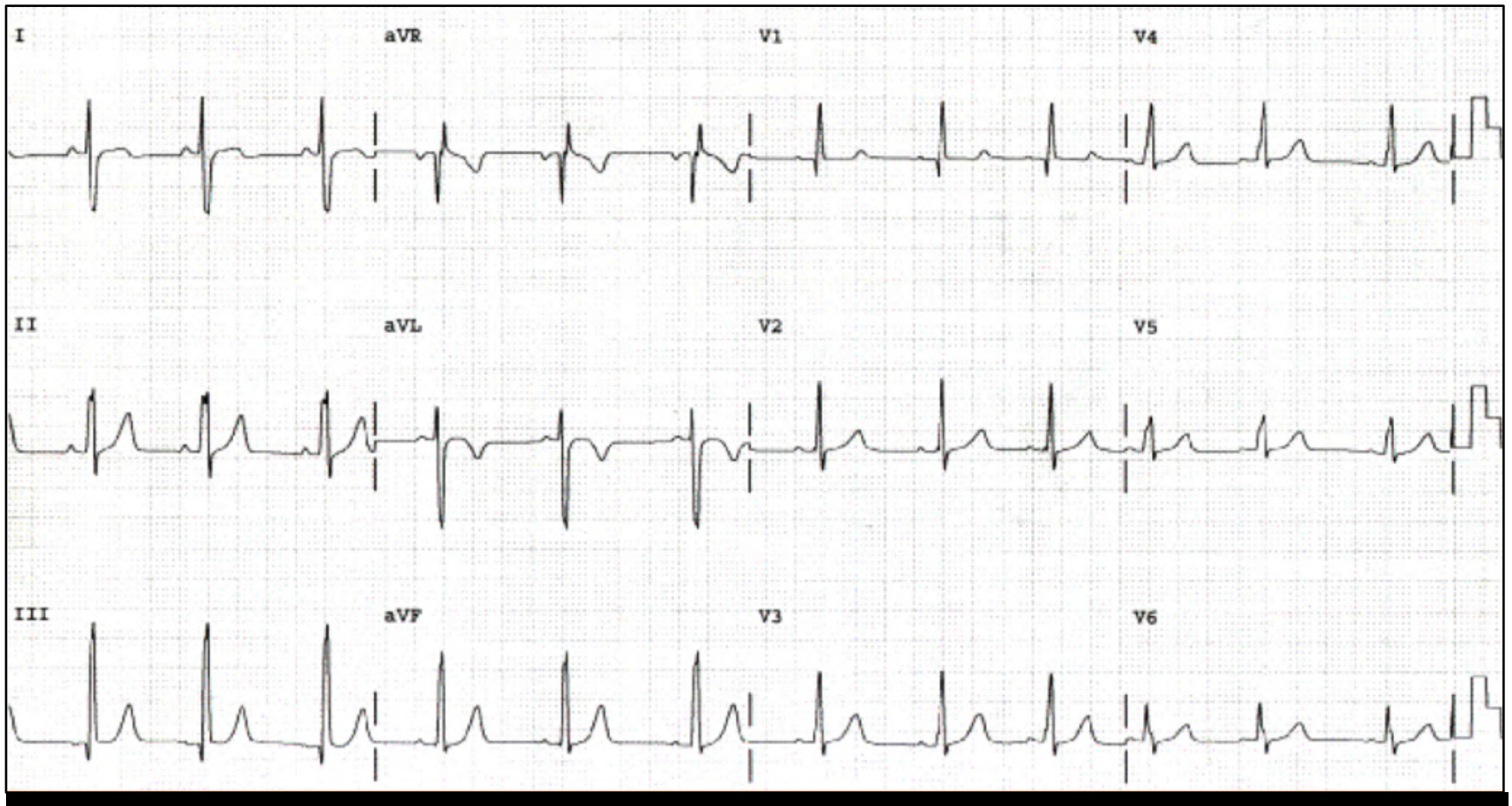
MANAGEMENT OPTIONS	
GOALS	Correct hypoxia and acidosis Decrease PVR and RVOT obstruction Increase SVR
Calming	Provide a quiet environment with parents
Positioning	The knee-chest position increases SVR
Oxygen	Blow-by in a non-threatening manner Oxygen: Pulmonary vasodilator, systemic vasoconstrictor
Morphine	0.1-0.2 mg/kg SQ, IM, IV Calms the infants, decreases PVR. Decreases circulating catecholamines and relax RVOT
Ketamine	0.5 -1.0 mg/kg Sedative and mild sympathomimetic. Increases SVR. In prolonged spells the patient may be catecholamine depleted and Ketamine may precipitate an arrest
Beta Blockers	Relaxes the RVOT, ↓↑ HR → ↑ diastolic filling Esmolol: 500 mcg/kg over 1-minute IV, then 50 mcg/kg/min Can increase by 50 mcg/kg/min to max of 300 mcg/kg/min Ultrashort acting, selective (beta 1 receptor only) antagonist Propranolol: 0.01-0.2 mg/kg IV
Normal saline bolus	10-20 ml/kg Increases the SVR, especially if child is dehydrated. Increases right ventricular pre-load. Fluids should be given slowly in TOF patients who are pink” on diuretics due to pulmonary over circulation to prevent pulmonary edema
Sodium bicarbonate	1 mEq/kg IV Decreases acidosis. Acidosis may prolong the hyperpneic cycle. Consider in a protracted cyanotic spell
Vasoconstrictors	Increase the systemic vascular resistance Phenylephrine (alpha-agonist); 0.1 mg/kg bolus IV/SQ/IM followed by 2-10 mcg/kg/min IV Norepinephrine: 0.1-0.5 mcg/kg/min
Surgery	Emergent modified Blalock-Taussig shunt (subclavian artery to right pulmonary artery shunt) Temporizing until old enough to undergo definitive repair 1. TOF spell unresponsive to medical therapy 2. Occluded B-T shunt not improved by anticoagulation

APPENDIX: CHEST XRAY: TETRALOGY OF FALLOT



XRAY FINDINGS: “BOOT-SHAPED” HEART, ↓ PULMONARY VASCULAR MARKINGS

APPENDIX: EKG: TETRALOGY OF FALLOT



EKG FINDINGS: RIGHT SIDED DOMINANCE: POSITIVE T-WAVES IN LEADS V1 – V3, AXIS NOTED BY QRS DIRECTION IN LEADS I AND AVF.

VENTRICULAR ARRHYTHMIAS

INTRODUCTION (RACHEL KOWALSKY, M.D., MPH 11/2020)
Ventricular arrhythmias are abnormal and potentially fatal rhythms that originate in the ventricles. The majority of pediatric cardiac arrests are attributed to asystole often preceded by bradycardia. However, approximately 10% may involve ventricular arrhythmias. Ventricular arrhythmias are characterized by a QRS duration of greater than 0.09 seconds (90 milliseconds).

Both ventricular tachycardia and ventricular fibrillation negatively impact cardiac output
As the heart rate increases, the time available for ventricular filling decrease. This leads to a decreased stroke volume and subsequently cardiac output decreases. Ventricular tachycardia can deteriorate to ventricular fibrillation and ultimately asystole. Ventricular fibrillation represents disorganized cardiac electrical activity without effective cardiac output.

See: PEM Guide: Cardiology:: Arrhythmias: An Overview
See: PEM Guide: Resuscitation: PALS Update 2020: Advanced Life Support

ETIOLOGY

Many of the treatable causes of ventricular arrhythmias can be remembered using the American Heart Association mnemonic “The H’s and the T’s”:

H’s	T’s
Hypovolemia	Toxins (e.g. digitalis and catecholamines)
Hypoxia	Tamponade (cardiac)
Hydrogen ions (acidosis)	Tension pneumothorax
Hypo/hyperkalemia	Thrombosis (coronary)
Hypoglycemia other metabolic	Thrombosis (pulmonary)
Hypothermia	Trauma

ADDITIONAL CAUSES	
CARDIAC (STRUCTURAL)	CARDIAC (RHYTHM)
Myocarditis	Long QT syndrome
Cardiomyopathy	Brugada syndrome
Arrhythmogenic right ventricular dysplasia	Membrane channelopathy
Cardiac Tumors, Injury	Catecholamine polymorphic VT
TOXINS	ELECTROLYTES
Cyclic Antidepressants	Hyperkalemia
Sympathomimetics (e.g. Cocaine)	Hypokalemia
	Hypocalcemia

DIAGNOSIS

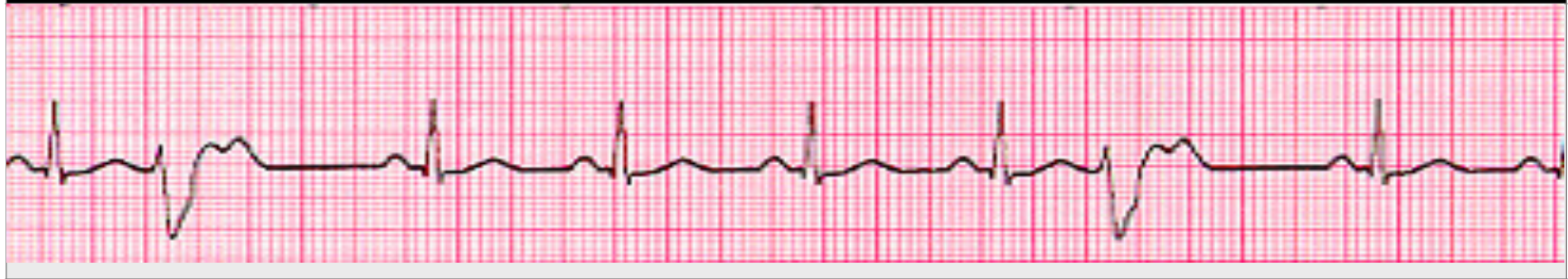
In clinically evaluating any arrhythmia, it is helpful to start with the following questions:

1. Is a pulse present or absent?
2. If there is a pulse, is there cardiopulmonary compromise (hypotension, signs of shock or an altered mental status)?

The diagnosis of a ventricular arrhythmia may be suggested by signs and symptoms such as syncope, altered mental status, chest pain, palpitations/tachycardia and shock.

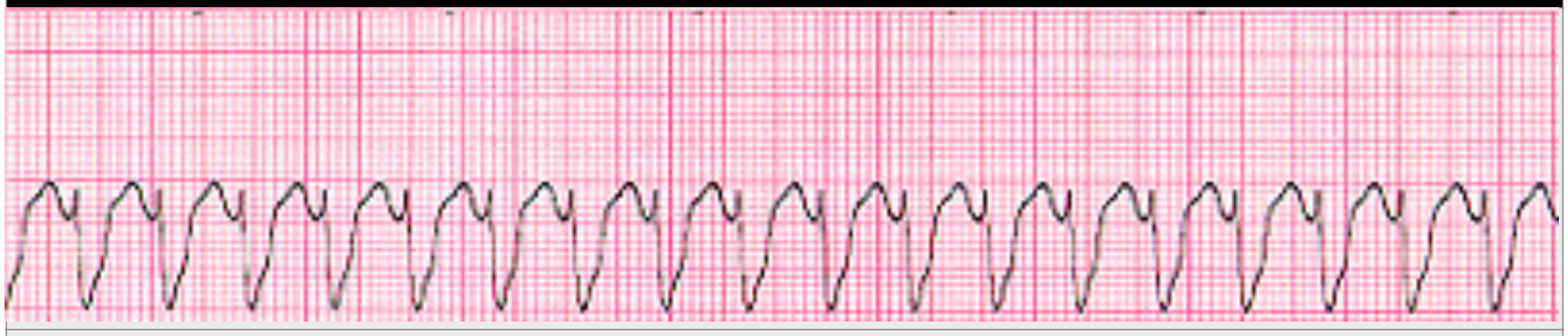
EKG: An ECG confirms the diagnosis. The primary distinguishing factors on the EKG are rate and QRS width. All of the ventricular arrhythmias are tachycardias with a wide QRS width (> 0.09 seconds or 90 milliseconds). They can be further defined as monomorphic (all waveforms similar) or polymorphic (varying waveforms). P waves may or may not be visible in ventricular tachycardia

PREMATURE VENTRICULAR CONTRACTIONS (PVC'S)



These wide complex beats result from an ectopic ventricular focus leading to early depolarization. They are most worrisome if they are associated with underlying heart disease, if they are worse with activity, if they are symptomatic, are multifocal or if they occur in couplets (two in a row).
Treatment, if required, consists of addressing the underlying cause.

VENTRICULAR TACHYCARDIA (VT)

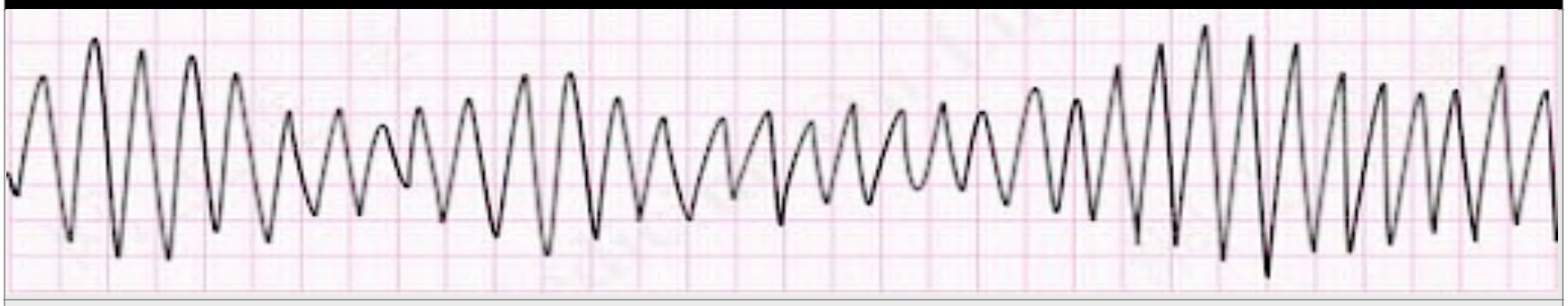


Rate usually 120-150 bpm. The P wave is dissociated, retrograde, or absent. There are 3 types of VT based on clinical status, all of which are managed differently (see the algorithms below):

- Pulseless VT
- VT with a pulse and cardiopulmonary compromise
- VT with a pulse and without cardiopulmonary compromise

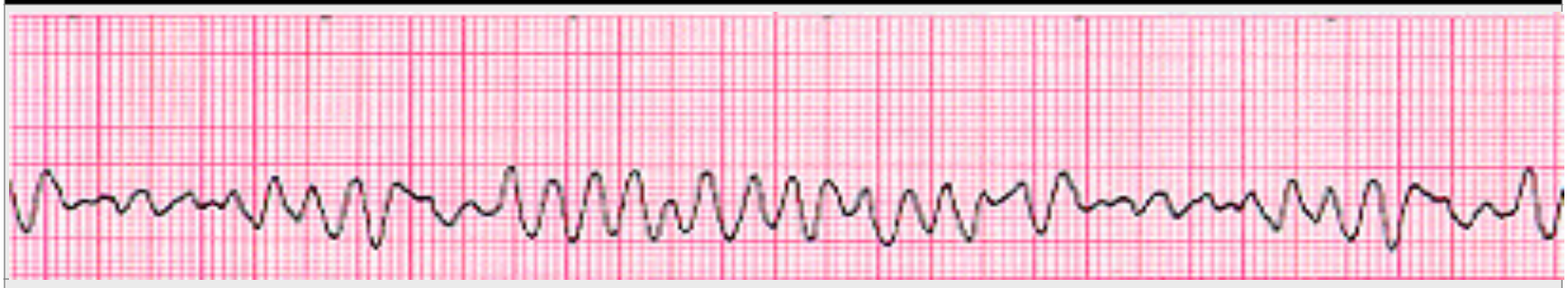
Cardiopulmonary compromise is defined as hypotension, altered mental status or signs of shock.
It can be difficult to distinguish VT from SVT with aberrancy; therefore, you should assume that the rhythm is VT unless the patient is known to have aberrant conduction. In patients with a pulse and without cardiopulmonary compromise Adenosine may be tried for a monomorphic VT

TORSADES DE POINTES (POLYMORPHIC VT)



Polymorphic VT with ↑ QT: Rate:150-250 bpm. QRS complexes change in polarity and amplitude, appearing to rotate around the EKG isoelectric line. ↑ QT acquired: ↓ K+, ↓ Mg++, ↓ Ca++, many medications or congenital. See Appendix.

VENTRICULAR FIBRILLATION (VF)



Ventricular fibrillation represents disorganized electrical activity and be described as coarse or fine. It is a pre-terminal rhythm which left untreated will deteriorate to asystole. QRS complexes of varying size and morphology and an irregular, rapid rate is seen. VF always occurs without a pulse, and requires immediate defibrillation.

MANAGEMENT

The American Heart Association has developed Pediatric Advanced Life Support algorithms for the management of cardiac arrhythmias. (see the cardiac arrest algorithm and the tachycardia with a pulse algorithm in the appendix). Ventricular arrhythmias require prompt recognition, initiation of chest compression and post pressure ventilation (if pulseless), cardioversion (electrical or pharmacologic) and treatment of underlying causes.

ELECTRICAL: Defibrillation should be used early in the patients with ventricular tachycardia without a pulse and ventricular fibrillation. Synchronous cardioversion is recommended or those with Ventricular tachycardia without a pulse and cardiopulmonary compromise and as an adjunct to pharmacologic therapy in the stable a patient. See Appendix: Cardioversion and Defibrillation.

PHARMACOLOGIC: See Appendix: Medications for Ventricular Arrhythmias

VENTRICULAR FIBRILLATION/VENTRICULAR TACHYCARDIA WITHOUT A PULSE

PEDIATRIC CARDIAC ARREST ALGORITHM: VF, pVT	
Basic Life Support: High quality CPR, O_2, attach monitor and defibrillator	
Defibrillation: 2 Joules/kg → 4 J/kg → 4 J/kg (To maximum of 10 J/kg or adult dose) Use an initial dose of 2-4 J/kg, consider 2 J/kg for ease of teaching Adult: Biphasic (manufacturers suggested) or 120-200J, Monophasic at 360J)	
No stacked shocks: Single shock followed by compressions (start with compressions)	
Continue CPR: 2-minute cycles with ventilations, then pulse and rhythm assessment	
Medications: Give during chest compressions	
Epinephrine	Within 5 min of chest compressions, repeat Q3-5 minutes until ROSC IV/IO: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/kg Epinephrine, Adult 1.0mg ETT: 0.1 mg/kg = 0/1 ml/kg of 1.0 mg/ml Epinephrine, Adult 2.5 mg
Amiodarone OR Lidocaine is an acceptable antiarrhythmic agent for shock-refractory pediatric ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT)	
Lidocaine	1 mg/kg IV, repeat Q5-10min, If successful → 20-50 mcg/kg/min
Amiodarone	5 mg/kg IV/IO push. Repeat x 2 to total of 15 mg/kg Maximum single dose: Adult 1st dose = 300 mg, 2nd dose = 150 mg
Magnesium Sulfate	Indicated for Torsade de points (a type of polymorphic VT) 25-50 mg/kg, Maximum dose: 2 grams
See: PEM Guide: Cardiology: Ventricular Arrhythmias	

H's	T's
Hypovolemia	Toxins (e.g. digitalis and catecholamines)
Hypoxia	Tamponade (cardiac)
Hydrogen ions (acidosis)	Tension pneumothorax
Hypo/hyperkalemia	Thrombosis (coronary)
Hypoglycemia other metabolic	Thrombosis (pulmonary)
Hypothermia	Trauma

WEBLINK: PEDIATRIC CARDIAC ARREST ALGORITHM (AHA 2020)

WEBLINK: ADULT CARDIAC ARREST ALGORITHM (AHA 2020)

WIDE COMPLEX TACHYCARDIA (QRS > 0.09 SECONDS) WITH A PULSE

WIDE COMPLEX TACHYCARDIA (QRS > 0.09 SECONDS) WITH A PULSE	
ALL PATIENTS	
Maintain airway, ventilation PRN, IV/IO access, 12 lead ECG, monitor/defibrillator Assess for cardiovascular compromise: Altered mental status, shock, hypotension? a. Ventricular Tachycardia with a pulse (VT) b. Wide-complex Supraventricular Tachycardia (SVT with aberrant conduction)	
CARDIOVASCULAR COMPROMISE: YES	
Synchronized Cardioversion: 0.5-1.0 Joules/Kg ® 2 Joules /Kg (Adult 100 Joules)	
CARDIOVASCULAR COMPROMISE: NO	
Expert consultation prior to antiarrhythmic No pediatric evidence for specific antiarrhythmic in wide complex tachycardia Antiarrhythmics complications may occur in cardiomyopathy, WPW, prolonged QT Do not give both Amiodarone and Procainamide. Both increase QRS, QTc	
Adenosine	Consider adenosine if rhythm is regular and monomorphic. Adenosine: 0.1 mg/kg (max 6 mg) then 0.2 mg/kg (max 12 mg) Distinguish between wide complex SVT and Ventricular Tachycardia
Amiodarone	Child: 5 mg/kg IV/IO over 30-60 minutes. Repeat x 2 to total 15 mg/kg Adult: 1st dose = 300 mg, 2nd dose = 150 mg
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes, monitor QRS width Adult: 20 mg/min infusion to max dose of 17 mg/kg

WEB LINK: PEDIATRIC TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

APPENDIX: MEDICATIONS FOR VENTRICULAR ARRHYTHMIAS

PALS MEDICATIONS (2020): ANTIARRHYTHMICS			
	DOSE	INDICATIONS	COMMENT
Adenosine	0.1 mg/kg IV/IO (maximum 6mg) Repeat PRN 0.2 mg/kg IV/IO (maximum 12mg)	SVT Monomorphic Wide-complex Tachycardia with a pulse	Monitor EKG Rapid IV/IO Push via 3-way stopcock
Amiodarone	5 mg/kg IV/IO Repeat x 2 to total of 15 mg/kg (maximum: 300 mg)	IV/IO push V Fibrillation V Tachycardia without pulse	Monitor QRS Don’t give with Procainamide
		Over 20-60 minutes V Tachycardia with a pulse Refractory SVT	
Epinephrine	0.01 mg/kg IV/IO 0.1 ml/kg of (1:10,000 = 0.1 mg/ml) (max: 1 mg IV/IO)	Asystole Bradycardia PEA V Fibrillation V Tachycardia without a pulse	May repeat every 3-5 minutes Do not give with HCO_3 in same line
	0.1 mg/kg Endotracheal 0.1 ml/kg (1:1,000 = 1 mg/ml) (max: 2.5 mg ET)		
Lidocaine	1 mg/kg IV 20-50 mcg/kg/min IV	V Fibrillation V Tachycardia without a pulse	Repeat bolus Q5-10min
Magnesium Sulfate	20-50 mg/kg over 12-20 minutes IV/IO (max: 2 grams)	Torsades: Polymorphic V Tachycardia	
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes Adult: 20 mg/min infusion (max dose of 17 mg/kg)	V Tachycardia with a pulse	Monitor QRS Don’t give with Amiodarone
Sodium Bicarbonate	1 meq/kg IV/IO slowly	Tricyclic Overdose	

APPENDIX: CARDIOVERSION AND DEFIBRILLATION

INTRODUCTION
Use of a defibrillator can be life-saving. A number of steps are required in order to use it both effectively and safely.
It is important to be familiar with whichever brand of defibrillator is available at sites that you will be working.
Think of the use of the defibrillator as hitting the electrical reset switch (as opposed to the pharmacologic reset switch). Essentially it stops whatever undesired rhythm is happening with the hope that a normal rhythm will restart
No stacked shocks. Shock → CPR x 2 minutes → Shock → CPR x 2 minutes
Give medications during CPR (no pause): Epinephrine, Amiodarone, Lidocaine

PROCEDURE: DEFIBRILLATION/CARDIOVERSION	
Sedation	Consider sedation and analgesia in an awake, cardiovascularly stable patient
Modes	1. Cardioversion: (synchronized): Supraventricular tachycardia, Ventricular tachycardia with pulse, atrial fibrillation/flutter
	2. Defibrillation: Ventricular fibrillation and tachycardia without a pulse
	3. Monitor: (including use of the paddles for a “quick look”)
	4. Pacemaker:
	5. AED: Some defibrillators may be used as an AED
Energy level: Defibrillation	Child: 2 → 4 → 8 Joules/kg Adult: Biphasic: manufacturer recommendation or 120-200 Joules, Monophasic 360 Joules (Biphasic at least as effective as monophasic and less harmful)
Energy level: Synchronized Cardioversion	Child: 0.5 →1.0 → 2.0 Joules/kg Adult: SVT: 50-100 Joules, ↑ PRN Adult: VT with a pulse monomorphic: 100 Joules, ↑ PRN
Paddle/Pad Size	Pediatric paddles < 10 kg (must remove adults paddles first)
Interface material	“Electrode” gel, paste, pads. No ultrasound gel or alcohol pads
Paddle/Pad Location	The heart goes between the paddles/pads 1. Sternum and apex OR 2. Anterior and posterior
Safety	“I’m clear, you are clear, we are all clear” The airway person is usually last to leave.
Charge	If using paddles, it is safer to charge while paddles are on the patient’s chest to avoid discharging them by accident on the way to the patient. Use of pads avoids this concern.
Discharge	Discharge can be initiated from the defibrillator or the paddles. Discharge is immediate for defibrillation but may require a second to attain synchronization with cardioversion
Re-evaluate	Both the patient and the monitor

APPENDIX: TORSADES DE POINTES

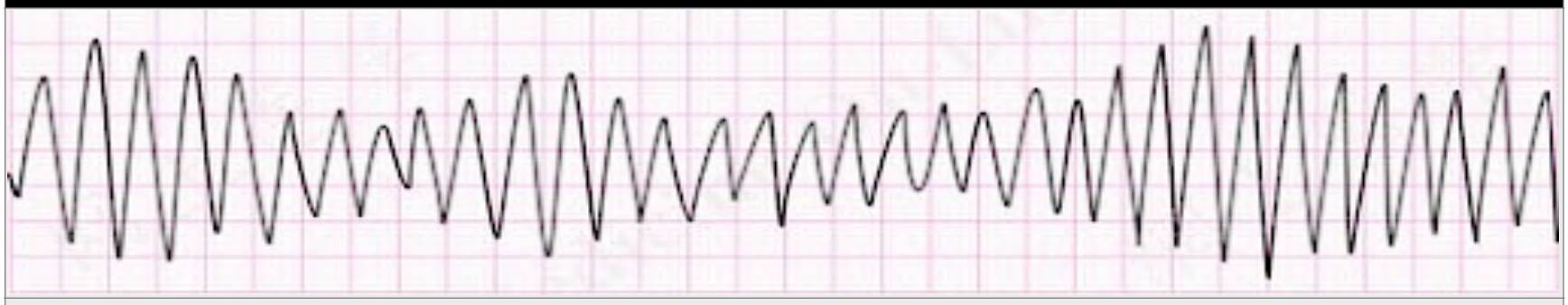
CLINICAL
Symptoms: Palpitations, dizziness, syncope, seizures, cardiac arrest
Generally short lived and self-terminating
Can rapidly develop hemodynamic instability/collapse
V Tach w/Pulse Stable → V Tach w/o Pulse Unstable → V Tach w/o Pulse → V Fib

PATHOPHYSIOLOGY
Form of polymorphic ventricular tachycardia (PVT) due to ↑ Q
PVT and ↑QT required for diagnosis
PVT without ↑ QT most commonly caused by MI
Prolonged QTc
Acquired (with bradycardia) or Congenital (with catecholamine surge)
Electrolyte abnormalities: ↓ Ca^{++}, ↓ K^{+}, ↓ Mg^{++}
Medications (Extensive list: See Link Below
Antiarrhythmic drugs: Procainamide, Amiodarone
Antimicrobials: Macrolides, Fluoroquinolones, some antifungal and antiviral
Psychotropic medications: Haloperidol, Thioridazine
Congenital long QT syndrome: Romano-Ward, Jervell and Lange-Nielsen syndrome
PATHOPHYSIOLOGY
Myocyte repolarization malfunction → Early after-depolarizations (EAD) (Tall U waves). If EAD reaches threshold → Premature ventricular contractions (PVC) PVC occurs during the preceding T wave (R on T phenomenon) → Vent Tachycardia

WEB LINK: QT PROLONGING MEDICATIONS

EKG
Prolonged QTc Interval
Best seen: Lead II, V5
QT Interval; Onset of the QRS complex to the point at which the T wave ends
Calculation: Do not include U wave. Use JT interval if bundle branch block
QTc: Corrected for HR (↑ HR → ↓ QTc), Bezett Formula: QTc = QT / (square root of the R-R interval)
Rhythm Strip
Look at the rhythm strip only. The limb and precordial leads change mimicking torsades
Characteristic morphology: Multiple ventricular foci → QRS complexes varying in amplitude, axis and duration. Cycling of the QRS axis around the isoelectric line through 180 degrees Q5-20 beats. Rate: 160-250 beats/min, irregular RR intervals,

TORSADES DE POINTES (POLYMORPHIC VT)



Polymorphic VT with ↑ QT: Rate:150-250 bpm. QRS complexes change in polarity and amplitude, appearing to rotate around the EKG isoelectric line. ↑ QT acquired: ↓ K+, ↓ Mg++, ↓ Ca++, many medications or congenital

MANAGEMENT

DEPENDENT ON CLINICAL STATUS
PALS/ACLS: Cardiac Arrest Algorithm: Ventricular Tachycardia without Pulse
PALS/ACLS: Tachycardia with a Pulse Algorithm: Ventricular Tachycardia with Pulse
CORRECT UNDERLYING CAUSE
Rapid correction of electrolyte abnormalities
Discontinuation of medications that prolong QT
MEDICATIONS
1. Magnesium (limited evidence on efficacy)
Effective in patients with normal magnesium
Dose: 50 mg/kg (max 2 grams) over 1-2 minutes (w/o pulse), 15 min (w/pulse)
Can repeat dose in 5-10 minutes, Followed by infusion: Adult 3-20 mg/min
2. Isoproterenol: Alternative to pacing. Goal (↑ HR → ↓ QT interval)
Children: 0.05-0.1 mcg/kg/min, Adults: 2 mcg/min
3. Beta-blockers: Indicated for congenital cause due do catecholamine surge
4. Class IB antiarrhythmic: Lidocaine, phenytoin. Less effective than pacing, isoproterenol
Lidocaine → ↓ QT interval (most effective in medication induced torsades)
5. No 1a, 1c and III antiarrhythmics (Amiodarone, Procainamide → ↑ QT interval)
ELECTRICAL CARDIOVERSION
1. Defibrillation: Torsades without a pulse
2. Synchronized Cardioversion: Torsades with a pulse
3. Overdrive pacing: Atrial or ventricular, if unresponsive to magnesium
Rate 100 beats/min (↑ HR → ↓ QT interval)
↓ Early after-depolarizations →↓ QT interval (particularly if bradycardic)

CHILD PROTECTION

CHILD ABUSE AND NEGLECT

INTRODUCTION (KATHERINE FULLERTON, M.D. 6/2021)
(Child Protection: Lori Legano M.D., Vincent Palusci M.D., Margaret McHugh, M.D.)
Currently, there are more than 700,000 confirmed cases of child abuse per year in the U.S. Many cases are never reported, so actual figures are likely much higher. Child abuse consists of physical abuse, sexual abuse, emotional abuse and neglect. Most cases are neglect and physical abuse, with fewer cases of sexual & emotional abuse. The definitions below are as defined by CAPTA (The Child Abuse Prevention and Treatment Act, 1974. Reauthorized 2010) and New York State laws.

ABUSE AND NEGLECT RISK FACTORS	
Family	Stress, poverty, homelessness, unemployment.
Parent	Abused as child, expectations mismatch child's development, single parent, psychiatric problems, impulsive behavior, substance abuse, developmental or intellectual delays, other domestic/family violence.
Social	No supports (friends, family), violence learned/acceptable socially.
Child	Stepchild, temperament, colic, child with special health or other needs (e.g. prematurity, chronic medical or psychiatric problems).

DEFINITIONS

CHILD ABUSE: Abuse occurs when a child has suffered intentional physical or emotional injury caused by a caregiver, such as a parent, legal guardian, or teacher, which results in mental distress, disability, disfigurement, or the risk of death.

CHILD NEGLECT: Neglect occurs when a child's physical, mental, or emotional condition has been endangered because the parents or legal guardians have failed to provide for basic needs (physical, mental, or emotional) including food, shelter, clothing, medical, dental, eye care and education or failure to provide proper supervision, including abandonment, parental substance abuse (excessive use of drugs or alcohol which interferes with the ability of the parent to supervise the child). Neglect includes neglectful supervision, medical neglect, physical neglect, abandonment and refusal to accept parental responsibilities.

PHYSICAL ABUSE: Physical abuse occurs when an inflicted physical injury results in injury, distress, disfigurement, or death of a child (e.g. punching, beating, kicking, biting, burning, shaking). CT findings suggestive of abusive head trauma include: intra-hemispheric falx hemorrhage, subdural hemorrhage, non-acute extra-axial fluid collection and basal ganglia edema. Other lesions include: bruises, burns, contusions, lacerations, hematomas and fractures.

EMOTIONAL ABUSE: Emotional abuse occurs when the parent or caregiver exhibits persistent behavior that assaults, demeans, diminishes, or debases the child, and interferes with the child's normal development. Emotional abuse is present with all other forms of child abuse, but can also occur by itself.

SEXUAL ABUSE: Sexual abuse consists of using, persuading, or coercing a child to engage in any sexually explicit conduct (e.g. fondling, intercourse, rape, molestation, sodomy, exhibitionism). See information for Commercial Sexual Exploitation of Children. See: PEM Guide: Child Protection: Sexual Abuse and Assault.

IDENTIFICATION OF SUSPECTED CHILD ABUSE

HISTORY

Some children may clearly detail abuse/neglect. However, often the history is vague and doesn't match physical findings or the developmental abilities of the child. The history may change from one telling to the next, or differ between caregivers. For neglect and other maltreatment, physical exam may be normal and history is essential.

INTERACTIONS

Suspect abuse with arguments, lack of parent holding or making eye contact with child, parent has impaired speech/motor consistent with intoxication, overt yelling, threatening, striking child in front of health care providers.

PHYSICAL EXAMINATION

Record full vital signs and growth parameters. Many cases of physical abuse occur without specific physical findings. Life threatening injuries may be occult. Thoroughly assess the neurologic, abdominal, skin and musculoskeletal systems. Certain injuries (facial bruises, pattern marks, specific fracture types) are 'sentinel' with high suspicion for abuse, particularly in young children.

CENTRAL NERVOUS SYSTEM INJURIES: Abusive head trauma (AHT) is the most common cause of abuse fatality and disability. Infants and younger children are at greatest risk given small size and development. For intracranial hemorrhage, consider an evaluation for bleeding disorders, birth and accidental trauma, and metabolic disease. Injury of brain parenchyma can lead to a cascade of fibrinolysis and thrombosis resulting in abnormal coagulation (↑ PT, PTT) and disseminated intravascular coagulation.

A multicenter, prospective validation and refinement of the Pittsburgh Infant Brain Injury Score (PIBIS) rule (Berger, Pediatrics 2016, PubMed ID: 27338699) included 214 cases of abusive head trauma and 826 controls and identified 4 prognostic factors. At a score of 2, the sensitivity was 93.3% (95% confidence interval 89.0%–96.3%) and a specificity of 53% (95% confidence interval 49.3%–57.1%).

PITTSBURGH INFANT BRAIN INJURY SCORE RULE	
CRITERIA	POINTS
Abnormality on dermatologic examination	2
Age ≥ 3.0 months	1
Head circumference > 85th percentile	1
Serum hemoglobin < 11.2 g/dl	1

ABUSIVE HEAD TRAUMA
Retinal Hemorrhages (> 80%, 100% fatal AHT)
Subdural/Subarachnoid Hemorrhages: Various stages of healing, interhemispheric
Metaphyseal Fractures
No External Signs of Trauma

RETINAL HEMORRHAGES: NON-ABUSIVE
Vaginal delivery (most resolve by 10 days, all before 6 weeks)*
High velocity accidents/falls
Traumatic asphyxia: Forceful compression of the chest. Facial plethora, petechiae
Vasculitis, Vascular disease
Coagulopathy
Thromboembolic disease
Hypertension
Superior vena cava syndrome
Meningitis
*Involve intraretinal layer only (all 3 layers typical of abuse)

CUTANEOUS BRUISING: Skin is the most common organ injured in child abuse. Look for cuts, scrapes, bruises (ecchymosis), lacerations, burns, bites, redness, and swelling. Typical abusive injuries include unusual locations (inner thighs, cheeks, buttocks, lower back), patterned bruises/burns, multiple injuries, and different stages of healing.

The TEN4-FACESp bruising clinical decision rule for children less than 4 years of age with at least one bruise on a comprehensive skin exam includes, age, location of bruise, frenulum injury and patterned bruises (Pierce, JAMA Netw Open. 2021, PubMed ID: 33852003)). TEN-4FACESp had a sensitivity of 95.6%, 95% (93.0, 97.3%) and specificity of (87.1% (85.4, 88.6%)). Identification of any of the predictors in the rule should prompt further evaluation for child abuse.

Use of the rule requires a comprehensive skin exam which may not be feasible in the emergency department. The rules requires external validation before it can be applied clinically. The impact of the rule on the rate of child abuse consultations requires further study.

TEN4-FACESp: BRUISING IN CHILDREN < 4 YEARS OF AGE[1]			
T	Torso[2]	F	Frenulum
E	Ear	A	Angle of the jaw (mandible)
N	Neck	C	Cheeks (fleshy)
4	Any bruise 4.99 months of age	E	Eyelids
		S	Subconjunctival
		p	Patterned bruises[3]

1. Positive response to any predictor signals the need for further evaluation
2. Torso: Chest, abdomen, back, buttocks and genitourinary area
3. Patterned Bruises: Bite, loop, hand slap, squeeze, grab, multilinear

CUTANEOUS BURNS: Approximately 10-20% of burns in children are intentional and burns constitute 20% of child abuse injuries. (See also: PEM Guide: Environmental Injuries: Burns). It is essential to maintain a high level of suspicion for abuse in all children with burns. Understanding burn types can be helpful to determine if the observed injury is consistent with the history provided. Scald burns are the most common burn associated with intentional injury. Patterned burns, such as multiple cigarette burns are also concerning for intentional injury.

Scald burns can be subclassified as: 1. spill or splatter pattern, 2. flow and 3. immersion/submersion. A spill or splatter pattern typically occurs when a toddler reaches for and spills a cup or pot full of hot liquids. Burns typically occur on the anterior, upper chest and upper extremities, are of varying depth, are asymmetric and have peripheral/satellite splash burns. In contrast, intentional burns are more likely to be sharply demarcated (e.g. linear), of uniform depth, symmetrical and circumferential. Flow scald burns occur when a liquid of poured over a body part. Submersion burns occur when a child is placed or dipped in a liquid. There may be sparing the soles and/or buttocks (in contact with cooler tub surface).

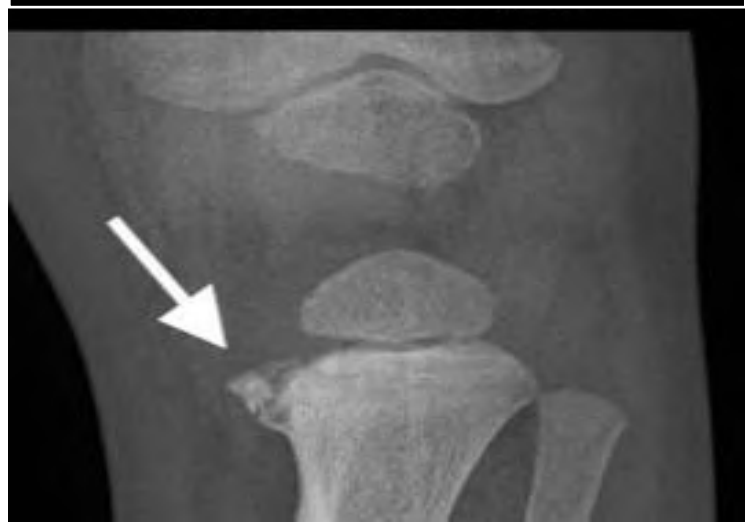
ABDOMINAL INJURIES: Abdominal trauma is second most common cause of abuse fatality (after CNS injury), more than half without external bruises. A classic, abdominal injury due to trauma is a duodenal hematoma. A blow to the upper mid-abdomen compresses the mid-duodenum as it crosses the midline against the adjacent vertebrae. It is important to adequately assess bowel sounds, tenderness, gastrointestinal history. Screen with liver function tests.

MUSCULOSKELETAL INJURIES: Consider other causes (osteogenesis imperfecta). Skeletal surveys (SCAMP series) are usually indicated in children under age 2 years being reported for suspected physical abuse but are usually only done during regular business hours. Metaphyseal fractures occur at the junction of the meta-physis and physis and include metaphyseal chip (corner) fracture and “bucket handle” fractures. They result from traction/torsional forces when the infant’s extremity is pulled and/or twisted forcefully. Chip (corner) fractures are seen as a discrete avulsion of the metaphysis. “Bucket handle” fractures are seen as a horizonal avulsion with discrete proximal and distal segment.

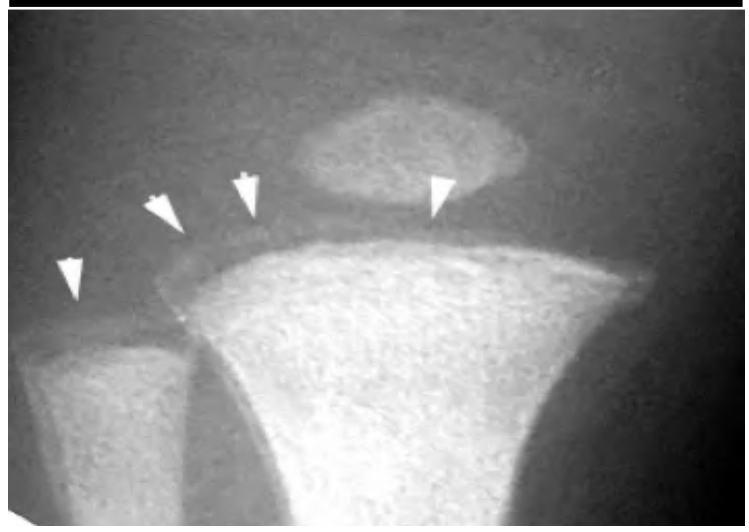
FRACTURES ASSOCIATED WITH ABUSE
Fractures at various stages of healing
Fracture not explained by reported mechanism
Fracture not consistent with child developmental level
Delayed presentation of fractures
Skull fractures: Complex, multiple, cross suture lines
Vertebral fractures
Femur fractures in children < 1 year
Scapula fractures
Rib fractures (particularly posterior-lateral)
Metaphyseal chip fractures
Bucket handle fractures

EASILY FRACTURED	
CONDITION	EXAMPLE
Genetic bone disorder	Osteogenesis imperfecta
Nutritional deficiencies	Rickets (Vitamin D)
Metabolic deficiencies	Hyperparathyroidism
Infection	Osteomyelitis
Benign bone cysts	Non-ossifying fibromas
Bone tumors	Primary and metastatic

METAPHYSEAL CORNER OR CHIP FRACTURE



BUCKET HANDLE FRACTURE



MANAGEMENT

1. Consult Social Work.
2. Consult Child Protection

MEDICAL CARE: The physician must first care for life or limb threatening medical and psychiatric problems as well as other medical needs. Admit only if there is a medical reason for admission. Safe discharge is part of medical management.

REPORTING: All licensed physicians and other hospital staff are mandated reporters and must report (based on state law) suspicion of child abuse/neglect. Mandated reporters are required to report suspected child abuse or maltreatment when they are presented with a reasonable cause to suspect child abuse or maltreatment in a situation where a parent, or other person legally responsible for the child has caused or allowed to be caused the conditions identified. “Other person legally responsible” refers to a guardian, caretaker, or other person 18 years of age or older who is responsible for the care of the child.

SOCIAL WORK: The social worker will gather information, write the report, and make the report to the State Central Register. If the case is accepted, it will be referred to Administration for Children’s Services (New York City). The attending will need to provide the medical diagnosis and sign the report.

HOSPITAL POLICE: To provide for your safety and prevent the caregiver from eloping with the child. Hospitals can take **protective custody** if there is **imminent danger**. This should be discussed with the attending staff, and hospital police should be notified as soon a necessary. The Administration for Children’s Services (ACS) is called when this is needed.

DOCUMENTATION: Clearly and objectively include the history, physical, and tests that created the suspicion of abuse for the report. It is best to use the caregiver’s exact language for the history in “quotes” and exactly describe physical exam findings (photos should be taken by as well) and to avoid legal terms like “alleged” “rule out” or “perpetrator”. List the specific injuries and “suspected” physical abuse, neglect, or maltreatment as appropriate.

PLACEMENT OF CHILD WITH CHILD PROTECTIVE SERVICES

COMMUNICATING WITH CAREGIVERS: This is an emotionally charged situation. Expect caregivers to be upset and angry. Acknowledge and validate these emotions. Always ensure your own safety (have another healthcare provider with you, make sure you have ready access to an exit, have hospital police/ security present). These discussions are best handled with/by the attending with Social Work involvement.

SUGGESTED COMMUNICATION SCRIPT
The baby has injuries (explain what the injuries are and their clinical significance) and the information we have does not explain the injuries.
I am concerned that the injuries are not explained and may be from someone hurting the child. When we have these concerns, we are required by state law to report this to Child Protective Services.
If the parent asks: Do you think I abused my child? I am not accusing you but we have concerns that someone may have hurt the baby.
If the parent asks: Are they going to take my baby away? Once the case has been accepted for investigation, the NYC Administration for Children’s Services will make the decision of where the child will go after leaving the hospital.

COMMUNICATING WITH INVESTIGATORS: These can be medically complex situations. Do not expect investigators to fully understand the significance of the injuries or the medical evaluation. It is best to be simple and clear by listing the injuries, medical evaluation planned, and potential causes and prognosis. Investigators may under or over respond to what you perceive as the level of seriousness. If being discharged, follow-up plans, appointments and medications need to be carefully spelled out so the investigators and the hospital team can assure proper follow-up.

Discussions with investigators are best left to the Attending and Social Work to prevent miscommunications which could severely affect the investigation and safety of the child and family.

SEXUAL ABUSE AND ASSAULT

INTRODUCTION (KATHERINE FULLERTON, M.D. 3/2023)
Child abuse is defined by the Child Abuse Prevention and Treatment act as: “at a minimum, any recent act or failure to act on the part of a parent or caretaker, which results in death, serious physical or emotional harm, sexual abuse of exploiting, or an act or failure to act which presents an imminent risk of serious harm” (WEB LINK: CAPTA). Sexual exploitation/trafficking was added to this definition in 2015.

Many states have developed more detailed definitions. It is essential to understand the definitions as they apply to your state. Child abuse is typically categorized as physical abuse, emotional abuse, neglect and sexual abuse. This PEM guide focuses on child sexual abuse and sexual assault. For a discussion of other forms of abuse, see PEM Guide: Child Protection: Child Abuse and Neglect

SEXUAL ABUSE
Employment, use, persuasion, inducement, enticement or coercion of any child to engage in, or assist any other person to engage in any sexually explicit conduct or any simulation of such conduct for the purpose of producing any visual depiction of such conduct.
Rape, and in cases of caregiver or interfamilial relationships, statutory rape, molestation, prostitution, or other form of sexual exploitation of children or incest with children

TYPES OF CHILD SEXUAL ABUSE	
Non-contact	Exhibitionism (with inappropriate sexualized contact)
	Pornography
Contact	Penetrative: Penetration of the mouth, anus or vagina
	Non-Penetrative: Touching/fondling, masturnbation

RAPE	
A person commits a felony when he or she engages in forced sexual intercourse with another person	
1	By forcible compulsion
2	By threat of forcible compulsion that would prevent resistance by a person of reasonable resolution
3	Who is unconscious
4	Who is so mentally deranged or deficient that such person is incapable of consent

STATUTORY RAPE: Statutory rape laws assume that minors are not capable of providing consent. States vary on the age of consent (16-18 years, 17 years in New York) and whether the sex was consensual or not. In New York State a person who is 18 years of age or older commits a felony when he or she engages in sexual intercourse with another person not his or her spouse who is younger than 17 years of age even if the sex is consensual. Sexual assaults may also be tried under a state assault and battery laws.

HISTORY
Patients may present with signs and symptoms consistent with trauma or a sexually transmitted infection. Children may also present with non-specific and behavioral symptoms. The perpetrator is frequently known by the child and in a position of authority. The sexually abused child if often worried about the negative consequence to themselves, the perpetrator and their family. They may lack the knowledge that what happened to the is wrong. There are often feelings of embarrassment or guilt and the may distrust authority figures to whom to report.

SIGNS OF POSSIBLE SEXUAL ABUSE	
Distress at the medical visit	Refusal to get undressed and unwillingness to separate from caregiver or to be examined.
Change in behaviors	Associated with sleep/bedtime: Nightmares, refusal to sleep alone, bedwetting, fear of the dark.
	Changes in mood: Sadness, irritability, anger
	Abnormal sexual behaviors (see table below)
Physical symptoms	Often vague, general: Headache, fatigue, abdominal pain

NORMAL SEXUAL BEHAVIORS (SEXUAL PLAY)	
Infancy	Oral gratification, penile erections with bowel and bladder distention, genital self stimulation in both genders by 18 months
2-3 years	Gender identification, enjoy displaying the nude body
3-6 years	Display sexual behavior, understands gender differences. Masturbation common, Like to touch bodies, may include genitals and breast of parents. Identities with same sex parent
6-7 years	Still interested in sexuality but overt behaviors diminished. Remains curious about sex. Use “dirty” words but more modest than younger children. Learn from pears
Puberty	Display fewer family related sexual behaviors. More interested in peers
Chiesa, Pediatr Rev 2017, PubMed ID: 28250071	

ABNORMAL SEXUAL BEHAVIORS	
Puts mouth on sex parts	Makes sexual sounds
Asks to engage in sex acts	Engages in kissing with tongue
Masturbates with object	Undresses other people
Inserts objects in vagina/anus	Asks to watch explicit videos
Imitate sexual intercourse	Imitates sexual behavior with dolls

PHYSICAL EXAMINATION

A complete physical examination that includes a thorough anogenital examination and forensic evidence collection should be completed. It may be prudent to delay an attempt at obtaining a history and performing the examination in an asymptomatic, hemodynamically stable children until someone trained in sexual abuse evaluation can perform it. For children (< 13 years old), that would include the child protection team. For adolescents and young adults (≥ 13 years old) the Sexual Assault Response Team (SART) should be consulted. Don’t overlook non-genital signs of physical abuse

For children, the knee-chest or frog-legs positions may facilitate the physical examination. Greater than 90% of children evaluated for sexual abuse have normal physical examinations. Even when physical findings are present initially, they often resolve within 3 days. Those undergoing penile presentation and repeated assault are more likely to manifest exam findings. Abnormalities may involve the posterior fourchette, fossa navicularis, posterior hymen, or perianal tissues.

Less than 5% of male victims have findings. If present this often includes bruising and abrasions of the penis. A laceration of the anus with involvement of mucosal tissue is the best physical exam evidence of anal penetration. Anal fissures due to hard stool do not involve the mucosa. Skin tags are normal findings. Other normal findings that can be confused with anal injury are: a purple-bluish discoloration of the perianal area can occur in the supine position due to venous pooling and will resolve with a change in position, dilatation of the anus with hard stool in the vault and perianal warts. Perianal warts are no longer pathognomonic for abuse as they can be transmitted perinatally and occur at any age.

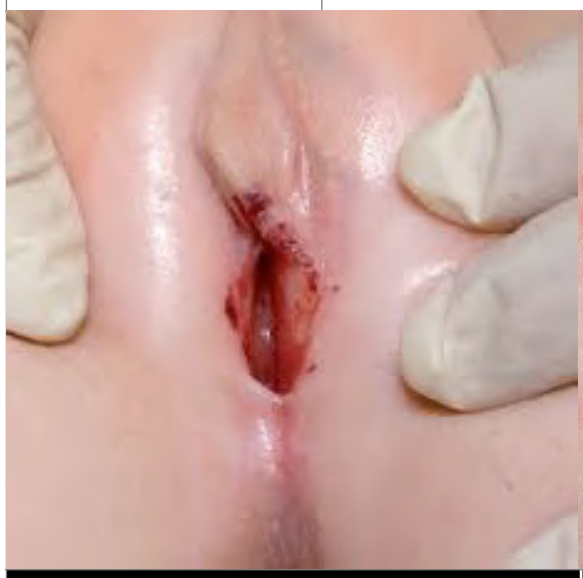
HYMEN ANATOMY	
Birth	Annular (circumferential) and redundant (fimbriated) hymen
Preschool Early school	The posterior rim of the hymen thins out into a crescent shape with a prominent vaginal orifice
Puberty	Thickened, annular (circumferential) appearance of the hymen with scalloped edges. Notching at 3 and 9 o'clock is normal

NONSPECIFIC FINDINGS
Vaginal discharge
Vulvar erythema
Perianal skin tags
Hymenal ridges
Thinning of the hymenal ring
Urethral dilatation with labial traction
Labial adhesions

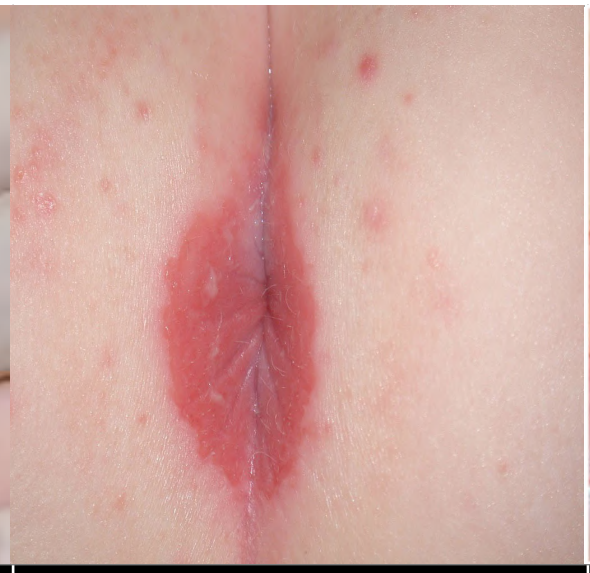
DIFFERENTIAL DIAGNOSIS

There are many nonspecific findings that are found in normal children but may be mistaken for signs of sexual abuse. Conditions that mimic sexual abuse include: urethral prolapse, vaginitis, straddle injuries, vaginal foreign body and lichen sclerosis.

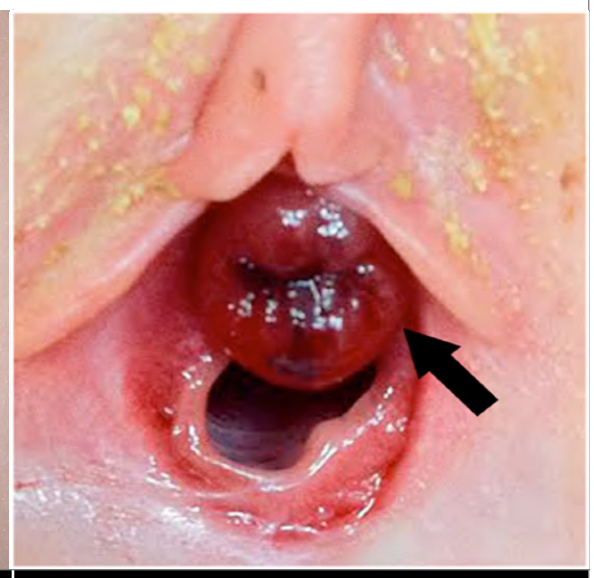
DIFFERENTIAL DIAGNOSIS: OFTEN MISTAKEN FOR SEXUAL ABUSE	
Lichen Sclerosis	Skin condition most commonly mistaken for sexual abuse
	Initial lesion is a white or yellow papule
	Skin becomes atrophic, fissures and/or sub-epidermal hemorrhages
	Perianal hypo-pigmentation with an "hour glass" appearance
Strep A Strep	Vulvar or perineal erythema with discrete borders
Urethral Prolapse	Blood in the underwear
	Donut shaped protrusion above the vaginal orifice



LICHEN SCLEROSUS



PERIANAL STREP



URETHRAL PROLAPSE

LABORATORY TESTING

Sexually transmitted infections (STI) occur in less than 5% of prepubertal and less than 15% of adolescent victims of sexual abuse. Cases with a high likelihood of STI include those with genital-to-genital or genital-to-anal contact, examination findings consistent with penetration, genital discharge or a perpetrator with a suspected STI. In general, do not test sexual assault victims for baseline sexually transmitted infections (with the exception of HIV). The presence of a baseline infection may have a negative impact on the patients case in the court room. See evidence collection below for information about testing for suspected drug facilitated sexual assault.

INFECTIONS ASSOCIATED WITH SEXUAL ABUSE		
EVIDENCE	CONFIRMED INFECTION	ACTION
Diagnostic	GC[1], HIV, Syphilis, Chlamydia	Report
Highly Suspicious	Trichomonas, HSV2[2]	Report
Suspicious	Condylomata acuminata[3]	Consider Report
Inconclusive	Bacterial Vaginosis	Medical Follow up
1. GC most common 2. HSV1 can be auto-inoculated from the oropharynx 3. Can be transmitted by vaginal delivery and occur at any age		

SEXUAL ASSAULT LABORATORY TESTING		
TEST	SOURCE	PATIENT
HIV AB/AG Testing	X	X
Hepatitis B: Surface antigen/antibody, core antibody	X	X
Hepatitis C: Antibody	X	X
Syphilis serology	X	
Gonorrhea	X	
Chlamydia	X	
HIV: Viral load, genotypic resistance	X	
Serum creatinine (will receive PEP)		X
Serum hepatic transaminases (will receive PEP)		X
Pregnancy testing (female patient)		X

MANAGEMENT

Managing the patient with sexual abuse requires collaboration with social work, children services, child protection and pediatric infectious disease. Managing the patient with a sexual assault requires collaboration with rapid crises counseling, the police and infectious disease. Additional interventions include evidence collection (See Appendix) and the provision or sexually transmitted disease and pregnancy prophylaxis (See Appendix).

It is important document essential information without providing information that could possible do damage to the patient’s case. Use patient quotes when possible, note people present for the examination and the position the patient was examined in. DO NOT use terms such as, “alleged” or “rule out sexual abuse.”

The police may be contacted by the patient prior to arrival in the Emergency Department. If a patient has not contacted law enforcement officers before arriving at a health care facility, the patient should be informed of the right to report the crime. It is the adult patient’s choice whether or not to involve law enforcement personnel. If the patient so chooses, providers should assist her in contacting law enforcement officials.

DISPOSITION

The majority of victims of sexual abuse or assault can be discharged to their home if that is deemed safe. These patients are at high risk of long term psychosocial adverse events and would benefit from ongoing counseling. Patients started on HIV prophylaxis should follow-up with pediatric or adult infectious disease.

APPENDIX: MANAGEMENT SUMMARY

MANAGEMENT SUMMARY
Avoid secondary abuse phenomenon. An overzealous physical examination can assume a assualt-like quality in child's mind.
If abuse is within 72 hours and without acute symptoms may refer to a child protection center for evaluation as soon as possible
Address acute medical injuries immediately, Hospitalization may be required
If internal bleeding is suspected an exploration and repair under anesthesia may be required
Interview the patient separately if possible and avoid leading questions
Provide emotional support. Reaffirm the importance of what the child has revealed
Physical exam can be in the parent's lap, knee-chest, frog-leg or lithotomy positions
Pre-pubertal female: External genital exam only
Post-pubertal female: Full genital exam (modify as needed)
Rectal and oropharyngeal exam on all victims
Evidence collection: Within 120 hours (though may be collected later at your discretion) Age ≥ 13 years, Notify SART, Age < 13 years, Notify Child Protection Maintain the evidence chain (See Appendix)
STI prophylaxis for post-pubertal patients including HIV prophylaxis (See Appendix)
Pregnancy prophylaxis for all post-pubertal girls within 120 hours (See Appendix)
Involve child protection, social work, rape crisis advocate
Documentation: Be meticulous. Use quotes as much as possible, note people present for the exam and the position the patient was in during the exam DO NOT use the terms, "alleged" or "rule out sexual abuse."
Useful assessment terminology**:** "The history obtained reveals risk factors and indicators suspicious for sexual abuse. Interpretation of the evaluation and physical findings is deferred for later review with expert consultation."
All sexually abused or assaulted patients need to be followed by integrated team involving mental health professionals, physicians, and social work.
Reporting is mandated for all child abuse or maltreatment by a parent, or other person legally responsible for the child. Social work will notify the Administration for Children's Service and NYPD.

MANAGEMENT TIME INTERVALS	
HIV prophylaxis	Within 72 hours
Evidence collection (rape) kit	Within 120 hours
Pregnancy prophylaxis	Within 120 hours

APPENDIX: EVIDENCE COLLECTION

It is our responsibility to meet the evidentiary needs of law enforcement. The evidence kits are both medical and legal documents. It is essential to follow instructions carefully and maintain a clear chain of evidence. In New York State there are two kits: the NYS Sexual Offense Evidence Collection Kit (Part A) and the NYS Drug Facilitated Sexual Assault Evidence Collection Kit (Part B). Part B should not be collected without Part B The recommendation is to complete the kits within 120 hours of an assault but DNA evidence may be present for a longer duration and use of the kit beyond 120 hours is at your discretion.

Ensure that the kit is sealed prior to use. Follow all instructions. The patient must sign the consent form in the kit and the NY State Office of victim's services form. The drug facilitated sexual assault kit consists of both urine and blood samples. Alcohol is the most commonly identified drug (70%) on toxicology screen in sexual assault. Flunitrazepam (Rohypnol) and gamma hydroxy butyrate (GHB) have been associated with "date rape". The samples should be obtained as soon as possible after arrival and the patient must sign the separate authorization. The examiner may elect not to complete one or more steps, based on the patient's well being and preferences.

NYS SEXUAL OFFENSE EVIDENCE COLLECTION KIT STEPS (UPDATED 2023)		
1	Trace Evidence and Debris	Evidence Collection
2	Underwear	Evidence Collection
3	Clothing	Evidence Collection
4	Oral Swabs	Evidence Collection
5	Buccal Swabs	Control Sample
6	Fingernail Swabs	Evidence Collection
7	External Dried secretions and bite marks	Evidence Collection
8	Pubic Hair Combing	Evidence Collection
9	Perinal/Anal Swabs	Evidence Collection
10	Vulvar or Penile Swabs	Evidence Collection
11	Vaginal/Cervicle Swabs	Control Sample
12	Tampon/Pad Liner Collection	Evidence Collection
Swabs: Separate the swabs on the collection table to avoid contamination. Allow swabs ro properly dry before sealing in the envelope		

Envelopes that are not used should be marked "No" on the line, which asks, "Was sample collected?" All sample swabs and smears must be dry before packaging. Upon completion of the kit remove the police evidence seal from the box. Return all evidence envelopes and instruction sheets to the box. If photographs were taken, do not include them in the kit. Include photos in the patient's medical record, or release to investigating officer as determined by your institution's policy. Sign the Police Evidence Seal and use it to seal the box. Signature must be partly on seal and partly on box. Fill out information requested on the top of the box. Give the sealed kit and clothing bags to the investigating officer. If an officer is not present, place sealed kit in a secure area, in accordance with established protocol (Bellevue = Hospital Police Office). It is essential to ensure that the chain of evidence is properly maintained, and the chain of custody is documented. New York State requires hospitals to hold evidence for 30 days to give the patient an opportunity to decide to report to law enforcement if they do not initially elect to.

APPENDIX: SEXUAL ASSAULT MEDICATION PROPHYLAXIS

A. SEXUALLY TRANSMITTED INFECTION PROPHYLAXIS (WEB LINK: CDC 2021)

GONORRHEA, CHLAMYDIA AND TRICHOMONAS PROPHYLAXIS
Indication: All patients
Ceftriaxone 500 mg IM (1,000 mg if > 150 kg) PLUS Doxycycline 100 mg PO BID x 10 days PLUS Metronidazole 500 mg PO BID x 10 days (Women only)
Risk of cross-reaction between penicillin and 3rd generation cephalosporin negligible Severe cephalosporin allergy (Anaphylaxis, Steve's-Johnson): Gentamycin 240 mg IM PLUS Azithromycin 2 grams PO

HIV POST-EXPOSURE PROPHYLAXIS (See Appendix: HIV Exposure Risk Algorithm)
Recommendation for HIV PEP are made on a case-by-case basis according to risk
HIV testing is not required but encouraged to provide a baseline status (and at 6 weeks and 3 months)
Provide a starter pack of medication and prescribe the remainder of the 28 day course
New York State law requires that a patient be provided with at least a 7-day supply
Schedule an early follow-up visit to discus test results and provide additional counseling

HIV POST-EXPOSURE PROPHYLAXIS (PEP): NYU AND BELLEVUE	
MEDICATION	DOSING
Truvada (Tenofovir 300 mg, Emitricitabine 200 mg)	1 TAB PO Daily x 28 days
Raltegravir (Isentress) 400 mg Tab	1 TAB PO BID x 28 days
Bellevue: Follow up with Child Protection, Pediatric ID clinic (< 18 yrs), Virology clinic (> 18 yrs) NYU: Follow up with Pediatric Infectious Disease (< 18 years) or Infectious Disease (> 18 yrs)	

HIV POST-EXPOSURE PROPHYLAXIS (PEP): CDC 2021	
PREFERRED REGIMEN	DOSING
Truvada (Tenofovir 300 mg, Emitricitabine 200 mg)	1 TAB PO Daily x 28 days
PLUS Raltegravir (Isentress) 400 mg Tab	1 TAB PO BID x 28 days
OR Dolutegravir 50 mg Tab	1 TAB PO Daily x 28 days
ALTERNATIVE REGIMEN	
Truvada (Tenofovir 300 mg, Emitricitabine 200 mg)	1 TAB PO Daily x 28 days
PLUS Darunavir 800 mg Tab	1 TAB PO Daily x 28 days
PLUS Ritinovir 100 mg	1 TAB PO Daily x 28 days

HEPATITIS B PROPHYLAXIS
Indication: Non-immune patients (Not previously vaccinated)
Perpetrator Status (+): Hepatitis B Immunoglobulin 0.06 ml/kg IM AND Hepatitis B Vaccine 1.0 ml IM
Perpetrator Status Unknown: Hepatitis B Vaccine 1.0 ml IM only
Hepatitis B Vaccine follow-up doses at 1-2 months and 4-6 months after the first dose

TETANUS PROPHYLAXIS
Indication: Last tetanus booster > 5 years
Tetanus/Diptheria Toxoid 0.5 ml IM

HUMAN PAPILLOMA VIRUS PROPHYLAXIS
Female and Male 9-26 years: Not vaccinated or incompletely vaccinated
HPV vaccine
Initiating vaccine >15 years: 3 dose regimen: Follow-up at 1-2 months (2nd) and 6 months (3rd) Initiating vaccine >15 years: 2 dose regimen: Follow-up at 1-2 months (2nd)

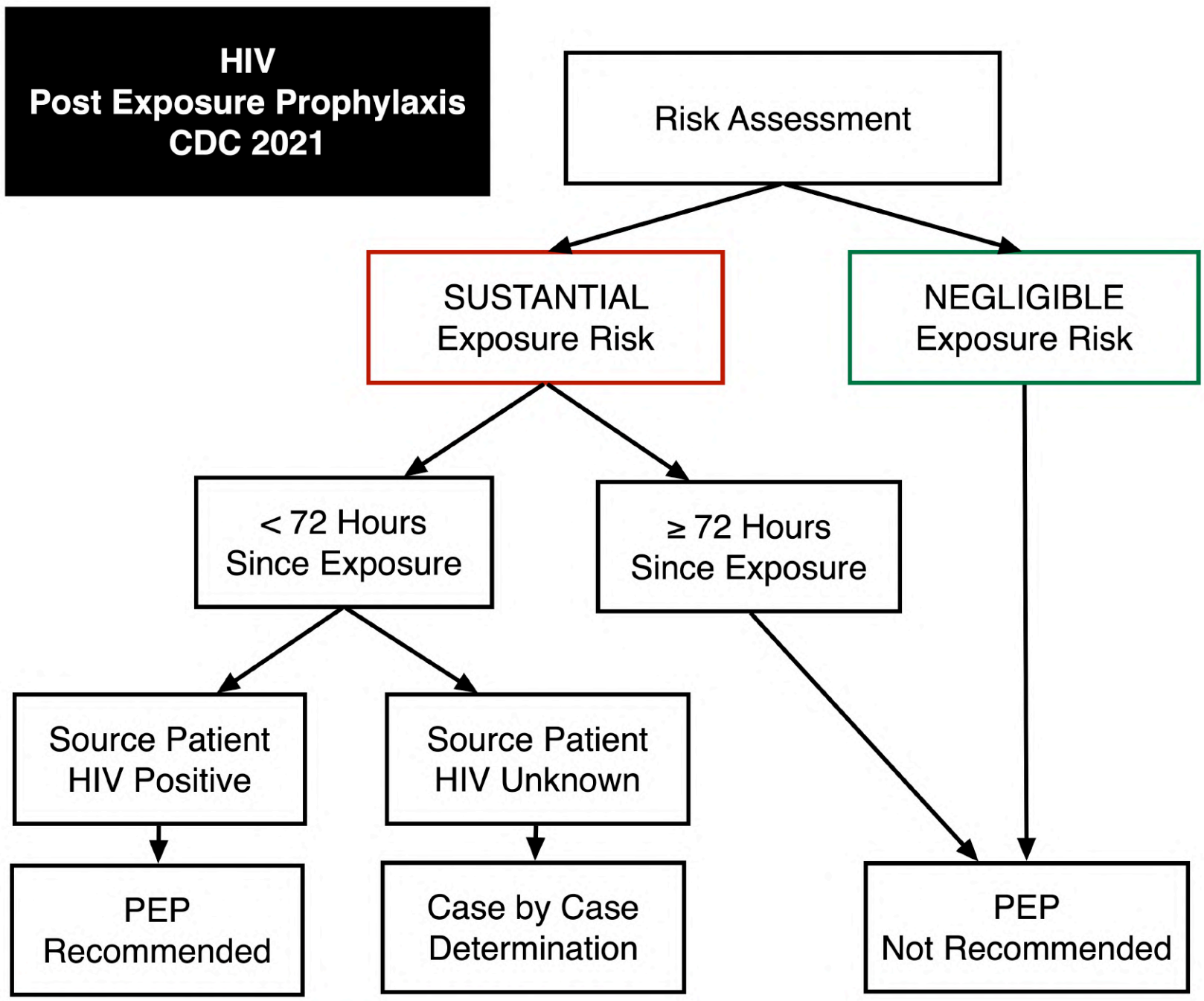
B. NON-INFECTION PROPHYLAXIS

PREGNANCY PROPHYLAXIS
Indication: Within 120 hours (5 days) of event in post-pubertal females
a. Plan B (Levonorgestrel): 0.75 mg TAB, 2 Tablets PO x 1
Can also give 1 TAB PO with second tab in 12 hours but no compliance issues with 2 TABS in the ED Evidence suggests that patients > 165 pounds may require higher doses
b. Ella (Ulipristal): 30 mg TAB, 1 Tablet PO x 1
May be more effective at preventing ovulation and pregnancy at days 1, 3 and 5. Does not require dosage adjusting for patients > 165 pounds

NAUSEA AND VOMITING PROPHYLAXIS
Indication: Prior to emergency contraception (especially if Azithromycin and Metronidazole for STI prophylaxis)
Antiemetic: Zofran 4 or 8 mg PO or Reglan 10 mg PO

APPENDIX: HIV POST EXPOSURE PROPHYLAXIS

WEB LINK: CDC GUIDELINE 2021



SUBSTANTIAL EXPOSURE RISK

EXPOSURE OF: Vagina, rectum, eye, mouth or other mucous membrane, non-intact skin or percutaneous contact

WITH: Blood, semen, vaginal secretions, rectal secretions, breast milk or any body fluid visually contaminated with blood

WHEN: The source of the fluid is known to be HIV positive

NEGLIGIBLE EXPOSURE RISK

EXPOSURE OF: Vagina, rectum, eye, mouth or other mucous membrane, non-intact skin or percutaneous contact

WITH: Urine, nasal secretions, saliva, sweat or tears when not visibly contaminated with blood

REGARDLESS OF: The known or suspected HIV status of the source

EXPOSURE TYPE	HIV ACQUISITION
PARENTERAL	
Blood transfusion	9,250/10,000 (1 in 1.1)
Needle sharing during injection drug use	63/10,000 (1 in 159)
Percutaneous	23/10,000 (1 in 435)
SEXUAL	
Receptive anal Intercourse	138/10,000 (1 in 72)
Receptive penile-vaginal intercourse	8/10,000 (1 in 1,250)
Insertive anal intercourse	11/10,000 (1 in 909)
Insertive penile-vaginal intercourse	4/10,000 (1 in 2,500)
Receptive or Insertive oral intercourse	Low
OTHER (Technically possible though unlikely)	
Biting, spitting, throwing body fluids, sharing sex toys	Negligible
Risk based on HIV positive source. Factors below not included in risk assessment Increased Risk: STI, acute or late stage HIV infection, high viral load Decreased Risk: Condom use, circumcision, antiretroviral Rx, pre-exposure Rx	

SUDDEN INFANT DEATH

INTRODUCTION (EVAN YANNI, M.D., VINCENT PALUSCI, M.D., M.S.,1/2022)
Every year, approximately 3,500 infants in the United States die suddenly and unexpectedly without a clear cause (Lambert, Pediatr 2018, PubMed ID: 29440504). As many as 1 in 7 infant deaths and 1 in 3 post-neonatal deaths are first attributed to this (Shapiro-Mendoza, Pediatrics 2014, PubMed ID: 24913798). Sudden Infant Death Syndrome (SIDS) was initially defined by Dr. Bruce Beckwith in 1969 as “the sudden death of any infant or young child, which is unexpected by history, and in which a thorough post-mortem examination fails to demonstrate an adequate cause for death” (Beckwith, Curr Prob Ped 1973, PubMed ID: 4351768). The SIDS definition has been since been refined (table below).

SUDDEN INFANT DEATH: DEFINITION
Infant less than 1 year of age
Sudden death: Within 24 hours of first symptoms
Unexpected death: Lack of an underlying illness expected to produce death
Onset of the fatal episode apparently occurring during sleep
Remains unexplained after a thorough investigation: Including: a complete autopsy, scene investigation and review of the clinical history”
Krous, Pediatrics 2004, PubMed ID: 15231934.

There is ongoing debate among experts that “syndrome” is an inaccurate description because these deaths occur in otherwise healthy infants without a clear group of preceding or concurrent signs or symptoms. Newer efforts argue for a shift to use the term sudden unexplained infant death (SUID), and such efforts are proposed for future International Coding of Disease (ICD) nomenclature (Shapiro-Mendoza, Pediatrics 2021, PubMed ID: 34544849). At this time, it is customary in the United categorize SIDS into three groups (table below).

SUDDEN INFANT DEATH: US CATEGORIES
SIDS (ICD-10 code R95)
Unknown or unspecified causes (ICD-10 code R99)
Accidental suffocation and strangulation in bed (ICD-10 code W75)
Shapiro-Mendoza: Pediatrics 2021, PubMed ID: 34544849

PATHOPHYSIOLOGY

The underlying cause of SIDS is unknown. Postmortem examinations most commonly demonstrate intrathoracic petechiae in over 80% of SIDS cases, which suggests attempts to breathe against an obstructed upper airway in the moments preceding death (Krous, Arch Pathol Lab Med 1984, PubMed ID: 6546345). It has also been suggested that altered or immature cardiorespiratory autonomic control in the brain stems of young infants impairs arousal mechanisms when an infant is in a hypoxic sleep environment (Paterson, JAMA 2006, PubMed ID: 17077377).

A number of risk factors have been proposed including prematurity, and maternal cigarette or substance use, and a “triple risk” hypothesis was formulated with
1. Vulnerable infant and
2. Exogenous stressors, and
3. A critical developmental period.

CLINICAL MANIFESTATIONS

In addition to a complete and thorough standard medical and family history by the pediatrician, key history also begins with the first responders.

HISTORY: IMPORTANT ELEMENTS
Location and positioning of the infant when found
Type of sleep environment and any defects in bedding
Amount and position of additional clothing and bedding materials
Room temperature, type of ventilation, and type of heating
Marks on the body at the scene, pattern and distribution of livor mortis, rigor mortis,
Reaction of caregivers

HISTORY: HIGH RISK OF NON-ACCIDENTAL TRAUMA
Recurrent cyanosis, apnea, brief resolved unexplained events (BRUEs), or deaths while in care of the same individual
Age > 6 months at time of death
Prior sibling(s) with unexplained death
Death of twins or siblings occurring simultaneously
Palusci, Pediatrics 2019, PubMed ID: 31451610

On physical examination, there is no anatomic feature that is pathognomonic for asphyxia, and it is often impossible to differentiate SIDS from accidental or intentional suffocation on external features alone (Coe, J Pediatr 1960, PubMed ID: 3810850). In the emergency department, a thorough head-to-toe examination of the infant should be conducted with detailed documentation of any patterns, skin findings, injuries, or other external physical findings. The medical examiner will also conduct a thorough exam within 24 hours, which includes internal and microscopic evaluation.

DIAGNOSTIC TESTING

There are no immediate labs required in the emergency department setting. Careful consideration should be given to toxicology and other labs in the “near-SIDS” child based on the clinical assessment. However, the medical examiner will perform often post-mortem laboratory testing pertaining to toxicology, clinical pathology/histology, microbiology, and inborn error of metabolism testing (Palusci, Pediatrics 2019, PubMed ID: 31451610).

There is no immediate imaging required in the emergency department setting. Careful consideration should be given to head and body imaging in the “near-SIDS” child based on the clinical assessment. However, the medical examiner will perform often radiographic skeletal surveys and CT imaging prior to the autopsy (Palusci, Pediatrics 2019, PubMed ID: 31451610).

DIFFERENTIAL DIAGNOSIS

In addition to child abuse, a number of investigations have increasingly identified cardiac, genetic, neurologic and other inborn errors of metabolism which may predispose to sudden, unexpected death. Because sudden unexplained infant death is a diagnosis of exclusion, a growing consensus suggests these deaths can be diagnosed once all the relevant alternative etiologies have been considered and ruled out below (Palusci, Pediatrics 2019, PubMed ID: 31451610). See also: PEM Guide: Child Protection: Child Abuse and Neglect for a discussion of physical examination and imaging findings commonly seen in non-accidental trauma.

DIFFERENTIAL DIAGNOSIS: EXCLUSION
Complete autopsy fails to demonstrate an anatomic cause of death
No evidence of inflicted trauma or significant natural disease by radiologic imaging, postmortem exam, and history
No evidence of meningitis, sepsis, aspiration, pneumonia, myocarditis, trauma, dehydration, fluid and electrolyte imbalance, significant congenital defect, inborn metabolic disorders, asphyxia, drowning, burns, and poisoning.
Laboratory testing reveals no evidence of toxic exposure to alcohol, drugs, or other substances
Investigation of the medical history and death- and incident- scene reveal no cause of death

MANAGEMENT

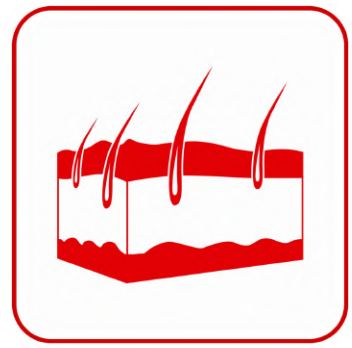
The AAP and the National Association of Medical Examiners recommend that all cases of sudden unexplained infant death should have an autopsy performed by a forensic pathologist certified by the American Board of Pathology. This should occur within 24 hours of death and include: examination of all major body cavities; microscopic examination of organs; photographs; skeletal survey and CT scans; pathology, toxicological, and metabolic screening; collection of medical history through interviews of caregivers and key medical providers by a trained professional; review of previous medical charts (Palusci, Pediatrics 2019, PubMed ID: 31451610).

Remaining management centers around providing information and support needs to the family or caregiver. In the emergency department setting, it should be remembered that the body of the deceased child is in the care of the medical examiner, who should be notified on all cases of sudden, unexplained death. Policies should be established as regarding such notification as well as responding to family needs.

Most importantly, never assign blame to the family or induce feelings of guilt, even when child abuse is suspected (Shapiro-Mendoza, Pediatrics 2021, PubMed ID: 34544849). Resources and education on safe sleep practices are essential, but should be delivered in a compassionate and emotionally intelligent manner. Support should be sought for the family from hospital sources such as social work and chaplaincy, and referrals can be made to outside long-term resources such as FirstCandle.org.

CRITICAL INFORMATION TO PROVIDE TO THE FAMILY
Time with the deceased child (a member of the clinical team should remain with the caregiver or family to supervise against any potential tampering of the body or artifacts)
A description and timeline of what to expect in the post-mortem process
Points of contact for questions or concerns
Referral and resources for grief and support
Palusci et al, Chapter 12 (pp. 177-202): Family needs and follow-up care after the sudden, unexpected death of a child In *Unexplained Pediatric Deaths: Investigation, Certification and Family Needs.* San Diego, CA: Academic Forensic Pathology International, 2019.

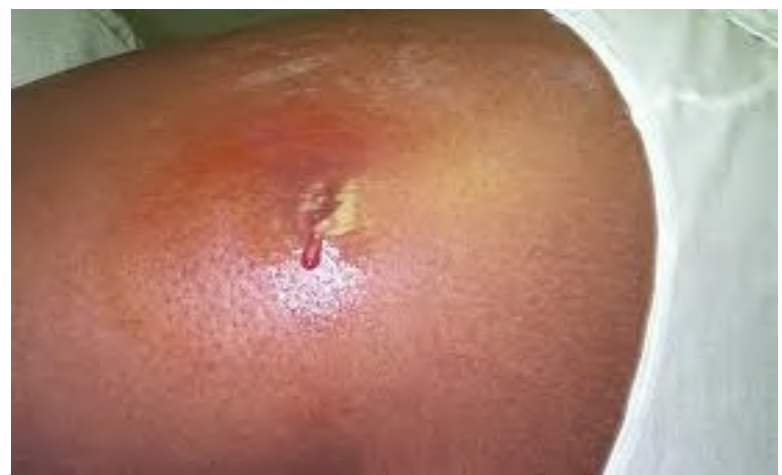
DERMATOLOGY



ABSCESS INCISION & DRAINAGE

INTRODUCTION (ALVIRA SHAH M.D., 1/2018)
A cutaneous abscess is a collection of pus within the dermis and underlying soft tissues. It typically presents as a warm, red, tender, fluctuant area surrounded by a rim of indurated, erythematous tissue. Abscesses occur when the normal skin barrier is breached and bacteria invade the underlying tissue.

Common pathogens include *Staphylococcus* and less commonly *Streptococcus* that are found naturally on the skin. Abscesses can occur anywhere on the body, but most commonly in the axilla, buttocks/perianal area, breast, and extremities.

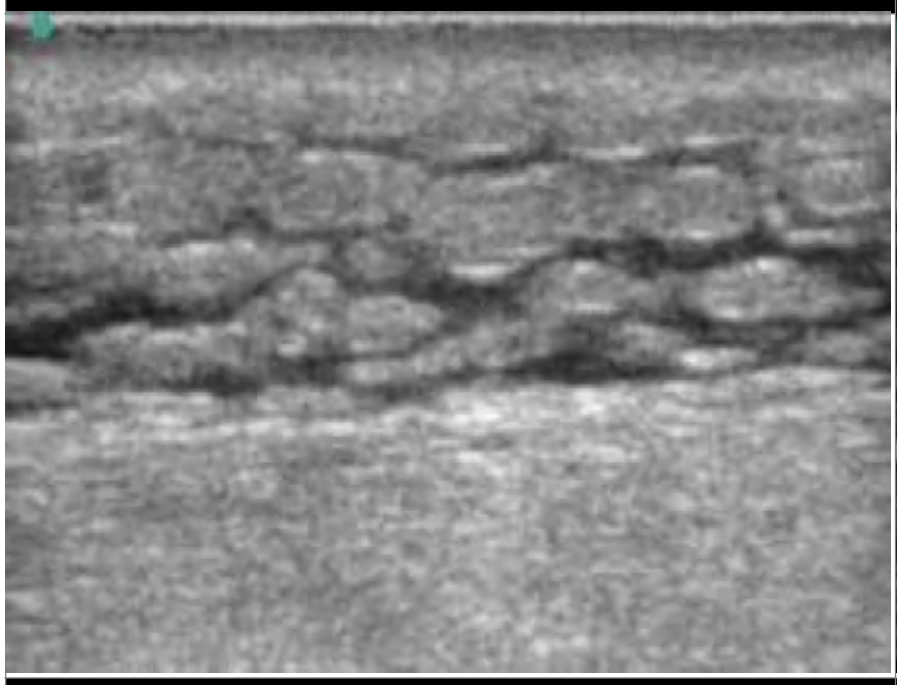
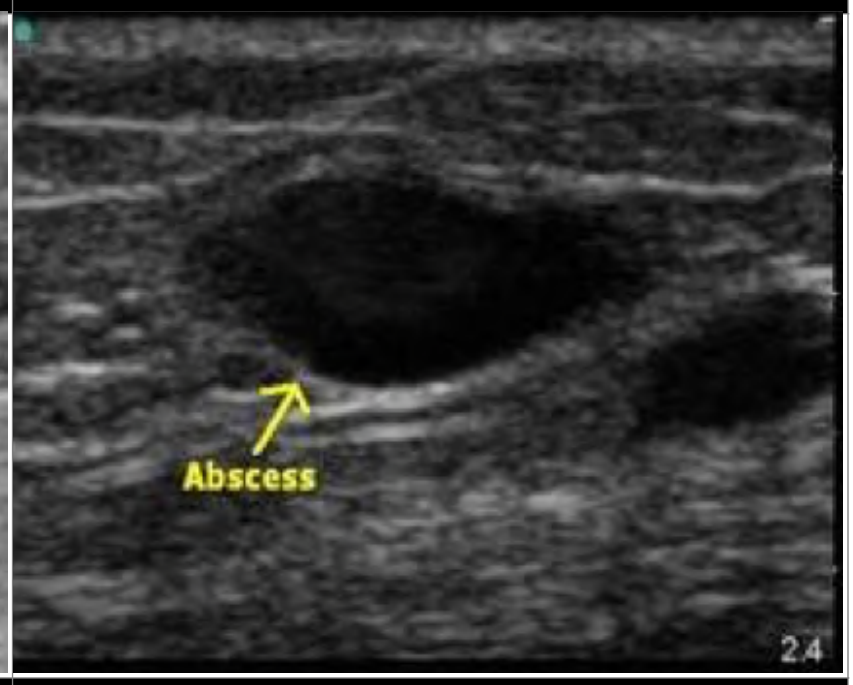


DRAINING CUTANEOUS ABSCESS

DIAGNOSIS: SONOGRAPHY

Bedside ultrasound can be used to distinguish between cellulitis and abscess in situations when the distinction is clinically ambiguous. It can help detect an occult abscess that would not have been drained otherwise. It can also avoid incision and drainage if no significant abscess is present. It can also avoid damaging nearby nerves and blood vessels. A study of 148 pediatric patients with suspicion of a cutaneous abscess (Adams, J Pediatrics 2016, PubMed ID: 26563535), both sensitivity and specificity of point of care ultrasound (Sensitivity: 96% (90, 99%), Specificity 87% (74-95%)) were higher than for physical examination (Sensitivity: 84% (75, 90%), Specificity: 60% (44, 73%). The authors concluded that “for every 4 ultrasounds performed, these was 1 correct change in management”.

Most subcutaneous abscesses are relatively superficial. A high-frequency (7-12 MHz) linear array transducer is commonly used. An abscess appears as a spherical or oblong anechoic or hypo-echoic collection without or without hyper-echoic debris. Cellulitis has a cobblestone appearance, with no distinct fluid collection.

CELLULITIS	ABSCESS
	
COBBLE-STONING	ANECHOIC CAVITY

INDICATIONS

An abscess on the skin that is palpable and fluctuant by exam or seen via ultrasound is treated with incision and drainage. Small abscesses (< 1 cm in diameter) are usually treated with warm compresses to promote spontaneous drainage, and antibiotic treatment may be considered. Larger abscesses require incision and drainage. This is because the walled off abscess will not allow adequate penetration by antibiotics and conservative measures such, as soaks are ineffective.

CONTRAINDICATIONS

A surgical specialist should drain abscesses that have a higher rate of complications.

ABSCESSES REQUIRING SUBSPECIALTY CONSULTATION
Peri-rectal abscesses
Neck abscesses potentially arising from congenital cysts
Hand abscesses (not including felons and paronychia)
Abscesses adjacent to vital nerves or blood vessels
Naso-labial folds abscess: risk of septic phlebitis, extension through the cavernous sinus
Breast abscesses, especially those near the areola/nipple
Recurrent and multiple interconnected abscesses that may have fistulas
Very large/deep abscesses as determined by palpation or ultrasound
Rapidly progressing abscess in toxic patient (necrotizing fasciitis)
Patients at increased risk of complications of procedural sedation
Patients with a bleeding disorder

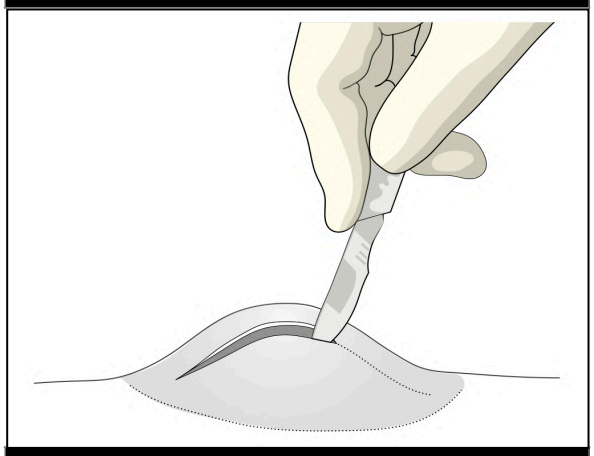
EQUIPMENT
Personal protective equipment: Sterile gloves, drapes, face-mask with eye protection
Antiseptic: Povidone-Iodine or Chlorhexidine
Local anesthetic: 1 or 2% Lidocaine (with/without Epinephrine depending on location)
3 to 10 mL syringe and needle of 25, 27, or 30 gauge
Culture swab
Number 11 scalpel
Gauze
Curved hemostats
Forceps
Scissors
30 - 60 mL syringe, 19 gauge angiocatheter with splash shield
Basin with sterile saline solution (for irrigation)
Packing material (e.g. Iodoform or plain gauze packing tape)
Dressing of choice

PRE-PROCEDURE

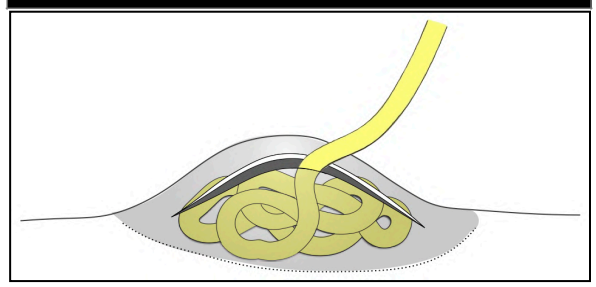
In a retrospective, multicenter study of pediatric patients with cutaneous abscess the application of a topical anesthetic cream (LMX: 4% Lidocaine) and an occlusive dressing resulted in spontaneous abscess rupture in 24% (26/110) of patients. (Cassidy-Smith Amer J Emerg Med, 2012, PubMed ID: 21129885).The authors conclude that: “topical anesthetic cream application before drainage procedures promotes spontaneous drainage and decreases the need for procedural sedation for pediatric cutaneous abscess patients”.

PROCEDURE	
1	Explain the procedure with risks and benefits to the patient and obtain informed consent. Consider procedural sedation.
2	Use universal precautions. Clean site over/around abscess with Betadine/Chlorhexadine. Drape to create a sterile field.
3	Use a field block with a local anesthetic. The injection can be performed with 1 puncture if needle inserted into dome of abscess, then syringe is held parallel to the skin and rotated while injecting to distribute anesthetic circumferentially. Allow 2-3 minutes for anesthetic to take effect.
4	Incise widely over abscess with a #11 blade, cutting through the skin into the abscess cavity in the normal skin cleavage planes (Langer’s lines) if possible. (See illustration: Step 4)
5	Allow the pus to drain, soak up drainage with gauze
6	Take a culture of abscess contents, swabbing from inside the abscess cavity
7	Use the hemostat to gently explore the abscess cavity and break up any loculations via blunt dissection. Probing is painful and may require additional anesthetic.
8	Irrigate the abscess cavity copiously with isotonic saline solution until all visible pus is removed (questionable utility)
9	Pack the abscess cavity with packing strip to prevent closure of wound margins. Do not pack tightly since excessive pressure can cause tissue necrosis and prevent granulation and wound closure. Leave a ‘tail’ hanging to serve as wick for drainage. (See illustration: Step 9)
10	Place gauze dressing over wound, and tape in place.
11	Give instructions to follow up for reevaluation and packing change in 24-48 hours.

STEP 4: INCISION



STEP 9: PACK LOOSELY



LOOP DRAINAGE TECHNIQUE: Evidence supports the loop drainage technique over simple incision and drainage. A meta-analysis of 4 studies including 470 patients reported a failure rate of 9.4% in the incision and drainage group and 4.1% in the loop drainage group (OR: 2.63, 95% CI (1.04, 6.63) (Gottlieb, Amer J EM, 2017, PubMed ID: 28917436).

VIDEO LINK: SIMPLE INCISION AND DRAINAGE

VIDEO LINK: LOOP DRAINAGE TECHNIQUE

COMPLICATIONS

Lack of adequate pain control is the most common limiting factor in achieving adequate incision and drainage. Local infiltration is less effective due to lower pH of infected tissue that reduces the proportion of anesthetic in the more active uncharged form. Depending on the size, location, and age of patient you should consider procedural sedation in the emergency department or general anesthesia in operating room. Complications are uncommon but can occur from under or over drainage. Inadequate drainage may lead to local extension of abscess (osteomyelitis; tenosynovitis; septic thrombophlebitis; necrotizing fasciitis; fistula formation). Overaggressive drainage with sharp dissection can result in nerve and/or vessel damage.

PACKING

The benefit to packing small abscesses in healthy patients is debated as it may cause unnecessary pain and recurrent revisits. A few small studies have shown packing does not change outcomes. It is recommended to pack an abscess cavity if: the abscess greater than 5 cm in diameter, pilonidal abscess or abscess in immunocompromised or diabetic patients.

ANTIBIOTICS

Treatment for a simple abscess is incision and drainage alone. This has been shown to be true even in the setting of methicillin resistant staph aureus infection. (Duong, Annals EM, 2010 PubMed ID: 19409657). A clinical trial compared placebo to trimethoprim/sulfamethoxazole in approximately 1,200 adult patients with uncomplicated cutaneous abscesses and demonstrated a 7.2% (95% CI, 3.2, 11.2) improvement in clinical cure in patients receiving antibiotics (Talan, NEJM 2016, PubMed ID: 26962903). Many of the secondary outcomes also favored antibiotics. The investigators included some patients with diabetes, chronic skin diseases and possibly those with cellulitis who may have met criteria for antibiotics. It remains unclear if antibiotics are warranted in the truly “uncomplicated” cutaneous abscesses in patients who do not have co-morbid conditions.

Patients with extensive cellulitis or with comorbidities may require supplemental antibiotic treatment. It is important to assess for cellulitis after incision and draining is completed because a tensely fluctuant abscess may mimic the induration and surrounding erythema seen in cellulitis. Antibiotic choice should include coverage of both MSSA and MRSA. This includes Trimethoprim/Sulfamethoxazole or clindamycin (guidelines recommend against clindamycin if resistance rates are greater than 10-15% in your community.). A first generation cephalosporin may be added to the regimen if there is a concern for streptococcus infection. Single antibiotic coverage with Doxycycline can be used in older patients.

ANTIBIOTIC INDICATIONS
Abscess > 5cm
Ill appearing (fever, etc.)
Surrounding cellulitis
Abscess site difficult to drain (genital, face)
Co-morbid conditions, immunocompromised
Rapidly advancing disease: Necrotizing fasciitis
Failure of simple drainage

FOLLOW-UP

Reevaluation should be scheduled within 24-48 hours. The patient should return in this time frame to ensure the wound is healing, there is no abscess recurrence or expanding cellulitis, and no signs of systemic illness such as fever or chills are present. Packing can be discontinued is the wound has granulated in from the bottom sufficiently so that if the skin closed no cavity would remain.

The packing is removed and the patient can begin warm wet soaks several times a day until healing occurs. If the wound continues to drain, develops additional signs of infection or worsening clinical signs such as pain or fever then the wound should be re-explored to determine if residual abscess cavities are present. Bedside ultrasound can help to identify a residual abscess. The culture results should guide selection. If antibiotics are now required

RECURRENT ABSCESSES AND MRSA COLONIZATION

Patients with a history of multiple or recurrent abscesses, family members with abscesses, extensive antibiotic use, or living in shelters may be colonized with methicillin-resistant staphylococcus aureus (MRSA). (Shahara, ID Clinics NA 2020, PubMed ID: 33303331). These patients and their cohabitants may benefit from decontamination. A randomized clinical trial found that a regimen of intranasal 2% Mupirocin (applied to both anterior nares twice a day for 5 days) and dilute bleach baths (1 cup bleach – 6% Na hypochlorite (e.g. Clorox) in a tub of water soaking for 15 minutes on five consecutive days) was the most effective at eliminating colonization at four months (Fritz, Infection Control Hosp Epid 2011, PubMed ID: 21828967). A combination of mupirocon and chlorhexadine wipe has also been used for decolonization (Noto, Intensive Care Med 2015, PubMed ID: 26088910).

APPROACH TO RASHES

INTRODUCTION (JOE BENNETT, MD, CHRISTOPHER CASPERS, MD, 5/2019)
Rash is a common pediatric chief complaint in the Emergency Department. Rashes can range from those that are benign and self-limited to those that are life-threatening.
Rashes may be localized to the skin or represent a systemic process. Rashes can be caused by a variety of disease processes affecting any layer of the skin. These include vascular dilatation/leakage and inflammation or interruption of the junctions between the skin layers.

Many providers admit that they have difficulty diagnosing rashes. This is primarily because they approach rashes solely by visual pattern recognition. If they have seen it before they know it. If they haven't seen it before they don't know it. Rashes should be approached in the same manner as any other differential diagnoses. A series of questions based on the rash's primary and secondary characteristics and the patient's history and examination findings can help to narrow the differential diagnosis.

DESCRIBING A RASH: PRIMARY AND SECONDARY* CHARACTERISTICS	
Lesion type(s)	Macule, papule, vesicle, bullae, plaque, petechiae, purpura
Lesion shape/size	Circular, oval, annular (central clearing)
Lesion color	Erythematous, skin-colored, hypo or hyperpigmented
Lesion border	Regular, irregular, no border (confluent lesions)
Lesion feel	Firm, fluctuant, tender, smooth, rough, scaly, blanching
Lesion stage	Same or different stages of development
Lesion distribution	Discrete, confluent, distinct pattern, symmetric, unilateral
Lesion location	Generalized vs focal (sun-exposed, flexor/extensor, hairy areas)
*Secondary skin lesions: Modification of primary lesions: Scale, crust, erosion, fissure, ulceration, excoriation, lichenification (thickened, skin) due to trauma or evolution of the primary lesion.	

DESCRIBING A RASH: LESION TYPES				
	COLOR CHANGE	SIZE[1]	RAISED/PALPABLE	BLANCHING
Macule	Yes	< 1 cm	No	Yes
Patch	Yes	> 1 cm	No	Yes
Papule	Yes/No	< 1 cm	Yes	Yes
Plaque	Yes/No	> 1 cm	Yes	Yes
Petechiae	Yes	< 1 cm	No	No
Purpura	Yes	> 1 cm	Yes/No[2]	No
Vesicle	Clear fluid filled	< 1 cm	Yes	NA
Pustule	Opaque fluid filled	< 1 cm	Yes	NA
Bullae	Clear fluid filled	> 1 cm	Yes	NA
1. No consensus on size definitions, generally divided into < or > 1 cm 2. Palpable purpura suggest an inflammatory vasculitis (Henoch-Schonlein Purpura)				

DESCRIBING A RASH: LESION SHAPE AND DISTRIBUTION	
SHAPE	DISTRIBUTION
Circular (round) (Tinea corporis)	Discrete
Discoid (oblong, oval) (Pityriasis rosea)	Confluent (Measles on the face)
Irregular boarders (Erythema migrans)	Palms/Soles (2nd Syphilis, Gonorrhea)
Annular (central clearing) (E multiforme)	Linear (Scabies)
Umbilicated (Molluscum contagiosum)	Serpiginous (Cutaneous larva migrans)
	Dermatomal (Shingles)
	Tree shaped (Pityriasis rosea)

DIAGNOSIS

The diagnosis of a rash is made primarily on clinical grounds. The history and physical examination are the most important diagnostic tools. The goal is to describe and categorize the rash. It may not be possible to arrive at a definitive diagnosis in the ED. Identification of the class of etiology as infectious (viral, bacterial, fungal), allergic, rheumatologic or inflammatory can guide the initial approach to therapy, disposition and referral.

HISTORY: RED FLAGS	
PMH	Immunocompromised, chemotherapy, diabetes, valve disease
HPI	Fever: Infectious vs rheumatologic, ill contacts
	Severe pain: Necrotizing infections
	Difficulty swallowing or breathing: Anaphylaxis, SJS-TEN
Medications	TEN/SJS, anaphylaxis, most medication reactions benign
Progression	Fast moving rashes are associated with dangerous disease
	Anaphylaxis: Minutes
	Meningococcemia: Petechiae/purpura spread within hours
	RMSF: 4 days after illness petechiae appear and spread rapidly
Spread	Vasculitis (e.g. RMSF): Peripheral → Central
	Viral exanthem: Central → Peripheral
	Measles: Cranial → Caudal
Travel	Northeast: Petechial rash: RMSF, Ehrlichiosis
	Northeast: Bullseye, irregularly bordered lesion: Lyme
	Caribbean: Maculopapular rash: Dengue, chikungunya
	Sub-Saharan Africa: Maculopapular rash: Ebola
Other	Occupation: Teen lifeguard, loves lemonade: Phyto-photodermatitis Exposures: Outdoors, animals

EXAMINATION: Ensure that lighting is adequate. Undress the patient fully. It is helpful to have them lie in a supine position then flip over to the prone position to view the entire skin surface. Often overlooked areas include the groin, buttocks, axilla and scalp. All mucosal surfaces should be examined. The mid-upper back is difficult to reach so it is a good location to look for un-excoriated lesions. Feel the rash. Does it blanch? Is it palpable? Is there fluctuance or tenderness? Does the skin slough with gentle rubbing?

PHYSICAL EXAMINATION: RED FLAGS	
Toxic appearance	Altered mental status, respiratory distress, poor perfusion
Abnormal vital signs	Fever, hypotension, tachycardia, tachypnea
Adenopathy	Kawasaki, rheumatologic disease, rubella
Arthritis	Lyme, acute rheumatic fever, Lupus, JIA, rubella, gonorrhea
Mucosal involvement	SJS-TEN, angioedema (anaphylaxis), conjunctivitis
Skin sloughing (exfoliation)	Staphylococcal scaled skin syndrome, TEN, Toxic shock syndrome, Kawasaki disease, Scarlet fever
Necrosis	Ecthyma, anthrax, brown recluse bite, necrotizing fasciitis
Tenderness	Necrotizing soft tissue infections, erysipelas (strep)
Petechiae/Purpura	RMSF, meningococcemia, leukemia, HSP, ITP, HUS
Vesiculo-bullous	HSV, varicella, smallpox, staph impetigo/scalded skin

DIAGNOSTIC TESTING

Laboratory testing rarely yields the diagnosis in the time frame of an ED visit. A biopsy may be required for unusual rashes.

MANAGEMENT

If a dangerous etiology is suspected, involve consultants early and begin empiric treatment. Withdraw any potential offending agents. Isolate the patient and wear appropriate personal protective equipment if a contagious infectious rash is suspected (e.g. measles, meningococcemia). Abnormal vital signs should be addressed first. Early airway protection should be considered for those at risk for airway obstruction (e.g. anaphylaxis, Stevens-Johnson syndrome). Antibiotics should be administered to those with a suspected serious bacterial infection (meningococcemia, toxic shock syndrome, staphylococcal scaled skin, necrotizing fasciitis). The suspected etiology of the rash will dictate treatment options. Patients with dangerous rashes will require admission and potentially transfer to a burn center.

APPENDIX: MACULOPAPULAR RASHES

DIFFERENTIAL DIAGNOSIS: MACULOPAPULAR RASHES		
VIRAL	BACTERIAL	NON-INFECTIOUS
Adenovirus[2]	Gonorrhea (disseminated)	Bites (insect)[4]
Coxsackie virus[2,4]	Scarlet fever	Contact derm: Allergic[3]
Dengue[1]	Syphilis	Contact derm: Irritant[3]
Epstein-Barr virus	FUNGAL	Drug reaction
Echovirus	Pityriasis versicolor[4]	Erythema multiforme[1,4]
Enterovirus[2]	OTHER INFECTION	Lichen nitidus
Erythema infectiosum[2,4]	Ehrlichiosis[1]	Papular urticaria
Molluscum contagiosum[4]	Mycoplasma	Pityriasis lichenoides
Non-specific viral[2]	Rocky Mountain Spotted [1]	Psoriasis: Guttate
Roseola infantum[2,4]	UNCLEAR (VIRAL?)	Scabies[3]
Rubella	Pityriasis rosea[2,4]	
Rubeola (Measles)[1,4]	Kawasaki[1]	
Varicella (early)	Papular acrodermatitis	
1. Potentially life-threatening. 2. Generalized		3. Localized, 4. Characteristic clinical appearance

APPENDIX: PAPULAR AND PAPULOSQUAMOUS RASHES

DIFFERENTIAL DIAGNOSIS: PAPULAR AND PAPULOSQUAMOUS RASHES	
PAPULAR	PAPULOSQUAMOUS[1]
Granuloma annulare[2]	Acrodermatitis enteropathica[3]
Insect bites[2]	Drug reactions[2,3]
Juvenile xanthogranuloma	Lichen nitidus
Lichen nitidus	Lichen planus
Mastocytomas, urticaria pigmentosa	Nummular eczema[2]
Milia[2]	Para-psoriasis
Molluscum contagiosum[2]	Pityriasis rosea[2]
Pyogenic granuloma[2]	Pityriasis rubra pilaris
Spitz nevi	Psoriasis
Warts[2]	Reiter’s syndrome
Xanthomas	Seborrheic dermatitis
	Syphilis (secondary)[2]
1. Papulosquamous rashes have both a papular and a scaling component 2. Common. 3. Potentially life-threatening	

APPENDIX: ECZEMATOUS RASHES

DIFFERENTIAL DIAGNOSIS: ECZEMATOUS RASHES		
INFECTIOUS	IMMUNOLOGIC	EXOGENOUS
Candida	Agammaglobulinemia	Asteototic eczema
Dermatophyte (fungal)[2]	Graft versus host	Contact Derm: Irritant[2]
Eczema Herpeticum	Hyperimmunoglobulin E	Dyshydrotic Eczema
HIV	Immune dysregulation	Frictional lichenoid derm
Pityriasis rosea	Polyendocrinopathy	Intertrigo
Molluscum contagiosum[2]	Enteropathy	Lichen simplex chronicum
Scabies[2]	X-linked (IPEX)	Photo-allergic reaction
Seborrheic Dermatitis	Wiskott-Aldrich syndrome	NUTRITIONAL
ALLERGY	ONCOLOGIC	Acrodermatitis enteropathy
Atopic dermatitis[2]	Histiocytosis	OTHER
Auto-eczematization (Id)	Cutaneous T Cell lymphoma	Exfoliative dermatitis[1,3]
Contact Derm: Allergic[2]	Leukemia	Netherton's syndrome
Drug Reaction		Psoriasis
1. Potentially life-threatening, 2. Common 3. See table below for differential diagnosis of exfoliate dermatitis		

APPENDIX: EXFOLIATION/ERYTHRODERMA

DIFFERENTIAL DIAGNOSIS: EXFOLIATIVE RASHES[3] AND ERYTHRODERMIA		
INFECTIONS	DERMATOLOGIC	IMMUNOLOGIC
HIV[1]	Atopic dermatitis	Cutan T Cell lymphoma[1]
Staph scaled skin[1]	Contact dermatitis	Graft versus host[1]
Scarlet fever	Diffuse mastocytosis	Hypogammaglobulinemia
Toxic shock syndrome[1]	Ichthyosis	Kawasaki disease[1]
DRUG REACTIONS	Pemphigus foliaceus	Omenn's syndrome
Antiepileptics[1]	Pityriasis rubra pilaris	Severe Com Immune Def[1]
Cephalosporins[1]	Seborrheic dermatitis	Wiskott-Aldrich syndrome[1]
DRESS[2]	METABOLIC/NUTRITION	OTHER
Penicillins[1]	Acrodermatitis enteropath[1]	Leukemia, lymphoma[1]
Sulfonamides[1]	Kwashiokor[1]	Netherton's syndrome
Toxic epidermal necrolysis[1]	Phenylketonuria[1]	
	Leiner's disease	
1. Potentially life-threatening, 2. Drug Reaction with Eosinophilia and Systemic Symptoms 3. Exfoliative dermatitis includes a component of skin sloughing/desquamation		

APPENDIX: PETECHIAL AND PURPURIC RASHES

DIFFERENTIAL DIAGNOSIS: PETECHIAL AND PURPURIC RASHES	
DISRUPTED VASCULAR INTEGRITY	PLATELET, COAGULATION DISORDER
Acute glomerulonephritis	↓ Platelet Survival
Acute rheumatic fever	Immune: ITP, collagen vascular
Drugs and Toxins[1]	Immune: Drugs[1], sepsis[1]
Ehlers-Danlos syndrome	DIC[1], HUS[1], TTP[1], Wiskott-Aldrich1
Infections	↓ Platelet Production
Viral exanthem[2]	Leukemia[1], neuroblastoma[1]
Infectious mononucleosis	Sepsis[1]: Viral, bacterial
Bacterial endocarditis[1]	Aplastic Anemia
Rickettsial disease[1,2]	Drugs: Bone marrow suppression[1]
Streptococcal infections[2]	↓ Platelet Function
Henoch-Schonlein purpura	Glanzmann thrombasthenia[1]
Langerhans cell histiocytosis	Aspirin, antihistamines
Other collagen vascular diseases	Phenothiazines, Guaifenesin
Trauma: Accidental, intentional[1,2]	Platelet Sequestration
Vitamin C deficiency	Congestive splenomegaly
	Kasabach-Merritt syndrome
	Glycogen storage disorders
	Factor Deficiencies: Congenital
	Von Willebrand disease
	Hemophilia A (VIII) [1], B (IX) [1], others[1]
	Factor Deficiencies: Acquired
	DIC[1,] Liver, heart, renal disease[1]
	Vitamin K deficiency
	Warfarin[1] Circulating anticoagulants[1]
1. Potentially life-threatening, 2. Common	

APPENDIX: VESICULAR AND BULOUS RASHES

DIFFERENTIAL DIAGNOSIS: VESICULAR AND BULOUS RASHES	
VESICULAR	BULOUS
Varicella-Zoster	Staphylococcal impetigo[1], scalded skin[2]
HSV, eczema herpeticum	Erythema multiforme
Small pox (Variola virus)[2]	Bullous pemphigoid
Staphylococcal pustulosis/folliculitis[1]	Epidermolysis bullosa
Rhus dermatitis (e.g. Poison Ivy)	Toxic epidermal necrolysis[2]
Dyshidrotic eczema	Heat, cold, friction blisters[1]
Vesicular tinea	Bullous tinea
Scabies	Lupus[2]
Hand-foot-mouth (Coxsackie)[1]	Urticaria pigmentosa
1. Common, 2. Potentially life-threatening	

APPENDIX: RASH CLASSIFICATION BY LESION TYPE

RASH CLASSIFICATION BY LESION TYPE[1]	
VESICULAR	YELLOW LESIONS: SMOOTH
Herpes	Xanthelasma
Varicella-Zoster	Necrobiosis lipoidica diabeticum
Vesicular tinea pedis	Sebaceous gland hyperplasia
Dyshidrotic eczema	YELLOW LESIONS: ROUGH
Scabies	Actinic Keratosis
Eczema herpeticum	Crusted: impetigo
BULLOUS	RED PAPULES: NON-SCALING
Poison Ivy (Rhus dermatitis)	Insect bites
Bullous impetigo (Staphylococcal)	Cherry angiomas
Steven Johnson Syndrome	Spider angiomas
Pemphigoid, Pemphigus	Granuloma annulare
PUSTULAR	RED NODULES: NON-SCALING
Acne Vulgaris	Furuncles
Acne Rosacea	Inflamed epidermoid cyst
Folliculitis: Bacterial, Fungal	Hydradenitis suppurativa
Candidiasis	Erythema nodosum
Gonorrhea (systemic)	VASCULAR REACTIONS:NO PURPURA
SKIN COLORED: ROUGH	Exanthems, medications, photosensitivity
Warts: Plantar, paronychial	Urticaria
Actinic keratosis	Erythema multiforme
Seborrheic dermatitis	Cellulitis, erysipelas
Corns and calluses	VASCULAR REACTIONS: PURPURIC
SKIN COLORED: SMOOTH	Vasculitis (palpable purpura)
Warts: Genital	Actinic (senile) purpura
Basal, squamous cell carcinoma	Petechiae
Sebaceous (epidermoid) cysts	Ecchymoses
Lipomas	PAPULOSQUAMOUS: PLAQUES
Molluscum contagiosum	Psoriasis: Vulgaris
Intra-dermal nevi	Tinea corporis, capitis, pedis, cruris
	Discoid Lupus
	Parapsoriasis-mycosis fungoides
CONTINUED ON NEXT PAGE	

RASH CLASSIFICATION BY LESION TYPE (CONTINUED)[1]	
WHITE PATCHES AND PLAGUES	PAPULOSQUAMOUS: PAPULES
Pityriasis alba	Pityriasis rosea
Tinea versicolor	Lichen planus
Vitiligo	Secondary syphilis
Post inflammatory hypo-pigmentation	Psoriasis: Guttate type
WHITE PAPULES	ECZEMATOUS: SEVERE EXCORIATED
Milia	Atopic dermatitis
Keratosis pilaris	Dyshidrotic eczema
Molluscum contagiosum	Tinea: Cruris, pedis, capitis
Sebaceous gland hyperplasia	Psoriasis
Lentigines	Candidiasis
BROWN MACULES	ECZEMATOUS: MILD EXCORIATED
Freckles	Seborrheic dermatitis
Junctional nevi	Contact dermatitis
BROWN PAPULES/NODULES	Impetigo (streptococcal)
Compound and Intra-dermal Nevi	ECZEMATOUS
Seborrheic keratosis	Hand and foot eczema
Melanoma	Diaper dermatitis
BROWN PATCHES/PLAQUES	Nummular eczema
Café-au-lait patches	Exfoliative erythrodermatitis
Post inflammatory hyperpigmentation	Auto-eczematization (ID reaction)
Giant congenital nevi	
GENERALIZED HYPER-PIGMENTATION	
Systemic disease, post inflammatory	
1. Polymorphous rashes may be listed in more than 1 category	

Adapted from Lynch, Annals of Emergency Medicine 1984, PubMed ID: 6465632

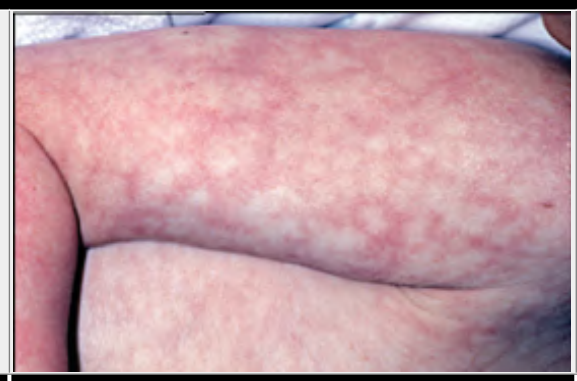
BENIGN NEWBORN RASHES

INTRODUCTION (ELLEN DUNCAN, MD, PHD, 2/2020)
Newborn rashes are quite common and can be a source of concern and confusion to parents and providers alike. There are many benign neonatal rashes that require no work up or intervention, and being able to distinguish these from the concerning rashes is crucial for any provider who sees pediatric patients. Rashes associated with systemic illness requiring additional evaluation and/or treatment are not discussed in this PEM Guide.

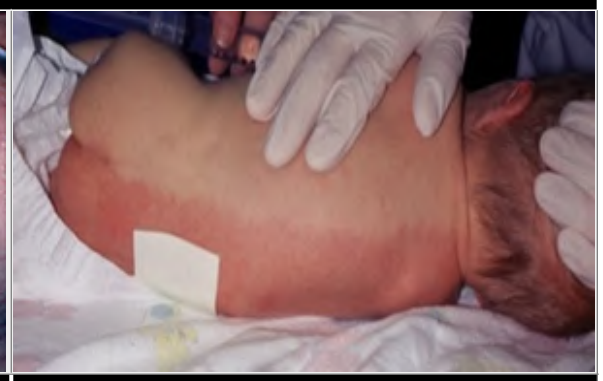
Before delving into a discussion of neonatal rashes, it is important to discuss normal skin changes that occur in newborns. One such example is the desquamation that commonly occurs after birth, which is most pronounced on the hands, feet, and ankles Additionally, newborns may experience cutis marmorata, a lacy reticular mottling of the skin in response to cold. Newborns may also have an entity known as harlequin color change, which is characterized by erythema to dependent areas, with concomitant blanching of the non-dependent skin. Harlequin skin change appears suddenly, can last for up to 30 minutes, and resolves spontaneously. No intervention is needed for any of these conditions.

NORMAL NEWBORN SKIN CHANGES

DESQUAMATION



CUTIS MARMORATA

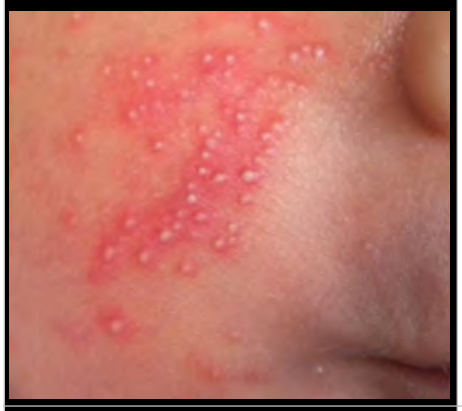
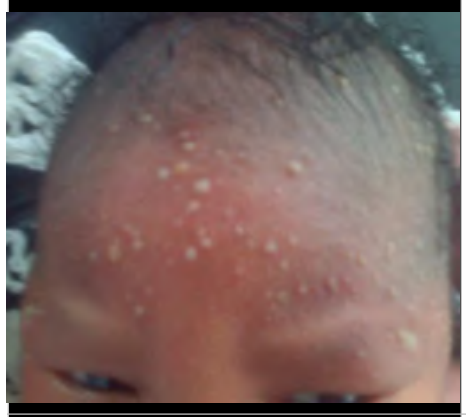
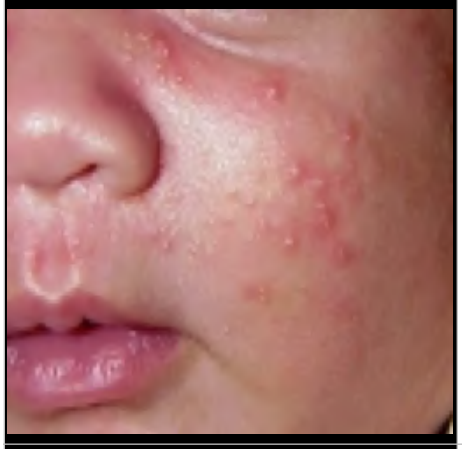
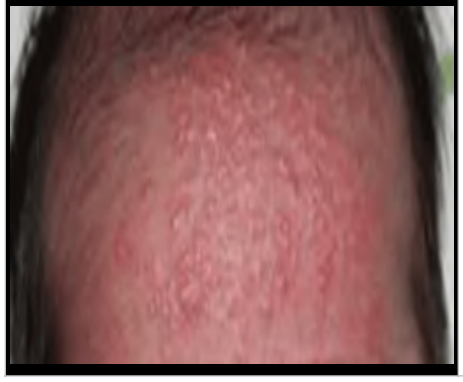


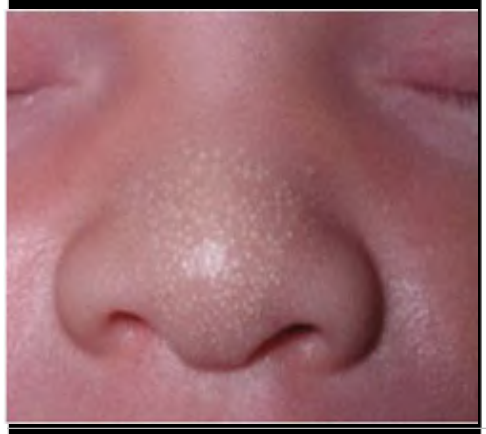
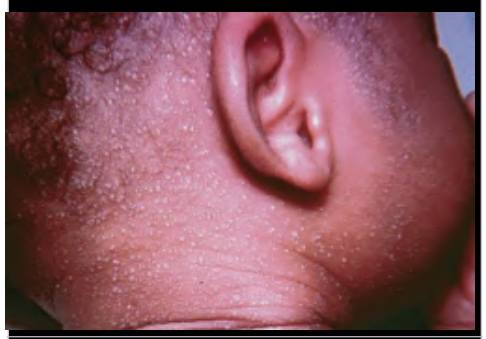
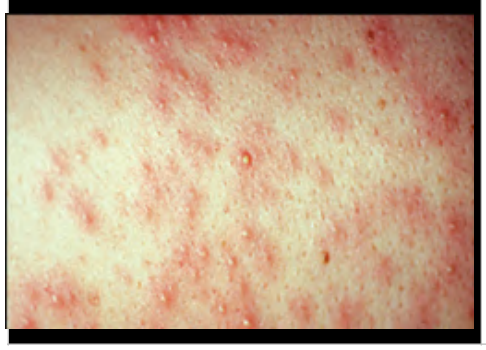
HARLEQUIN COLORS

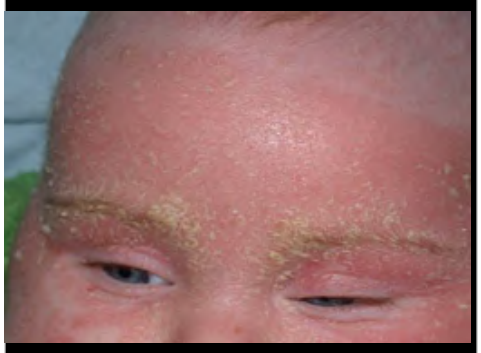
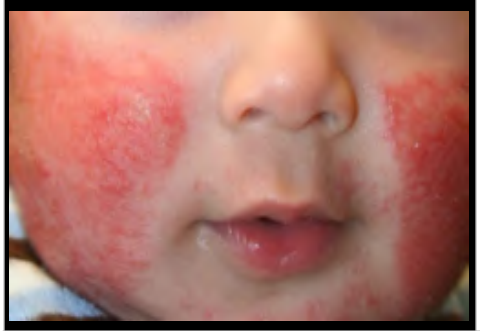
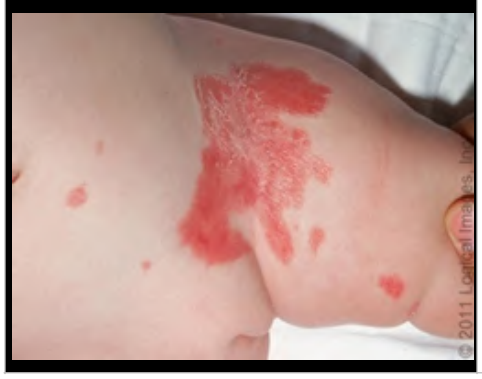
HISTORY
As with any neonate, it is crucial to ask about systemic symptoms (most importantly fever) that might indicate a systemic infection. Infants with rashes indicative of systemic disease require a full sepsis work up, including testing of lesions where possible. Parents should be asked about the onset of the rash, as well as about its distribution or spread, and its evolution. Additionally, because of the sensitivity of newborn skin, information should be gathered regarding soaps, lotions, and detergents. Many products marketed towards babies can be heavily fragranced and cause significant irritation.

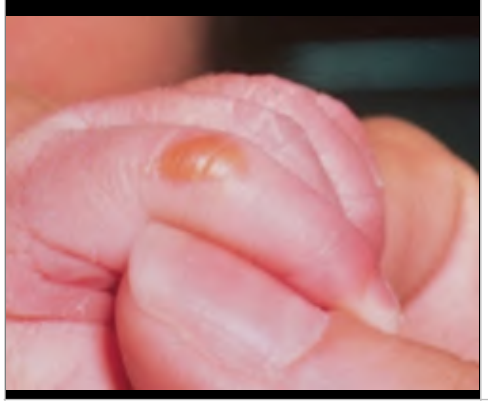
EXAMINATION
Benign newborn rashes can have many different morphologies. It is crucial to note not only the characteristics of the rash (e.g. macular vs papular vs pustular vs vesicular) but also the distribution. The following tables provide a differential diagnosis of benign newborn rashes based on their appearance.
See: PEM Guide: Approach to Rashes for information regarding rash types and how to describe them.

NEWBORN RASHES BY MORPHOLOGY

PUSTULAR RASHES				
CONDITION	EPIDEMIOLOGY	RASH LESIONS	DISTRIBUTION	TREATMENT
ERYTHEMA TOXICUM NEONATORUM (“E TOX”) 	Up to 40-70% of infants Usually DOL 2-5 Can be present at birth	Erythematous, 2-3 mm macules and papules → pustules Surrounding blotchy “flea-bitten” erythema	Face, trunk, and proximal extremities Does NOT include palms or soles.	No treatment Usually resolves within two weeks
TRANSIENT NEONATAL PUSTULAR MELANOSIS 	Up to 5% Black, 1% White Appears within the first month of life	1-3 mm fragile pustules or pigmented macules without surrounding erythema Lesions rupture and leave behind a collarette of scale and a hyperpigmented macule that can take days to months to fade	Any area Usually chin, neck, forehead, trunk, and buttocks Included palms and soles	No treatment Usually resolves by three months of life
ACNE NEONATORUM 	Up to 20% of newborns Presents in first month Related to maternal and endogenous androgens	Closed or open comedones, inflammatory papules, and pustules	Most commonly on the forehead, nose, and cheeks	No treatment Can use 2.5% benzoyl peroxide for extensive or persistent lesions (test first in antecubital fossa)
NEONATAL CEPHALIC PUSTULOSIS 	Up 20% of infants Mean age of onset at 3 weeks NOT related to androgens	Inflammatory papules and pustules	Face and scalp	No treatment Can use Ketoconazole or hydrocortisone

PUSTULAR RASHES (CONTINUED)				
CONDITION	EPIDEMIOLOGY	RASH LESIONS	DISTRIBUTION	TREATMENT
MILIA 	50% of Newborns Often present at birth	1-2 mm white or yellow papules of retained keratin within the dermis	Most common on forehead, cheeks, nose, and chin Can occur on trunk, limbs, penis, and mucous membranes	No treatment Resolves spontaneously within first few months of life
MILIARIA CRYSTALLINA  **MILIARIA RUBRA** 	Up to 40% of infants; usually develops in the first month of life	Miliaria crystallina: 1-2mm vesicles surrounded by erythema that rupture and desquamate Miliaria rubra (prickly heat rash): erythematous papules and vesicles on covered or heat-exposed skin	Appear in locations with eccrine sweat glands Miliaria crystallina: head, neck, and trunk Miliaria rubra: covered areas	No treatment

ERYTHEMATOUS AND/OR SCALY RASHES				
CONDITION	EPIDEMIOLOGY	LESION TYPE	DISTRIBUTION	TREATMENT
SEBORRHEIC DERMATITIS 	Within first month of life	Greasy scales and erythema	Scaling common on scalp, face, ears, and neck; erythema in flexural and intertriginous areas (including diaper area)	No treatment required Symptomatic treatment with: - Petrolatum - Tar or Ketoconazole shampoos - HC 1% cream may help
ATOPIC DERMATITIS 	Usually occurs after three months of age Infantile atopic dermatitis described at right	Erythroderma	Diffuse erythema more common than flexural distribution seen in older infants and children	Emollients Topical Corticosteroid ointments
INFANTILE PSORIASIS 		Glossy, erythematous skin with superficial erosions; may be pustular	Diaper area, scalp, axillae, extremities	No treatment

BULLOUS RASHES				
CONDITION	EPIDEMIOLOGY	LESION TYPE	DISTRIBUTION	TREATMENT
SUCKING BLISTERS 	None	Vesicular or bullous lesions present at birth due to sucking behavior in utero	Forearms, wrists, hands, or fingers	No treatment

FEBRILE RASHES

INTRODUCTION (JOE BENNETT, MD, 5/2019)
Fever and rash are a common pediatric complaint in the Emergency Department. Rashes associated with fever can range from those that are benign and self-limited to those that are life-threatening. This PEM Guide provides an overview of those rashes associated with fever that are either common or life-threatening. However, this overview is by no means comprehensive.

DIAGNOSIS

The diagnosis of a rash is made primarily on clinical grounds. The history and physical examination are the most important diagnostic tools. The goal is to describe and categorize the rash. Some rashes are readily identifiable based on a characteristic lesions or distribution. Many rashes can be described as generalized maculopapular. For these rashes, associated history and physical exam findings can help to narrow the differential diagnosis. It may not be possible to arrive at a definitive diagnosis in the ED. Identification of the class of etiology as infectious (viral, bacterial fungal) or allergic or rheumatologic can guide the initial approach to therapy, disposition and referral. (See: PEM Guide: Dermatology: Approach to Rashes).

HISTORY: A thorough history should include associated symptoms, travel, exposures (insects, animals, sexual history), illness in close contacts and immunization history.

HISTORY: RED FLAGS	
PMH	Immunocompromised, diabetes, valve disease, vaccination status
HPI	Fever, ill contacts
	Severe pain: Necrotizing infections
	Difficulty swallowing or breathing: Anaphylaxis, SJS/TEN
Medications	TEN/SJS, anaphylaxis, most medication reactions benign
Progression	Fast moving rashes are associated with dangerous disease
	Anaphylaxis: Minutes
	Meningococcemia: Petechiae/purpura spread within hours
	RMSF: 4 days after illness petechiae appear and spread rapidly
Spread	Vasculitis (e.g. RMSF): Peripheral → Central
	Viral exanthem: Central → Peripheral
	Measles: Cranial → Caudal
Travel	Northeast: Petechial rash: RMSF, Ehrlichiosis
	Northeast: Bullseye, irregularly bordered lesion: Lyme
	Caribbean: Maculopapular rash: Dengue, chikungunya
	Sub-Saharan Africa: Maculopapular rash: Ebola
Other	Occupation, exposures (insects, animals, sexual contacts)

EXAMINATION: Ensure that lighting is adequate. Undress the patient fully. It is helpful to have them lie in a supine position then flip over to the prone position to view the entire skin surface. Often overlooked areas include the groin, buttocks, axilla and scalp. All mucosal surfaces should be examined. The mid-upper back is difficult to reach so it is a good location to look for lesions that have not been excoriated by scratching.

DIFFERENTIAL DIAGNOSIS

PALPATE THE RASH
Does it blanch?
Is it palpable (above the skin, below the skin)?
Is there fluctuance?
Is there tenderness?
Does the skin slough with gentle rubbing (Nikolsky sign)?

PHYSICAL EXAMINATION: RED FLAGS	
Toxic appearance	Altered mental status, respiratory distress, poor perfusion
Altered Mental status	Lupus (cerebritis), typhoid fever,
Shock	Toxic shock, bacterial sepsis, hemorrhagic fever
Abnormal vital signs	Fever, hypotension, tachycardia, tachypnea
Relative bradycardia	Typhoid, typhus, medication fever
Abdomen tenderness	Typhoid fever, scarlet fever, Lupus (serositis)
Adenopathy	Kawasaki, rheumatologic disease, rubella, EBV, strep
Splenomegaly	Lupus, EBV, rubella, typhoid fever
Arthritis	Lyme, acute rheumatic fever, Lupus, JIA, rubella, gonorrhea
Mucosal involvement	SJS-TEN, angioedema (anaphylaxis)
Conjunctivitis	Kawasaki, measles, toxic shock, adenovirus
Exfoliation (sloughing)	Staphylococcal scaled skin syndrome, TEN, Toxic shock syndrome, Kawasaki disease, Scarlet fever
Necrosis	Ecthyma, anthrax, brown recluse bite, necrotizing fasciitis
Tenderness	Necrotizing soft tissue infections, erysipelas (strep)
Petechiae/Purpura	RMSF, meningococcemia, leukemia, HSP, gonorrhea
Vesicular-bullous	HSV, varicella, smallpox, staph impetigo/scalded skin

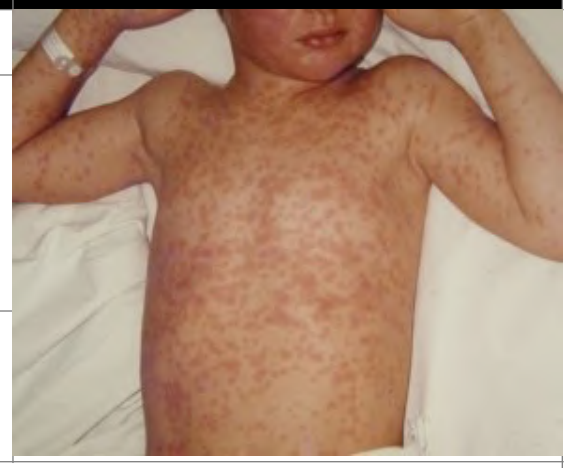
MANAGEMENT

The suspected etiology of the rash will dictate treatment options. If a dangerous etiology is suspected, involve consultants early and begin empiric treatment. Withdraw any potential offending agents. Isolate the patient and wear appropriate personal protective equipment if a contagious, infectious rash is suspected (e.g. measles). Abnormal vital signs should be addressed first. Early airway protection should be considered for those at risk for airway obstruction (e.g. anaphylaxis, Stevens-Johnson syndrome). Antibiotics should be administered to those with a suspected serious bacterial infection (meningococcemia, toxic shock syndrome, staphylococcal scaled skin, necrotizing fasciitis). Patients with dangerous rashes will require admission and potentially transfer to a burn center.

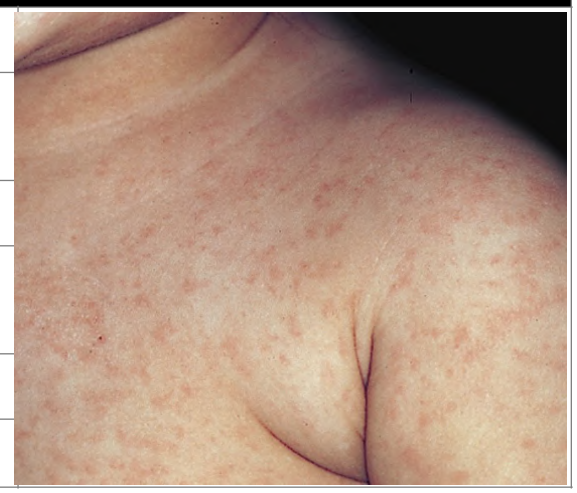
FEBRILE RASHES: DIFFERENTIAL DIAGNOSIS		
VIRAL/SUSPECTED VIRAL		
1	Rubeola (Measles)*	Maculopapular: Cranial → Caudal
2	Rubella (German measles)	Maculopapular, lymphadenopathy
3	Erythema infectiosum: Parvovirus B19	Slapped cheeks, lacy trunk/extremities
4	Roseola (human herpes virus 6)	Maculopapular after high fever
5	Hand-Foot-Mouth (Coxsackie)*	Papular-vesicular, hands, feet, buttocks
6	Varicella	Vesicles at various stages of healing
7	Infectious mononucleosis (EBV)*	Maculopapular, exudative pharyngitis
8	Gianotti-Crosti	Papular: face, extremity extensor surface
9	Pityriasis rosea	Discoid lesion, tree pattern, herald patch
BACTERIAL		
1	Streptococcal scarlet fever*	Fine (sandpaper), erythematous papules
2	Rocky mountain spotted fever*	Distal extremity macules → petechiae
3	Meningococcemia	Petechiae, purpura, skin necrosis
4	Gonococcemia	Pustular, vesiculo-pustular
5	Strep/Staph toxic shock syndrome*	Diffuse erythroderma
6	Staphylococcal scaled skin*	Desquamation, bullae
7	Erythema multiforme minor	Red raised border, central clearing
8	Stevens-Johnson Syndrome*	Bullae, skin sloughing, mucosa involved
9	Erysipelas*	Red, indurated, tender/painful patch
RHEUMATOLOGIC/IMMUNOLOGIC		
1	Kawasaki disease*	Polymorphous (morbilliform)
2	Systemic Lupus Erythematosus*	Malar rash, discoid plaques
3	Juvenile Immune arthritis	Evanescent, oval, macular, salmon colored
4	Dermatomyositis	Groton’s papule, heliotrope facial rash
5	Acute rheumatic fever*	Erythema marginatum, SubQ nodules
*Reviewed in detail in a separate PEM Guides		

APPENDIX: VIRAL FEBRILE RASHES

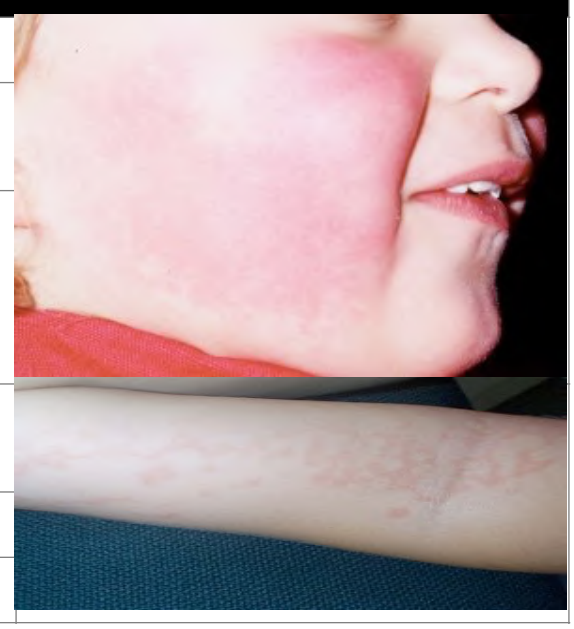
1. MEASLES (RUBEOLA) (FIRST DISEASE)	
Etiology	Rubeola virus
Prodrome	High fever, malaise, anorexia. 3 C's: Cough, Conjunctivitis, Coryza. Koplik spots (oropharynx) 1-3 mm white, grey/blue lesions on an erythematous base. Slough when exanthem appears
Rash	Maculopapular, red-brown "morbilliform" rash. Cranial to caudal: Discrete on face → confluent on face, discrete on trunk/extremities
Other	30% complications rate: Pneumonia most common, encephalitis
Treatment	Symptomatic treatment, Vitamin A
Prevention	Measles, mumps, rubella vaccine: 1st dose 12-14mo, 2nd dose 4-6yrs
See: PEM Guide: Infections: Measles	

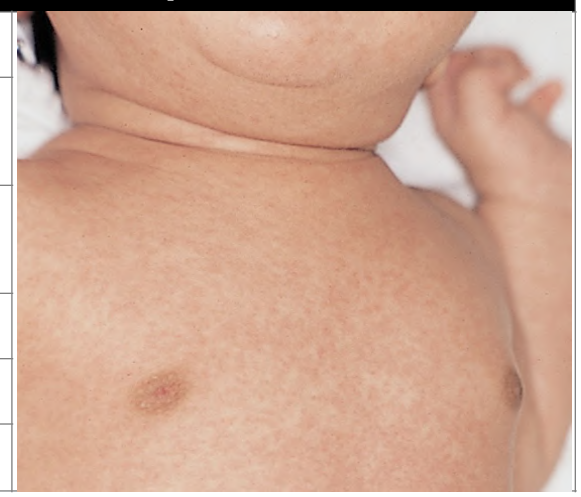


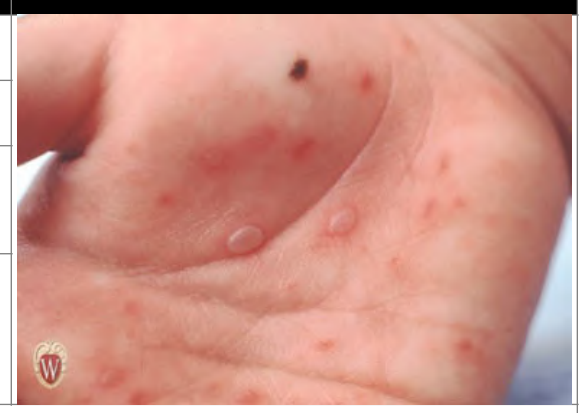
2. RUBELLA (AKA GERMAN MEASLES, THIRD DISEASE)	
Etiology	Rubella virus
Prodrome	Arthralgias, low grade fever. Typically 3 days ("simple measles")
Rash	Pink macules, spread cranial → caudal
Other	Prominent lymphadenopathy: posterior auricular, cervical, occipital
Treatment	Symptomatic management
Prevention	MMR vaccine: 1st 12-14 months, 2nd 4-6 years

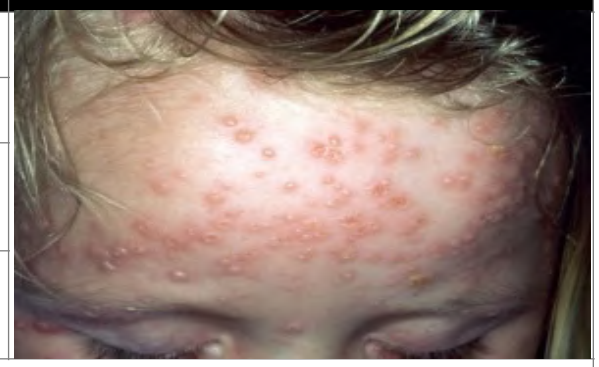


3. ERYTHEMA INFECTIOSUM (FIFTH DISEASE)	
Etiology	Parvovirus B19
Prodrome	Fever, rash onset with fever, diarrhea, myalgias, URI symptoms
Rash	Abrupt onset rash with bright red cheeks "slapped cheeks" Spreads to arms and legs on second day with a "lacy" appearance
Other	Sickle cell disease: Risk of aplastic anemia Pregnancy: Severe anemia, miscarriage
Treatment	Symptomatic management
Prevention	None



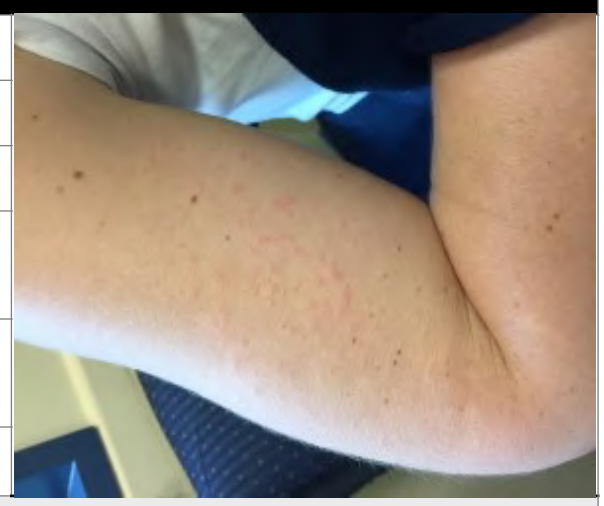
4. ROSEOLA INFANTUM (ERYTHEMA SUBITUM, SIXTH DISEASE)		
Etiology	Human herpes virus 6	
Prodrome	Irritability. High fever x 3-4 days, rash occurs after fever resolves	
Rash	Pink macules and papules on trunk, spread to neck, face, extremities	
Other	Febrile seizures common	
Treatment	Symptomatic management	
Prevention	None	

5. COXSACKIE: HAND FOOT MOUTH DISEASE		
Etiology	Coxsackie A and B, echoviruses and enterovirus A71	
Prodrome	Fever, cough, coryza, mild GI Symptoms	
Rash	Red/flesh colored vesicles-papules on palms, soles and buttocks	
Other	Herpangina: Painful vesicles on posterior pharynx, tongue, soft palate, leaving shallow ulcerations when rupture	
Treatment	Symptomatic management	
Prevention	None	
See: PEM Guide: Head and Neck Infections: Upper Respiratory Illness		

6. VARICELLA (CHICKEN POX)		
Etiology	Varicella-Zoster virus	
Prodrome	Fever, malaise, cough, coryza	
Rash	Crusting vesicles at various stages of development “Dew drop on a rose petal”	
Other	Avoid salicylates (Reye’s syndrome) Risk of group A strep sepsis, pneumonia, cerebellitis	
Treatment	Supportive, skin hygiene to prevent secondary bacterial infection	
Prevention	Varicella vaccine: 1st dose: 12-18 months, 2nd dose: 4-6 years	

7. INFECTIOUS MONONUCLEOSIS

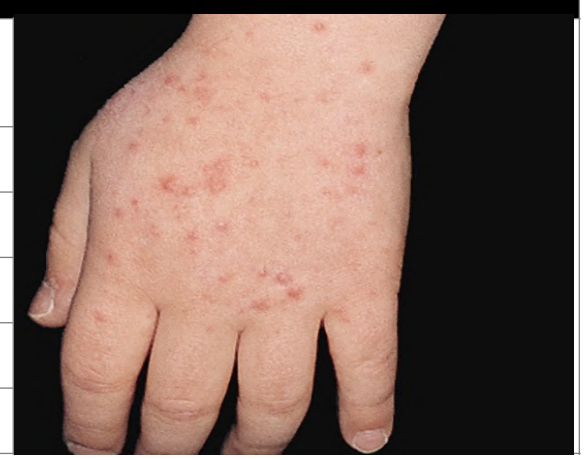
Etiology	Epstein-Barr virus
Prodrome	Fever, malaise, sore throat
Rash	Diffuse maculopapular
Other	Exudative pharyngitis, cervical adenitis, splenomegaly
Treatment	Supportive, corticosteroids for significant tonsillar enlargement
Prevention	None



See: PEM Guide: Infections: Infectious Mononucleosis

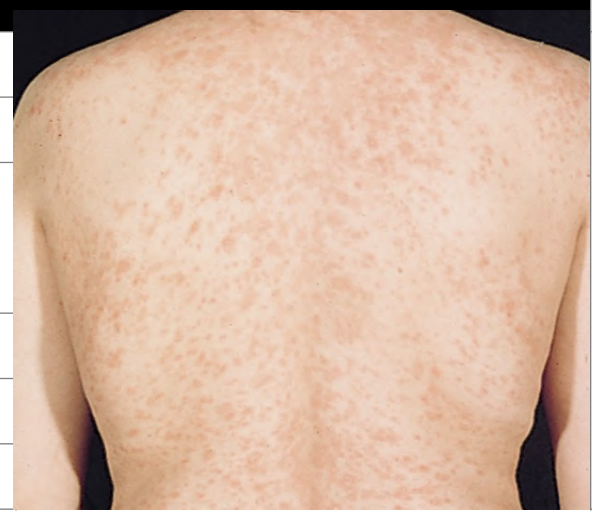
8. GIANOTTI-CROSTI

Etiology	Associated with hepatitis B, other viruses, exact etiology unclear
Prodrome	Fever, cough, coryza
Rash	Papular, face and extremity extensor surfaces
Other	Lymphadenopathy
Treatment	None
Prevention	None

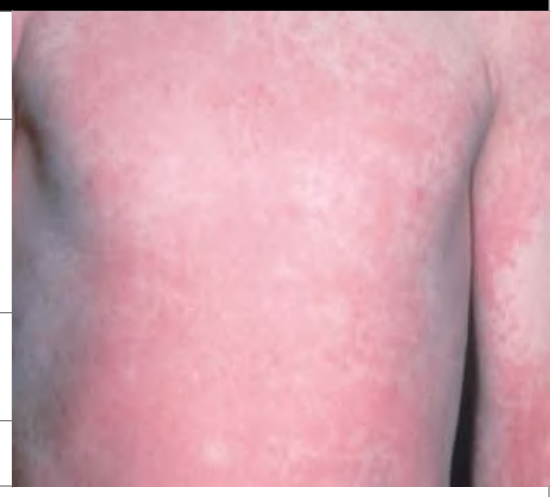


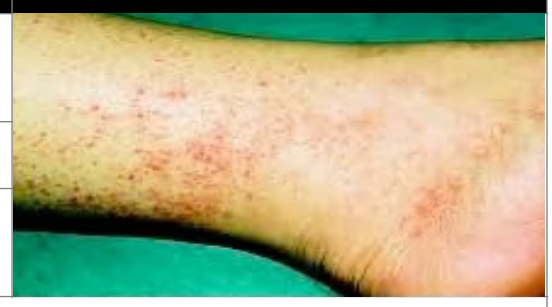
9. PITYRIASIS ROSEA

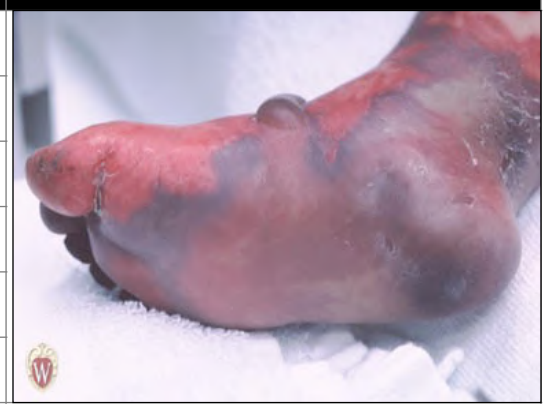
Etiology	Suspected viral etiology, ?HHV6, HHV7
Prodrome	Spring, fall, children, adolescents, fever
Rash	Herald patch: Erythematous scaly patch Discrete, oval, salmon colored lesions, XMAS tree pattern (dermatomal)
Other	Intense pruritis
Treatment	Antihistamines, emollients, ?steroids
Prevention	None

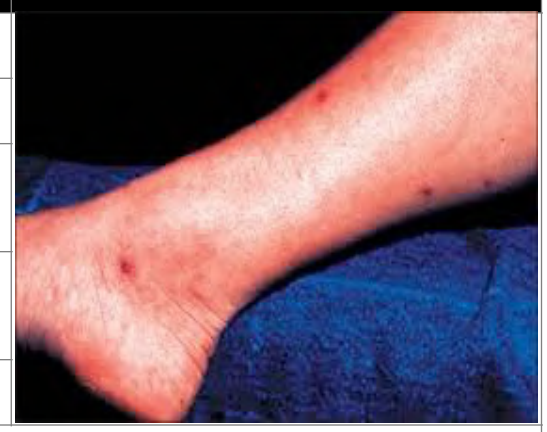


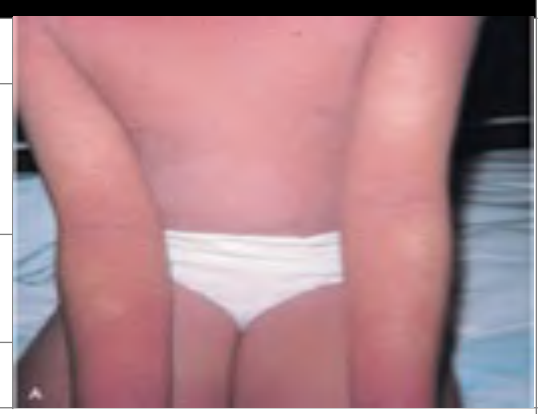
APPENDIX: BACTERIAL FEBRILE RASHES

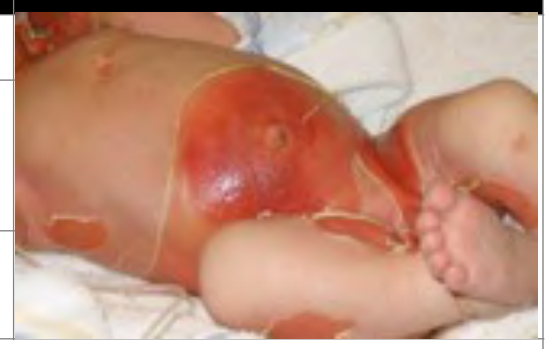
1. SCARLET FEVER (SECOND DISEASE)		
Prodrome	High fever, febrile seizures common, absence of URI symptoms	
Rash	Fine (Sandpaper), erythematous rash begins 12-72 hours after fever Pastia's lines: Erythematous papules in the creases of antecubital fossa	
Other	Exudative pharyngitis, cervical adenitis, palatal petechiae	
Treatment	Penicillin or Amoxicillin	
Prevention	None	
See: PEM Guide: Head and Neck Infections: Pharyngitis		

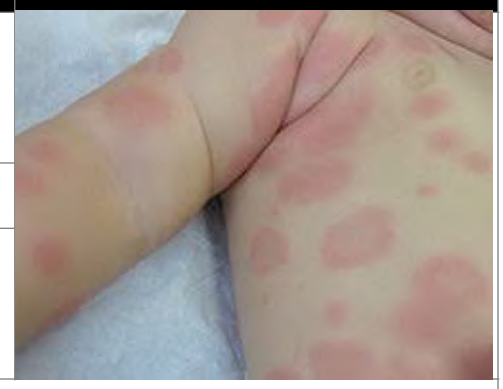
2. ROCKY MOUNTAIN SPOTTED FEVER		
Etiology	Rickettsia rickettsii (gram negative coccobacilli) (via a tick vector)	
Prodrome	Fever, headache, malaise, myalgias, arthralgias	
Rash	Macular→ Petechial Distal extremities → Trunk	
Other	Encephalo-cardiogenic pulmonary edema, hyponatremia, necrosis	
Treatment	Doxycycline	
Prevention	Insect/Tick repellant, clothing covering exposed skin	
See: PEM Guide: Infections: Rocky Mountain Spotted Fever		

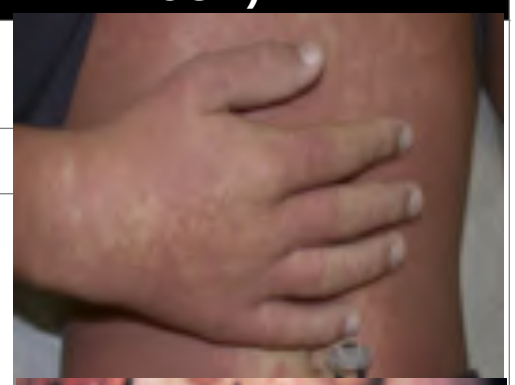
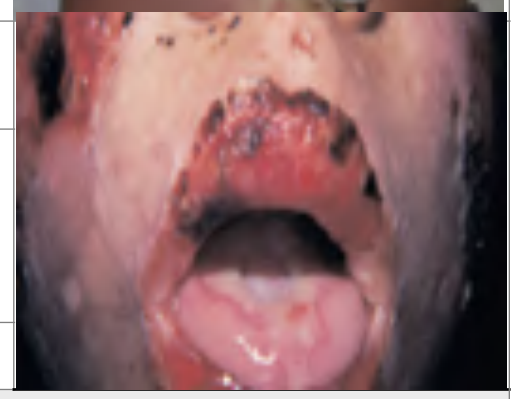
3. MENINGOCOCCEMIA		
Etiology	Neisseria meningitides (gram negative)	
Prodrome	Fever, malaise	
Rash	Petechiae, purpura, skin necrosis	
Other	Shock	
Treatment	Ceftriaxone	
Prevention	Meningitis vaccine	

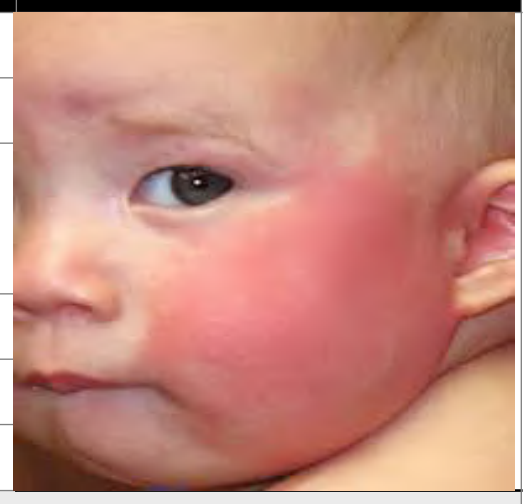
4. GONOCOCCEMIA		
Etiology	Neisseria gonorrhea (gram negative),	
Prodrome	Fever, malaise, arthralgia, tenosynovitis	
Rash	Pustular, vesiculo-pustular, erythema nodosum or multiforme	
Other	Arthritis, endocarditis, myopericarditis, meningitis, osteomyelitis	
Treatment	Ceftriaxone	
Prevention	Barrier contraception	

5. STREPTOCOCCAL & STAPHYLOCOCCAL TOXIC SHOCK SYNDROME		
Etiology	Streptococcal or Staphylococcal toxin	
Prodrome	Fever, malaise, myalgias, weakness, headache, fatigue, sore throat, abdominal pain, vomiting, profuse watery diarrhea, non-pitting edema.	
Rash	Diffuse erythroderma, fine erythematous papules, confluent (flushed appearance)	
Other	Multi-organ involvement: Renal failure, shock	
Treatment	Streptococcal/Staphylococcal antibiotics PLUS Clindamycin	
Prevention	None	
See: PEM Guide: Dermatology: Toxic Shock Syndrome		

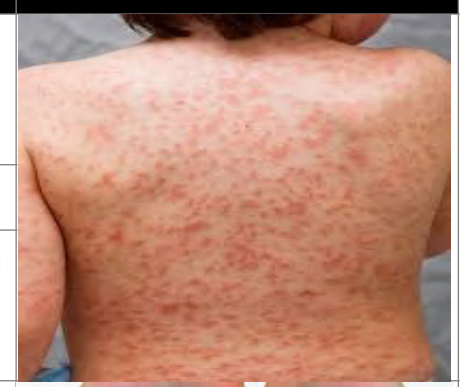
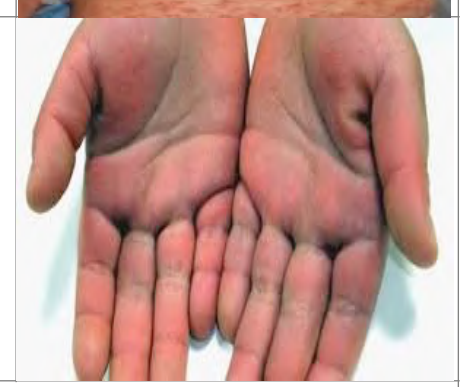
6. STAPHYLOCOCCAL SCALED SKIN SYNDROME		
Etiology	Staphylococcal toxin mediated	
Prodrome	Preceding staph infection (may be subclinical) Sudden-onset of fever, malaise, irritability, ± skin tenderness.	
Rash	Initial: Tender, diffuse erythroderma Exfoliation phase: Bullae with desquamation	
Other	Crusting around the eyes and mouth, pharyngitis, conjunctivitis, superficial erosions of lips. Intraoral mucosal surfaces spared.	
Treatment	Staphylococcal antibiotics, burn center transfer?	
Prevention	None	
See PEM Guide: Dermatology: Staphylococcal Scaled Skin Syndrome		

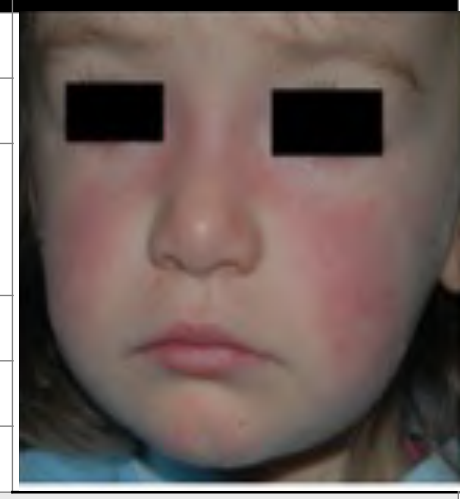
7. ERYTHEMA MULTIFORME MINOR		
Etiology	Hypersensitivity reaction to: Medication (Sulfonamide) Infection (Staph, strep, mycoplasma, HSV)	
Prodrome	Fever, headache, malaises	
Rash	Highly variable, papules, vesicles. Classic: irregular shape, erythematous borders, central clearing (“targetoid’)	
Other	Thought to be on spectrum with Stevens-Johnson syndrome	
Treatment	Withdrawal of offending medication, treatment of associated infection	
Prevention	None	

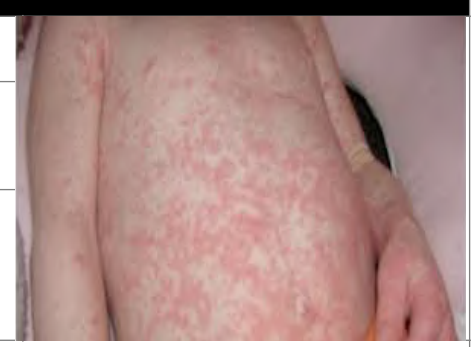
8. STEVENS-JOHNSON SYNDROME (ERYTHEMA MULTIFORME MAJOR)		
Etiology	Medications (ibuprofen, sulfonamides), infections (mycoplasma, HSV)	
Prodrome	Malaise, flu-like symptoms, fever	
Rash	Early: Erythematous macules with purpuric centers, may be targetoid. Late: Vesicles and bullae, skin sloughing (Nikolsky’s sign) Mucosal involvement: Pharynx, eye, genital	
Other	Photophobia, conjunctival itching/burning, rash with burning sensation, paresthesias	
Treatment	Discontinuation of offending agent. Fluids, electrolyte replacement, skin care similar to burn management May require transfer to a burn center	
Prevention	None	
See: PEM Guide: Dermatology: Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis		

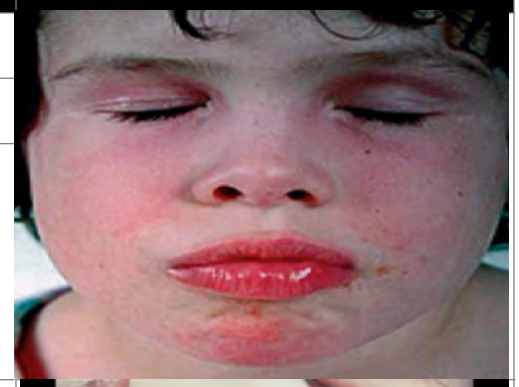
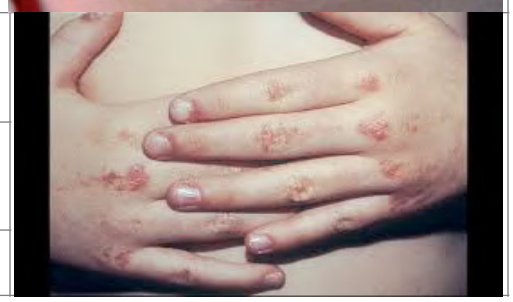
9. ERYSIPELAS		
Etiology	Beta hemolytic Streptococcus	
Prodrome	Fever, lesion pain	
Rash	Erythematous patches on the face, genitals, hands or feet, sharply demarcated from surrounding normal skin (superficial cellulitis)	
Other	Tender to light palpation	
Treatment	Anti-streptococcal antibiotics	
Prevention	None	
See: PEM Guide: Dermatology: Skin and Soft Tissue Infections: Overview		

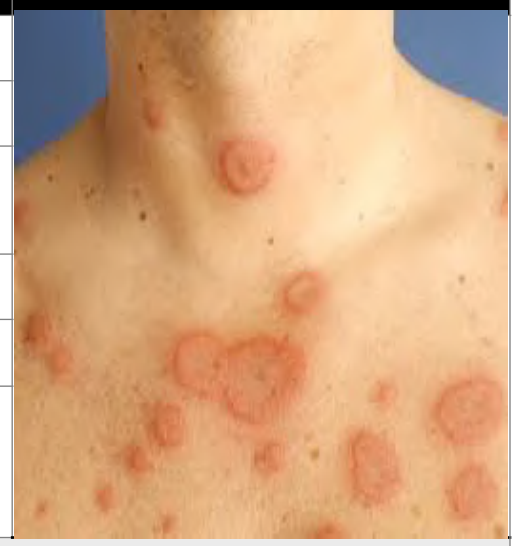
APPENDIX: RHEUMATOLOGIC FEBRILE RASHES

1. KAWASAKI DISEASE		
Etiology	Unknown, epidemics suggest an infectious/immune source leading to systemic vasculitis (primary concern is coronary artery aneurysms)	
Prodrome	Acute febrile illness	
Rash	Variable: Morbilliform, maculopapular, erythroderma, targetoid Early: Erythema/swelling of palms and soles, Late: Desquamation of fingers	
Other	Major criteria: Fever > 5 days AND 4 of 5 1. Conjunctival injection: Bulbar only 2. Oral mucous membrane: Strawberry tongue, fissured/cracked lips 3. Enlarged cervical lymph nodes: Typically, anterior, unilateral 4. Polymorphous rash (see above) 5. Extremity changes (see above)	
Treatment	High-dose aspirin, intravenous immune globulin	
Prevention	None	
See PEM Guide: Rheumatology: Kawasaki Disease		

2. SYSTEMIC LUPUS ERYTHEMATOSUS		
Etiology	Autoimmune, may be medication induced	
Prodrome	Fever, mucositis, arthritis, fatigue, weight loss	
Rash	Face: Malar rash (spares nasolabial fold) Extremities: Discoid, erythematous plaques Chronic: Chill blains, panniculitis, alopecia	
Other	Arthritis, renal, neurologic, hematologic	
Treatment	Immunosuppressants	
Prevention	None	
See PEM Guide: Rheumatology: Systemic Lupus Erythematosus		

3. JUVENILE IDIOPATHIC ARTHRITIS (SYSTEMIC)		
Etiology	Auto-inflammatory disorder	
Prodrome	High, daily, intermittent fever (return to normal), arthralgia, intense pruritis	
Rash	Evanescent, oval, macular, salmon colored lesions of varying sizes (more prominent during fever). May appear with trauma or stroking of the skin (Koebner phenomenon)	
Other	Arthritis, lymphadenopathy, hepatomegaly, splenomegaly, pericarditis	
Treatment	NSAIDs, Interleukin 1,6 inhibitors	
Prevention	None	

4. JUVENILE DERMATOMYOSITIS		
Etiology	Autoimmune myopathy	
Prodrome	Fever, weakness/fatigue	
Rash	Heliotrope rash: Red-purple on upper eyelids with periorbital edema Grottron papules: Erythematous, papulosquamous lesion on dorsal knuckles Grotton sign: Erythematous rash over dorsal knuckles	
Other	Symmetric proximal muscle weakness, interstitial lung, GI disease. Rare myocardial, neurologic	
Treatment	1° Glucocorticoids, methotrexate, 2° Immune globulin, hydroxychloroquine	
Prevention	None	

5. ACUTE RHEUMATIC FEVER		
Etiology	Autoimmune reaction to streptococcus	
Prodrome	Fever, arthralgia	
Rash	Erythema marginatum Subcutaneous nodules (late)	
Other	Arthritis, carditis, chorea	
Treatment	Anti-inflammatories, Treatment of strep infection.	
Prevention	Primary: Treatment of initial streptococcal infection: Penicillin, Amoxicillin within 10 days Secondary: Prophylactic antibiotics	
See: PEM Guide: Rheumatology: Acute Rheumatic Fever		

NECROTIZING ACUTE SOFT TISSUE INFECTION

INTRODUCTION (REBECCA BURTON, M.D. 10/2021)
The vast majority of rashes seen in the pediatric emergency department are benign in nature. However, there are several relatively uncommon rashes can be associated with significant morbidity and mortality and need to be identified and treated expeditiously. This PEM Guide reviews the pathophysiology, clinical presentation, diagnosis and ED management of Necrotizing Acute Soft Tissue Infections (NASTI).

The term Necrotizing Acute Soft Tissue Infections encompasses necrotizing forms of fasciitis and myositis, which are characterized by fulminant soft tissue destruction associated with systemic signs of toxicity and high mortality. Necrotizing fasciitis, which is much more common than necrotizing myositis, is an infection of the deeper tissues that results in progressive destruction of the muscle fascia and overlying subcutaneous fat. The infection tends to spread rapidly along the fascia due to poor blood supply. The incidence of necrotizing fasciitis is estimated at 3.5 cases/100,000 people/year.

Necrotizing myositis is a rarer entity than necrotizing fasciitis. It is thought that this is because ample blood supply to the muscle itself usually prevents infection from spreading from the fascia to the muscle. Necrotizing myositis affects all ages, males and females equally, and usually occurs in otherwise healthy individuals. Risk factors are skin abrasions or other skin injury, blunt trauma, and heavy exercise.

NECROTIZING ACUTE SOFT TISSUE INFECTION: TYPE I
Account for 55-75% of all NASTI
Older patients with significant medical comorbidities. Diabetes mellitus and immunosuppression are important risk factors
Polymicrobial infection
At least one anaerobic species such as *Bacteroides*, *Clostridium*or, *Peptostreptococcus* AND
One or more facultative/anaerobic streptococci (other than group A strep) AND
A member of enterobacteriaceae such as E *coli*, *Enterobacter*, *Klebsiella*, and/or *Proteus*
Less commonly, an obligate aerobe such as *Pseudomonas aeruginosa* is involved.
The anatomic site of involvement can predict what pathogens is involved
Head and neck NASTI tends to involve oral anaerobes
Fournier’s gangrene (external genitalia/perineum) has prominent bacteriaceae involvement
With unusual mechanisms of trauma, unique pathogens may be implicated
Trauma in fresh water suggests *Aeromonas hydrophila* involvement
Trauma in sea water suggests *Vibrio vulnificus* involvement.

NECROTIZING ACUTE SOFT TISSUE INFECTION: TYPE II
Patients are more likely to be young and healthy at baseline
Risk factors: Most involve a breach in the skin barrier or trauma to the soft tissues (i.e. blunt trauma, recent surgery, laceration or abrasion, intravenous drug use, childbirth, chickenpox).
Group A or other beta-hemolytic streptococcal spp. such as Group B *Streptococcus*, Group G *Streptococcus*, or *Streptococcus milleri*, alone or in combination with other species, particularly *Staphylococcus aureus* (mainly MSSA, though CA-MRSA is increasing and may be the cause of some cases of NASTI on its own (case reports.

PATHOPHYSIOLOGY

The pathophysiology of NASTI involves two major mechanisms: bacterial invasion with direct damage to soft tissues via exotoxins, and a super-antigen response. The rapid necrotizing process begins with direct invasion of subcutaneous tissue from external trauma such as a surgical incision, intravenous injection, abscess, insect bite, or ulcer. Less commonly, there is direct spread of bacteria from a perforated viscus such as the colon, rectum, or anus. Rarely, the process develops spontaneously. Risk factors for this include diabetes and underlying malignancy.

In type II infection, it is thought that the group A strep are able to localize to the site of muscle injury via increased myocyte expression of a protein called vimentin, which directly binds the microbe.

Whatever the mechanism of invasion, once bacteria arrive in the soft tissue they proliferate, invade subcutaneous tissue and deep fascia, and release exotoxins that lead to liquefaction necrosis and systemic toxicity, including a super-antigen response that results in shock, tissue ischemia and destruction, and multi-organ system failure.

Finally, the skin involvement seen in NASTI is thought to be secondary to vasculitis and thrombosis of perforating blood vessels. This creates an ischemic tissue environment that promotes bacterial growth, propagating the process and resulting in rapid spread of the infection. Infection can spread as fast as 1 inch per hour. Since thrombosis of large numbers of capillary beds must occur before skin findings develop, early on there may be minimal or even no change in the overlying skin. However, as the disease progresses, widespread gangrene of the skin, subcutaneous fat, fascia, and rarely even skeletal muscle occur.

CLINICAL PRESENTATION

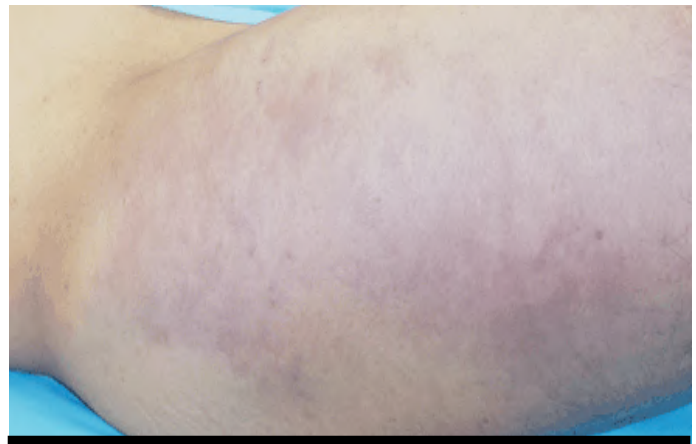
NASTI is typically an acute process, although subacute cases have been reported. Patients are often febrile, ill appearing, tachycardic, and hypotensive. The tachycardia is often out of proportion to the fever. Patients may appear anxious and have diaphoresis, or they may complain of malaise, myalgias, anorexia, and/or diarrhea. Less commonly, patients may be somnolent, confused, or have other change in mental status.

Early dermatologic manifestations are often minimal but patients often report severe tissue or skin pain out of proportion to the clinical exam findings. The skin overlying the involved area may be erythematous, swollen, warm, shiny, and exquisitely tender to palpation. Patients may also have edema at the site of involvement. Often this is subtle early on, but it can be marked, particularly with necrotizing myositis, even to the point of causing compartment syndrome.

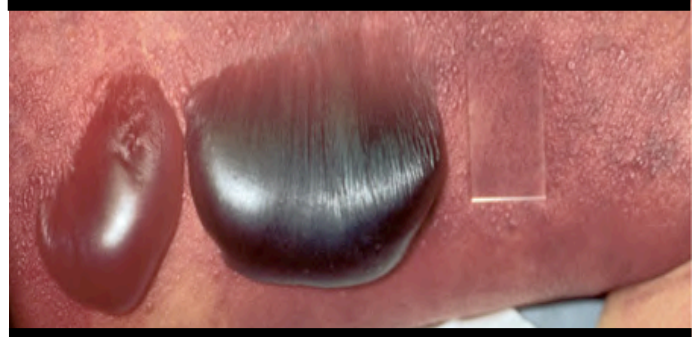
Over several days, this rapidly progresses, with a change in skin color from red-purple to patches of blue-grey. Within 3-5 days of onset, skin breakdown occurs with formation of bullae filled with thick pink or purple fluid, and frank cutaneous gangrene develops. At this point, skin is often insensate due to thrombosis of small blood vessels and destruction of superficial nerves in the subcutaneous tissue. However, anesthesia can precede skin necrosis, and this should be considered an ominous sign.

Subcutaneous gas can be seen in type I infection, particularly in patients with diabetes mellitus. If the infection is of a surgical wound, copious drainage, dusky friable subcutaneous tissue, and pale, devitalized fascia may be seen at the surgical wound site.

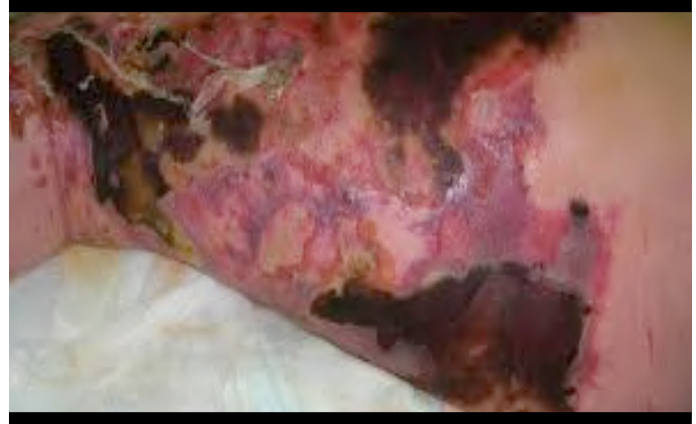
With necrotizing myositis, there is usually exquisite pain and swelling and induration of the involved muscle; once again, the overlying skin usually appears normal, but then becomes erythematous and warm, and then bullae, vesicles, and petechiae can develop; necrotizing myositis is not associated with gas (contrast *Clostridial* myonecrosis).



ERYTHEMA



BULLAE



NECROSIS

DIFFERENTIAL DIAGNOSIS
Cutaneous abscess
Staphylococcal scaled skin
Pyomyositis
Gangrene with secondary super infection
Brown recluse spider bite
Septic arthritis
Warfarin induced skin necrosis
Deep vein thrombosis
Compartment Syndrome

DIAGNOSIS

NASTI is a clinical diagnosis. Labs findings may support the diagnosis and include leukocytosis with a left shift, anemia, thrombocytopenia and a coagulopathy. Elevated CKP, lactate, creatine, and liver transaminases (AST/ALT) may be seen. Myoglobinemia and myoglobinuria can also occur. Blood culture is usually positive in necrotizing myositis, and is positive in type I necrotizing fasciitis in about 20%, and in type II necrotizing fasciitis about 60% of the time.

Imaging may be useful, particularly in determining whether there is muscle involvement and to plan the surgical approach to debridement but should not delay surgical intervention. Plain films may reveal subcutaneous gas but will not show deep fascial gas and is therefore a poor screening tool. More often it just shows soft tissue swelling. CT scanning is more sensitive (80%) and can demonstrate fascial thickening and edema, deep tissue collections, and gas formation. Intravenous contrast provides no additional benefit. MRI has better sensitivity (90% to 100%) but imposes delays to treatment. Ultrasound has not been studied in NASTI.

Biopsy and cultures from the involved tissue are sent from the operating room and show extensive tissue destruction, thrombosed blood vessels, abundant bacteria spreading along fascial planes, and infiltration of acute inflammatory cell. In necrotizing myositis, you will also see degeneration and necrosis of skeletal muscle fibers, infiltration of granulocytes, and numerous bacteria in the areas of muscle necrosis.

MANAGEMENT

Surgical consultation should be obtained as soon as the diagnosis is entertained to plan for source control through aggressive surgical exploration and debridement of necrotic tissue. Mortality is 100% in patients with NASTI who receive appropriate antibiotics without surgical intervention. Patients should be admitted to the intensive care unit after the operative intervention.

Hemodynamic support including fluid resuscitation and vasopressors is often needed
Parenteral antibiotics should be chosen to include a wide range of possible pathogens. Intravenous immune globulin has not been formally studied in NASTI.
Hyperbaric oxygen may also be a useful as an adjunctive therapy in the future.

ANTIBIOTIC SELECTION*
Vancomycin AND Piperacillin/Tazobactam AND Clindamycin
Alternative to Vancomycin: Linezolid
Alternative to Piperacillin/Tazobactam: Aztreonam AND Metronidazole
*NYU Pediatric Antimicrobial Stewardship Guidelines (2021)

SKIN AND SOFT TISSUE INFECTIONS: OVERVIEW

INTRODUCTION (ERIC WEINBERG, M.D. 10/2021)
Skin and soft tissue infections (SSTI) are among the most common bacterial infections encountered in young children. They represent an interruption in the skins natural host defenses. The majority are the result of infection with Staphylococcal aureus and Streptococcal pyogenes. Infections range from superficial infections of the epidermis (impetigo, erysipelas), to deeper infections of the dermis (cellulitis). Pyogenic collections can occur (cutaneous abscess) as well as infections of accessory cutaneous structures (folliculitis). The extension of the local infection to adjacent structures (lymphangitis, adenitis, osteomyelitis) and systemic infections (bacteremia, meningitis, sepsis) can also occur. While most infections are self-limited and respond well to appropriate skin care and antibiotics, some may be life or limb threatening infections. See: PEM Guides: Dermatology: Necrotizing Acute Soft Tissue Infections (NASTI), Steven-Johnsons Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) , Staphylococcal Scaled Skin Syndrome (SSSS), Toxic Shock Syndrome (TSS).

ANTIBIOTIC SELECTION
The management of skin and soft tissue infection requires an understanding of the bacteriology of each entity and in particular the role of methicillin resistant Staph aureus (MRSA). MRSA appears to be more virulent due to the presence of the Panton-Valentine leukocidin (PVL) gene which increase likelihood of tissue necrosis resulting in purulent infections as well as adjacent and systemic infections. Treatment decisions must take into account the severity of the infection and the presence/potential for adjacent and systemic spread.

MRSA RISK FACTORS
Recent admission
Antibiotic use within 90 days
Previous MRSA infection: Patient or household member
High MRSA prevalence communities

The Infectious Disease Society of America recommends that skin infection with purulent drainage be considered to be due to staph aureus and skin infections without evidence of purulence be considered due to Strep species. Source control (e.g. abscess drainage) is an important component of therapy. See Appendix: Antibiotic Selection, Appendix: Specific skin and soft tissue infections.

Topical treatment with mupirocin can be considered for focal, mild infections. Oral antibiotic choices for MRSA include: Trimethoprim/Sulfamethoxazole (Bactrim), Clindamycin and Doxycycline. Bactrim should not be used in infants less than 2 months. Group A Strep isolates are commonly resistant. There may be inducible resistance to clindamycin. This is when MRSA sensitive to clindamycin in vitro develops resistance during treatment.

Alternatives to clindamycin should be considered if there is greater than 10% community resistance. Doxycycline is typically considered in those older than seven years of age. However, Doxycycline is chemically different from Tetracycline and recent evidence suggests Doxycycline is not associated with dental staining in children (Pöyhönen, J Antimicrob Chemother. 2017, PubMed ID: 29091225). Linezolid use should be limited (high cost, potential toxicity). If the patient fails to respond to oral therapy or meets indications for intravenous therapy with Vancomycin.

Whenever possible, cultures should be sent of purulent fluid to determine the prevalence of MRSA in your community and it's antibiotic resistance pattern in order to guide empiric treatment as well as management of patients who fail to respond to initial therapy.

ANTIBIOTIC COVERAGE: OUTPATIENT			
	Clindamycin	Bactrim	Keflex
MSSA	YES	YES	YES
MRSA	YES[1]	YES	NO
Strep	YES	NO	YES
1. Not recommended if local Clindamycin resistance > 10-15%			

INFECTIOUS DISEASE CONSULTATION	
< 3 months	Burn or traumatic wound
Immunocompromised	Infections involving water sources
Indwelling device	Orbital cellulitis
Febrile, neutropenic	Post-operative Infection
Necrotizing fasciitis	Staphylococcal scaled skin

DISPOSITION

The majority of skin and soft tissue infections may be managed with outpatient antibiotics. However, patients with signs of systemic toxicity (fever, hypoperfusion, altered mental status), rapidly spreading infections and deep tissue infections (e.g. necrotizing fasciitis) should be admitted for intravenous antibiotics.

ANTIBIOTIC SELECTION: SKIN AND SOFT TISSUE INFECTIONS

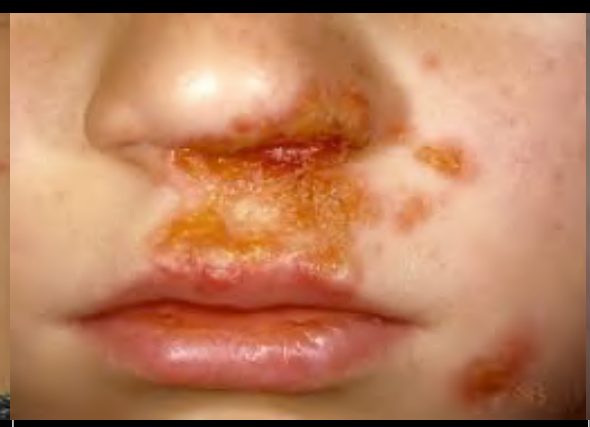
ANTIBIOTIC SELECTION*		
Impetigo	Oral	Mupirocin ointment TID Extensive or bullous: Cephalexin or TMP/SMX Ultraorthodox (>2mo): Retapamulin ointment
	Duration	5-7 days
Non-purulent Cellulitis	Oral	Cephalexin
		MRSA risk: Add TMP/SMX
		Cephalexin Failure: Add TMP/SMX
	IV	Cephazolin
	IV Alternative	MRSA risk: Vancomycin (or Linezolid)
		Cephazolin Failure: Vancomycin (or Linezolid)
	Duration	5-7 days
Purulent Cellulitis or Abscess Cellulitis	All	Source Control: Incision and Drainage PRN
	Oral	TMP/SMX
		Alternative: Linezolid or Doxycycline
	IV	Vancomycin
		Alternative: Linezolid
	Duration	7 days if adequate drainage
Traumatic (including post-operative)	Oral	Amoxicillin/Clavulanate
		MRSA Risk: TMP/SMX
	IV	Vancomycin AND Piperacillin/Tazobactam
		Alterative to Vancomycin: TMP/SMX
		Alternative to Zosyn: Levofloxacin[1]
	Duration	5-7 days
Dog/Cat Bite	Vaccine?	Tetanus, Rabies
	Oral	Amoxicillin/Clavulanate (Augmentin)
	IV	Ampicillin/Sulbactam (Unasyn)
	Duration	Treatment: 10-14 days, Prophylaxis: 3-5 days
	Alternative	Clindamycin AND TMP/SMX
Human Bite	Vaccine?	Tetanus
	Oral	Amoxicillin/Clavulanate (Augmentin)
	IV	Ampicillin/Sulbactam (Unasyn)
		Alternative: Clindamycin AND Levofloxacin[1]
	Duration	Treatment: 10-14 days, Prophylaxis: 3-5 days
1. Levofloxacin: Use limited to specific circumstances in pediatrics due to arthropathy		
*NYU PEDIATRIC ANTIBIOTIC STEWARDSHIP PROGRAM 2021		

SPECIFIC SKIN AND SOFT TISSUE INFECTIONS

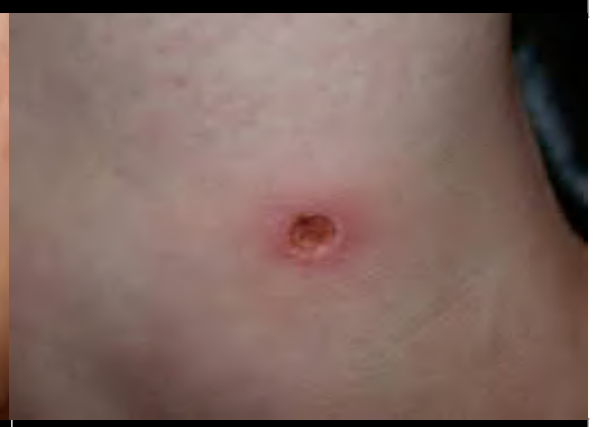
CLASSIFICATION OF SKIN AND SOFT TISSUE INFECTIONS		
Mild	Moderate	Severe
Impetigo (Strep)	Furunculosis	Cutaneous abscess
Bullous Impetigo (Staph)	Carbuncles	Lymphangitis
Folliculitis	Cellulitis	Staph Scalded Skin
	Erysipelas	Necrotizing Fasciitis

IMPETIGO/ECTHYMA	
Bacteriology	Staph aureus (most common) and/or Strep pyogenes. Transferred to skin from URI (strep) or nasal colonization (staph).
Diagnosis	Impetigo: Discrete lesions, exposed areas of body (face, extremities) Non-bullous lesions (Strep): Papules → Vesicles → Pustules → Honey crusted lesions. Bullous lesions (Staph): MSSA > MRSA with exfoliate toxin Appearance of an unroofed bullae similar to a burn
	Ecthyma: Deeply ulcerated single lesion. Strep > Staph. Differential diagnosis includes brown recluse spider bite, cutaneous anthrax
Treatment	The nature of the lesion (bullous vs non-bullous, purulent vs non-purulent) may be used to guide therapy. For isolated lesions, Mupirocin topical TID is effective. For extensive or bullous lesions or MRSA risk, oral antibiotics are recommended (Cephalexin or Bactrim).

STAPH IMPETIGO



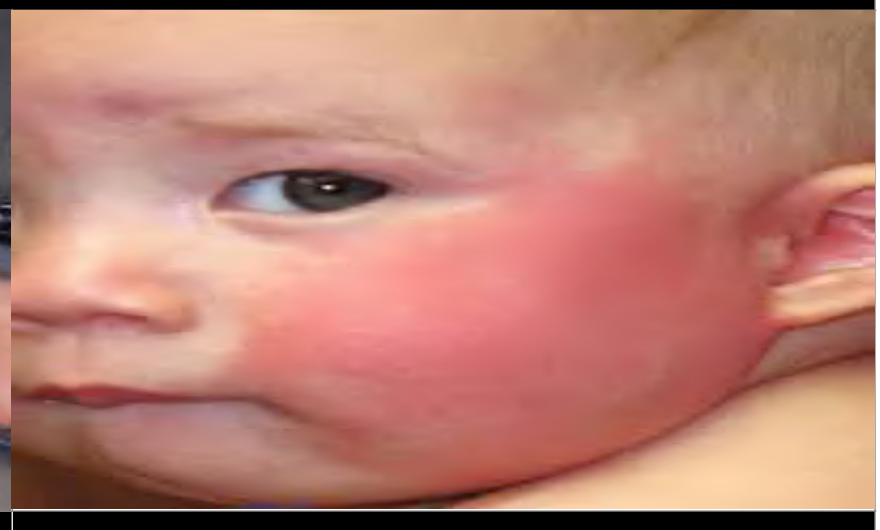
STREP IMPETIGO



ECTHYMA

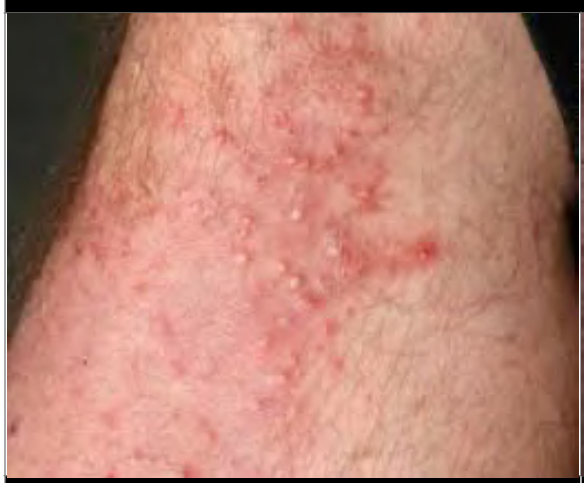
CELLULITIS/ERYSIPELAS	
Bacteriology	Strep pyogenes, rare Group B Strep or Staph
Diagnosis	Erysipelas: Involves the upper dermis and is typically associated with streptococcal infection. Cellulitis involves the deeper dermis and subcutaneous fat. To distinguish, erysipelas has raised fiery red lesions with a clear line of demarcation between abnormal and normal tissue, and occurs more often in infants and young children. Erysipelas also tends to be markedly tender to palpation.
	Cellulitis: Organisms enter through a break in skin and cause infection. Rapidly spreading areas of edema (induration), erythema, and warmth, +/- lymphadenitis. Vesicles, bullae, and petechiae/ecchymosis may develop. May have systemic manifestations (fever, chills, ↑ WBC).
	Ancillary Testing: Blood culture is of low yield (positive 5%) Skin culture is of low yield unless purulent drainage is present.
Treatment	Oral therapy can be used in nontoxic patients with slowly progressing disease and with reliable follow up.
	Indications for hospital admission and parenteral antibiotics include rapidly progressing disease, systemic signs (fever, shock), unreliable follow-up, or unable to tolerate the medication (e.g. persistent vomiting). Elevation of affected area will encourage drainage and healing.
Non-purulent Cellulitis	Outpatient: Cephalexin, Follow-up 2d to evaluate response to treatment. Inpatient: Cephazolin Add Vancomycin (or Linezolid) for suspected MRSA, treatment failure
Purulent Cellulitis +/- Abscess	Source Control: Abscess incision and drainage Outpatient: TMP/SMX, Alternatives: Linezolid, Doxycycline Inpatient: Vancomycin, Alternative: Linezolid

CELLULITIS/LYMPHANGITIS

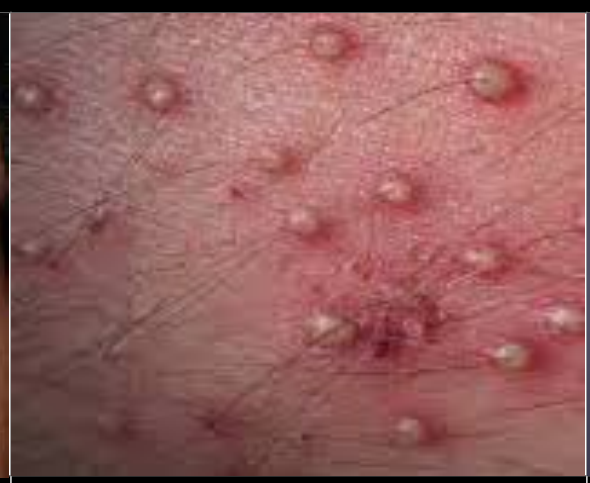


ERYSIPELAS

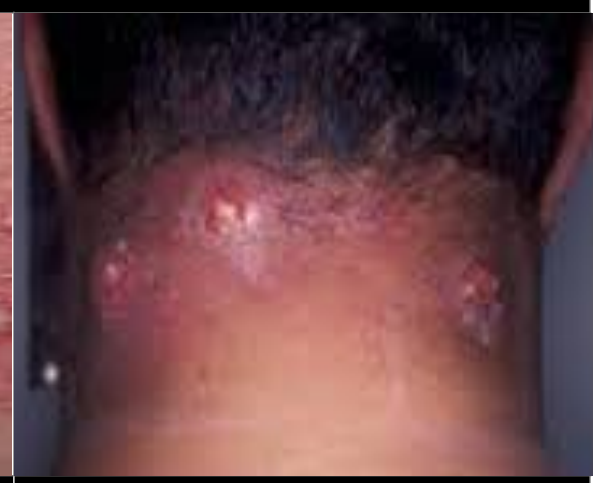
FOLLICULITIS/FURUNCULOSIS/CARBUNCLES	
Bacteriology	Staph aureus, Strep species
Diagnosis	Folliculitis is a localized area of superficial inflammation +/- epidermal pus surrounding the hair follicle.
	Furuncles (“boils”) represent a similar infection with penetration through the dermis into the subcutaneous tissue with small abscess formation. Can occur anywhere on hairy skin.
	Carbuncle is a coalesced mass of infected follicles, usually on the back of the neck/ trunk.
Treatment	Folliculitis and small furuncles respond to warm compresses to promote drainage. Larger furuncles and all carbuncles require incision and drainage. No antibiotics necessary unless signs of concomitant cellulitis.



FOLLICULITIS



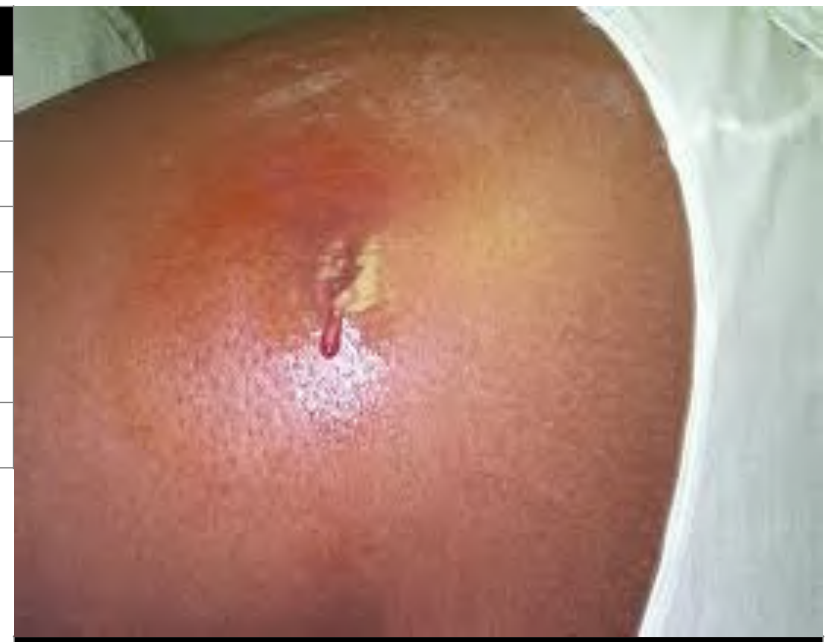
FURUNCULOSIS



CARBUNCLES

SIMPLE CUTANEOUS ABSCESS	
Bacteriology	Often polymicrobial, regional skin flora. Likely Staph aureus
Diagnosis	Painful tender fluctuant red nodules, often with central pustule and surrounded by a rim of induration.
	Wound culture unhelpful unless multiple lesions, cutaneous gangrene, immunocompromised, surrounding cellulitis, or severe systemic symptoms (e.g. high fever). However, wound culture is indicated if there is a high prevalence of MRSA in the community.
	Ultrasound may be used to reveal location and dimensions of the fluid cavity prior to incision and drainage. It may also distinguish between abscess and cellulitis
Treatment	Incision and drainage (source control) A sizeable incision should be made to allow exploration of the abscess cavity and to break up loculations.
	Traditionally, wounds have been then packed and dressed. There is recent evidence that packing may not be necessary and that primary closure may be considered thought these options are not the standard of care at present.
	Patients should return for follow-up to assess the wound progression and dressing change in 48 hours.
	Oral antibiotics are typically not necessary unless specific indications are present (See table below) though these is recent evidence in adults for their routine use.
See: PEM Guide: Dermatology: Abscess Incision and Drainage	

ANTIBIOTIC AFTER ABSCESS DRAINAGE
Large abscesses > 5 cm
Ill appearing (fever, chills,)
Abscess site difficult to drain (genital, face)
Co-morbid conditions, immunocompromised
Rapidly progressive disease
Failure of simple drainage



DRAINING CUTANEOUS ABSCESS

STAPHYLOCOCCAL SCALDED SKIN SYNDROME

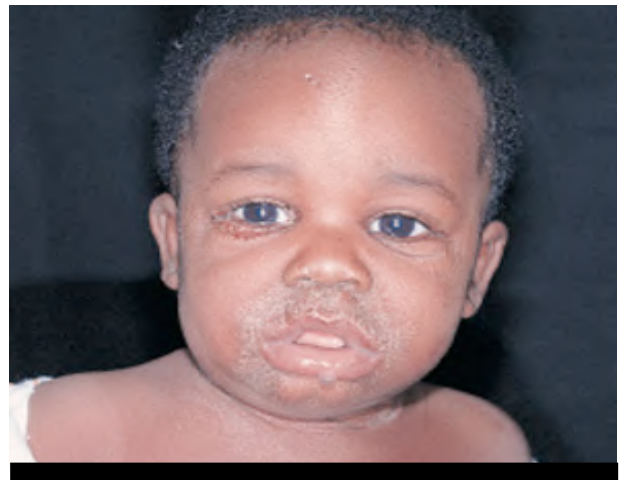
INTRODUCTION (REBECCA BURTON, M.D. 10/2021)
The vast majority of rashes seen in the pediatric emergency department are benign in nature. However, there are several relatively uncommon rashes that can be associated with significant morbidity and mortality and thus require rapid identification and management. This PEM Guide will review the pathophysiology, clinical presentation, diagnosis and ED management of Staphylococcal Scalded Skin Syndrome (SSSS).

Staphylococcal Scalded Skin Syndrome is a toxin-mediated exfoliative dermatitis caused by toxin producing strains of Staphylococcus aureus. Toxin-mediated *staphylococcal* syndromes actually comprise a group of blistering skin diseases, which range in severity from localized bullous impetigo to SSSS. Historically, SSSS was denoted “Fourth Disease.”

Epidemiological studies have shown that approximately 3-6% of the pediatric population are carriers of the toxin-producing strains of Staph aureus that can cause SSSS. Despite this, the incidence of SSSS is very low, with an overall incidence of approximately 0.5 cases/million patients/year. SSSS is a disease of infants and young children, with 60% of cases occurring in children < 2 years, and 90% in children < 6 years of age. It is rare in adults, and those adults affected usually are Immunocompromised (e.g. HIV) or have other significant medical comorbidities (e.g. malignancy). Cases occur more frequently during the autumn and winter months, and outbreaks have been reported, especially in newborn nurseries and day care centers.

PATHOPHYSIOLOGY
SSSS is a toxin-mediated exfoliative dermatitis that occurs in the setting of infection by one of a small subset of Staph aureus strains. In SSSS, the origin of infection may be obvious, such as a purulent conjunctivitis or acute otitis media, or it may be subtle or even occult, such as subclinical infection of the nasopharynx, umbilicus, or circumcision site. Whatever the infective locus, SSSS arises when certain strains of Staph aureus produce Exfoliative Toxins A & B (ET-A (80%), ET-B (20%)), which are subsequently released into the circulation and travel to the skin. There, they target keratinocytes in the stratum granulosum layer of the epidermis lysing these cell-to-cell connections. Disruption of these intercellular bridges in turn leads to the formation of fragile, tense bullae, which easily rupture and slough off.

CLINICAL PRESENTATION
The infant or child initially has a clinical or subclinical Staph infection, most commonly of the conjunctiva, middle ear, nasopharynx, umbilicus, or circumcision site, though other origins of infection have been reported. Then the patient usually experiences sudden-onset of fever, malaise, irritability, and possibly skin tenderness.


EYE/MOUTH CRUSTING

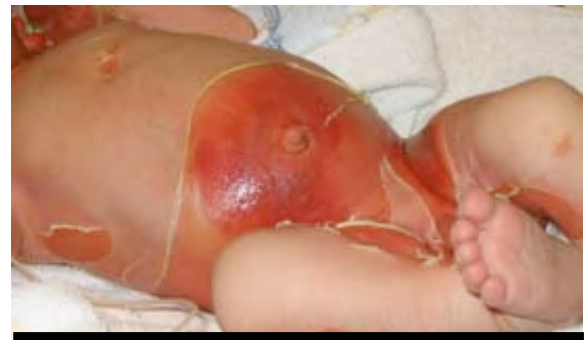
The dermatologic findings in SSSS can generally be divided into an early prodrome and then three distinct phases (initial, exfoliative, and desquamative)

EARLY PRODROME: The rash of SSSS initially appears as prominent crusting around the eyes and mouth. The patient may also have exam findings of pharyngitis, conjunctivitis, or superficial erosions of lips. However, the intraoral mucosal surfaces are spared.

INITIAL PHASE: The initial phase of the rash is characterized by an exquisitely tender, diffuse erythroderma (rarely localized instead of diffuse). The rash may feel sandpapery to the touch. It is usually most prominent in the perioral, periorbital, and flexural regions (neck, axillae, groin, and antecubital and popliteal fossae).

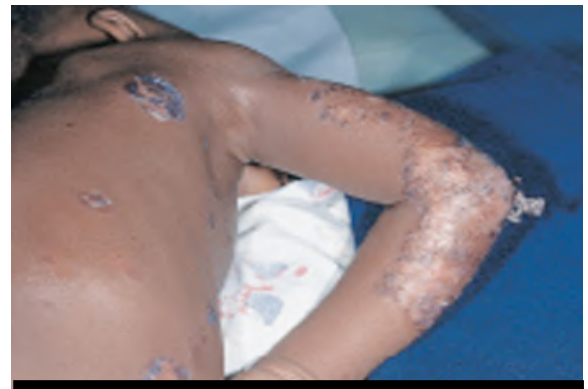
ERYTHRODERMA

EXFOLIATIVE PHASE: During the 2nd, exfoliative phase of SSSS, which occurs over the next 24 to 48 hours, the skin wrinkles and flaccid bullae develop, followed by exfoliation in sheets revealing a moist, red, shiny scalded-looking surface. The bullae rupture very easily, and are often not intact at the time of examination. The borders of exfoliating skin are rolled like wet tissue paper. Nikolsky sign is positive (slight lateral pressure applied to normal-looking adjacent skin results in separation of the upper epidermis results in blistering). This exfoliation can spread to cover the entire body surface area in the most severe form of SSSS.



EXFOLIATION

DESQUAMATIVE PHASE: In the 3rd, desquamative phase of the disease, the exfoliated areas desiccate, followed by flaky desquamation lasting 3 to 5 days.Hair and nails may also be shed during this recovery phase. Healing of the rash occurs without scarring over 7 to 14 days.



DESQUAMATION

DIAGNOSIS

There are currently no specific laboratory findings for the diagnosis of SSSS. An assay for ETA and ETB titers may be available shortly, Cultures are often sent from blood, urine, nasopharynx, umbilicus, abnormal skin, and any other suspected focus of infection. Intact bullae are sterile (toxin-mediated).

Skin biopsy is sometimes useful to confirm the diagnosis and to distinguish SSSS from Stevens-Johnsons Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). SSSS is characterized by intra-epidermal split in the region of the lower stratum granulosum layer with minimal keratinocyte necrosis. In contrast, SJS/TEN is characterized by full-thickness epidermal necrosis and a cleavage plane just above the basement membrane.

DIFFERENTIAL DIAGNOSIS	
Stevens-Johnson Syndrome (Unlike SSSS, involves the mucous membranes)	
Toxic Epidermal Necrolysis (Unlike SSSS, involves the mucous membranes)	
Group A Streptococcal skin infections	
Neonatal TORCH infections: HSV, VZV, Syphilis, Listeriosis	
Congenital genodermatoses	
	Epidermolysis bullosa (especially EB simplex)
	Epidermolytic hyperkeratosis
	Aplasia cutis congenita

MANAGEMENT

Management of SSSS in the entails prompt administration of anti-staphylococcal antibiotics and supportive measures.

Intravenous antibiotics should include a penicillinase-resistant penicillin such as Nafcillin or Oxacillin. If there are concerns for methicillin resistant Staph aureus (MRSA) or if there is a poor initial response to treatment, Vancomycin and/or clindamycin are preferred. Clindamycin resistance has been increasing in the Northeast U.S. though Clindamycin may also be beneficial by reducing toxin production.

ANTIBIOTIC SELECTION	
First Line	Oxacillin AND Linezolid
Alternative	Vancomycin AND Clindamycin
NYU Pediatric Antibiotic Stewardship (2021)	

Supportive care entails fluid and electrolyte repletion as losses may be considerable due to disruption of the skin barrier. Skin care with emollients can improve barrier function. Steroids are not indicated. The patient should be admitted to the intensive care unit, and may require admission to a burn center.

STEVENS-JOHNSON & TOXIC EPIDERMAL NECROLYSIS

INTRODUCTION (REBECCA BURTON, M.D. 10/2021)
The vast majority of rashes seen in the pediatric emergency department are benign in nature. However, there are several relatively uncommon rashes that can be associated with significant morbidity and mortality and thus require rapid identification and management. This PEM Guide will review the pathophysiology, clinical presentation, diagnosis and ED management of Stevens-Johnson Syndrome (SJS) (AKA erythema multiforme major) & Toxic Epidermal Necrolysis (TEN).

SJS and TEN are severe immunologic reactions that are characterized by fever and mucocutaneous lesions followed by necrosis and sloughing of the epidermis. Previously, it was unclear if these were separate or related conditions. Currently, it is thought that SJS and TEN exist on a spectrum. They are most commonly triggered by certain medications, though other triggers exist. Erythema multiforme minor is characterized by papular, acrally-distributed, target lesions with or without mild mucosal involvement. Erythema multiforme minor is typically infectious in origin. In contrast, SJS and TEN are commonly medication related and are initially macular.

SJS/TEN SPECTRUM		
	SEVERITY	SKIN SLOUGHING
SJS	Less severe	< 10% of total BSA
SJS/TEN	Overlap syndrome	10-30% of total BSA
TEN	Most severe	> 30% of total BSA

RISK FACTORS: SJS AND TEN	
Concomitant infection	Important risk factor for SJS in children Pathogens: mycoplasma pneumoniae and herpes viruses.
Genetic factors	Specific HLA types (1,502, 3,101), being a “slow acetylator,” and IL-4 receptor gene polymorphisms.
Immunodeficiency	Especially in adults, includes HIV, malignancy.
Physical factors	Exposure to radiation or UV exposure Increased risk is observed in patients with lupus.

PATHOPHYSIOLOGY
The pathophysiology of SJS/TEN is very poorly understood. The diseases represent an idiosyncratic inflammatory skin reaction that is triggered by specific medications or less commonly other things. At a histologic level, there is epidermal cleavage just above the basement membrane, resulting in first vesicles and bullae and then later skin sloughing and denudation. This process may involve a cytotoxic protein called granulysin, which is secreted by cytotoxic T calls and Natural Killer cells, though the stimulus to do this is unknown. Other studies suggest a role for drug metabolites, both via direct toxicity and immunologic mechanisms. Other proteins and cytokines, such as perforin, TNF-alpha, and granzyme B, may be involved.

TRIGGERS	
MEDICATIONS	Most frequent of an extensive list
Antibiotics	Sulfa drugs #1, Trimethoprim/Sulfamethoxazole (Bactrim)
Antiepileptics	Phenobarbital, valproate, carbamazepine, lamotrigine
Analgesics	Acetaminophen, combination of ibuprofen and azithromycin
INFECTIONS	More common in pediatrics, triggers SJS, not TEN
	Mycoplasma pneumoniae (most common)
	Herpes viruses, EBV, HBV
OTHER	Less common triggers
	Vaccines
	Systemic disease
	Chemical exposure, including herbal medications
	Some foods.

CLINICAL PRESENTATION

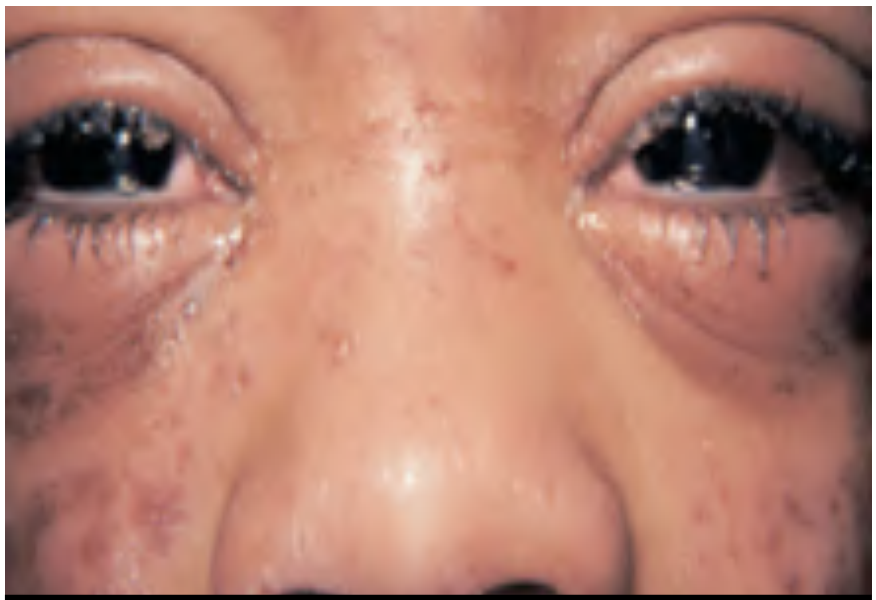
Trigger exposure occurs 1-3 weeks (average 14 days) prior to the onset of symptoms Prodrome includes systemic symptoms such as malaise, flu-like symptoms and fevers (higher in TEN than SJS). Skin tenderness may or may not occur but is more likely in TEN, where skin tenderness is out of proportion to physical findings. Photophobia, conjunctival itching and burning occur 1-3 days later and then mucocutaneous lesions develop.

DERMATOLOGIC MANIFESTATIONS

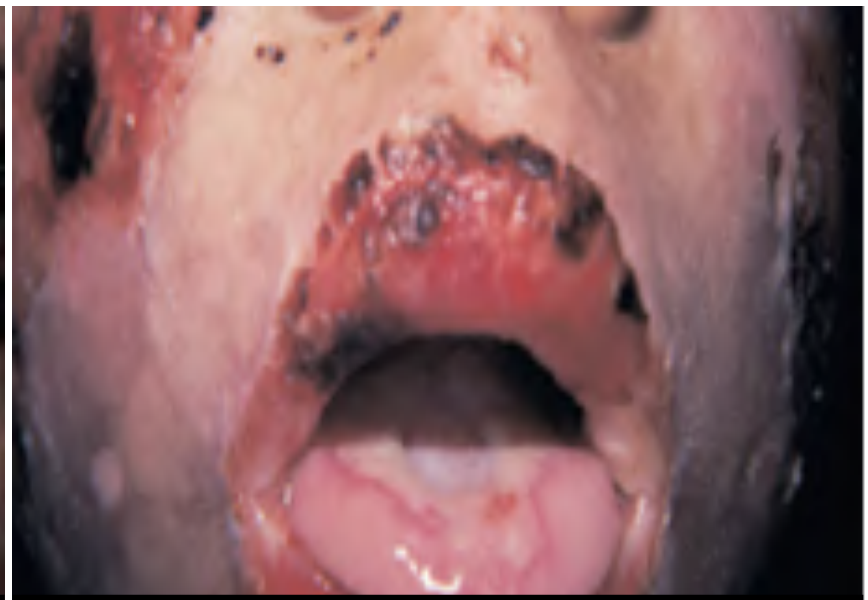
Initially, the skin lesions begin as ill-defined erythematous macules with purpuric centers, though 50% of TEN cases begin with diffuse erythroderma. In SJS, the lesions may be targetoid (similar to erythema multiforme minor), while in TEN the targets are more atypical and less well demarcated lesions are usually symmetrically distributed, and typically start at the face and thorax, then spread to other parts of the body. Palms, soles, and scalp are often spared.

The rash may be associated with a burning sensation or other paresthesias. Skin pain is often out of proportion to exam findings, particularly in TEN. The rash may be associated with facial edema or have prominent central facial involvement. Mucous membrane involvement is common. 92-100% of SJS and nearly 100% of TEN cases have mucous membrane involvement. Mucous membrane involvement usually begins 1-2 days after the onset of rash. Frequently at 2 or more sites, most commonly the oropharynx, ocular, and genital regions (i.e. the painful crusts and erosions in the oral mucosa demonstrated above)

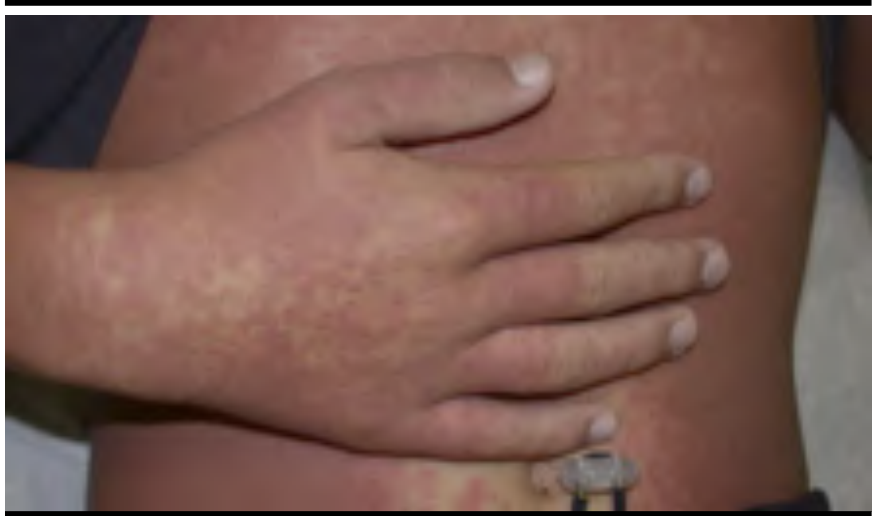
Vesicles and bullae then form due to full-thickness epidermal detachment just above the basement membrane. A positive Nikolsky sign may be present (lateral pressure applied to an uninvolved area results in new blister formation). Within days vesicles and bullae rupture, and skin sloughs off. Re-epithelialization begins after several days, and usually takes approximately 2-3 weeks. Total time course from onset to recovery (barring complications) is about 2-4 weeks



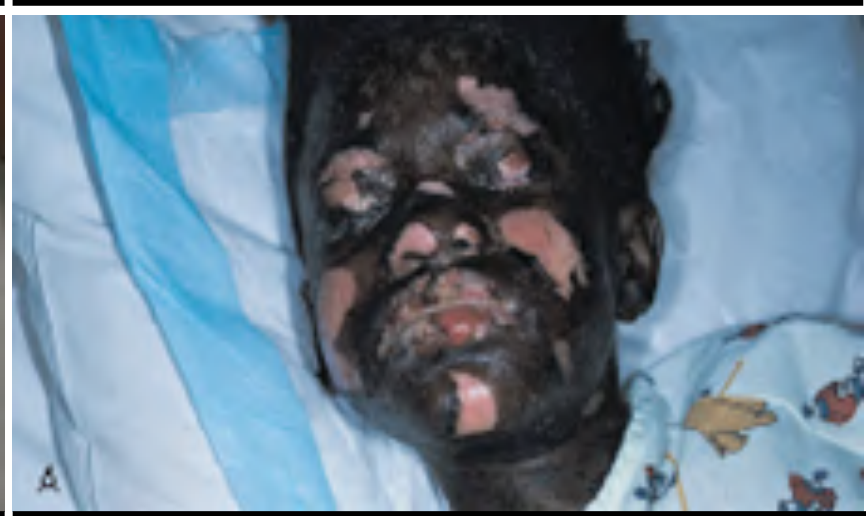
MACULES



MUCOUS MEMBRANES



ERYTHRODERMA



SLOUGHING/NECROSIS

DIFFERENTIAL DIAGNOSIS
Erythema multiforme minor
Staphylococcal scaled skin syndrome
Gangrene with secondary super infection
AGEP: Acute Generalized Exanthematous Pustulosis)
Drug eruptions
Photo-toxic eruptions
Warfarin induced skin necrosis
Toxic Shock Syndrome: Staphylococcal, Streptococcal
Paraneoplastic pemphigus
Kawasaki disease

DIAGNOSTIC EVALUATION

The diagnosis of SJS and TEM is made on clinical grounds. Laboratory results are nonspecific and may include, anemia, leukopenia with neutropenia and elevated liver transaminases. Granulysin, a cytotoxic, lipid-binding protein that induces cell apoptosis, is found in high concentrations in blister fluid from patients with SJS and TEN. Significantly elevated serum granulysin levels are present in patients with SJS/TEN though this test is not readily available.

Mycoplasma titers may be positive and cultures should be sent for Staph aureus to distinguish between Staph scalded skin syndrome. Skin biopsy reveals complete epidermal detachment above the basement membrane as well as full-thickness keratinocyte necrosis

MANAGEMENT

The most critical aspects of management of SJS/TEN in the ED are prompt removal of any potential triggers and supportive measures, including hemodynamic support with appropriate intravenous resuscitation, electrolyte repletion, and wound care. Ophthalmology should be consulted if there is ocular involvement. Patients are typically admitted to the intensive care unit or if severe, to a burn center.

Studies of intravenous immune globulin suggest a benefit if given at high doses, particularly in adults, but possibly also in children. There is limited evidence supporting plasmapheresis or cyclosporine. There is some evidence for the use of tumor necrosis factor inhibitors such as Etanercept (Enbrel). There is no evidence to support the use of corticosteroids. They may actually increase morbidity and mortality.

TOXIC SHOCK SYNDROME

INTRODUCTION (REBECCA BURTON, M.D. 8/2013)
The majority of rashes seen in the pediatric emergency department are benign in nature. However, there are several relatively uncommon rashes that can be associated with significant morbidity and mortality and thus require rapid identification and management. This PEM Guide will review the pathophysiology, clinical presentation, diagnosis and emergency department management of toxic shock syndrome.

Toxic Shock Syndrome is a toxin-mediated, severe, life-threatening syndrome characterized by diffuse erythroderma, high fever, profound hypotension, mucous membrane hyperemia, pharyngitis, diarrhea, and constitutional symptoms. It can progress rapidly to multisystem dysfunction with severe electrolyte disturbances, renal failure, shock, and death.

The term Toxic shock syndrome encompasses two different syndromes: Staphylococcal toxic shock syndrome and Streptococcal toxic shock syndrome. The syndromes are similar except that Streptococcal toxic shock syndrome usually develops in association with a severe soft tissue infection and requires surgical intervention. The pathophysiology, clinical presentation, diagnosis, and management differ enough that we will focus on each syndrome separately.

STAPHYLOCOCCAL TOXIC SHOCK SYNDROME

INTRODUCTION
Staphylococcal toxic shock syndrome, which is the classic form, was originally described in the 1970s and often associated with tampon use. Staphylococcal toxic shock syndrome is caused by strains of Staphylococcus aureus that produce specific exotoxins and enterotoxins. Historically, cases were caused by Methicillin Sensitive Staphylococcal aureus, but cases due to Methicillin Resistant Staphylococcal aureus are increasing. There is an estimated 30-50% Staphylococcal aureus carriage rate (skin, mucous membranes) in healthy children and adults.

Young women, particularly Caucasians, appear to be at highest risk, though some studies suggest that incidence in males and females is equal if menstrual, postpartum, and mastitis related cases are excluded. Other risk factors include vaginal foreign bodies (tampons, contraceptive sponges, diaphragms); postpartum or post-surgical wound infection; other infections (i.e. sinusitis, osteomyelitis, septic arthritis, respiratory infections (especially. influenza, varicella zoster), enterocolitis; and any condition that poses a potential breach of the skin or mucosa, burns, cutaneous and subcutaneous lesions (especially those involving the extremities, perianal, axillary regions), tattooing, and piercing. The current incidence is estimated at 0.8-3.4 cases/100,000 people/year.

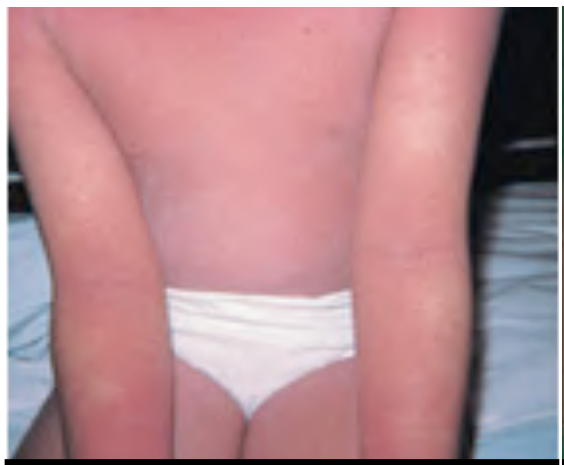
PATHOPHYSIOLOGY
Staphylococcal toxic shock syndrome is a toxin-mediated process. Toxins include: Toxic Shock Syndrome Toxin 1 (TSST-1) (90-100% menstrual related cases, 40-60% non-menstrual related cases) and enterotoxin B (seen in 38-62% non-menstrual toxic shock syndrome.) Other toxins include enterotoxin A, (a cofactor of TSST-1), and enterotoxins C, D, E, and H. These toxins act as super antigens, bypassing normal antigen processing mechanisms and stimulating a massive and rapid T cell activation and proliferation (up to 20% of T-cells activated). T cell activation generates a massive cytokine release, including IL1, IL2, TNF-alpha, TNF-beta, and IFN-gamma. These cytokines are responsible for the signs and symptoms characteristic of toxic shock syndrome, including distributive shock, high fevers and skeletal muscle proteolysis. Inhibition of neutrophils results in lesions with minimal purulence. The toxins may also cause direct damage.

CLINICAL PRESENTATION

In Staphylococcal toxic shock syndrome, the signs and symptoms generally develop rapidly. Systemic symptoms are common, particularly fever, dizziness and fatigue. Vasodilation and third spacing result in decreased systemic vascular resistance and hypotension (distributive shock). Hypotension is also due to depressed cardiac function and decreased total body water due to vomiting, diarrhea, fever, and poor intake. The patient may also have chills, malaise, myalgias, weakness, headache (the most common complaint), fatigue, sore throat, abdominal pain, vomiting, profuse watery diarrhea, non-pitting edema. Less commonly, the patient presents with acute encephalopathy.

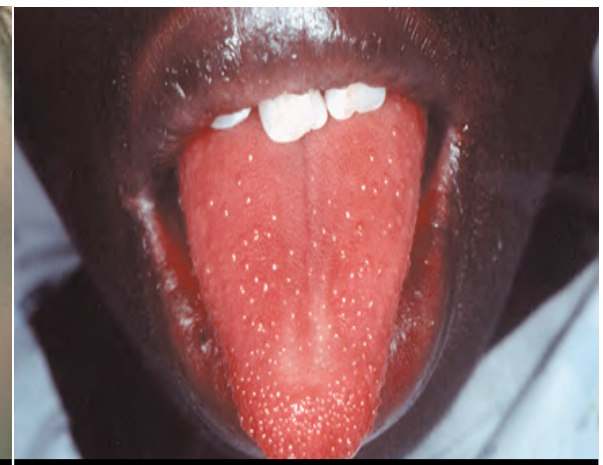
DERMATOLOGIC FINDINGS

The patient usually presents with a diffuse, blanching, non-painful erythroderma of the skin and mucous membranes. This has been described as a “painless sunburn”. The rash can also appear as a more patchy, erythematous, macular rash. This rash can involve the palms and soles and may be subtle or fleeting. If the patient is post-operative, it can be more prominent at the surgical wound site. Patients may also have a strawberry tongue and pharyngitis (50-75%), and may have conjunctival hyperemia or hemorrhage.



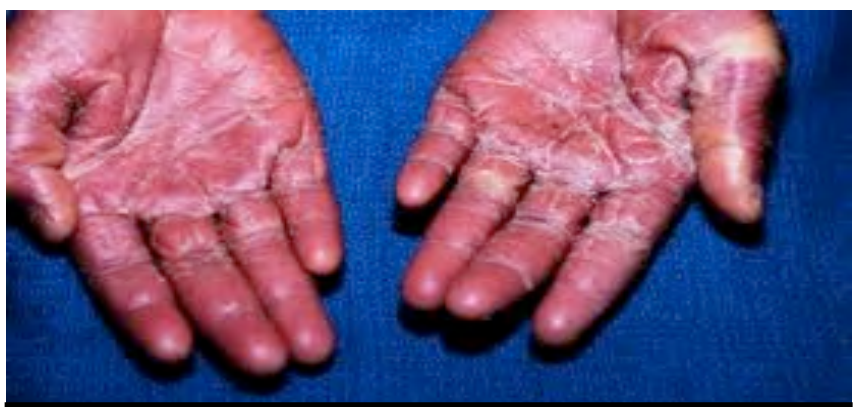
ERYTHRODERMA

CONJUNCTIVAL HEMORRHAGE

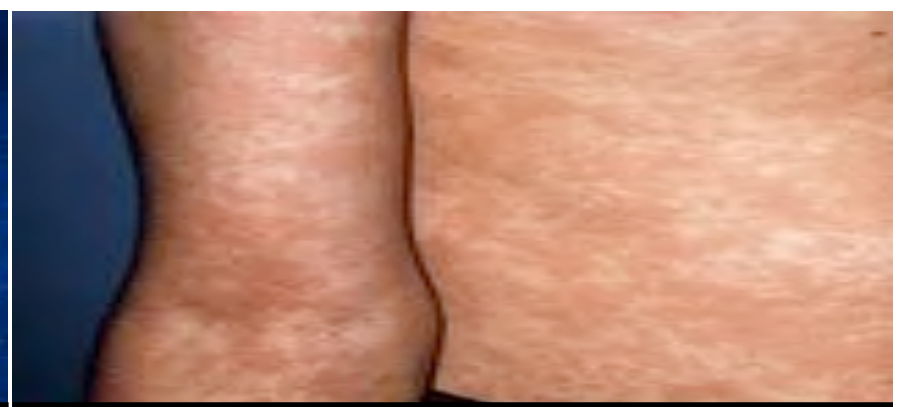


GLOSSITIS

At 1-2 weeks, patients develop a pruritic maculopapular rash. As these resolves, there is development of a fine, generalized desquamation of the skin, with peeling over the soles, fingers, toes, and palms. Desquamation typically occurs from 6 to 14 days after the onset of illness. Most severely ill patients experience loss of hair and nails 2 to 3 months later.



DESQUAMATION



MACULOPAPULAR RASH

DIAGNOSIS

The diagnosis of toxic shock syndrome is made on a clinical basis (see CDC criteria below). Laboratory findings include: leukocytosis with left shift, thrombocytopenia, evidence of disseminated intravascular coagulation and organ failure. Cultures are not required to make the diagnosis. Blood cultures are positive in approximately 5% of cases (In contrast to 60% for Streptococcal toxic shock syndrome). Cultures of wound or mucous membrane may be useful, but are not required.

DIFFERENTIAL DIAGNOSIS
Streptococcal toxic shock syndrome
Meningococcemia
Rocky Mountain Spotted Fever
Kawasaki
Nosocomial sepsis
Others: Leptospirosis, Dengue hemorrhagic fever, Typhoid fever, Measles

CDC DEFINITION: STAPHYLOCOCCAL TOXIC-SHOCK SYNDROME	
CLINICAL CRITERIA: An illness with the following clinical manifestations	
Fever	Temperature ≥ 102.0°F (≥ 38.9°C)
Rash	Diffuse macular erythroderma
Desquamation	1-2 weeks after onset of rash
Hypotension	Systolic BP ≤ 90 mm Hg (adults), < fifth percentile by age < 16 years
MULTISYSTEM INVOLVEMENT: Three or more of the following organ systems	
GI	Vomiting or diarrhea at onset of illness
Muscular	Severe myalgia or creatine phosphokinase level at least twice the upper limit of normal
Mucous membrane	Vaginal, oropharyngeal, or conjunctival hyperemia
Renal	Blood urea nitrogen or creatinine at least twice the upper limit of normal urinary sediment with pyuria (greater than or equal to 5 leukocytes per high-power field) in the absence of urinary tract infection
Hepatic	Total bilirubin, alanine aminotransferase enzyme, or asparate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory
Hematologic	Platelets less than 100,000/mm3
CNS	Disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent
LABORATORY CRITERIA: Negative results on the following tests, if obtained	
Cultures	Blood/CSF Culture, may be positive for *Staphylococcus aureus*)
Serologies	Negative for Rocky Mountain spotted fever, leptospirosis, measles
CASE CLASSIFICATION	
Probable	Meets laboratory criteria AND Four of the five clinical criteria described above are present
Confirmed	Meets laboratory criteria AND All five of the clinical criteria described above are present, including desquamation, unless the patient dies before desquamation occurs

WEB LINK: NON-STREPTOCCOCAL TOXIC SHOCK (CDC CRITERIA 2011)

MANAGEMENT

The primary therapy for toxic shock syndrome is aggressive hemodynamic support and source control. The goal is to maintain perfusion in the setting of intractable hypotension and capillary leak. Fluid resuscitation up to 10-20 liters per day and vasopressors are often required.

Any foreign material in the vagina or nose should be removed immediately. Any identified focus of infection should be drained. If the patient is post-operative, surgery should be consulted to explore the surgical wound.

It is currently unclear whether parenteral antibiotics alter the acute course of disease in Staphylococcal toxic shock syndrome. Nevertheless, most authorities recommend parenteral antibiotics to eradicate toxin-producing Staphylococcus and to decrease the recurrence rate. The typical regimen of antibiotics includes Vancomycin for coverage of Methicillin Sensitive Staphylococcal aureus and Methicillin Resistant Staphylococcal aureus. Clindamycin is added to reduce toxin production. Linezolid is substituted if the patient is clindamycin allergic or resistant.

Studies on the use of intravenous immune globulin, particularly early during cases of severe toxic shock syndrome, are promising. However, the evidence is stronger for the use of intravenous immune globulin in Streptococcal toxic shock syndrome than Staphylococcal toxic shock syndrome. There is currently no evidence to support the use of high dose corticosteroids.

STREPTOCOCCAL TOXIC SHOCK SYNDROME

INTRODUCTION

Streptococcal toxic shock syndrome, (toxic shock “like” syndrome) is associated with invasive and less commonly local Group A Streptococcus infection. It is generally more serious than Staphylococcal toxic shock syndrome, with case fatality rate estimated at 30-60% (2-6% in Staphylococcal toxic shock syndrome). Cases of the syndrome caused by Streptococcus suis and Groups B, C, and G Streptococcus species. have been reported as well. Invasive group a streptococcus disease includes: bacteremia, pneumonia, necrotizing fasciitis, and gangrenous myositis. When group A Streptococcus causes invasive disease, it is estimated to cause toxic shock syndrome in approximately 1/3 of cases. The incidence of Streptococcal toxic shock syndrome is thought to be increasing in the U.S. and Europe, with recent estimates of incidence of 3.5-cases/100,000 people/year. Streptococcal toxic shock syndrome can affect all ages, males and females equally, and victims are typically healthy.

Risk factors include diabetes mellitus; alcoholism; trauma, which can be minor, or any injury that causes a hematoma, bruising, or muscle strain; surgical procedures, including liposuction, vaginal delivery, c-section, hysterectomy, bunionectomy, bone pinning, or breast reconstruction; viral infection (especially influenza, varicella, which is a major risk factor for children); and possibly use of NSAIDs (mechanism unclear).

PATHOPHYSIOLOGY

Streptococcal toxic shock syndrome occurs in the setting of Group A Streptococcus infection, which is most commonly a deep-seated soft tissue infection like necrotizing fasciitis or myonecrosis that arises within 24-72 hours at the exact site of a minor trauma such as a bruise, strained muscle or sprained ankle. There is often no visible break in the skin. Less commonly, it arises in the setting of other forms of invasive group A streptococcus disease (i.e. bacteremia, pneumonia). Other potential portals of entry include the skin, vagina, and pharynx. However, the etiology is unknown in up to 45% of cases.

The pathophysiology of Streptococcal toxic shock syndrome is like that of Staphylococcal toxic shock syndrome, though the exotoxins involved differ. The toxins involved include Streptococcal pyogenic exotoxins A, B, and C and Streptococcal super antigen mitogenic factor. As in Staphylococcal toxic shock syndrome, the toxins act as super-antigens but are more effective than those in Staphylococcal toxic shock syndrome.

The toxins also induce cytotoxicity, pyrogenicity, and enhance lethal effects of endotoxin M protein, a protein with anti-phagocytic properties, on the Streptococcal bacterial cell membrane. There are over 80 different Group A streptococcus serotypes identified by their M protein; M-types 1, 3, 12, 28, & 89 are the types most frequently found in Streptococcal toxic shock syndrome.

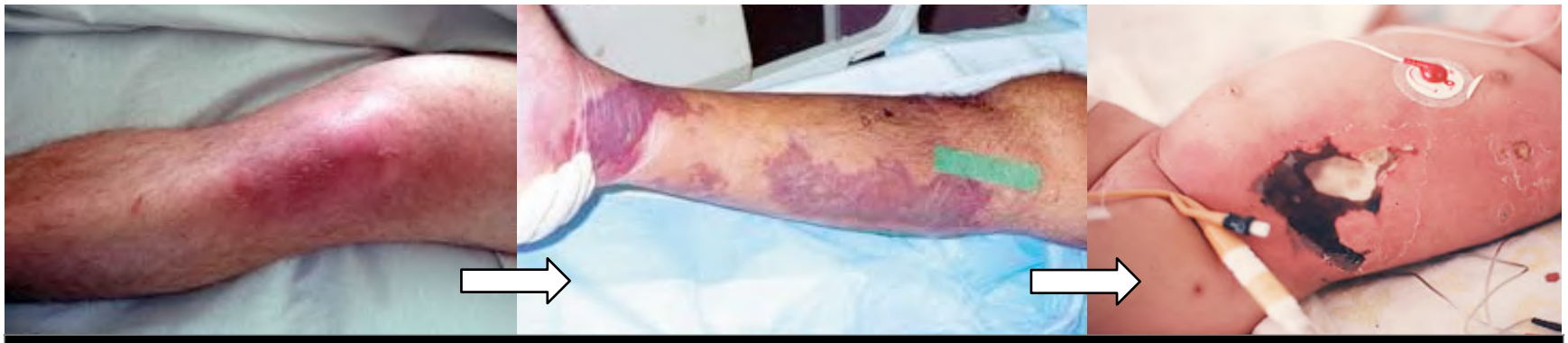
CLINICAL PRESENTATION

As with Staphylococcal toxic shock syndrome, the signs and symptoms in Streptococcal toxic shock syndrome tend to develop rapidly. Patients may present with acute onset of severe pain, usually involving the soft tissue of an extremity, but occasionally mimicking peritonitis, pelvic inflammatory disease, pneumonia, acute myocardial infarction, pericarditis, or cholecystitis. The pain is usually out of proportion to physical findings, which may be absent. Systemic symptoms are common, and patients often present with a flu-like syndrome of fever, chills, nausea, vomiting, myalgia, and/or diarrhea. Mental status changes are seen in approximately 50% at presentation. Patients are often normotensive initially, but rapidly progress to fluid-refractory hypotensive shock within 4-6 hours of presentation.

DERMATOLOGIC FINDINGS

Unlike Staphylococcal toxic shock syndrome, a diffuse erythroderma or scarlatiniform rash is uncommon in Streptococcal toxic shock syndrome. If the patient has pain at the soft tissue of an extremity, it will often appear normal at presentation. Later, swelling and erythema can develop at that site. The degree of swelling may result in a compartment syndrome.

The initial erythema and swelling are often followed by ecchymosis and sloughing of skin. Violaceous (bluish) vesicles or bullae may be seen and are a sign of necrotizing fasciitis or myositis. Necrotizing fasciitis or myositis occur in approximately 70-80% of patients. See PEM Guide: Dermatology: Necrotizing Acute Soft Tissue Infections.



RASH PROGRESSION: STREPTOCOCCAL TOXIC SHOCK SYNDROME (NOTE: DIFFERENT PATIENTS)

DIFFERENTIAL DIAGNOSIS
Staphylococcal Toxic Shock Syndrome
Meningococcemia
Rock mountain spotted fever
Kawasaki
Nosocomial sepsis
Others: Leptospirosis, dengue hemorrhagic fever, typhoid fever, measles

DIAGNOSIS

The diagnosis of Streptococcal toxic shock syndrome is made based on clinical and culture findings. Laboratory results are nonspecific and may include, anemia, leukocytosis with a left shift, elevated creatine phosphokinase (CPK), coagulopathy and other findings of organ failure. Blood cultures are positive in 60% of cases, and tissue cultures from the locus of infection are positive greater than 90% of the time. In the appropriate clinical setting, culture of pericardial, pleural, or joint space fluid may be performed.

DIAGNOSIS: GROUP A STREPTOCOCCAL TOXIC SHOCK SYNDROME	
Isolation of GAS from a normally sterile site	Blood, cerebrospinal, pleural, or peritoneal fluid, tissue biopsy, or surgical wound culture. Surgical specimens of infected fascia or muscle, showing gram-positive cocci in pairs and chains provides an early and definitive diagnosis.
PLUS	
Hypotension	Adults: Systolic BP ≤ 90 mmHg Children: < 5th percentile for age in children (< 16 years)
PLUS TWO OR MORE OF THE FOLLOWING	
Renal	Adults: Creatinine ≥ 2 mg/dl Children: Creatine ≥ 2-times the upper limit of normal for age Pre-existing renal disease: ≥ 2-times baseline
Coagulopathy	Thrombocytopenia, disseminated intravascular coagulation
Hepatic	≥ 2-times upper limit of normal for age of transaminases or bilirubin Pre-existing liver disease: ≥ 2-times elevation over baseline
Pulmonary	Adult respiratory distress syndrome
Skin	Erythematous macular rash, may desquamate Soft tissue necrosis: Necrotizing fasciitis/myositis, gangrene

WEB LINK: STREPTOCOCCAL TOXIC SHOCK SYNDROME (CDC CRITERIA 2010)

PROBABLE GAS TOXIC SHOCK SYNDROME: Occurs when group A streptococcus is isolated from a non-sterile site (e.g. throat, vagina, skin lesion) but the other criteria are fulfilled and if no other etiology is identified.

MANAGEMENT

The primary goal is to maintain perfusion in the setting of intractable hypotension and capillary leak (distributive shock). Hemodynamic support includes aggressive fluid resuscitation. Patients often requiring up to 10-20 liters per day. Vasopressors are often required and should be initiated early.

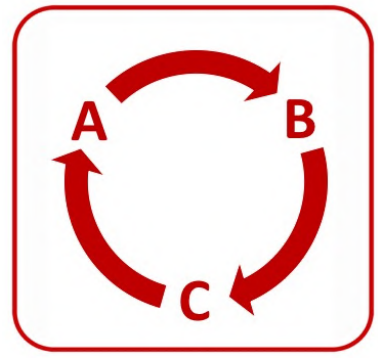
ANTIBIOTIC SELECTION: (A OR B) + C
Broad spectrum; Coverage of Gram (+), Gram (-) and anaerobes
A. A Beta lactam/Beta lactamase Combination: Zosyn or Unasyn or Timentin OR
B. A Carbapenem: Meropenem or Imipenem or Ertapenem AND
C. Clindamycin (inhibition of toxin production)

Parenteral antibiotics should be initiated as soon as possible. Studies have demonstrated a high morbidity and up to 85% mortality if patients are treated with Penicillin alone even though group a Streptococcus is almost universally sensitive in vitro. The hypothesis is that Penicillin fails if large numbers of organisms are present.

Surgery should be consulted early for prompt surgical exploration, debridement, and sometimes fasciotomy and amputation. Tissue cultures can also be sent from the operating room for definitive diagnosis.

There is growing evidence to support the use of intravenous immune globulin in Streptococcal toxic shock syndrome (though more in adults than children). There are case reports of benefit of hyperbaric oxygen therapy, but currently no randomized clinical trials. Animal studies have demonstrated improved outcomes with anti-tumor necrosis factor antibodies.

ENDOCRINE & METABOLIC



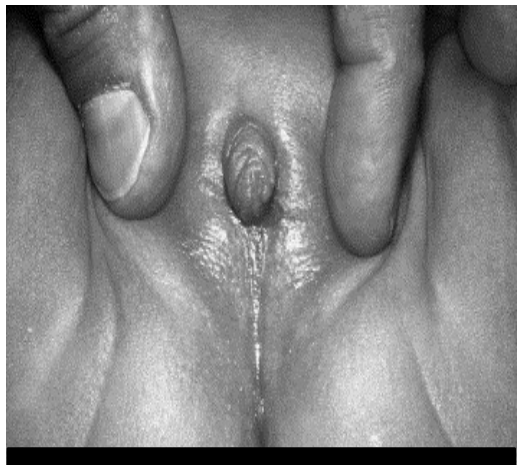
CONGENITAL ADRENAL HYPERPLASIA

INTRODUCTION (MICHAEL MOJICA, MD, 4/2020)
Congenital adrenal hyperplasia (CAH) is a type of adrenal insufficiency. CAH is a group of autosomal recessive, inherited disorders of adrenal steroid hormone synthesis. The most commonly form of CAH is due to deficiency of the enzyme 21 hydroxylase (95%) limiting the conversion of 17-hydroxyprogesterone (17OHP) to 11-deoxycortisol and the and conversion of progesterone to deoxycorticosterone.

CAH results in glucocorticoid (cortisol) and mineralocorticoid (aldosterone) deficiency. Glucocorticoid deficiency causes shock and hypoglycemia. Aldosterone deficiency causes renal loses of water (dehydration) and sodium (hyponatremia) and a decrease in renal excretion of potassium (hyperkalemia). The decrease production of adrenal steroids → ↑ corticocotropin releasing hormone (CRH: Hypothalamus) → ↑ secretion of adrenocorticotropin hormone (ACTH: Pituitary) → adrenal simulation. Shunting to alternate synthesis pathways results → ↑ male androgenic steroids.

ADRENAL INSUFFICIENCY
PRIMARY: ADRENAL CAUSES
Congenital Adrenal Hyperplasia: Multiple enzyme deficiencies
Infection: TB, meningococcal sepsis
Autoimmune disease (Addison's)
Adrenal hemorrhage
SECONDARY: HYPOTHALAMIC-PITUITARY CAUSES
Steroid use with suppression of ACTH secretion
Congenital hypopituitarism
CNS: Tumor, structural abnormality, surgery, radiation therapy

PRESENTATION
There is great variety in the phenotypic presentation of this disorder. Classic CAH includes both salt-wasting and simple virilization without salt-wasting. Two-thirds of patients present with acute-salt wasting crisis at 1-2 weeks of life. The other one-third present during childhood with simple virilization without salt wasting. This manifests in newborn females as atypical genitalia (clitoromegaly, common urethral-vaginal orifice (urogenital sinus)) and in males 2-4 years of age with precocious puberty. Non-classic disease in adults may present as infertility, oligomenorrhea and hirsutism.



VIRILIZATION CLITOROMEGALY

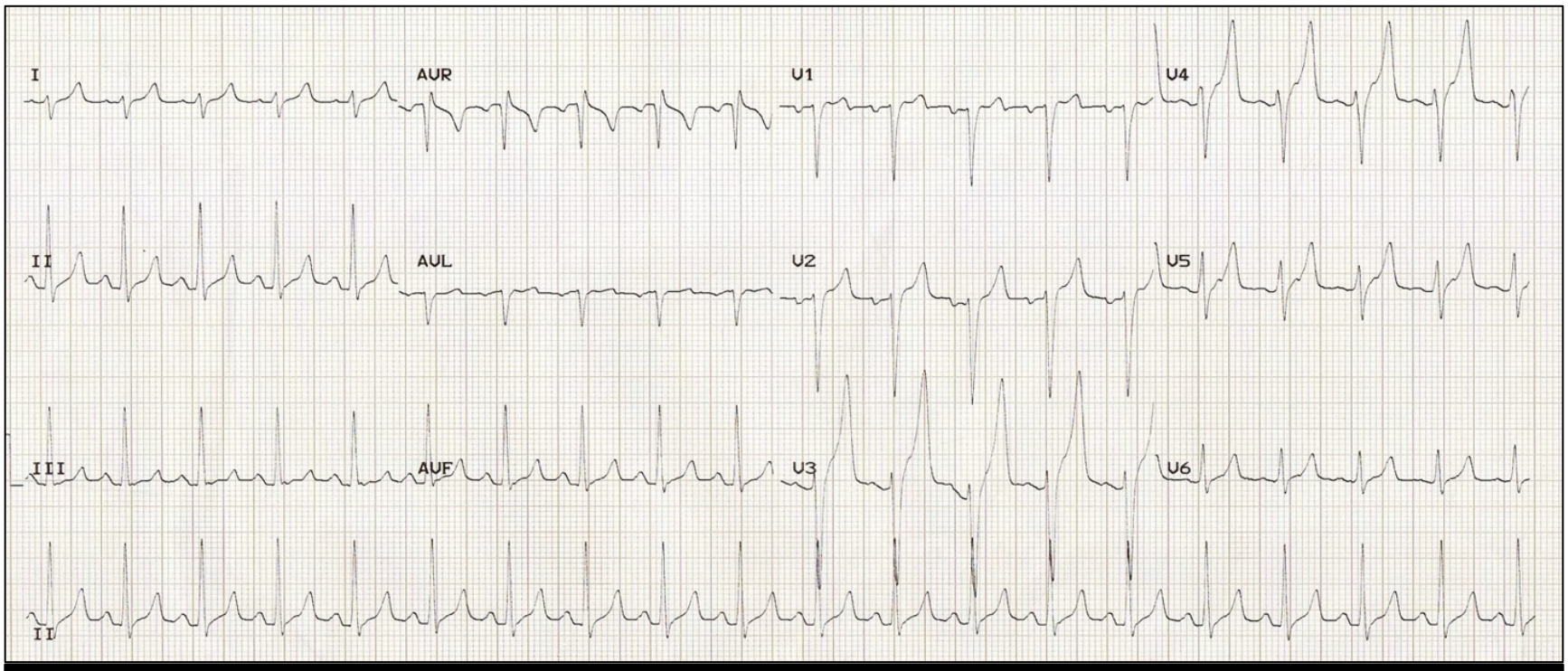
DIAGNOSIS
Diagnosis is based on clinical suspicion. The hallmark of adrenal insufficiency is rapid deterioration when stressed. Minor illness, such as an upper respiratory tract infection, can result in an increased need for glucocorticoids and mineralocorticoids. All newborns in the US are screened for 21-hydroxylase deficiency. Non-classic CAH is not screened for an may present in later childhood or adulthood.

HISTORY: Nonspecific Symptoms may include: malaise, weakness, nausea, vomiting, poor feeding and abdominal pain.

EXAM: Examination findings include hypotension, signs of poor perfusion, altered mental status, hyperpigmentation (due to ↑ ACTH) and signs of virilization (atypical genitalia in females newborns (due ↑ androgenization). In children, precocious puberty, rapid growth and short stature due to premature termination of growth may be seen.

LABORATORY TESTING: Serum electrolytes demonstrate both mineralocorticoid deficiency (hyponatremia, hyperkalemia) and glucocorticoid deficiency (metabolic acidosis, hypoglycemia). Definitive laboratory testing for 21 hydroxylase deficiency includes an elevated 17 hydroxyprogesterone (the substrate to 12 hydroxylase). Additional testing may be necessary to diagnose CAH not due to 21 hydroxylase deficiency (serum 11-deoxycortisol, 17-hydroxypregnenolone, androstenedione, dehydroepiandrosterone (DHEA), and cortisol)

IMAGING: Changes in the adrenal gland can be identified on abdominal ultrasound.



EKG FINDINGS: PEAKED T WAVES DUE TO HYPERKALEMIA

CONGENITAL ADRENAL HYPERPLASIA: DIAGNOSIS	
Adrenal Insufficiency	Shock: Hypotension, signs of poor perfusion
Exam: Skin	Hyperpigmentation due to increased ACTH
Exam: Genitalia	Atypical genitalia: Clitoromegaly in females due to the increased production of androgens by alternative pathways
Labs: Electrolytes	Glucocorticoid deficiency: Hypoglycemia, Metabolic Acidosis Mineralocorticoid deficiency: Hyponatremia, Hyperkalemia
Labs: Definitive Diagnosis	Accumulation of precursor hormones to 21-hydroxylase: 17-hydroxyprogesterone

MANAGEMENT

Treatment of CAH depends on the type and severity of disease. The primary goal of management is to replace deficient adrenal steroids and reduce excess androgen production in order to prevent adrenal crisis and ensure optimal growth and reproductive function. Anti-androgen therapy is beyond the scope of this PEM Guide.

KNOWN CAH: Patients with existing congenital adrenal hyperplasia are frequently managed with Hydrocortisone (glucocorticoid), Fludrocortisone (mineralocorticoid) and salt supplementation. Any significant incurrent illness (infection, trauma, surgery) presents a stress to the body. Stress steroids should be administered in conjunction with pediatric endocrinology consultation. As a general rule, in the well appearing child, oral glucocorticoid dosing should be doubled or tripled for the duration of illness. Parental glucocorticoids may be required. Changes in mineralocorticoid dosing is not required.

SALT-WASTING CRISIS: The management of acute salt-wasting crisis involves the restoration of normal perfusion, correction of electrolyte abnormalities and the administration of glucocorticoids and mineralocorticoids.

CAH ACUTE SALT-WASTING CRISIS: MANAGEMENT	
Shock Metabolic Acidosis	Fluid resuscitation: 20 ml/kg bolus of NS or D5NS until restoration of normal perfusion (avoid hypotonic solutions) Hydrocortisone: 25 mg (< 3yrs), 50 mg (3-12yrs), 100 mg (> 12yrs) (Hydrocortisone has glucocorticoid and mineralocorticoid activity)
Hypoglycemia	Hydrocortisone (see above) Dextrose: 0.5-1.0 gm/kg = D10: 5-10 ml/kg, D25: 2-4 ml/kg, D50: 1-2 ml/kg
Hyponatremia	Hydrocortisone has some mineralocorticoid activity
Hyperkalemia	Typically, no treatment required unless arrhythmia then Calcium and/or Insulin and glucose
Other	Treatment of precipitating factors: e.g. Antibiotics for infection

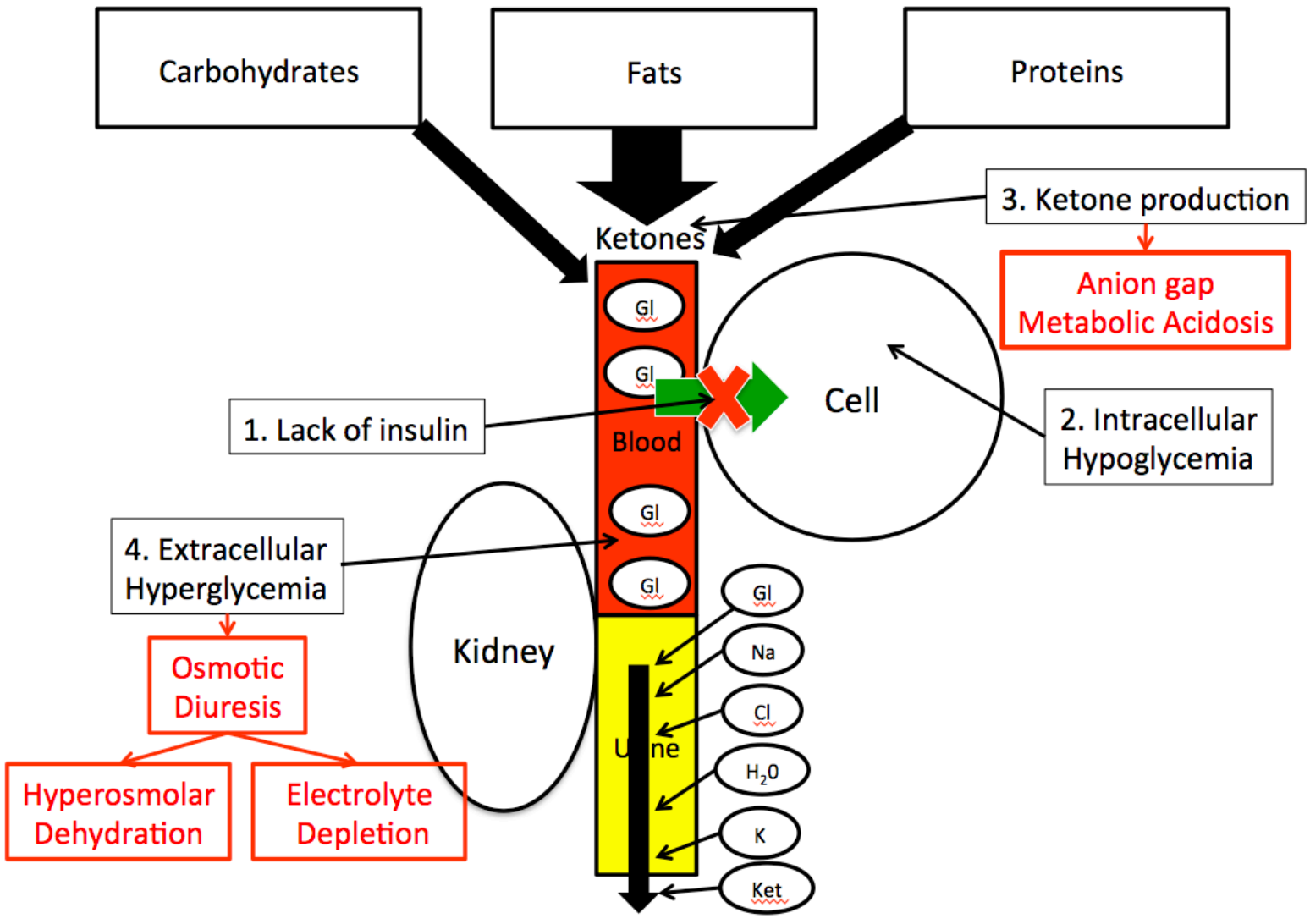
HYPERKALEMIA MANAGEMENT: CALCIUM	
Mechanism	Stabilizes cardiac cell membranes to effect of hyperkalemia
Indications	Prolonged QRS
Timing	Onset: 2-3 minutes, duration 30-60 minutes
Calcium Chloride	Calcium Chloride 10% (1 gram/10ml) (13.6 meq elemental Ca+/10ml) Child: 0.2 ml/kg (20 mg/kg), maximum dose 1 gram (10 ml) Adult:10 ml (1 gram) More rapid dissociation in the blood stream than Calcium Gluconate Risk of tissue necrosis with extravasation use CVL or large PVL
Calcium Gluconate	Calcium Gluconate 10% (1 gram/10ml) (4.6 meg elemental Ca+/10ml) Child: 0.6 ml/kg (60 mg/kg), maximum dose 3 grams (30 ml) Adult: 30 ml (3 grams) Requires hepatic metabolism → Slower onset than Calcium Chloride Avoid in liver failure, shock
Frequency	Repeat Q5 minutes if EKG changes persist or recur
Caveat	Slow infusion on cardiac monitor over 3-5 minutes Do not give in same IV with $NaHCO_3$ ($CaCO_3$ precipitates) Contraindicated in digoxin toxicity

HYPERKALEMIA MANAGEMENT: INSULIN AND GLUCOSE	
Mechanism	Enhances activity of Na-K-ATPase pumps Shifts K+ from extracellular to intracellular space Glucose administered concurrently to avoid hypoglycemia
Indications	EKG changes or K+ > 6.5-7.0 meq/l
Timing	Onset 10-20 minutes, peak at 30-60 minutes, duration 4-6 hours
Adult Dosing	Regular Insulin: 10 units Glucose: 25 grams (50 ml of D50)
Child Dosing	Regular Insulin: 0.1 units/kg (maximum dose 10 units) Glucose: 0.5 grams/kg over 20 minutes D10 = 5 ml/kg (infant), D25 = 2 ml/kg (child), D50 = 1 ml/kg (adult)
Caveats	Provide glucose infusion after bolus to avoid hypoglycemia Monitor bedside glucose closely

DIABETIC KETOACIDOSIS

INTRODUCTION (ETHAN WIENER, M.D. 9/2021)
Diabetic ketoacidosis (DKA) is a metabolic state of insulin deficiency that leads to extracellular hyperglycemia with hyperosmolar dehydration and electrolyte depletion and intracellular hypoglycemia with an anion gap metabolic acidosis. DKA is the number one cause of death in children with diabetes. Mortality is primarily due to cerebral edema (See Appendix: Cerebral Edema). This PEM Guide focuses on the initial management of DKA in the Emergency Department.

PATHOPHYSIOLOGY	
1	Lack of insulin → Intracellular hypoglycemia →
2	→ ↑ Counter regulatory hormones →
3	→ Ketoacid production → Anion gap metabolic acidosis
4	Lack of insulin → Extracellular hyperglycemia → Increased osmolarity → Osmotic diuresis of water, electrolytes → Hyperosmolar dehydration, electrolyte depletion



DKA PRECIPITANTS
New onset insulin dependent diabetes
Insulin pump failure
Noncompliance with insulin regimen
Stressors such as infection, trauma

CLINICAL FINDINGS

The classic presentation of DKA includes the triad of polyuria, polydipsia and weight loss. Virtually all patients are dehydrated. Dehydration manifests as dry mucous membranes, delayed capillary refill, tachycardia, and poor skin turgor. Because the dehydration is hyperosmolar, clinical signs and symptoms may underestimate the degree of dehydration. Other associated symptoms may include: abdominal pain, vomiting and altered mental status. Abnormal (Kussmaul) respirations, are characterized by deep, sighing respirations (hyperpnea) alternating with short, rapid breaths (tachypnea). A careful examination should be undertaken to identify potential sources of infection that may precipitate DKA.

LABORATORY TESTING

LABORATORY TESTING	
EXISTING IDDM	NEW ONSET IDDM
POCT: Glucose	Thyroid peroxidase antibody
POCT: BMP, VBG/Lactate, Hb/HCT	Thyroglobulin antibody
Serum BMP, mg, phosphorus, LFT's	Tissue transglutaminase antibody
Serum Osmolarity	Glutamic acid decarboxylase antibody
Serum Beta hydroxybutyrate	Immunoglobulin A
Hemoglobin AIC	Insulin antibody
Urinalysis, urine beta HCG	C-peptide
TSH, free T4	Insulin
Urine toxicology screen, cultures PRN	
EKG if serum potassium is elevated	

DKA CRITERIA	
Hyperglycemia	> 200 mg/dl (> 11 mmol/L)
Ketosis	Moderate to large Ketonuria OR beta-OH butyrate >3 mmol/L
Acidosis	Venous pH < 7.3 OR HCO_3 < 15 mmol/L

DKA CLASSIFICATION		
	pH	HCO_3
Mild	7.2-7.3	10-14
Moderate	7.1-7.2	5-9
Severe	< 7.1	< 5

ANION-GAP METABOLIC ACIDOSIS: Counter regulatory hormones stimulate gluconeogenesis and glycogenolysis in the liver as well as proteolysis and lipolysis in the peripheral tissues. Lipolysis accounts for much of the acidosis due to the production of the ketoacids, ß-hydroxy butyrate, and acetoacetic acids. Of note, acetone is a ketone body but is not a ketoacid. Hyperglycemia results in a hyperosmolar diuresis that results in a depletion of electrolytes and loss of fluids. The combination of ketoacidosis and hypoperfusion with lactic acidosis can result in a severe anion gap metabolic acidosis. Metabolic acidosis may be partially compensated by hyperventilation.

SODIUM: Serum sodium is generally low. This is due to urinary losses and occasionally due to vomiting. In addition, the serum sodium may be falsely lowered due to the osmolar contribution of hyperglycemia. For every 100 mg/dl increase in glucose over 100 mg/dl, there is an expected decrease of 1.6 meq/L of sodium that is measured. It is important to monitor the sodium to ensure that it is rising as the blood glucose is falling. Failure of serum sodium increasing during therapy for DKA has previously been associated with an increased risk of cerebral edema. Recent evidence suggest that this is not the case (see Appendix: Cerebral Edema).

POTASSIUM: There is a total body loss of potassium secondary to urinary losses (the hyperosmolar, high flow state does not allow reabsorption of K+ in the distal tubule). Serum potassium however may be measured as normal (pseudo-normokalemia) or even high. This occurs due to the shift of potassium out of the cells in response to metabolic acidosis. Cells trade potassium for hydrogen ions to try to maintain normal intracellular pH. As the acidosis resolves, the K+ begins to flow back into the cells and the serum potassium will fall unless potassium supplementation has occurred. Potassium is held if > 5.5 mEq/L on two successive specimens that are not hemolyzed.
Maintain potassium > 3.5 mEq/L

PHOSPHORUS: Hypophosphatemia is also observed in DKA. This occurs because of osmotic diuresis and is exacerbated when insulin is administered as phosphate reenters the cells. The clinical relevance of hypophosphatemia is uncertain. Replacement can contribute to hypocalcemia. Replace phosphorous if less than 1.5 mg/dl and monitor calcium, magnesium and phosphorus.

HYPEROSMOLAR DEHYDRATION: Electrolyte disturbances occur in the setting of an overall hyperosmolar state due to hyperglycemia. The osmolality can be calculated by 2(Na) + glucose/18 + BUN/2.8. Care should be taken to avoid rapid shifts in serum glucose and sodium and therefore serum osmolality. Previously, rapid shifts in serum osmolality was thought to result in rapid fluid shifts across cell membranes, particularly in the central nervous system. More recent evidence suggests that rapid replacement of fluid deficits and hypotonic fluids are not associated with cerebral edema (see Appendix: Cerebral Edema).

ELECTROLYTE INTERPRETATION IN DKA		
Na+	↓	Na^+ decreased 1.6 meq/L for every 100 mg/dl Glucose over 100 mg/dl
K+	Any	Diuresis due to hyperglycemia → Urinary loss of K+ ® Total body K+ depletion. Acidosis shifts K+ out of the cell ® Falsely normal levels
Cl-	↓	Diuresis due to hyperglycemia ® Loss of Cl- in urine
HCO3-	↓	Anion gap metabolic acidosis ® Accumulation of ketones, lactic acid Anion gap = Na – (Cl + HCO3), normal = 8-12 Do not replace HCO3 in DKA
BUN	↑	Dehydration
Cr	↑	Dehydration and analyzer measures ketones as creatinine
Glucose	↑	Insulin deficiency
SOsm	↑	Serum osmolality = 2(Na) + BUN/2.8 + Gl/18, normal = 275-295

ONGOING LABORATORY TESTING		
TESTING	FREQUENCY	CONTINUE UNTIL
Point of care glucose	Q1 hour	Insulin discontinued
Beta-OH butyrate	Q2 hours	< 1 mmol/L
Venous blood gas (pH)	Q2 hours	Normalized
BMP, Mg, Phosphorus	Q4 hours	Normalized

MANAGEMENT

Management of DKA is focused on replacement of fluids and electrolytes and reversing the catabolic state by administration of exogenous insulin. This should be done in consultation with an endocrinologist familiar with diabetic care. A DKA-specific flowsheet will simplify the documentation and management of DKA. Continuously monitor the patient's cardiorespiratory parameters, fluid in and fluid out and neurologic status. Serial laboratory testing should monitor electrolytes and acid-bases status.

MANAGEMENT GOALS	
1	Correct anion gap metabolic acidosis, hyperglycemia: Insulin infusion
2	Correct hyperosmolar dehydration: Intravenous fluids
3	Correct electrolyte abnormalities: e.g. Na^+, Cl^-, K^+ supplementation
4	Avoid treatment complications: Hypoglycemia, hypokalemia, cerebral edema
5	Identify and treat potential precipitants such as infections

FLUIDS AND ELECTROLYTES REPLETION: Initial management involves administration of isotonic fluid (normal saline or lactated ringers) as a bolus at a dose of 10 mL/kg up to 1 liter over one hour. Fluid may be administered faster in cases of hypotension or severe dehydration (shock). The initial bolus administration should not exceed 40 mL/kg as a total fluid dose over the first four hours of treatment. Some experts recommend limiting the initial fluid bolus and delaying insulin administration as the serum glucose may fall significantly with fluid administration alone. After the initial isotonic fluid administration, intravenous fluid solution should contain normal saline with electrolytes added. Typically add 20 mEq/L of potassium chloride per liter in combination with 20 mEq/L of potassium acetate.

The two-bag system is intended to allow flexibility in fluid and electrolyte administration. One bag contains fluid and electrolytes while the other bag contains fluid and electrolytes with glucose added. When serum glucose is below 300 mg/dl dextrose containing fluid and electrolytes can be added to avoid hypoglycemia without having to discontinue insulin therapy before ketoacidosis is corrected.

INSULIN ADMINISTRATION: A continuous infusion of insulin is used to reverse the catabolic state in DKA. An initial bolus of intramuscular or intravenous insulin bolus is not indicated. The aim is to have the serum glucose fall by approximately 50-100 mg/dl per hour with a target blood glucose level in the 150-250 mg/dl range. Insulin should not be administered without potassium. A rise in pH with insulin will shift potassium into the cells resulting in severe serum hypokalemia.

INSULIN
Initiated after the completion of the crystalloid bolus and DKA diagnosis confirmed
Regular human insulin (HumuLIN R): 0.05 - 0.1 units/kg/hour
Children < 5 years: Recommend 0.05 units/kg/hour
Infusion should be made by adding insulin to normal saline
Patients with insulin pump: Remove pump, tubing and SQ catheter prior to insulin

APPENDIX: 2-BAG SYSTEM OF FLUIDS AND ELECTROLYTES

FLUID AND ELECTROLYTE REPLACEMENT: INITIAL 4-6 HRS (PHASE I)	
Bolus	Initial fluid bolus of normal saline 10 ml/kg over 1 hour
	Consider additional fluid boluses or a faster rate if hemodynamically unstable
Rate	1.5 x Maintenance (1-1.25 x maintenance if > 30 ml/kg boluses)
Bag 1	Normal Saline + 20 meq/L K Chloride + 20 meq/L K Acetate
Bag 2	D10 Normal Saline + 20 meq/L K Chloride + 20 meq/L K Acetate

1. Start Bag 2 if glucose is < 300 mg/dl or rate of glucose decline is > 100 mg/dl/hour
2. Total fluid rate per hour remains constant. As the rate of one bag increases the rate of the other bag is decreased proportionately
3. Do not add potassium if serum K+ > 5.5 meq/L
4. Maintenance (ml/day) = 100 ml/kg for the 1st 10 kg + 50 ml/kg for the 2nd 10 kg + 20 ml/kg for each kilogram above 20 kg
5. Phase 2 fluid and electrolyte replacement (after 4-6 hours)
   a. Low risk of cerebral edema with GCS 14: Change Normal Saline to ½ NS
   b. High risk of cerebral edema or corrected Na < 140 meq/L: Continue Normal Saline

2-BAG SYSTEM			
BLOOD SUGAR	BAG1 (D0)	BAG2 (D10)	DEXTROSE
> 300	100%	0%	D0 (none)
201-300	50%	50%	D5
151-200	25%	75%	D7.5
< 150	0%	100%	D10

Dextrose is added to the intravenous solution to avoid hypoglycemia when the blood glucose falls below 300 mg/dl (see 2-bag system above). A common error is to decrease the insulin infusion to avoid hypoglycemia before the ketonemia and acidosis has resolved. Continuous intravenous insulin is continued until there is evidence of resolution of ketoacidosis including: pH > 7.3, HCO_3 > 15, beta hydroxybutyrate < 1 mmol/L and closure of the anion gap. The patient is then transitioned to intermittent, subcutaneous, basal and rapid-acting insulin.

APPENDIX: CEREBRAL EDEMA IN DIABETIC KETOACIDOSIS

BACKGROUND: The most concerning complication of diabetic ketoacidosis (DKA) and its treatment is cerebral edema. It is the primary cause of death in childhood DKA. Cerebral edema is estimated to occur in 0.5-1.0% of patients with a mortality of 20-25% and significant morbidity among survivors.

The etiology of cerebral edema is unclear. One theory suggests that it may result from rapid osmotic shifts in the central nervous system. Recent evidence suggests that cerebral hypoperfusion/reperfusion and neuroinflammation may be causative.

Guidelines acknowledge that the etiology or cerebral edema in DKA is incompletely understood and that the impact of the rate/volume of fluids/sodium administration is controversial. No strategy can be definitively recommended as superior based on current evidence (ISPAD, Pediatric Diabetes 2018, PubMed ID: 29900641).

HIGH RISK FACTORS FOR CEREBRAL EDEMA	
CLINICAL	LABORATORY
Age 24 months	Calculated SOsm < 350 meq/L[1]
Abnormal neurologic exam after fluids	Corrected Na^+ < 140 meq/L[2]
Compromised communication	Corrected Na^+ decreasing at 2 hours[2]
Development delay	Initial BUN > 30 mg/dl
Double vision	Initial HCO_3 < 5 meq/L
GCS 13 after initial fluids	Initial PCO_2 < 10 mmHg
New onset diabetes	Initial pH 7.15
Other organ system dysfunction	
Received IV HCO_3 or Insulin bolus or > 40 ml/kg initial fluids	
1. Calculated SOsm = (Na*2) + (Glucose/18) + (BUN/2.8) 2. Corrected Na^+ = Measured Na^+ + [1.6 x (Serum Glucose – 100/100)]	

A well-designed, case-control study including 61 episodes of confirmed cerebral edema (Glaser, NEJM 2001, PubMed ID: 11368049) demonstrated that younger age, new onset of IDDM, the degree of acidosis, level of hypocapnia, degree of dehydration (as indicated by BUN measurement), and a slower rate of increase in serum sodium was associated with the development of cerebral edema. A bolus of sodium bicarbonate was the only treatment variable associated with the development of cerebral edema. The level of hyperglycemia did not correlate with risk of cerebral edema.

A multicenter randomized clinical trial was conducted in 13 Urban Children's Hospital emergency department in the PECARN Network from 2/2001 to 9/2016. (PECARN, NEJM 2018, PubMed ID: 29897851) Patients were randomized to 1 of 4 treatment groups based on the rate of deficit fluid administration and the tonicity of the fluids (0.9% NS versus 0.45% NS). Fast fluid administration was defined as one half of the fluid deficit replaced over 12 hours and the remainder of the deficit and maintenance fluids over subsequent 24 hours. Slow fluid administration was defined as the fluid deficit replaced with maintenance fluids over 48 hours. The primary outcome was the proportion, magnitude and duration of the decline of 2 consecutive GCS to less than 14 during any hour within the first 24 hours of enrollment. The secondary outcome of clinically apparent brain injury was defined as deterioration in neurologic status leading to: hyperosmolar therapy, endotracheal intubation, or death.

1,389 DKA episodes were included with a baseline GCS of 15 (91%), GCS 14 (7%), and GCS less than 14 (2%). Clinically apparent brain injury occurred in 12 (0.9%) episodes. 11 of the 12 recovered without overt neurologic injury. One patient (0.07%) died. There was no difference in the 4 study groups in the proportion or patients developing a GCS of less than 14 as well as the magnitude and duration of the decline in GCS or in clinical apparent brain injury requiring treatment or death. There were no differences in either of these outcomes in the subgroups specified by age or prior history of DKA. A secondary study demonstrated that a decline in serum sodium was not associated with a decrease in GCS to less than 15 or clinically apparent cerebral edema (PECARN, Pediatrics. 2021, PubMed ID: 34373322).

CLINICAL MANIFESTATIONS: The peak incidence of cerebral edema occurs from 4-12 hours of initial presentation but can occur before presentation and up to 24 hours. Treatment of cerebral edema should be initiated based on clinical suspicion. The absence of evidence of edema on a CT scan does not exclude cerebral edema.

CLINICAL SIGNS OF CEREBRAL EDEMA	
Neurologic	Altered mental status: Irritability, increased drowsiness, incontinence, in GCS (exclude hypoglycemia and hyponatremia as cause for AMS
	Focal neurologic findings, seizures, headaches, CN palsies
Cardiac	Bradycardia, hypertension, widened pulse pressure
Ocular	Blurry vision, anisocoria
Respiratory	Cheyne-Stokes breathing: Hyperpnea (fast/slow) followed by apnea

CEREBRAL EDEMA: CLINICAL DIAGNOSTIC CRITERIA
DIAGNOSTIC CRITERIA (ANY 1)
Abnormal motor or verbal response to pain
Decorticate or decerebrate posture
Cranial nerve palsy (especially III, IV, and VI), may result in double vision
Abnormal neurogenic respiratory pattern (e.g., grunting, tachypnea, Cheyne-Stokes respiration, apneusis)
MAJOR CRITERIA (ANY 2)
Altered mentation/fluctuating level of consciousness (GCS 13)
Sustained heart rate deceleration (decline > 20 beats/minutes) not attributable to improved intravascular volume or sleep state
Age-inappropriate incontinence
MINOR CRITERIA (ANY 2 WITH 1 MAJOR)
Vomiting
Headache
Lethargy or being not easily aroused from sleep
Diastolic blood pressure > 90 mmHg
Age < 5 years
Muir, Diabetic Care 2004, PubMed ID: 15220225 (Sensitivity 92%, Specificity 96%)

MANAGEMENT

CEREBRAL EDEMA: MANAGEMENT	
Indications	Treatment should be initiated based on clinical suspicion. CT findings are late (slit-like ventricles, loss grey/white differentiation)
Fluids	Decrease rate of intravenous fluids by 1/3
Mechanical	Elevate the head of bed to 30 degrees, keep the head positioned in the midline
Hyperosmolar Therapy	Mannitol: 1.0 gram/kg over 20 min, repeat if no response in 30 min
	3% Saline: Central line preferred, if no response to Mannitol Bolus: 5 ml/kg Infusion targeted to Na of 150-160 meq/L
Endotracheal intubation	Avoid if possible. Indicated for airway compromise, respiratory failure The patients hyperpnea is in compensation for the metabolic acidosis. Ventilator settings should match the patient's pre-intubation respiratory rate and tidal volume to avoid a precipitous drop in pH and cardiac arrest Avoid medications that increase ICP: Succinylcholine, ?Ketamine
Consultation	Neurosurgery for placement of an ICP monitor
Imaging	Consider imaging if no response to therapy or other CNS complication suspected

APPENDIX: PEDIATRIC GLASGOW COMA SCALE

GLASGOW COMA SCALE				
	< 1 YEAR	>1 YEAR		
Eye Opening	Spontaneous	Spontaneous		4
	To Verbal Command	To shout		3
	To Painful	To Painful		2
	No response	No response		1
Motor Response	Spontaneous	Obeys Commands		6
	Localizes Pain	Localizes Pain		5
	Withdraws to Pain	Withdraws to Pain		4
	Flexion-Decorticate	Flexion-Decorticate		3
	Extension-Decerebrate	Extension-Decerebrate		2
	No Response	No Response		1
	< 2 YEARS	2-5 YEARS	> 5 YEARS	
Verbal	Smile/Coos Appropriately	Appropriate Words/ Phrases	Oriented	5
	Cries and is Consolable	Inappropriate Words	Confused / Disoriented	4
	Persistent Inappropriate crying and/or screaming	Persistent Cries Screams	Inappropriate Words	3
	Grunts, Agitated or Restless	Grunts	Incomprehensible Sounds	2
	No Response	No Response	No Response	1

HYPERKALEMIA

INTRODUCTION (MICHAEL MOJICA, M.D. 6/2011)
Hyperkalemia is defined as serum potassium greater than 5.5 meq/liter.
Serum potassium may be elevated through three primary mechanisms.
1. Decreased urinary excretion
2. Redistribution of potassium from intracellular to extracellular space
3. Cell lysis

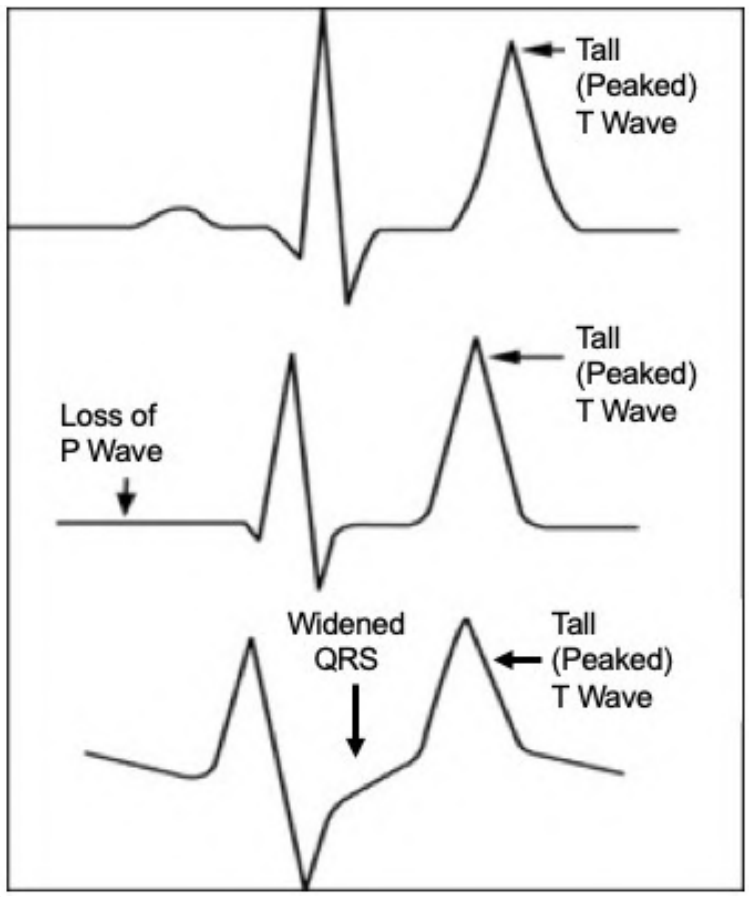
HYPERKALEMIA: ETIOLOGY	
K+ release from cells	Metabolic acidosis
	Hyperosmolar states e.g. diabetic ketoacidosis
	Beta receptor antagonists e.g. beta blockers
	Periodic paralysis
	Digoxin
	Succinylcholine
↓ K+ urinary excretion	Renal failure
	Urinary tract obstruction
	Hypoaldosteronism
	Addison's Disease
	Congenital Adrenal Hyperplasia
	NSAIDs
	Renal Tubular Acidosis (Type 4)
	Angiotensin converting enzyme Inhibitors
Cell lysis	Hemolysis
	Rhabdomyolysis
	Tumor lysis
	Crush injuries
	Burns
Pseudo-hyperkalemia	Hemolysis (phlebotomy)
	Extreme leukocytosis
	Thrombocytosis

CLINICAL PRESENTATION
The presentation of hyperkalemia may be nonspecific. Patients may complain of fatigue, muscle weakness or cramps, paralysis or paresthesias, palpitations, nausea and vomiting. Clinical signs may include: altered mental status, dysrhythmias, weakness/paralysis and decreased deep tendon reflexes.

Potassium depolarizes cell membranes, slows conduction and increases myocardial excitability. EKG changes progress from peak T waves to a sine wave QRS pattern and asystole though these changes do not correlate well with a specific potassium level.

DYSRHYTHMIAS
Sinus bradycardia
Slow idio-ventricular rhythm
First, second and third degree heart blocks
Wide complex tachycardia
Ventricular fibrillation
Asystole

EKG CHANGES
Peaked T
Prolonged PR interval
Absent P wave
Prolonged QRS interval
Sine wave pattern



See Appendix for EKG Examples

MANAGEMENT

Three methods are used to treat hyperkalemia.
1. Antagonize the membrane effects of potassium (Calcium)
2. Drive extracellular potassium into cells (Beta agonists, glucose/insulin, $NaHCO_3$)
3. Remove excess potassium from the body (diuretics, exchange resins, dialysis)

The management of hyperkalemia will be dependent on the etiology, degree of hyperkalemia and clinical manifestations. The first two methods above provide only transient decreases in potassium but do not decrease total body potassium.

In some patients withdrawal of potassium increasing medications may be sufficient. Etiology specific treatments should be initiated (e.g. Corticosteroids for congenital adrenal hyperplasia, Digoxin specific antibodies for Digoxin toxicity).

In some circumstances such as diabetic ketoacidosis the hyperosmolar state and metabolic acidosismay result in hyperkalemia while total body potassium is depleted through renal excretion. In this situation, correction of the underlying illness and provision of potassium will be required.

Hemodialysis can be used if other efforts fail to lower potassium in patients with significant clinical manifestations. It is favored in situations such as renal failure or in those with ongoing cell lysis in which hyperkalemia is expected to be persistent or increasing in severity.

CALCIUM	
Mechanism	Stabilizes cardiac cell membranes to effect of hyperkalemia
Indications	Prolonged QRS
Timing	Onset: 2-3 minutes, duration 30-60 minutes
Calcium Chloride	Calcium Chloride 10% (1 gram/10ml) (13.6 meq elemental Ca+/10ml) Child: 0.2 ml/kg (20 mg/kg), maximum dose 1 gram (10 ml) Adult:10 ml (1 gram) More rapid dissociation in the blood stream than Calcium Gluconate Risk of tissue necrosis with extravasation use CVL or large PVL
Calcium Gluconate	Calcium Gluconate 10% (1 gram/10ml) (4.6 meg elemental Ca+/10ml) Child: 0.6 ml/kg (60 mg/kg), maximum dose 3 grams (30 ml) Adult: 30 ml (3 grams) Requires hepatic metabolism. Slower onset than Calcium Chloride Avoid in liver failure, shock
Frequency	Repeat Q5 minutes if EKG changes persist or recur
Caveat	Slow infusion on cardiac monitor over 3-5 minutes Do not give in same IV with $NaHCO_3$ ($CaCO_3$ precipitates) Contraindicated in digoxin toxicity

$NaHCO_3$	
Mechanism	Increase H+ ion out of cell to buffer HCO_3. K+ into cell in exchange for H+
Dose	Adult: 150 meq $NaHCO_3$ in 1 liter D5W at 250 ml/hour Do not give hyperosmolar concentration (e.g. 50 meg/50ml)
Caveat	Limited efficacy. Do not give with Ca++ ($CaCO_3$ precipitates) Not indicated in the absence of metabolic acidosis

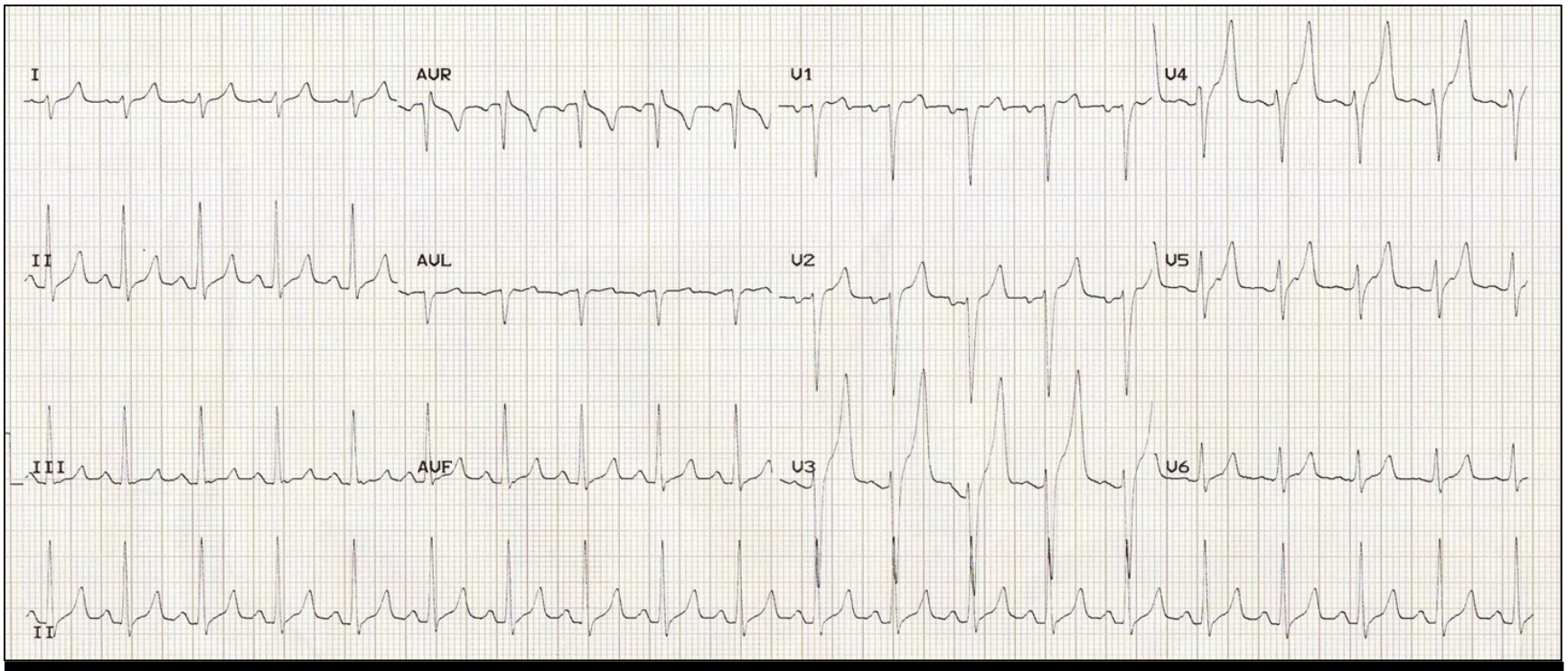
INSULIN/GLUCOSE	
Mechanism	Enhances activity of Na-K-ATPase pumps Shifts K+ from extracellular to intracellular space
Indications	EKG changes, K+ > 6.5
Timing	Onset 10-20 minutes, peak at 30-60 minutes, duration 4-6 hours
Indications	EKG changes or K+ > 6.5-7.0 meq/l
Adult Dosing	Glucose: 25 grams (50 ml of D50) Regular Insulin: 10 units
Child Dosing	Glucose:1 gram/kg D10 = 10 ml/kg, D25 = 4 ml/kg, D50 = 2 ml/kg) Regular Insulin: 0.2 units per gram of glucose
Caveats	Provide glucose infusion to avoid hypoglycemia Monitor bedside glucose closely

FUROSEMIDE (LASIX)	
Mechanism	Loop diuretic. Enhances excretion of K+
Dose	Adult: 20-40 mg IV Child: 1-2 mg/kg IV
Caveat	Higher dose may be required in renal insufficiency
	Limited short term efficacy
	Replace fluid losses (unless the patient is volume overloaded)

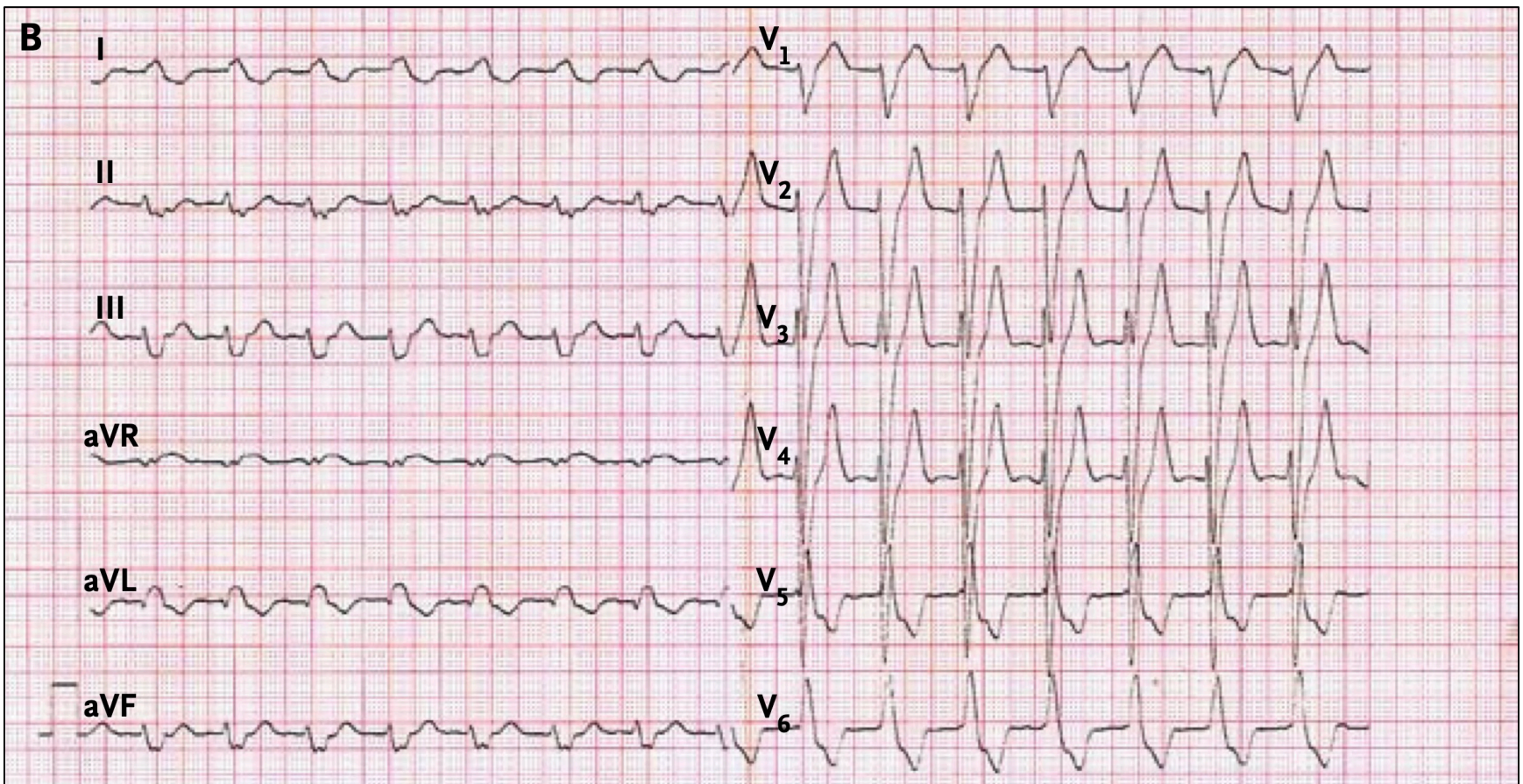
BETA AGONISTS	
Mechanism	Decrease potassium release from cells,
Albuterol	10-20 mg/4ml via nebulizer over 10 minutes, duration 2 hours Note: This is 4-8 times the typical asthma dose of 2.5-5.0 mg

SODIUM POLYSTYRENE SULFONATE (KAYEXALATE)	
Mechanism	Binds potassium in GI tract, releases Na+ in exchange
Timing	Onset: 1-2 hours
Dose	Adult: 15-30 grams PO Child: 1 gm/kg PO
	May also be given as a retention enema (50 gm in 250 ml D5W)
	May repeat dose in 4-6 hours based on repeat K+
Caveat	Do not use with sorbitol. May cause intestinal necrosis
	Do not use in post-op or renal transplant patients

APPENDIX: HYPERKALEMIA EKG CHANGES



EKG FINDINGS: PEAKED T WAVES DUE TO HYPERKALEMIA



EKG FINDINGS: WIDENED QRS DUE TO HYPERKALEMIA

HYPOKALEMIA

INTRODUCTION (MICHAEL MOJICA, MD, 7/2020)
Hypokalemia is defined as a serum potassium of less than 3.5 meq/Liter. Potassium is a predominantly (98%) intracellular cation. The correct ratio of intracellular to extracellular potassium is essential for the propagation of cellular action potentials. Potassium movement across cell membranes is mediated by Na^+/K^+ ATPase in the cell membrane. Potassium renal excretion is mediated by the mineralocorticoid aldosterone. Aldosterone is secreted from the adrenal gland in response to hypovolemia. Sodium and water are resorbed from the kidney and potassium is excreted to maintain electrical neutrality. Infants have higher normal potassium levels of due to a decrease in urinary potassium excretion as a result of a lower glomerular filtration rate and decreased sensitivity to aldosterone.

HYPOKALEMIA CLASSIFICATION (>1 YEAR OF AGE)	
Mild	3.0-3.5 meq/L
Moderate	2.5-3.0 meq/L
Severe	< 2.5 meq/L

NORMAL POTASSIUM BY AGE	
Premature Infant	4.0-6.5 meq/L
Newborn	3.7-5.9 meq/L
Infant	4.1-5.3 meq/L
> 1 year	3.5-5.0 meq/L

PATHOPHYSIOLOGY
Hypokalemia is a result of potassium losses via the kidneys, gastrointestinal tract or skin or redistribution of potassium from the extracellular to the intracellular space. Decreased intake of potassium is rarely the sole cause of hyperkalemia because of the kidney's ability to reabsorb potassium. However, inadequate intake can exacerbate other causes of hypokalemia. Gastrointestinal losses are the most common cause of hypokalemia in children.

GASTROINTESTINAL LOSSES: Diarrheal stool has a high concentration of potassium (20-50 meq/L). In contrast, the potassium concentration of vomit or nasogastric tube contents is relatively low (5-10 meq/L). In both diarrhea and vomiting, dehydration (hypovolemia) stimulates aldosterone secretion that increases sodium and water resorption and renal potassium excretion. With vomiting, the resulting metabolic alkalosis increase renal hydrogen resorption in exchange for potassium excretion as well as redistribution of potassium from the extracellular to the intracellular space.

RENAL LOSSES: Renal potassium losses can be due to: increased aldosterone and increased sodium and water reaching the distal nephron. In both situations, increased sodium and water resorption results in increased potassium excretion. Both of these mechanisms can occur as the result of diuretic therapy. Polyuria due to osmotically active agents (e.g. DKA, mannitol) can also increase urinary potassium excretion.

POTASSIUM REDISTRIBUTION: Alpha agonists, beta agonists and insulin activity on Na^+-K^+ ATPase results in transfer of potassium from the extracellular to the intracellular space. Decreases in potassium can be seen in stress settings such as head trauma in response to endogenous Epinephrine release. Similarly, over-the-counter sympathomimetics such as decongestants (pseudoephedrine) and diet aides (ephedrine) can also result in hypokalemia.

Both metabolic and respiratory alkalosis can result in a shift of potassium into the cells in exchange for hydrogen (H^+) out of the cells to maintain electrical neutrality. Potassium decreases 0.4 meq/L for every 0.1 increase in pH. These causes may result in transient hypokalemia with a normal total body potassium.

HYPOKALEMIA ETIOLOGY
GASTROINTESTINAL LOSSES
Diarrhea (K^+ = 20-50 meq/L), vomiting, nasogastric drainage (K^+ = 5-10 meq/L)
Laxative abuse
Decreased oral intake: Anorexia, malnutrition (rarely, the sole cause of hypokalemia)
REDISTRIBUTION: EXTRACELLULAR → INTRACELLULAR SPACE
Alkalosis: H^+ exits the cell in exchange for K+ entering the cell
Increased insulin activity: Shifts K^+ from the extracellular to intracellular space
Beta agonists: Shifts K^+ from the extracellular to intracellular space, e.g. Epinephrine, Albuterol
Hypokalemic Periodic Paralysis; Defect in Ca^{++}, Na^+ channels → Severe weakness Hereditary (autosomal dominant) or acquired (hyperthyroidism) forms Precipitated by rest after exercise, stress or carbohydrate load
Medications: Risperidone, Quetiapine, Chloroquine
Other: Hypothermia, increased blood cell production (↑ new cell uptake of potassium)
RENAL LOSSES
↑ Na^+ to the distal nephron: Diuretics, osmotic diuretics (mannitol), tubular injury, DKA
Renal tubular acidosis: Types 1 and 2
↑ Mineralocorticoid: Primary hyperaldosteronism. Hypovolemia → ↑ Aldosterone (2°)
Tubulopathies: Bartter syndrome, Gitelman syndrome
Hypomagnesemia
Polyuria
CUTANEOUS LOSSES
Cystic Fibrosis, excessive sweating

CLINICAL MANIFESTATIONS

In general, symptoms of hypokalemia are rare in healthy children above a level of 3.0 meq/Liter. However, symptoms can occur at higher levels with a rapid decrease in potassium. Muscle and cardiac effects are related to alteration of the transmembrane gradient. History should include as assessment of gastrointestinal illness, medications, a family history of periodic paralysis and symptoms of thyrotoxicosis (weight loss, heat intolerance, tremors, palpitations and anxiety). Physical examination should assess for muscle strength, tone and reflexes and signs of hypovolemia.

SKELETAL MUSCLE: Skeletal muscle weakness typically progresses from the lower extremities to the trunk and upper extremities. Severe muscle weakness typically occurs at a potassium of < 2.5 meq/L if hypokalemia develops slowly. However, it can occur at higher levels if hypokalemia develops rapidly (e.g. periodic or thyrotoxic period paralysis). Severe weakness can progress to flaccid paralysis. It is essential to monitor for signs of respiratory failure (respiratory rate, effort, oxygen saturation, end tidal CO2, negative inspiratory flow). Severe hypokalemia can also result in muscle cramps, fasciculations, rhabdomyolysis and myoglobinuria. The release of intracellular potassium from rhabdomyolysis can mask the degree of hypokalemia.

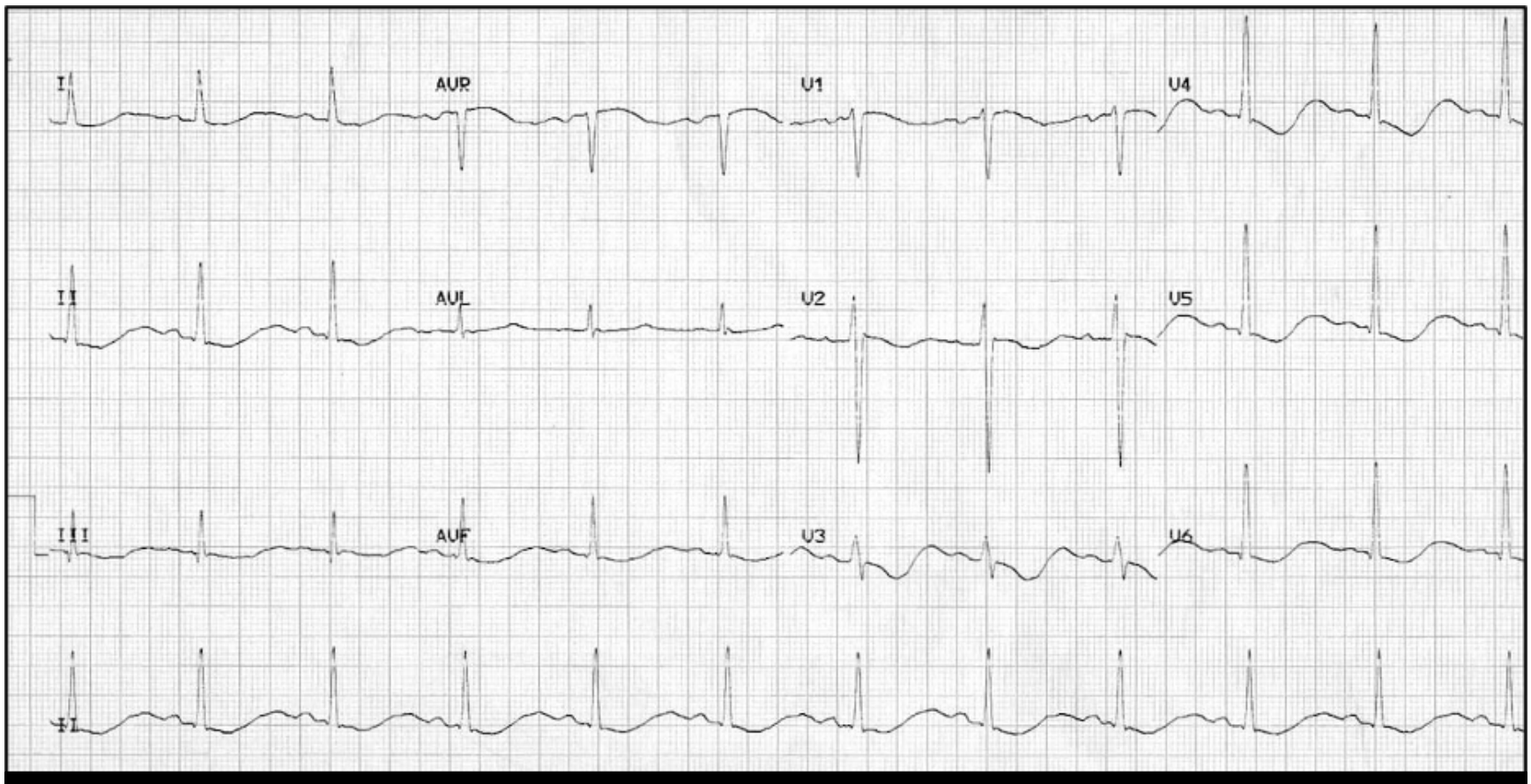
SMOOTH MUSCLE: Intestinal smooth muscle relaxation can result Olgilvie's syndrome (acute colonic pseudo obstruction) with symptoms of nausea, vomiting, anorexia and constipation and signs of ileus and abdominal distention.

CARDIAC: Hypokalemia can cause EKG changes and life-threatening arrhythmias. There is significant variability in the potassium level at which EKG changes and arrhythmias occur. In addition, concomitants factors such as beta agonist therapy, stress (endogenous Epinephrine) and hypomagnesemia can increase the risk of lethal ventricular arrhythmias. Continuous cardiac monitoring is essential for any patient with cardiac complaints (chest pain, palpitations, syncope), exam findings (irregular heart rate, bradycardia, tachycardia) or EKG changes.

Hypomagnesemia (< 0.8 meq/L) due to diarrhea and diuretic use, can increase the QT interval, cause atrial and ventricular ectopy, atrial tachycardias and torsades de points. Hypomagnesemia is often present with hypokalemia. In addition, hypomagnesemia increases renal losses of potassium. Hypokalemia may be refractory to potassium supplementation if hypomagnesemia is not corrected first. Treatment to a potassium of > 4.0 meq/L and magnesium > 1.0 meq/L can stabilize the myocardium.

EKG	
EKG CHANGES	ARRHYTHMIAS
↑ P wave height and width	Premature atrial or ventricular contractions
↑ PR interval	Paroxysmal atrial tachycardias
T waves flattened or inverted	Paroxysmal junctional tachycardia
ST depression	Atrioventricular blocks
↑ QT (Due to fusion of T, U waves)	Ventricular Tachycardia or Torsades
U waves*	Ventricular Fibrillation
*Most common in precordial leads (V4-6), typically > 50% height of adjacent T wave Normal U waves in patients with slow HR are < 50% height of adjacent T wave	

WEB LINK: LIFE IN THE FAST LANE: EKG LIBRARY



EKG FINDINGS: K+ = 1.7, ↓ ST, T wave inversion, prominent U waves, ↑ QU interval

RENAL: Prolonged hypokalemia can cause functional and structural renal changes. Impaired renal concentrating ability can present with polyuria and polydipsia. Polyuria can further exacerbate renal potassium losses. Reno-vascular hypertension may also be present.

DIAGNOSTIC TESTING

Extensive diagnostic testing is not required if a clear etiology of hypokalemia can be determined (diarrhea, alkalosis, medications, hypovolemia, family history of periodic paralysis). A basic metabolic profile, magnesium, CPK, venous pH and urinalysis should be obtained. Management of hypokalemia takes precedent over identification of rare causes of hypokalemia (See Appendix: Diagnosis of hypokalemia of unclear etiology).

It is essential to remember that potassium is 98% intracellular and that the serum potassium may not reflect total body potassium. The serum potassium should be interpreted with care in the setting of an acid-base disturbance or medications that redistribute potassium across cell membranes. For example, the serum potassium may be normal or elevated in diabetic ketoacidosis despite total body potassium depletion.

MANAGEMENT

Treatment of hypokalemia is based on the etiology, degree of hypokalemia, presence of severe symptoms and the patient's ability to tolerate oral intake.

MANAGEMENT GOALS
Prevent and treat life-threatening complications such as paralysis (e.g. respiratory failure), arrhythmias and rhabdomyolysis
Replace potassium deficit
Identify and treat the cause of hypokalemia

If supplemental potassium is required, oral supplementation is typically preferred. It has similar efficacy with fewer adverse effects compared to intravenous supplementation. Continuous cardiac monitoring is required for intravenous supplementation due to the risk of hyperkalemia with arrhythmia. (See Appendix: Potassium Supplementation).

Hypokalemia may be refractory to supplementation if hypomagnesemia (diarrhea, diuretics) is not corrected first. In patients with GI or renal potassium loss, serum potassium levels will increase and subsequently decrease are potassium is taken up into the cells until the total potassium deficit is replaced.

POTASSIUM SUPPLEMENTATION: INDICATIONS	
1	Renal and gastrointestinal potassium losses: Total body potassium depletion
2	Potassium redistribution: Severe hypokalemia, symptoms or EKG changes

POTASSIUM REDISTRIBUTION: Shifts in potassium across cell membranes may be transient and total body potassium may be normal. Correction of the underlying cause (correction of alkalosis, cessation of beta agonists) may be sufficient. Care should be taken to avoid rebound hyperkalemia due to potassium supplementation followed by correction of the cause of redistribution (most common in patients with hypokalemic or thyrotoxic periodic paralysis).

GASTROINTESTINAL LOSS: Correction of hypovolemia will improve metabolic acidosis due to lactate and hypokalemia due to secondary hyperaldosteronism. Potassium chloride (PCL) is preferred in those with a normal pH and those with metabolic alkalosis. PCL also replaces the chloride that is lost with

vomiting. In those with a metabolic acidosis due to loss of bicarbonate from diarrheal stools, potassium bicarbonate or it's precursors potassium acetate or citrate is preferred.
RENAL LOSS: Potassium supplementation is incompletely effective in those with chronic, stable hypokalemia due to diuretic therapy or primary hyperaldosteronism. As the serum potassium increases, renal reabsorption decreases. Resulting in a hypokalemia steady state. Potassium sparing diuretics are more effective in these circumstances. An aldosterone antagonist, such as Spironolactone, is

OTHER THERAPIES	
Magnesium	Lost with K^+ via GI or renal route. Can also ↑ renal K^+ excretion 50 mg/kg (maximum dose 2 grams) IV
Amiloride*	Renal collecting tube Na channel antagonist Diuretics, Tubulopathies (Bartter syndrome, Gitelman syndrome)
Spironolactone*	Aldosterone antagonist, Treatment for hyperaldosteronism
Beta-blocker	Congenital ↓ K^+ Propranolol, indicated for ↑ sympathetic tone
*Potassium sparing diuretics	

recommended for primary hyperaldosteronism. A renal collecting tube sodium channel antagonist, such as Amiloride, is recommended for those on chronic diuretic therapy.

APPENDIX: POTASSIUM SUPPLEMENTATION

POTASSIUM FORMULATIONS	
Chloride	Most commonly used. Preferred for hypochloremia, metabolic alkalosis (vomiting)
Phosphate	Renal loss of K+ and phosphorus
	1. Diabetic ketoacidosis
	2. Proximal tubule dysfunction: Fanconi syndrome, cystinosis
Acetate, Citrate	Metabolized to bicarbonate. Hypokalemia due to acidosis (e.g. RTA 1 and 2, diarrhea)

POTASSIUM SUPPLEMENTATION: DOSING[1]			
		ADULT	PEDIATRIC
Daily requirement		40-80 meq/day	50 kg: 2-4 meq/kg/day > 50 kg: 1-2 meq/kg/day
Prevention (Maintenance IV Fluids)		20-40 meq/day Divided QD-BID	1-2 meq/kg/day Divided QD-BID Max dose: 20 meq
Mild-Moderate Hypokalemia (2.5-3.5 meq/L)	PO	40-100 meq/day PO Divided in 2-5 doses Max dose: 40 meq	2-5 meq/kg/day PO Divided BID Max dose: Lowest of 1-2 meq/kg or 20 meq
	IV	10 meq Max conc: 40 meq/L Max rate: 10 meq/hour	0.2-0.5 meq/kg Max dose: 20 meq Max conc: 20 meq/L Max rate: 0.5 meq/hour
Severe Hypokalemia (< 2.5 meq/L) OR Severe Symptoms (arrhythmia, marked muscle weakness, paralysis)	PO	40 meq PO Q6-8 hours or 20 meq PO Q2-3 hours Max dose: 40 meq	5-10 meq/kg/day PO Divided BID Max dose: Lowest of 2 meq/kg or 40 meq
	IV	40 meq Max conc: 40 meq/L Max rate: 40 meq/hour (Central line or IO)	0.5-1.0 meq/kg Max dose: 20 meq Max conc: 40 meq/L Max rate: 0.5 meq/kg/hr

1. Little evidence on the safety and efficacy of specific regimens. Dosing adapted from Lexicomp
2. Dosing should be adjusted lower to account for renal or hepatic insufficiency
3. Central line and cardiac monitoring for > 10 meq/hour IV or > 0.5 meq/kg/hour
4. Avoid Dextrose containing IV fluids → ↑ Insulin secretion → ↓ K^+
5. 10 meq IV KCL → ↑ K^+ by 0.1 meq/L
6. Hypokalemia may be refractory to supplementation if hypomagnesemia (diarrhea, diuretics) is not first corrected

APPENDIX: DIAGNOSIS: HYPOKALEMIA OF UNCLEAR ETIOLOGY

TESTING IF HYPOKALEMIA OF UNCLEAR ETIOLOGY	
Blood	BMP, Ca^{++}, Mg^{++}, phosphorous, pH, renin, aldosterone, thyroid function
Urine	Na^{+}, K^{+}, Chloride-, Ca^{++}, Creatinine

A spot urine potassium to creatinine ratio can be used to determine the etiology of hypokalemia. In those with a high urine potassium to creatinine ratio, blood pressure, pH and a urine chloride can be used to determine the etiology.

SPOT URINE POTASSIUM TO CREATININE RATIO	
>15 meq/gm Cr	↑ Mineralocorticoid, tubular dysfunction
a. Hypertension	1. ↓ Aldosterone, ↓ Renin: Apparent mineralocorticoid excess (ACE), Liddle syndrome, adrenal hyperplasia
	2. ↑ Aldosterone, ↓ Renin: Hyperaldosteronism
b. Normal BP	1. Acidosis: Renal Tubular Acidosis 1, 2, diabetic ketoacidosis
	2a. Alkalosis: Urine Creatinine < 10-15 meq/L: Emesis, diuretics
	2b. Alkalosis: Urine Creatinine > 20 meq/L: Barter syndrome (± ↓ Ca^{++}), Gitelman Syndrome, (± ↓ Mg^{++})
	3. Normal pH: Drug effect, ↓ Mg^{++}, osmotic effect (non-ketotic)
<15 meq/gm Cr	Gastrointestinal losses, poor oral intake Cellular shifts due to alkalosis, medications and diuretic use

HYPONATREMIA

I**NTRODUCTION** (ELLEN DUNCAN, M.D., PhD., 4/2017)

Hyponatremia is one of the most common electrolyte abnormalities in the pediatric population. Severe hyponatremia can cause significant morbidity and mortality due to complications of cerebral edema (herniation, status epilepticus).

PHYSIOLOGY

Sodium and water homeostasis are tightly integrated by both volume and osmole receptors regulate. Sodium is primarily regulated by the intake or excretion of water and to a lesser extent by sodium resorption and excretion. Osmolality is maintained in the range of 275-290 mosmol/kg. Plasma osmolality can be calculated using the formula: 2 Na + Glucose/18 + BUN/2.8. Measured serum osmolality can be compared to the calculated osmolality to determine if an osmolar gap exists. The term tonicity differs from osmolality in that it refers only to molecules that cannot readily move across cell membranes. The calculation of tonicity is the same as that as osmolality but excludes the BUN term because BUN moves freely across cell membranes. A decrease in plasma tonicity results in movement of water from the extracellular to the intracellular space. An increase in plasma tonicity results in movement of water from the intracellular to the extracellular space.

Total body water makes up about 60% of body weight for adults and a higher percentage for children. Total body water consists of intracellular fluids (ICF 2/3) and extracellular fluids (ECF 1/3). The extracellular fluid can be further divided into the effective circulating volume and interstitial fluids. Starling's law describes the factors which result in shifts of fluid between the effective circulating volume (capillaries) and extravascular space (interstitial and intracellular space). Increased capillary hydrostatic pressure (e. g. congestive heart failure), increased capillary permeability (e.g. sepsis) and a decreased plasma oncotic pressure (e.g. nephrotic syndrome) result in the movement of water from the vascular to extravascular space. The term third spacing refers to the movement of water from the intravascular space to the interstitial space.

SODIUM AND WATER REGULATION	
SYSTEM	ACTION (RECEPTOR LOCATION)
Renin-ANGIOTENSIN-Aldosterone	Vasoconstriction, Na resorption (renal arteriole)
Renin-Angiotensin-ALDOSTERONE	Na resorption (Renal arterioles)
Pituitary-Renal: Antidiuretic Hormone	H_2O resorption (Hypothalamus)
Thirst	H_2O intake (Hypothalamus)
Sympathetic nervous system	Vasoconstriction, Na resorption (Carotid sinus)
Natriuretic peptides	Vasodilation, Na excretion (Atria, Ventricles)

PATHOPHYSIOLOGY

Hyponatremia is defined as a sodium concentration of < 135 meq/liter. A low sodium concentration can be seen with a low (hypovolemia), normal (normovolemia) of high (hypervolemia) total body water.

HYPONATREMIA CLASSIFIED BY VOLUME STATUS
HYPOVOLEMIC HYPONATREMIA
Loss of Na >> Loss of water. Hypovolemia → ↑ ADH → ↑ Free water retention. Exacerbated by hypotonic fluid replacement. e.g. Pedialyte
Gastrointestinal: Diarrhea, vomiting, 3rd Spacing of fluids: Ascites, ileus, burns Hemorrhage: Internal and external Adrenal: Mineralocorticoid Deficiency: e.g. congenital adrenal hyperplasia Cerebral Salt Wasting: Trauma, encephalitis/meningitis, CNS surgery Renal Salt Wasting: Renal tubular or interstitial defects, diuretics Intense Exercise: Sweating, heat exposure Others: Cystic fibrosis, Improperly mixed infant formulas (too much water)
NORMOVOLEMIC HYPONATREMIA
Inappropriate ADH secretion →↑ Free water retention OR Excessive free water intake
Syndrome of inappropriate ADH secretion (SIADH); See table below H_2O Intoxication: Psychogenic polydipsia, extreme exercise with free water intake Hypothyroidism Medications: Chemotherapy, antiepileptic agents, MDMA (Ecstasy)
HYPERVOLEMIC HYPONATREMIA
Increase in total body water but a decrease in effective circulating volume ® ↑ ADH ® ↑ Free water retention.
Congestive heart failure, renal failure, liver failure, nephrotic syndrome
PSEUDO/FICTITIOUS HYPONATREMIA
Normal sodium and normal total body water
PSEUDO: Laboratory methods corrupted: Hyperproteinemia, Hyperlipidemia
FICTITIOUS: ↑ Serum osmolality: Hyperglycemia (DKA), Mannitol

HYPOVOLEMIC HYPONATREMIA: Hyponatremic dehydration (hypovolemia) is the most common cause of hyponatremia in pediatrics. There is a loss of both sodium and water but a greater loss of sodium than water. Alternatively, there is a loss of isotonic fluids (equal amount of sodium and water) and an extra sodium deficit. Appropriate ADH secretion and stimulation of the Renin-Angiotensin system occur to improve the effective circulating volume. Studies have demonstrated a significantly higher relative risk of iatrogenic hyponatremia in hospitalized patients receiving hypotonic versus isotonic fluids. In patients receiving oral rehydration it is often overlooked that Pedialyte is hypotonic (D2.5, 1⁄4 Normal Saline, KCL 20 meq/L, Base 20 meq/L). Hypovolemic hyponatremia may also be seen in patients with: cystic fibrosis, cerebral salt wasting (head trauma, encephalitis), obstructive uropathy and with thiazide diuretics.

HYPERVOLEMIC HYPONATREMIA: In edematous states such as congestive heart failure, renal failure and nephrotic syndrome there is an increase in total body water more than the increase in sodium. Alternatively, there is an increase in isotonic fluids (equal amount of sodium and water) and an additional free water excess. Despite an increase on total body water there is a decreased in the effective circulating volume and this stimulates ADH secretion.

NORMOVOLEMIC HYPONATREMIA: There are also hyponatremic states in which the total body water is normal and the total body sodium is normal. In the syndrome of inappropriate ADH secretion (SIADH), ADH causes free water retention resulting in a dilutional hyponatremia. Patients with primary psychogenic polydipsia have a dilutional, normovolemic hyponatremia caused by excessive free water intake. Medications such as antiepileptics (Valproate, Carbamazepine) and chemotherapeutic agents can also result in normovolemia hyponatremia.

SYNDROME OF INAPPROPRIATE ADH SECRETION (SIADH)	
CNS	Stroke, hemorrhage, infection, trauma
Pulmonary	Lung cancer, pneumonia, bronchiolitis, pneumothorax, asthma
Surgery	Major thoracic or abdominal surgery
Medications	Psychiatric: Haloperidol, SSRIs, MAO's, tricyclics Drugs of abuse: Ecstasy (MDMA), Opiates, Nicotine Antiepileptics: Valproate, Carbamazepine, Chemotherapy: Vincristine, Cyclophosphamide Others: Amiodarone, Ciprofloxacin, NSAIDS, oxytocin, ACE inhibitors
Mimics	Cerebral salt wasting (hypovolemic, hyponatremia) Exogenous vasopressin: DDAVP for nocturnal enuresis

PSEUDO-HYPONATREMIA: The laboratory method used to determine serum sodium is ineffective under certain conditions. The total body water and sodium are normal but the measurement of serum sodium is artificially depressed. This may be seen with hyperproteinemia and hyperlipidemias. Fictitious hyponatremia can be seen in states with a high serum osmolality as seen with an elevated glucose in diabetic ketoacidosis or with the administration of Mannitol.

ASSESSMENT
Fluid losses: Vomiting, diarrhea, hemorrhage, diuretics, diabetes (mellitus & insipidus)
Excessive water intake: Psychogenic, extreme exercise with free water intake
Underlying disease: CNS, pulmonary, endocrine pathology, infections
Ascites and edema: CHF, liver/renal failure, nephrotic syndrome
Oliguria or anuria: May indicate inability to excrete free water
Cerebral salt wasting: CNS trauma/surgery, meningitis, encephalitis
Kidney failure or renal tubular disorders
Cutaneous losses: Cystic fibrosis, intense exercise/sweating
Medications: Diuretics, antiepileptic agents (Valproate, Carbamazepine)

CLINICAL MANIFESTATIONS

Assessment of the patient with hyponatremia is aimed at determining the severity of symptoms, the patient's volume status and the etiology of hyponatremia. In hyponatremic dehydration more fluid is lost from the intravascular space when compared to isotonic dehydration. Clinical signs of dehydration are more pronounced than in isotonic dehydration and the extent of dehydration may be overestimated. Symptoms of hyponatremia are related to a shift in water from the extracellular to the intracellular space. Severe cerebral edema can result in brainstem herniation and status epilepticus.

Symptoms reflect the degree of cerebral edema and are more closely related to rapidity of onset of hyponatremia than the absolute level of hyponatremia. A rapid fall in serum sodium can cause cerebral edema because of the rapid shift of water from the extracellular to the intracellular space. Normal compensatory mechanisms are insufficient in the face of acute changes. In patients with chronic hyponatremia cerebral edema is less likely as the cerebral cell volume has had sufficient time to adapt to the low sodium concentration. More subtle symptoms such as restlessness, weakness, fatigue, or irritability may be present.

MILD-MODERATE SYMPTOMS: Acute hyponatremia may be asymptomatic. Although hyponatremia is defined as plasma or serum sodium level <135 mEq/L, clinical manifestations generally occur when levels are <130 mEq/L. Early symptoms include nausea, vomiting, anorexia, weakness and muscle cramping.

SEVERE SYMPTOMS: At lower sodium levels (<120 mEq/L) or with more rapid declines in sodium, central nervous system signs and symptoms predominate. These include: seizures, altered mental status, hyporeflexia and pseudo-bulbar palsy (difficulty with chewing, swallowing, and speech, as well as inappropriate emotional outbursts). Patients may be hypothermic and have Cheyne-Stokes respiration (periodic respirations, alternating periods of deep and shallow respiration and possibly apnea).

LABORATORY TESTING
Basic electrolytes and a urinalysis are ordered to assess renal function. Urine sodium and urine osmolality are measured to determine the integrity of kidney function and to determine if ADH and the Renin-Angiotensin-Aldosterone system are activated. These systems are activated in states where there is decreased renal blood flow (volume receptors) or there is deceased flow of sodium to the kidneys.

LABORATORY STUDIES
Serum sodium: Normal 135-145 mEq/L
Plasma osmolality: Normal 275-290 mosmol/kg)
Basic metabolic panel: Renal function (BUN, Creatine), acid-base status
Urine osmolality: Normal <100 mosmol/kg)
Urine sodium: Normal 20 meq/L
Urinalysis

URINE SODIUM: A low urine sodium concentration indicates intact renal sodium resorption and/or the presence of a stimulus to conserve sodium. A decrease in urine sodium (< 20 meg/L) can be seen in patients with a decreased total body water (e.g. dehydration due to gastroenteritis), in patient with an increase in total both water but with a decrease in the effective circulating volume. (e.g. congestive heart failure), and in patients with increased free water intake (e.g. psychogenic polydipsia).

In the hypovolemia patient, a decreased urine sodium is indicative of a pre-renal etiology of hyponatremia. This includes. gastrointestinal fluid losses, hemorrhage (internal or external), 3rd spacing of fluids (bowel obstruction, burns, pancreatitis). In the hypervolemic patient (edematous states), a decrease urine sodium can occur with cirrhosis and nephrotic syndrome.

A high urine sodium concentration may signify salt wasting etiologies. An increase in urine sodium (>20-40 meq/L) is associated with: the use of thiazide or loop diuretics, renal failure, cerebral salt wasting, SIADH and osmotic diuresis (diabetic ketoacidosis, mannitol)

In the hypovolemia patient, an increased urine sodium is indicative of a renal etiology of hyponatremia. This include: the diuretic phase of renal failure, salt losing nephropathy (e.g. renal tubular acidosis), cerebral salt wasting, thiazide diuretics and osmotic diuresis (e.g. DKA, Mannitol). In the hypervolemic patient (edematous states), an increased urine sodium can occur with renal failure, diuretic use and hypothyroidism.

URINE OSMOLALITY: The comparison of urine to serum osmolality can be helpful to determine the etiology of hyponatremia. ADH is secreted in response to a decrease in plasma volume or an increase in plasma osmolality. A urine osmolality that is lower than serum osmolality is seen with water intoxication (e.g. psychogenic polydipsia). A urine osmolality that is greater than serum osmolality occurs with hypervolemia (appropriate ADH secretion), SIADH (inappropriate ADH secretion) and cerebral salt wasting.

	SIADH	CEREBRAL SALT WASTING
Urine Na^+	Increased	Increased
Urine: Serum Osmolality	Urine > Serum Osmolality	Urine > Serum Osmolality
Urine Output	Decreased or Normal	Increased
Volume status	Normal or elevated	Decreased
Treatment	Fluid Restriction	Fluid Resuscitation

MANAGEMENT

Treatment depends on the severity of symptoms of cerebral edema, volume status and the underlying etiology. Treatment options included replenishment of sodium or fluid restriction and treatment of the underlying condition.

HYPERTONIC SALINE: 3 NORMAL SALINE (463 MEQ/LITER)	
Adults	100 ml bolus
Children	3-5 ml/kg bolus
• The optimum period over which the bolus should be given is unclear • If severe symptoms worsen or persist a second bolus may be administered • Sodium levels should be monitored closely to assess for overly rapid correction	

SEVERE SYMPTOMS: In patients with altered mental status or seizures, hyponatremia should be corrected quickly but only to the extent that is required to reduce severe symptoms from cerebral edema. A too rapid increase in sodium can result in osmotic demyelination syndrome (previously called central pontine myelinolysis but found to occur in other locations than the pons). Patients with acute hyponatremia (< 48 hours) can withstand a more rapid correction with hypertonic saline. Patients with chronic hyponatremia are protected from cerebral edema by cerebral adaption, but may be more susceptible to osmotic demyelination.

The goal is to increase the serum sodium no more than 6-8 meg/liter/day. A smaller, more rapid correction of not faster than 2-3 meg/liter/hour and no more than 5 meg/liter over the first several hours can be obtained with hypertonic saline (3% Saline = 3 x 154 = 462 meg/liter). For severely symptomatic patients, the morbidity from cerebral edema is significantly greater than the morbidity from a too rapid correction. Hyponatremic seizures are typically refractory to antiepileptic agents.

MILD-MODERATE SYMPTOMS: Patients who are asymptomatic or have mild symptoms do not require hypertonic saline. The underlying cause of hyponatremia should be addressed.

HYPOVOLEMIC HYPONATREMIA: The management of hypovolemic hyponatremia consists of the replacement of fluid deficits with isotonic or near isotonic fluids. This corrects both the hypovolemia and the hyponatremia. When volume is restored, ADH secretion will decrease and reduce the amount of free water that is resorbed. After the initial fluid bolus, the fluid deficit and maintenance fluids are provided over 24 hours. Potassium in the replacement fluids is osmotically active and contributes to the fluids tonicity. The potassium provided in the extravascular space is exchanged for intracellular sodium further reducing the degree of hyponatremia (See also: Appendix: Hypertonic dehydration: Fluid and Electrolyte Calculations)

HYPERVOLEMIC HYPONATREMIA: Those with volume overload may be treated with diuretics such as furosemide.

NORMOVOLEMIC HYPONATREMIA: Patients with SIADH should be fluid-restricted and the underlying cause be treated. Patients with adrenal insufficiency should be treated with corticosteroids.

DISPOSITION

Patients with symptomatic hyponatremia should be transferred to the pediatric ICU as soon as they are hemodynamically stable. If any doubt exists about the cause of the hyponatremia, or if the sodium levels remain difficult to control, a pediatric endocrinology consult may be beneficial. If the cause of hyponatremia is renal, pediatric nephrology should be consulted. If brain pathology (e.g. intracranial tumor) is causing low sodium levels, neurosurgical care may be required.

APPENDIX: HYPONATREMIC DEHYDRATION: ELECTROLYTES

HYPONATREMIC DEHYDRATION: FLUID AND ELECTROLYTE CALCULATIONS	
1. H_2O REPLACEMENT	
Prior weight known	Fluid deficit (liters) = Prior weight (kg) - Current weight (kg)
Prior weight unknown	Prior weight = Current weight (kg) x (1 + % dehydration/100)
H_2O Deficit (liters)	= Prior weight (kg) - Current weight (kg)
H_2O Replacement	= [Maintenance Fluid + Fluid Deficit] – Fluid bolus
2. SODIUM (Na^+) REPLACEMENT	
Na^+ lost with H_2O	= 135 meq/L x 0.6 x H_2O deficit (L)
Extra Na+ Deficit	= (135 – Measured Na^+) x 0.6 x Weight (kg)
Maintenance Na^+	= 3 meq/dl of daily maintenance fluids
Na+ Replacement	= Na^+ deficit + Extra Na^+ deficit + Na^+ maintenance
3. POTASSIUM (K^+) REPLACEMENT	
K^+ Deficit	= 150 meq/L x 0.4 x H_20 deficit (L)
Maintenance K^+	= 2 meq/dl of maintenance fluids
K^+ Replacement	= K^+ deficit (A3) + Maintenance K^+ (B3)
FINAL FLUID (Over 24 hours) = H_2O + Na^+ + K^+	H_2O deficit (liters) + Na^+ Replacement + K^+ Replacement If fluid replacement = 1.5 L and Na replacement is 115 meq Fluid is: 115 meq/1.5 liter = 77 meq/liter = 1/2 Normal Saline Addition of K+ to fluid adds to its tonicity

MAINTENANCE FLUIDS (ML/KG/DAY): CALORIC EXPENDITURE METHOD
100 ml/kg/day for the first 10 kg
50 ml/kg/day for the second 10 kg
20 ml/kg/day for every kg above 20 kg
Example: 25 kg child: 10 Kg + 10 Kg + 5 kg Maintenance = (100 ml/kg/day x 10kg) x (50 ml/kg/day x 10kg) + (20 ml/kg/day x 5 kg) Maintenance = 1000 ml/day + 500 ml/day + 100 ml/day = 1600 ml/day or 67 ml/hour

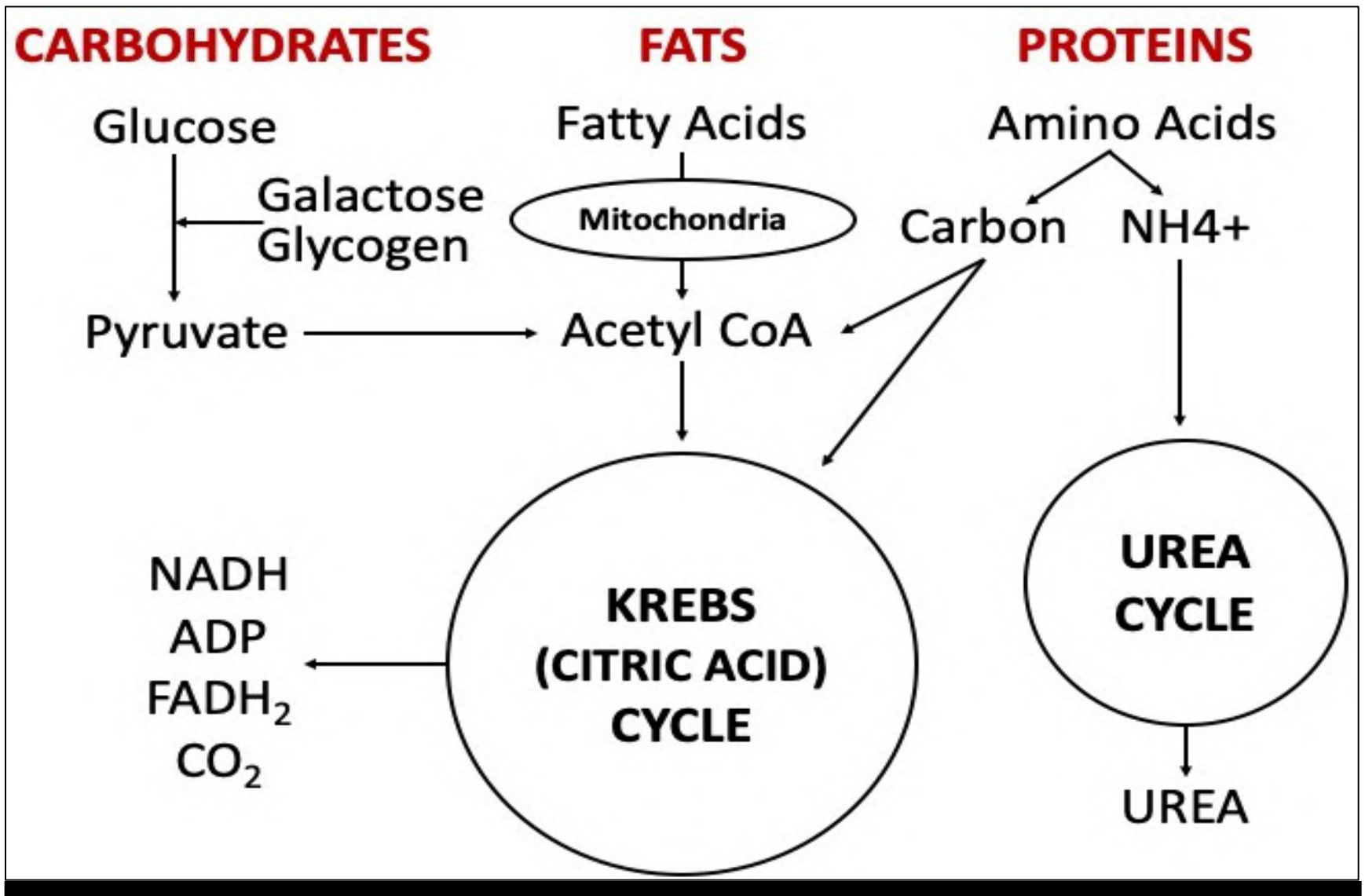
CLINICAL MANIFESTATIONS OF DEHYDRATION			
	MILD (< 5 %)	MODERATE (5-10%)	SEVERE (>10%)
Skin Turgor	Slightly Decreased	Decreased	Very Decreased
Skin Color	Pale	Sallow	Ashen
Oral Mucosa	Dry	Very Dry	Parched
Tears	Decreased	Absent	Absent
Fontanel	Normal	Normal	Decreased
Pulse	Increased	Increased	Marked Increase
Blood Pressure	Normal	Normal	Decreased
Urine Output	Mild Oliguria	Oliguria	Anuria
Mental Status	Irritable	Lethargic	Unresponsive

INBORN ERRORS OF METABOLISM

INTRODUCTION (RAMONA WARREN, M.D. MPH. 3/2020)
Inborn errors of metabolism are a diverse set of genetic disorders. The enzymatic defect results in an accumulation of substrate and a decrease in product. Both of these conditions can have deleterious effects. In addition, enzymatic defects can result in the use of alternative pathways and accumulation of harmful products.

This PEM Guide will focus on disorders of intermediate metabolism. These disorders are the result of enzyme deficiencies in the catabolism of carbohydrates, protein and fats.

DISORDERS OF INTERMEDIATE METABOLISM		
Food	Disorder	Primary Manifestation
Carbohydrates	Organic acidurias (Krebs cycle)	Anion gap, metabolic acidosis
Proteins	Urea cycle defects (Urea cycle)	Hyperammonemia
Fats	Fatty Acid Oxidation (Mitochondria)	Hypoketotic, hypoglycemia



OVERVIEW: CATABOLISM OF CARBOHYDRATES, FATS AND PROTEINS

CLASSIFICATION: INBORN ERRORS OF METABOLISM
Carbohydrate metabolism disorders. e.g. Galactosemia
Urea cycle defects: Ornithine Transcarbamylase Deficiency
Fatty acid oxidation disorders: Medium Chain Acyl Dehydrogenase Deficiency
Organic acidemias/acidurias: Methylmalonic Acidemia
Amino acid disorders
Lysosomal storage disorders
Peroxisomal disorders
Porphyrias
Purine or pyrimidine metabolism disorders
Disorders of steroid metabolism. e.g. Congenital Adrenal Hyperplasia
Mitochondrial function defects

NEWBORN SCREENING

The New York State newborn screening program tests for over 50 disorders (WEB LINK: NYS SCREENED DISORDERS**)**. The disorders tested for vary from state to state. Not all of the tests are for inborn errors. For example, HIV and sickle cell disease are included. Results are usually available within the first two weeks of life. There are conditions that are not included in the screening tests or are not present in the first two weeks of life, so normal newborn screening does not rule out an inborn error of metabolism.

PRESENTATION

Inborn errors can present as a neonatal catastrophe. Infants are usually normal at birth due to placental clearance of toxic metabolites. Symptoms begin after change from breast milk to formula or introducing a new food. A history of recurrent vomiting despite formula changes and failure to thrive is often present. Stressors such as infection, trauma or surgery can trigger these disorders. Symptoms are typically out or proportion with a normally self-limited illness.

In a small series of patients that presented to the emergency department and who were ultimately diagnosed with an inborn error of metabolism, the most common findings were neurologic signs (85%), including an altered mental status, seizures and hypotonia. The second most common findings were gastrointestinal complaints (58%) (Calvo, Pediatric Emergency Care 2000, PubMed ID: 11138882). Half of the patients had a combination of neurologic and gastrointestinal signs and symptoms. Older children and adults can present to the ED with a previously undiagnosed inborn error. The urea cycle defects, can present as late as adulthood.

The presentation of an inborn error is nonspecific and overlaps considerably with other childhood disease so a high index of suspicion is warranted. A family history of unexplained infant deaths or consanguinity should raise suspicion.

INFANT PRESENTATIONS	
Neurologic	Acute decline: Lethargy, seizures, hypotonia.
Gastrointestinal	Poor feeding, vomiting, diarrhea and dehydration,
Respiratory	Quiet Tachypnea: Tachypnea without increased work of breathing and normal oxygen saturation, chest examination and chest XRAY. In compensation for metabolic acidosis or direct CNS stimulation.

CHILDHOOD PRESENTATIONS
Severe symptoms or rapidly deteriorate with mild childhood illnesses
Recurrent episodes of lethargy, emesis leading to alteration of mental status.
Failure to thrive, food aversions
Unexplained seizures, dystonia, myoclonus, hypotonia, ataxia
Mental retardation or cerebral palsy without a clear etiology
Hepatosplenomegaly
Unusual odors
Disorders of multiple organ systems

PHYSICAL EXAMINATION	
Pulmonary	Quiet tachypnea
Cardiac	Cardiomegaly, dysrhythmias
Gastrointestinal	Hepatomegaly, splenomegaly
Neurologic	Altered mental status, hypotonia
Hematologic	Neutropenia, thrombocytopenia
GU	Ambiguous genitalia
General	Unusual rashes, odors, cataracts

UNUSUAL ODORS	
Maple syrup urine disease	Burnt sugar
Isovaleric acidemia	Sweaty socks, cheese
Methylmalonic aciduria	Fruity (ketosis), ammonia
Phenylketonuria	Mouse urine, musty
Tyrosinemia	Cabbage
Methionine malabsorption	Malt or hops
3-Methylcrotonic aciduria	Tomcat urine
3-OH-3methylglutaric	Tomcat urine
Propionic acidemia	Fruity (ketosis), ammonia

LABORATORY TESTING

In general, the diagnostic workup of an inborn error is extensive, but a few common laboratory features include: an anion gap metabolic acidosis, hyperammonemia and hypoglycemia without ketosis. If suspicions are high, set aside, on ice, an extra vial of blood, urine, and CSF so there is a sample of each at the baseline state. These are important, as abnormalities may only be present when they are ill.

LABORATORY TESTING	
Initial Testing	Definitive Testing
CBC, coagulation profile	Serum for:
VBG/ABG with lactate	Amino acids
BMP, bedside glucose	Beta hydroxybutyrate
Ammonia level	Urine for:
Liver function tests	Reducing substances
Urinalysis (ketones, crystals)	Organic acids
Infection evaluation: Blood, urine culture	Amino acids

MANAGEMENT

After addressing airway, breathing and circulation the primary goals are to remove toxic metabolites and decrease production of toxic intermediaries by preventing catabolism and promoting anabolism. A definitive identification of the disorder should not delay treatment. The severity of the metabolic derangement will guide therapy.

MANAGEMENT OVERVIEW	
1	Supportive Care: Oxygenation, ventilation as needed, fluid resuscitation
2	Don’t delay treatment until a definitive diagnosis is made
3	Decreased production of the toxic metabolites through prevention of catabolism
4	Decreased production of the toxic metabolites through promotion of anabolism
5	Increased excretion/removal of the toxic metabolite
6	Treat precipitation factors: e.g. antibiotics for infection
7	Cofactor administration

1. ORGANIC ACIDEMIAS/ACIDURIAS

INTRODUCTION

In the organic acidurias, enzyme deficiencies result in the accumulation of metabolic or organic acids. The concept is similar to the accumulation of organic acids in the absence of substrate. Lactate and ketoacids are organic acids. Lactate accumulates as a result of cellular hypoxia. Ketoacids accumulate as a result of intracellular hypoglycemia.

The majority of organic acidurias are due to the impaired catabolism of the carbohydrate portion of amino acids. These patients present with severe anion gap metabolic acidosis. Organic acid accumulation can cause hepatic, neurologic, and hematologic (bone marrow suppression) toxicity.

PRESENTATION

Patients present from newborn to early infancy. Patients will present with quiet or effortless tachypnea in compensation (respiratory alkalosis) for metabolic acidosis. There is no increase work of breathing. Respiratory examination, oxygen saturation and chest XRAY are normal. Neurologic symptoms include an altered mental status, seizures and hypotonia. Bone marrow toxicity can result in hemorrhage due to thrombocytopenia and infection due to neutropenia. Unusual odors may be present

LABORATORY DIAGNOSIS

The primary laboratory feature of the organic acidurias is an anion gap metabolic acidosis due the accumulation of substrate organic acids that are not processed into their usual product due to enzyme deficiency. A mild hyperammonemia may be present. This should be distinguished from the severe hyperammonemia that is seen in the urea cycle defects. The accumulation of intermediate organ acids can result in liver toxicity and bone marrow suppression.

LABORATORY DIAGNOSIS: ORGANIC ACIDURIAS:	
Accumulation of organic acids	Anion gap metabolic acidosis
Hepatic	Hypoglycemia (impaired gluconeogenesis) Transaminitis, hyperammonemia*
Hematologic	Neutropenia, thrombocytopenia
Urinalysis	Ketonuria (inhibition of ketone oxidation)
Definitive diagnosis	Urine for organic acids, plasma amino acids
*Not elevated to the extent seen with urea cycle defects	

DIFFERENTIAL DIAGNOSIS: ANION GAP METABOLIC ACIDOSIS			
C	Carbon monoxide, Cyanide	P	Paraldehyde, Propylene glycol
A	Aminoglycosides, Acetaminophen	I	Iron, Isoniazid, Inborn errors
T	Theophylline, Toluene	L	Lactic acid
M	Methanol, Metformin	E	Ethylene Glycol, Ethanol (lactate)
U	Uremia	S	Salicylate
D	Ketoacidosis: Diabetic ketoacidosis, alcoholic ketoacidosis, starvation ketosis		
Anion Gap = ((Na^+ - [Cl^- + $HCO3^-$]), normal = 8-12), *e.g. Organic acidurias			

MANAGEMENT

Management of the organic acidurias focuses on supportive care (hydration) as well as efforts to correct the metabolic acidosis by removal and decreased production of organic acids. Empiric antibiotics may be required due to bone marrow suppression.

Care should be taken in intubating and mechanically ventilating a patient with a respiratory alkalosis in compensation for a metabolic acidosis (organic acidosis, salicylate toxicity, diabetic ketoacidosis). If these patients are not hyperventilated to the extent they were prior to intubation, the pH can plummet and precipitate cardiopulmonary arrest.

MANAGEMENT: ORGANIC ACIDURIAS
INCREASED REMOVAL
Fluid resuscitation
Correct acidosis: $NaHCO_3$ promotes organic acid excretion $NaHCO_3$: 1-2 meq/kg or Based on base deficit: HCO_3 deficit = Weight (kg) x base deficit x 0.3
DECREASED PRODUCTION
Dextrose: Corrects hypoglycemia, promotes anabolism Bolus: 0.5-1.0 gm/kg = D10: 5-10 mg/kg, D25: 2-4 ml/kg, D50: 1-2 ml/kg Maintenance: D10 NS @ 1.5 x maintenance provided 6-8 mg/kg/hour
Avoid precursors: No protein intake (many due to amino acid catabolism)
OTHER
If ventilation is absolutely necessary must hyperventilate to the same extent that the patient is compensating for metabolic acidosis or pH will drop precipitously and may result in cardiac arrest
“Antidotes”: Biotin, Thiamine, Glycine
Consider sepsis evaluation, empiric antibiotics

2. UREA CYCLE DEFECTS

INTRODUCTION

The urea cycle defects are enzyme deficiencies in the urea cycle that result in the reduction of catabolism of the nitrogen component of amino acids and the accumulation of ammonia. Ammonia is central nervous system toxin. Many of the urea cycle defects are named after the amino acid that is being metabolized.

PRESENTATION

These patients typically present 24-48 hours after birth with neurologic symptoms due to severe hyperammonemia. This may include an altered mental status, seizures or hypotonia.

DIFFERENTIAL DIAGNOSIS: ALTERED MENTAL STATUS:	
A	Alcohol, Abuse
E	Encephalitis, Electrolytes, Endocrine
I	Insulin, Intussusception, Inborn errors of metabolism
O	Overdose, oxygen deficiency (hypoxia)
U	Uremia
T	Trauma, tumor (CNS),
I	Infection
P	Poisoning, psychogenic
S	Seizures, shock, stroke, space occupying lesion

LABORATORY DIAGNOSIS

The hallmark of the urea cycle defects is extreme hyperammonemia due to the inability to catabolize the nitrogen component of amino acids. A transaminitis can develop secondary to the severe hyperammonemia. Electrolytes are typically normal. A respiratory alkalosis is present due to direct central nervous system stimulation. This is in contrast to the organic acidurias with respiratory alkalosis in compensation for metabolic acidosis. Ornithine transcarbamylase deficiency (OTC) is the most common urea cycle defect and orotic acid crystals are seen in the urine.

LABORATORY DIAGNOSIS: UREA CYCLE DEFECTS	
Hyperammonemia	Severely elevated
Electrolytes/ABG	Typically normal electrolytes (no anion gap metabolic acidosis) Respiratory alkalosis via direct CNS stimulation
Urinalysis	Orotic acids crystals (Ornithine transcarbamylase deficiency)
Hepatic	Transaminitis secondary to hyperammonemia
Definitive diagnosis	Serum amino acid profile, specific enzyme assays

MANAGEMENT

The management of the urea cycle defects if focused on decreasing ammonia production and increasing ammonia excretion. Protein intake should be halted to decrease catabolism and dextrose provided to promote anabolism.

MANAGEMENT: UREA CYCLE DEFECTS:
DECREASE AMMONIA PRODUCTION
Avoid precursors: No protein intake (all related to amino acid catabolism)
Dextrose: Promotes anabolism Bolus: 0.5-1.0 gm/kg = D10: 5-10 mg/kg, D25: 2-4 ml/kg, D50: 1-2 ml/kg Maintenance: D10 NS @ 1.5 x maintenance provided 6-8 mg/kg/hour
GI tract sterilization: PO Neomycin, prevents bacterial ammonia production
INCREASE AMMONIA EXCRETION
Fluid resuscitation
Avoid alkalization: Increases NH_4 that crosses the blood brain barrier
Hemodialysis
Lactulose: Inhibits GI tract NH_4 production/absorption
Antidotes: Sodium benzoate, Sodium phenylacetate (nitrogen scavengers)

3. FATTY ACID OXIDATION DISORDERS

INTRODUCTION

Fatty acid oxidation disorders are a group of autosomal recessive enzymatic defects in the catabolism of fatty acids. This includes failures of mitochondrial beta oxidation of fatty acids or failure of carnitine based transport of fatty acids into the mitochondria. Over 30 enzymes or carriers are involved in this process. The most common disorder is medium chain acyl-CoA dehydrogenase deficiency (MCAD).

Small and medium chain fatty acids enter the mitochondria directly while long chain fatty acids require transport into the mitochondria via the carnitine shuttle.In the mitochondria, fatty acids are catabolized to NADH+ and $FADH_2$ and Acetyl Coenzyme A (Acetyl-CoA). NADH+ and $FADH_2$ are further metabolized by the respiratory chain via oxidative phosphorylation to ATP. Acetyl Coenzyme A (Acetyl-CoA) is metabolized via the tricarboxylic acid cycle into 1. reducing equivalents for the electron transport chain, 2. ketone bodies (an alternative fuel) and 3. cholesterol synthesis.

PRESENTATION

The primary result of fatty acid oxidation disorders is deficient energy production. Severe forms, such as long chain fatty acid oxidation disorders present in the first few days of life. MCAD, a medium chain disorder presents in later infancy or early childhood. Signs and symptoms of hypoglycemia predominate. These include both central nervous system and adrenergic findings. The majority of these findings are nonspecific symptoms such as lethargy/altered mental status or failure to feed. Symptoms occur over a shorter duration of fasting in infants than for older children. Long chain disorders can present with cardiomyopathy and arrhythmias.

HYPOGLYCEMIA: SIGNS AND SYMPTOMS	
CNS	Irritability, lethargy/coma, fatigue, seizure, syncope, coma
Adrenergic	Palpitations, tremors, anxiety, diaphoresis

LABORATORY TESTING

The hallmark of fatty acid oxidation disorders is the presence of hypoglycemia in the absence of ketoacidosis/ketonuria. Newborn screening varies by state. **DIFFERENTIAL DIAGNOSIS:** The primary disorders to consider are hyperinsulinism (hypoketotic hypoglycemia), cardiomyopathy, rhabdomyolysis and Reye syndrome (encephalopathy liver dysfunction.

LABORATORY DIAGNOSIS: FATTY ACID OXIDATION DISORDERS	
Electrolytes/ABG	Hypoglycemia with absent ketosis/ketonuria
	Mild metabolic acidosis due to dehydration
Hepatic	Transaminitis
	Hyperammonemia (mildly elevated) if severe liver involvement
CPK	Myopathy (cardiac, skeletal), rhabdomyolysis
Differential diagnosis	Insulin, cortisol, ACTH, beta hydroxy butyrate
Definitive diagnosis	Plasma acyl carnitine profile, total and free carnitine

DIFFERENTIAL DIAGNOSIS: HYPOGLYCEMIA	
Etiology	Example
↓ Available	Poor intake
	↓ Absorption (diarrhea)
↓ Production	Abnormal glycogenolysis, ↓ glycogen stores
	Abnormal gluconeogenesis
	Fatty acid oxidation disorders
	Adrenal insufficiency
	Hypothyroid, hypopituitarism
	Organic acidemia/aciduria
↑ Utilization	Hyperinsulinism, tumors, sepsis, shock
↓ Alternatives	↓ fat stores, ↓ ketones (Fatty acid oxidation disorders)
Medications	Ethanol, hypoglycemic agents, salicylates, beta blockers

MANAGEMENT

The focus of management of fatty acid oxidation disorders is in preventing decompensation. Fasting, for any reason (viral infection) can result in life-threatening hypoglycemia in a short time frame. Oral or intravenous glucose should be administered. Patients with known disease should have a letter from their metabolic specialist outlining the patient's specific regimen to follow.

SAFE FASTING TIME	
< 6 months	Q3 hours
6-12 months	Q4 hours (day), Q6-8 hours (night)
> 12 months	Q4 hours (day), Q8 hours (night)
Intercurrent illness can shorten safe fasting times	

MANAGEMENT: FATTY ACID OXIDATION DISORDERS
Dextrose: Promotes anabolism Bolus: 0.5-1.0 gm/kg = D10: 5-10 mg/kg, D25: 2-4 ml/kg, D50: 1-2 ml/kg Maintenance: D10 NS @ 1.5 x maintenance provided 6-8 mg/kg/hour

APPENDIX: DISORDERS OF INTERMEDIATE METABOLISM

COMPARISON: LABORATORY DIAGNOSIS AND MANAGEMENT			
	Organic Acidemia/ Aciduria	Urea Cycle Defects	Fatty Acid Oxidation Disorders
AG[1] metabolic acidosis	YES	NO[2]	NO[2]
Respiratory alkalosis (Quiet tachypnea)	YES (compensation)	YES (direct stimulation)	NO
↑ Ammonia	Mild-Moderate	Severe	Mild-Moderate
Transaminitis	YES	YES	YES
Hypoglycemia,	YES	NO	YES
Ketosis, ketonuria	YES	NO	NO
↓ WBC, hb/hct, platelets	YES	NO	NO
Fluid resuscitation	YES	YES	YES
↑ Glucose → ↑ Anabolism	YES	YES	YES
↓ Protein → ↓ Catabolism	YES	YES	YES
$NaHCO_3$	YES	NO	NO
Hemodialysis	RARELY	YES	?
“Antidotes”	B12, Biotin	NaX[3], Arginine	?Carnitine

1. AG = Anion Gap
2. Unless, dehydration and shock
3. NaX = Na phenylacetate and Na benzoate

RHABDOMYOLYSIS

INTRODUCTION (ELLEN DUNCAN, MD PhD, 12/2018)
Rhabdomyolysis is characterized by necrosis of skeletal muscle and the release of intracellular muscle contents. It is similar in concept to tumor lysis syndrome in that as cells dies, cell contents are released, resulting in metabolic abnormalities that have the potential to cause end organ damage. Potassium, phosphates (acids), and myoglobin are the principle substances released with myocyte breakdown. It is thought that the mechanism of injury is related to ATP depletion and an increase in intracellular calcium. Acute kidney injury is the most common complication.

The causes of rhabdomyolysis can be divided into exertional and non-exertional causes. Non-exertional causes can be further divided into traumatic and non-traumatic etiologies. Patients with exertional rhabdomyolysis tend to fare better than those with non-exertional causes. Infection, congenital disorders, trauma, and exercise are the most common causes in children.

CAUSES OF RHABDOMYOLYSIS	
EXERTIONAL	
Physical activity in untrained individuals	
Exercising in hot conditions, e.g. athletes on sports teams, sickle cell disease/trait	
Intense physical activity such as cross fit training and spinning	
Eccentric exercises: e.g. movement against the natural direction of muscle activity, such as lowering weight during biceps curls	
NON-EXERTIONAL: TRAUMATIC	
Multiple injuries, crush injuries	
Immobilization e.g. coma, restraint of the agitated patient	
Compartment syndrome	
High-voltage electrical injury	
NON-EXERTIONAL: NON-TRAUMATIC	
Drugs	Drugs: Alcohol, heroin, cocaine, amphetamines, methadone, LSD Medications: Statins, colchicine
Toxins	Carbon monoxide, snake and insect bites, poisonous mushrooms
Foods	Licorice, quail
Infections	Viral: Influenza, EBV, HSV, CMV, HIV, coxsackievirus Bacterial: *Mycoplasma pneumoniae*, legionella, *Strep pyogenes*, necrotizing fasciitis, sepsis
Metabolic-Endocrine	Diabetic ketoacidosis, hyperthyroid crisis Hypokalemia, hyponatremia
Rheumatology	Dermatomyositis, polymyositis
Genetic	Metabolic myopathies, muscular dystrophy
Hyperpyrexia syndromes	Malignant hyperthermia, neuroleptic malignant syndrome, serotonin syndrome
Neurologic	Status epilepticus, psychotic agitation

COMPLICATIONS	
Acute kidney injury (AKI)	Due to a combination of the following: 1. Pre-renal azotemia 2. Pigment cast deposition leading to tubular obstruction 3. Tubular injury from free iron released by myoglobin breakdown 4. Metabolic acidosis Rare in exertional rhabdomyolysis Most commonly oliguric, dialysis may be required
Compartment syndrome	Especially after fluid resuscitation Crush injury, necrotizing fasciitis
DIC	Severe rhabdomyolysis with release of prothrombotic substances
Arrhythmias Cardiac arrest	Due to electrolyte abnormalities such as hyperkalemia, hypocalcemia, metabolic acidosis

CLINICAL MANIFESTATIONS

The spectrum of disease can range from asymptomatic to life-threatening. In patients with severe disease, fatigue, fever, tachycardia, and gastrointestinal symptoms may also be present. Muscle tenderness may be present on examination. If present, muscle swelling is typically seen after fluid resuscitation. Hypovolemia results from third spacing of fluids into the injured muscles.

"CLASSIC TRIAD" OF RHABDOMYOLYSIS (ONLY IN 50% OF PATIENTS)
1. Myalgias, muscle stiffness, cramping (often in proximal muscle groups)
2. Dark or red urine: Myoglobinuria (+) urine dipstick for blood, negative RBCs (50%)
3. Weakness: Weakness is greatest proximally. Muscle lesions typically associated with normal reflexes and normal sensation.

DIFFERENTIAL DIAGNOSIS
Metabolic myopathies (consider if recurrent episodes)
Myocardial infarction (high CK-MB)
Hemolysis leading to hematuria
Foods, dyes, and drugs causing dark urine
Inflammatory myopathies (myalgias and elevated CK)
Hematuria: Renal stones, post infectious glomerulonephritis

DIAGNOSTIC TESTING

Laboratory testing should target markers of disease (e.g. CPK), disease complications (e.g. BUN/creatinine), and the cause of rhabdomyolysis (e.g. urine toxicology screen). An EKG should be obtained early to assess for arrhythmias and/or changes consistent with electrolyte abnormalities.

LAB	FINDING
Creatine phosphokinase (CPK) or Creatine kinase (CK)	Typically ≥ 5 times the upper limit (>1,000 IU/L) CPK > 5,000 indicates risk of kidney injury Onset 2-12 hours post injury, peaks 24-72 hours Consider compartment syndrome if persistent/worsening elevation MM (skeletal muscle) fraction elevated MB (myocardial) fraction may be mildly elevated
Urinalysis	(+) heme on dipstick with < 5 RBC/HPF (80% SN), +/- proteinuria
Urine Myoglobin	Poor sensitivity due to rapid clearance, often a send out test
Basic Metabolic Profile	Metabolic acidosis Anion gap: Release of intracellular organic acids Non-Anion gap: Lactate Hypocalcemia (early: 1st few days) due to entry into muscle Hypercalcemia (late) due to release from muscle Hyperkalemia Hyperphosphatemia
Transaminases	May be slightly elevated
Other	Hyperuricemia (elevates before CPK) CBC to exclude hemolytic anemia ESR, CRP elevations are nonspecific and vary with etiology DIC: Coagulation profile, fibrin split products, fibrinogen
EKG	Arrhythmia, signs of hyperkalemia, hypocalcemia

MANAGEMENT

The primary focus of management is fluid resuscitation and the correction of metabolic abnormalities to prevent complications. Management of disease complications may also be required (e.g. hemodialysis). There is little evidence to support most treatment recommendations.

OVERVIEW: MANAGEMENT OF RHABDOMYOLYSIS	
Electrolyte correction:	Hyperkalemia: Calcium, Lasix, insulin/glucose, albuterol, HCO_3, Hypocalcemia: Ca Chloride: 0.2 ml/kg, Ca Gluconate: 0.6 ml/kg (Only be used for severe ↓ Ca or ↑ K, could exacerbate the late↑ Ca) Hyperuricemia: Allopurinol PO for the Uric acid > 8 mg/dl Hyperphosphatemia: Consider oral phosphate binders Metabolic acidosis: Fluid resuscitation, consider HCO3
Fluid resuscitation	1-2 liters/hour (adult), 20-40 ml/kg/hour (children) Target is hypervolemia. Maintain urine output at 1-3 ml/kg/hour
Na HCO3	Add 3 ampules NaHCO3 to D5W, run at 1.5-2 x maintenance rate Contraindications: ↓ Ca, serum pH > 7.5, HCO3 > 30 Discontinue if urine pH does not rise to greater than 6.5 after 3-4 hours of if develops any of the contraindication above
Treat Causes	Malignant hyperthermia (Dantrolene), hyperthermia (cooling), infection (antibiotics), compartment syndrome (fasciotomy), agitation (sedative)
Complications	e.g. hemodialysis for renal failure

FLUID RESUSCITATION: Fluid resuscitation is aimed at restoring perfusion and increasing renal blood flow to prevent pigment deposition and subsequent kidney injury. The optimal volume and rate of fluid resuscitation has not been established. In general, isotonic saline at 1-2 liters/hour (adults) or 20-40 ml/kg/hours (children) is recommended. Fluid administration should be tailored to trends in CPK and should continue until CPK is less than 5,000. Loop diuretics may be considered for those patients with volume overload due to renal failure.

URINARY ALKALINIZATION: Urinary alkalization has been recommended. However, its use is controversial, as no randomized clinical trials have demonstrated its efficacy. Urinary alkalinization may decrease pigment deposition in the kidney. It is contraindicated if there is hypocalcemia or metabolic alkalosis (serum pH > 7.5, HCO3 > 30). Urinary alkalinization can be achieved by adding 3 ampules of NaHCO3 to D5W and running it at 1.5 to 2 times the normal maintenance rate. The goal is to maintain urine Ph in the range of 7.5-8.0. It is essential to avoid hypokalemia; in the setting of hypokalemia, the renal tubule re-absorbs potassium in exchange for hydrogen ions. Hydrogen ions acidify the urine, thus reducing the efficacy of alkalinization.

DISPOSITION

Patients with mild exertional rhabdomyolysis without comorbidities or evidence of complications and who have a down-trending CPK and/or CPK < 5,000 may be discharged after sufficient hydration. Patients not meeting these conditions should be admitted.

APPENDIX: MEDICATIONS FOR HYPERKALEMIA

CALCIUM	
Mechanism	Stabilizes cardiac cell membranes to effect of hyperkalemia
Indications	Prolonged QRS
Timing	Onset: 2-3 minutes, duration 30-60 minutes
Calcium Chloride	Calcium Chloride 10% (1 gram/10ml) (13.6 meq elemental Ca+/10ml) Child: 0.2 ml/kg (20 mg/kg), maximum dose 1 gram (10 ml) Adult:10 ml (1 gram) More rapid dissociation in the blood stream than Calcium Gluconate Risk of tissue necrosis with extravasation use CVL or large PVL
Calcium Gluconate	Calcium Gluconate 10% (1 gram/10ml) (4.6 meg elemental Ca+/10ml) Child: 0.6 ml/kg (60 mg/kg), maximum dose 3 grams (30 ml) Adult: 30 ml (3 grams) Requires hepatic metabolism → Slower onset than Calcium Chloride Avoid in liver failure, shock
Frequency	Repeat Q5 minutes if EKG changes persist or recur
Caveat	Slow infusion on cardiac monitor over 3-5 minutes Do not give in same IV with $NaHCO_3$ ($CaCO_3$ precipitates) Contraindicated in digoxin toxicity

INSULIN/GLUCOSE	
Mechanism	Enhances activity of Na-K-ATPase pumps Shifts K+ from extracellular to intracellular space
Indications	EKG changes, K+ > 6.5
Timing	Onset 10-20 minutes, peak at 30-60 minutes, duration 4-6 hours
Indications	EKG changes or K+ > 6.5-7.0 meq/l
Adult Dosing	Glucose: 25 grams (50 ml of D50) Regular Insulin: 10 units
Child Dosing	Glucose:1 gram/kg D10 = 10 ml/kg, D25 = 4 ml/kg, D50 = 2 ml/kg) Regular Insulin: 0.2 units per gram of glucose
Caveats	Provide glucose infusion to avoid hypoglycemia Monitor bedside glucose closely

$NaHCO_3$	
Mechanism	Increase H+ ion out of cell to buffer HCO_3. K+ into cell in exchange for H+
Dose	Adult: 150 meq $NaHCO_3$ in 1 liter D5W at 250 ml/hour Do not give hyperosmolar concentration (e.g. 50 meg/50ml)
Caveat	Limited efficacy. Do not give with Ca++ ($CaCO_3$ precipitates) Not indicated in the absence of metabolic acidosis

BETA AGONISTS	
Mechanism	Decrease potassium release from cells,
Albuterol	10-20 mg/4ml via nebulizer over 10 minutes, duration 2 hours Note: This is 4-8 times the typical asthma dose of 2.5-5.0 mg

FUROSEMIDE (LASIX)	
Mechanism	Loop diuretic. Enhances excretion of K+
Dose	Adult: 20-40 mg IV Child: 1-2 mg/kg IV
Caveat	Higher dose may be required in renal insufficiency
	Limited short-term efficacy
	Replace fluid losses (unless the patient is volume overloaded)

SODIUM POLYSTYRENE SULFONATE (KAEXOLATE)	
Mechanism	Binds potassium in GI tract, releases Na+ in exchange
Timing	Onset: 1-2 hours
Dose	Adult: 15-30 grams PO Child: 1 gm/kg PO
	May also be given as a retention enema (50 gm in 250 ml D5W)
	May repeat dose in 4-6 hours based on repeat K+
Caveat	Do not use with sorbitol. May cause intestinal necrosis
	Do not use in post-op or renal transplant patients

THYROTOXIC CRISIS

INTRODUCTION (KATRINA KNAPP, D.O., 4/2016)
Thyrotoxicosis is the clinical manifestation of hyperthyroidism. Thyrotoxic crisis, otherwise known as thyroid storm, is a life threatening condition that involves multi-organ system dysfunction including severe cardiovascular, thermoregulatory, gastrointestinal, and neurobehavioral symptoms. It is seen in less than 1% of adults with hyperthyroidism and is rarer in children. It has a high mortality rate (10-30%) if not recognized early and treated aggressively.

PATHOPHYSIOLOGY
Thyroid hormones are produced in the thyroid gland under the influence of thyroid stimulating hormone (TSH). Thyroid releasing hormone (TRH) from the hypothalamus stimulates TSH release from the pituitary. In order to maintain thyroid hormone levels in normal range, circulating levels of thyroid hormones exert feedback inhibition on the hypothalamus and pituitary axis (HPA).

There are 2 active thyroid hormones: triiodothyronine (T3) and L-thyroxine (T4). T4 is exclusively made in the thyroid gland. T3 is also made in the thyroid but 80% is made in the peripheral tissues by de-iodination of T4. Iodine is essential for thyroid hormone synthesis.

T4 is more abundant than T3 and a greater proportion is protein bound (e.g. TBG, thyroid binding globulin). Only 0.03% of T4 is unbound. It is the unbound (“free”) hormones that are active. A greater proportion of T3 is the free form, and has a greater affinity (10 fold) for tissue thyroid hormone receptors than T4. T4 can also be metabolized to reverse T3 which is completely inactive. Most of the biologic activity of thyroid hormones is due to T3, but it is less reliably identified which is why we typically measure free T4.

Thyroid hormones increase oxygen consumption in all tissues except the brain, spleen, and testes. They also stimulate adrenergic receptors sites in myocardial cells and glucocorticoid receptors in lung tissue. In addition, thyroid hormones accelerate the metabolism of other hormones (insulin, cortisol).

Thyrotoxicosis can develop in patients with longstanding untreated hyperthyroidism or it can be precipitated by an acute event (see table below). Thyroid storm is a hyper-metabolic and beta-adrenergic driven state. Over production of thyroid hormones increase the density of beta-adrenergic receptors enhancing the effect of catecholamines. 90% of thyrotoxicosis is caused by hyperthyroidism. The most common cause in children is Grave’s Disease. Grave’s disease is an autoimmune disorder that results in antibody production (TSH receptor stimulating immunoglobulins) that stimulate TSH receptors resulting in excessive stimulation of the thyroid gland.

COMMON CAUSES/PRECIPITATING FACTORS OF THYROTOXICOSIS
Primary hyperthyroidism (Grave’s disease, toxic multi-nodular goiter)
Secondary hyperthyroidism (pituitary adenoma)
Thyroiditis (postpartum, radiation thyroiditis)
Drug Induced (Lithium, Iodine, Amiodarone, excessive thyroid hormone ingestion, anticholinergic drugs, adrenergic drugs, salicylates)
Abrupt cessation of anti-thyroid medications
Thyroid or non-thyroid surgery in a patient with unrecognized hyperthyroidism
Acute illness (diabetic ketoacidosis, sepsis), labor and delivery
Trans-placental passage of maternal thyroid stimulating immunoglobulins

CLINICAL MANIFESTATIONS

The diagnosis of thyrotoxic crisis is based upon the presence of severe life threatening symptoms (cardiovascular dysfunction, altered mental status, hyperpyrexia) in a patient with biochemical evidence of hyperthyroidism. Symptoms may be nonspecific

A clinical scoring system for diagnosing thyroid storm was published (See table below, Burch, Endo-Metab Clinics of NA 1993, PubMed ID: 8325286) but has not been validated.

DIFFERENTIAL DIAGNOSIS	
Endocrine	Pheochromocytoma, adrenal crisis
Infections	Sepsis, gastroenteritis
Toxicologic	Hyperpyrexia syndromes: malignant hyperthermia, neuroleptic malignant syndrome, serotonin syndrome
	Anticholinergics, Sympathomimetics (cocaine, amphetamine)
	Medication withdrawal: cocaine, opiates
Environmental	Heat stroke
Psychiatric	Anxiety/panic attack

PHYSICAL EXAMINATION	
Eyes	Staring appearance due to upper eyelid retraction, eyelid lag (both due sympathetic over-activity). Light sensitivity
	Grave's ophthalmopathy (periorbital edema, proptosis) is an autoimmune mediated inflammation and edema of extraocular muscles and intra-orbital connective tissue. 50-70% of children.
Neck	Smooth, diffusely and symmetrically enlarged goiter. No palpable nodularity. Typically, non-tender to palpation. Bruit over a large vascular gland possible
Cardiac	Most common cardiac finding is sinus tachycardia. Heart failure and arrhythmia (atrial fibrillation) more common in adults. High cardiac output produces bounding pulse, widened pulse pressure.
Skin	Warm (cutaneous vasodilation) and moist (diaphoresis)
	Grave's dermatopathology (bilateral non-pitting edema with associated thickening and induration of the skin) Typically seen over the ankles and feet. Rare in children
Neurologic	Altered mental status, tremor, agitation, psychosis, hyperreflexia, weakness

PRESENTATION	
Metabolic	Fever, sweating, metabolic acidosis, hyperventilation, amenorrhea, weight loss
GI	Nausea, vomiting, diarrhea, abdominal pain, hepatic dysfunction
Cardiac	Sinus tachycardia out of proportion to the degree of fever Hypotension, congestive heart failure Atrial fibrillation (up to 20% of adults, rare in children), Prolonged QT interval
Neuro-Psychiatric	Agitation, delirium, psychosis, stupor, coma
Newborns	Irritable, unable to feed appropriately, and have inadequate weight gain.

POINT SCALE FOR THE DIAGNOSIS OF THYROID STORM			
TEMPERATURE		GASTROINTESTINAL DYSFUNCTION	
99.0-99.9	5	Absent	0
100.0-100.9	10	Moderate (N,V,D, abd pain)	10
101.0-101.9	15	Severe (Jaundice)	20
102.0-102.9	20	PRECIPITANT HISTORY	
103.0-103.9	25	Positive	0
≥ 104.0	30	Negative	10
TACHYCARDIA		CNS DYSFUNCTION	
100-109	5	Absent	0
110-119	10	Mild (Agitation)	10
120-129	15	Moderate*	20
130-139	20	Severe (Seizure, Coma)	30
≥ 140	25	*Delirium, psychosis, severe lethargy	
ATRIAL FIBRILLATION			
Absent	0		
Present	10		
CONGESTIVE HEART FAILURE			
Absent	0	**TOTAL SCORE**	
Mild	5	THYROID STORM	> 45
Moderate	10	IMPENDING STORM	24-44
Severe	20	STORM UNLIKELY	< 25

LABORATORY TESTING

Laboratory findings are consistent with primary hyperthyroidism (Low TSH, high FT4/T3). Values are similar to those seen in uncomplicated hyperthyroidism. Abnormal liver function tests (thyroid hormones play a role in the metabolism of bilirubin) and an elevated glucose (catecholamine induced inhibition of insulin and increase glycogenolysis), elevated calcium (increased bone resorption) and leukocytosis or leukopenia may be seen.

MANAGEMENT

Initially treatment is directed at inhibiting the peripheral effects of thyroid hormone and decreasing metabolic rate and cardiac workload. Subsequent treatment is directed at decreasing thyroid hormone production, inhibiting release and enhancing clearance as well as recognition and treatment of precipitating factors. The patient should be admitted to an ICU to monitor for clinical deterioration and to provide ongoing care. See also: Hyperthyroidism Guidelines: American Association of Clinical Endocrinologists 2011: PubMed ID: 21700562

THIONAMIDES (Propylthiouracil (PTU), Methimazole). Decreases synthesis of thyroid hormones within 1-2 hours by inhibiting iodine oxidation. Do not effect release of preformed hormone. One or the other is administered and not both. PTU preferred in life-threatening illness. Methimazole for less severe illness.

INITIAL STABILIZATION
Airway protection, oxygenation, ventilation PRN
EKG, cardiac monitoring, avoid medications that can prolong the QT interval
Supportive measures including aggressive cooling e.g. cooling blankets
Fluid resuscitation (increased insensible fluid losses)
Acetaminophen for temperature regulation*
Decrease metabolic rate: Beta blockers (e.g. Propranolol)
Decrease thyroid hormone production: Methimazole, Propylthiouracil, Iodine
Consider corticosteroids, bile acid sequestration (e.g. Cholestyramine)
Treatment of precipitating factors
Admit to Intensive Care Unit
*DO NOT GIVE ASPIRIN - May increase T4 by displacing thyroid hormone from protein binding sites and increase metabolic demand due to uncoupling of oxidative phosphorylation

PROPRANOLOL	
Action	Inhibits the peripheral effects of thyroid hormone Beta-blocker. Limits B-adrenergic activity and block peripheral conversion of T4 to T3. Highly lipid soluble, crosses the blood brain barrier so may help with neurologic symptoms
Indications	Tachycardia, hypertension, agitation
Dose	0.5 – 1 mg IV over 10 minutes then 1-2 mg every few hours Adolescent/Adult: 60-80 mg PO every 4-6 hours Infants/Children: 0.5 to 2 mg/kg/day PO divided Q6 hours
Contra-indications	Congestive heart failure, hypotension Asthma: choose a cardio-selective agent e.g. Atenolol, Metoprolol Severe asthma: consider rate control with calcium channel blocker
Alternatives	Esmolol: Loading 250-500 mcg/kg then 100 mcg/min infusion
Adverse effects	Hypotension, hypoglycemia, bronchospasm, heart block

PROPYLTHIOURACIL (PTU)	
Action	Decreases synthesis of thyroid hormones within 1-2 hours Decreases peripheral conversion of T4 to T3
Indications	Preferred for life-threatening illness: Decreases synthesis of thyroid hormones within 1-2 hours, may more rapidly decrease T3 Preferred during first trimester in pregnancy due to less teratogenicity compared to Methimazole (can cross the placenta)
Dose	Adolescent/Adult: 500-1000 mg then 250 mg PO Q4 hours Child: 5-7 mg/day PO divided Q8 hours (maximum 1,200 mg/day)
Adverse effects	Risk of hepatotoxicity with liver failure in 1 of 2,000-4,000 children Reports of fulminant hepatic necrosis requiring liver transplant

METHIMAZOLE	
Action	Decreases synthesis of thyroid hormones within 1-2 hours
Indications	Preferred for severe illness: Longer duration of action, less hepatotoxic, ultimately results in euthyroidism faster than PTU Readily crosses placenta and distributes into breast milk, can be used in pregnancy. Safer in children
Dose	Adolescent/Adult: 60-80 mg/day PO/NG divided Q4-6 hours Infants/Children: 0.5 – 0.7 mg/kg/day PO/NG divided Q8 hours
Adverse effects	Adverse effects seen up to 20% of children. Allergic reactions, fever, myalgias, arthralgias, rash, hepatitis, headache Agranulocytosis in 0.3% of adults (unknown risk in children)

IODINE	
Action	Blocks synthesis and release of T4 and T3
Indications	At least 1 hour after synthesis blockade with PTU or Methimazole
Dose	Lugol solution: 5% Iodine and 10% Potassium Iodide (126 mg Iodine/ml or 8 mg Iodine per drop) Children/Adolescents: 10 drops PO TID
	SSKI (Saturated Solution of Potassium Iodide (38 mg Iodine/drop) Infants < 1 year: 150-200 mg PO TID Children/Adolescents: 300 to 500 mg PO (5 drops) Q6 hours) Adults: 5 drops (0.25 ml or 250 mg) PO Q6 hours
Contra-indications	Do not administer until 1 hour after the dose of thionamide If given prior to synthesis blockade the addition of iodine will act as a substrate promoting further hormone production

GLUCOCORTICOIDS	
Action	Inhibit thyroid hormone release from the thyroid and decreases peripheral conversion of T4 to T3 Decrease autoimmune process in Grave’s disease
Indications	Used in extreme cases; patient with CHF, arrhythmias, or shock.
Dose	Dexamethasone 0.2 mg/kg (1-2 mg Q6 hours) or Hydrocortisone (adolescent/adult): 300 mg IV, then 100 mg Q8H Hydrocortisone (infant/child): 1-2 mg/kg Q8 hours

CHOLESTYRAMINE	
Action	Thyroid hormones are metabolized in the liver, get secreted into bile and get reabsorbed if not bound by enterohepatic circulation. Bile acid sequestrants interfere with enterohepatic circulation and reduce thyroid hormone levels
Dose	Adult: 4 grams PO QID

ENVIRONMENTAL ILLNESS

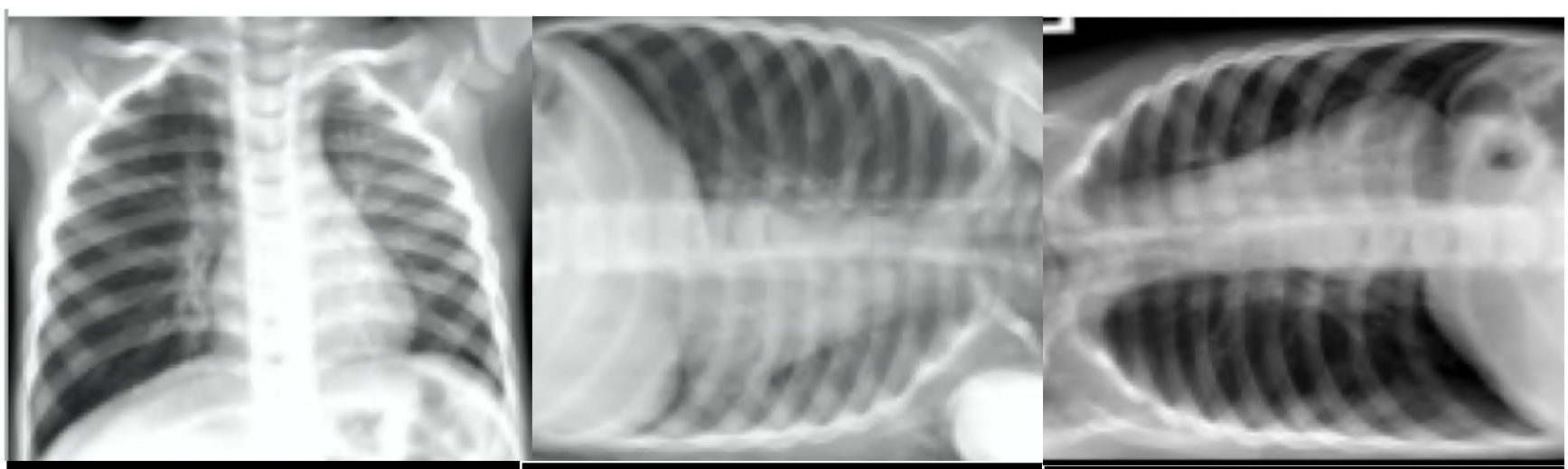
AIRWAY FOREIGN BODIES

INTRODUCTION (ETHAN WIENER, M.D. 2/2018)
Children are at particularly high risk of foreign body aspiration. The peak age of aspiration in otherwise healthy children is during the second year of life with most occurring before the age of 3 years. Common foreign bodies include: hot dogs, hard candies, peanuts, and popcorn. Nonfood objects include coins, batteries, and similarly shaped objects commonly found in and around the home. (See: PEM Guide: Environmental Injuries: Gastrointestinal Foreign Bodies)

CLINICAL MANIFESTATIONS
In the majority of cases, there is no discreet history that secures the diagnosis. A choking history is 76-92% sensitive. A careful discussion with the parents and maintaining a high index of suspicion leads to the diagnosis. Signs and symptoms of airway foreign body can be very mild such as a persistent cough or life threatening with asymmetry on chest auscultation due to partial or complete upper airway obstruction. There is typically an initial symptomatic phase with coughing, choking or shortness of breath followed by a relatively quiescent phase and finally a symptomatic complication phase due to obstruction or infection.

COMPLICATIONS
Acute pneumonia
Recurrent pneumonia
Lung abscess
Bronchiectasis
Hemoptysis

DIAGNOSIS
Evaluation begins with a PA and lateral chest radiograph. The absence of XRAY findings does not exclude the presence of a foreign body. Svedstrom et al (Pediatric Radiology 1989, PubMed ID: 2797935) showed a routine chest XRAY had a sensitivity of 68-76% and specificity of 45-67%. Forced expiratory or decubitus views with the suspected effected side down are often obtained. The purpose is to look for air trapping and the inability of a part of the lung to lose volume due to airway obstruction.



PA VIEW RIGHT LUNG	L LATERAL DECUBITUS LEFT LUNG	R LATERAL DECUBITUS RIGHT LUNG

Brown et al (Annals EM 2013, PubMed ID: 22841172) assessed the utility of adding expiratory or decubitus views to identify pediatric airway foreign bodies. Standard views had a sensitivity of 56% and specificity of 79%, Decubitus views had a sensitivity of 56% and specificity of 64%. Expiratory views had a sensitivity of 62% and specificity of 72%. The authors concluded that:

1. The addition of decubitus view to standard views increases false positives without increasing true positives and lacks clinical benefit
2. The addition of expiratory view to standard views increases true positives without increasing false positives, but accuracy remains low and clinical benefit is uncertain.

Chest CT or rigid bronchoscopy for direct visualization may be required to confirm the diagnosis.

MANAGEMENT

Initiate consultation with ENT/Anesthesiology/pulmonology early in the care of persistently symptomatic patients. (See: PEM Guide: Resuscitation: Airway)

In the case of complete airway obstruction foreign body obstructed airway maneuvers are indicated. The Heimlich maneuver is recommended for children older than 1 year of age who are responsive. It they become unresponsive then they receive abdominal thrusts in either the standing or kneeling. Infants younger than 1 year receive sequences of 5 back blows followed by 5 chest thrusts. A blind finger sweep should not be done in a pediatric patient, as it is more likely to push the object further into the oropharynx and decreasing the likelihood or removal.

If this is unsuccessful, advanced airway procedures should be initiated. Direct laryngoscopy and endotracheal intubation should be attempted. A Magill forceps can be used to remove a visualized foreign body above the vocal cords. An attempt can be made to pass an endotracheal tube through a soft foreign body such as a grape or push the foreign body into the right mainstem bronchus and ventilating the left lung. If these efforts are unsuccessful a cricothyrotomy can be life saving. (See: PEM Guide: Airway Procedures: Cricothyrotomy)

GUIDELINE FOR CONSULTING PEDIATRIC ENT/PULMONARY
Consultation should be considered strongly for every choking episode when aspiration in the airway is suspected
Who should be consulted depends on the probability that foreign body is in the airway.
High Probability of Airway Foreign Body: Consult ENT History of choking episode plus physical exam findings and/or XRAY changes requires removal of foreign body with rigid bronchoscope
Low/Medium Probability of Airway Foreign Body: Consult: Pediatric Pulmonology History of choking episode without any other findings, or, when a foreign body could have been aspirated long ago. Pediatric Pulmonology will assess the patient and decide if ENT is to be involved. Further strategy will be decided between ENT and Pediatric Pulmonology. Most likely diagnostic flexible bronchoscopy would be done with ENT available for further assistance with rigid bronchoscope if needed.

Rigid bronchoscopy is the standard of standard of care for the evaluation and removal of children with suspected foreign body aspiration and non-emergent presentation. It is successful in removing the foreign body 95% of the time with a complication rate of less than 1%. It provides control of the airway, good visualization, manipulation of the object with a wide variety of forceps, and ready management of mucosal hemorrhage. It however, requires general anesthesia.

DISPOSITION

Foreign bodies in the trachea or larynx are medical emergencies and should not be discharged. Discharge with follow up with pulmonology is reasonable if the patient is asymptomatic and the foreign body is not suspected to be in the trachea or larynx. In asymptomatic patients with a normal chest XRAY follow up of less than 1 week with pediatric pulmonology is reasonable. Follow up longer than this period is not recommended because granulation tissue and swelling related to infection may significantly complicate the removal.

ANIMAL BITES

INTRODUCTION (MICHAEL MOJICA, M.D. 10/2021)
There are 1-2 million animal bites per year. The majority result in trivial injury. The “biters” in greater than 95% of cases are domestic dogs and cats. Male animals of certain breeds (Shepard’s, pit bulls, Chows, Rottweiler, Doberman), who are reproductively intact have been most commonly implicated. “Provoked” attacks are more common in children less than 5 years of age. Children tend to have more bites, fatal injuries, bites to face/head/neck and are more likely to have been at home with their own pet that has not previously demonstrated aggressive behavior.

CLINICAL MANIFESTATIONS
Clinical manifestations are related to the location, number and degree of injury as well as infectious complications.

INJURIES: Injuries include: lacerations, puncture wounds, crush injuries and penetrating injuries to underlying structures (e.g. tendon, nerve, bone, joint, vasculature, body cavity, skull). Complications of bite wounds include cosmetic and functional deformity, infections and death. Deaths occur most commonly in those less than 10 years of age.

INFECTIOUS COMPLICATIONS: Infections Include: local infections such as cellulitis, abscess, septic arthritis, osteomyelitis, and tenosynovitis. Distant infections can occur as well and include: bacteremia, sepsis, and meningitis. Infections of particular concern to animal bites include: rabies and cat scratch disease. In general, infection rates of simple animal bite wounds are similar to those found for non-bite simple lacerations (approximately 5%).

The animal’s oral flora rather than host skin flora is most predictive of the bacteriology of bite wound infections. Infections are generally mixed including aerobes and anaerobes. Specific organisms include: Staph aureus, Streptococcal species, Pasteurella multocida and anaerobes such as Peptococcus and bacteroides species. Pasteurella multocida is a small coccoid gram negative. It is present in 50-60% of dog secretions and is the causative organism in up to 10-25% of infections. Pasteurella is found in 70-90% of cats and is responsible for up to 50% of infections. Pasteurella infections are rapidly progressing (usually < 24 hours) with an intense inflammatory response. Pasteurella is generally susceptible to penicillin G and its derivatives as well as 2nd and 3rd generation cephalosporins.

EVALUATION
Evaluation of the patient with an animal bite first involves a primary trauma survey to rule out life-threatening penetrating injuries. Further evaluation includes an assessment of the incident (time, location, animal-type, behavior, availability, animals vaccine history). Radiographs may be helpful in evaluating the presence of fractures, foreign bodies and penetration of adjacent structures and body cavities.

WOUND EVALUATION
Location, type (laceration, crush) and depth of the injury
Signs of infection
Involvement of adjacent structures
Neurovascular status distal to the injury site
Presence of foreign bodies

MANAGEMENT

The management of animal bites involves:
1. Local wound care
2. Treatment of established infections
3. Infection prophylaxis
4. Mandated reporting

1. **LOCAL WOUND CARE:** Local wound care consists of high-pressure irrigation, wound exploration and debridement of devitalized tissues. Clean wounds with soap and water. Operative evaluation should be considered for full thickness wounds of the hands and face and suspicion of penetrating structures. Delayed fracture pinning and nerve and/or tendon repair is recommended. Classically bite wounds have been managed by secondary or delayed primary closure. Primary closure of certain low risk wounds may be possible. In particular, those in areas where cosmesis is of high concern (e.g. face).

2. **TREATMENT OF ESTABLISHED INFECTIONS:** Treatment of established infections includes coverage of the primary organisms involved. Combination therapy (Penicillin for Strep, anaerobes, Pasteurella and Cephalexin for methicillin sensitive Staph aureus) may be administered. Alternatively, a single agent such as Amoxicillin/clavulanate may be used. Clindamycin and Trimethoprim Sulfamethoxazole are recommended in the Penicillin allergic child. Azithromycin, Trimethoprim Sulfamethoxazole, Cefdinir, and Doxycycline do not provide adequate coverage for anaerobes or *Pasteurella*. High risk (injuries and more severe infections, may require parenteral therapy (Ampicillin/Sulbactam).

3. **INFECTION PROPHYLAXIS:** Antibiotic prophylaxis for bite wounds is commonly administered. A Cochrane systematic review concluded that "There is no evidence that the use of prophylactic antibiotics is effective for cat or dog bites. There is evidence that the use of antibiotic prophylactic after bites of the hand reduces infection but confirmatory research is required". (Medeiros, Cochrane Review 2011, PubMed ID: 11406003). Cultures should be obtained only in the presence of an established infection. Cultures of non-infected wounds do not reliably predict infecting organism. If prophylactic antibiotics are administered their selection for should be guided by the principles outlined above for treatment of established infections.

WOUNDS AT HIGH RISK OF INFECTION
Bites to the hand, wrist, feet (increased risk of involvement of underlying structures)
Wounds involving fractures, joints, tendons, or ligaments,
Crush injuries requiring extensive debridement
Puncture wounds
Cat bites
Old wounds (> 12 hours)
Wounds in patients with impaired host defenses (steroids, diabetes, HIV).

ANTIBIOTIC SELECTION: BITE WOUNDS[1]		
Dog/Cat Bite	Vaccine Status? (animal, patient)	Tetanus vaccine PRN Rabies vaccine and immune globulin PRN
	Oral	Amoxicillin/Clavulanate (Augmentin)
	IV	Ampicillin/Sulbactam (Unasyn)
	Alternative	Clindamycin AND TMP/SMX
	Duration	Treatment: 10-14 days, Prophylaxis: 3-5 days
Human Bite	Vaccine Status?	Tetanus vaccine PRN
	Oral	Amoxicillin/Clavulanate (Augmentin)
	IV	Ampicillin/Sulbactam (Unasyn)
		Alternative: Clindamycin AND Levofloxacin[2]
	Duration	Treatment: 10-14 days, Prophylaxis: 3-5 days
1. NYU PEDIATRIC ANTIBIOTIC STEWARDSHIP PROGRAM 2021 2. Levofloxacin: Use limited to specific circumstances in pediatrics due to arthropathy		

TETANUS: Dog and cat wounds are considered tetanus prone and tetanus prophylaxis should be administered if tetanus vaccination is deficient.

TETANUS PROPHYLAXIS				
	CLEAN, MINOR WOUNDS		ALL OTHER WOUNDS[1]	
History	Td[2]	TIG[3]	Td[2]	TIG[3]
< 3 doses	YES	NO	YES	YES
≥ 3 doses	NO[4]	NO	NO[5]	NO
1. Wounds contaminated by dirt, feces, soil, saliva, puncture wounds, avulsions. wounds from missiles, crushing, burns, frostbite				
2. Children < 7 years DTAP or DT recommended, > 7 years Td recommended				
3. TIG 250 Units IM				
4. Yes if > 10 years since last dose				
5. Yes if > 5 years since last dose				

RABIES: Rabies virus infection results in an acute, atypical encephalomyelitis. Infection may occur due to a bite from a rabid animal as well as from contact with saliva on non-intact skin or mucous membranes. Rabies is a relatively rare event in the United States. Between 1990 and 2004, 47 cases were reported. 10 of these were acquired abroad. Of the remaining 37 cases, 34 were found to involve the bat variant of the rabies virus while 1 came from a raccoon. Rabies prophylaxes should be administered to those with bite wounds in endemic areas (in particular the East Coast of the U.S.) in which the animal's vaccine status cannot be reliably established or the animal is unavailable for observation and testing. Local wound care is an essential component of rabies prevention. Post exposure immune-prophylaxis consists of delivery of the human diploid cell vaccine (passive) and the human rabies immune globulin (active). Until recently rabies has been universally fatal. An experimental regimen (The Milwaukee Protocol), has resulted in survival in a handful of those infected with only one of those patients intact neurologically (Lampejo, J Hosp Infect 2017, PubMed ID: 28559126).

RABIES PROPHYLAXIS	
Rabies Vaccine	1 ml Intramuscularly on Days 0, 3, 7 and14* Intra-gluteal injection has been associated with lower response and prophylaxis failure
Rabies Immune Globulin	20 International Units/kg on day 0. Dose is infiltrated around the wound if feasible Remaining dose delivered at site distinct from the vaccine site.
*A 4 dose regimen is recommended by Advisory Committee of Immunization Practices .	

The 5th dose at 28 days is no longer advised (CDC, MMWR 2010, PubMed ID: 20648715).

4. MANDATED REPORTING: The event should be reported to the animal control officer or health department. 10 days of observation is considered to sufficiently to determine the presence of infection.

CONTACTS (NEW YORK CITY)		
Business Hours	Bureau of Communicable Diseases	212-788-9830
	Veterinary Public Health Service	212-676-2483
Off Hours	NYC Poison Control Center	212-764-7667

NYCDOHMH: GUIDE TO RABIES POSTEXPOSURE PROPHYLAXIS

WEB LINK: https://www1.nyc.gov/assets/doh/downloads/pdf/cd/cd-cdrab-pvtalgo.pdf

Rabies

Postexposure Prophylaxis

Administer Postexposure Prophylaxis (PEP) if a patient was bitten or otherwise exposed* to

1. A rabies-positive animal
2. A rabies vector species** that is unavailable for testing

Raccoons and bats are the most commonly reported rabid animals in New York City. Other animals that have tested positive include skunks, cats and opossums. For the most recent rabies statistics, visit nyc.gov/health/rabies.

Report bites to the Animal Bite Unit at 646-632-6074.

Once the bite is reported, the Health Department will contact the animal owner and the potentially exposed victim and provide guidance.

Do not start PEP if the patient was bitten by a dog or cat that is healthy and can be observed for 10 days. If the animal remains healthy during the observation period, the bite victim does not need PEP. If the dog or cat is unavailable for observation or testing, the need for PEP should be assessed on a case-by-case basis.

Patient's Status:	Never Vaccinated Patient has never received a complete regimen of either rabies pre-exposure or rabies PEP	Previously Vaccinated Patient has received a complete regimen of either rabies PEP for a previous exposure or rabies pre-exposure vaccination
1. Clean the Wound(s) Thoroughly irrigate with water or a dilute water povidone-iodine solution.	**Always**	**Always**
2. Administer Human Rabies Immune Globulin (HRIG) 20 IU/kg Thoroughly infiltrate the area in and around the wound(s) with a full dose of HRIG if possible. Otherwise, inject remaining volume IM in a site distant from the vaccine.	**Always**	**Never**
3. Vaccinate – IM Deltoid The lateral thigh can be used for children.	**Always** on days 0, 3, 7 and 14 Immunocompromised patients should receive an additional dose on day 28.	**Always** on days 0 and 3 only

DON'T

- ✘ Start PEP if the patient was bitten by a dog or cat that is healthy and can be observed for 10 days.
- ✘ Inject HRIG and vaccine at the same site.
- ✘ Inject vaccine or HRIG in the gluteus.
- ✘ Give HRIG to patients who have already received a complete regimen of PEP or rabies preexposure prophylaxis.

DO

- ✔ Infiltrate all wounds with HRIG, unless patient was previously vaccinated.
- ✔ Inject rabies vaccine in deltoid. In children, the thigh may also be used.
- ✔ Give tetanus booster, if appropriate.

Call the Health Department's Provider Access Line at 866-692-3641 if:

- HRIG was administered, but NOT at the bite site.
- HRIG was indicated, but not administered on day 0. If given more than 7 days after the first rabies vaccine, HRIG can interfere with the immune response.
- There are significant deviations in the vaccination schedule. Rabies PEP should be given on days 0, 3, 7 and 14. Deviations of a few days are not a great concern and the patient should resume the series. Maintain the recommended spacing between doses.
- PEP was initiated overseas.
- You are not sure if PEP is indicated.

* Rabies virus is most commonly and most efficiently transmitted through the bite of a rabid animal. While rare, the virus may also be transmitted through exposure of infectious saliva or neural tissue to a mucous membrane or an open wound. Always consider the possibility of an unrecognized exposure if a bat was found near someone who may have been unaware or unable to communicate if an exposure occurred.

** Rabies vector species in the United States include raccoons, bats, skunks, foxes, coyotes and mongooses (in Puerto Rico).

NYC Health

BURNS

INTRODUCTION (JULIETTE QUINTERO-SOLIVAN, M.D. 7/2020)
Burns and related injuries are the 3rd leading cause of death in children. 75% of burn injuries occur in the home. Males and children under 5 years are at greatest risk. Burns can be described by their etiology as: thermal, chemical, friction, electrical, or radiation. Thermal burns occur from direct contact with steam, hot objects, or flames. Scald burns are thermal burns that are caused by a wet substance, such as hot liquids or steam. Scald burns are the most common cause of burns encountered in young children.

BURN ETIOLOGY	
Thermal	Direct contact with steam, hot items, or flames
	Scald: Caused by contact with something wet (steam, liquid)
Electrical[1]	Conduction of heat from an electrical current
	Surface injury does not correlate with underlying injury
	Bite electrical cord → Labial commissure → Delayed labial artery bleed
	Lightning → Ferning pattern
Chemical[2]	Longer contact time, injury evolves slowly
	Caustic → Skin necrosis
	Acids → Coagulation necrosis (proteins) → Eschar → Limits depth
	Alkali's → Liquefaction necrosis (fats) → Deeper penetration
Friction	Heat generated by mechanical friction
	± Crush or shear stress injuries
Radiation	Exposure to: Sun, radiation therapy, nuclear burns
1. See PEM Guide: Environmental Injuries: Electrical Injuries 2. See PEM Guide: Toxicology: Caustics	

INTENTIONAL BURNS: Approximately 10-20% of burns in children are intentional and burns constitute 20% of child abuse injuries (See PEM Guide: Child Protection: Child Abuse and Neglect). It is essential to maintain a high level of suspicion for abuse in all children with burns. Understanding burn types can be helpful to determine if the observed injury is consistent with the history provided. Scald burns are the most common burn associated with intentional injury.

Scald burns can be sub-classified as: 1. spill or splatter pattern, 2. flow and 3. immersion/submersion. A spill or splatter pattern typically occurs when a toddler reaches for and spills a cup or pot full of hot liquids. Burns typically occur on the anterior, upper chest and upper extremities, are of varying depth, are asymmetric and have peripheral/satellite splash burns. In contrast, intentional burns are more likely to be sharply demarcated (e.g. linear), of uniform depth, symmetrical and circumferential. Flow scald burns occur when a liquid of poured over a body part. Submersion burns occur when a child is placed or dipped in a liquid. There may be sparing the soles and/or buttocks (in contact with cooler tub surface).

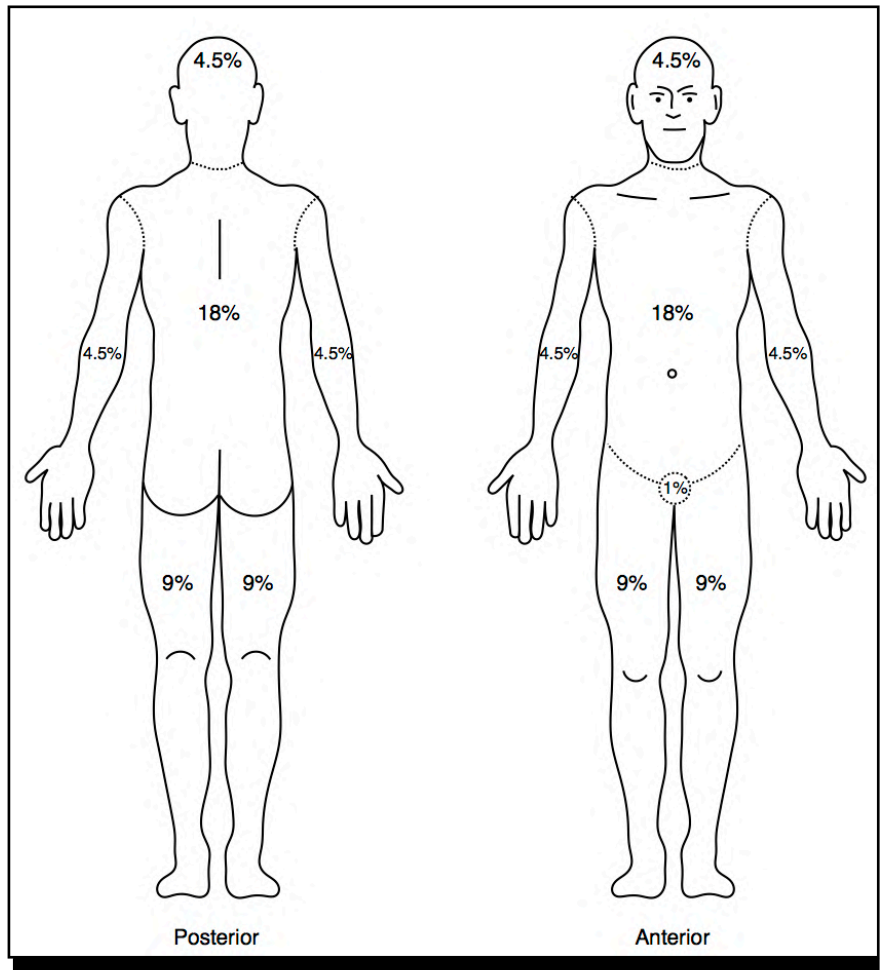
CLINICAL MANIFESTATIONS
Estimation of burn depth is based on: bleeding or needle prick, sensation, appearance, and blanching to pressure. Complications vary with the severity of injury and include primarily hypovolemia/shock, electrolyte abnormalities, sepsis, pain and contracture formation.

BURN CLASSIFICATION	
First Degree (Superficial thickness)	Involve injury to the epidermis only Not included is body surface area (BSA) calculations Present with erythema and extreme pain (e.g. mild sunburn) No blistering, Sensation is intact Resolves in 3-5 days without scarring
Second Degree (Partial thickness: Superficial and Deep)	<u>Superficial Partial Thickness</u> Injury to the epidermis and superficial dermis Appears with thin blisters, erythematous, edematous and moist Sensation is intact Heal in 2-3 weeks without scarring
	<u>Deep Partial Thickness</u> Involve injury to epidermis and both superficial and deep dermis Often intermixed with 3rd degree burns Appears dry or moist and pale or red. Thick ruptured blisters Extreme pain or no pain (insensate) May have decreased 2-point discrimination Heals in 3-6 weeks. Potential for scarring
Third Degree (Full thickness)	Involve injury to the epidermis and the entire dermis Appear pale, charred, white and leathery Minimal tenderness due to the destruction of dermal pain receptors Skin grafting always necessary
Fourth Degree	These burns involve deep injury to muscle, fascia and bone

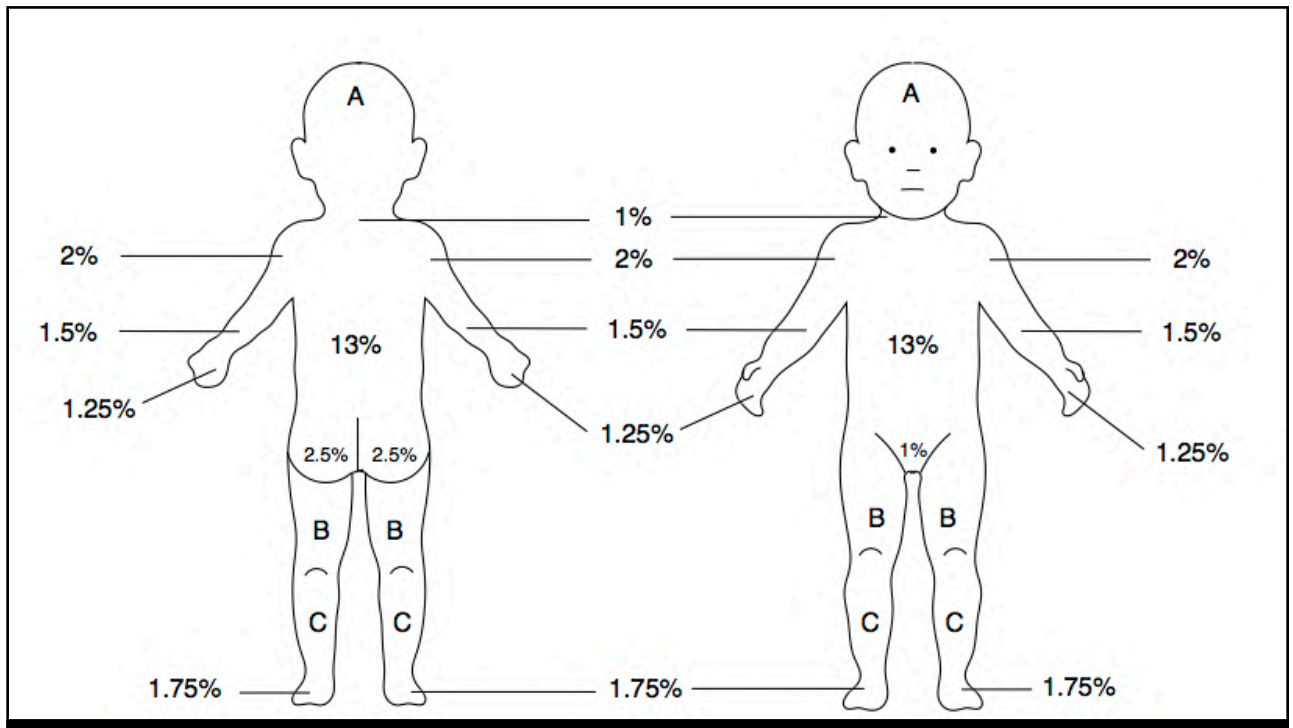
LABIAL BURNS: Labial burns are typically electrical injuries after a young child bites on an electrical cord. Saliva is a conductor and completes the circuit. Labial burns usually affect the commissure (corner) of the mouth. Minor burns are managed with analgesia, soft diet and good oral hygiene. The primary complication of labial burn is retraction of the eschar and labial artery bleeding at 5-8 days.

ASSESSMENT OF BURNED SURFACE AREA (BSA): The Rule of Nines is used to assess BSA in adults but cannot be used in children less than 10 years old. In adults, the head is 9%, each upper extremity is 9%, each lower extremity is 18%, the back and front of the trunk are each 18% and the perineum is 1%.

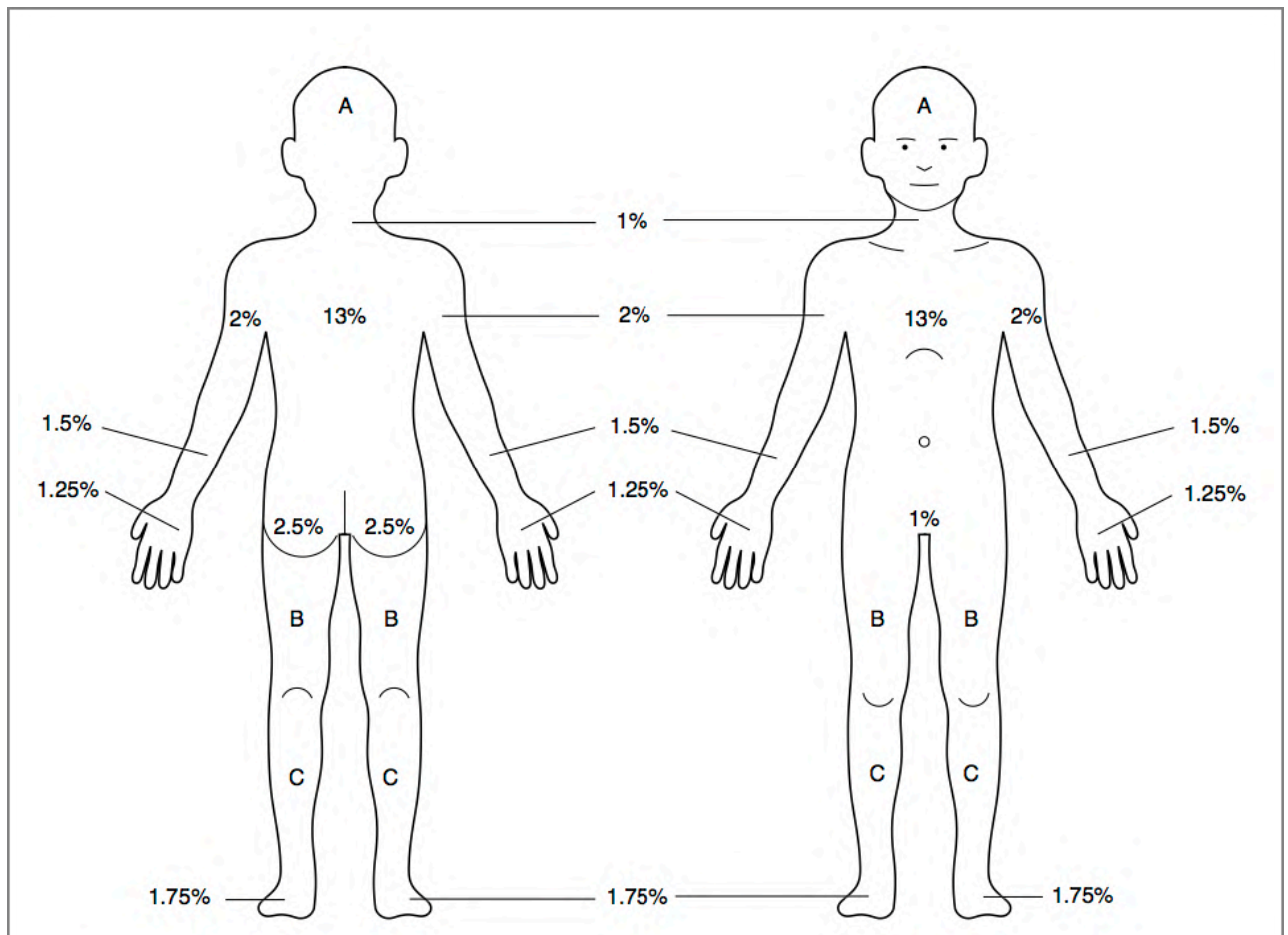
Young children have relatively large heads and smaller extremities. The Lund Browder chart is should be used for children under 10 years. Alternatively, the child's palm (not including fingers), which is approximately 1% of body surface area, can be used as an estimate.



RULE OF NINES (> 10 YEARS)



LUND BROWDER (BIRTH TO 5 YEARS)



LUND BROWDER (5-9 YEARS)

	BIRTH-5 YEARS			5-9 YEARS		
AREA	Birth	1 year	5 years	10 years	15 years	Adult
A = 1/2 head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
B = 1/2 1 Thigh	2 3/4	3 1/4	4	4 1/2	4 1/2	4 3/4
C = 1/2 1 Leg	2 1/2	2 1/2	2 3/4	3	3 1/4	3 1/2

MANAGEMENT

RESUSCITATION: Assessment of the airway, breathing and circulation and removal of smoldering clothing occurs first. Airway edema can progress rapidly and early intubation should be considered for signs of upper airway obstruction such include soot in the nares or mouth. Racemic epinephrine and humidified O_2 may facilitate intubation. Be prepared for a surgical airway. Analgesia should be provided. Benzodiazepines may be required for anxiolysis. Patients should be assessed with co-oximetry for carbon monoxide toxicity. Cyanide toxicity should be considered in patients with a severe metabolic acidosis. Patients with deep burns should be monitored for rhabdomyolysis.

See:
PEM Guide: Airway Procedures: Cricothyrotomy
PEM Guide: Airway Procedures: Difficulty Airway
PEM Guide: Environmental Injuries: Smoke Inhalation
PEM Guide: Toxicology: Carbon Monoxide
PEM Guide: Toxicology: Cyanide

FLUID RESUSCITATION: Fluid therapy is calculated by several available fluid resuscitation formulas. These are helpful in the initial resuscitation phase though frequent adjustments should be made, especially in small children, based on response to therapy such as urine output and vital signs. Some pediatric burn centers are using a Revised Parkland formula with 3 ml/kg/%BSA instead of 4 ml/kg/%BSA. Fluid should be replaced with isotonic solutions such as normal saline or ringers lactate. Dextrose containing maintenance fluids are typically added for children under 2 years of age.

FLUID RESUSCITATION				
	FORMULA	FIRST 8 HR	NEXT 16 HR	MAINTENANCE
Parkland	4 ml/kg/%BSA*	50%	50%	Add for < 2 years
Carvalhal	5,000 ml/m^2/%BSA*	50%	50%	Add 2,000 ml/m^2/day
*%BSA = 2nd and 3rd degree burns only				

WOUND CARE: Initial wound care for 1st and 2nd degree burns involves irrigation with sterile saline, debridement of loose skin and ruptured bullae, topical antibiotic application and sterile dressing. Full thickness circumferential burns may require escharotomy. Silver sulfadiazine was traditionally used but recent evidence supports to the use of bacitracin. Silver sulfadiazine should be avoided in infants less than 2 months of age and on the face due to the possibility of staining. Tetanus prophylaxis should be administered. Prophylactic antibiotics are not recommended as they increase the risk of resistance

TETANUS PROPHYLAXIS				
	Clean, Minor Wounds		All Other Wounds[1]	
History	Td[2]	TIG[3]	Td[2]	TIG[3]
< 3 doses	YES	NO	YES	YES
≥ 3 doses	NO[4]	NO	NO[5]	NO
1. Wounds contaminated by dirt, feces, soil, saliva. Puncture wounds, avulsions. Wounds from missiles, crushing, BURNS, frostbite				
2. < 7 years: DTAP or DT recommended, > 7 years Td recommended				
3. TIG 250 Units Intramuscularly				
4. Yes if > 10 years since last dose				
5. Yes if > 5 years since last dose				

DISPOSITION

The decision to manage the burn patient as an inpatient should be individualized, but general guidelines exist for admission and referral to a burn center. WEB LINK: Burn Center Transfer Criteria (2017)

ADMISSION CRITERIA	
Burn Depth	Full thickness > 2% BSA
	Partial thickness > 10% BSA
Burn Location	Face
	Hands, feet
	Perineum
	Circumferential
Mechanism	Inhalation
	Electrical, high voltage
	Chemical
	Child Abuse
Associated Issues	Trauma
	Co-morbid conditions
	Carbon monoxide, cyanide

AMERICAN BURN ASSOCIATION: BURN CENTER TRANSFER
Partial thickness burns > 10% total body surface area
Burns that involve the: Face, hands, feet, genitalia, perineum, or major joints
Third-degree burns
Electrical burns including lightning injury
Chemical burns
Burns associated with inhalation injury
Patient with preexisting medical disorders that could complicate management, prolong recovery, or affect mortality
Any patients with burns or concomitant trauma (e.g., fracture) in which the burn injury poses the greatest risk of morbidity or mortality.
Burned children in hospitals without qualified personnel or equipment for the care of children
Burn injury in patients who require special social, emotional or rehabilitative intervention
WEB LINK: BURN CENTER TRANSFER CRITERIA (2017)

PREVENTIVE MEASURES
Limit sun exposure, use sunscreens
Smoke detectors
Lower home water temperature to < 120 F
Firework bans
Pan handles positioned to rear of stove

DROWNING

INTRODUCTION (MICHAEL MOJICA, M.D. 1/2017)
In the United States, submersion injuries are the second leading cause of injury related death in the 1-4-year-old age group. The World Health Organization (2002) defines drowning as the process of respiratory impairment from submersion/immersion in a liquid. Many terms are utilized and make comparisons between studies difficult. The terms fatal and non-fatal drowning are preferred. The terms near drowning, dry drowning, wet drowning and delayed drowning should not be utilized.

RISK FACTORS
Like many environmental injuries there is a bimodal distribution of those involved. The first peak is the toddler age group (“the young”). Risk factors for toddler submersion include: inadequate supervision, limited water safety skills, access to residential swimming pools and bodies of water close to or in the home (including bath tubs, hot tubs, spas, whirlpools and large containers such as 5 gallon buckets). Intentional submersion should be considered in this population. The second peak is the adolescent male (“the restless”). Risk factors for adolescent males include risk-taking behaviors such as diving in shallow bodies of water, use of alcohol, drugs and boating mishaps.

Patients with seizures, autism and arrhythmias are at increased risk. Adequate anticonvulsant levels may not be protective and these patients should be specifically counseled regarding water safety. Those who hyperventilate prior to free diving are also at risk for drowning. They hyperventilate in order to increase the oxygen reserve. In doing so, they decrease their PCO_2 and when they become hypoxic the low PCO_2 is insufficient to stimulate breathing.

PATHOPHYSIOLOGY
Submersion leads to aspiration and pulmonary injury with resulting multi-organ hypoxia. Struggle during submersion can hasten the effects of hypoxia. At about 4 minutes there is circulatory inadequacy and by six minutes microscopic CNS damage ensues. There is a period of time in which return of spontaneous circulation is possible but the patient will suffer permanent neurologic sequelae.

The distinction between salt and fresh water drowning is not clinically relevant as the amount of fluid aspirated/ingested is insufficient to result in electrolyte abnormalities. The presence of chlorine does not influence the clinical course. The temperature of the water (particularly the rate of development of hypothermia) and the presence of contaminants (particularly infectious and chemical) may influence outcomes.

SYSTEM INJURIES	
Pulmonary	Surfactant washout results in damage to the alveolar-capillary membrane, atelectasis, pulmonary edema, vasoconstriction, and bronchospasm. Similar to acute respiratory distress syndrome.
Neurologic	Hypoxia → Neuronal injury and cerebral edema → Increased intracranial pressure (late), 20% with permanent damage
Cardiovascular	Arrhythmias due to hypoxia and hypothermia. Arrest: Tachycardia → Bradycardia → PEA → Asystole Ventricular arrhythmias rare Sinus tachycardia, sinus bradycardia, atrial fibrillation with a pulse don't require treatment other than ventilation and rewarming
Metabolic	Metabolic and respiratory acidosis, normal electrolytes
Renal	Acute tubular necrosis: hypoxia, hemoglobin, myoglobin deposition

MANAGEMENT

The goals of management are the prevention of further anoxic damage and the identification and treatment of complications. Evidence on the management of the drowning victim is limited to case series and case-control studies.

The focus is on establishing adequate ventilation. Efforts at promoting clearance of lung fluid are not effective. The American Heart association guidelines state that “the routine use of abdominal thrusts or the Heimlich maneuver for drowning victims is not recommended”. (AHA, Circulation 2015, PubMed ID: 26472998). These maneuvers increase the risk of vomiting and delay the onset of adequate ventilation.

Areas of additional concern in the submersion victim include cerebral resuscitation and the management of hypothermia and dysrhythmias. Precipitants of drowning such as seizures, trauma, myocardial infarction, toxins and arrhythmias should be considered and managed appropriately.

PREHOSPITAL CARE: Ventilatory support should be initiated as soon as possible. In-water resuscitation in the unconscious person may improve outcomes (Szipilman, Resuscitation 2004, PubMed ID: 15451583). This consists of ventilations only and should be attempted only by highly trained rescuers. If there is no response to ventilations, the victim should be brought quickly to solid ground and chest compressions initiated. High flow oxygen should be provided to the spontaneously breathing patient via a combination of non-rebreather face-mask and nasal cannula. The apneic patient requires endotracheal intubation. Routine cervical spine immobilization is not recommended unless there are signs of trauma or there is a suspicious mechanism of injury (e.g. diving). Passive rewarming efforts such as removal of wet clothing can be initiated in the pre-hospital phase of care.

The approach the cardiopulmonary resuscitation differs from non-drowning situations as ventilation is prioritized over chest compressions (Traditional A-B-C, rather than the current sequence of C-A-B). Pulses may be weak and slow. A minute should be taken to assess for pulse before compressions are initiated. Compressions should not delay ventilation efforts and may precipitate ventricular arrhythmias in the hypothermic myocardium. Arrhythmias are managed as per Pediatric Advanced Life Support guidelines. Efforts to improve ventilation and correct hypothermia may effectively treat arrhythmias. Epinephrine may be administered for asystole or pulseless electrical activity not responsive to ventilation and chest compressions. Endotracheal delivery of medications is not recommended.

EMERGENCY DEPARTMENT CARE: Endotracheal intubation should be initiated in the apneic patient, those with an oxygen saturation below 90% despite high-flow oxygen and those with a PCO_2 above 50 mm Hg. Non-compliant lungs require positive end expiratory pressure (PEEP) and either an increased minute ventilation or peak pulmonary pressures. Non-invasive ventilation techniques may be considered in the spontaneously breathing patient. Blood pressure and heart rate should be carefully monitored in any patient receiving positive pressure ventilation as it can increase intrathoracic pressure and decrease cardiac output. Bronchodilators may be required. The routine use of corticosteroids is not recommended. Antibiotics are not recommended unless potential infectious contaminants are present. Regurgitation is a common complication of resuscitation. An oral-gastric or nasal-gastric tube should be placed to relieve gastric distention.

Fluid resuscitation should be balanced to treat shock and avoid worsening pulmonary edema. In the hypothermia patient, vasoconstriction results in a shift of fluids centrally. Central baroreceptors increase antidiuretic hormone secretion in response to a high central pressure and a “cold” diuresis ensures.

Central nervous system resuscitation is aimed at reducing cerebral hypoxia and maintaining perfusion. The head of bed should be elevated to 30 degrees, seizures controlled and euglycemia maintained. The roles of hyperventilation, barbiturate coma, hyperosmolar therapy and invasive monitoring have not been convincingly established.

HYPOTHERMIA: The possible neuro-protective effects of hypothermia have been publicized in multiple case reports as well as in the media. The theorized benefit is due to a rapid decrease in basal metabolic rate and oxygen consumptions. This however has not been conclusively demonstrated with higher level evidence. In a 2014 study involving over 1,000 Washington state residents, lower water temperature was not associated with improved outcomes (Quan, Resuscitation 2014, PubMed ID: 24607870). In a study of 98 children who presented with cardiac arrest and hypothermia after drowning and required resuscitation for more than 30 minutes, 89% died and the 11% that survived were in a persistent vegetative state or had severe neurologic disability. The authors conclude that “drowned children in whom return of spontaneous circulation is not achieved within 30 minutes of advanced life support have an extremely poor outcome. These findings question the therapeutic value of resuscitation beyond 30 minutes in drowned children with cardiac arrest and hypothermia” (Kieboom, British Medical Journal 2015, PubMed ID: 25670715). See: PEM Guide: Environmental Injuries: Hypothermia, PEM Guide: Environmental Injuries: Frostbite

However, current guidelines recommended that resuscitative efforts be continued until a temperature of 32-35 C (90-95 F) is achieved. Core temperature should be measured with an esophageal or rectal probe. Active and passive external rewarming techniques include: warm blankets, heating pads, radiant heaters and forced warm air. Active internal (core) rewarming techniques include: humidified oxygen via an endotracheal tube and heated irrigation of the pleural or peritoneal cavities. Some institutions have the capability to utilize endovascular and extracorporeal rewarming techniques. The evidence to support therapeutic hypothermia in submersion injuries is limited. See also PEM Guide: Environmental Injuries: Hypothermia

TERMINATION OF RESUSCITATION: The termination of resuscitative efforts is always a difficult decision and should be based on the available evidence.

FACTORS ASSOCIATED WITH POOR OUTCOMES
Submersion time > 5 minutes (most predictive)
Time to effective Basic Life Support > 10 minutes
Resuscitation > 25 minutes
Glasgow Coma Scale < 5
Persistent apnea in the Emergency Department
pH < 7.1 at presentation

DISPOSITION

Patients who remain asymptomatic after a 4-6-hour observation period and who have normal chest XRAYS at the end of that period may be safely discharged. A retrospective cohort study of patients with near-drowning were studied to determine predictors of safe discharge. The authors concluded that “children who present to the ED with GCS ≥ 13 and have normal physical examination and respiratory effort and a room air oxygen saturation > 95% at 4 to 6 hours after ED presentation can be safely discharged home” (Causey, American J Emergency Medicine 2000, PubMed ID: 10674523). Patients not meeting these criteria should be admitted to a monitored setting, preferably an intensive care unit.

PREVENTION

It is estimated that 85% of drowning are preventable by supervision, swimming instruction, technology, regulation and public education. Prevention efforts should focus on education, enforcement (legislation) and engineering. First aid/resuscitation training should be encouraged for all caregivers.

Infant swimming programs may lead to a false sense of security and should not take the place of close supervision. In a 2010 policy statement on prevention of drowning the American Academy of Pediatrics (PubMed ID: 20498167) re-evaluated the age at which swimming lessons can be considered as protective based on new evidence. The AAP continues to support swimming instruction for children 4 years of age and older. Several recent studies have indicated that children aged 1 to 4 years may also benefit from lessons. There is no longer a recommendation against swimming lessons in this age group though lessons are not recommended.

POOL SAFETY RECOMMENDATIONS: AAP 2010
Isolation fence (encloses pool on all sides, can’t enter pool directly from house)
Fence height ≥ 4 feet, Bottom of fence < 4” from ground, vertical supports < 4” apart
Fence gate opens outward away from pool and is self-closing
Gate latch > 4.5 feet and self-latching
Climb resistant (e.g. vertical bars are better than open steel mesh)
Inflatable toys stored away from pool and out of sight
Pool covers alone are not adequate prevention

EAR CANAL FOREIGN BODIES

INTRODUCTION (MICHAEL MOJICA, M.D., 7/2015)
Many of the same principles apply to removal of a foreign body from the otic canal and the nasal cavity. For example, there are manual extraction and suction techniques applicable to both areas. There are also location specific techniques. (e.g. Irrigation of ear canal foreign bodies). A cooperative patient, the correct tools and experience with foreign body removal can ensure a successful removal for the majority of patients without complications. (See also PEM Guide: Procedures: Removal of Nasal Foreign Bodies)

Foreign bodies in the ear canal are common. Children with special needs, attention deficit hyperactivity disorder and those with ear complaints such as cerumen impaction and otitis media or externa are at increased risk. Common foreign bodies include: seeds, beads, pebbles, popcorn kernels, small toys and insects.

CLINICAL EVALUATION
A patient with an ear canal foreign body may be asymptomatic, present with ear pain or discharge or after a witnessed foreign body insertion. Ear canal foreign bodies are apparent on direct visualization of the otic canal with an otoscope. The other ear and both nares should be examined as well. The location, size, shape and texture of the foreign body should be noted. These foreign body characteristics and well as the presence of trauma to the canal or tympanic membrane and a parental assessment of the child likelihood of cooperating, will assist in determining the appropriate removal technique, the need for urgent removal and the need for procedural sedation.

MANAGEMENT
Techniques to remove ear canal foreign bodies include: irrigation, mechanical extraction and suction. An emergency physician with the correct tools, experience and a cooperative patient, can remove the majority of foreign bodies. Patients with distal foreign bodies adjacent to the tympanic membrane, those with significant trauma to the canal or tympanic membrane should be removed in consultation with an otolaryngologist. Indications for urgent removal are presented in the table below. Other foreign bodies in the asymptomatic patient can be referred to ENT for removal at a later date if they are not readily removable in the emergency department. Insects (frequently cockroaches) must be killed prior to removal. This can be accomplished by instilling mineral oil or 2-4% Lidocaine into the canal with the patient lying on their side with the ear with the foreign body facing up. The insect can then be removed with an alligator forceps or irrigation.

URGENT REMOVAL
Button (disc) batteries: Electrical current and pressure necrosis
Live Insects
Penetration of the tympanic membrane
Ataxia, vertigo, hearing loss or facial nerve injury

REMOVAL TECHNIQUES
There are a numbers of techniques that vary with the ease or performance, invasiveness and likelihood of complications. For example, irrigation is simple to perform, is not invasive, does not require a great degree of cooperation and has a low likelihood of complication. Techniques that require passage of an instrument past the foreign body may require procedural sedation and have a high likelihood of damage to the ear canal or tympanic membrane.

The characteristics of the foreign body also assist also determine the most appropriate technique. For example, irrigation should not be used with an organic foreign body such as a bean that will swell in the presence of water while irrigation is the best technique with friable foreign bodies. Soft, irregularly shaped foreign bodies that are easily grasped with a forceps. Hard, round foreign bodies are best removed with an instrument that passed distally (e.g. a ear current or balloon tipped catheter) or a suction technique.

REMOVAL TECHNIQUE SELECTION	
TECHNIQUE	FOREIGN BODY TYPE
Irrigation	Best for friable, can be for any except those likely to swell
Forceps	Soft, irregular, can be firmly grasped from the front
Hooks	Hard, round that can not be grasped with forceps
Balloon Tipped Catheter	Hard, round that can not be grasped with forceps
Suction	Any

IRRIGATION: Irrigation is the technique least likely to cause complications and does not require a cooperative patient. A butterfly needle with the needle cut off or a 20 gauge angiocatheter (without the needle) may be used in conjunction with a 60 ml syringe and a basin to catch the effluent. The water used should be approximately body temperature.

The tip is directed around the foreign body. It is often helpful to have the effected ear down so allow gravity to assist the process. It is particularly useful for friable foreign bodies that would require multiple attempts and removal with mechanical techniques. Irrigation should not be used for objects that are likely to expand in contact of water such as beans or seeds, in the presence of tympanic membrane perforation or with a button battery (can cause corrosion and leakage).

MECHANICAL EXTRACTION: Mechanical extraction requires a cooperative patient and may result in damage to the canal approximately 50% of the time. It is helpful to inform caregivers that the procedure is likely to cause some bleeding. An ENT ear speculum and headlamp will improve visualization. Procedural sedation may be required.

Attempts at removal of distal foreign bodies may result in perforation of the tympanic membrane. Multiple unsuccessful attempts may prevent the otolaryngologist from visualizing the foreign body and performing a definitive procedure.

A number of instruments can be used including: alligator forceps, a right ankle loop, cerumen removal loops, balloon tipped catheters, and adhesive tipped instruments.

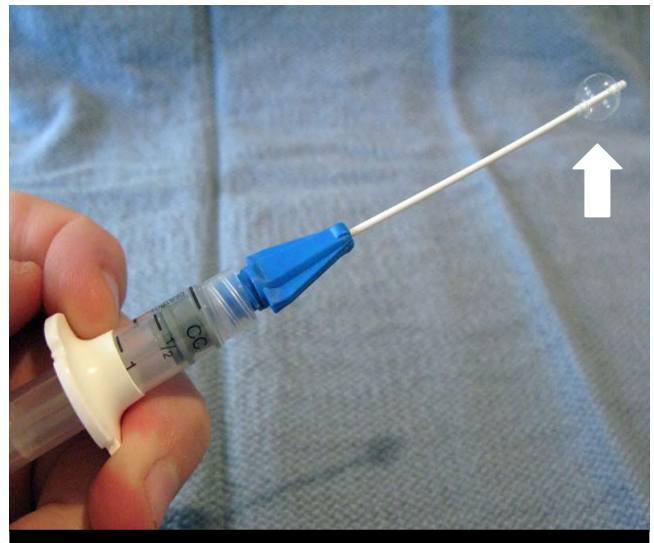
Alligator forceps as best suited to soft or irregularly shaped foreign bodies that can easily be grasped from the front. Forceps removal has less likelihood of damage to the ear canal because it does not have to be passed distal to the foreign body.

Smooth and hard foreign bodies may be difficult to grasp with forceps. An instrument that can be passed distal to the foreign body then manipulated to remove the foreign body with gentle traction may be effective. These however, cannot be used to remove foreign bodies that occlude the canal because the instrument cannot be passed distal to the foreign bodies. Examples of instruments include angled ear cerumen curettes and balloon tipped catheters.

The Katz extractor is a balloon tipped catheter that is primarily intended for nasal use but has been used for ear canal foreign bodies as well. The catheter is inserted past the foreign body, the balloon is inflated with saline and the foreign body is extracted with gentle traction.

Tissue adhesives applied to the end of a wood or plastic swab stick have also been used to snare ear foreign bodies with variable levels of success. This requires a cooperative or sedated patient as it takes up to 60 seconds for the glue to dry.

SUCTION: A fine tipped suction catheter such a tonsil suction may be used for retrieval of may types of.foreign todays. It does not require passage around and distal to the foreign body.



KATZ EXTRACTOR

COMPLICATIONS
Canal laceration (up to 50%)
Tympanic membrane perforation
Middle ear damage
Conversion from easy to difficult to remove
Distal to proximal
Obscured visualization due to trauma with blood or swelling

DISPOSITION

If trauma to the canal occurs then the patient should be started on topical otic drops and the parent advised to return from persistent bleeding or discharge from the ear.

ELECTRICAL INJURIES

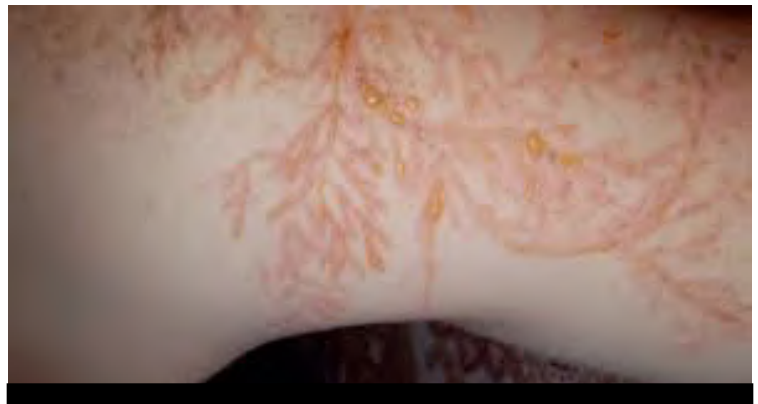
INTRODUCTION (KATHERINE FULLERTON, M.D. 8/2016)
Electrical injuries result in approximately 700 deaths/yr in the U.S. Those at highest risk are young children 0-6 years (due to exploratory behaviors such as pulling on or placing an electrical cord in their mouth or placing an object into an electrical socket), and 12-18 years (particularly adolescent males with risk taking behaviors such climbing telephone/electric poles, playing in abandoned buildings) and adults with occupational exposures (electricians). People who spend a lot of time out of doors are at risk for lightning injuries. The effects of electrical injuries include: the direct effect of the electrical current on tissue, the conversion of electrical current to thermal injury and blunt trauma.

FACTORS DETERMINING THE EXTENT OF ELECTRICAL INJURY	
Resistance	Injury extent inversely related to resistance High resistance tissue heats up, develop coagulation necrosis Resistance: Oral mucosa < Dry skin < Thick skin on palms/soles
Current Type	AC current used in households Cause tetanic contractions, unable to release hand from electrical source. Increases contact time and therefore tissue penetration
	DC used in medical setting (defibrillation, pacing), railroad tracks, auto electrical systems, lightning Can trigger asystole, ventricular fibrillation
Frequency	Low voltage (< 1000 Volts) versus High Voltage (> 1000 Volts) Low voltage follows the path of least resistance High voltage follows a direct path High voltage injury can cause muscle contraction enough to throw the victim. Decreases time of contact but increases the risk of blunt trauma
Contact Duration	Longer contact will lead to more severe symptoms. However even a very brief contact with a high voltage source can lead to significant injury
Pathway	Entry and exits wounds do not correlate with extent of internal injury Hand to hand flow: Mortality from spinal cord transection C4-C6 Hand to foot flow: Mortality from cardiac arrhythmia

LIGHTNING INJURIES

Lightning strikes have an approximate 5-20% risk of mortality resulting in 100 deaths/year in the U.S.)**.** They are very high voltage (up to a million volts) and of a short duration. “Flash over” is common with electricity traveling superficially over the skin and exiting at ground level. A characteristic “feathering” pattern of the skin, that is transient, may be seen.

There is 70% morbidity in survivors**.** Injuries include: blast injury, superficial burns and central nervous system injury. CNS is more common and superficial burns are less common than non-lightning, high voltage injuries. Keraunoparalysis is transient paralysis and sensory deficits as the result of vasospasm and can present with a blue, mottled, pulseless extremity.



FEATHERING BURN

TASER INJURIES

Taser injuries are becoming more common as they are used more frequently by law enforcement agencies. They produce a burst of high voltage, low DC current. There is no evidence that with brief exposure (< 15 seconds) their use results in dangerous laboratory abnormalities and either immediate or delayed myocardial ischemia or arrhythmias. Concurrent use of sympathomimetics, such as PCP, cocaine or methamphetamines may, increase the risk of complications.

ELECTRICAL INJURY COMPARISON			
	LOW VOLTAGE	HIGH VOLTAGE	LIGHTNING (VERY HIGH)
Duration	Long	Brief	Instantaneous
Cardiac	Ventricular Fibrillation	Ventricular Fibrillation	Asystole
Burns	Superficial	Deep Common	Rare, Superficial “Flashover”
Rhabdomyolysis	Common	Very Common	Common
Blunt trauma	Rare, Fall	Fall (Tetany)	Blast Injury
Mortality	Low	Moderate	High

CLINICAL MANIFESTATIONS

Every system may be involved with an electrical injury so a complete history and physical examination is essential. The degree of external injury does not necessarily correlate with internal injury.

*See: PEM Guide: Environmental Injury: Burns

MANIFESTATIONS OF ELECTRICAL INJURY BY SYSTEM	
Cardiovascular	Asystole and arrhythmias. Tachycardia’s (ventricular fibrillation and SVT) and heart blocks are most common Myocardial ischemia is rare Myocardial contusion due to direct electrical injury or trauma
Neurologic	Loss of consciousness, amnesia, intracranial hemorrhage, peripheral neuropathy, autonomic dysfunction, SIADH (delayed), brainstem (medullary) paralysis Fixed and dilated pupils can be seen with lightning injury and should not be used to determine the end point of resuscitation
Musculoskeletal	Tetanic contractions, fractures (including C-spine), rhabdomyolysis, compartment syndrome, dislocations (e.g. shoulder)
Ocular	Hyphema, corneal lesions, retinal detachment, cataracts and optic atrophy (delayed)
Lungs	Pleural effusions, respiratory arrest
Skin*	Burns (also burns to internal organs in injury pathway)
Oral/facial	Airway compromise with significant swelling Orofacial/labial burns (in children chewing on electric cords) Significant bleeding when eschar detaches in 2-3 weeks

ELECTRICAL INJURY MANAGEMENT	
Pre-hospital	Remove from the current, high quality CPR, C-spine immobilization
	After lightning strikes, victims often recover from cardiac arrhythmias and die from respiratory arrest
History	Nature of contact: AC/DC. High/Low voltage, pathway
	Current complaints
Physical	Assess ABCDE's (Helpful to approach as a trauma patient)
	Complete head-toe exam with emphasis on the following areas
	Oral burns/edema: can lead to airway compromise
	Pulses, perfusion
	Neurologic exam
	Eye and ear exam
	Chest wall and abdomen
	Entry and exit wounds may suggest injury pathway
Testing	Indicated for: 1. high voltage injury or 2. low voltage injury with significant symptoms or physical examination findings
	CBC, BMP (K+, BUN/Cr), CPK
	Urinalysis, myoglobin
	EKG, troponin
	X-RAYS, e.g. C-spine (identify fractures, dislocations)
	CT head (neurologic deficits, persistent altered mental status)
Monitor	Continuous cardio-respiratory monitor
	High voltage injuries may cause delayed cardiac arrhythmias.
Management	Assess airway/ breathing. Endotracheal intubation
	Maintain hydration with volume expansion as needed. Burn formulas, such as the Parkland formula may significantly under-estimate fluid requirements
	Maintain urine output > 1-2 ml/kg/hour (child), 100 ml/hour (adult)
	Restrict fluids if CNS injury suspected
	Rhabdomyolysis: consider diuretics, urinary alkalinization
	Tetanus vaccine: burns considered tetanus prone (see table below)
	Treat arrhythmias as per ACLS, PALS algorithms
	Consider surgery consult for fasciotomy for compartment syndrome
	Minor burn care: topical antibiotic ointment
	Transfer to burn center (see table below for criteria)

TETANUS PROPHYLAXIS				
	CLEAN, MINOR WOUNDS		ALL OTHER WOUNDS[1]	
History	Td[2]	TIG[3]	Td[2]	TIG[3]
< 3 doses	YES	NO	YES	YES
>= 3	NO[4]	NO	NO[5]	NO
1: Wounds contaminated by dirt, feces, soil, saliva. Puncture wounds, avulsions. Wounds from missiles, crushing, BURNS, frostbite				
2: For children < 7years: DTAP or DT, > 7 years Td recommended				
3: TIG (Tetanus Immune Globulin): 250 Units Intramuscularly				
4: Yes if > 10 years since last dose				
5: Yes if > 5 years since last dose				

DISPOSITION

A review of pediatrics electrical injuries (Chen, Annals EM 2007, PubMed ID: 17141143) found that "Healthy children exposed to common household currents (120 to 240 Volts and without water contact), if asymptomatic at ED presentation and without a ventricular arrhythmia or cardiac arrest in the field, are at very low risk for developing cardiac arrhythmias. Patients with a normal initial ECG result do not develop late dysrhythmias, and those with nonfatal arrhythmias or nonspecific ECG abnormalities typically resolve spontaneously within 24 hours".They conclude that the "available literature supports the practice of safely discharging these children without an initial ECG evaluation or inpatient cardiac monitoring after a common household current exposure. Our recommendations do not pertain to patients who might require admission for other injuries."

ADMISSION CRITERIA	
High Voltage Exposures	Admit all for cardiac monitoring
Low Voltage Exposures	Initial loss of consciousness Persistent altered mental status Cardiac arrest arrhythmia Suspicion of significant internal, deep tissue injury

AMERICAN BURN ASSOCIATION: BURN CENTER TRANSFER CRITERIA (2017)*
Partial thickness burns > 10% total body surface area
Burns that involve the: Face, hands, feet, genitalia, perineum, or major joints
Third-degree burns
Electrical burns including lightning injury
Chemical burns
Burns associated with inhalation injury
Patient with preexisting medical disorders that could complicate management, prolong recovery, or affect mortality
Any patients with burns or concomitant trauma (e.g., fracture) in which the burn injury poses the greatest risk of morbidity or mortality.
Burned children in hospitals without qualified personnel or equipment for the care of children
Burn injury in patients who require special social, emotional or rehabilitative intervention

FROSTBITE

INTRODUCTION (MICHAEL MOJICA, MD, 4/2021)
Frostbite occurs when soft tissue freezes. The pathophysiology of frostbite is multifactorial. Direct tissue damage occurs to due cold-related ischemia (vasoconstriction, vascular thrombosis) and crystal formation. This is compounded by reperfusion inflammatory changes. The fingers, toes, ears, nose, chin and cheeks are most commonly affected. Rapid diagnosis and treatment are the key to preserving tissue viability. See: PEM Guide: Environmental Injuries: Hypothermia

Other cold-induced soft tissue injuries include chilblains, immersion foot and frostnip. Chilblains (pernio) occur due to exposure to moist environment above the freezing point. Localized inflammation presents as edematous, red or purple lesions that be painful and/or pruritic. Immersion foot (aka trench foot) occurs after prolonged exposure to dampness and non-freezing cold resulting in injury to the sympathetic nerves and vasculature of the foot. Signs and symptoms included erythema, edema, numbness and pain. Severe cases can be associated with hemorrhagic bullae and tissue loss. The term frostnip denotes cold induced paresthesias that resolve with rewarming.

CLINICAL MANIFESTATIONS
Frostbite commonly presents with numbness and tingling and appears white or grey and hard or waxy to touch.

FROSTBITE CLASSIFICATION		
Superficial	First Degree	No blistering Pallor, anesthesia, surrounding edema
	Second Degree	Large, clear blisters, surrounding erythema, edema
Deep	Third Degree	Small, hemorrhagic blisters, Deep: Necrosis, blue/back
	Fourth Degree	Deep tissue necrosis to muscle/bone

EXTREMITY FROSTBITE CLASSIFICATION				
	Grade 1	Grade 2	Grade 3	Grade 4
Cyanosis Day 0[1]	None	Distal phalanx	Middle/Proximal Phalanx	Carpal/Tarsal
Bone Scan Day 2[1]	NA	Hypo-fixation of radio-tracer	Absent Uptake Digit	Absent Uptake Carpal/Tarsal
Blister Day 2[1]	None	Clear	Hemorrhagic Digit	Hemorrhagic Carpal/Tarsal
Amputation	None	Tissue	Bone	Bone Limb Systemic
Sequelae	None	Fingernail	Function Loss	Function Loss
1. Days after reperfusion				

COMPLICATIONS

Complications of frostbite are the result of tissue necrosis, neurovascular injury and abnormalities of sympathetic tone. Short term complications include gangrene/infection, throbbing pain in the first 2-3 days after rewarming and paresthesias, burning and electric shock type pain for weeks to months. Auto-amputation can take weeks. Therapeutic amputation may be required earlier for deep infection. Long term complications can include scarring and contracture, peripheral neuropathy, chronic pain and arthritis. Patients develop hypersensitivity to cold and are at increased risk of subsequent frostbite. Patients should be advised to avoid cold exposure for 6 months after mild frostbite and for a year after moderate to severe frostbite.

IMAGING

Imaging studies can determine the extent of injury, progression after rewarming and need for debridement/amputation (tissue viability). Bone scan (Technetium (Tc)-99m scintigraphy) can be used to examine the microcirculation and identify those for whom thrombolytic therapy may be warranted after rewarming. Recent case reports suggest that MRI/MRA may be superior to bone scan though evidence is limited. Plain XRAYs, are indicated only in those with suspected trauma.

MANAGEMENT

Prehospital care includes moving to a warm environment, removal of wet clothing and splinting to minimize injury. Patients should not walk on frostbitten feet. Avoid rewarming if it is possible that the tissue can refreeze as tissue damage can be exacerbated by thawing then refreezing. Rewarming may include immersion in warm water. Hot temperatures should be avoided as insensate skin can burn without notice.

Emergency department care should prioritize management of possible trauma or systemic hypothermia. Rapid rewarming can occur in a warm (not hot) water bath (37-40°C). Complete thawing typically occurs within 15-30 minutes and is indicated by a red or purple color and tissue that is soft to the touch. Analgesia will be required for moderate to severe injury as rewarming and reperfusion occurs.

ANTITHROMBOTIC THERAPY: (See the American Burn Association guideline (Hickey S, J Burn Care Res 2020, PubMed ID: 31899512). Tissue Plasminogen Activator (TPA) can be used to reverse thrombosis and improve perfusion. It is less effective after 24 hours or if freeze-thaw-refreezing has occurred. TPA can be administered both intravenously and intra-arterially. It is typically combined with intravenous heparin or subcutaneous Enoxaparin (Lovenox). The reversal of thrombosis must be balanced against the risk of hemorrhage.

ANTITHROMBOTIC THERAPY: INDICATIONS
Within 24 hours of injury AND
Grade 3 or 4 injury AND
Loss of perfusion at or proximal to the middle phalanx on bone scan immediately after rewarming AND
No TPA absolute contraindications

TPA CONTRAINDICATIONS
Absolute
Active internal bleeding
Concurrent or past history of intracranial hemorrhage
Concurrent subarachnoid hemorrhage
Endocarditis
Intracranial arteriovenous malformation, aneurysm or neoplasm
Known bleeding diathesis: e.g. Heparin or oral anticoagulant use, thrombocytopenia
Neurosurgery, head trauma or stroke within the past 3 months
Uncontrolled hypertension: Adult: Systolic > 185, diastolic > 110
Relative
Major surgery or serious head trauma within 2 weeks
Gastrointestinal or urinary tract hemorrhage within 3 weeks
Recent lumbar puncture or arterial puncture at a non-compressible site
Pregnancy

ANTITHROMBOTIC THERAPY: ADULT DOSING[1]
Alteplase (Intravenous)
Bolus: 0.15 mg/kg IV over 15 minutes
Infusion: 0.15 mg/kg/hour x 6 hours
Maximum total dose of 100 mg
Alteplase (Intra-arterial): Divide dosage if > 1 extremity involved
Bolus: 2-4 mg IA (brachial or femoral artery) over 15 minutes
Infusion: 0.5-1.0 mg/hour
Repeat angiogram Q8-12 hours
Heparin OR Enoxaparin
Heparin: 500-1,000 units/hour x 6 hours (target a twice normal PTT)
Enoxaparin (Lovenox): 1 mg/kg subcutaneously BID x 14 days
1. Consult pediatric hematology for pediatric dosing

VASODILATOR THERAPY: Prostacyclin is a vasodilator that has been shown to decreased amputation rates for severe frostbite. It can be administered with TPA or alone if TPA is contraindicated or more it has been more than 24 hours since injury. It is indicated for grade 2-4 injury within 48 hours.

PROSTACYCLIN DOSING
0.5 nanograms/kg/minute
Q30 minutes by 0.5 nanograms/kg/minute to a maximum of 2.0 nanograms/kg/min
by 0.5 nanograms/kg/minute for headache or hypotensive
Administer for 6 hours/day at the maximum tolerable rate for 5 days

WOUND CARE: Wound care includes a soft, bulky dressing, elevation to prevent edema and splinting to avoid contractures. Let tissue dry completely before dressing. Non-adherent gauze should be used as the first layer. Sterile cotton should be placed between digits. Avoid the use of occlusive dressings. There is no consensus on the management of blisters. One approach is to leave small bullae intact, debride large, clear bullae that impede mobility (e.g. involving a joint) and aspirate large hemorrhagic bullae.

Further management involves, analgesia and debridement. Tetanus prophylaxis should be administered as wounds resulting from frostbite are considered tetanus prone. Prophylactic antibiotics are not routinely recommended due to a dearth of evidence. Treatment of established infection should include intravenous antibiotics with coverage for staphylococcus, streptococcus and pseudomonas.

TETANUS PROPHYLAXIS				
	CLEAN. MINOR WOUNDS		ALL OTHER WOUNDS[1]	
History	Td[2]	TIG[3]	Td[2]	TIG[3]
< 3 doses	YES	NO	YES	YES
≥ 3 doses	NO[4]	NO	NO[5]	NO
1. Wounds contaminated by dirt, feces, soil, saliva, Puncture wounds, avulsions, wounds from missiles, crushing, burns, frostbite				
2. < 7 years DTAP or DT recommended, > 7 years Td recommended				
3. Tetanus Immune Globulin 250 Units IM				
4. Yes if > 10 years since last dose				
5. Yes if > 5 years since last dose				

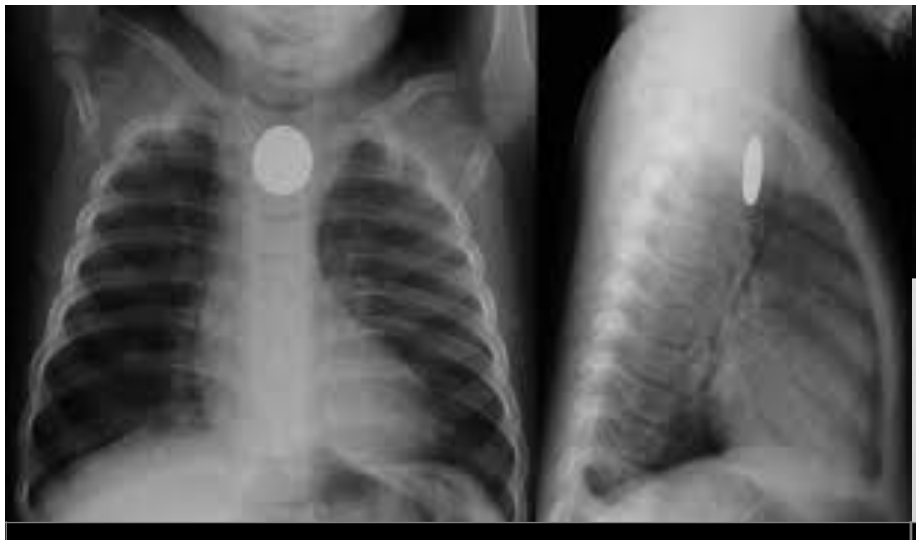
GASTROINTESTINAL FOREIGN BODIES

INTRODUCTION (ETHAN WIENER, M.D. 5/2023)
Ingested foreign bodies are common. The most common ingested foreign bodies are coins. Many of these will pass uneventfully into the stomach and proceed naturally due to peristalsis. Others may lodge initially in the esophagus.

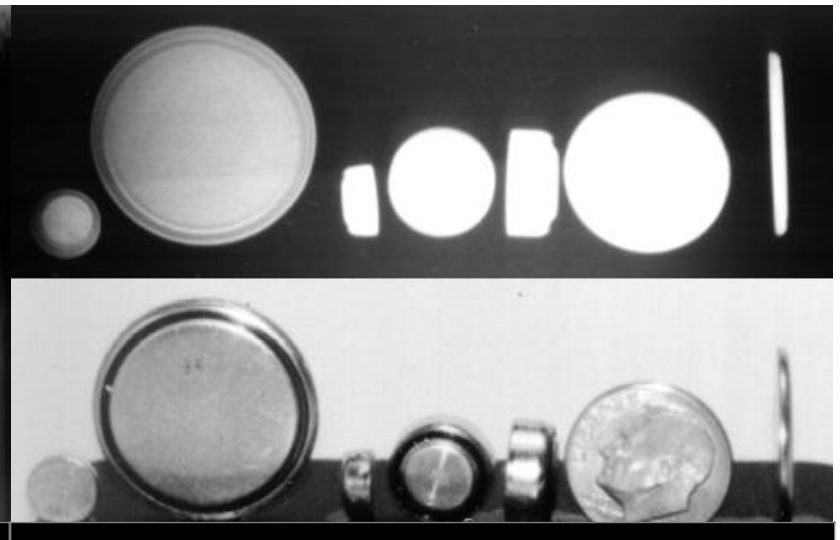
Common sites for foreign bodies in the esophagus are at the level of the cricopharyngeus muscle (thoracic inlet) (65%), the level of the aortic arch (10%), and the lower esophageal sphincter (20%). These sites are associated with anatomic narrowing of the esophageal canal. Distal coins may be lodged in the lower GI tract at the pylorus, the ligament of Treitz and at the ileocolic junction.

DIAGNOSIS
A history of a choking episode, drooling and intolerance of food may suggest a GI foreign body. Patients may report symptoms of a “stuck” sensation, retrosternal chest pain, dysphagia or refusal to feed. A physical exam should focus on the neck (swelling, erythema, crepitus), the chest (stridor, wheezing, decreased aeration) and the abdomen (tenderness, distention, peritoneal signs).

XRAYs will determine the presence and location, shape and number of a radio-opaque foreign body. Biplane XRAYS (AP and Lateral), soft tissue lateral neck XRAYS and abdominal XRAYS are typically ordered. If another example of the foreign body is available it is helpful to XRAY it as well to determine if it is radio-opaque on XRAY.



XRAY: RADIOPAQUE FB (COIN) THORACIC INLET (CORONAL PLAIN)



XRAY: COINS & DISK BATTERIES

IMAGE FROM: RADIOLOGY CASES IN PEDIATRIC EMERGENCY MEDICINE

30-40% of foreign body ingestions are radiolucent. XRAYS can help in identifying signs of perforation (free air) or obstruction (hyperinflation of a lung, air fluids levels of the intestines). Further imaging by CT or MRI may be required if there is a high suspicion, a symptomatic patient or based on potential object characteristics (length > 5 cm, sharp, potential toxic material).

MANAGEMENT

Most gastrointestinal foreign bodies will pass spontaneously. Approximately 10-20% require endoscopic removal and less than 1% require surgery. Spontaneous passage is more likely in older children and coins located in the distal third of the esophagus. See: NAGSPAN Guideline, JPNG 2015, PubMed ID: 25611037). Management is based on the type of foreign body (coin, button battery, magnet, other) its location and the patients symptoms.

GLUCAGON: Glucagon has been found to increase peristalsis, decrease esophageal transport time and relax the lower esophageal sphincter tone. A 2019 meta-analysis of Glucagon compared to control for esophageal food impaction or foreign body included 5 studies and 1,085 patient (Peksa, Pharmacotherapy 2019, PubMed ID: 30779190). There was no difference in the rate of passage but a higher rate of adverse events in those receiving Glucagon. However, only one study including 14 children with an esophageal coin was included. The remaining patient were adults with esophageal food impaction.

OBSERVATION: A period of observation of up to 24 hours is recommended in many children found to have esophageal coins prior to intervention. In a randomized clinical trial of management of esophageal coins in children the authors concluded that “Because 25% to 30% of esophageal coins in children will pass spontaneously without complications, treatment of these patients may reasonably include a period of observation, in the range of 8 to 16 hours, particularly among older children and those with distally” (Waltzman, Pediatrics 2005, PubMed ID: 16140701).

REMOVAL: Removal techniques include flexible and rigid endoscopy. Flexible endoscopy is generally preferred. Removal of esophageal objects is done to prevent significant complications such as esophageal perforation from erosion, esophageal-aortic fistulas, and stricture formation due to inflammation. Removal, however, is not without risks. These include aspiration, bleeding complications, bronchospasm, and esophageal perforation.

URGENT EVALUATION AND MANAGEMENT
Long objects (> 5cm)
Super-absorbent materials that will expand in the GI tract
Disk (button) batteries in the esophagus
Ingestion of a magnet with another magnet or metallic foreign body
Patients with airway compromise
Inability to tolerate secretions
Signs of gastrointestinal obstruction/perforation

BUTTON (DISC) BATTERIES

Most batteries that are ingested are button batteries. A button battery that is lodged in the esophagus should be removed expeditiously to prevent complications from esophageal erosion due to leakage of battery contents into the esophagus. Mucosal necrosis can occur within 2 hours of ingestion and perforation can occur within 8 hours. Erosion into adjacent vessels (e.g., the aorta) can led to life-threatening hemorrhage. WEB LINK: BUTTON BATTERY MANAGEMENT GUIDELINE

There is some evidence that honey or Sucralfate can decrease esophageal injury (Anfang, Laryngoscope 2019, PubMed ID: 29889306). Honey is restricted to those over 1 year of age due to botulism concerns. 10 ml of either Q10 minutes is recommended if within 12 hours of ingestion. The National Button Battery Ingestion Hotline can be reached at 202-625-3333.

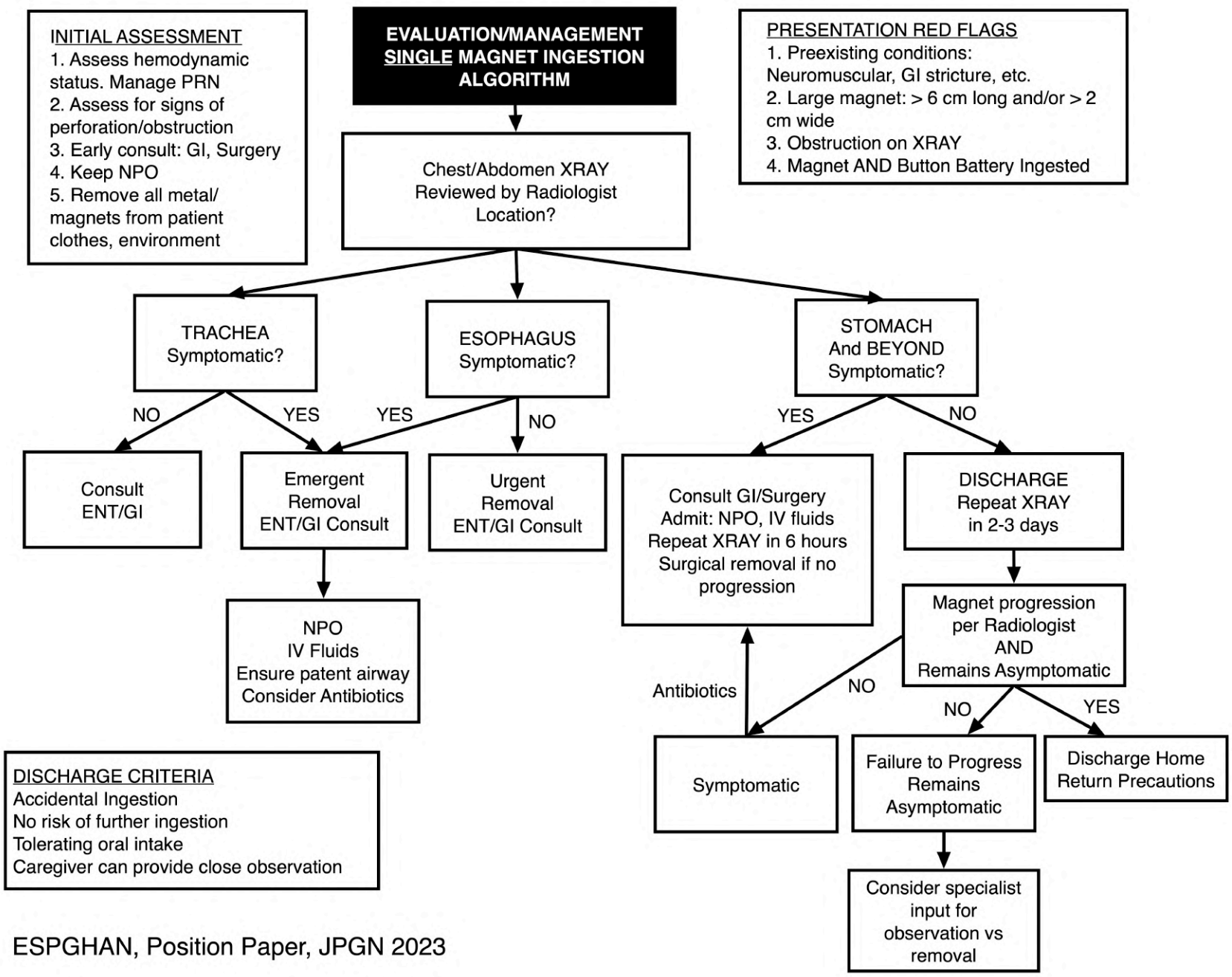
Buttons that pass into the stomach in an asymptomatic patient should be followed for several days to ensure passage. Those less than 6 years of age or with a > 20mm diameter button battery should have a repeat XRAY in 4 days. Those not meeting these criteria should follow up in 10-14 days for a repeat XRAY

ENDOSCOPY INDICATIONS: BUTTON BATTERIES
Esophageal
Symptomatic: Pain, drooling: May cause esophageal injury prior to distal passage
≥ 1 Button Battery
Button battery with magnet co-ingestion

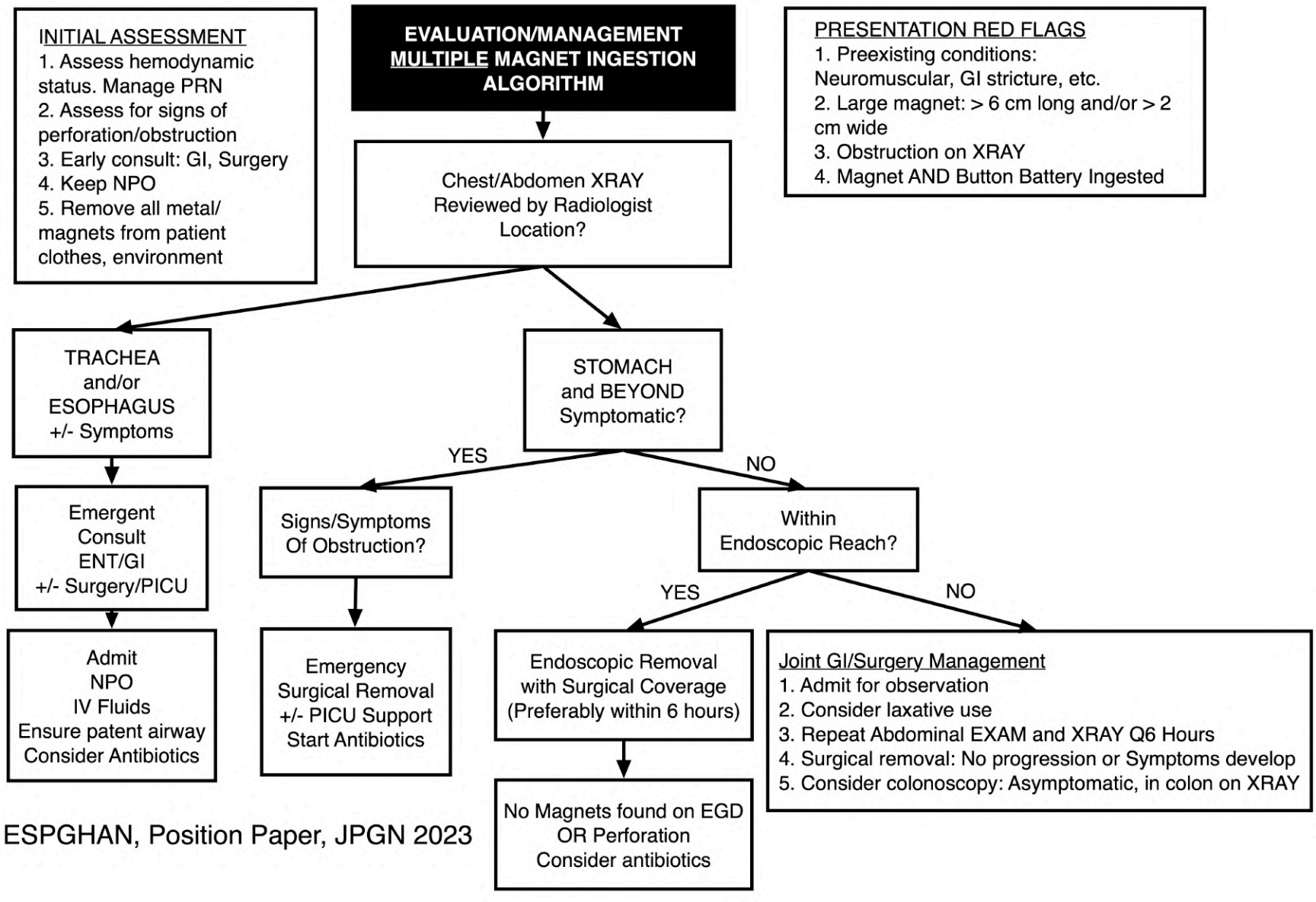
MAGNETS

Magnets present a problem when more than one magnet is ingested (or 1 magnet and a metallic foreign body) and there is a risk of adherence across the intestinal walls of adjacent lumens and resultant ischemia.

The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) provide algorithms for the evaluation and management of single and multiple magnet ingestions based on the location of the magnet(s) and symptom status (ESPGHAN, JPGN 2023, PubMed ID: 36947000).. Magnet ingestions are generally managed in tandem by pediatric gastroenterology and pediatric surgeon. Single magnet ingestions in asymptomatic patients are generally safe. Multiple magnets that are joined firmly together in the stomach can generally be managed with watchful waiting. Surgical management is indicated if there are signs of obstruction or perforation of is the magnets can not be reached endoscopically. Antibiotics such as Piperacillin/Tazobactam or Meropenem may be considered in patients with complications such as obstruction, perforation, peritonitis or sepsis.



ESPGHAN, Position Paper, JPGN 2023



ESPGHAN, Position Paper, JPGN 2023

STRAIGHT PINS: Surprisingly, straight pins generally pass without incident, especially if there is a weighted tip on one end. The micro-perforations that are assumed to occur have not been shown to have clinical significance.

OTHER FOREIGN BODIES: Many types of foreign bodies can lodge in the esophagus as well. The most problematic ones tend to be radiolucent. These include food, toys, and other household items. This can lead to a delay in diagnosis. If a radiolucent foreign body is suspected, the diagnostic study of choice after the negative plain XRAY is a contrast esophagram.

DISPOSITION

Any patient who presents with symptoms of drooling, dysphagia, stridor or vomiting should proceed to intervention. The intervention of choice is often institution-dependent and varies from fluoroscopic removal by a radiologist to endoscopic removal under general anesthesia by a pediatric gastroenterologist or pediatric surgeon. Interventions are more common the younger the patient and the more proximal the foreign body.

HIGH ALTITUDE ILLNESS

INTRODUCTION: (SHWETA IYER, M.D., 11/2021)
Cities in the western U.S., South America, and Asia frequently have altitude elevations greater than 2000-3000 meters above sea level. Additionally, climbers, athletes, and skiers often ascend to elevations greater than this. Children are more susceptible to hypoxia than adults. Infants < 6 weeks of age should avoid ascent over 2500 meters. Pregnancy does not appear to affect altitude illness, and travel to moderate altitudes is safe. High altitude illness (HAI) is a collective term that includes several specific disease manifestations (see table). Acute mountain sickness (AMS) is the most frequent form of high-altitude illness. Other forms are relatively rare but include life-threatening conditions such as high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE).

DEFINITIONS	
High Altitude Illness (HAI)	Collective term that includes the clinical manifestation listed below
Acute Mountain Sickness (AMS)	Typically, an early manifestation with nonspecific symptoms such as headache, fatigue and malaise.
High Altitude Cerebral Edema (HACE)	Characterized by encephalopathic symptoms: ataxia, progressive depression in mental status
High Altitude Pulmonary edema (HAPE)	Characterized by non-cardiogenic pulmonary edema Develops a few days after ascent and is life threatening Most common cause of death
Other altitude related illness	Other symptomatic manifestations of altitude illness: High altitude retinal hemorrhage Periodic breathing of sleep

PATHOPHYSIOLOGY
The oxygen in inspired air diffuses across alveoli into the blood. The amount of oxygen which reaches the bloodstream is dependent on the partial pressure of oxygen. The fall in atmospheric pressure at higher altitude decreases the partial pressure of inspired oxygen. In addition, the ability for oxygen to diffuse from capillaries to the mitochondria is also reduced in higher altitudes. These factors lead to tissue hypoxia at high altitudes (hypobaric hypoxia). Children are at higher risk of high-altitude periodic breathing and have an increased risk of pulmonary hypertension leading to acute right heart failure.

HIGH ALTITUDE CEREBRAL EDEMA: High altitude illness is a spectrum from acute mountain illness to high altitude cerebral edema. High altitude cerebral edema is a result of increased extravascular fluid (vasogenic edema) in the brain. HACE is thought to be due to increased cerebral blood flow, loss of cerebral auto-regulation and multiple chemical factors that result in increased permeability of the blood brain barrier. HACE is more common in patients with HAPE. Cerebral herniation is the primary cause of death.

HIGH ALTITUDE PULMONARY EDEMA: HAPE is thought to occur because of breakdown in the pulmonary blood/gas barrier. Pulmonary artery pressure increases due to compensatory mechanisms to hypobaric hypoxia. Hypoxic pulmonary vasoconstriction results in pulmonary hypertension. This process is variable throughout the lungs resulting in increased flow to non-affected areas. Chemical and genetic factors also lead to the accumulation of extracellular fluid, protein and cells in the alveoli. The presence of HAPE increased the likelihood of HACE. 50% of patients with HAPE will not have other symptoms of acute mountain sickness.

ACCLIMATIZATION

Acclimatization is the process by which the body partially compensates for higher altitudes. In response to hypoxia, several mechanisms improve oxygen delivery and utilization. This process typically takes days to weeks and varies widely. The most common change with altitude is an increase in minute ventilation (the hypoxic ventilator response). This results in a respiratory alkalosis. Circulatory changes include increased sympathetic activity resulting in increases in cardiac output, heart rate and vascular tone (both systemic and pulmonary). Stroke volume decreases due to a decrease in plasma volume as a result of bicarbonate diuresis. Cerebral blood flow is typically well maintained until late stages. Hypoxemia stimulates erythropoietin production creating an increased hemoglobin concentration within the first few days.

CLINICAL MANIFESTATIONS

Symptoms of acute mountain illness typically occur within 6-12 hours after ascent, but range from 1 hour to 1 day after ascent. There are no objective markers of acute mountain sickness. A scoring system such as the Lake Louise Score or Children's Lake Louise Score can be used. (See Appendix).

RISK FACTORS	
General	Genetic susceptibility Hypoxic stress Cold temperature Degree of exertion Rate of ascent Final elevation achieved (especially sleeping elevation)
Pediatric	Viral upper respiratory infection: Otitis media, pneumonia Congenital cardiopulmonary disease: Cardiac disease with R→L shunts, sickle cell disease, cystic fibrosis, and chronic lung disease Trisomy 21 Systemic pulmonary disease (e.g. asthma, bronchopulmonary dysplasia) Neuromuscular disorders affecting respiratory reserve

HISTORY	
History	Ascent (absolute altitude, rate of ascent) History of prior high-altitude illness Comorbidities: ischemic heart disease, lung disease, sleep apnea, baseline need for supplemental oxygen Exercise history. Those regularly exercising at high altitudes are less likely to be affected
Common symptoms	Headache Fatigue, Malaise Dizziness and/or Lightheadedness Nausea, Vomiting Dyspnea Poor sleep Anorexia
Common symptoms (infants)	Crying Irritability Decreased playfulness/activity Poor feeding or vomiting Poor sleep
HAPE (Infants/ Children)	Respiratory distress, Nonspecific symptoms (such as fussiness) Pallor Decreased level of activity and consciousness
HAPE (Adolescents)	Low grade fever (<101F) Breathlessness, difficulty breathing Cough Sputum production: Early: frothy, pink, Late: frank blood
HACE	Ataxia Progressive loss of consciousness: Irritability, drowsiness, coma Decreased activity/sleepiness (especially in infants)
Other altitude related illness	High altitude retinal hemorrhage: Blurry vision High altitude periodic breathing of sleep: Alternating deep and shallow breathing with/without apneic periods (a type of Cheyne-Stokes respiration)

PHYSICAL EXAMINATION

Physical examination findings are limited in those with mild to moderate acute mountain sickness. Physical exam findings may be present in those with severe high-altitude illness. Findings in those with high altitude pulmonary edema may include: cyanosis, tachypnea, jugular venous distention, hepatomegaly, diffuse rales and cardiac murmur. Findings in those with high altitude cerebral edema may include: ataxia, depressed mental status and impaired coordination. Focal neurologic deficits are rare and should prompt an evaluation for other etiologies (e.g. stroke).

DIFFERENTIAL DIAGNOSIS

Since high altitude illness often presents with non-specific symptoms, several alternative diagnoses should be considered. These include: carbon monoxide poisoning, dehydration, migraines, viral illness, and toxic ingestions. In infants, the differential includes undetected intra-cardiac or fetal shunts. Consider alternative diagnoses if a patient has symptoms such as the absence of headache, symptoms continuing for more than 2 days after reaching an altitude, failure to improve with oxygen, or shortness of breath without exertion.

LABORATORY/RADIOLOGY TESTING

Diagnosis is made clinically in a patient who lives at a low altitude who has ascended to a high altitude (> 2000 meters). There are no specific labs or imaging that definitively diagnose high altitude illness. Pulse oximetry and blood gas analysis may show hypoxemia or decreased oxygen saturation, but this is not reliable. Lumbar puncture findings are typically normal, and WBC count may or may not be elevated. Targeted testing can be useful to exclude other diagnoses.

HIGH ALTITUDE PULMONARY EDEMA: A chest XRAY may reveal the diffuse interstitial changes of non-cardiogenic pulmonary edema. The XRAY appearance is typically worse than the patient's clinical appearance. An EKG and echocardiogram can be obtained to identify right heart failure because of pulmonary hypertension. HAPE and pneumonia can co-exist.

HIGH ALTITUDE CEREBRAL EDEMA: A CT may show cerebral edema. A brain MRI reveals characteristic findings of intense T2 signal in the white matter without grey matter lesions.

MANAGEMENT

Treatment is based on the severity of acute mountain sickness. Treat of mild symptoms is generally supportive only. Moderate to severe illness may require medications, supplemental oxygen and descent. Evidence for pharmacologic treatment of acute mountain sickness is limited.

MILD ACUTE MOUNTAIN SICKNESS
Rest, limited physical activity
Avoid further ascent, cold temperatures, alcohol, other respiratory depressants
Analgesics: NSAIDs, Acetaminophen
Antiemetics: Ondansetron
Supplemental oxygen. Rapid resolution of symptoms virtually diagnostic of mild AMS
1º Acetazolamide: ↑ HCO_3 in urine resulting in acidemia. Increases minute ventilation Adults: 125-250 mg PO Q12H, Children: 2.5 mg/kg (max dose 250 mg) PO Q12H Continue for 24 hours after symptom resolution or descent completed
2º Dexamethasone: Anti-inflammatory response Adults: 2-4 mg PO Q6H, Children: 0.15 mg/kg (max dose 4 mg) PO Q6H Continue for 24 hours after symptom resolution or descent completed but < 7 days
Should not ascend further until symptoms resolve

HIGH ALTITUDE PULMONARY EDEMA
Immediate descent is not always required
Rest, limited physical activity, limit cold exposure
Supplemental oxygen, potable hyperbaric therapy (simulated descent)
Hallmark of HAPE is rapid improvement with oxygen and/or decent
Medications: Limited evidence of efficacy. Use only if oxygen is not available and descent is not possible
1º Nifedipine: Calcium channel blocker: ↓ pulmonary vascular resistance, ↓ pulmonary artery pressure. May require IV fluids due to decreased systemic vascular resistance
2º Tadalafil/Sildenafil: Augments nitric oxide pulmonary vasodilation ↓ pulmonary artery pressure without ↓ systemic vascular resistance (benefit over Nifedipine)
No longer recommended: Diuretics, Morphine, Nitrates

MODERATE-SEVERE ACUTE MOUNTAIN SICKNESS
Rest, limited physical activity, avoid alcohol and other respiratory depressants
Analgesics: NSAIDs, Acetaminophen, Antiemetics: Ondansetron
More severe illness may require descent
Supplemental oxygen
Portable hyperbaric therapy (simulated descent)
1º Dexamethasone: ↓ symptoms, does not improve acclimatization Can be used in conjunction with Acetazolamide Adults: 4 mg PO/IM Q6H, Children: 0.15 mg/kg (max dose 4 mg) PO/IM Q6H Continue for 24 hours after symptom resolution or descent completed but for < 7 days Should not ascend further if on Dexamethasone alone due to lack of acclimatization
2º Acetazolamide: ↓ symptoms, ↑ acclimatization, Contraindicated: sulfa allergy Adults: 125-250 mg PO Q12H, Children: 2.5 mg/kg (max dose 250 mg) PO Q12H Continue for 24 hours after symptom resolution or descent completed Avoid further ascent until symptoms have subsided

HIGH ALTITUDE CEREBRAL EDEMA
Immediate descent may be life-saving and is the definitive treatment
1º Dexamethasone: Adults: 8-10 mg PO/IM/IV x 1 then 4 mg PO/IM/IV Q6H Children: 0.15 mg/kg (max dose 4 mg) PO/IM/IV Q6H Continue for 24 hours after symptom resolution or descent completed but for < 7 days
2º Acetazolamide: With DEX, not as monotherapy. Contraindicated: sulfa allergy Adults: 250 mg PO Q12H, Children: 2.5 mg/kg (max dose 250 mg) PO Q12H Continue for 24 hours after symptom resolution or descent completed
Supplemental Oxygen to maintain SpO2 > 90%
Portable hyperbaric therapy (simulated descent)
Intubated patients: Avoid hyperventilation. May result in cerebral ischemia due to preexisting respiratory alkalosis
Intravenous fluids: Avoid hypotension. Can lead to cerebral ischemia
Admit to ICU setting, neurology/neurosurgical consultation

APPENDIX: COMPARISON HIGH ALTITUDE ILLNESS

SUMMARY: HIGH ALTITUDE ILLNESS				
	High-Altitude Illness (HAI)	Acute Mountain Sickness (AMS)	High-Altitude Cerebral Edema (HACE)	High-Altitude Pulmonary Edema (HAPE)
Prevention	Gradual Ascent[1]	Gradual Ascent[1] Acetazolamide Dexamethasone	Gradual Ascent[1]	Gradual Ascent[1]
Symptoms	Headache	Headache with 1 of: nausea, vomiting, fatigue, anorexia, dizzy, poor sleeping	Early: Drowsy, apathy, withdrawal	Mild-Moderate: Cough, frothy sputum, dyspnea
			Late: Altered, ataxia, +/- headache	Severe: Hemoptysis, Irritability
Onset	Hours (<24 hrs) Resolves 2-3 d at same altitude Can recur on assent	Hours (<24 hrs) Resolves 2-3 d at same altitude Can recur on assent	Appears 1-2 days at altitude	Appears 2-4 days at altitude
Exam	Normal	Normal	Altered, Ataxia	Rales, RV heave, P2 heart sound
Lab	None	None	None	ABG: Respiratory alkalosis, hypoxemia EKG: Right heart strain
Imaging	None	None	CT or MRI	Chest XRAY
Treatment	Analgesics[2] Antiemetics[2]	Descent O_2 if Sat < 90% Analgesics[2] Antiemetics[2] Acetazolamide Dexamethasone	Descent[2] O_2 if Sat < 90% Analgesics Antiemetics Acetazolamide Dexamethasone Portable hyperbaric chamber	Descent O_2 if Sat < 90%[2] Analgesics Antiemetics Nifedipine CPAP Portable hyperbaric chamber

1. Gradual ascent
   a. Staged ascent: Few days at intermediate elevation
   b. Sleep < 500 meters higher than previous night, “climb high, sleep low”
   c. 1 day of rest for every 1,000-meter increase in elevation
2. Primary treatment, other treatments if primary is unsuccessful

APPENDIX: LAKE LOUISE SCORE: ACUTE MOUNTAIN SICKNESS

Self-reported scoring tool for patients with a rise in altitude within the past 4 days. Headache and at least one other symptom must be present for the diagnosis of AMS

LAKE LOUISE SCORE: ACUTE MOUNTAIN SICKNESS	
HEADACHE	
None	0
Mild headache	1
Moderate headache	2
Severe headache	3
APPETITE	
Good appetite	0
Poor appetite or nausea	1
Moderate nausea or vomiting	2
Severe, incapacitating nausea and vomiting	3
FATIGUE AND/OR WEAKNESS	
Not tired or weak	0
Mild fatigue/weakness	1
Moderate fatigue/weakness	2
Severe fatigue/weakness	3
DIZZINESS/LIGHTHEADEDNESS	
None	0
Mild	1
Moderate	2
Severe, incapacitating	3
DIFFICULTY SLEEPING	
Sleep as well as usual	0
Did not sleep as well as usual	1
Woke many times, poor night’s sleep	2
Could not sleep at all	3
TOTAL SCORE (Mild 3-5, Moderate-Severe ≥ 6)	

APPENDIX: CHILDREN'S LAKE LOUISE SCORE FOR AMS

Parent reported
Child with a history of rise in altitude within the past 4 days.
Total Score = Total Fussiness Score (0-12) + Pediatric Symptom Score (0-9).

CHILDREN'S LAKE LOUISE SCORE: ACUTE MOUNTAIN SICKNESS		
Amount of unexplained fussiness	0 1-5 6	No fussiness Intermittent fussiness Constant fussiness
Intensity of fussiness	0 1-5 6	No fussiness Moderate fussiness Hard crying and extreme fussiness
A. TOTAL FUSSINESS SCORE (0-12)		
Eating	0 1 2 3	Normal Slightly less than normal Much less than normal Vomiting or not eating
Playfulness	0 1 2 3	Normal Playing slightly less Playing much less than normal Not playing
Sleeping	0 1 2 3	Normal Slightly less or more than normal Much less or more than normal Not able to sleep
B. TOTAL SYMPTOM SCORE (0-9)		
TOTAL SCORE (A + B) (0-21)		
Total Fussiness Score (0-12) = Unexplained Fussiness + Intensity of FussinessTotal Score ≥ 7 (including a fussiness score ≥ 4 and pediatric symptom score ≥ 3) is considered diagnostic of acute mountain sickness		

HYPERTHERMIA

INTRODUCTION (JULIETTE QUINTERO-SOLIVAN, M.D. 5/2021)
Hyperthermia is defined as an elevated core temperature greater than 38.5°C. Heat may be generated either from extreme environmental temperatures, from increased heat production or from the inability to properly dissipate heat. Environmental and exertional heat illness occurs when the ability of the body to dissipate heat is overwhelmed.

ETIOLOGY	
Infants/Children	Non-exertional: Left in a closed vehicle on a hot day
Adolescents	Exertional: Prolonged exercise in a hot environment, particularly on humid days or if fluid intake is inadequate.
	Third leading cause of mortality among high school athletes.

PHYSIOLOGY: TEMPERATURE REGULATION

Core temperature is closely regulated to within 0.6°C (1°F) via central and peripheral thermoregulatory mechanisms. Heat production results from: basal metabolism, muscle activity, thyroxine and sympathetic stimulation of cellular processes. Heat loss results from: conduction to objects and air, convection through liquids and air, evaporation and radiation. Regulatory mechanisms include control by the posterior hypothalamus (regulates sympathetic tone (vasodilation) and the anterior hypothalamus (regulates autonomic tone (cholinergic stimulation to sweat glands)). The average person sweats 0-1.5 liters/hour in hot weather (4 liters/hour in tropical climates).

DEFINITIONS	
Fever	Hypothalamic set point is increased by circulating cytokines most typically in response to infection
Hyperthermia	Hypothalamic set point is normal, body is unable to dissipate heat effectively.
	External heat exposure and internal heat production overtake the body’s ability to dissipate heat effectively.

Individuals at risk for heat illness are un-acclimatized individuals, the elderly, laborers, athletes, and individuals with chronic illness or physical disabilities. Children at higher risk for heat related illness include: cystic fibrosis, impaired sweating (anhidrosis), infants, young athletes, obesity and those with diabetes insipidus, anorexia or cardiac disease.

PEDIATRIC RISK FACTORS
Greater ratio of body surface area to mass
Less ability to produce sweat effectively
Generation of proportionally more body heat
Lower cardiac output in relation to metabolic rate.

HYPERTHERMIA: ETIOLOGY	
TOXINS/MEDICATIONS	MEDICAL
Anticholinergic poisoning	Thyrotoxicosis
Serotonin syndrome	Pheochromocytoma
Neuroleptic malignant syndrome	Thalamic injury.
Salicylate	Intracranial hemorrhage
Malignant hyperthermia	Cystic fibrosis
Sympathomimetics/Stimulants	Infections, rheumatologic disease
Alcohol, sedative hypnotic withdrawal	PHYSICAL EXERTION
Diuretics	Obese
Tricyclic antidepressants	Non-acclimated athletes

CLINICAL MANIFESTATIONS

Heat illness manifests as three principle entities: heat cramps, heat exhaustion, and heat stroke. Heat cramps represent relatively mild illness, but heat exhaustion and heat stroke are considered to be one entity on a continuum of severity. Morbidity and mortality are directly related to the degree and duration of hyperthermia. There is poor prognosis with core temperatures over 42°C (107.6F).

COMPARISON: HEAT RELATED ILLNESS					
	TEMP	MENTAL STATUS	BLOOD PRESSURE	DEHYDRATION	SWEATING
Heat Cramps	Normal	Normal	Normal	Mild	Yes
Heat Exhaustion	< 39 C	Confusion	Orthostatic	Moderate	Yes
Heat Stroke	> 41 C	Lethargy	Hypotension	Severe	No

HEAT CRAMPS: Heat cramps are severe, brief episodes of muscular cramping which occurs in the fatigued muscles of acclimated individuals. These muscular cramps are thought to be related to a salt deficiency, which occurs in the setting of hypotonic fluid replacement. Laboratory findings reveal hyponatremia and hypochloremia. Most cases occur after exercise has ceased and are treated with oral salt solutions. The severest of cases may need intravenous isotonic crystalloid. Patients should evaluated for rhabdomyolysis.

HEAT EXHAUSTION: Heat exhaustion is an acute syndrome characterized by hyperthermia (rarely beyond 39°C, 102.2°F), malaise, fatigue, nausea, vomiting, dizziness, vertigo, sweating, headache, tachycardia, orthostatic hypotension with or without dehydration and muscle cramping and in the absence of major central nervous system dysfunction. If untreated, heat exhaustion can progress to heat stroke and the development of thermoregulatory failure.

Management of a heat exhaustion patient involves rest in a cool environment, and correction of fluid and electrolyte losses. Differentiating heat exhaustion from heat stroke can be difficult. Therefore, having a high index of suspicion for the presence of heat stroke may reduce the morbidity and mortality associated with it.

HEAT STROKE: Heat stroke is a medical emergency with an estimated mortality rate of 17-70% depending on the severity of illness. Heat stroke occurs when thermoregulatory mechanisms fail. The result is an elevation in core body temperature to extreme levels (beyond 40.5°C, 105°F) with resulting end-organ injury and multi-system failure.

Head stroke is a clinical diagnosis. Signs and symptoms are similar to those of heat exhaustion but with the additional development of central nervous system dysfunction. This may include altered mental status, confusion, hallucinations, coma, and seizures. Absence of sweat is typical of heat stroke but is not necessary for the diagnosis. Multi-organ system failure may include cardiovascular collapse, arrhythmias, respiratory failure, coagulation abnormalities and acute liver and renal failure.

EVALUATION: LABORATORY/IMAGING	
Metabolic	BMP, lactate, blood gas
Hematology	CBC (anemia, thrombocytopenia), PT/PTT, INR
Cardiac	Troponin, electrocardiogram, echocardiogram
Liver	LFTS (transaminases, bilirubin)
Muscle	Creatine kinase, urine myoglobin
CNS	Head CT to evaluate for cerebral edema
Other	D-dimer

MANAGEMENT

Management involves stabilization of the airway, breathing and circulation and aggressive cooling measures; as well as identification and correction of metabolic, electrolyte and coagulation derangements resulting from organ failure. The goal is to decrease rectal temperature to less than 40 C within 30 minutes. (See also: PEM Guide: Endocrine-Metabolic: Rhabdomyolysis)

RAPID COOLING INDICATIONS	
1	Temperature > 40C rectally associated with an altered mental status
2	Hyperthermia associated with hemodynamic instability
3	Suspected Malignant hyperthermia or Neuroleptic malignant syndrome

RAPID COOLING TECHNIQUES	
Noninvasive	Evaporative Cooling (slow): Water mist circulated with fans (moderate)
	Ice water immersion (Except head): Difficult resuscitation (severe)
	Whole body ice packing (moderate-severe)
	Strategic ice packing: Axilla, groin: Minimal efficacy (mild-moderate)
Invasive	Gastric lavage (severe): Requires airway protection
	Peritoneal lavage (severe)
	Cardiopulmonary bypass/ECMO (refractory severe)
	Cool air jet ventilation
	Ice water rectal lavage
	Intravascular cooling with cold crystalloid (limited evidence)

OTHER TREATMENTS: Antipyretics have not been found to be effective in controlling environmental hyperthermia. Malignant hypothermia and neuroleptic malignant syndrome can be treated with Dantrolene. Dantrolene decrease intracellular skeletal muscle calcium which decreased contractility. Benzodiazepines and paralytics may be necessary to reduce shivering and minimize metabolic heat production.

DANTROLENE		
	Initial Dose	Subsequent Dose
Malignant Hyperthermia	2.5 mg/kg IV	1 mg/kg Q4-6H IV[1]
Neuroleptic Malignant Syndrome[2]	1-2.5 mg/kg IV	1 mg/kg Q6H IV[1]
1. To a maximum dose of 10 mg/kg 2. Off-label use		

SUMMARY: HEAT STROKE MANAGEMENT	
Arrival	Removal from hot environment (EMS)
	Remove clothing
Monitor	Rectal or esophageal core temperature probe continuous monitoring
	HR, BP, urine output, neurologic exam/mental status
Breathing	Mechanical ventilation of respiratory failure
Circulation	Fluid resuscitation: 20 ml/kg NS or LR as needed
	Rapid Vasopressor for fluid refractory hypotension (e.g. Dobutamine) (Avoid alpha agonists and anticholinergic agents)
Myoglobinuria	Diuresis. Maintain urine output > 1ml/kg/hour Consider Lasix 1 mg/kg and/or Mannitol 0.25-1.0 gm/kg
Cooling* (best method controversial)	Goal: Core temperature to 39C within 30 minutes
	Ice pack application to axilla, groin, neck
	Cooling blanket
	Evaporation: Wet sheets, sprayed water with fan
	Cooled intravenous fluids
	Ice water immersion
	Peritoneal/thoracic lavage (no pediatric data, consider if severe
Other	Treat coagulopathy if hemorrhage
	Treat seizures
*Antipyretics are not useful in treating the hyperthermia due to environmental heat exposure. Acetaminophen could aggravate liver injury.	

DISPOSITION

DISPOSITION	
Heat Stroke	Admit to ICU
Heat Exhaustion	Vital signs not normalized OR significant lab abnormalities → Admit
	Vital signs normalized AND No significant lab abnormalities → D/C
Heat Cramps	Discharge after symptom resolution

RECOMMENDATIONS: ATHLETE RETURN TO PLAY AFTER HEAT STROKE
No exercise for at least 1 week after release from medical care
Medical follow-up about 1 week after the heat stroke incident for physical examination and possible laboratory testing of affected organs.
Supervised return to play protocol involving gradual increases in exercise duration, intensity, and heat exposure over 2 weeks.
Return to full activity in hot environments may take more than 4 weeks
American College of Sports Med: Current Sports Med R 2010, PubMed ID: 20827100

HYPOTHERMIA

INTRODUCTION (JULIETTE QUINTERO-SOLIVAN, M.D. 4/2021)
Hypothermia is defined as a core temperature less than 35°C (95°F). Populations most at risk are the elderly, children (particularly newborns), trauma victims, individuals with physical disabilities or chronic illness, those involved in cold weather recreation and those who use drugs and alcohol. (See: PEM Guide: Environmental Injury: Frostbite).

Environmental exposure is the most common cause of hypothermia in children. Younger children are at increased risk due to a proportionally greater body surface area, limited subcutaneous fat and glycogen stores needed for heat production. They are also at increased risk of exposure by becoming lost outdoors and having submersion injuries. Adolescents (particularly males) participate in risky behaviors. This is often compounded by alcohol intoxication and the use of other substances that result in peripheral vasodilation, facilitating heat loss.

PATHOPHYSIOLOGY
Heat can be lost by radiation, conduction, convection, evaporation and respiration or any combination of these factors. Regulation of body temperature involves a number of different body systems. Accordingly the differential diagnosis of hypothermia is broad.

HYPOTHERMIA: DIFFERENTIAL DIAGNOSIS	
Endocrine-Metabolic: Utilization, BMR	Drugs: CNS Depression, Vasodilation
Adrenal Insufficiency	Antidepressants e.g. Nortriptyline
Diabetes Mellitus	Antipsychotics e.g. Chlorpromazine
Hypoglycemia (stores)	Barbiturates
Hypopituitarism	Benzodiazepines
Hypothyroidism, Hypoparathyroidism	Clonidine
Menkes disease	Ethanol
Organic or Amino Acidemias	Opioids
CNS: Hypothalamic, Autonomic regulation	Systemic Infection
Brain or spinal cord injury	Encephalitis/Meningitis
Brain tumors	Sepsis
Congenital brain malformations	↓ Intake, production, subcutaneous fat
Familial dysautonomia	Anorexia nervosa
Stroke	Malnutrition
Loss of Dermal Integrity	Other
Burns	Child abuse
Staph scalded skin, Steven’s Johnson	Hyponatremia

CLINICAL MANIFESTATIONS

As core temperature falls below 37°C shivering increases to increase the metabolic rate. As core temperature falls further the basal metabolic rate begins to drop and shivering is extinguished. With severe hypothermia (< 28°C) the individual's ability to conserve heat is eliminated. Identifying the clinical features of hypothermia may be easy when there is a history of environmental exposure . However, symptoms of mild hypothermia may be subtle and nonspecific.

CORE TEMPERATURES: Rectal temperatures may not be reflective of core body temperature. Nasopharyngeal, esophageal or central venous probes with dedicated low temperature thermometers should be utilized instead.

HYPOTHERMIA: CLASSIFICATION (CORE TEMPERATURE)			
Category	Centigrade	Fahrenheit	Clinical Manifestations
Mild	32-35 C	90-95 F	Shivering pallor, clumsiness, slurred speech
Moderate	28-32 C	82-90 F	Confusion, loss of compensatory signs
Severe	< 28 C	< 82 F	Flushing, muscle rigidity, edema, stupor
Some include a classification of "profound hypothermia (< 25 C, < 77 F)			

MILD HYPOTHERMIA (32-35C, 90-95F): Patients with mild hypothermia may display nausea, dizziness, chills, confusion, moodiness, poor coordination, apathy, and tachycardia. Compensatory mechanisms manifest as shivering (↑ BMR), signs of poor peripheral perfusion due to vasoconstriction, cessation of sweating and piloerection (to trap a layer of insulating air against the skin).

MODERATE HYPOTHERMIA (28-32C, 82-90F): Compensatory shivering fails. Moderate hypothermia is characterized by worsening mental status, decreasing pulses, bradycardia, hypoventilation, abnormal reflexes, and pupillary dilation. Arrhythmias can include sinus bradycardia, atrial flutter or atrial fibrillation. These are typically well tolerated and revert with rewarming.

Shock may be due to bradycardia, hypovolemia, vasodilation or arrhythmias. Vasoconstriction shift blood centrally resulting in a cold diuresis (early) and renal tubular dysfunction (late). Hypovolemia is exacerbated by increased capillary permeability.

Impaired cerebral perfusion is due to decreased cerebral blood flow and increased blood viscosity due to hemoconcentration. This is manifested as a depressed mental including lethargy, confusion, apathy and/or irrational behavior.

SEVERE HYPOTHERMIA (< 28C, < 82F): Severe hypothermia results is a profound reduction in metabolic activities. Circulatory and respiratory failure are common. Severe bradycardia and hypotension are often present and vital signs may be absent. Myocardial irritability increases the risk of lethal ventricular arrhythmias. With profound hypothermia the EKG flattens and asystole develops. Central nervous system function is progressively impaired as temperature falls with loss of consciousness and coma.

MANAGEMENT

Management of the hypothermic patient involves support of airway, breathing, and circulation and rewarming techniques. Signs of drug or alcohol overdose or trauma should be sought. Initial management priorities are to reducing ongoing heat loss by removing wet clothing and insulating the patient from further exposure using dry blankets (passive rewarming).

REWARMING: Patients may be rewarmed actively or passively. Efforts are made to prevent further heat loss and to begin to rewarm the patient. All patients should have wet clothing removed and should be insulated from further environmental exposure. The degree of hypothermia and the presence of absence of a perfusing rhythm determines the approach to rewarming.

MILD HYPOTHERMIA: Prevent additional evaporative heat loss by removing wet clothing and insulating the victim from further environmental exposures. Passive rewarming is generally adequate for patients with mild hypothermia.

MODERATE HYPOTHERMIA: Passive rewarming is inadequate. External rewarming techniques are appropriate for those with a perfusing rhythm.

SEVERE HYPOTHERMIA: Those with a perfusing rhythms should be treated with active internal rewarming techniques with ECMO reserved for those who do not adequately rewarm. ECMO, if available, is the preferred rewarming technique in patients with severe hypothermia and a non-perfusing rhythm.

REWARMING STRATEGIES			
Hypothermia	Circulation	Primary Rewarming	Secondary Rewarming
Severe	No	ECMO	Maximal, Active Internal[1]
Severe	Yes	Active Internal	ECMO[2]
Moderate	Yes	Passive + Active External[3]	Active Internal[2], ECMO[2]
Mild	Yes	Passive + Active External[3]	
1. If ECMO is not available 2. If clinical deterioration or rewarming < 1 degree C/hour or < 1.8 degree F/hour 3. Active external rewarding may be ineffective or harmful in severe hypothermia			

REWARMING TECHNIQUES	
External Rewarming: Passive	Internal (Core) Rewarming: Non-invasive
Removal of wet clothing	Warm humidified oxygen < 45ºC
Warm blankets	Warm intravenous fluids 40-44ºC
External Rewarming: Active	Internal (Core) Rewarming: Invasive
Plumbed garments	Heated Saline Lavage: Pleural (preferred) and peritoneal are more effective than bladder or stomach
Heating pads, hot water bottles	
Radiant heat sources	
Forced warm air (e.g. Bear Hugger)	ECMO or Bypass (extracorporeal)
Passive rewarming requires the body to generate heat. This ability may have been exhausted. Pair with active external rewarming methods	

CORE AFTER-DROP: The trunk should be warmed first to prevent an after-drop in core temperature. If extremities are warmed first, perfusion returns to the extremities and shifts cold, acidotic blood centrally potentially inducing ventricular arrhythmias

BODY CAVITY LAVAGE: Pleural lavage with heated saline is the preferred method of lavage. Two pleural catheters are place on the left side (more direct lavage of the heart than the right side). An anterior pleural catheter (ICS2, midclavicular line) is for fluid influx and a posterior catheter (ICS5, midaxillary line) for fluid efflux.

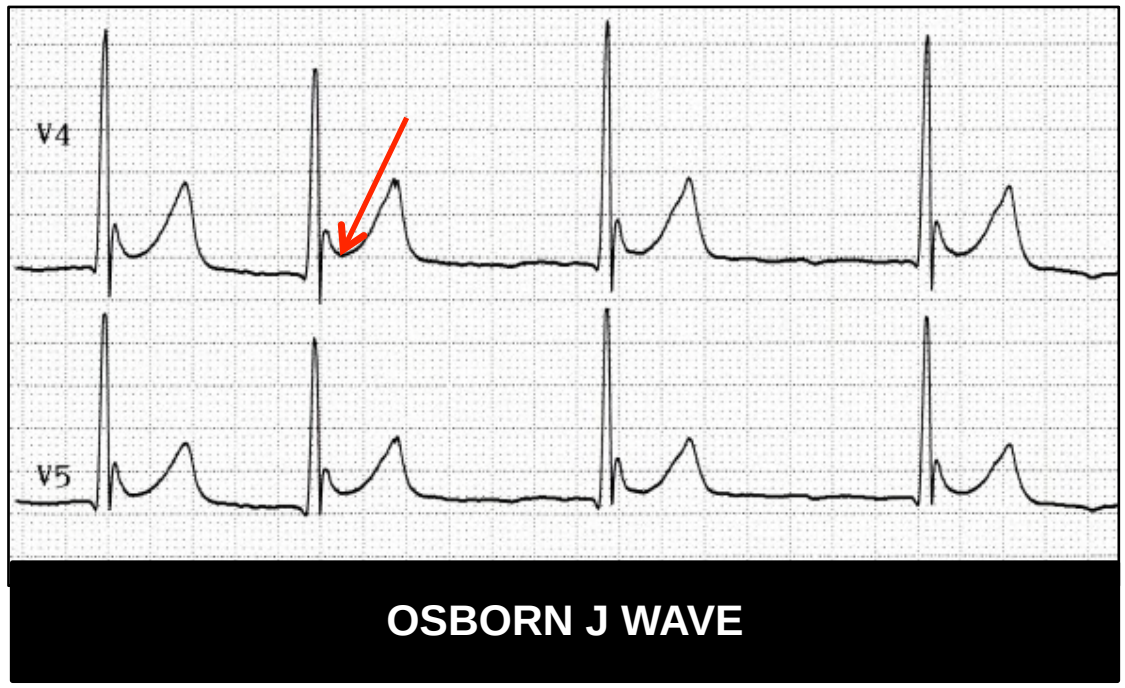
EXTRACORPOREAL REWARMING: Extracorporeal methods of rewarming have the advantage of circulatory support, oxygenation and rapid rewarming. ECMO is preferred over bypass due to anticoagulation, pulmonary edema and prolonged use.

FLUID RESUSCITATION
Fluid losses may be significant in moderate to severe hypothermia due to a cold diuresis (peripheral vasoconstriction shifts blood volume centrally, activating central baroreceptors to induce diuresis) as well as increased capillary permeability
Fluids should be warmed to a temperature of 40-44C (104-111F) Room temperature fluids (21C) can worsen hypothermia and precipitate asystole or ventricular fibrillation.
Standard blood warmers are in insufficient. Trauma-style fluid warmers with short, large bore, insulated or concurrent tubing should be used
A bladder catheter should be placed to measure fluid losses

CARDIAC INJURY: The hypothermic myocardium is particularly susceptible to ventricular dysrhythmias that are refractory to treatment. Efforts should be made to limit cardiac stimulation (e.g. defer the use of intracardiac catheters). Management includes aggressive rewarming techniques and limited attempts at pharmacologic and electrical cardioversion. If ventricular tachycardia or ventricular fibrillation are present, defibrillation should be attempted. The ideal temperature at which to attempt defibrillation and the number of attempts has not been firmly established. It has been postulated that medication efficacy is diminished with severe hypothermia.

ARRHYTHMIAS
Pulses may be difficult to perceive and a pulse check should take as long as a minute
Chest compressions at standard rates should be initiated in those with a non-perfusing rhythm
Perfusing Bradycardic Rhythms: Sinus bradycardia, 1st Degree atrioventricular block, Atrial Fibrillation with slow ventricular response
In severe hypothermia, these rhythms are thought to provide adequate oxygen delivery
Typically treated with rewarming only
Cardiac pacing and medications for bradycardia (Epinephrine, Atropine) are indicated if these rhythms persist after rewarming to 32-35C.
Non-perfusing Rhythms: Ventricular Tachycardia without a Pulse, Ventricular Fibrillation, Pulseless Electrical Activity, Asystole
Common in moderate and severe hypothermia
Treatment: ECMO (preferred) or aggressive, active internal rewarming. May not respond until rewarming occurs.
The temperature at which defibrillation is attempted and the number of attempts has not been firmly established. Some recommend that defibrillation and antiarrhythmic medications may be tried once. If unsuccessful should be held until rewarming to a temperature of 32-35 C.
Epinephrine may result in a perfusing rhythm in moderate hypothermia (use a widened dosing interval (e.g. Q20 minutes rather than Q3-5 minutes)

Osborn J Wave:
2nd bump in terminal QRS complex. The size of the bump increases as temperatures decreases



There are no clear recommendations for vasopressors or antiarrhythmics. Animal evidence suggests that vasopressors may improve outcomes while the use of antiarrhythmics does not. The American heart association states that, “It may be reasonable to consider administration of a vasopressor during cardiac arrest according to the standard ACLS algorithm concurrent with rewarming strategies (AHA, Circulation 2010, PubMed ID: 20956228).

DISCONTINUING RESUSCITATION
The theorized benefit of hypothermia is due to a rapid decrease in basal metabolic rate and oxygen consumptions
Traditional electrolyte (e.g. extreme hyperkalemia) and physical exam findings (e.g. dilated, non-reactive pupils) associated with death have been present in patients with eventual neurologically intact survival
Current recommendations are to continue resuscitative efforts until a core temperature of 32-35 C (93-95 F) or until return of spontaneous circulation is achieved. The exception if for patients with life-ending injuries
CPR may be required for many hours until sufficient warming can recur in order to establish the need for continuing/discontinuing resuscitation. Patients should not be considered dead before warming has been achieved.

MARINE ENVENOMATIONS: INVERTEBRATES

INTRODUCTION (MARIJU F. BALUYOT, MD, 4/2020)
This PEM Guide reviews invertebrate marine envenomations. This includes envenomations from Cnidarians (Jellyfish, man-of-war, coral) as well as the Echinoderms (starfish, sea urchins, sea cucumbers), Annelida (sea worms), and Porifera (sea sponges). See also: PEM Guide: Environmental Injuries: Marine Envenomations: Vertebrates (venomous fish, sharks, sea snakes and sting rays) and PEM Guide: Environmental Injuries: Marine-Related Toxic Ingestions.

CNIDARIANS (JELLYFISH, MAN-OF-WAR, CORAL)

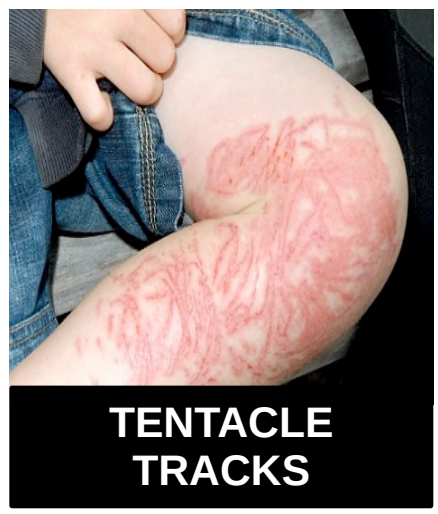
INTRODUCTION
Cnidaria is a phylum which includes over 11,000 species of venomous invertebrate animals, of which about 100 are known to cause injuries to humans. Cnidarian envenomation accounts for the vast majority of marine envenomations worldwide. Clinically relevant species are divided into classes that include jellyfish, man-of-war, sea anemone, and coral. While they do not actively seek humans, they can cause injury from people inadvertently swimming into their tentacles or from divers touching them.

Knowledge of general geographical distribution can help with identification and potential treatment of symptoms, however changing climates and ocean currents in recent decades have caused changes in distribution of many marine species.

PATHOPHYSIOLOGY
These animals cause injury through thousands to several billions of microscopic nematocysts (also called cnidae or cnidocysts) on their tentacles that help them incapacitate prey or provide a means of defense. These nematocysts can function without the animal being alive (e.g. outside of the water on the beach) and without the tentacle being attached.

A nematocyst is composed of an encapsulated, hollow-barbed thread surrounded by venom. After mechanical contact (such as with the skin) or chemical changes (such as with osmotic changes), the nematocyst discharges its barbed thread and injects its toxin into the victim's skin.

CLINICAL MANIFESTATIONS
Depending on the type of cnidarian, length of its barbs, and the amount of contact with the victim's skin, the toxin can cause a range of severity of skin eruptions and/or enter the victim's circulation and cause systemic effects. Toxins can contain a mixture of cytolytic or proteolytic enzymes causing local cutaneous toxicity as well as neurotoxins, and other bioactive components such as serotonin and histamine that cause systemic toxicity. It is thought that some cases of systemic toxicity in children may be due to their thinner dermis (allowing for ease of penetration) and lower body mass than adults (resulting in a higher ratio of toxin to body mass).


TENTACLE TRACKS

DERMAL FINDINGS: Dermal findings include local skin eruptions caused by both toxin-mediated damage as well as the host immune response. Victims often experience immediate pain with skin lesions appearing minutes to several hours later. They may not see the cnidarian causing the envenomation, particularly if it is small or if only a portion of its tentacle is floating in the water. Typical skin reactions range include maculopapular or urticarial rash with varying degrees of pain, pruritus, and local edema that resolve within several hours. Rarely, vesicles, ecchymosis and skin necrosis may be seen.

OCULAR INVOLVEMENT: Anyone with eye involvement warrants an urgent ophthalmologic evaluation as they are at risk for iritis and increased intraocular pressure. Corneal ulceration is also common. Corneal stings should be irrigated with copious saltwater or saline if available. Treatment varies based on the injury sustained and may include ophthalmic antibiotic drops, corticosteroids, and cycloplegics.

SYSTEMIC FINDINGS: Systemic envenomation can occur from certain species and can range from anaphylaxis, cardiorespiratory arrest, catecholamine surge, and neurotoxicity. Species-specific toxicity is reviewed below.

MANAGEMENT: PREHOSPITAL CARE (See Appendix: Prehospital Algorithm)

Pre-hospital management of cnidarian stings involves an initial assessment of cardiopulmonary status, particularly if the sting occurs in the Australian, Indonesian, or southeast Asian/Pacific Island regions. Initial basic life support measures may be warranted if the victim has had significant toxicity, with consideration that the victim may have concurrent drowning injury (See PEM Guide: Environmental Injuries: Submersion Injuries)

If the victim's cardiopulmonary status is stable or while bystander CPR is in process, removing and disabling attached nematocysts from the victim's skin is warranted to prevent further pain and toxicity. Initial topical treatments have historically included various alcohols, shaving cream, meat tenderizer, urine, water, baking soda and sand. Additionally, limb immobilization and application of pressure bandages to prevent lymphatic spread have also been proposed to help prevent toxicity. Studies have shown either no effect or increased nematocyst discharge with these treatments and they should thus be avoided.

MILD STINGS (IN AUSTRALIA) OR ANY STINGS (NOT IN AUSTRALIA)*:* Initial skin treatment for mild stings occurring in the Australian/Indo-Pacific regions, as well as any stings occurring in the continental United States is manual removal of nematocysts and rinsing with seawater. Significant pain is further treated with immersion of the affected area in hot water (40-45 Celsius (104-113°F), the hottest water tolerated if no thermometer is available) or hot packs for 20 minutes. If hot water is not available, ice packs in dry bags can also be placed on stings for pain control. Victims with eye involvement, persistent and/or intolerable pain, or development of systemic symptoms should be transferred to a medical facility.

MODERATE-SEVERE STINGS (IN AUSTRALIA): The general consensus for initial skin management for moderate to severe stings occurring in the Australian/Indonesian/Pacific Island regions including Hawaii is to disable nematocyst discharge with topical application of vinegar, if available, with manual removal of visible tentacles by hand if possible. The rescuer should then rinse his/her hands with seawater and rinse the victim's stings with seawater. Caution should be taken with manual removal as the pressure may trigger nematocyst discharge, and application of seawater may spread nematocysts to other areas. Freshwater should not be used and rubbing the area should be avoided as these will trigger nematocyst discharge. Ice packs in dry bags should be placed on stings for pain control and the victim should be transferred to a medical facility for further care.

MANAGEMENT: EMERGENCY DEPARTMENT CARE

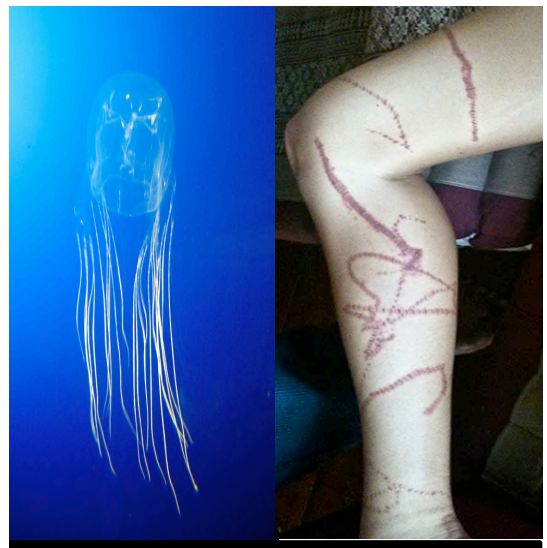
Hospital management involves pain control, local wound care (see table) and close monitoring of neurologic and cardiopulmonary status. Pain control may require intravenous opioids. Patients required nerve blocks should never be immersed in hot water due to the risk for significant burns.

PROPHYLACTIC ANTIBIOTICS: Empiric antibiotics are recommended for coral laceration and retained sea urchin spines. Antibiotics should provide coverage for skin flora (staph and strep), Vibrio species (salt water) and Aeromonas specific (fresh water). A number of other uncommonly encountered organisms may be responsible for infection. Aeromonas species are generally susceptible to third- and fourth-generation cephalosporins, fluoroquinolones and aminoglycosides. Vibrio species are generally susceptible to third-generation cephalosporins, fluoroquinolones and Doxycycline. Recommended empiric antibiotics include a first-generation cephalosporin OR Clindamycin AND a fluoroquinolone AND Doxycycline is sea water is involved.

LOCAL WOUND CARE
Copious cleansing and irrigation/immersion
Removal of foreign bodies: Nematocysts, sea urchin spines
Imaging for possible retained foreign bodies: XRAY, ultrasound
Debridement of devitalized tissue
Laceration should be left open OR delayed primary closure for cosmetically important areas
Tetanus prophylaxis
Antibiotic prophylaxis: Coverage for skin flora (staph, strep) and Vibrio species

SPECIFIC CNIDARIAN

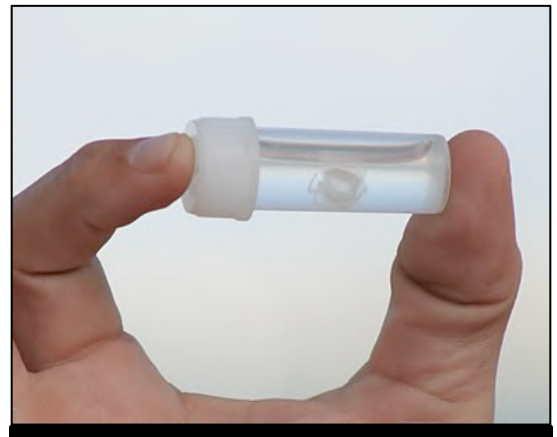
CHIRONEX FLECKERI: The sea wasp (*Chironex fleckeri*) is a type of box jellyfish native to Australia, Indonesia, and southeast Asia. Its tentacles can be up to 2 meters long and are known to cause excruciating pain, local skin eruptions including necrosis, and systemic toxicity such as cardiac arrest and cardiogenic shock. Pain often requires intravenous analgesia and lasts several hours. The maculopapular pruritic rash may be present for several days to weeks. Some people may even have flare-ups of their rash months to years after being stung. The rash is linear and whip-like. Skin findings are treated with topical corticosteroids and oral antihistamines.



CHIRONEX FLECKERI

Patients stung by *C. fleckeri* can receive anti-venom if presenting to medical care within 1 hour. A maximum of 3 doses can be given to patients in cardiogenic shock or cardiac arrest. Based on anecdotal experience, most deaths from severe *C. fleckeri* envenomation occur within 5-20 minutes of the sting.

IRUKANDJI JELLYFISH: Irukandji jellyfish comprise a group of 16 jellyfish that are known to cause Irukandji Syndrome. These jellyfish are small, with bodies approximately 1-2 cm in diameter, with varying lengths of tentacles. The most well-known species in this group include *Carukia barnesi, Malo kingi, Malo maxima, and Malo filipina.* They are also found in the waters of Australia, Indonesia, and southeast Asia, however several case reports of Irukandji Syndrome have also been described in Hawaii and southern Florida from unidentified species.



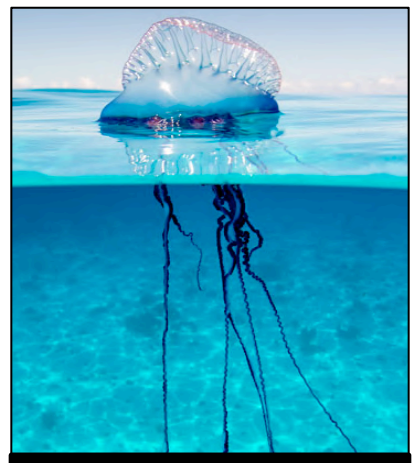
IRUKANDJI JELLYFISH

Irukandji Syndrome is characterized by severe systemic symptoms developing after 5-45 minutes from the initial sting. Pain is typically mildly and without skin findings. The toxin is thought to induce a dramatic catecholamine release and is not dose-dependent.

The severe hypertension puts victims at risk for intracerebral hemorrhage, acute coronary syndrome, and heart failure. Patients may develop cardiogenic pulmonary edema with global ventricular dysfunction identified on echocardiogram. EKG changes are nonspecific. More than half of victims that present to medical care are admitted for further management which focuses on control of pain and blood pressure. Intravenous opioids are often needed. There is no antivenom available. Severe hypertension is treated similarly as in patients who overdose on amphetamines with benzodiazepines and short-acting antihypertensives such as Nitroglycerine, Nitroprusside, or Phentolamine. Subsequent hypotension during the later stages of toxicity frequently requires pressor support.

IRUKANDJI SYNDROME: SYSTEMIC SYMPTOMS	
Tachycardia	Headache
Severe ↑ BP (Systolic >200 mmHg)	Altered mental status
Tachypnea	Severe muscle spasms: Abdomen, back
Diaphoresis	Piloerection
Vomiting	

MAN-OF-WAR: The cnidarians known as the man-of-war, man o'war, or blue bottle jellyfish are *Physalia physalis* (Portuguese man-of-war) and *Physalia utriculus* (Pacific man-of-war, or Australian blue bottle). The man-of-war is not actually a true jellyfish and it lacks a means of active movement other than using its air-filled body as a sail above the water. Its body is up to 25cm long with tentacles up to 30 meters long. Stings usually cause local dermal eruptions that can cause necrosis. Rare systemic symptoms include; vomiting, abdominal pain, muscle spasms, headache, syncope, altered mental status, chest pain, and shortness of breath. Treatment is supportive care and pain control. There is no available antivenom.



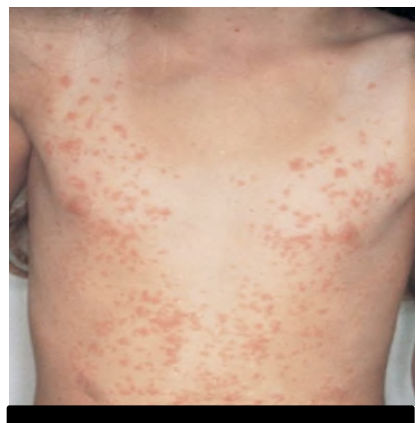
MAN-OF-WAR

SEA ANEMONE AND CORAL: Skin reactions from sea anemone and coral stings are generally milder in severity with infrequent systemic symptoms. Fire coral (*Millepora alcicornis*) stings are common in divers in the southern United States and the Caribbean, causing moderate pain which lasts 1-2 hours and urticaria that resolve over several days. Treatment is supportive and includes oral antihistamines and topical corticosteroids.

CORAL

Coral contact can result in lacerations, particularly if diving and falling or accidentally stepping onto the coral. These lacerations can be prone to secondary infection and victims may require both tetanus and antibiotic prophylaxis (see section on antibiotic prophylaxis above).

SEABATHER'S ERUPTION: Seabather's Eruption (also called sea lice) is caused by is floating cnidarian larvae, approximately 0.5 mm in size. Their immature nematocysts require more mechanical stimulation than they do in their mature stage, such as friction between bathing suits and skin. The immature nematocysts are also triggered by the osmotic change of freshwater showers after swimmers exit the water. They can cause repeated symptoms if the contaminated swimsuit is worn again without washing with detergent.



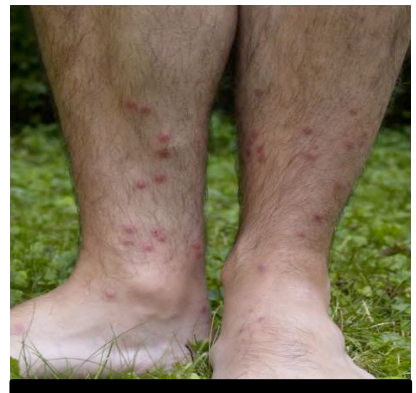
SEABATHER'S ERUPTION

Seabather's eruption consists of a pruritic papular rash that is characterized by delayed onset of symptoms in swimsuit-covered areas and particularly at points of suit constriction. It begins as pruritus and subsequent skin lesions develop over several hours as clustered urticaria, papules, and/or vesicles, with new lesions developing over several days and lasting 1-2 weeks. Treatment includes oral antihistamines, topical corticosteroids, and in severe cases, oral corticosteroids.

SWIMMER'S ITCH: Seabather's Eruption should not be confused with Swimmer's itch (cercarial dermatitis), which is caused by skin penetration of schistosomes larvae. Victims are usually swimming in fresh or brackish water and pruritic macules and papules develop in areas that are submerged in the water rather than underneath the swimsuit area. The schistosomes usually reproduce in an avian host thus are self-limited in human hosts. Treatment includes oral antihistamines and topical corticosteroids.

OTHER INVERTEBRATE ENVENOMATIONS

The phyla of Echinodermata (starfish, sea urchins, sea cucumbers), Annelida (sea worms), and Porifera (sea sponges) include venomous invertebrate animals which are generally sessile or slow-moving. These cause injury to people who mistakenly step on them or handle them while diving. They generally cause mild to moderately painful skin eruptions which can be treated with topical corticosteroids and oral antihistamines.

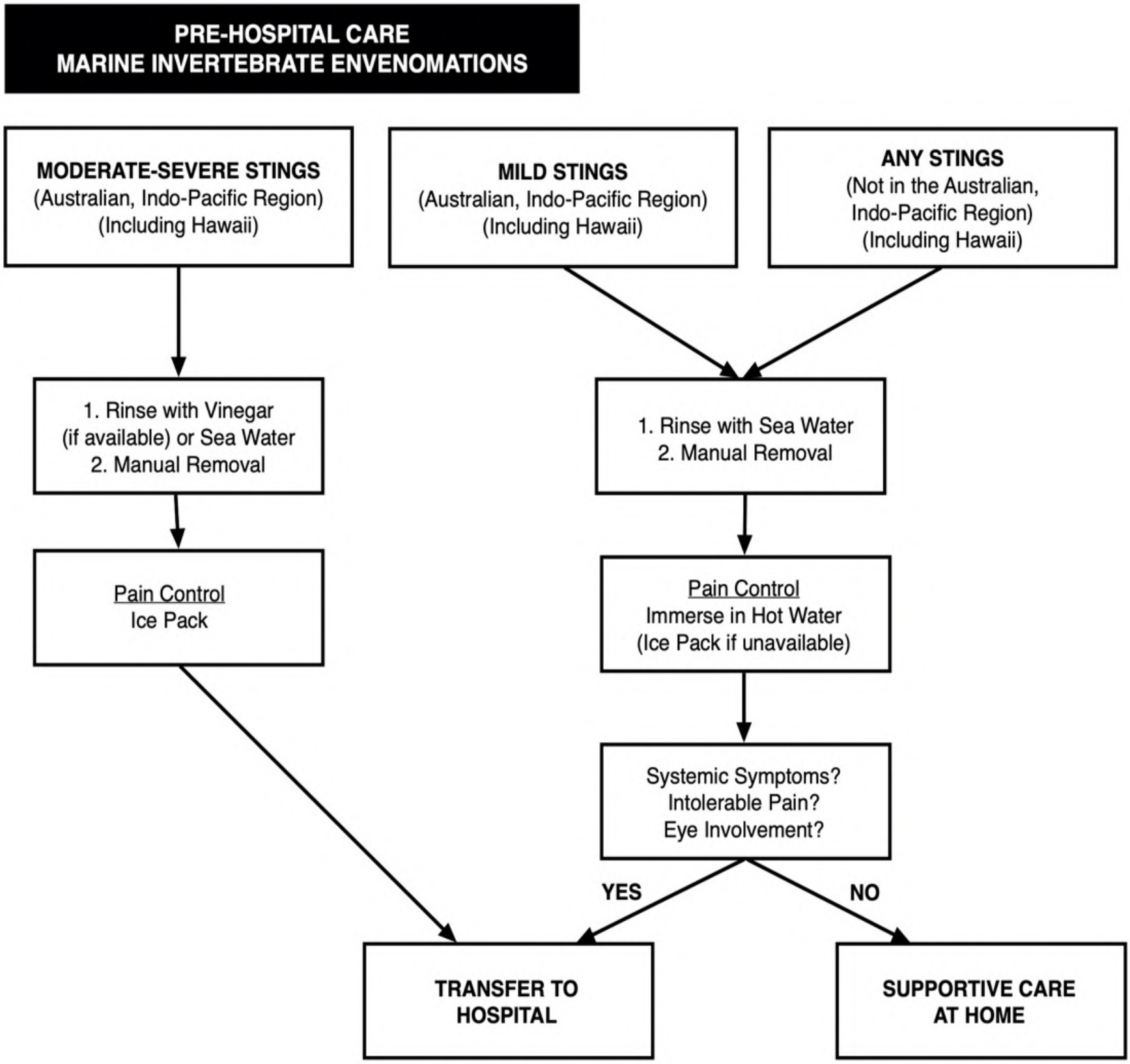


SWIMMERS ITCH

Echinodermata species that feature long, venom-containing spines, most notably sea urchins and some species of starfish, can cause additional injury as these spines can penetrate flesh, wet suits, and rubber soles and may break off within the wound and lead to secondary infection. Patients typically sustain multiple puncture wounds. Wounds should be assessed for retained foreign body with XRAY (as spines are composed of calcium carbonate) but XRAY may miss a significant percentage of spines. A period of observation is reasonable for those spines that cannot be readily removed as they may be resorbed over time. If signs and symptoms or inflammation persist for over a week then surgical exploration may be required. Tetanus and/or antibiotic prophylaxis may be required (see section on antibiotic prophylaxis above).

SEA URCHIN

APPENDIX: PREHOSPITAL MANAGEMENT ALGORITHM



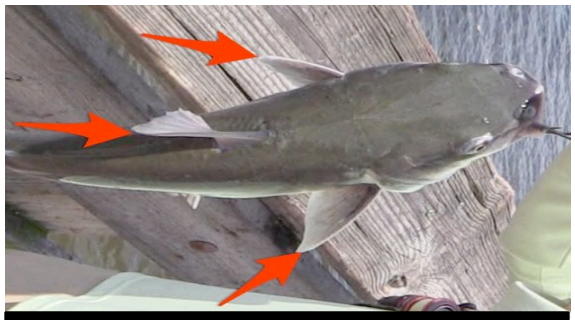
MARINE ENVENOMATIONS: VERTEBRATES

INTRODUCTION (MARIJU BALUYOT, MD, 4/2020)
There are many venomous marine vertebrates that have varying levels of toxicity to humans. Unlike invertebrate envenomation, these animals universally use sharp spines to inject venom into their victims and cause significant physical trauma and place these wounds at risk for secondary infection. There are few well-documented cases of people dying from envenomation itself. Most morbidity and mortality arise from infectious complications or bleeding, placing importance on proper wound care, treatment with antibiotics, and tetanus prophylaxis. The exception in this category of animals is sea snakes, which can have significant systemic effects from envenomation without serious physical trauma. See: PEM Guide: Environment Injuries: Marine Envenomations: Invertebrates.

VENOMOUS FISH

CATFISH: Freshwater catfish are found worldwide, with marine catfish found in the Indonesian and Pacific Island region. They typically cause injury to the upper limbs of humans when they are removed from fishing lines. They have venomous spines on their dorsal and pectoral fins.

SCORPIONFISH AND LIONFISH: These fish are found in tropical and temperate water and are frequently kept as pets in aquariums. They can cause injury to hands and fingers when they are being handled by owners or when their aquariums are being cleaned. They have 12-13 dorsal, 2 pelvic, and 3 anal spines containing venom.



CATFISH SPINES

SCORPIONFISH

LIONFISH

SHARKS: The Port Jackson shark, horn shark, and spiny dogfish are among several sharks that have defensive venomous spines in front of their dorsal fins.

SHARK SPINES

STONEFISH AND WEAVERFISH: Stonefish are found along the coasts of the Indian, Australian, Indonesian, and Pacific Island regions. They have a similar spine distribution as scorpionfish and lionfish. Weaverfish are found along the coasts of the Atlantic Ocean and the Mediterranean Sea, with several venomous spines along their dorsal fin. These fish cause injuries to lower extremities when they are inadvertently stepped on because they are bottom-dwellers. Stonefish can be particularly hard for swimmers to see as they are covered in algae.

WEAVERFISH

STONEFISH

CLINICAL MANIFESTATIONS

Local skin eruptions from venom injection and the puncture wound itself result in immediate pain, erythema, cyanosis, and swelling. Pain usually peaks at 30-90 minutes and resolves over 6-12 hours, though some patients have pain for days especially if there is secondary infection or retained foreign body. Stonefish stings may also cause significant edema of the affected extremity and lead to compartment syndrome. Additionally, wound healing from stonefish stings often takes months.

More serious findings are poorly reported and include systemic effects such as nausea, vomiting, headache, diaphoresis, hypotension, and syncope. However, these symptoms could also be attributed to severe pain. Deaths from these venomous fish have been infrequent and poorly documented.

LOCAL WOUND CARE
Thorough cleansing and copious irrigation
Removal of foreign bodies: Spines, stingray tails
Imaging for possible retained foreign bodies: XRAY, Ultrasound
Debridement of devitalized tissue
Lacerations should be left open or delayed primary closure in cosmetic areas
Tetanus prophylaxis
Antibiotic prophylaxis: Coverage for skin flora (staph, strep) and Vibrio species

MANAGEMENT

Pain and nausea symptoms should be treated based on severity as well as cardiopulmonary support if victims present to the hospital. Hot water irrigation has been shown to provide adequate relief in studies involving stonefish stings.

FOREIGN BODIES: Retained spines may not show up on XRAY and may need ultrasound or wound exploration to detect. Spines may break off of the fish and embed within skin, often becoming hard to remove if they have barbs. These wounds are at risk of developing secondary infection and should be closely monitored and tetanus prophylaxis administered.

PROPHYLACTIC ANTIBIOTICS: Empiric antibiotics are recommended for stonefish stings, penetrating wounds by stingrays, retained foreign bodies, deep puncture wounds and significant devitalized tissue. Antibiotics should provide coverage for skin flora (staph and strep), Vibrio species (salt water) and Aeromonas specific (fresh water).

A number of other uncommonly encountered organisms may be responsible for infection. Aeromonas species are generally susceptible to third- and fourth-generation cephalosporins, fluoroquinolones and aminoglycosides. Vibrio species are generally susceptible to third-generation cephalosporins, fluoroquinolones and Doxycycline. Recommended empiric antibiotics include a first-generation cephalosporin OR Clindamycin AND a fluoroquinolone AND Doxycycline is sea water is involved.

STINGRAYS

STINGRAY

INTRODUCTION

Stingrays are responsible for about 2,000 injuries in the United States yearly, mostly in temperate and semitropical areas during the late summer and early fall. They are found in shallow sandy areas. Swimmers may inadvertently step on a stingray or otherwise frighten or stimulate it, causing it to fling its barbed tail upward and inject its venom through its spine.

CLINICAL MANIFESTATIONS

There is immediate and severe pain, and wounds are usually deep and jagged. Injuries are usually on lower limbs but there have been cases of significant penetrating trauma to the torso as well. Victims are also at risk of having vascular and tendon disruption and developing compartment syndrome. Death is rare but is typically from complications of penetrating trauma rather than venom toxicity. Venom causes vasospasm and local edema, cyanosis, and eventual necrosis. Systemic effects are rare but may include: weakness, vertigo, vomiting, diarrhea, headache, muscle cramps, hypotension, and dysrhythmias.

MANAGEMENT

Initial treatment involves cardiopulmonary support, management of penetrating trauma, and wound care with tetanus and/or antibiotic prophylaxis. Adequate pain control can typically be achieved with hot water irrigation or infiltration of Lidocaine. Stingray spines are denser than human tissue and will be seen on XRAY. However, management may include ultrasound or wound exploration if retained tail fragments are a concern. Similar to stonefish strings, wounds are at high risk of developing secondary infection and empiric treatment with fluoroquinolones and cefazolin is recommended.

SEA SNAKES

SEA SNAKE

INTRODUCTION

See snakes belong to the family Elapidae (the same as coral snakes). They are found in the Indian and Pacific Oceans and come ashore to replenish their freshwater stores. Most envenomation cases occur in southeast Asia and the Persian Gulf and most often in fishermen when the snakes get caught in fishing nets and are brought brought aboard. There are over 50 known species and they are all venomous, however the most common species implicated in human envenomation are *Enhydrina schistosa* (beaked sea snake) and *Pelamis platurus* (yellow-bellied sea snake). Venom is injected through small front fangs and has a similar effect as coral snake venom.

CLINICAL MANIFESTATIONS

The initial bite is typically painless or minimally uncomfortable as sea snake venom contains less inflammatory and necrotizing components. Symptoms of neuromuscular blockade from neurotoxin plus muscle breakdown from myotoxin develop over minutes to hours depending on the amount of venom injected. Painful muscle rigidity, rhabdomyolysis, and subsequent myoglobin nephropathy occur. Hyperkalemia from cellular damage and acute kidney injury can lead to fatal dysrhythmias. Victims also develop cranial nerve involvement with ptosis, ophthalmoplegia, drooling, and dysarthria. Finally, respiratory arrest can result from diaphragm paralysis, seizures and coma.

MANAGEMENT

Management is similar to envenomation from the coral snake, with initial immobilization of the extremity. No attempt should be made to incise the wound and/or extract the venom. Antivenom is not readily available, requires refrigeration, has variable efficacy from limited evidence and anaphylaxis and anaphylactoid reactions are common. Anticholinesterase inhibitors, typically neostigmine, have been shown to be effective for elapids that have post-synaptic neurotoxins.

Asymptomatic patients should be admitted for observation because neurologic symptoms may be delayed by up to 12 hours. Hospital management includes respiratory support and intravenous hydration and pain control. (See: PEM Guide: Environmental Injuries: Snake Bites)

MARINE-RELATED TOXIC INGESTIONS

INTRODUCTION (MARIJU BALUYOT, MD, 4/2020)
There are a number of toxic ingestions related to marine animals that are relevant to clinical practice. As with any toxin ingestion, knowing general toxidrome patterns and good history-taking if possible are helpful in management of these patients, as confirmatory testing is frequently unavailable. The New York City Poison Control Center (212-POISONS) or the national number for the American Association of Poison (1-800-222-1222) may be helpful resources management decisions.

SCOMBROID (HISTAMINE TOXICITY)


TUNA

INTRODUCTION
Scombroid is the most common cause of histamine toxicity. It is characterized by skin flushing, urticarial rash, vomiting, diarrhea, headache, tachycardia, and other symptoms similar to allergic reaction and anaphylaxis, occurring shortly after eating improperly stored fish. It accounts for almost 40% of seafood-borne illness in the United States and Europe, however this may be an underestimate as its symptoms may frequently be confused with other illnesses.

Histidine that is present in fish that live in temperate or tropical waters (such as tuna, mackerel, mahi-mahi, sardines, marlin, tilapia, trout, and salmon). It is converted into histamine by the bacterial enzyme histidine decarboxylase when the freshly killed fish is stored at 20°C (68°F) or higher for several hours. Toxic levels of histamine can accumulate in 2-3 hours. Histamine accumulation has also occurred in fish that were stored improperly at any time prior to consumption (including canned fish) as well as in Swiss cheese due to bacterial contamination.

Histamine is not degraded by refrigeration, freezing, or cooking. Affected fish smell and appear fresh, however some patients have recalled fish tasting “peppery” or “spicy.” Affected fish have also been described as having a honeycombed skin appearance.

CLINICAL MANIFESTATIONS
Symptoms develop within 1 hour of eating contaminated fish (or cheese). In addition to flushing of the skin and an urticarial rash, gastrointestinal symptoms, and headache, patients may also have perioral burning, itching, or swelling, dizziness, blurred vision, shortness of breath, and rarely arrhythmias and hypotension. Duration of illness depends on amount of fish consumed and usually resolves within 12-48 hours without treatment. There are no reported long-term sequelae. Patients taking Isoniazid and MAOIs may have more prolonged course or pronounced findings because these medications inhibit histamine metabolism.

MANAGEMENT
Initial cardiopulmonary may be required, particularly if patients are having upper airway obstruction and/or significant dehydration. Presuming a patient is having anaphylaxis and treating as such until proven otherwise is warranted given the acuity of symptoms. Treatment with H1- and H2-blockers will help with symptoms and patients may need to continue 1-2 days of treatment after discharge. (See: PEM Guide: Respiratory: Anaphylaxis)

CIGUATERA FISH POISONING (CIGUATOXIN)

BARRACUDA

INTRODUCTION

Ciguatera fish poisoning is characterized by a range of gastrointestinal and neurologic symptoms that occur several hours to days after ingesting fish containing ciguatoxin and other neurotoxins. Though most cases happen in tropical and subtropical regions, 16,000 estimated cases occur in the United States each year.

Over 400 species of tropical fish are known to cause toxicity, particularly reef fish such as barracuda, amberjack, grouper, and snapper. The toxins arise from algae that is found on coral reefs. Fish feed on the algae and do not experience toxicity. Affected fish do not taste or smell different from unaffected fish, and cooking and freezing the fish does not degrade the toxins.

CLINICAL MANIFESTATIONS

Ciguatoxin opens Na+ channels and triggers depolarization, leading to a range of symptoms. Gastrointestinal symptoms (vomiting, diarrhea, and abdominal pain) are seen 3-6 hours after ingestion but can occur up to 30 hours after. Cardiotoxicity has also been seen within hours after ingestion. This includes bradycardia, heart block, and hypotension. Gastrointestinal and cardiac toxicity usually resolve within 1-2 days.

Neurologic symptoms are seen approximately 3-72 hours after ingestion. These include blurry vision, perioral numbness, diaphoresis, pruritus (without rash), painful or abnormal sensation of teeth, dysuria, cerebellar dysfunction, and paresis. Notably, ciguatera fish poisoning is known for causing temperature-related dysesthesias (reversal of hot and cold sensation). Neurotoxicity symptoms can persist for days to weeks, even months to years. Toxicity has also been associated with long-term neuropsychiatric and reproductive sequelae such as chronic fatigue, fibromyalgia, dyspareunia, painful ejaculation, and premature labor or spontaneous abortions. Recurring symptoms from a variety of triggers have been described, including ingestion of fish, alcohol, caffeine, and nuts, as well as overexertion with dehydration.

Symptoms can differ by geography depending on the composition of toxins ingested. Contaminated fish from the Caribbean waters usually cause GI symptoms followed by neurotoxicity without mental status changes. In contrast, contaminated fish from the Indian and Pacific Ocean usually cause GI symptoms, neurotoxicity with altered mental status including coma, and more serious cardiovascular or respiratory complications.

Slow resolution of symptoms, long term sequelae, and lack of paralysis or weakness can differentiate ciguatera fish poisoning from neurotoxic and paralytic shellfish poisonings, pufferfish poisoning, and other neurologic pathologies.

MANAGEMENT

Initial management should focus on cardiopulmonary support with symptomatic care for vomiting (antiemetics), pain (analgesia), and pruritus (antihistamines). Various treatments for neuropathic symptoms including Gabapentin, Pregabalin, and Amitriptyline have been described with limited supporting data. A single dose of 0.5-1 grams/kg of intravenous mannitol within the first 48 hours of symptom onset has been shown to reduce neurologic symptoms in limited, uncontrolled trials, with no difference in efficacy compares to normal saline placebo in one randomized controlled trial (Mullins, Clinical Tox 2017, PubMed ID: 28535116). If given, adequate intravenous hydration should be given as there is potential for further dehydration from vomiting and diarrhea symptoms. Long-term management has included counseling, dietary and behavior modifications to reduce potential triggers of symptom recurrence.

SHELLFISH POISONING

SCALLOPS

RED TIDE

INTRODUCTION

The most common type of shellfish poisoning is toxin-mediated diarrheal illness within 2 hours of ingestion and resolves after 2-3 days with supportive care. Other relevant types of shellfish poisoning are paralytic shellfish poisoning (PSP) and neurotoxic shellfish poisoning (NSP). Hepatitis A infection from shellfish is not reviewed in the PEM Guide.

PSP and NSP are both caused by shellfish contaminated by toxins typically produced by algae blooms known as “red tides.” Outbreaks have mostly occurred with mussels or clams; however, crustaceans and fish have been implicated as well. PSP has been seen in temperate waters of the NE and NW continental United States and Alaska. NSP has been associated with the southeast United States, the Gulf of Mexico, the Caribbean, and New Zealand.

Red tides are composed of algae and plankton that form neurotoxins which are ingested by bivalve mollusks (clams, scallops, oysters, and mussels), crustaceans, and some species of fish. They do not cause toxicity to these hosts and are then ingested by humans. Affected animals do not look, smell, or taste differently from unaffected animals, and the toxins are not degraded by heat or freezing.

PARALYTIC SHELLFISH POISONING: PSP is caused by sodium channel-blocking saxitoxins that cause a wide range of neurologic symptoms: perioral tingling, dysphagia, dizziness, paresthesias, weakness, ataxia, and paralysis. Symptoms usually begin within minutes to hours of toxin ingestion, gradually improving after 12 hours to several days. Symptoms can progress to brain stem dysfunction and respiratory failure in 2-12 hours in serious cases. Treatment involves supportive care and airway protection.

NEUROTOXIC SHELLFISH POISONING: NSP is caused by hemolytic toxins and neurotoxins collectively called brevetoxins that cause increased Na+ channel permeability. Within 30 minutes to 3 hours after ingestion, victims develop gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal cramping), and neurologic symptoms similar to PSP (paresthesias, ataxia, and paralysis in severe cases) as well as muscle aches and dizziness. Seizures and coma have also been described in severe cases. Few fatalities have been reported. Treatment involves symptomatic care (antiemetics, pain control) and intravenous hydration. Symptoms usually resolve within several days without sequelae.

AEROSOLIZED RED TIDE RESPIRATORY IRRITATION (ARTRI): Inhalation of NSP toxins can cause irritation of the nasal and respiratory tract, causing rhinorrhea and bronchoconstriction. Treatment is with inhaled bronchodilators. Individuals with chronic lung diseases have shown increased susceptibility.

PUFFERFISH POISONING (TETRODOTOXIN)

PUFFER FISH

INTRODUCTION

Tetrodotoxin (TTX) poisoning is most notably seen in Japan, where puffer fish (fugu) is considered a delicacy, but cases involving other species of fish (globefish, blowfish) have been reported in other parts of the world, including outbreaks in California and Florida. TTX is also found in the blue-ringed octopus and various species of frogs and salamanders where it is used as a defensive measure against predators. It is thought to be produced by bacteria present in all of these animals.

BLUE RINGED OCTOPUS

CLINICAL MANIFESTATIONS

TTX blocks Na+ channels and can cause significant neurotoxicity. Symptoms after TTX ingestion typically occur within 10-45 minutes and include nausea, weakness, dizziness, paresthesias, and loss of reflexes. Severe cases can result in paralysis and respiratory failure. Victims often remain conscious without changes in mental status. Death may occur as early as 20 minutes after ingestion or after 24 hours of progressive symptoms. TTX envenomation has been described with bites sustained from the blue-ringed octopus defending itself with similar symptoms.

MANAGEMENT

Treatment includes supportive care and airway protection. Limited data support the use of anticholinesterases such as Edrophonium or Neostigmine to help with reversal of paralysis. Victims who live through the first 24 hours of acute intoxication typically have full recovery without any sequelae after several days.

Of note, pufferfish may also contain saxitoxins, which causes the clinical features described above with paralytic shellfish poisoning and is managed similarly.

NASAL FOREIGN BODIES

INTRODUCTION (MICHAEL MOJICA, M.D., 7/2015)
Foreign bodies in the nasal cavity are common. Common foreign bodies include: seeds, beads, pebbles, popcorn kernels, small toys and insects. The majority of patients are between 2 and 4 years of age.

CLINICAL EVALUATION
Patients may present with pain, unilateral foul-smelling discharge or rarely epistaxis
Anterior nasal foreign bodies canal are apparent on direct visualization of the nasal cavity with an otoscope. The other nares and both ear canals should be examined as well. A headlamp and a nasal speculum oriented as to not put pressure on the nasal septum will improve visualization.

MANAGEMENT: GENERAL PRINCIPLES
Many of the same principles apply to removal of a foreign body from the nasal passage and the otic canal. For example, there are manual extraction and suction techniques applicable to both areas. There are also location specific techniques. (e.g. Irrigation of ear canal foreign bodies). (See also PEM Guide: Procedures: Removal of Ear Canal Foreign Bodies)

Techniques to remove nasal foreign bodies include: positive pressure techniques, mechanical extraction and irrigation. An emergency physician with the correct tools, experience and a cooperative patient, can remove the majority of nasal foreign bodies without complications. Patients with posterior foreign bodies and those with significant trauma should be removed in consultation with otolaryngologist. Indications for urgent removal include button batteries or two magnets connecting across the septum.

Button batteries can cause major damage in a short period of time. In the moist environment of the nares an electrical current can be generated resulting in thermal injury, leakage of the alkaline content of the batter can cause chemical injury and direct pressure can result in necrosis.

REMOVAL COMPLICATIONS
Pain and discomfort
Epistaxis
Posterior displacement with ingestion or aspiration
Direct trauma to the nasal mucosa or septum with swelling and bleeding

TOPICAL AGENTS: Topical anesthetics such as 1% Lidocaine (max 3 mg/kg or 0.3 ml/kg) can be instilled prior to the procedure. The use of topical vasoconstrictors is generally not recommended due to the potential for posterior dislodgment of the foreign body with ingestion or aspiration. Use may be considered with a large, well visualized, anterior foreign body but appropriate airway equipment and providers skilled in advanced airway techniques and should be available. Instill 1-2 ml of 1:1,000 Epinephrine. Keeping the patient upright may lessen the risk of posterior displacement.

ANTIBIOTICS: Antibiotic prophylaxis is not indicated unless there are signs of septal perforation or secondary infection.

MANAGEMENT: REMOVAL TECHNIQUES
Selection of the removal technique is dependent upon the nature of the foreign body (soft, hard, friable, organic), its location (anterior versus posterior) and cooperation of the patient. Procedural sedation may be required for the more invasive mechanical extraction techniques

Many of the same principles apply to removal of a foreign body from the nasal passage and the otic canal. For example, there are manual extraction and suction techniques applicable to both areas. There are also location specific techniques. (e.g. Irrigation of ear canal foreign bodies). (See: PEM Guide: Environmental Injuries: Removal of Ear Canal Foreign Bodies)

REMOVAL TECHNIQUE SELECTION			
TECHNIQUE	TYPE	LOCATION	OBSTRUCTION
Positive Pressure	Any	Anterior/Posterior	Complete
Nasal Washout	Friable	Anterior/Posterior	Complete
Forceps	Soft	Anterior	Incomplete
Hooks	Hard	Anterior	Incomplete
Balloon Tipped Catheter	Any	Anterior	Incomplete
Adapted from Kiger, Pediatric Emergency Care 2008, PubMed ID: 19018225			

POSITIVE PRESSURE EXPULSION TECHNIQUES: There are a number of methods that use positive pressure to the mouth or unaffected nares to push the foreign body from behind. The techniques can utilize air or water. These techniques are less likely to result in posterior dislodgment of the foreign body and less likely to cause direct trauma to the nasal mucosa and nasal septum than mechanical extraction techniques. Because they do does not hinder subsequent removal attempts they should be considered in most situations and in particular with posterior nasal foreign bodies. Positive pressure expulsion techniques are less likely to be successful if the foreign body does not occlude the nasal cavity because airflow around the foreign body will limit the amount of pressure that builds up posteriorly. The simplest and least distressing to the child may be the “parents kiss”. The steps involved are provided in the table below.

PARENTS KISS TECHNIQUE	
1	Parent positions themselves on the child’s side opposite to the foreign body
2	Parent tells the child that they are going to give them a big kiss
3	Holds the mouth open with the inferior hand on the child’s chin
4	Occludes the nostril without the foreign body with the fingers of the superior arm
5	Cover the child’s mouth with the parent’s mouth resulting in a good seal
6	Provide a rapid, forceful breath (more than 1 attempt may be required)
Alternatively, a bag valve mask may be used if the parents are unwilling or unable to complete the procedure.	

Other positive pressure techniques involve providing pressure to the unaffected nares (rather than the mouth) while occluding the mouth. Air can be provided by blowing in the nostril with the parent’s mouth, through a rubber tube or with 10-15 liters/minute of oxygen with a male-to-male adapter.

NASAL WASHOUT: The saline washout technique uses the same principles as the posterior pressure techniques. 5-10 ml of normal saline is injected forcibly with a catheter tipped bulb syringe occluding the unaffected nares with the mouth closed. The object is propelled out of the affected nares by the force of the water flow. This is particularly helpful for friable foreign bodies that are difficult to remove using other techniques. There is however a possibility of aspiration of the irrigation fluid.

MECHANICAL EXTRACTION: Mechanical extraction requires a cooperative patient. Procedural sedation may be required. These techniques may result in damage to the nasal mucosa or septum with epistaxis occurring between 5 and 10% of the time. It is helpful to inform caregivers that the procedure is likely to cause some bleeding. In addition, mechanical extraction techniques they have an increased potential for dislodging the foreign body posteriorly with a risk of ingestion or aspiration. These techniques should not be used for poorly visualized, posterior foreign bodies.

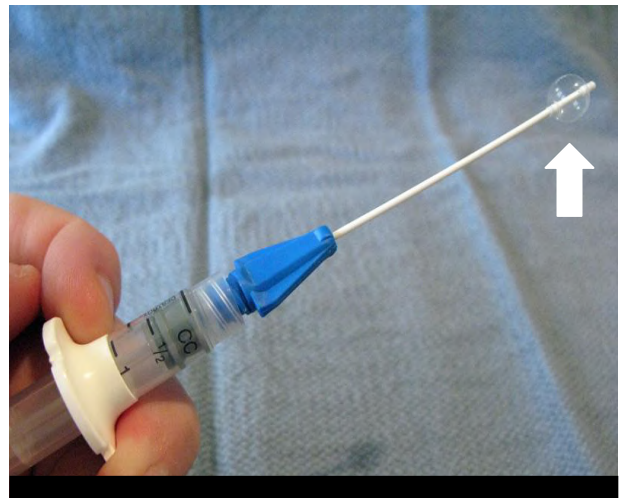
A number of tools can be used including: alligator forceps, surgical clamps, a right ankle hoop, cerumen removal loops, balloon tipped catheters and tissue adhesives.

In general clamps/forceps are indicated for soft, irregularly shaped foreign bodies such as paper or cloth. Forceps and clamps are less invasive than mechanical techniques such as hooks and balloon tip catheters that require placement of the instrument distal to the foreign body.

Hooks are indicated for hard objects. The tip of the hook is inserted beyond the foreign body and the instrument is rotated so that the hook is behind the foreign body and gentle traction is applied.

The Katz extractor is a balloon catheter tipped syringe. The catheter is inserted above and distal to the foreign body, the balloon is inflated and the foreign body is extracted with gentle retraction. Alternatively, a small Foley catheter may be used.

Tissue adhesives applied to the end of a wood or plastic swab stick have also been used to snare nasal foreign bodies with variable levels of success. This requires a dry environment and a cooperative or sedated patient as it takes up to 60 seconds for the glue to dry before removal can be attempted.



KATZ EXTRACTOR

SMOKE INHALATION

INTRODUCTION (KATHERINE FULLERTON, M.D. 4/2020)
There are approximately 5,000 fire-related deaths/year. Approximately half of these are due to smoke inhalation. The term smoke inhalation encompasses thermal injury to the airways, chemical injury from smoke to the airways and systemic effects of toxins in smoke such as carbon monoxide and cyanide. The airway can be divided into the upper airway, the tracheo-bronchial tree and the lung parenchyma. See also PEM Guide: Environmental Injuries: Burns, PEM Guide: Toxicology: Carbon Monoxide, PEM Guide: Cyanide).

PATHOPHYSIOLOGY

SMOKE INHALATION: INJURY MECHANISMS	
Thermal Burns	Typically, of the upper airway. Injury to the glottis is most common and the most immediately life-threatening. The lower airway is infrequently involved (e.g. steam)
Chemical Injury	Chemical components (acrolein, aldehydes, chlorine, phosgene, NO, NO_2), soot and particulate matter,
	Cause direct parenchymal injury. Cilia damage and thickened secretions lead to decreased clearance and obstruction, atelectasis and impaired gas exchange
	Symptoms include; bronchorrhea, dyspnea, wheezing, pulmonary edema, hypoxia, ARDS and bronchopneumonia
Toxins	Carbon Monoxide (CO) is most common cause of fire-related death. Displaces O_2 from hemoglobin leading to anoxia.
	Hydrogen Cyanide (HCN) is released from combustion of polyurethane, acrylonitrile, nylon, wool and cotton. Binds to cytochrome a-3 complex and inhibits electron transport chain. Causes severe lactic acidosis, coma, cardiovascular collapse, apnea, and death.

UPPER AIRWAY: Thermal injury most commonly effects the upper airway resulting in edema and ulceration. Edema can be exacerbated by aggressive fluid therapy recommended for extensive burns.

TRACHEO-BRONCHIAL TREE: Injury to the tracheobronchial tree is primarily due to chemicals in smoke. These result in bronchoconstriction, a major inflammatory response and transudate into the alveolar space.

LUNG PARENCHYMA: Smoke inhalation results in alveolar collapse and atelectasis, loss of surfactant and loss of hypoxic pulmonary vasoconstriction.

CLINICAL PRESENTATION
Essential history includes exposure to flame, smoke and chemicals, the duration of exposure (e.g. in an enclosed space) and loss of consciousness.

SMOKE INHALATION: PRESENTATION	
Thermal Burns	Laryngeal and laryngospasm up to 24 hours after exposure. Cough, tachypnea, hoarseness, stridor, carbon-tinged sputum. Burns to head/face/neck, singed nasal hairs.
Chemical Injury	Hoarseness, wheezing, rales, cough with soot-tinged sputum, shortness of breath. Pulmonary insufficiency, bronchospasm usually within 12 hours Pulmonary edema 6-72 hours post inhalation. May have a normal ABG and CXR in first 12-24 hours
Toxins	Carbon Monoxide: Presentation varies with level of exposure. Mild/moderate causes headache, nausea, more severe exposures may progress to severe systemic symptoms.
	Hydrogen Cyanide: Severe metabolic acidosis, rapidly progresses to coma, cardiopulmonary arrest and death

EVALUATION
CBC
BMP
ABG/VBG with co-oximetry panel (Venous sample sufficient for co-oximetry sample)
Chest XRAY: Findings lag behind, may underestimate injury. Abnormal XRAY indicates severe disease.
Direct or fiberoptic laryngoscope
Bronchoscopy

MANAGEMENT

The NYC Poison Center should be consulted for suspected CO and HCN exposure (212-POISONS). Jacobi Hospital Center and the New York Presbyterian Weill Cornell Medical Center are the NYC burn centers.

SMOKE INHALATION: MANAGEMENT
Upper Airway Management
Early intubation is indicated for impending upper airway obstruction
Surgical airway equipment (cricothyrotomy) should be readily available
Racemic Epinephrine may facilitate intubation
Steroids are not useful for localized upper airway thermal injury
Smoke Inhalation
100% humidified O_2 or positive pressure ventilation via endotracheal intubation.
A laryngeal mask airway should not be used: Above the level of airway obstruction
Fiberoptic bronchoscopy maybe helpful in determining the extent of injury
Albuterol for wheezing
Prophylactic antibiotics and steroids are not indicated
Carbon Monoxide (See Table Below)
Cyanide (See Table Below)

CARBON MONOXIDE	
Example	House fires, motor vehicle exhaust, methylene chloride metabolism
Mechanism	Carbon monoxide is the leading cause of “poisoning” deaths. Fetus/neonate are more sensitive to CO than adults. High affinity for hemoglobin results in the production of carboxy-hemoglobin which has decreased O_2 carrying capacity and shifts the O_2 dissociation curve to the left.
Presentation	Headache, confusion, dyspnea, chest pain, coma, shock, myocardial ischemia. May cause delayed neuropsychiatric effects.
Diagnosis	Co-oximetry panel (does not need to be arterial) PaO_2 will be normal: Measures O_2 dissolved in blood not attached to hemoglobin) Oxygen Saturation Monitor: Overestimates SaO_2 (wavelength of COHb similar to HbO_2)
Treatment	Carboxyhemoglobin: Half-life Room-air Oxygen: 320 minutes 100% FiO_2: 60-90 minutes (non-rebreather face mask + nasal cannula) Hyperbaric Oxygen: 15-30 minutes
See: PEM Guide: Toxicology: Carbon Monoxide	

CARBON MONOXIDE: CRITERIA FOR HYPERBARIC OXYGEN THERAPY
End organ toxicity (with CO level > 3-5%)
Persistent metabolic acidosis
Initial loss of consciousness or syncope
Altered Mental Status: Confusion, disorientation, cognitive defects, coma
Myocardial ischemia: Abnormal EKG, angina chest pain, (+) troponin
Pregnancy
CO level > 10%
Third trimester monitoring suggestive of fetal distress
CO Level > 25%

CYANIDE	
Example	House fires (burning wood, nylon, silk), lab chemicals, silver polish
Mechanism	Cyanide’s principal toxicity is the result of inactivation of cytochrome oxidase (binds to ferric iron) → Impairment of cellular respiration
Presentation	CNS depression, dyspnea, shock, profound anion gap metabolic acidosis, seizures, cyanosis (late finding), smell of bitter almonds
Treatment	100% FiO_2, mechanical ventilation $NaHC0_3$, Intravenous fluids and vasopressors for hypotension
Antidotes	Hydroxocobalamin is the preferred antidote. Some toxicologists recommend the addition of Sodium Thiosulfate if: 1. Severe toxicity 2. Insufficient Hydroxocobalamin available 2. Insufficient response to Hydroxocobalamin
See PEM Guide: Toxicology: Cyanide	

CYANIDE ANTIDOTE: HYDROXOCOBALAMIN	
Mechanism	Chelation: The central cobalt atom binds cyanide Hydroxocobalamin + CN → Cyanocobalamin (Vitamin B12) Rapidly enters the mitochondria Safer, faster, though not always readily available, higher cost
Indications	Suspected cyanide toxicity
Dosing	Adult: 70 mg/kg (max 5 grams) IV over 30 min (may push in an arrest) May repeat to max 15 grams. Subsequent doses given over 6-8 hours
	Pediatric: 70 mg/kg (max 5 grams), subsequent dose 35 mg/kg
	CAUTION! Do not give at same site or time as sodium thiosulfate. Sodium Thiosulfate binds to Hydroxocobalamin rendering it inactive
Adverse events	Dark red skin, mucous membranes and urine (hours-day) Allergic reactions, local reaction at the infusion site, lymphopenia Interfere with subsequent laboratory testing, particularly colorimetric testing (AST, bilirubin, creatine, magnesium, iron)

CYNIDE ANTIDOTE: SODIUM THIOSULFATE	
Mechanism	A slow acting sulfur donor. With the enzyme rhodanese uses cyanide to form thiocyanate which is excreted in the urine Works synergistically with Hydroxocobalamin
Indications	Suspected cyanide toxicity
Dosing	Adult: 12.5 grams (50 ml of 25% solution) bolus or over 10-30 min Child: 0.5 grams/kg (2 ml/kg of 25% solution) maximum is adult dose
	Administer as a bolus or over 10-30 minutes based on severity Onset up to 30 minutes. May be repeated at ½ the initial dose if manifestation reappear or at 2 hours as prophylaxis
	CAUTION! Do not give at the same site/time as Hydroxocobalamin. Thiosulfate binds Hydroxocobalamin rendering it inactive
Adverse events	Hypotension, nausea, vomiting

DISPOSITION

ADMISSION INDICATIONS
History of loss of consciousness
Facial burns or carbonaceous sputum
Documented injury of upper airway: PaO_2 > 60 mmHg
Smoke inhalation with lower airway injury
Meeting criteria for hyperbaric oxygen: CO > 15%
Any cyanide toxicity: Metabolic acidosis
History of significant smoke/fire exposure in enclosed area

SNAKE BITES

INTRODUCTION (MICHAEL MOJICA, M.D. 10/2019)
There are more than 8,000 snakebites per year in the US resulting in 6-16 deaths per year. 25% of victims are less than 18 years old. Pediatric patients exhibit severe envenomation earlier than adults due to the large dose of venom per kilogram. The NYC Poison Control Center (212-POISONS) can be helpful in managing these patients and in particular those requiring antivenom.

PIT VIPERS (CROTALIDS)

INTRODUCTION
Pit vipers (rattlesnakes, cotton mouths, copperheads) of the Crotalid family account for 90% of venomous snake bites in the US. Bites result in significant local and systemic reactions. Identifying characteristics of the snake include vertically oriented, elliptical pupils, a diamond shaped head, two fangs to directly inject venom and heat finding organs (pits) between the eyes and the nose.

CLINICAL FINDINGS
The venom is primarily hematotoxic though neurotoxicity can occur with some species.
Bites are characterized by early, intense local reactions and two distinct fang marks (in contrast to the Elapidae). Complications include disseminated intravascular coagulopathy (characterized by hemolysis, defibrination and thrombocytopenia), rhabdomyolysis, renal failure, shock and compartment syndrome.

BLEEDING MANIFESTATION PROGRESSION
Atraumatic local bleeding at the site of the envenomation
Bleeding from old scabs, cuts and wounds that reopen
Gingival bleeding (1st signs of systemic envenomation)
Hematemesis and/or melena*
Intracranial/subarachnoid hemorrhage or intra-peritoneal hemorrhage*
* Indicates severe envenomation, require twice the dose of antivenom as those with a moderate systemic envenomation

MANAGEMENT
On scene care includes compression bandages (no tourniquets). Incisions and suction devices are not indicated. Not only are they ineffective but they can result in greater local injury. Grading schemes are available to determine the extent of envenomation (see Table below). Clinical and laboratory parameters are used in this assessment. Consider early intubation if neurologic symptoms suggest imminent respiratory failure.

SUPPORTIVE CARE
Analgesia
Intravenous fluids
Tetanus prophylaxis
Splint, elevate extremity

LABORATORY TESTING
CBC with Platelets
PT, fibrinogen
UA
Cross matching
Electrolytes

In addition to supportive care, antivenin is prescribed for moderate to severe (Grades 2 and 3) local or systemic reactions. The Crotaline FAB Antivenom is safer than the previously used Antivenin Crotalidae Polyvalent which was frequently associated with severe anaphylactoid reactions. Skin testing is not recommended prior to Crotaline FAB. Crotaline FAB antivenom contains antibodies to Western diamondback rattlesnake, Eastern diamondback rattlesnake, Mojave rattlesnake, and cottonmouth (water moccasin). However, CroFAB has cross reactivity with other crotalids in the US. Fasciotomy may be required for compartment syndrome.

ENVENOMATION GRADING	
0	No envenomation
1	Minimal: Local swelling and pain without progression
2	Moderate: Swelling and pain beyond the site if injury with some systemic or laboratory findings
3	Severe: Severe local, systemic and laboratory findings

CROTALIDAE POLYVALENT IMMUNE FAB	
Indications	Pit viper envenomation (within 4 hours for grades 2 and 3) Significant local reaction Coagulation abnormalities Cardiovascular instability
Adverse Effects	20% hypersensitivity (anaphylaxis) 23% serum sickness
Initial dose	4-6 vials antivenom diluted in 250 ml of crystalloid
Subsequent dosing	May repeat initial dose in 1 hour if no arrest in progression of local reaction and return to normal coagulation profile. Then 2 vials Q6H x 3

Pit viper envenomation may show a secondary resurgence of envenomation between 24-72 hours after initial antivenom therapy. Monitoring patients for at least 96 hours is recommended.

CORAL SNAKES (ELAPIDAE)

INTRODUCTION

Elapidae are responsible for less than 2-3% of venomous snakebites in the US but envenomation can result in significant neurotoxicity. Prior to antivenom availability, a 10% mortality rate due to cardiopulmonary failure was reported. The Eastern, Texas and Arizona coral snakes are the only Elapidae encountered in the US. Other Elapidae include the Cobra (Southeast Asia), Black Mamba (sub-Saharan Africa), the Australian copper head and sea snakes (tropical and subtropical waters of the Indian and Pacific oceans). The pattern of banding may be helpful in identifying the snake (“red on yellow kill a fellow, red on black venom lack”). The rule of thumb is only applicable to the US where the comparison is between the coral snake (Eastern, Texas or Arizona) and the king snake. Coral snakes in other parts of the world do not adhere to this maxim.

CLINICAL FINDINGS

Coral snake envenomation results in systemic neurotoxicity. Patients may present with local paresthesias, altered mental status and complaints related to cranial nerve involvement (ptosis, drooling and dysphagia). Ptosis is pathognomonic, part of a descending paralysis along the cranial nerve pathways. Once ptosis and drooling/dysphagia are present, time is critical. Typically, there is about 20 minutes before respiratory arrest occurs due to paralysis of the diaphragm. Prophylactic endotracheal intubation should be strongly considered. Local reaction is generally limited to mild soft tissue swelling. The area of envenomation is often macerated and does not have distinct fang marks (in contrast to the crotalids)

MANAGEMENT

Treatment is primarily supportive. A compression bandage and immobilization of the affected area may limit systemic absorption. Incisions and suction devices are not indicated. Not only are they ineffective but they can result in greater local tissue injury. Patients in whom the snake has been positively identified or who exhibit signs of envenomation should be treated with the specific antivenom (Micrurus fulvius antivenom) though this is not often readily available. Skin testing is recommended. Anaphylaxis and anaphylactoid reactions should be anticipated.

A randomized, double-blind, placebo-controlled study including over 1,000 patients (de Sliva, PLOS 2011, WebLink) assessed the efficacy of pretreatment of snakebite patients with various drugs to prevent antivenom-induced anaphylaxis. They found that the only effective pretreatment was a subcutaneous dose of 0.25 ml epinephrine (1:1,000) administered immediately before antivenom administration, which reduced anaphylactoid reactions by more than 40%.

Anticholinesterase inhibitors, typically neostigmine, have been shown to be effective for elapids that have post-synaptic neurotoxins. However, they have not been studied on North American coral snake envenomations. Given that coral snake antivenom is no longer in production for the United States, anticholinesterase inhibitors may provide an effective alternative to antivenom.

Asymptomatic patients should be admitted for observation because neurologic symptoms may be delayed by up to 12 hours.

COMPARISON: SNAKE BITES		
	CROTALID	ELAPIDAE
Identification	Elliptical Pupils Triangular Heads Pit in central forehead (between eyes and nose)	Round Pupils Blunt Heads “Red on Yellow Kill a Fellow Red on Black venom lack” (Applicable only in the US)
		
Incidence in US	Common	Rare
Example	Rattle Snake	Coral Snake
Primary Clinical Findings	Severe Skin/Soft Tissue Characteristic fang marks Systemic (shock) Coagulopathy Rare neurologic	Limited local reaction Neurologic symptoms
Treatment	Supportive Care CroFAB Antivenom	Supportive Care Micrurus fulvius Antivenom

CLINICAL DIFFERENTIATION: INSECTS AND SNAKES BITES				
	INTENSE LOCAL REACTION	NEUROLOGIC SYMPTOMS	CHOLINERGIC SYMPTOMS	OTHER
Spider	Brown Recluse	Black Widow	Black Widow	Black Widow Severe abdominal pain (cramping)
Snake	Crotalid	Elapidae		Crotalids with hematotoxicity
Scorpion		Bark Scorpion	Bark Scorpion	Roving eyes Abdominal pain Pancreatitis[1]
1. Pancreatitis is only associated with the Brazilian yellow scorpion				

SPIDERS, SCORPIONS AND BEES

INTRODUCTION (MICHAEL MOJICA, M.D. 11/2021)
Insect bites are a common chief complaint in the emergency department. The majority are benign and limited to local erythema. However, some of these can become super-infected and a few may develop life threatening systemic reactions. The NYC Poison Control Center (212-POISONS) can be helpful in managing these patients and in particular those requiring antivenom.

This PEM Guide will review serious spider, scorpion and bee bites. See also PEM Guide: Infections: Lyme Disease and PEM Guide: Infections: Rocky Mountain Spotted Fever for a discussion of major tic born illnesses.

BROWN RECLUSE SPIDER (LOXOSCELES RECLUSES)

CLINICAL FINDINGS
Violin shaped markings on its body identify the brown recluse spider. It is responsible for a cutaneous injury associated with envenomation. The classic lesion has a blue/black central area (thrombosis) with concentric rings of pallor (ischemia) and erythema (vasodilation) (The red, white and blue sign). Local pain and vasospasm give way to a hemorrhagic vesicles at 24-72 hours and later to the characteristic necrotic eschar (approximately 50%). Ecthyma (Streptococcus) and Anthrax should be considered in the differential diagnosis.

Rare systemic reactions (loxoscelism), which occur more frequently in children, may develop 1-4 days after envenomation. Symptoms include: fever, a scarlatiniform rash, hematuria, oliguria, myalgias, nausea, vomiting and abdominal pain. Tachycardia, hypotension and renal failure may occur. Severe cases may develop hemolysis and coagulopathy (DIC) and may require blood transfusions.

MANAGEMENT
Local wound care consists of debridement, cool compresses and elevation. Patients with systemic reactions should be admitted. Analgesics and antihistamines are indicated. Corticosteroids, colchicine, dapsone and hyperbaric therapy have no proven clinical efficacy. Plastic surgery consultation for skin grafting may be required after disease resolution.

BLACK WIDOW SPIDER

CLINICAL FINDINGS
The hourglass shaped markings on its body identifies the black widow spider. It is located primarily in the Southwest United States. Its venom is neurotoxic inhibiting the release and preventing the re-uptake of acetylcholine and resulting in cholinergic excess (See PEM Guide: Toxicology: Cholinergics)

Local reaction is generally minimal. Cholinergic symptoms peak a few hours after the bite and can include tremors, muscle spasm, muscle rigidity, weakness, paresthesias and hyperesthesias. Severe abdominal pain is often seen. Other systemic signs include salivation, diaphoresis, hypertension, tachycardia and bronchorrhea (elements of the cholinergic toxidrome).

MANAGEMENT
Supportive treatment includes analgesics and sedatives (benzodiazepines). Calcium gluconate and muscle relaxants do not reliably reduce pain. A horse-derived antivenom (Lactrodectus Antivenin) is available for severe reactions though serum sickness and anaphylaxis may result. One vial is usually sufficient. Indications include: abdominal pain, hypertension, muscular pain and agitation/irritability.

COMPARISON: SPIDER BITES		
	BLACK WIDOW	BROWN RECLUSE
Markings	Hourglass	Violin
Clinical	Onset: Hours Neurologic Cholinergic Toxidrome Abdominal pain	Onset: Days Cutaneous Rare systemic
Treatment	Analgesics, Sedatives Antivenin	Supportive Care
		

SCORPION BITES

In the United States, the only native poisonous scorpion is the bark scorpion (*Centuroides sculpturatus*). It is found in Southwest desert regions and in particular Arizona. It gets its name from the tendency for being found under fallen tree trunks and rocks. Its venom that contains neurotoxins that cause the increased and repetitive firing of neurons, releasing acetylcholine and catecholamines. Cholinergic symptoms may mimic the effects of black widow spider bites.

CLINICAL MANIFESTATIONS

Often, there is no reported history of a sting. Patients complain of intense pain at the bite site and rapidly develop paresthesias of the affected extremity. Younger children tend to have more severe symptoms and may require antivenom to shorten the course of symptoms, as well as mitigate the need for other adjunct medications

CLINICAL MANIFESTATIONS	
Cutaneous	Burning pain, paresthesias. No cytolytic toxins Minimal or no swelling of erythema at the site (distinguishing scorpion bite from other arthropod bites)
Catecholamine	Tachycardia, hypertension, agitation, seizure
Muscarinic	Diaphoresis, salivation, lacrimation, urination, defecation. mydriasis
Nicotinic	Paresthesias, fasciculations, jerking movements, opisthotonus chaotic multidirectional conjugate saccades)

LABORATORY TESTING

Severe cases should be evaluated for end organ damage including rhabdomyolysis (CPK), liver (LFTs), renal (BMP, UA) and pancreatic (Lipase) dysfunction.

MANAGEMENT

Treatment is primarily supportive. Pain and paresthesia at the sting site can last for up to 2 weeks. Antivenom is indicated based on severity grading (Table below). More severe symptoms may require narcotic analgesia and benzodiazepines for muscle relaxation. Fentanyl is the preferred narcotic for analgesia because it does not cause histamine release. Other therapies include anticholinergics (e.g. atropine) and antihypertensives.

SCORPION ENVENOMATION		
GRADE	FINDINGS	TREATMENT
1	Local pain or paresthesias	Symptomatic care Analgesics, anxiolytics
2	Local and remote pain or paresthesias	Symptomatic care Analgesics, anxiolytics
3	Local pain with paresthesias and either: a. Cranial nerve abnormalities OR b. Skeletal neuromuscular dysfunction	Analgesics, anxiolytics Supportive Care, Antivenom
4	All of grade 3 and airway involvement	Analgesics, anxiolytics Supportive Care, Antivenom

HYMENOPTERA

Hymenoptera include bees, wasps, hornets and yellow jackets. They are responsible for one-third of all envenomations in the US (the most common cause) leading to 40-150 deaths per year. Clinical findings include local to systemic reactions. Four percent of the population is sensitized to bee stings. Management includes anaphylaxis therapy (epinephrine, antihistamines. corticosteroids, intravenous fluids, inhaled beta agonists and vasoactive infusions for hypotension). See also PEM Guide: Respiratory: Anaphylaxis. Patients should be instructed in the use of an Epi-Pen prior to discharge.

APPENDIX: COMPARISON: SNAKE, SPIDER AND SCORPION

SUMMARY: CLINICAL DIFFERENTIATION: SNAKE, SPIDER, SCORPION				
	INTENSE LOCAL REACTION	NEUROLOGIC SYMPTOMS	CHOLINERGIC SYMPTOMS	OTHER
Spider	Brown Recluse	Black Widow	Black Widow	Black Widow Severe abdominal pain (cramping)
Snake	Crotalid	Elapidae		Crotalids with hematotoxicity
Scorpion		Bark Scorpion	Bark Scorpion	Roving eyes Site of bite pain Paresthesias

GASTRO-ENTEROLOGY

1. Cholelithiasis and Cholecystitis.	Alexa Goldfard, DO Bridget Kiernan, MD
2. Clostridium Difficile	Michael Mojica, MD
3. Constipation	Arielle Grossman, MD Melanie Greifer, MD
4. Gallbladder POC Ultrasound	Adriana Manikin, MD
5. Gastritis-Peptic Ulcer Disease	Matthew Paik, MD
6. Gastroenteritis	Michael Mojica, MD
7. Gastrostomy Tube Complications	Michael Mojica, MD
8. Inflammatory Bowel Disease	Arielle Grossman, MD Melanie Greifer, MD
9. Pancreatitis	Roshni Patel, MD, Joseph Levy, MD
10. Umbilical Disorders	Didier Murillo-Parra, MD
11. Upper Gastrointestinal Hemorrhage	Michael Mojica, MD

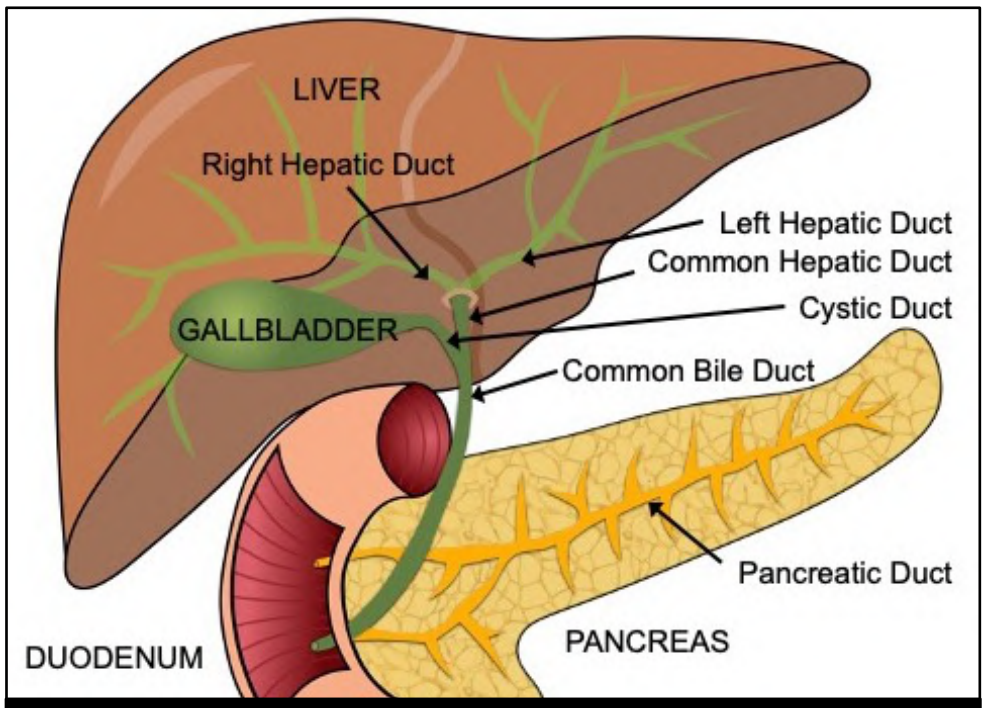
CHOLELITHIASIS AND CHOLECYSTITIS

INTRODUCTION (ALEXA GOLDFARB, D.O., BRIDGET KIERNAN, M.D, 2/2022)
The gallbladder stores and concentrated bile secreted by the liver. Biles aids in the digestion of fats. Gall stones form in response to a number of conditions (see Appendix: Characteristics of Gall Stones in Children). Gallstone disease is predominantly a disease of adulthood although the prevalence of gallbladder disease in children is increasing, likely due to the increasing prevalence of childhood obesity.

Most pediatric patients with gallstones have a predisposing condition. For example, gallstones in infancy are typically found in those with short bowel syndrome, after cardiac surgery, and in those receiving parenteral nutrition, diuretics, or cephalosporins. Gallstones found in children from the ages of 1 to 5 years are usually secondary to hemolysis (e.g. sickle cell disease). Gallstones found in adolescents are often associated with obesity, menarche, pregnancy, and the use of oral contraceptives.

ANATOMY

The gallbladder lies under the liver and superior and lateral to the duodenum and pancreas. The extrahepatic biliary tree consists of the left and right hepatic ducts that join to form the common hepatic duct. The cystic duct from the gallbladder joins the common hepatic duct to form the common bile duct. The common bile duct joins the pancreatic duct which enters the 2nd portion of the duodenum via the hepato-pancreatic ampulla (previously the ampulla of Vater) and through the hepato-pancreatic sphincter (previously sphincter o



GALLBLADDER ANATOMY

CLINICAL MANIFESTATIONS

COMPLICATIONS OF CHOLELITHIASIS	
Cholecystitis	Primarily inflammatory but infection can also occur Typically, due to obstruction but not always, 5-10% acalculous May be complicated by empyema, gangrene, gallbladder rupture, pericholecystic abscess Syndrome of RUQ abdominal pain, fever and leukocytosis
Choledocholithiasis	Stone obstructs a bile duct
Pancreatitis	Gall stone: Stone obstructs pancreatic duct or ampulla with reflux of bile into the pancreas
Cholangitis	Inflammation/Infection of the bile duct due to obstruction, ascending duodenal bacteria Presentation: Fever, jaundice, abdominal pain
Mirizzi Syndrome	Impacted stone in the cystic duct cause extrinsic compression of the common bile duct

CHARACTERISTICS OF GALLSTONES IN CHILDREN			
	Cholesterol Stones	Black Pigment Stones	Brown Pigment Stones
Number and morphology	Multiple: 2-25 mm faceted, smooth Solitary: 2-4 cm round, smooth	Multiple: <5 mm Irregular or smooth	Multiple: 10-30 mm Round, smooth
Composition	Cholesterol monohydrate (>50%) Glycoprotein Calcium salts	Bile pigment polymer (~40%) Calcium carbonate or phosphate salts (~15%) Cholesterol (~5%) Mucin glycoprotein (~20%)	Calcium bilirubinate (~60%) Calcium palmitate and stearate soaps (~15%) Cholesterol (~15%) Mucin glycoprotein (~10%)
Radiopaque	No	Yes (~50%)	No
Location	Gallbladder Common Bile Duct	Gallbladder Common Bile Duct	Common Bile Duct, Intrahepatic ducts
Clinical associations	Hyperlipidemia Obesity Clofibrate Pregnancy Cystic fibrosis Octreotide	Hemolytic anemia Cirrhosis Total parenteral nutrition Ileal disease Ceftriaxone	Bacterial infection (Escherichia coli) Parasitic infection Bile duct anomaly Birth control pills
Recurrent	Yes	No	Yes
Sex	Female > Male	No difference	No difference
Age	Pubertal: with age	Any: with age	Any: with age
Bacteria	No	No	Yes (found at core)
Soluble	Yes	No	No (minimally)

HISTORY: The majority of gall stones are asymptomatic and may never develop complications. Non-impacted stones may be asymptomatic or result in intermittent biliary colic. Impacted stones cause significant biliary colic and may lead to cholecystitis. If a fever is present, it usually indicates associated cholecystitis.
Older children and adolescents with cholelithiasis typically present with biliary colic. Pain is often described as intense, dull and constant and localized to the right upper quadrant and/or epigastric area. Despite its name, it is not colicky. Pain may radiate to the right upper back and may be associated with nausea, vomiting or diaphoresis. It may occur after fatty meals. It is thought to be due to intermittent obstruction of the gallbladder neck. Younger children tend to present with nonspecific symptoms. Jaundice may be encountered in infants. “Silent stones” are most commonly seen in infancy through the preschool years.

PHYSICAL EXAM: When distended and inflamed, the gallbladder lies on the anterior abdominal wall between the 9th and 10th costal cartilages, causing localized tenderness on palpation and Murphy’s sign. Ask the patient to take in and hold a deep breath while palpating the right subcostal area. Murphy's sign is positive if pain occurs on inspiration, when the inflamed gallbladder moves inferiorly into contact with the examiner's hand. Peritoneal signs are typically absent in cholelithiasis and present in cholecystitis.

DIFFERENTIAL DIAGNOSIS: RUQ ABDOMINAL PAIN	
BILIARY TRACT	OTHER
Cholelithiasis	Hepatitis, Peri-hepatitis (Fitz-High-Curtis)
Cholecystitis	Gastric/Duodenal ulcer
Choledocholithiasis	Right lower lobe pneumonia
Cholangitis	Retrocecal appendicitis
Gall stone pancreatitis	Sub-diaphragmatic abscess/hematoma

LABORATORY STUDIES

Laboratory evaluation is typically non-diagnostic in cholelithiasis. Occasionally patients will have leukocytosis and mildly elevated aminotransaminase levels and GGT. In patients with cholecystitis, leukocytosis is frequently found. Elevated aminotransferase levels and mild hyperbilirubinemia may be seen. Elevated lipase and amylase levels are also common even without pancreatitis.

IMAGING

Ultrasonography is the diagnostic imaging modality of choice. Plain-film radiography may be helpful in cases of black pigmented stones which would appear radiopaque. A significant proportion of cholesterol stones are iso-attenuating compared to bile and may be missed on CT scan. Cholescintigraphy using 99mTc-Hepatic IminoDiacetic Acid (HIDA scan) is indicated if the ultrasonography is negative.

Magnetic resonance cholangiopancreatography (MRCP) is purely diagnostic. It may be used to visualize the biliary and pancreatic ducts non-invasively to determine whether gallstones are lodged in any of the ducts surrounding the gallbladder. Endoscopic retrograde cholangiopancreatography (ERCP) is useful in the evaluation of ductal stones. ERCP is diagnostic and can be therapeutic (stone removal, stent placement). ERCP is more invasive and has a higher rate of complications than MRCP.

ULTRASOUND FINDINGS	
Cholelithiasis	Echogenic focus indicating a stone, in a dependent position that moves when the patient is moved and is associated with acoustic shadowing. Sludge may also be present
Obstruction	Dilated gallbladder or common bile duct
Cholecystitis	Thicken gallbladder wall, pericholecystic fluid
Sonographic Murphy's sign	Presence of maximal tenderness elicited by pressure with the transducer over the visualized gallbladder on inhalation
See: PEM Guide: Gastroenterology: Gallbladder Point of Care Ultrasound	

MANAGEMENT

There is limited pediatric data on which to manage cholelithiasis, cholecystitis and other biliary tract complications. Many management recommendation are based on extrapolation for adult data.

No treatment is required for infants with asymptomatic cholelithiasis. Gallstones in older children should be removed, with elective laparoscopic cholecystectomy as the surgical procedure of choice. Despite the use of medical therapy (e.g. Ursodiol) for adults, there is no approved medical treatments for gallstones in children.

Patient with biliary colic without gall stone complications are treated with analgesics, Ondansetron for nausea and vomiting and intravenous fluids for dehydration.

CHOLECYSTITIS: MANAGEMENT OVERVIEW
Intravenous fluids, correction of electrolyte abnormalities
Analgesia
Antibiotics
NPO, nasogastric tube may be required for persistent vomiting

ANALGESIA: Non-steroidal anti-inflammatory drugs (e.g. Toradol) are the preferred analgesic for biliary colic. A meta-analysis of adult patients with biliary colic demonstrated no difference between NSAIDS and opioids in pain relief (Colli, Aliment Pharmacol Ther 2021, PubMed ID: 22540869). Opioids are typically reserved for pain unresponsive to NSAIDS. It has been traditionally taught that hydromorphone is preferred over morphine due to less contraction of the hepato-pancreatic sphincter. However, all opioids cause contraction and the clinical significance is unclear.

CHOLECYSTITIS: In cholecystitis, hospitalization with intravenous fluids, cessation of oral feeding, and analgesics is appropriate.

SURGERY: Early laparoscopic cholecystectomy during the initial hospitalization is commonly recommended. Though guideline definitions of “early” varies from 3-10 days. Emergent cholecystectomy may be required for complicated cholecystitis and those who do not respond to supportive therapy. Percutaneous gallbladder drainage may be necessary if there is high risk of anesthesia or surgery complications.

Inter-operative cholangiography can be performed to identify common bile duct stones. Common bile duct stones can be managed surgically of endoscopically.

ANTIBIOTICS: Data on the use of antibiotics is inconclusive. Antibiotics may not be required in very limited cases. Antibiotics are indicated for persistent fever, clinical worsening, concern for obstruction/ complication and in those with co-morbid conditions.

E Coli is the most frequently encountered organism (approximately 50%) followed by Enterococcus, Klebsiella, and Enterobacter. Antibiotics should achieve adequate concentration in bile. Piperacillin/ Tazobactam is often used as single coverage. Combination therapy typically includes a cephalosporin (e.g. Cefoxitin) or a fluoroquinolone (e.g. Levofloxacin) with Metronidazole,

CLOSTRIDIUM DIFFICILE

INTRODUCTION (MICHAEL MOJICA, MD, 3/2023)
Clostridium (AKA Clostridioides*) difficile* (C. *difficile*) is a spore-forming, anaerobic, toxin producing, gram-positive bacillus. The spore form is resistant to heat, acid, antibiotics and most disinfectants. It is spread via the fecal-oral route. Toxins are responsible for colonic mucosal damage and fluid secretion. While pediatric C. *difficile* infection is less common than in adults, it has been increasing in frequency. *C difficile* can be seen during or within 3 weeks of antibiotic exposure or in children with other risk factors.

Asymptomatic carriage of C. *difficile* spores is common in children less than 2 years of age with a peak colonization rate of approximately 40% in infants 6-12 months of age. It is thought that infants do not manifest symptoms because they lack toxin receptors. Asymptomatic carriage has also been found in hospitalized children with comorbidities such as cancer or inflammatory bowel disease. C. *difficile* may be pathogenic in this age group under select circumstances.

C. DIFFICILE: RISK FACTORS
Antibiotics: Augmentin, cephalosporins, clindamycin, fluoroquinolones
Cystic fibrosis
Enteral feeding tubes
Hirschsprung disease
Inflammatory bowel disease, structural or post-operative intestinal disorders
Immunodeficiency: Malignancy, transplantation
Acid Suppression: Proton pump inhibitors, H_2 receptor antagonists
Recent hospitalization
Renal insufficiency

CLINICAL MANIFESTATION
C. difficile manifestations range from asymptomatic carriage to fulminant disease based on the presence of systemic symptoms and symptom severity. The most common symptoms are an acute-onset of profuse and watery diarrhea with 3 or more unformed stools within 24 hours. Frequency may reach 10 episodes per day at peak. Fever, abdominal pain, cramping and vomiting are common. Grossly bloody stools are atypical (<15%). Rarely, diarrhea may be absent in the setting of colonic ileus or toxic dilation (megacolon). There patients present primarily with abdominal pain and distention.

FEATURES SUGGESTIVE OF C. DIFFICILE	
Clinical	Severe diarrhea (> 6 stools/day), abdominal pain
	Fever > 102 F
Laboratory	WBC ≥ 15K
	Fecal leukocytes of occult blood
	Albumin, Creatinine, Lactate
Imaging	XRAY: Bowel wall thickening and/or dilation, ascites, “thumbprinting”
	CT: Bowel wall thickening, ascites, mural enhancement, fat stranding

CLASSIFICATION			
NON-SEVERE		SEVERE	FULMINANT (COMPLICATED)
MILD	MODERATE		
No Fever	Fever	Fever, Rigors	Fever. Rigors
Diarrhea	Profuse Diarrhea	Profuse Diarrhea	Shock/Hypotension
	Abdominal Pain	Severe Abd Pain	Severe Abd Pain
		Abd Tenderness	Severe Abd Tender
		Abd Distention	Paralytic Ileus
		Pseudomembranes	Toxic Megacolon
		WBC ≥ 15,000	WBC, Lactate
		Creatinine 1.5 x	Albumin

Common complications of C *difficile* include dehydration with shock and electrolyte abnormalities. Pseudomembranous colitis is severe inflammation of the inner bowel lining most commonly confirmed by its characteristic adherent, yellow plaques on colonoscopy or biopsy. Pseudomembranous colitis is uncommon in children. In toxic megacolon, ileus and distention result in colonic ischemia and necrosis with peritonitis and sepsis.

Extra-colonic manifestation of disease are rare and may include soft tissue infection, osteomyelitis, bacteremia and reactive arthritis. Recurrence is defined as the return of symptoms within 2 months of the initial infection. The etiology of recurrence is unclear.

DIAGNOSTIC TESTING

Diagnosis in children can be difficult. There are no validated scoring systems for children and testing does not distinguish between carriage and disease.

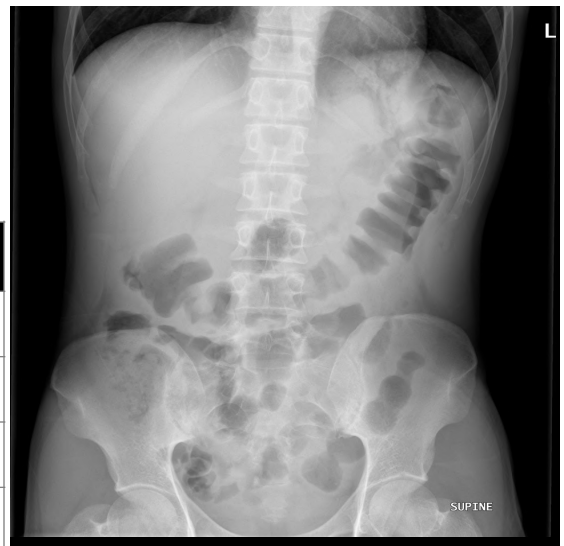
LABORATORY: Leukocytosis (WBC > 15,000/μL) is common and is often associated with bandemia. Elevated levels of creatinine and lactate and decreased albumin are typical of severe to fulminant disease. There is no definitive laboratory study to differentiate asymptomatic carriage from active infection.

C. DIFFICILE TESTING: *Clostridioides difficile* can be diagnosed by identifying the toxin or toxin genes in the stool. Testing does not distinguish carriage from disease. Testing should be limited to patients for whom the clinical suspicion is moderate to high, based on clinical features and the presence of risk factors. Limit testing in those less than 12 months of age to those with high clinical suspicion due to their high carriage rates. In children 12-24 months of age do not test for C difficile unless other, more common causes of diarrhea have been excluded. Consider testing those 2 years of age or older with more than at least 3 stools within 24 hours with persistent or worsening diarrhea with risk factors (e.g., antibiotics in the past two months) or relevant exposures (e.g., recent hospitalization). This excludes patients who have received gastrografin, tube feeds or a bowel regimen within 24 hours.

NYU utilizes a real time C. *difficile* PCR for the detection of the toxin gene with a sensitivity of 94.4% and specificity of 96.3% (compared to 58.3% and 94.7% for enzyme immunoassay (EIA) test). The test will remain positive over the next 30 days. If PCR is not available, use a stool toxin test as part of a multistep algorithm (glutamate dehydrogenase plus toxin), arbitrated by nucleic acid amplification test (NAAT).

IMAGING: Imaging studies are not routinely indicated but can be used to identify complications, Thumbprinting or large bowel fold thickening due to edema, may be seen on XRAY. It is a finding indicative of colitis in general and is not specific to C. difficile colitis.

C. DIFFICILE COMPLICATIONS: IMAGING	
Paralytic ileus	May have an absence of diarrhea
Intestinal perforation	Free air
Intussusception*	Absent liver edge, target, crescent signs
Pneumatosis intestinalis	Air within the bowel wall
Toxic megacolon*	Dilated colon
*Reviewed in detail in a separate PEM Guide	



THUMBPRINTING

DIFFERENTIAL DIAGNOSIS

It is difficult to distinguish C. *difficile* from other causes of gastroenteritis based solely on clinical features. As described in the testing section above, other, more common causes of gastroenteritis should be excluded before diagnosing C Difficile in children less than 2 years of age due to their high rate of C. *difficile* carriage (See: PEM Guide: Gastroenterology: Gastroenteritis). Abdominal pain, in those with ileus without diarrhea, may mimic appendicitis and intussusception.

MANAGEMENT

Appropriate contact precautions should be maintained including patient isolation and appropriate personal protection equipment (gown, gloves, face mask). All caregivers must perform hand hygiene after patient contact. Soap and water are preferred. Hand sanitizer may be considered if gloves remain intact and are not viably soiled.

MANAGEMENT OVERVIEW
Apply appropriate contact precautions, isolation, use of PPE
Consult pediatric ID, GI, surgery for severe illness (e.g., shock, ileus, toxic megacolon)
Discontinue non-essential antibiotics
Discontinue anti-peristaltic agents and opioids
Discontinue proton pump inhibitors, H2 receptor antagonists
Initiate C. *difficile* antibiotic regimen (See Table below)
Supportive Care: Fluid resuscitation, correction of electrolyte abnormalities
Surgery: Toxic megacolon, colonic perforation, acute abdomen, or septic shock

Discontinuing non-essential antimicrobial agents is the first step of treatment. Continued use of antibiotics may increase the duration of illness and the risk of recurrence.

Discontinue all anti-peristaltic medications and opioids. These decrease transit time and can increase the exposure to C. *difficile* toxin and theoretically increase the risk of ileus and toxic megacolon. Consider discontinuing proton pump inhibitors and histamine-2 receptor antagonists as these had been associated with recurrence.

Recommendation for antibiotics for C. *difficile* infection in children are primarily derived from evidence in adults. Antibiotics are not indicated for asymptomatic carriage as they do not reduce the rate for carriage. For non-severe disease, the Infectious Disease Society of American pediatric guidelines recommend the use of Fidaxomicin over a standard course of Vancomycin due to its safety and efficacy (Guideline: IDSA 2021, (PubMed ID: 34164674).

Management of recurrent C. *difficile* infection (within 8 weeks of prior infection) and prophylaxis are not reviewed in this PEM Guide. Contact pediatric infectious disease for antibiotic recommendations for recurrent disease or prophylaxis.

ANTIBIOTIC RECOMMENDATIONS: INITIAL DISEASE (>12 MONTHS)	
Non-Severe	Metronidazole: 7.5 mg/kg/dose (max dose 500 mg) PO Q8H x 10 days[1]
	May take 4-6 days for the diarrhea to resolve
	If no improvement after 4 days, consider change to Vancomycin
	OR Vancomycin: 10 mg/kg/dose (max dose 125 mg) PO Q6H x 10 days
	Total course of Metronidazole + Vancomycin = 14 days
	No evidence for combination Vancomycin + Metronidazole IV
	May Vancomycin to 14 days if improved but without resolution
Severe[2]	Vancomycin: 10 mg/kg/dose (max dose 500 mg) PO/NG[3] Q6H x 10 days[4]
	+/- Metronidazole: 10 mg/kg/dose (max dose 500 mg) IV[5] TID x 10 days
	Metronidazole + Vancomycin: Fulminant, comorbidities
	Complete Ileus: Vancomycin to 125 mg PO Q6H
	Toxic Megacolon: Fecal transplant (consult pediatric ID, GI, surgery)
1. Metronidazole contraindicated: Ethanol intake, medications with ethanol (e.g., Tipranavir), disulfiram reaction, pregnancy, hypersensitivity → Vancomycin 2. ICU, shock, hypotension, ileus, megacolon. Consult pediatric ID, GI and surgery 3. Rectal dosing is also available for those with complete ileus or who cannot tolerate PO 4. Long course → High concentrations, renal failure. Monitor trough 5. Add IV metronidazole if ileus since reduced PO Vancomycin delivery to the colon	
NYU Pediatric Antibiotics Stewardship Guideline (Revised 2/2023)	

DISPOSITION

Patients with fulminant disease should be admitted to the ICU. Patients with non-severe or severe disease may require admission for hydration as are those with significant comorbidities.

CONSTIPATION

INTRODUCTION (ARIELLE GROSSMAN, MD, MELANIE GREIFER MD, 3/2022)
Constipation is a common problem in pediatric patients. It is described subjectively as the infrequent passage of dry, hardened stools, large stools, infrequent stools, and/or discomfort with stooling. 95% of constipated pediatric patients do not have an underlying organic etiology and are diagnosed with functional constipation.

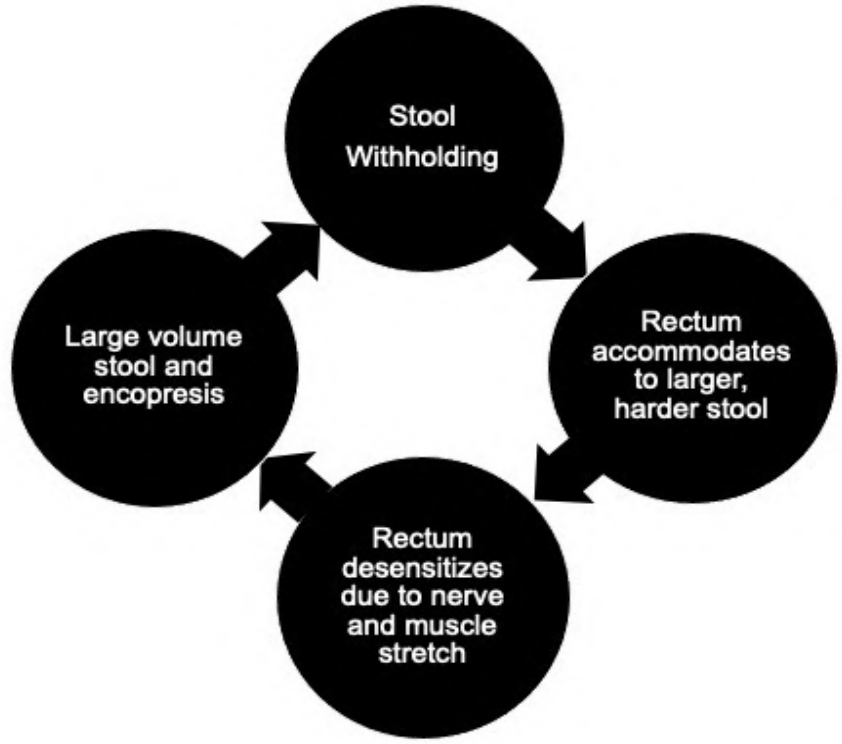
FUNCTIONAL CONSTIPATION: ROME IV PEDIATRIC CRITERIA
≥ 2 of the following occurring for ≥ 1 time per week for ≥ 1 month (with insufficient criteria for irritable bowel syndrome*)
≤ 2 defecations in the toilet per week in a child of a developmental age of ≥ 4 years
≥ 1 episode of fecal incontinence per week
History of retentive posturing or excessive volitional stool retention
History of painful or hard bowel movements
Presence of a large fecal mass in the rectum
History of large diameter stools that can obstruct the toilet

WEBLINK: MD CALC: ROME IV PEDIATRIC IRRITABLE BOWEL SYNDROME

PATHOPHYSIOLOGY

While constipation can occur at any age, there are certain phases when it is more likely to occur:

- Infants: Introduction of solids
- Toddlers: Toilet training
- Older children: Avoidance of school bathroom and withholding



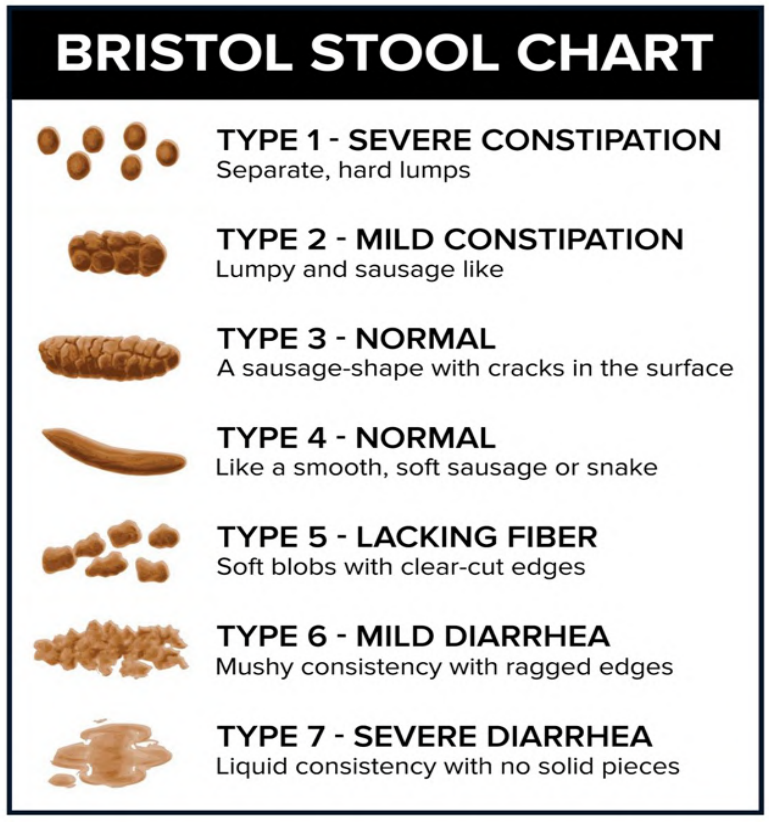
DIFFERENTIAL DIAGNOSIS	
Organic Constipation	Cystic fibrosis, hypokalemia, lead intoxication hypo/hypercalcemia, infant botulism, hypothyroidism, celiac disease, cow's milk intolerance
Acute Abdomen	Assess for presence of fever, nausea, vomiting, abdominal guarding, rebound tenderness, localized tenderness. Patient may require blood work, ultrasound or cross-sectional imaging and surgical consult.
Intestinal Obstruction	Consider in the presence of bilious vomiting. A 2-view abdominal X-ray and surgical consult should be considered.

COMPLICATIONS	
Fecal Impaction	A hard mass in the lower abdomen identified on physical examination, a dilated rectum filled with a large amount of stool on rectal examination, or excessive stool in the distal colon on abdominal X-ray.
Encopresis	Involuntary loss of stool after acquisition of toilet training skills, likely related to functional constipation.
Hemorrhoids	Swollen blood vessels at the anal verge. Most commonly present with painless rectal bleeding or anal pruritus. Initial treatments include treatment of underlying constipation, dietary modifications/fiber, sitz baths, and over the counter medications to treat symptoms.
Anal Fissure	Tear in skin around anus due to large, hard stools. Typically presents with rectal bleeding and pain. Initial treatments include treatment of underlying constipation, dietary modifications/fiber, and sitz baths.
Rectal Prolapse	Protrusion of the rectum through the anus commonly caused by chronic constipation and straining. Medical management is preferred and includes treatment of underlying constipation, dietary modifications/fiber, and pelvic floor exercises.

CLINICAL MANIFESTATIONS

HISTORY: A complete history includes characteristics of stooling as well as past medical history or medication use that increase the risk of constipation. Medications associated with constipation include opioids, iron supplement, selective serotonin reuptake inhibitors and anticholinergics. Further history should be elicited to identify the presence of alternative diagnoses (e.g. appendicitis, intestinal obstruction). Vomiting is rare in functional constipation.

STOOLING PATTERN
Age of onset, any potential triggering event around start of constipation
Frequency of stooling, timing of last stool
Consistency (can use Bristol stool scale as visual aid)
Size of stools (can ask if they clog toilet)
Presence of blood (may be due to anal fissure in presence of large, hard stools)
Pain with defecation or retentive posturing (crossing legs, body stiffening or shaking)
Fecal soiling or presence of stains on underwear
Treatment strategies already attempted



PREDISPOSING MEDICAL DISORDERS
Neuromuscular disorders (i.e. spinal cord disorders, cerebral palsy)
Decreased tone can predispose to constipation
Neurodevelopmental disorders (i.e. Autism spectrum disorder)
Sensory issues can lead to stool withholding
Anatomical conditions (i.e. Hirschsprung disease, anorectal malformation)
Mechanical obstruction, poor tone before or after repair.

PHYSICAL EXAMINATION: A targeted physical examination should include an abdominal, perianal and digital rectal examination. On the abdominal examination, assess for bowel sounds, presence of distention and the presence of a hard mass. The perianal examination should assess for perianal tags or fissures which can be associated large, bulky stools and lead to rectal bleeding. Presence of perianal stool staining may be associated with encopresis. A digital rectal examination can detect presence of a fecal impaction as well as assess rectal tone/sensation but may be a traumatic experience. 73% (169/233) of children meet the Rome Criteria without a rectal exam (Pradhan, J Ped GI Nutrition 2018, PubMed ID: 29601443).

DIAGNOSTIC TESTING

The diagnosis of functional constipation only requires history and physical exam. Labs are not required in the acute setting unless an organic etiology of constipation is suspected. A pediatric gastroenterologist may consider the need for laboratory tests as an outpatient including testing for thyroid disease, hypercalcemia, and celiac disease.

Imaging, such as abdominal XRAY, is not required for the diagnosis of constipation. Abdominal X-ray is only useful to determine presence of a fecal rectal mass when rectal exam is unable to be performed. This may include patients with obesity, behavioral difficulties, autism spectrum disorder, or history of sexual abuse. Importantly, the presence of significant stool on XRAY does not preclude an alternative diagnosis such as appendicitis. Additional imaging may be warranted if appendicitis or bowel obstruction is suspected.

MANAGEMENT

NON-PHARMACOLOGIC TREATMENT: Infants with functional constipation may respond with sorbitol containing juices, such as prune, pear or apple juice. Toilet-trained children should be instructed to sit on the toilet after breakfast and/or dinner to try to defecate, with knees elevated above hips (may require a stool under feet), for 5 minutes without distractions. Finally, it is important to ensure adequate hydration in all children.

PHARMACOLOGIC TREATMENT: Laxative medications can treat the underlying constipation and as well as prevent it from reoccurring. Osmotic laxatives (e.g. polyethylene glycol, lactulose) help draw water into the colon and soften the stool. Stimulant laxatives (e.g. senna, bisacodyl) help activate colonic contractions and the urge to defecate.

In general, osmotic laxatives may increase gas and stimulant laxatives may increase cramping. These side effects must be considered in the individual patient. Stimulant laxatives may be particularly useful in patients with stool withholding. Finally, the doses listed are a useful starting point; however, they must be titrated up/down based on the patient’s clinical response to with the goal of one soft stool per day. Patients with encopresis or a fecal impaction may require a bowel “clean out.” For most children, this can be accomplished with an oral regimen with polyethylene glycol at a dose of 1-1.5g/kg/day for up to 6 days. Rectal medications may be required for more severe impactions as they work quickly; however, this may be traumatic for some.

PHARMACOLOGIC MANAGEMENT OF CONSTIPATION			
MEDICATION		STARTING DOSE	NOTES
Oral Osmotic Laxatives	Polyethylene glycol 3350 (Miralax)	0.2-0.8 mg/kg/day mixed in 8 ounces fluid.	Drink within 15 minutes for best effectiveness. Can mix into any non-carbonated beverage.
	Lactulose	1-2 mL/kg/day	Consider in infants
Oral Stimulant Laxatives	Senna (Ex-lax)	2–6 y/o: 2.5–5 mg once or twice/day	Senna comes in liquid or tablets. Ex-lax comes in chocolate squares (15 mg senna) that children may be more likely to take. Expect effect 6-8 hours after administration. Diapered children should have diapers changed right away to prevent diaper rash.
		6–12 y/o: 7.5–10 mg/day	
		>12 y: 15–20 mg/day	
	Bisacodyl (Dulcolax)	3–10 y/o: 5 mg/day	Often used as step-up therapy from senna.
		>10 y/o: 5–10 mg/day	
Suppos-itories	Glycerin	1 pediatric suppository	No medication (glycerin is a wax that distends the rectum, leading to colonic stimulation).
	Bisacodyl	2–10 y/o: 5 mg	
		>10 y/o: 5-10 mg	
Enemas	Sodium Phosphate (Fleet)	1–18 y/o: 2.5 mL/kg, max 133 mL/dose	Avoid frequent dosing due to risk of hyperphosphatemia and hypocalcemia.
	Mineral Oil	2–11 y/o: 30-60 mL	Can help soften stool.
		>11 y/o: 60-150 mL	
Dosing from: WEB LINK: GUIDELINE: FUNCTIONAL CONSTIPATION: NORTH AMERICAN SOCIETY OF PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION (2014)			

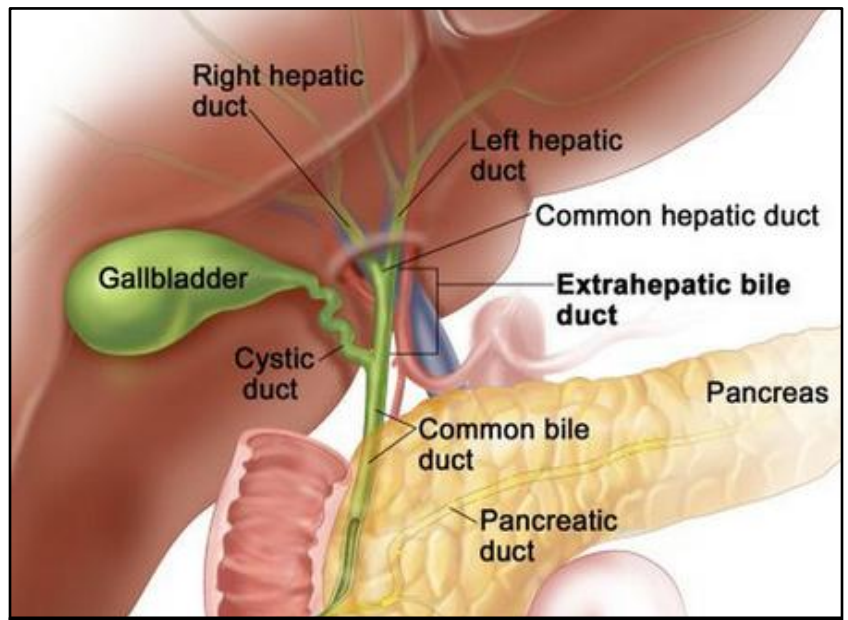
DISPOSITION

Patients can generally be discharged home with an appropriate laxative regimen with pediatrician follow-up. If a patient requires a bowel clean-out and has either failed outpatient management and/or are unable to orally take the medications, they may require inpatient hospitalization for a nasogastric tube placement and a bowel clean-out. This may be required in children with autism spectrum disorder or other neurodevelopmental delays.

GALLBLADDER POINT OF CARE ULTRASOUND

INTRODUCTION (ADRIANA MANIKIAN, MD 2/2022)
Point of care ultrasound of the gallbladder and biliary tract has been proven accurate in the identification of cholelithiasis and cholecystitis in adults. In a systematic review, test characteristics for history, physical examination and laboratory findings were poor. In contrast, in 5 studies, point of care ultrasound for cholecystitis had an average sensitivity of 86% (range: 78%-94%) and a specificity of 71% (range: 66%-76%); (Jain, Acad EM 2017, PubMed ID: 27862628). See: PEM Guide: Gastrointestinal: Cholelithiasis and Cholecystitis.

ANATOMY
Knowledge of the anatomy of the biliary tree is essential to ultrasound interpretation. The gallbladder lies under the liver and superior and lateral to the duodenum and pancreas. The extrahepatic biliary tree consists of the left and right hepatic ducts that join to form the common hepatic duct. The cystic duct from the gallbladder joins the common hepatic duct to form the common bile duct. The common bile duct subsequently joins the pancreatic duct which enters the 2nd portion of the duodenum via the hepato-pancreatic ampulla (previously ampulla of Vater) and through the hepato-pancreatic sphincter (previously sphincter of Oddi).



GALLBLADDER ANATOMY

BILIARY TRACT POCUS: QUESTIONS	
Gallstones?	Yes/No? Location? (body, neck)
Obstruction?	Yes/No? Gallbladder distended, common bile duct distended?
Cholecystitis?	Wall thickness? Pericholecystic fluid?

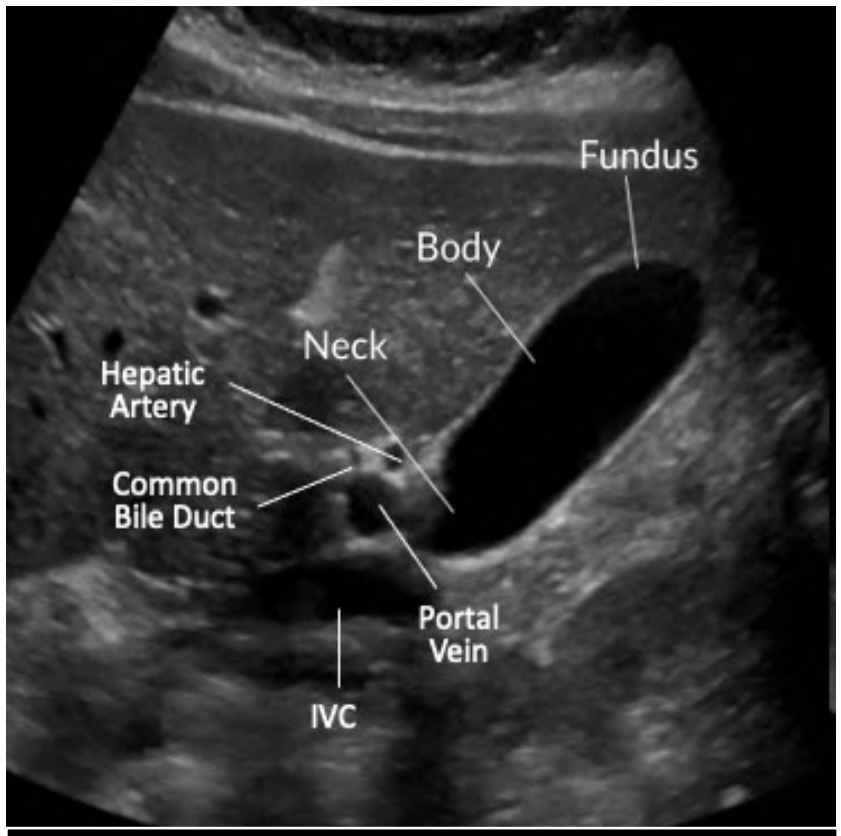
BILIARY TRACT POCUS: SET UP	
Equipment	Curvilinear probe (older patients) or phased array: Abdominal preset
Patient	Fasting state ideally, contracted GB may be difficult to find and interpret
Positioning	Supine or left lateral decubitus with right arm raised above head
Approaches	Subcostal Sweep: Probe marker cranial or to the L shoulder, patient supine or on their left side, patient holds breath in inhalation (diaphragm contraction moves gallbladder inferiorly). Intestinal gas (e.g. bowel or stomach) can interfere with this approach and duodenum can be mistaken for gallbladder with gallstones (dirty shadowing)
	Intercostal: XY-7 (7 cm to the right of the xiphoid), probe placed between ribs, oriented to maximize window space. If not visualized, continue to sweep laterally while fanning through the liver
	Mid-axillary view: Best window to the gall bladder in obese patients

BILIARY TRACT POCUS: REQUIRED VIEWS	
Longitudinal	“Long” including neck, fan through (Longitudinal Sagittal plane)
Transverse	“Short”, 90 degrees counter-clockwise, fan through
Gallbladder wall	Best measured on the anterior wall from outer to inner margins Posterior wall obscured by posterior acoustic enhancement Wall: Mucosa (interior), muscularis (middle), serosa (external) Separate wall layers best seen in contracted gallbladder Edema within the wall can also be seen as area of anechoic fluid
Portal Triad Bonus view (transverse view)	Follow main lobar fissure from gallbladder Dilated CBD = Choledocholithiasis (stone in CBD or distal) Doppler: CBD (No flow), Hepatic artery and Portal vein (Yes flow) CBD: Thicker walled than hepatic artery and portal vein

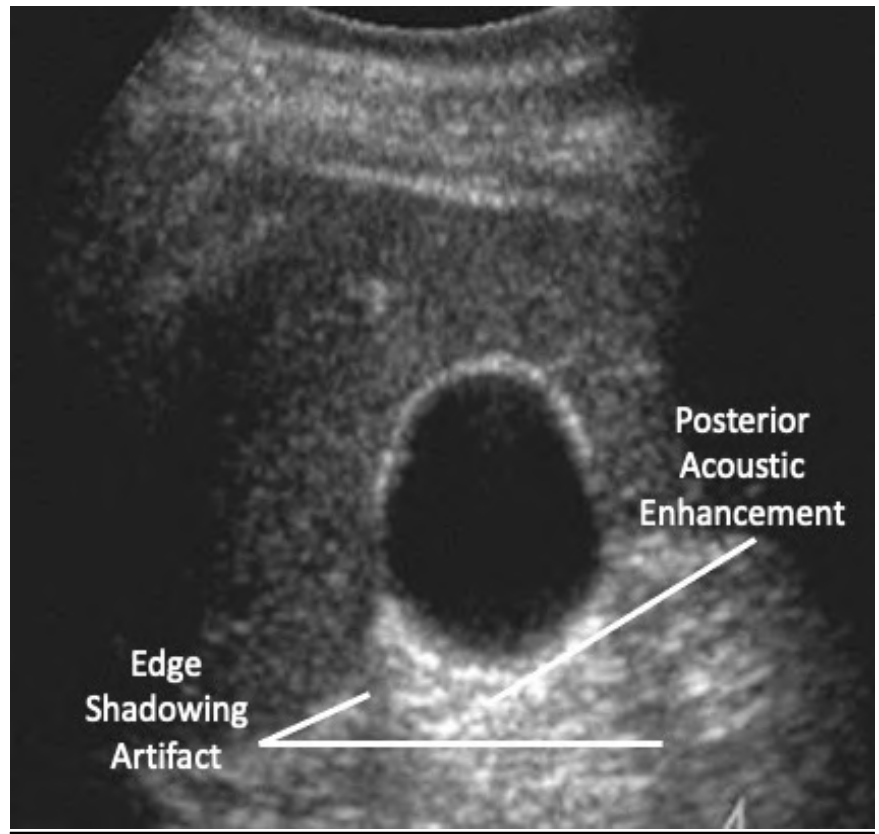
ULTRASOUND FINDINGS	
Cholelithiasis (Stone)	Echogenic focus in a dependent position that moves when the patient is moved with acoustic shadowing sludge. No movement: Impacted neck stone, polyp
Obstruction (Distention)	Dilated gallbladder = Impacted neck stone, may also be seen in common bile duct stone Gallbladder (transverse view): > 5 cm (Distended), 3-4 cm (Normal), < 3 cm (Contracted)
	Dilated common bile duct = Choledocholithiasis (CBD or distal) Measured from the inner wall to inner wall Normal size: 1 mm per decade of life Most 2-5 mm, 6-8 mm (requires clinical correlation), > 8 mm (abnormal), up to 10 mm (seen post cholecystectomy)
Cholecystitis (Inflammation)	Thickened gallbladder wall: Anterior wall on transverse or long view, measure perpendicular to the wall. ≤ 3 mm (Normal), ≤ 4 mm (Contracted)
	Pericholecystic fluid: Hypoechoic, typically, between liver and GB
Murphy Sign (Tenderness)	Sonographic Murphy’s sign: Maximal tenderness elicited by pressure with the transducer over the identified gallbladder

BILIARY POCUS: PEARLS
Know the anatomy
Fan through the gallbladder on both longitudinal and transverse views
Visualize neck, Special attention to neck stones. Can be confused with edge artifact
Not all gallstones shadow. Small stones may not
Preemies with TPN: Wall thickening without stones = Acalculous cholecystitis
Use Doppler to distinguish CBD with blood vessels:
Dirty shadowing due to air in stomach or duodenum may mimic gallstones.
Duodenum has hypoechoic wall (thick muscle layer). Gallbladder has echogenic wall

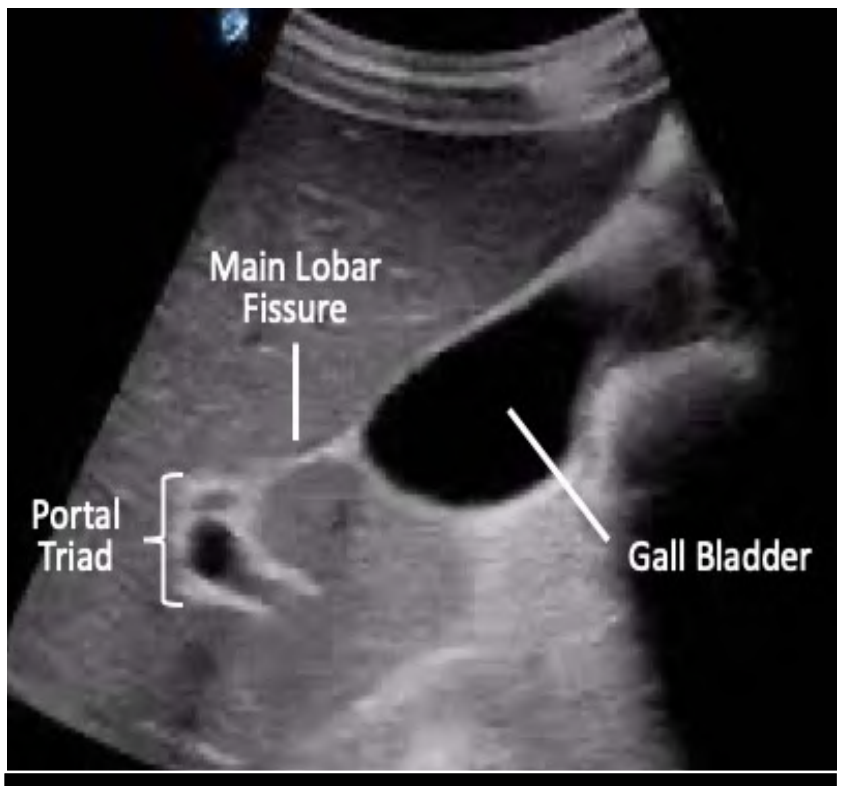
NORMAL ANATOMY (WIDE ANATOMIC VARIATION)



LONGITUDINAL VIEW



TRANSVERSE VIEW

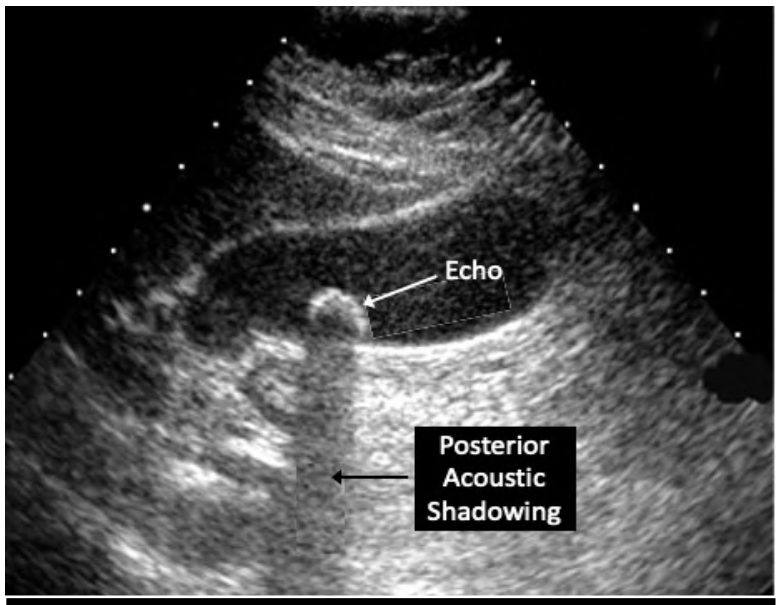


EXCLAMATION POINT SIGN

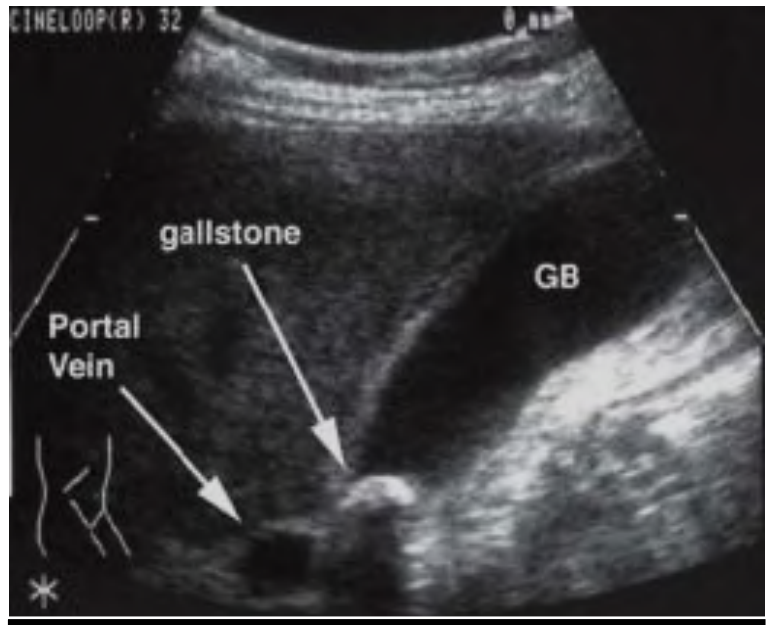
VIDEO LINK: GALLBLADDER ULTRASOUND: NORMAL

GALL STONES/OBSTRUCTION

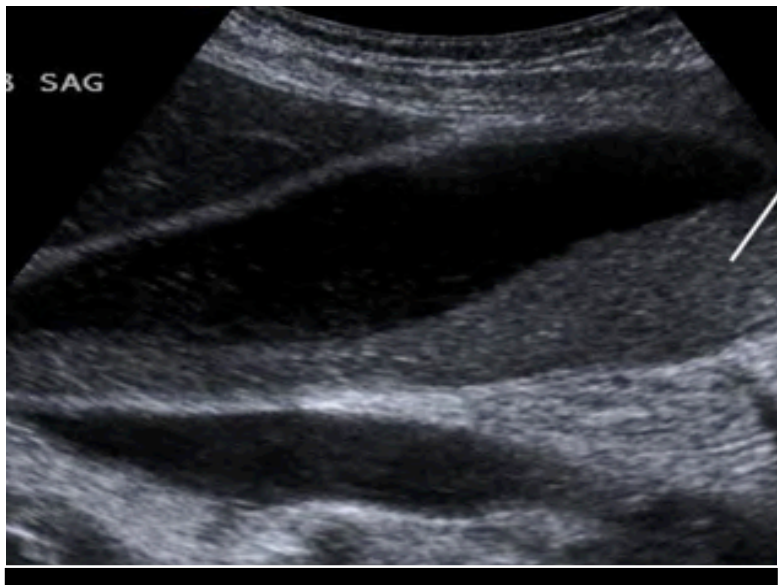
ULTRASOUND FINDINGS: GALL STONES/OBSTRUCTION
Highly echogenic
Posterior acoustic shadow: May be absent if small. Don’t confuse with edge artifact
Dependent position, typically inferior, polyp may be anterior or posterior
Moves with position change: Stone, No movement: Stone in neck or polyp
Large > 6 mm Neck impaction, Medium 3-6 mm, Small < 3 mm CBD obstruction
Wall Echo Shadow (WES): Stone filled or large stone within contracted gallbladder



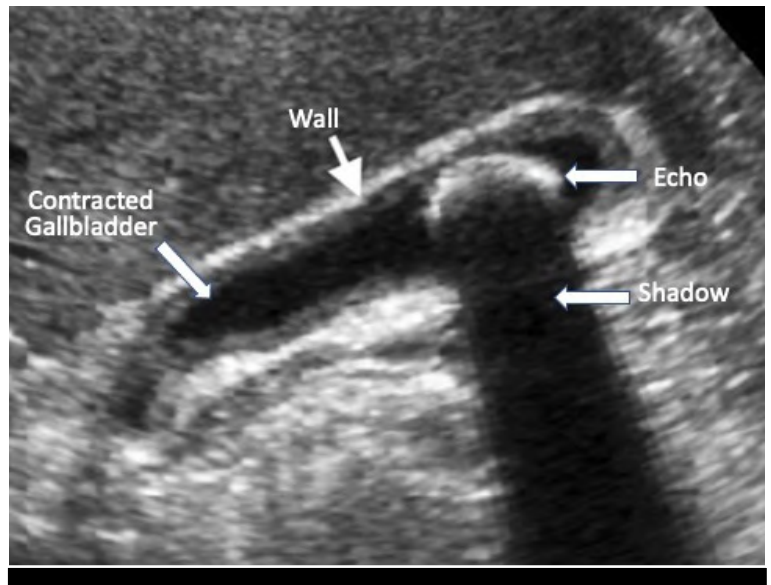
STONE IN BODY



STONE IN NECK (SIN)



SLUDGE



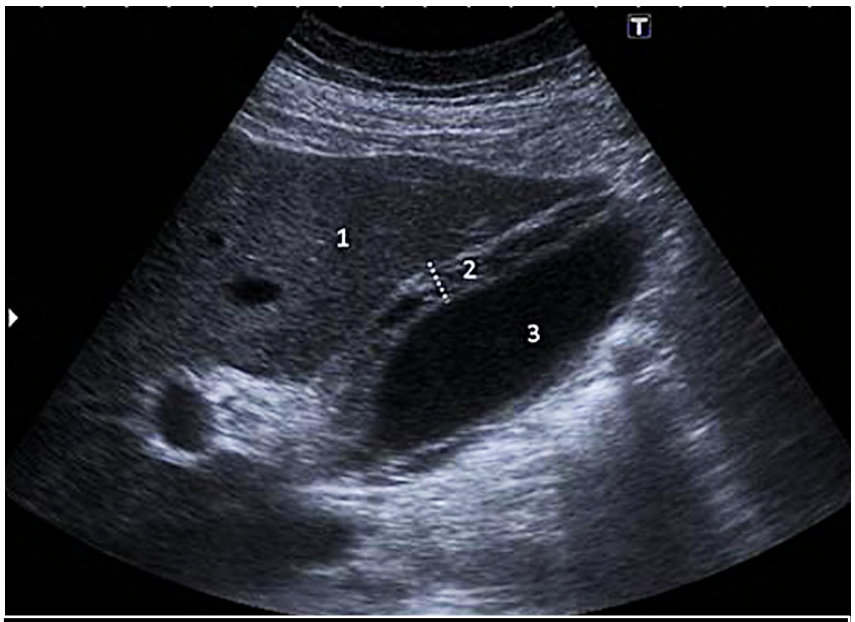
WALL ECHO SHADOW

SLUDGE
Microcrystals Small stones Large stones
Does not produce acoustic shadowing, layers out

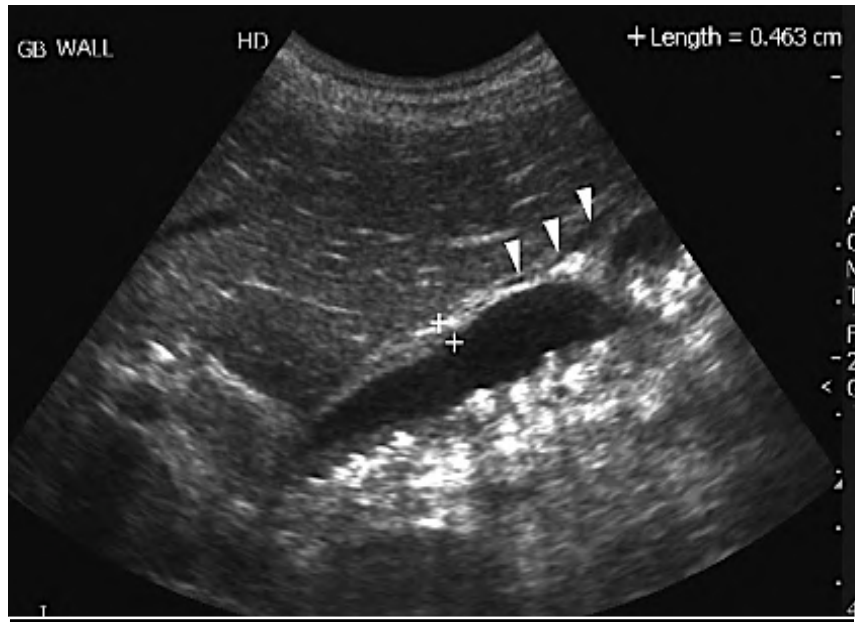
VIDEO LINK: GALLBLADDER ULTRASOUND: CHOLELITHIASIS

CHOLECYSTITIS

ULTRASOUND FINDINGS: CHOLECYSTITIS
Gallbladder wall edema: Measure anterior wall inner to outer: Thickening ≥ 4mm
+/- Gallstones: Echogenic with acoustic shadowing
Sonographic Murphy's sign: Pressure to fundus of the gallbladder with probe Pain
Peri-cholecystic fluid: Anechoic. Typically, between liver and gallbladder fundus
Distended GB > 5 cm on transverse view (if obstructed)
Most Predictive: Stone + Murphy Sign = Predictive Value (+) 92%, PV(-) 95%



WALL THICKENING



PERICHOLECYSTIC FLUID

DIFFERENTIAL DIAGNOSIS[1]: GALLBLADDER WALL EDEMA	
Ascites	Hypoalbuminemia
Congestive heart failure	Pancreatitis
Contracted gallbladder	Peptic ulcer disease
Hepatitis	Renal Failure
HIV	Sepsis
1. Not all wall thickening is cholecystitis. If no stones, look for other causes	

VIDEO LINK: GALLBLADDER ULTRASOUND: CHOLECYSTITIS

GASTRITIS-PEPTIC ULCER DISEASE

INTRODUCTION (MATTHEW PAIK, MD, 3/2023)
Gastritis is defined as gastric mucosal injury accompanied by inflammation. In contrast, gastropathy is gastric mucosal injury with minimal to no inflammation. Gastritis, which involves the stomach, should be differentiated from gastroesophageal reflux disease (GERD), which involves the esophagus. When left untreated, both gastritis and gastropathy can progress to peptic ulcer disease defined by ulcerations in the stomach and proximal duodenum. Peptic ulcer disease can lead to perforations, gastrointestinal bleeding, strictures and bowel obstruction. Rates in the pediatric population are much lower than in adults. However, rates are increasing with the use of NSAIDs, steroids, and immunosuppressive mediations.

PATHOPHYSIOLOGY
Disruptions in the balance between protective and destructive forces in the stomach can progress to gastritis/gastropathy and peptic ulcer disease. Both hydrochloric acid, secreted by H+/K+ ATPase (the proton pump), and pepsin, secreted gastric chief cells, aid digestion but can damage the gastric and duodenal mucosa. To protect itself, mucin, is secreted by surface alveolar cells, and bicarbonate is secreted by epithelial cells to create a pH neutral buffer zone. Prostaglandins mediate mucin and bicarbonate secretion. Tight epithelial cell junctions and an intact mucosal blood supply to distribute protons that reach the lamina propria protection also contribute to protection

The gastric mucosa consists of 4 layers, the mucosa (epithelium, lamina propria and muscularis mucosae), submucosa, muscularis and serosa. An ulcer occurs with disruption of the mucosal and submucosal layers exposing the submucosa. Ulcer perforation occurs when the serosa of the gastric or duodenal wall is penetrated.

FACTORS DISRUPTING THE GASTRIC MUCOSAL BARRIER	
Infections	Bacterial: Helicobacter pylori (Most common, See Appendix) Viral: Cytomegalovirus, EBV Fungal: Candida albicans, histoplasmosis, Cryptosporidium Parasites: Giardia lamblia, ascariasis
Medications	NSAIDS, high-dose corticosteroids, iron supplements, valproic acid, chemotherapeutic agents
Stress	Sepsis, burns, multisystem trauma Local ischemia
Ingestions	Iron, caustics, button batteries
Chronic Conditions	Inflammatory bowel disease, chronic renal failure Systemic macrocytosis (histamine), hyperparathyroidism
Hypersecretory States	Zollinger-Ellison syndrome (gastrin secreting tumor)

CLINICAL MANIFESTATIONS
Given the nonspecific nature of the symptoms related to gastritis and peptic ulcer disease, clinicians must gather a thorough history with attention to medication history and any medical, social, or family history which might make gastritis/peptic ulcer disease more likely. In addition, determine the onset and duration of symptoms and alleviating/exacerbating factors.

Younger patients may present with irritability, poor feeding, regurgitation, vomiting or poor weight gain. School-age and adolescent patients can present with abdominal pain describe as dull or burning that is either generalized or localized to the epigastric area. Bloating and/or nausea are often present. Recurrent nocturnal awakenings from abdominal discomfort are also common as symptoms are exacerbated by emptying of gastric contents at night.

Patients with gastric ulcers, may report epigastric abdominal pain immediately after meals whereas patients with duodenal ulcers report that their symptoms occur a few hours after eating. On exam, patients with gastritis will often have benign physical exams with mild epigastric tenderness as an isolated physical exam finding.

Patients with chronic untreated gastritis or peptic ulcer disease may develop symptoms related to anemia due to long standing occult gastrointestinal bleeding and may present conjunctival pallor, tachycardia, or a flow murmur. As the erosions and ulcers worsen, patients can also present with overt gastrointestinal bleeding with hematemesis, melena, or hematochezia.

With perforated ulcerations, patients present with abrupt and severe worsening of their epigastric symptoms. Erosions leading to a posterior perforation can also lead to pancreatitis and patients can present with mid-back radiation of their abdominal pain. Patients with perforated ulcers and peritonitis may have a rigid abdomen develop sepsis.

DIFFERENTIAL DIAGNOSIS

It is important to keep a broad differential when treating patients with possible gastritis since nausea, bloating, epigastric, or periumbilical abdominal pain are not specific to gastritis alone.

DIFFERENTIAL DIAGNOSIS	
Appendicitis	Inflammatory bowel disease
Bowel obstruction	Ingested foreign body: Button battery
Celiac disease	Lactose intolerance
Cholelithiasis	Pancreatitis
Food intolerance or allergy (e.g. lactose)	Parasitic infections
Gastroesophageal reflux disease	
Hepatitis	

LABORATORY TESTING

Testing is aimed at narrowing the differential diagnosis or identifying sequelae of long-standing gastritis or peptic ulcer disease.

LABORATORY TESTING	
Albumin	Albumin (chronic disease)
CBC	Anemia (bleeding), leukocytosis (infection)
Electrolytes	Hyperparathyroidism: phosphate, chloride, acidosis
Inflammatory markers	ESR, CRP, thrombocytosis (chronic disease)
Transaminases	Hepatis
Lipase	Pancreatitis
Stool studies	Culture, ova and parasites, PCR

IMAGING

An abdominal ultrasound may reveal that patient had a cholelithiasis or cholecystitis or even an early manifestation of appendicitis with periumbilical discomfort.

An upper endoscopy (EGD) is required for a definitive diagnosis. Patients with persistent symptoms after initial trial of antacid therapy and those with alarming features in their evaluation (see table below) should be referred to a pediatric gastroenterologist to discuss whether an EGD is indicated.

INDICATIONS FOR ESOPHAGOGASTRODUODENOSCOPY (EGD)
Gastrointestinal bleeding
Dysphagia, odynophagia, refusal to eat
Persistent pain despite acid suppression treatment
Upper abdominal pain with weight loss or anemia
Persistent vomiting of unknown etiology
Unexplained iron deficiency anemia

MANAGEMENT

Initial treatment of gastritis and peptic ulcer disease begins with treatment of underlying etiologies such as discontinuation of inciting medications or treatment of H. pylori. See also: PEM Guide: Gastroenteritis: Upper Gastrointestinal Hemorrhage.

Acid suppression via proton pump inhibitors (PPIs)(ending in …PRAZOLE) or histamine-2 antagonists (H2Ras)(ending in …TIDINE) is often used to relieve symptoms and promote healing over a course of 4-8 weeks. H2RAs are associated with tachyphylaxis (diminishing response to successive doses). If patients need prolonged therapy, such as for peptic ulcers, PPIs are preferred. H2Ras have a more rapid onset of action and shorter duration. Of the PPIs, Omeprazole has the shortest time to peak levels. PPIs are activated in the acidic environment of the stomach and binds to the H+/K+ ATPase (the proton pump). PPI should be administered before the first meal of the day and are typically given once daily. PPI use has been associated with C difficile infection.

MEDICATIONS FOR GASTRITIS	
MEDICATION	DOSE
Famotidine (H2RA)	0.5-1 mg/kg/day QHS or divided twice daily (max 40 mg/day)
Omeprazole (PPI)	5 kg to <10 kg: 5 mg once daily 10 kg to <20 kg: 10 mg once daily ≥20 kg: 20 mg once daily
	Alternative: 1-4 mg/kg/day (maximum 40 mg/day)
Pantoprazole (PPI)	Children ≥5 years 15 to <40 kg: 20 mg once daily ≥40 kg: 40 mg once daily
	Alternative: 1-2 mg/kg/day (maximum 40 mg/day)
Lansoprazole (PPI)	2 mg/kg daily (maximum 30 mg/day
Esomeprazole (PPI)	Infants: 3 to 5 kg: 2.5 mg once daily >5 to 7.5 kg: 5 mg once daily >7.5 kg: 10 mg once daily
	Children 1-11 years <20 kg: 10 mg once daily for 8 weeks. ≥20 kg: 10 or 20 mg once daily for 8 weeks.
	Children ≥12 years: 20 to 40 mg once daily (maximum 40 mg/day)

DISPOSITION

Most pediatric patients with gastritis or peptic ulcer disease can be safely managed in the outpatient setting and often have resolution of symptoms after 4-8 weeks of medical management. They will rarely have severe complications such as gastrointestinal bleeding , perforation, or obstruction as a complication requiring admission and emergent pediatric gastroenterology or surgical intervention.

APPENDIX: HELICOBACTER PYLORI

INTRODUCTION: H pylori is a gram negative bacillus with a spiral shape. The prevalence increases with age and it is estimated that approximately one quarter of patients are infected by adulthood. Most patients are asymptomatic. H pylori infection has been associated with gastritis and peptic ulcer disease but also with significant long term sequelae such as gastric adenocarcinoma and lymphoma.

DIAGNOSIS: On endoscopy, if there is evidence of peptic ulcer disease or nodular gastritis on endoscopy, biopsies will be taken for Helicobacter pylori testing. Unlike adults, non-invasive testing such as stool antigen assay or urea breath tests are not recommended for the initial diagnosis of H. pylori in children. In children, non-invasive testing is recommended only for post treatment assessment at least 4 weeks after treatment. H pylori testing should not be done within 2 weeks of taking a PPI and 4 weeks of antibiotics. In contrast, H2RAs can be taken up to 24 hours before H. pylori testing without affecting results.

CRITERIA FOR DIAGNOSIS OF H. PYLORI
a. Positive culture for H. pylori OR
b. Evidence of H. pylori on histopathology + 1 of the following:
A positive Rapid Urea Test OR PCR OR Fluorescence in situ hybridization

MANAGEMENT: Treatment of H. pylori should be directed by the pediatric gastroenterologist as H. pylori is always diagnosed via endoscopy and biopsy. Guidelines recommend triple therapy with two antibiotics and a PPI for a 2 week course. Which antibiotics are guided by susceptibility testing. The majority of patients will have resolution of ulcers by 4-8 weeks. The routine addition of probiotics is not supported by the evidence

ANTIBIOTIC SELECTION		
Clarithromycin	Metronidazole	Regimen
Susceptible	Susceptible	PPI + AMOX + CLAR x 14 days OR
		Sequential Therapy: PPI + AMOX x 5 days then PPI + CLAR + METR x 5 days (total 10 days)
Resistant	Susceptible	PPI + AMOX + METR x 14 days[1]
Susceptible	Resistant	PPI + AMOX + CLAR x 14 days[1]
Resistant	Resistant	PPI + High dose AMOX + METR x 14 days[1, 2]
Unknown	Unknown	PPI + High dose AMOX + METR x 14 days[1, 2]
AMOX = Amoxicillin, CLAR = Clarithromycin, METR = Metronidazole 1. Alternative: Bismuth subsalicylate quadruple therapy a. < 8 years: Bismuth + PPI + AMOX + METR b. > 8 years: Bismuth + PPI + AMOX + Tetracycline 2. Alternative: PPI + AMOX + CLAR + METR x 14 days		
Penicillin Allergy	a. Susceptible to CLAR and METR PPI + METR + CLAR x 14 days b. Resistant to CLA, > 8 yrs Bismuth + PPI + Tetracycline + MET x 14 days	
Guideline Link: ESPGHAN/NASPGHAN (2016)		

RECOMMENDED DOSING			
		AM Dose	PM Dose
Proton Pump Inhibitor (PPI)[1]	15-24 kg	20 mg	20 mg
	25-34 kg	30 mg	30 mg
	≥ 35 kg	40 mg	40 mg
Amoxicillin	15-24 kg	500 mg	500 mg
	25-34 kg	750 mg	750 mg
	≥ 35 kg	1,000 mg	1,000 mg
Amoxicillin High-dose	15-24 kg	750 mg	750 mg
	25-34 kg	1,000 mg	1,000 mg
	≥ 35 kg	1,500 mg	1,500 mg
Clarithromycin	15-24 kg	250 mg	250 mg
	25-34 kg	500 mg	250 mg
	≥ 35 kg	500 mg	500 mg
Metronidazole	15-24 kg	250 mg	250 mg
	25-34 kg	500 mg	250 mg[2]
	≥ 35 kg	500 mg	500 mg
Bismuth Subsalicylate	< 10 years	262 mg	None
	> 10 years	524 mg	None

1. Dosing for Esomeprazole or Rabeprazole. Preferred, when available, due to less susceptibility to rapid metabolizers. If another PPI is used then must review that PPI's dosing
2. If Metronidazole suspension is used, the dose can be equally divided

Guideline Link: ESPGHAN/NASPGHAN (2016)

GASTROENTERITIS

INTRODUCTION (MICHAEL MOJICA, M.D. 12/2021)
Diarrhea is defined as 3 or more loose or liquid stools or when bowel movements occur more frequently than it typical in a 24-hour period. This does not include formed or pasty stools. An acute diarrheal illness is defined as symptoms lasting for less than 2 weeks. Acute gastroenteritis is very common. The CDC estimates that in the U.S. acute diarrheal illness account for more than 1.5 million pediatric outpatient visits, 200,000 hospitalizations and 300 deaths annually. Diarrheal illness may be associated with dehydration and hypovolemic shock and both infectious and para-infectious complications.

GASTROENTERITIS COMPLICATIONS
Dehydration/Hypovolemic shock*
Electrolyte abnormalities: Hyponatremia*/Hypernatremia, metabolic acidosis
Bacteremia/Sepsis*
Meningitis*: Salmonella, Listeria monocytogenes (most common < 3 months of age)
Extra-intestinal and Post infection complications (Only GI causes listed)
Methemoglobinemia*: NADH methemoglobin reductase not fully active <4 months of age and fetal hemoglobin is more readily oxidized to methemoglobin
Guillain-Barre*: Campylobacter
Erythema Nodosum: Yersinia, Salmonella, Campylobacter, Shigella
Glomerulonephritis*: Yersinia, Campylobacter, Shigella
Hemolytic uremic syndrome*: E Coli: O157:H7, Shigella, Salmonella
Reactive arthritis: C difficile, Campylobacter, Salmonella, Shigella and Yersinia
*Reviewed in detail in a separate PEM Guide

PATHOGENS
Prior to vaccination, rotavirus was the most common pathogen in children less than 5 years of age. Currently noroviruses are the most common pathogen in the U.S. Viral infections are typically accompanied by a low-grade fever and watery, non-bloody diarrhea. Bacterial etiologies are more frequently accompanied by high fever, severe abdominal pain and tenderness and bloody stools.

GASTROENTERITIS PATHOGENS		
VIRAL	BACTERIAL	PROTOZOA
Noroviruses	Campylobacter jejuni	Cryptosporidium
Rotavirus	Salmonella: Typhi and Paratyphi[1]	Giardia lamblia
Enteric adenoviruses	Salmonella: Non-typhoid species[1]	Entamoeba histolytica
Enteroviruses	Yersinia enterocolitica	
Calicivirus	Escherichia coli: Enteropathogenic	
Astrovirus	Escherichia coli: Shiga toxin producing	
	Shigella species	
	Vibrio cholerae	
1. See Appendix: Salmonella		

CLINICAL MANIFESTATIONS

Diarrheal illness may be accompanied by nausea, vomiting, fever, anorexia and abdominal pain. Either vomiting or diarrhea may be the initial symptom. Acute gastroenteritis is the most common initial diagnosis in missed cases of appendicitis and intussusception. This is particularly important with intussusception for which gastroenteritis can cause hypertrophy of intestinal lymph nodes (Peyer's patches) which can then serve as a lead point for intussusception.

When vomiting occurs in the absence of diarrhea the differential diagnosis should be expanded to include, gastrointestinal obstruction, increased intracranial pressure, non-gastrointestinal infection such a pyelonephritis and a range of toxic and metabolic conditions. The history should focus on the presence of associated symptoms and on questions assessing the hydration status as well as characterizing the diarrhea and emesis. Emesis and diarrhea can be characterized by frequency, relationship to oral intake and the presence or absence of blood.

HISTORY
Hydration Status: Oral intake, urine output, tears, mucous membranes, mental status
International travel, camping
Animal exposure
Recent antibiotics
Immunocompromising conditions, medications
Setting: Long term care facility, child care facility
Recent hospitalization
Foodborne or waterborne exposures

WEB LINK: CDC YELLOW BOOK FOR INTERNATIONAL TRAVELERS

DEHYDRATION ASSESSMENT: The diagnosis of dehydration is based on clinical assessment. A documented recent weight loss is the most reliable sign of dehydration. A clinical decision rule was derived in 186 infants 1 month to 5 years of age with an assessment of fluid deficit based on weight gain following resolution of illness. 10 predictor variables were evaluated and no single variable was both highly sensitive and specific. Regression analysis generated 4-independent predictors of dehydration (Table below) with an area under the receiver operating characteristic curve of 0.90. The presence of greater than or equal to two of the four predictors had a sensitivity of 79% and specificity of 87% for 5% dehydration. The presence of greater than or equal to three of the four predictors had a sensitivity of 82% and specificity of 85% for 10% dehydration (Gorelick, Pediatrics 1997, PubMed ID: 9113963).

PREDICTOR	ADJUSTED ODDS RATIO (95% CI)
Capillary Refill > 2 seconds	13.3 (3.4, 5.1)
Dry Mucous Membranes	4.3 (1.5, 12.6)
Absent Tears	4.3 (1.5, 12.4)
Abnormal General Appearance	3.0 (1.0, 8.8)

LABORATORY TESTING

PATHOGEN IDENTIFICATION: Testing may be indicated to determine the etiology of gastroenteritis and to aid in the assessment of dehydration. Testing is typically targeted to those who are at high risk for a bacterial pathogen. Traditionally, stool culture has been the test of choice to determine the etiology of infection as well as antimicrobial susceptibility.

Recently, cultures have been replaced by culture independent diagnostic tests that primarily use nucleic acid amplification techniques. The benefit of these tests includes the rapidity of results and the ability to detect a larger number of pathogens including pathogens that were previously difficult to detect. The downside of rapid testing is that antimicrobial susceptibility cannot be determined. In general, if a culture independent test identifies a bacterial pathogen, a stool culture should be sent.

STOOL TESTING INDICATIONS (IDSA GUIDELINE 2017)*
Fever with bloody or mucoid stools
Immunocompromised patient
Severe abdominal pain and/or tenderness
Signs of sepsis
Suspected enteric fever (Fever, abdominal pain due to Salmonella Typhi or Paratyphi)
Outbreaks of diarrheal illness
International travelers who have been previously treated with antibiotics
*Infectious Disease Society of America: Infectious Diarrhea. PubMed ID: 29194529

NYU GI PATHOGEN PANEL	
Campylobacter	Yersinia Enterocolitica
Clostridium difficile*	Cryptosporidium
Plesiomonas Shigelloides	Cyclospora Cayetanensis
Salmonella	Entamoeba Histolytica
Vibrio	Giardia Lamblia
Vibrio Cholerae	Adenovirus F 40/41
Enteroaggregative E Coli (EAEC)	Astrovirus
Enteropathogenic E. Coli (EPEC)	Norovirus GI/GII
Enterotoxigenic E. Coli (ETEC)	Rotavirus
Shigella/Entero-invasive E. Coli (EIEC)	Sapovirus
Shiga-like Toxin (X1/X2) Producing E. Coli (STEC)	
*Clostridium difficile not reported < 1 year. Frequently positive, don’t manifest disease.	

DEHYDRATION TESTING: The presence of urinary ketones, an elevated urine specific gravity, a decreased serum bicarbonate, and an elevated blood urea nitrogen may aid in the diagnosis of dehydration. Recent studies have demonstrated that these may not be helpful except in those with severe dehydration.

ADDITIONAL TESTING: In patients with severe disease or those who have E Coli 0157 identified, an evaluation for hemolytic uremic syndrome would include a CBC (anemia, thrombocytopenia) with a reticulocyte count (elevated) and a peripheral smear (schistocytes) and a basic metabolic panel (renal function). See also PEM Guide: GU-Renal: Hemolytic Uremic Syndrome). Fecal leukocytes or stool lactoferrin are not indicated.

BLOOD CULTURE INDICATIONS
< 3 months of age with fever
Signs of sepsis
Immunocompromised
Hemolytic anemia
International traveler with fever of unknown etiology

MANAGEMENT

Management of diarrheal illness generally consists of supportive care focusing on dehydration. Antimicrobial therapy is not frequently indicated in children. The use of Ondansetron to decrease vomiting is effective (Freedman, NEJM 2006, PubMed ID: 16625009) though the use of other anti-emetics is not recommended due to the high risk of adverse events. Antidiarrheal agents are not recommended.

ANTIBIOTICS: Empiric antibiotics are generally not indicated in patients who are immunocompetent with bloody or mucoid diarrhea as disease is self-limited and treatment is associated with only minor benefit. Antibiotics are indicated in those who are febrile and less than 3 months of age, those who are immunocompromised, those with severe disease complicated by sepsis, in those with identified typhoid (enteric) fever and those with Shigella, Cholera, amebiases or giardiasis. Empiric antibiotics for adults typically included a fluoroquinolone (e.g. Ciprofloxacin) or Azithromycin. Empiric antibiotics for children typically included a 3rd generation cephalosporin (< 3 months of age) or Azithromycin.

Definitive treatment is based on identification of a specific pathogen and antibiotic susceptibility (See: Appendix: Antimicrobial Therapy for Non-viral Diarrhea). If a patient is asymptomatic, treatment may not be indicated unless they are health care providers who work with children or the elderly and those who work in the food service industry. Antibiotics administration may have significant adverse events in some infections. Antibiotics may increase the risk of relapse and prolonged carriage in patients with non-typhoidal Salmonella infections. Antibiotics may increase the risk of hemolytic uremic syndrome in infection with shiga-toxin producing E Coli.

REHYDRATION: Hypovolemic shock, if left untreated it may lead to cardiopulmonary failure. The goal of therapy is the restoration of normal perfusion through replacement of fluid deficits and the provision of maintenance fluids.

MAINTENANCE FLUIDS		
	ml/kg/day	ml/kg/hour
First 10 kg	100	4
Second 10 kg	50	2
Each additional kg > 20 kg	20	1
A 25-kg child would require 1600 ml/day or 65 cc/hour as maintenance fluids (10kg x 100ml/kg/day) + (10kg x 50ml/kg/day) + (5kg x 20ml/kg/day) = 1600 ml/day)		

ORAL REHYDRATION THERAPY (ORT): Glucose/electrolyte solutions typically contain a low concentration of glucose (e.g. D2.5) to facilitate GI water transport, as well as sodium, potassium, chloride and a base (e.g. HCO_3). Pedialyte contains 2.5% dextrose, ¼ normal saline with 20 meq/liter of potassium chloride and 20 meq/liter of citrate (a base). Prolonged use of Pedialyte does not provide sufficient calories or sodium. A negative carbohydrate balance can result in ketosis and worsening vomiting and metabolic acidosis. Sports drinks, ginger ale and fruit juices should not be used as rehydration solutions. These contain minimal electrolytes and a high sugar concentration that is an osmotic load that may worsen diarrhea.

ORAL REHYDRATION THERAPY		
	Over 4 hours	Every 5 minutes
Mild dehydration	50 ml/kg	1 ml/kg
Moderate dehydration	100 ml/kg	2 ml/kg
Frequency and volume administered per feed dictated by tolerance. Vomiting is replaced ml for ml. Diarrheal is replaced as 10 ml/kg per unformed stool.		

MILD HYPOVOLEMIA (3-5%)**:** The majority of infants and children present with mild-moderate dehydration and fluid deficits and maintenance fluids can be provided with an oral glucose electrolyte solution (Spandorfer, Pediatrics 2005, PubMed ID: 8780476). The CDC and AAP recommend oral rehydration therapy (ORT) in dehydration due to gastroenteritis (CDC, MMWR 2003, PubMed ID: 14627948). Vomiting is not a contraindication to ORT but ORT should be avoided in patients with ileus or suspected bowel obstruction.

An ORT regimen consists of a rehydration phase in which the fluid deficit is replaced over a 4-hour period and a maintenance phase in which maintenance calories and fluids are delivered. A rehydration regimen for a mildly dehydrated child consists of 50 ml/kg over 4 hours or 1 ml/kg every 5 minutes. If ORT fails due to insufficient oral intake then nasogastric rehydration may be considered (Fonseca, Arch Ped Adol Med 2004, PubMed ID: 15123483)

MODERATE HYPOVOLEMIA (5-9%): Moderate dehydration may also be treated with ORT. An oral rehydration regimen for a moderately dehydrated child consists of 100 ml/kg over 4 hours or 2 ml/kg every 5 minutes. If ORT fails or is contraindicated then nasogastric or intravenous rehydration should be initiated. One half of the fluid deficit is replaced over the first 8 hours and the second half over the next 16 hours. Maintenance fluids and replacement of ongoing losses also occur. Rapid intravenous rehydration therapy using boluses of 20 ml/kg has also been shown to be safe and effective in preventing hospital admission (Reid, Annals EM, 1996, PubMed ID: 8780476).

SEVERE HYPOVOLEMIA (> 10%): Severe dehydration requires immediate and aggressive intravenous fluid resuscitation. If intravenous access cannot be obtained then intraosseous access should be considered. Initial fluid boluses of an isotonic crystalloid such as normal saline or Ringer's lactate at 20 ml/kg are given until restoration of normal perfusion. Vasoactive infusions should be avoided in hypovolemic shock since peripheral vasoconstriction may lead to end organ ischemia.

See Appendix: Management: Non-isotonic (Hyponatremic/Hypernatremic) Dehydration.

ADJUNCTIVE THERAPY

ANTIEMETICS: Oral Ondansetron has been demonstrated to reduce vomiting, improve oral rehydration and decrease intravenous rehydration rates (Freedman, NEJM 2006 PubMed ID: 16625009). The study used a dosing scheme of 8-15 kg: 2mg, 15-30 kg: 4mg and >30kg: 8mg. Alternatively a dose of 0.15 mg/kg could be used. The oral dissolving tablets are better tolerated. The primary concern with its use is the possibility of masking significant underlying illness such as intussusception and appendicitis. Other antiemetics such as Promethazine and Metoclopramide are not recommended due to the high rate of adverse events.

ANTIDIARRHEALS: The use of antidiarrheal agents is not recommended. Anti-motility agents such as Loperamide (Diphenoxylate) can result in opiate induced drowsiness and ileus. Bismuth subsalicylate (Pepto Bismol) has demonstrated limited efficacy. Antimotility agents (e.g. anticholinergic agents, opioids) increase the risk of hemolytic uremic syndrome and central nervous system manifestations without improving gastrointestinal symptoms.

PROBIOTICS: A randomized multicenter clinical trial in the PECARN network including 943 patients with acute gastroenteritis found no difference in the proportion of patients developing moderate to severe gastroenteritis, in the duration and frequency of diarrhea and vomiting, unscheduled health care visits, days of daycare missed or hours of caregiver absence from work comparing probiotics (Lactobacillus rhamnosus) twice a day for 5 days to placebo (Schnadower, NEJM. 2018, PubMed ID: 30462938).

ZINC: Zinc supplementation has proven efficacious in the developing world particularly in those with malnutrition though the efficacy in other settings has not been established.

REFEEDING: In the past bowel rest has been recommended. Recent evidence suggests that early refeeding results in a decrease in the severity and duration of symptoms. Breast feeding and an age appropriate diet should be initiated as soon as possible.

PREVENTION

Most infectious diarrhea is spread through the fecal-oral route. Good hygiene can be used to limit the spread of infection. This includes: hand washing, proper food preparation and storage and avoidance of unsafe water or high-risk foods (e.g. unpasteurized milk or cheese). Infants currently received the rotavirus vaccine. Cholera and typhoid vaccines are available for travelers.

APPENDIX: TREATMENT OF NON-VIRAL DIARRHEA

ANTIMICROBIALS FOR BACTERIAL AND PARASITIC DIARRHEA		
BACTERIAL	1ST CHOICE	ALTERNATIVE
Campylobacter	Azithromycin	Ciprofloxacin
Clostridium difficile	Vancomycin PO	Fidaxomicin
Salmonella: Non-typhoidal	Not indicated for uncomplicated infections	
	< 3 months, immunosuppression or invasive disease If susceptible: Ceftriaxone or Ciprofloxacin, or TMP-SMX or Amoxicillin	
Salmonella: Typi or Paratyphi	Ceftriaxone or Ciprofloxacin	Ampicillin or TMP-SMX or Azithromycin
Shigella	Azithromycin or Ciprofloxacin or Ceftriaxone	TMP-SMX or Ampicillin if susceptible
Shiga-Toxin Producing E. Coli (STEC)	None. May increase risk of hemolytic uremic syndrome	
Non-Vibrio cholerae	Invasive disease Ceftriaxone and Doxycycline	Invasive disease TMP-SMX and Aminoglycoside
Vibrio cholerae	Doxycycline	Ciprofloxacin or Azithromycin or Ceftriaxone
Yersinia Enterocolitica	TMP-SMX	Cefotaxime or Ciprofloxacin
PARASITES	1ST CHOICE	ALTERNATIVE
Cryptosporidium	Nitazoxanide (+ Combination anti-retrovirals if HIV+)	
Cyclospora cayetenensis	TMP-SMX	Nitazoxanide
Cystoispora beli	TMP-SMX	Pyrimethamine or Ciprofloxacin or Nitazoxanide
Giardia Lamblia	Tinidazole or Nitazoxanide	Metronidazole
Trichinella spp	Albendazole	Mebendazole
GUIDELINE: INFECTIOUS DIARRHEA: IDSA 2017. PubMed ID: 29194529		

APPENDIX: NON-ISOTONIC DEHYDRATION

HYPOTONIC HYPOVOLEMIA (SODIUM < 130 MEQ/LITER)

Hypotonic (hyponatremic) dehydration occurs when more sodium is lost then water. This may occur in patients whose deficits are replaced with free water, with adrenal insufficiency, and with gastrointestinal or renal losses. More fluid is lost from the intravascular space when compared to isotonic dehydration. Clinical dehydration may be overestimated. (See also: PEM Guide: Endocrine-Metabolic: Hyponatremia).

The management of hypotonic dehydration consists of administration of intravenous isotonic saline. Water maintenance and deficit are calculated and replaced as for isotonic dehydration. Because sodium is lost in greater proportion than water an extra sodium deficit must be calculated:

Extra Na^+ deficit (in mEq) = (135 - current Na^+) x 0.6 x prior weight (kg)

In patients with severe neurological symptoms or seizures, rapid elevation of sodium may be accomplished by the administration of hypertonic saline (e.g. 3% Normal Saline at 5 ml/kg over 20 minutes).

HYPERTONIC HYPOVOLEMIA (SODIUM > 150 MEQ/LITER)

Hypertonic (hypernatremic) dehydration occurs when more water is lost then sodium. This may occur in patients who are taking improperly mixed infant formulas. Fluid volume in the intravascular space is maintained compared to isotonic dehydration, therefore clinical dehydration may be underestimated.

The management of severe hypertonic dehydration consists of administration of intravenous isotonic saline. Care should be taken to slowly lower serum sodium (<10 – 15 mEq/l/24 hours) to protect against cerebral edema. Water maintenance is calculated as for isotonic dehydration, and fluid replacement should occur over a 48-hour period. Because water is lost in greater proportion than sodium the extra water deficit must be calculated:

Free water deficit = (Current Na+ - 145 mEq/ml) x 4ml/kg x prior weight (kg)

APPENDIX: SALMONELLA

NONTYPHOIDAL SALMONELLA (NTS) INFECTION

INTRODUCTION: Transmission in the United States is most commonly due to contaminated eggs, poultry or beef. Ingestion of contaminated water or contact with infected animals or humans can also lead to infection.

NTS infection typically, manifests as a self-limited gastroenteritis presenting with diarrhea, abdominal pain, and fever. NTS may be complicated by urinary tract infection, bacteremia, meningitis, osteomyelitis, and brain abscess. Patients at higher risk of complications include infants less than 3 months, patients with hemoglobinopathies or chronic gastrointestinal disease and those who are immune compromised.

MANAGEMENT: Supportive care is recommended for uncomplicated gastroenteritis due to NTS in an immunocompetent child. Antimicrobials may prolong the duration of fecal excretion in these patients. Oral therapy with Azithromycin, trimethoprim-sulfamethoxazole or fluoroquinolones may be considered for well-appearing, low-risk patients without invasive disease. High risk patients and those with infectious complications require treatment with parenteral Ceftriaxone. A blood culture should be obtained prior to initiating antibiotics.

ENTERIC FEVER

INTRODUCTION: Enteric fever is due *Salmonella* typhi or paratyphi serotypes. It is characterized by prolonged bacteremia. It is rare in the United States with most cases the result of international travel.

HISTORY: Older children have a gradual onset with non-specific symptoms of headache, malaise, lethargy, anorexia, and abdominal pain as well as persistent fevers. Constipation rather than diarrhea may be the presenting symptom. Young infants have a higher rate of invasive complications such as meningitis.

EXAMINATION
Hepatosplenomegaly
Dactylitis
Rose spots (skin bacterial emboli, small, red macules on chest and abdomen
Altered mental status
Shock
Rare: Myocarditis, endocarditis

MANAGEMENT: Enteric fever requires empiric antimicrobial therapy. This most typically includes ceftriaxone or cefotaxime. Dexamethasone has demonstrated a reduction in mortality in enteric fever complicated by shock and/or altered mental status. Aminoglycosides have *in vitro* activity but are not clinically effective. Trimethoprim-sulfamethoxazole, chloramphenicol and amoxicillin are not recommended for fist line therapy due to high rates of treatment failure and relapse. Patients may be transitioned to oral antibiotics when blood cultures are negative.

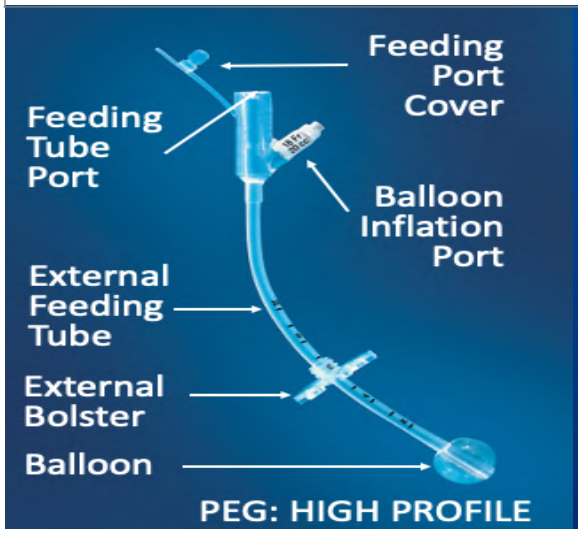
GASTROSTOMY TUBE COMPLICATIONS

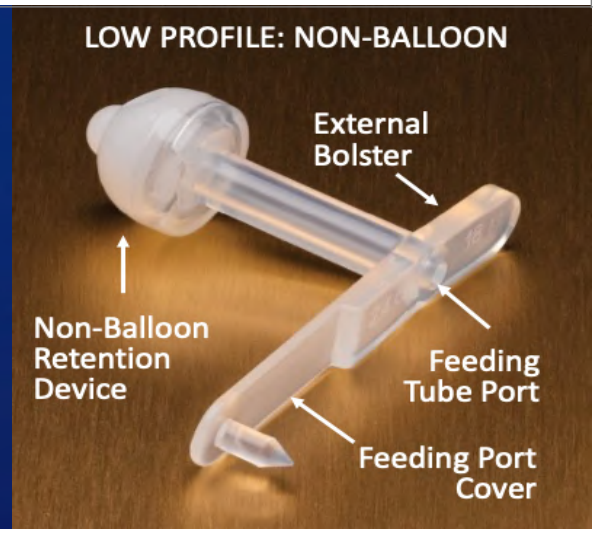
INTRODUCTION: (MICHAEL MOJICA, MD, 9/2020)
Gastrostomy tubes, are placed into the stomach through the abdominal wall to provide enteral access for feeding and medications. G-Tubes can be placed endoscopically (most common), surgically or under fluoroscopic guidance. The distal end of the tube can extend into the stomach (G-Tube) or advanced into the jejunum (GJ-Tube). Jejunal tubes (J-Tube) are placed directly into the jejunum through the abdominal wall. GJ-Tubes and J-Tubes are preferred for patients with a high pulmonary aspiration risk.

This PEM Guide focuses on G-Tube complications outside of the immediate post-operative period. The most common ED G-Tube complications are a dislodged G-Tube and leakage/skin breakdown/concern for infection at the site of entry. It is essential to determine how long feeding has been missed or if essential medications (such as antiepileptics) have been delayed if the G-Tube is dislodged. These should be administered by alternate routes (NG: Feeds, NG/IV: Medications)

ANATOMY OF A G-TUBE: G-Tubes types can be defined by whether the require an extension tube (high vs low profile), whether they have a balloon or other type of retention devise and the number/type of ports that they have.

G-TUBE CHARACTERISTICS
PROFILE: LOW (AKA BUTTONS) VS HIGH (AKA PEG)
Low: Sit as the skin level and require an extension tube for use
Less conspicuous, less easily dislodged, length and caliber listed on device
High Profile (i.e. PEG Tubes): Typically placed first until stoma matures
PORTS
Balloon: Minimum of 2 ports: Feeding tube port, balloon inflation port
Additional Ports: 2nd feeding tube port and/or gastric decompression port
GJ Tubes: Jejunal port (feeds), Gastric port (medications)
RETENTION MECHANISM
Balloon serves as internal retention mechanism
Non-Balloon (e.g. Bard, Malecot): Internal segment compresses/widens at rest. A stylet/device is needed to extend the distal segment for insertion and removal.





G-TUBE DISLODGMENT: It is not considered safe to replace a tube without fluoroscopic guidance if it has been less than 4-12 weeks since initial placement (NYU: 6 weeks). This time allows the abdominal wall, stomach wall and peritoneum to adhere. Tube replacement before maturation can created a false passage into the abdominal cavity. Patients with poor wound healing (malnutrition, chemotherapy) may take longer for the site to mature. Consult surgery if the site is not mature. GJ-tubes and J-tubes require endoscopic or fluoroscopic replacement.

The majority of G-Tubes can be replaced by an emergency physician with the appropriate equipment and technique. Closure of the stoma can occur over hours. If the tube cannot be replaced quickly then an alternative tube (e.g. Foley catheter, feeding tube, NG tube) can be placed in the stoma to prevent closure.

G-TUBE REPLACEMENT PROCEDURE: BALLOON DEVICE	
PREPARATION	
1	Ensure that the G-tube site is mature (> 6 weeks (NYU) since initial placement).
2	Equipment: G-Tube of same length/caliber, sterile water for balloon, water-soluble lubricant, syringes for inflation, infusions. aspiration (Leuer lock, catheter tip)
3	If a delay in replacement is anticipated, place a Foley catheter, nasogastric tube or feeding tube to prevent stoma closure
4	Flush all feeding tube ports prior to insertion to assess patency
5	Inflate/deflate the balloon to ensure it does both adequately, assess for leaks
6	Consider alternate access for food (NG) and essential medications (NG, IV)
7	Consider sedation or topical anesthetic (e.g. Lidocaine gel)
8	Dilation of the stoma may be required. Insertion of progressively larger Foley catheters or surgical dilators (e.g. Hager) can reestablish the ostomy site caliber.
PLACEMENT	
1	Apply lubricant generously to the skin site and replacement tube
2	Position the patient reclined in bed to relax the abdominal wall
3	Guide the tube through the stoma perpendicular to the abdominal wall with gentle pressure. Never force it. A stylet or cotton tipped swab can be used to stiffen the tube for placement if bending prevents insertion
4	After placement, inflate the balloon with sterile water (saline may precipitate and impede deflation of the balloon), 12 French: 3 ml, 14-24 French: 5 ml, This should be painless. Apply gentle traction to secure the balloon against the gastric wall
5	If an external bolster is present (PEG tube) move it 1 cm from the abdominal wall
CONFIRM PLACEMENT	
1	Flush the feeding port with 10-20 ml of water and aspirate gastric contents. Alternatively, instill 10-15 ml of air and auscultate for borborygmi
2	Radiologic/Ultrasound confirmation is not required if the following criteria are met. a. The tube is replaced perpendicularly without significant force b. The balloon is inflated without pain or resistance c. The tube flushes easily and gastric aspirate (pH < 4) is obtained
3	If there are any difficulties with placement, obtain an upright abdominal XRAY after instilling 10-20 ml of water-soluble contrast such are Gastrografin

G-TUBE REPLACEMENT PROCEDURE: NON-BALLOON DEVICE	
Similar to the insertion of a balloon tipped G-Tube with the following exceptions	
Preparation	The stylet of the new G-Tube should be released to ensure the retention device contracts (shortens and widens).
Pre Insertion	The stylet should be used to extend (lengthen) the retention device
Post Insertion	The stylet should be removed to shorten/widen the retention device

VIDEO LINK: NON-BALLOON G-TUBE INSERTION

OTHER G-TUBE COMPLICATIONS: Vomiting (particularly hematemesis), persistent bleeding and rapidly developing infection (necrotizing fasciitis) are the most concerning complications of gastrostomy tubes.

G-TUBE COMPLICATIONS	
Infection	Cellulitis, peritonitis, necrotizing fasciitis
Irritation	Skin breakdown, bleeding
Leaking	Leaking: Common before stoma maturation
Bleeding	Granulation tissue
Vomiting	Gastric outlet obstruction: Balloon → pylorus/beyond, overinflation Gastric volvulus: Hematemesis, severe pain
Clogged	Failure to flush or aspirate tube
Unremovable	Unable to Remove

LOCAL IRRITATION/LEAKAGE: Local erythema is frequently encountered as a result of skin exposure to acidic gastric contents. New or loose G-tubes can allow for more leakage then a mature G tube. Irritation due to leakage can be treated with topical application of Carafate or Zinc oxide. Worsening or expanding erythema indicate the possibility of infection. Pain can results from any of the conditions above but may also be due to a tight external bumper and if the bumper is accidentally pulled into the tract (“buried bumper syndrome). The site should be examined closely for herniation of gastric tissue.

INFECTION: Most infections are localized to the peristomal skin. Mild, local infection can be treated with a topical anti-fungal or oral antibiotics. Methicillin resistant Staph Aureus is the most common pathogen. A first generation cephalosporin is adequate if MRSA is not a concern. Peritonitis. necrotizing fasciitis and intraabdominal abscess are rare. Necrotizing fasciitis is more common in patients with diabetes, malnutrition, immune compromise (disease or medications) and with pressure/traction at the stomal site.

BLEEDING: Granulation tissue may bleed and if resistant to direct pressure, can be treated with silver nitrate. Endoscopic evaluation is warranted for persistent bleeding, significant bleeding with a decrease in hemoglobin, hemodynamic instability, gastric aspirate with frank blood, melena or hematochezia.

VOMITING: Vomiting, and in particular hematemesis can represent life-threatening complications such as gastric volvulus. Vomiting can also be due to gastric outlet obstruction as a result of overinflation of the balloon or balloon migration into the pylorus or beyond. Patients with constipation, gastroparesis or high volume feeds may have high residuals after feeding leading to nausea and vomiting.

INABILITY TO REMOVE A G-TUBE: Inability to remove a G-Tube is more commonly the result of failure of the balloon to deflate. A guidewire can be passed through to balloon inflation port to puncture the balloon. In addition, an intravenous catheter can be carefully passed through the stoma immediately adjacent to the tube to puncture the balloon.

CLOGGED FEEDING PORT: A G-Tube should be flushed after normal usage for feedings or medication to prevent blockage. Attempts to unclog the tube can be made by flushing or mechanical means. Cola, meat tenderizer and cranberry juice are no more efficacious than warm water. If unable to unclog the tube, it should be replaced.

UNCLOGGING A BLOCKED G-TUBE
FLUSHING
Pressure-flushing with warm water with a small syringe
Chemical Solutions: Pancrelipase, Clog Zapper. Instill x 30-60 min then flush
MECHANICAL
Attempt to milk the precipitant proximally
Attempt to pass a small guidewire or stylet to the proximal tube only (not internally)
Replace the G-Tube with a new one

CONSULTATION
Dislodged Immature G-Tube
Inability to replace a dislodged G-Tube
Dilation of the stoma is required
Significant infection: Extensive cellulitis, peritonitis, necrotizing fasciitis, abscess
Significant bleeding: Refractory to pressure
Gastric volvulus: Severe pain, hematemesis, frank blood in gastric aspirate

INFLAMMATORY BOWEL DISEASE

INTRODUCTION (ARIELLE GROSSMAN, M.D., MELANIE GREIFER, M.D., 4/2021)
Inflammatory bowel disease (IBD) is an umbrella term that includes Crohn's disease (CD), ulcerative colitis (UC), and IBD-unspecified (IBD-U). The incidence and prevalence of IBD is rising, particularly in very young children. Approximately one-quarter of patients with IBD are diagnosed in childhood. Children often have a more severe disease course than adults. It is important for the emergency room provider to recognize symptoms/signs of active IBD and be aware of IBD-related potential complications.

INFLAMMATORY BOWEL DISEASE: DIFFERENCES		
	CROHN'S DISEASE	ULCERATIVE COLITIS
Location	Anywhere in the gastrointestinal tract (from mouth to anus)	Colon only
	Patchy, "skip lesions" Often involves terminal ileum	Contiguous Any amount of colon; Extends proximally from rectum
Inflammation	Transmural	Submucosal/Mucosal
Symptoms	Colon: Diarrhea, rectal bleeding Small bowel: Abdominal pain, weight loss	Colon: Diarrhea, rectal bleeding
Complication	Fistulae, abscess, strictures	Hemorrhagic shock Toxic megacolon

CLINICAL MANIFESTATIONS

HISTORY: Patients with IBD can present to the emergency room with varied symptoms due to an IBD flare or IBD-related complication. The following symptoms are central to the focused IBD history.

HISTORY	
SYMPTOM	QUESTIONS
Pain	Location, severity, interference with activities, association with stooling
Stooling	Consistency (watery, loose and unformed, formed) Number of stools in 24 hours, presence of nocturnal stools, urgency, tenesmus (sensation of needing to stool, but unable)
Bleeding	Presence/Amount: Only on toilet paper, mixed with some/all stools, fills up toilet bowl
Other	Weight loss, fever, nausea/vomiting, energy level, joint pain, rashes, mouth sores

It is additionally important to know when a patient was diagnosed, prior complications, current treatment and adherence, recent labs and imaging, and recent esophagogastroduodenoscopy and colonoscopy findings.

PHYSICAL EXAM: Vital signs are the first step in the evaluation. Fever may be present with disease flares, concurrent infection, or toxic megacolon. Tachycardia and/or hypotension may occur with anemia, dehydration, toxic megacolon, and/or sepsis due to an immunocompromised state. General appearance should assess pallor or fatigue.

The abdominal exam is a central part of the focused physical exam. A distended abdomen may represent a partial small bowel obstruction due to a small bowel stricture or can be due to toxic megacolon. Bowel sounds may be normal, hypoactive, or hyperactive in the setting of a partial small bowel obstruction. On palpation, the provider should pay close attention to areas of fullness or pain, which may reflect areas of disease.

A perianal and rectal examination is particularly significant for Crohn's disease patients with known perianal disease. The provider should inspect for areas of erythema, tenderness, induration, fistulae, and large tags.

EXTRA-INTESTINAL MANIFESTATIONS: Extra-intestinal manifestations of inflammatory bowel disease can occur at any time. The activity of these manifestations typically mirrors gastrointestinal activity and typically improves with treatment of underlying disease.

EXTRA-INTESTINAL MANIFESTATIONS	
SYSTEM	MANIFESTATIONS
Musculoskeletal	Peripheral arthritis/arthralgia, ankylosing spondylitis, sacroiliitis
Dermatologic	Erythema nodosum, pyoderma gangrenosum
Ophthalmologic	Episcleritis, scleritis, uveitis
Hepatobiliary	Primary sclerosing cholangitis

LABORATORY STUDIES

Blood work should include a complete blood count, comprehensive metabolic panel, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). These may show leukocytosis, anemia, thrombocytosis, hypoalbuminemia, and elevated ESR/CRP. Further, patients with IBD often have blood work checked; therefore, the trend of these values from previous levels can be helpful. It may be useful to check a drug level based on the treatment of the patient in order to evaluate its effectiveness and presence of drug antibodies.

Stool studies are an essential part of the work-up. A stool calprotectin can evaluate for inflammation in the colon and is used as a biomarker of disease. There may additionally be an underlying infectious etiology leading to (or causing the) onset of symptoms. Patients with IBD are more likely to have a *Clostridium difficile* infection. Therefore, patients presenting with worsening diarrhea should be checked for *C.difficile*. *C.difficile* nucleic acid amplification testing is more sensitive, but can reflect *C.difficile* colonization. *C.difficile* Toxin A and B enzyme immunoassay is less sensitive, but is specific for active infection. Available testing for *C.difficile* is center specific. Furthermore, IBD patients that are immunocompromised may be at risk for other opportunistic gastrointestinal infections. The provider should consider testing for other gastrointestinal pathogens.

IMAGING

Imaging depends on the symptoms of the patient. There should be low threshold for an abdominal X-RAY to rule out toxic megacolon. Magnetic resonance enterography (MRE) with oral contrast of the abdomen and pelvis is a helpful study to evaluate the gastrointestinal tract for inflammation, strictures, abscesses, and fistulae. MRE is preferred over CT due to risk of radiation. Finally, ultrasound has been used more recently and can be useful, though operator dependent, to evaluate specific parts of the bowel.

MANAGEMENT

Treatment varies depends on disease severity, location, and individual factors and includes 5-aminosalicylates, antibiotics, steroids (i.e. Prednisone, budesonide), exclusive enteral nutrition, immunomodulators (i.e. 6-MP, methotrexate), biologics (i.e. infliximab, adalimumab, vedolizumab), and surgery.

DISEASE FLARES: Steroids may be required for disease flares, oral or intravenous depending on severity and need for hospitalization. The use of steroids should be discussed with the pediatric gastroenterologist, as the benefits must be considered against the associated risks. Further, the pediatric gastroenterologist may elect to use alternate IBD treatment instead of initiating steroids.

Pain control may include heat packs, acetaminophen and/or non-steroidal anti-inflammatory drugs (NSAIDs). There is concern for possible disease exacerbation with NSAIDS; however, we use ketorolac at our center to help manage pain. Opioids must be used with extreme caution and in low doses due to risk of toxic megacolon (see below).

Red blood cell transfusions should be used for anemia, particularly if symptomatic with tachycardia and/or hypotension. Fluids may be required for dehydration, particularly with excess diarrhea or inadequate oral hydration intake in setting of pain.

Antibiotics should be given concurrently if *C.difficile* infection is found. First line treatment is with oral vancomycin. Recurrent infections treatment can be found in the clinical practice guideline (McDonald, *Clin Infect Dis* 2018, PubMed ID: 29462280).

TOXIC MEGACOLON: Toxic megacolon is a rare complication of acute severe colitis, but carries a high mortality rate. It is characterized by non-obstructive colonic dilation with systemic toxicity. Patients are at higher risk soon after diagnosis. Risk factors include cytomegalovirus infection, *C.difficile* infection, and opiate use.

Diagnosis involves radiographic evidence of transverse colon diameter 56mm (or 40mm if < 10 years of age) and evidence of systemic toxicity. Systemic toxicity includes fever, tachycardia, hypotension, dehydration, electrolyte disturbances, or altered level of consciousness.

Initial therapy should include prompt surgical evaluation, correction of electrolyte imbalances, and fluid resuscitation. Patients should be made NPO with a nasogastric tube placed for decompression. Parenteral antibiotics should cover gram negative bacteria and anaerobic bacteria. Parenteral corticosteroids are initiated. Admission to intensive care is required.

PANCREATITIS

INTRODUCTION (ROSHNI PATEL, M.D., JOSEPH LEVY, M.D. 8/2017)
Acute pancreatitis occurs among all age groups and has been increasing in incidence during the past few decades. The incidence of acute pancreatitis of 1 in 7,500 per year. Given the many complications of pancreatitis, early diagnosis and management in the emergency department is essential.

PATHOPHYSIOLOGY

While the exact mechanism(s) are not completely elucidated, pancreatic injury stems from intra-acinar pancreatic enzyme activation, leading in some way to auto-digestion of the gland. Aberrant calcium signals within the pancreatic acinar cells leads to premature activation of proenzymes such as trypsin. This in turn leads to pancreatic edema and cytokines release such as TNF alpha. This can cause pancreatic necrosis and provoke a systemic inflammatory response, with shock multiorgan failure.

COMMON ETIOLOGIES	
Biliary Disease	Structural Defects (Pancreatic Divisum), Gallstones, biliary sludge
Medications	Most common: L Asparaginase, Valproic acid, Azathioprine, 6MP and Mesalamine, Alcohol
Multisystem Disease	Sepsis, Shock, hemolytic uremic syndrome, Lupus, Inflammatory bowel disease
Trauma	Motor vehicle accidents, child abuse, bicycle handlebar injuries
Infections (Most Common)	Mumps, Hepatitis A/E, Rotavirus, Mycoplasma pneumonia, Moraxella Catarrhalis, Adenovirus, Coxsackie B4
Metabolic Abnormalities	Diabetic ketoacidosis, Hypertriglyceridemia, Hypercalcemia, Inborn errors of metabolism
Hereditary Causes	Autoimmune pancreatitis Types 1 and 2, specific mutations

DIAGNOSIS

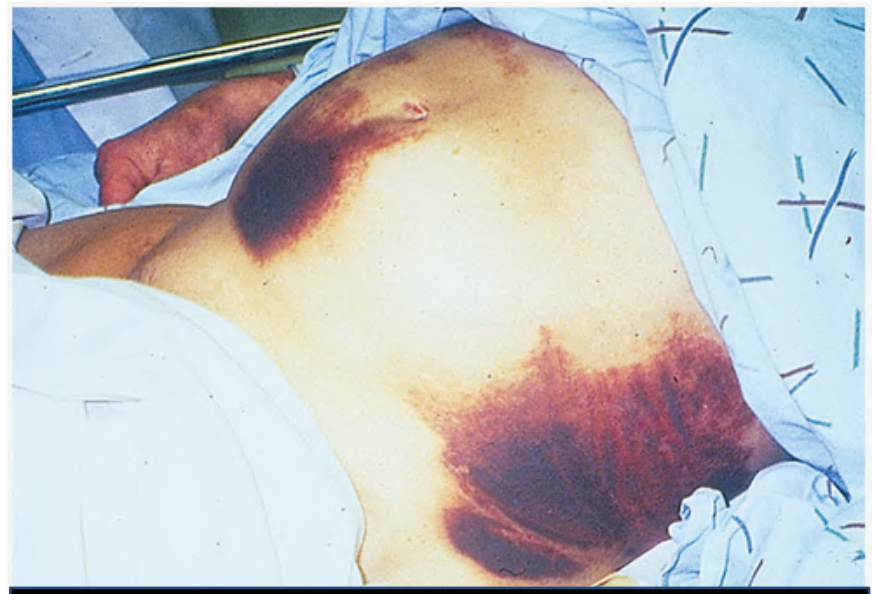
PANCREATITIS CRITERIA (≥ 2 OF THE FOLLOWING)
Typical abdominal pain (acute and epigastric)
Elevated Amylase/Lipase > 3 times the upper limit of normal
Confirmatory findings on cross sectional imaging

HISTORY: The most common symptom is sharp and sudden abdominal pain triggered or aggravated by eating as well as nausea and vomiting. The “classic” presentation of epigastric pain radiating to the back actually only occurs in only 1.6% cases. In younger children abdominal distention and fever are more likely than abdominal pain. A detailed history should include a history of medications, recent trauma, family history and alcohol intake.

DIFFERENTIAL DIAGNOSIS	
Peptic Ulcer disease	Hepatitis
Choledocholithiasis or Cholangitis	Pneumonia
Cholecystitis	Gastroenteritis
Intestinal obstruction or perforation	Ectopic Pregnancy

PHYSICAL EXAMINATION: Accurate vital signs should be obtained initially and repeated often. Orthostatic changes may occur with third spacing of fluids and hypotension. Patients may appear jaundiced if biliary tract obstruction is at the source of the pancreatitis. The abdominal exam might reveal abdominal distention and peritoneal signs.

In the more severe cases, hemorrhage or necrosis of the pancreas can occur. Grey's and Cullen's sign may be present. Grey's sign is a blue discoloration of the flanks and Cullen's sign is a blue discoloration around the umbilicus (See Image). These changes are caused by tracking of blood to the dependent flanks or around the umbilicus. Ascites may be present and the abdomen will be tender to palpation. Some patients will experience relief when the knees are flexed, as this maneuver relives tension on the visceral peritoneum which surrounds this retroperitoneal organ.



GREY SIGN (FLANK)
CULLEN SIGN (PERIUMBILICAL)

LABORATORY STUDIES

The two most reliable laboratory tests for pancreatitis are Amylase and Lipase. Amylase rises 1-12 hours after onset of the pain, peaking at 12-72 hours. Lipase rises 4-8 hours after the injury, peaking at 24 hours and slowly decreasing over 8-14 days. Although both are commonly measured, the Lipase is marginally more sensitive than the Amylase, which can be elevated from a salivary gland source. The diagnostic criteria for acute pancreatitis includes either an Amylase or Lipase greater than 3 times the upper limit of normal.

A complete blood count with differential, chemistry panel, hepatic panel and coagulation profile should also be obtained. There may be leukocytosis with bandemia, hemo-concentration, abnormal electrolytes, elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT) and hyperbilirubinemia. Hypocalcemia or hypercalcemia and disseminated intravascular coagulation may occur.

RADIOGRAPHIC STUDIES

Imaging can confirm the diagnosis of acute pancreatitis, determine the extent of injury and inform therapeutic options. Transabdominal ultrasound is the most practical modality for initial evaluation. However, air within the stomach may degrade image quality. CT provides high resolution images of the pancreas and takes seconds to obtain. CT is better at visualizing calcific densities but has a poor sensitivity for ductal anatomy. MRI provides better imaging of the ductal anatomy. MRI is ideal in non-acute situations. The scan can take up to an hour to complete and may require general anesthesia in patients who cannot still. Both CT and MRI are appropriate to monitor for complications of acute pancreatitis such as pseudocysts and abscesses that can occur months following an attack of acute pancreatitis.

ERCP (Endoscopic Retrograde Cholangiopancreatography) may be necessary in cases of acute pancreatitis caused by gallstone obstruction. It is both diagnostic and therapeutic but predominantly used for its therapeutic benefits. ERCP injects contrast under pressure to delineate anatomy, place stents and incise the sphincter of Oddi to relieve obstruction. It is invasive, exposes the patient to fluoroscopic radiation and can cause post-ERCP pancreatitis.

ACUTE PANCREATITIS SCORES

Scoring the severity of pancreatitis at can guide management and offer prognostic implications. The severity of the inflammation has traditionally been assessed using the Ranson or APACHE II criteria. These scores cannot be applied with confidence to the pediatric population as they have not been validated.

CLASSIFICATION OF ACUTE PANCREATITIS	
Mild	Absence of organ failure and local or systemic complications
Moderately Severe	Transient organ failure resolving within 48 hours
Severe	Persistent organ failure, may involve one or multiple organs

The Ranson criteria help predict the severity of acute pancreatitis and the risk of mortality at presentation, separately for gall-stone associated and non-gallstone related pancreatitis in the first 48 hours after admission.

WEB LINK: MDCALC: RANSON SCORE

RANSON CRITERIA			
0 HOURS		48 HOURS	
Age	> 55	Hematocrit	Fall by ≥ 10%
WBC Count	> 16,000	BUN	↑ by ≥ 5% despite fluids
Blood Glucose	> 200	Ca	< 8
LDH	> 350	PO2	< 60 mmHg
AST	> 250	Base Deficit	> 4
		Fluid Sequestration	> 6000 mL

RANSON SCORE	MORTALITY
≤ 3	0 to 3%
≥ 3	11 to 15%
≥ 6	40%

The APACHE II (Acute Physiology and Chronic Health Evaluation II) score provides a measure of the severity of disease within 24 hours of admission to the ICU. (Knaus, Crit Care Med 1985, PubMed ID: 3928249). It has not been validated for children under age the age of 16 years. This score helps make decisions as to which medications and interventions should be implemented and help normalize based on level of morbidity and outcomes. It is calculated once, at admission to the intensive care unit.

WEB LINK: MDCALC: APACHE II SCORE

COMPLICATIONS

Complications of pancreatitis can be divided into early and late onset. Early complications include shock and multiorgan dysfunction. The most common organs commonly affected include the lung (acute respiratory distress syndrome (ARDS), pneumonia effusion) and the kidney (acute renal failure). In addition, circulating cytokines can activate and interfere with the coagulation cascade resulting in life-threatening disseminated intravascular coagulopathy.

Late onset complications include glandular necrosis with abscess and pseudocyst formation. A pseudocyst is a homogenous collection of pancreatic fluid encased in granulation tissue. It might take weeks to develop. This may present with recurrent pain or with abdominal distention and a mass effect on the physical examination. Some pseudocysts are managed conservatively while other might require drainage. The drainage can be performed either by Interventional Radiology or by Gastroenterology via endoscopic transgastric placement of drains.

LOCAL COMPLICATIONS	SYSTEMIC COMPLICATIONS
Ileus	Shock or Sepsis
Pancreatic Edema	Hypermetabolic State
Pancreatic Necrosis	Hypocalcemia or Hypercalcemia
Pancreatic Abscess	Vascular Leak syndrome
Fat necrosis pancreatic hemorrhage	Multiorgan system failure
Pancreatic Pseudocyst	Disseminated Intravascular Coagulation
Pancreatic duct rupture	Pleural Effusion
Pancreatic duct stricture	Acute Renal Failure
Thrombosis of adjacent blood vessels	Splenic Artery Pseudoaneurysm

MANAGEMENT

Management of pancreatitis is largely supportive and includes pain control, fluid and electrolyte replacement, and, initially, bowel rest.

ANALGESIA: The pain can be quite severe so opioids (Morphine, Dilaudid) are often required. Alternatives include intravenous Acetaminophen and Ketorolac.

ANTIBIOTICS: Necrotizing pancreatitis is associated with infection with gut bacteria such as E. coli, Klebsiella, Pseudomonas or Enterococcus. Antibiotics with good penetrance inside the pancreas, such as Cefepime or Ceftazidime are recommended. Provide anaerobic coverage with Metronidazole.

INTRAVENOUS FLUIDS: Fluid management includes aggressive intravenous resuscitation with crystalloid solutions. Aggressive fluid resuscitation is defined as administration greater than ½ of the calculated 72-hour maintenance infusion within the first 24 hours of treatment. Initial fluid rate in the ED can safely be started at 1.5 times maintenance. The recommended fluid for resuscitation is Ringer's Lactate which was found to result in a lower incidence of systemic inflammatory response syndrome (SIRS) compared to normal saline, presumably because of its pH buffering capacity.

BOWEL REST: Bowel rest is recommended for any patient with suspected acute pancreatitis. The rationale for this is the decrease in pancreatic stimulation brought about when food is withheld and the consequent inhibition of digestive enzyme production leading to less glandular destruction. The newest recommendations for resuming oral feeds shy away from a target decrease in the amylase/lipase numbers and rather focus on the patient's pain and his ability to tolerate feeding without nausea, vomiting and aggravated pain. If feasible, enteral feeds can be started slowly within 24-48 hours after stabilization.

DISPOSITION

Patients are admitted for intravenous fluid management, pain control and observation. Depending on the patient's clinical status, it may be appropriate to monitor in an ICU setting, especially when the metabolic derangements are complex and dynamic and will require close monitoring and appropriate corrections.

Most patients with acute pancreatitis can be managed on the inpatient service. Pediatric gastroenterology consultation should be considered in cases of recurrent pancreatitis or in patients with more complicated clinical courses or those with other underlying gastrointestinal conditions (e.g. Inflammatory bowel disease). About 15-35% of children have a recurrence of pancreatitis which would warrant more extensive metabolic, ductal and hereditary work up.

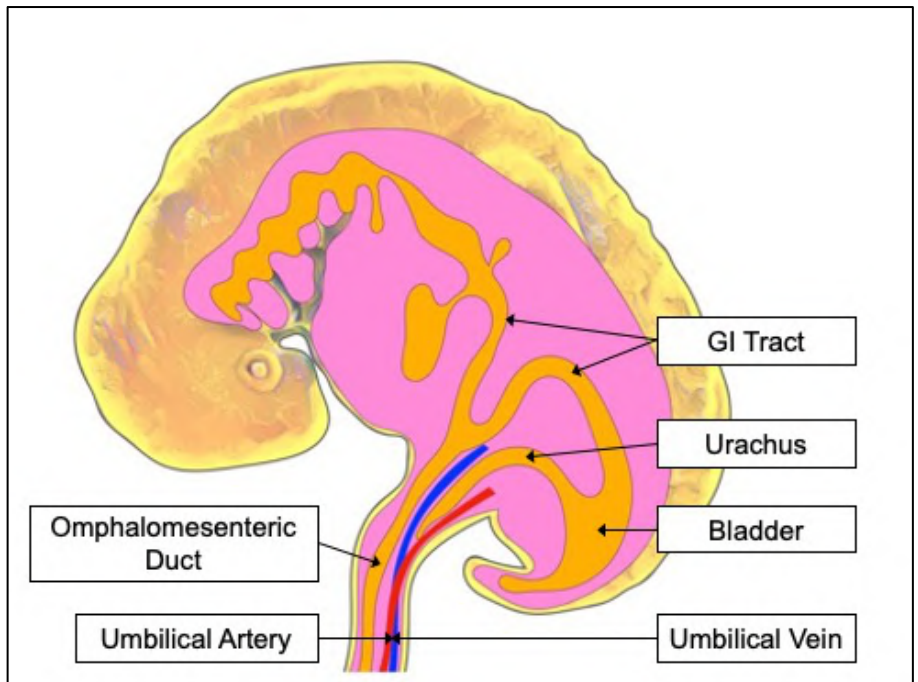
UMBILICAL DISORDERS

INTRODUCTION (DIDIER MURILLO-PARRA, M.D. 2/2023)
The umbilical cord, which provides vascular flow between the fetus and the placenta as well as embryologic gastrointestinal and genitourinary function The umbilical cord is clamped and cut at birth. The remnant umbilical cord stump separates from the neonate within the first few weeks of life, creating the umbilicus. Disorders of the umbilicus typically present in infancy and can have a wide range of signs and symptoms, depending on the underlying pathophysiology. Umbilical drainage/infection and umbilical masses are the most common presentations. While many of these disorders can be successfully managed in the outpatient setting, they can cause high levels of parental anxiety and often present to the emergency department (ED). However, some complications may require urgent or emergent care. Severe anomalies, such as cloacal exstrophy, omphalocele and gastroschisis will be readily apparent at birth. This PEM Guide focuses on umbilical disorders in the neonate, infant and young child.

EMBRYOLOGY/ANATOMY

UMBILICAL CORD: The umbilical cord begins to form around the fifth week of embryogenesis. It consists of the umbilical vessels, the omphalomesenteric duct, and the allantois, a diverticulum of the caudal hindgut.

The umbilical cord contains two arteries and one vein. The arteries carry deoxygenated blood from the fetus to the placenta, and the vein carries oxygenated blood from the placenta to the fetus. After birth, the intraabdominal portions of the umbilical vessels degenerate. The umbilical arteries become the lateral ligaments of the bladder. The umbilical vein becomes the round ligament of the liver.



UMBILICAL ANATOMY

The omphalomesenteric (AKA vitelline) duct connects the developing gastrointestinal tract to the umbilicus. The distal allantois becomes the urachus. It is a fibrous structure connecting the developing genitourinary tract to the umbilicus. During normal development they involute. However, persistent remnants, may occur.

During fetal life, the umbilical cord exits the fetal abdomen through the umbilical ring, a fascial opening with a fibrous ring. The umbilical opening is reinforced posteriorly by Richet fascia and peritoneum as well as by multiple ligaments. The umbilical ring contracts throughout gestation and begins closing after birth. Complete closure of the umbilical ring occurs in most children by 5 years of age, but it can remain patent into adolescence.

Once the umbilical cord is cut, the structures it contained begin to degenerate. The remnant umbilical stump separates from the neonate within the first three weeks of life. The resulting umbilicus is composed of three distinct areas: the mamelon, or central depression; the cicatrix, which is a dense scar and the cushion, which is a slightly raised margin between the Mamelon and cicatrix.

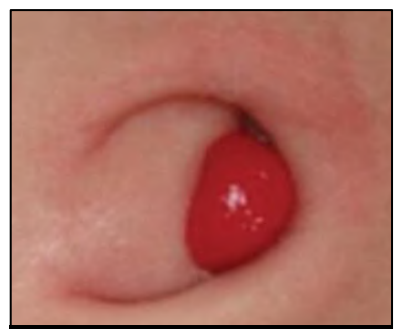
CARE OF THE UMBILICAL STUMP

Most newborns require very little care of the umbilical stump. The stump should fall off in the first few weeks of life without any intervention. Alcohol or other astringents do not provide any benefit and can cause local irritation. Prior to separating, the umbilical stump may develop a wet appearance or have scant serous discharge. If it is pulled off prematurely or traumatically some bleeding may result and if necessary can be treated with silver nitrate cautery. Parents should be counseled that until the stump has fallen off and is well healed, they should not submerge the area in a bath as this can increase the risk of infection (e.g., omphalitis). Separation beyond three weeks of life may be a result of leukocyte adhesion deficiency or urachal anomalies.

UMBILICAL GRANULOMA

Umbilical granulomas are the most common umbilical masses in neonates. They are formed in the first few weeks of life, growing from excess tissue that persists at the base of the umbilicus after separation of the umbilical cord.

CLINICAL PRESENTATION: Umbilical granulomas occur after cord separation and present with a mass or persistent drainage. Umbilical granulomas commonly present as a soft, moist, red, pedunculated lesion of friable granulation tissue. They typically measure 3-10 mm. They present in the first few weeks of life and are associated with delayed of irregular separation of the umbilical stump. The granulation tissue can cause persistent drainage of serous or serosanguinous fluid. The differential diagnosis include other causes of umbilical masses, such as umbilical hernias and urachal and omphalomesenteric duct anomalies. These conditions should be considered when lesions fail to respond to silver nitrate cautery or ligation.



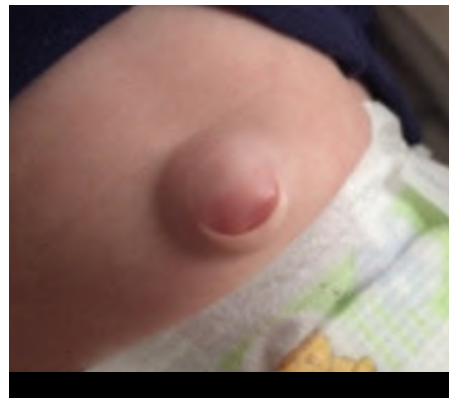
UMBILICAL GRANULOMA

MANAGEMENT: Umbilical granulomas are usually treated by cauterizing the tissue using topical 75% silver nitrate. Silver nitrate can be applied once or twice a week, but usually only a few applications are required. Silver nitrate must be applied carefully only onto the granulation tissue, as it may cause chemical burns or staining of the surrounding tissues. It may be helpful to coat the umbilical fold with an ointment such a surgilube to protect adjacent tissue from burns. If lesions fail to respond to topical silver nitrate, ligation of the granulation tissue can also be performed. However, the umbilicus should be examined carefully before ligation to rule out other possible conditions such as an umbilical polyp. Patients can be followed by their primary care pediatrician for monitoring and additional treatment.

UMBILICAL HERNIA

An umbilical hernia is caused by complete or partial failure of attachment by Richet fascia or the supporting ligaments, leading to weakness and persistent patency of the umbilical rink. At a minimum, the hernia includes peritoneum and skin but may also include peritoneal fluid, fat, intestine and the omentum. Umbilical hernias are more likely in preterm infants, African-American infants, those with a fascial opening of greater than 1.5 cm, Beckwith-Widemann syndrome, Trisomy 21, congenital hypothyroidism, Ehlers-Danlos and mucopolysaccharidoses.

CLINICAL PRESENTATION: Umbilical hernias commonly present as an intermittent, easily reducible umbilical mass. There are most prominent during periods of crying when there is increased intra-abdominal pressure. The borders of the fascial defects can be palpated through the skin.



UMBILICAL HERNIA

Umbilical hernias rarely become incarcerated or strangulated. Incarceration refers to a hernia that cannot be manually reduced. An incarcerated hernia presents as a hard, tender and non-reducible umbilical mass, usually surrounded by edema and erythema of the overlying skin. Infants are usually irritable. Vomiting and abdominal distention may occur if there is intestinal obstruction. Infants with incarcerated hernias and signs of intestinal

obstruction are at high risk of dehydration and hypovolemic shock.
Strangulation refers to vascular compromise of the contents of an incarcerated hernia. It is caused by progressive edema from venous and lymphatic obstruction. This limits blood flow and results in ischemia. Strangulation may occur within hours of incarceration. If prolonged, it may lead to necrosis of the incarcerated tissues. Patients may present toxic appearing with signs of peritonitis and possibly septic shock.

DIFFERENTIAL DIAGNOSIS: Other disorders of the umbilicus, such as umbilical polyps, may present as umbilical masses. However, they are usually unchanged by changes in intra-abdominal pressure. Care must be taken to differentiate umbilical hernias from supraumbilical hernias, which occur superior to the umbilicus secondary to congenitally weakened linea alba. These do not close spontaneously over time.

MANAGEMENT: Most umbilical hernias will spontaneously resolve as the umbilical ring eventually closes. Umbilical hernia repair is usually deferred until 5 years of age due to the high rate of spontaneous closure. There is a higher rate of recurrence when repair occurs before 4 years of age. Surgical repair may be done before 4 years of age in children who: have large, proboscoid hernias without a decrease in the size of the umbilical ring over the first 2 years of life, hernias secondary to genetic or syndromic conditions or who have poor feeding or behavioral concerns (bullying, pulling on hernia). Adhesive taping of umbilical hernias is not adhesive as it is ineffective and may leader to skin breakdown and infection.

Manual reduction may be attempted for an incarcerated hernia, in patients who are not ill or toxic appearing,. The patient should be made NPO as emergent surgery may be required if manual reduction is unsuccessful. Patients presenting with a reducible umbilical hernia and who are asymptomatic, do not require immediate surgical intervention. Patients presenting with an incarcerated hernia and signs of intestinal obstruction, peritonitis, or toxicity from gangrenous bowel or patients with a strangulated hernia require stabilization and pediatric surgery consultation for emergent operative reduction.

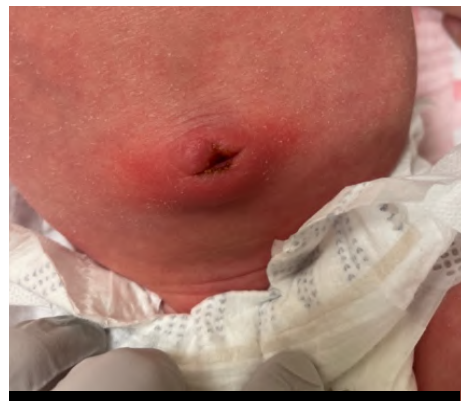
OMPHALITIS

Omphalitis is a life-threatening infection of the umbilicus and surrounding tissue. Bacteria begin to colonize the umbilicus immediately after birth. Devitalized tissue of the umbilical cord stump provides an excellent growth medium. In addition, thrombosed blood vessels in the umbilical cord, can provide a path of entry for bacteria into the bloodstream, increasing the risk of sepsis.

A case series of 566 infants identified MSSA (62%), MRSA (11%), E Coli (10%), Enterococcus (6%), Klebsiella (4%), Group A Strep (4%), Group B Strep (4%) and other (4.6%) in cultures from the infection site (Total > 100% due to polymicrobial infection).

OMPHALITIS RISK FACTORS
Cord care: Cultural practices, cow dung, charcoal dust, cooking oil, baby powder
Immunodeficiencies: e.g. Leukocyte Adhesion Deficiency
Low birth weight
Maternal chorioamnionitis
Non-sterile delivery, home birth
Prolonged labor or prolonged rupture of membranes
Umbilical catheterization

CLINICAL PRESENTATION: Omphalitis is characterized by discoloration of the umbilical cord stump, purulent discharge, periumbilical erythema and induration and tenderness of the surrounding tissues. The majority of infants are well appearing (95%) and afebrile (89%).. Systemic symptoms such as fever, lethargy and difficulty feeding are suggestive of severe infection. Prematurity, fever and age less than 28 days are risk factors for complications of omphalitis.



OMPHALITIS

OMPHALITIS COMPLICATIONS
Sepsis (most common)
Portal vein thrombosis
Liver abscess
Peritonitis
Intestinal gangrene
Necrotizing fasciitis

Concurrent serious bacterial infection is rare in patients with omphalitis. Bacteremia occurred in 1.1%, 95% CI (0.3, 2.5%), UTI in 0.9%, 95% CI (0.2, 2.7%) and bacterial meningitis is 0.9%, 95% CI (0.1, 3.2%) (Kaplan, Pediatrics 2022, PubMed ID: 35441224). These number are likely inflated because not all infants had blood (83%), urine (58%) and CSF (39%) cultures sent. In this case series, sepsis or shock occurred in 2.1%, 95% CI (1.1, 3.7%), severe cellulitis of necrotizing soft tissue infection in 0.4%, 95% CI (0.0, 1.3%) and 0.2% (1/566) died. Serious complication occurred only in those less than 28 days of age.

DIFFERENTIAL DIAGNOSIS: Mild, non-purulent, discharge from the umbilicus can be normal, even when accompanied with some odor. Absence of inflammatory signs, such as erythema and induration, make omphalitis less likely. Conditions secondary to urachal and omphalomesenteric duct remnants may also present with umbilical discharge (see below), but are unlikely to present with inflammatory signs.

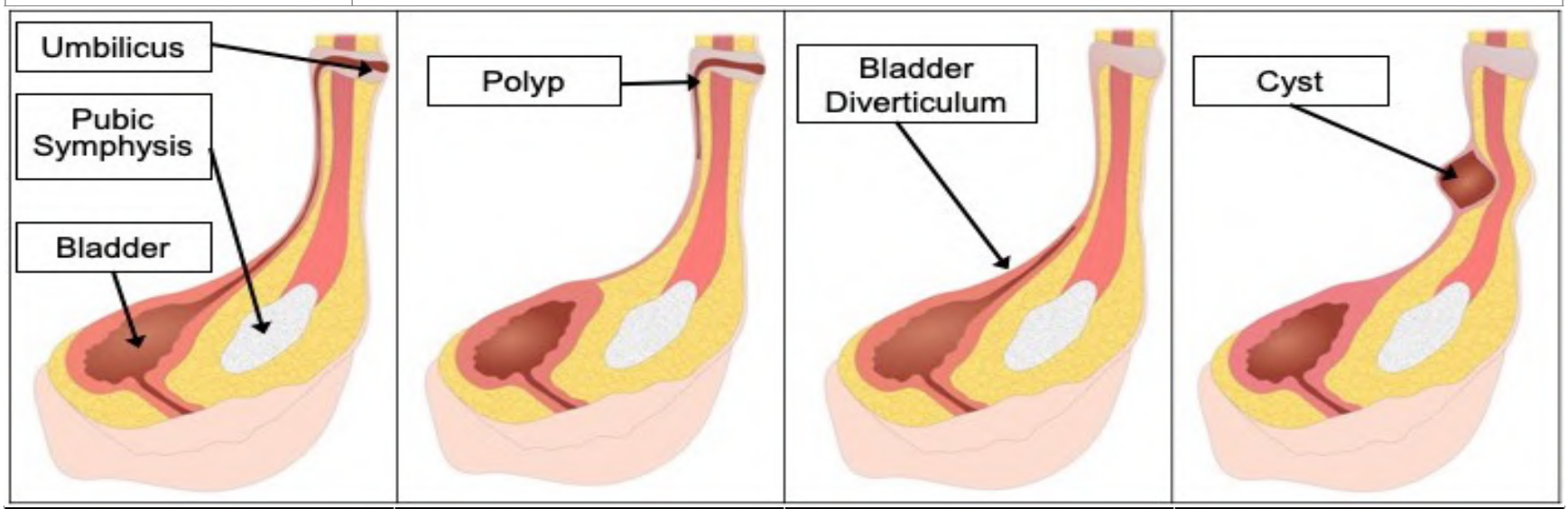
MANAGEMENT: Neonates presenting with systemic signs or symptoms, such as fever, should be evaluated for bacteremia, in addition to cultures of the umbilical discharge. Parenteral antibiotic treatment directed against gram-positive and gram-negative organisms is recommended. Vancomycin and an aminoglycoside are most commonly recommended. Anaerobic coverage (e.g., Metronidazole) and anti-pseudomonal coverage should be consider in those with systemic signs or rapid progression of illness. Necrotizing fasciitis requires surgical debridement.

DISPOSITION: Neonates diagnosed with omphalitis should generally be admitted to the inpatient unit to complete a 10-day course of parental antibiotics, and to monitor for progression to disseminated bacterial infection. In the case series described above, 88% of patients were hospitalized with 16% of those admitted to the ICU.

URACHAL ANOMALIES

The urachus is a fibrous structure that connects the umbilicus to the urinary bladder. It normally involutes, leaving a fibrous cord. When this process is disrupted, a number of rare anomalies can occur.

URACHAL ANOMALIES	
Urachal Sinus	Patency of the umbilical (external) segment of the urachus
Patent Urachus	Complete patency of the urachus with free communication between the bladder and the umbilicus.
Umbilical Polyp	Patency of the umbilical (external) segment of the urachus Firm mass comprised of intestinal epithelium or uroepithelium.
Bladder Diverticulum	Persistent urachal tissue at the bladder end without a connection to the umbilicus
Urachal Cyst	Mid urachal duct patency. Closure at the umbilicus and bladder
Ectopic Tissue	Colonic or intestinal epithelium may be found in urachal remnants. Rhabdomyosarcoma and neuroblastoma may originate there



PATENT URACHUS	UMBILICAL POLYP	BLADDER DIVERTICULUM	URACHAL CYST

CLINICAL PRESENTATION: Clinical manifestations of urachal anomalies can vary depending on the type of anomaly present. A large number of urachal anomalies are asymptomatic, and are found as incidental findings in patients undergoing imaging studies and evaluation for unrelated conditions. For this reason, the true incidence of urachal anomalies is unknown. Common manifestations of urachal anomalies include umbilical drainage, abdominal pain, palpable umbilical or periumbilical abdominal masses, with or without signs and symptoms of infection.

Imaging such as abdominal ultrasound or CT may be helpful when evaluating umbilical and peri-umbilical masses, to confirm the diagnosis of urachal cysts

PATENT URACHUS**:** A patent urachus may present at birth with the presence of a enlarged umbilical cord, as the umbilical cord may fill with urine. In older children, it often presents with a persistently wet or draining umbilicus, as urine exits the bladder through this connection. In some cases, children may present with urinary tract infections. Clear drainage from the umbilicus should always raise suspicion for a patent urachus. A urachal sinus occurs when only the external portion of the urachus remains patent.

UMBILICAL POLYPS: Umbilical polyps present as an umbilical mass, and may resemble an umbilical granuloma. However, umbilical polyps are less common and are usually larger than granulomas. Importantly, umbilical polyps do not respond to treatment with silver nitrate, and require surgical excision.

BLADDER DIVERTICULUM: A bladder diverticulum can cause ureteral obstruction at the urethra’s connection to bladder.

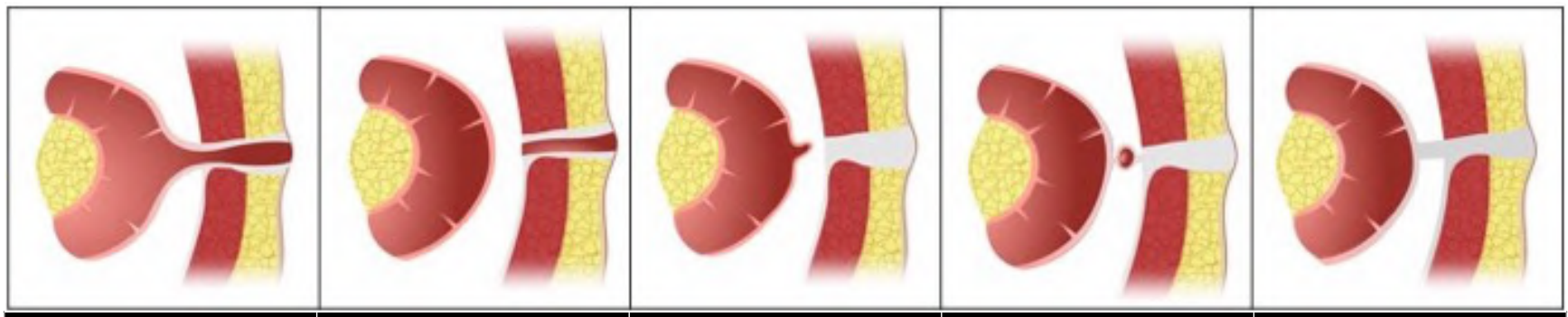
URACHAL CYSTS: Urachal cysts can present as an abdominal mass, especially in older children and adults. These are commonly located below the umbilicus. The cyst may get infected, presenting with associated symptoms of abdominal pain, erythema and swelling. A urachal cyst abscess can be mistaken for an incarcerated or strangulated umbilical hernia. Do not attempt reduction if a urachal cyst is considered.

MANAGEMENT: Surgical management is required for urachal anomalies. The approach depends on the nature of the anomaly. Identifying all umbilical structures is important for a definite diagnosis.

When frank urine is draining from the umbilicus, a thorough investigation of the urinary tract is required to look for bladder outlet obstruction, in which a patent urachus is functioning as an alternative bladder outlet. The patent urachus is ligated and transacted at the level of the bladder. When urachal cysts become infected and develop into abscess, they require drainage and should be allowed to heal prior to removing any residual cyst remnants.

OMPHALOMESENTERIC DUCT ANOMALIES

Omphalomesenteric duct remnants account for a wide variety of umbilical abnormalities. These include fistulas, sinus tracts, cysts, mucosal remnants and congenital bands. These abnormalities require surgical correction.



PATENT DUCT	UMBILICAL POLYP	MECKEL'S DIVERTICULUM	DUCT CYST	FIBROUS CORD

CLINICAL PRESENTATION AND MANAGEMENT:

Ultrasonography, a Meckel scan with 99m technetium pertechnetate and ultimately surgical exploration may be used to identify omphalomesenteric duct anomalies.

PATENT DUCT (AKA FISTULA): If the omphalomesenteric duct is patent from the terminal ileum to the umbilicus, fecal drainage will be present, which is likely to cause significant concern to parents. Prolapse of the proximal or distal ileum through the patent duct may also be seen. A patent omphalomesenteric duct should be excised with full exploration and identification of all umbilical structures. Once the defect is corrected, umbilicoplasty is performed.

POLYPS: Small remnants and sinuses may have less characteristic drainage, requiring the use of contrast injection to determine the specific abnormality. However, surgical exploration is needed for a definite diagnosis. All umbilical structures, including the intraperitoneal undersurface of the umbilicus, need to be visualized in order to identify and remove any bands attached to the small intestine.

MECKEL'S DIVERTICULUM: A Meckel's diverticulum arises from the ileum and may be associated with rectal bleeding when there is ectopic gastric mucosa. A Meckel's diverticulum may also serve as a lead point for intussusception. See also: PEM Guide: Surgery: Meckel's Diverticulum

DUCT CYST: Cystic remnants may become infected and lead to the formation of an abscess, even in older individuals. If an abscess forms due to an infected cystic remnant, surgical drainage may be required with later excision of any remnant.

FIBROUS CORD: The omphalomesenteric duct or any remnant attachment between the abdominal wall and intestines can cause volvulus or herniation of intestinal loops. This would present as mechanical intestinal obstruction, with constipation, abdominal pain, abdominal distention, and vomiting. The exact nature of the obstruction may only be revealed during laparotomy.

COMPARISON: URACHAL VS OMPHALOMESENTERIC DUCT ANOMALIES		
	URACHUS	OMPHALOMESENTERIC DUCT
Connection	Umbilicus → GU Tract	Umbilicus → GI Tract
Completely Patent	Patent Urachus (Urine)	Patent Duct (Stool)
Proximally Patent	Umbilical Polyp	Umbilical Polyp or Sinus
Centrally Patent	Urachal Cyst	Duct Cyst
Distally Patent	Bladder Diverticulum	Meckel’s Diverticulum
Incomplete Resolution	NA	Fibrous Cord

UPPER GI HEMORRHAGE

INTRODUCTION (MICHAEL MOJICA, 12/2020)
An upper gastrointestinal hemorrhage is defined as a source of bleeding above the ligament of Treitz (distal duodenum). Hematemesis is the vomiting of red blood or coffee ground material (due to coagulation of blood in the acidic environment of the stomach). An upper GI bleed is typically associated with melena (black or tarry stools). In general, bright red blood or clots in the stool is typically a sign of lower GI hemorrhage. However, stool color does not reliably distinguish between upper and lower GI sources as melena (heme oxidized to hematin by gut bacteria) can be seen with a proximal lower GI source and bright red blood (hematochezia) can be seen with an upper GI source due to rapid GI transport in infants and young children. The majority of upper GI hemorrhages in the pediatric population are benign and self-limited. However, some etiologies, such as esophageal variceal bleeding, can be life-threatening. The causes of upper GI bleeding are numerous and can be categorized by age.

DIFFERENTIAL DIAGNOSIS: PEDIATRIC UPPER GI HEMORRHAGE*		
NEONATE	INFANT	CHILD/ADOLESCENT
Swallowed maternal blood	Stress gastritis/ulcer	Mallory-Weiss tear
Vitamin K deficiency	Acid-peptic disease	Acid-peptic disease
Stress gastritis/ulcer	Mallory-Weiss tear	Gastric or esophageal varices
Esophagitis	Esophagitis	Esophagitis
Trauma (e.g. NG tube)	Vascular anomalies	Foreign body (e.g. battery)
Vascular anomalies	GI duplications	Ingestion: Caustic, Iron, Button battery
GI duplications	Gastric/Esophageal varices	Vasculitis e.g. HSP
Coagulopathy acquired	Duodenal or gastric webs	Crohn’s disease
Coagulopathy congenital	Bowel obstruction	Bowel obstruction
Milk protein intolerance[2]		Dieulafoy lesion[1]
*Displayed in order of relative frequency 1. Large, tortuous arterioles typically in the stomach but can occur elsewhere 2. More commonly associated with lower GI bleeding		

CLINICAL MANIFESTATIONS
The initial assessment should determine the patient’s hemodynamic status based on heart rate, blood pressure and perfusion. Hypotensive, hemorrhagic shock requires urgent therapy and should not be delayed in the search for a specific etiology.

The next priority is to determine if bleeding is from a systemic etiology or localized to the gastrointestinal tract. Is there bleeding from other sites (e.g. epistaxis, hematuria, mucous membrane bleeding, bruising, petechia, purpura)? Bleeding can occur from a GI location but from a non-GI etiology (e.g. coagulopathy, thrombocytopenia).

Signs and symptoms can aide in establishing an etiology of upper GI bleeding. Is there substernal chest pain (esophagitis) or epigastric abdominal pain (gastritis/ulcer). Has there been a recent choking episode (foreign body), binge drinking or recent/concurrent critical illness (stress gastritis/ulcer), new medications (pill esophagitis) or NSAID use (gastritis). Did vomiting without blood precede hematemesis (Mallory-Weiss tear). Is liver disease suggested by acholic stools, dark urine, right upper quadrant abdominal pain or jaundice (esophageal varices)?

A complete physical exam includes an evaluate of the skin (bruising, petechiae, hemangiomas) and mucous membranes (including the nasopharynx and oropharynx) and a complete abdominal examination for signs or portal hypertension (abdominal distention, splenomegaly and tenderness). Peritoneal signs suggest a perforation. A variety of red dyes in food and medications can be mistaken for blood when vomited.

LABORATORY TESTING

LABORATORY TESTING
CBC: Anemia (no change initially due to loss of whole blood), thrombocytopenia
BMP: Increased BUN in the absence of renal disease associated with UGI > LGI
Lactate: Perfusion/shock
Coagulation studies: PT, PTT, INR, fibrinogen
LFTs: Liver damage, function
Lipase: Pancreatitis associated with gastritis/peptic ulcer, duodenitis
Type and Screen: Significant bleeding with potential need for transfusion

Maternal blood can be swallowed during delivery or breast feeding. The Apt-Downey-Test can be used to distinguish fetal from adult hemoglobin. Fetal hemoglobin is only present in the first few months of life. It is resistant to denaturation in an alkaline environment and remains pink or red. In contrast, adult hemoglobin turns yellow to brownish.

Stool guaiac cards do not reliably detect blood in the acidic environment of the stomach. If available, gastroccult cards, that neutralize stomach acid, should be used instead.

IMAGING

Abdominal XRAYS may be indicated for concern for intestinal obstruction, foreign body (button battery, magnets, long-sharp objects or iron pill ingestion) or perforation. Abdominal ultrasound can identify splenomegaly and portal hypertension in patients with suspected esophageal varices. Angiography or radiolabeled red blood cell scan should be directed by gastroenterology consultation.

NASOGASTRIC ASPIRATION

The use of nasogastric (NG) lavage is controversial and it is not routinely recommended. It’s use has not been associated with a reduction in mortality, rebleeding or transfusion requirements. Placement of a nasogastric tube can help to assess the rapidity and location of bleeding and remove fresh blood and particulate matter to facilitate endoscopy. It should be considered in those with significant hematemesis with an unknown source of bleeding. Water or saline are used. Ice water lavage has not been found to reduce bleeding and is no longer recommended. NG placement is a very painful procedure. A meta-analysis of 10 randomized clinical trials and 734 adult patients demonstrated a decrease in the mean visual analog scale score of 26 mm, 95% CI (24, 28 mm) for nebulized, gel or spray Lidocaine prior to NG insertion (Lor, Medicine 2018, PubMed ID: 29384858).

The presence of bright red blood or coffee grounds is indicative of an UGI hemorrhage.
Bright red blood is indicative of rapid bleeding while coffee ground hematemesis is typically due to a slower rate of bleeding allowing for degradation of blood in the acidic environment of the stomach. Antacids can mask this distinction. The absence of aspirate blood may indicate bleeding cessation or UGI bleeding from a source that is below a closed pylorus. The absence of aspirated blood in the presence of bile (indicating an open pylorus) is indicative of bleeding cessation or an non-upper GI source.

SEVERE BLEEDING
Shock: Tachycardia, hypotension, orthostatic changes, poor perfusion, Lactate
Persistent hematemesis, melena or aspiration of blood aspirated via NG tube
Drop in hemoglobin of < 2 gm/dl or an absolute hemoglobin < 8 gm/dl

MANAGEMENT

The goals of management are to restore circulation blood volume and to target management to the likely cause of bleeding. Medical management options include the transfusion of blood products, acid suppression medications and the use of octreotide. If those options fail, endoscopic and surgical therapy may be considered. Upper GI bleeding from malrotation with midgut volvulus requires urgent surgical intervention. In general, patients should be stabilized, to the extent possible, prior to endoscopy or surgery. Significant ongoing hematemesis may require intubation for airway protection. This should be considered a difficult airway situation.

BLOOD TRANSFUSION: Patients with significant hemodynamic instability should be urgently transfused. The same principles that apply to traumatic hemorrhagic shock can be applied to gastrointestinal hemorrhagic shock (See PEM Guide: Trauma: Hemorrhagic Shock). A consumptive coagulopathy occurs with significant hemorrhage and when large volumes of PRBC's are transfused. In addition to packed red blood cells (10 ml/kg), platelets and fresh frozen plasma (FFP) may be indicated in a 1:1:1 ratio as part of a massive transfusion protocol. Some protocols add cryoprecipitate. Fully typed and cross matched PRBC's are preferred but takes the longest time to prepare. If time is not sufficient for fully typed and cross matched PRBC's then type specific PRBCs or O-negative PRBC (women of child bearing age or O-positive PRBCs (men, women not of child bearing age) can be transfused.

Patient with an acquired or medication induced coagulopathy are more likely to require FFP and platelets. Pharmacologic anticoagulation may require reversal with prothrombin complex concentrate. Patients with renal or cardiac disease should be carefully monitored for signs of fluid overload during transfusion. In addition, over transfusion is associated with an increased rate of variceal bleeding

Hemodynamically stable pediatric patients are typically transfused PRBC's for a hemoglobin of < 8 mg/dL. Patients with significant cardiac or pulmonary disease may require transfusion at a higher hemoglobin threshold.

ACID SUPPRESSION: Proton pump inhibitors are recommended based on good evidence in adults but pediatric evidence is limited. Acid suppression in adults is associated with a decreased risk of rebleeding. Intravenous therapy should be administered to those with large volume bleeding or hemodynamic instability. Intermittent intravenous therapy has been shown to be equivalent to a continuous infusion. Oral therapy is indicated for those not meeting criteria for intravenous therapy. H2 receptor antagonists have not been shown to reduce the risk of ulcer rebleeding.

INTRAVENOUS PROTON PUMP INHIBITOR DOSING		
	Esomeprazole (Nexium)	Pantoprazole (Protonix)
BOLUS DOSING		
< 1 year	0.5-1.0 mg/kg/day QD	< 40 kg: 0.5-1.0 mg/kg QD or BID
1-17 year	< 55 kg: 10 mg QD or BID	
	55 kg: 20 mg QD or BID	40 kg 10-20 mg QD or BID
Adult	40 mg BID	40 mg BID

OCTREOTIDE: Octreotide is a somatostatin analog. It reduces portal vein flow and intra-variceal pressure. It is typically indicated in those with known esophageal varices or those with an unknown source of upper GI hemorrhage with a history or examination consistent with cirrhosis).

OCTREOTIDE DOSING	
Bolus	1-2 mcg/kg (max 50 mcg), may repeat initial bolus in 1 hour PRN
Infusion	1-2 mcg/kg/hour (max 50 mcg/hour) titrated to effect. Typically weaned over 24 hours if bleeding stops.
Adverse Events	Bradycardia, hyperglycemia

ANTIBIOTICS: Ceftriaxone is indicated as prophylaxis against spontaneous bacterial peritonitis in patients with cirrhosis (Child: 50 mg/kg, Adult 1 gram). If bacterial peritonitis is present then the dose is increased to Child: 100 mg/kg, Adult: 2 grams.

ENDOSCOPY: Endoscopy may be required for both diagnostic and therapeutic purposes. Hemodynamically unstable patients should be stabilized, if possible, prior to endoscopy. Endoscopy is typically recommended within 24-48 hours in acute severe bleeding but may be required sooner. Immediate endoscopy may be indicated for esophageal button batteries and iron pill gastric concretions.

The Glasgow-Blatchford score is accurate in determining the need for ICU admission and early endoscopy in adults. A score > 0 is considered high risk. (WEB LINK: MD CALC: GLASGOW-BLATCHFORD SCORE). The Sheffield Scoring System was developed to predict the need for endoscopic therapy in children (Thomson, JPGN 2015, PubMed ID: 25539193). It was derived in population of 62 children with 69 bleeding episodes who had endoscopy for upper GI hemorrhage of which 50% underwent an intervention. The negative predictive value for the rule was 88.5%, 95% CI (73.2, 96.7%). Of note, this rule was derived at a single center in a small population (n=62), it has not been validated and inter-rater reliability of the rules parameters was not assessed.

Endoscopy therapeutic options include clips or electrical/thermal coagulation for bleeding ulcers and sclerotherapy, ligation or banding for variceal bleeding. Children often require deep sedation or general anesthesia and some therapeutic options are limited by the small caliber of the pediatric esophagus. Angiographic embolization or surgery may be indicated if endoscopic therapy fails.

SHEFFIELD SCORING SYSTEM (PEDIATRIC)		
CATEGORY	PARAMETER	POINTS
History	Significant preexisting condition[1]	1
	History of Melena	1
	History of large amount of hematemesis	1
Clinical Assessment	HR > 20 from mean HR of age	1
	Prolonged capillary refill	4
Laboratory Findings	Hb drop of > 2 mg/dl (20 gm/L)	3
Management and Resuscitation	Need for fluid bolus	3
	Need for blood transfusion (Hb < 8 mg/dl)	6
	Need for other blood product	4
Range: 0-24, Cutoff for intervention of 8 1. Liver disease with portal hypertension, malignancy, undifferentiated autoimmune inflammatory disease, eosinophilic enteropathy, Chron's disease, Glanzmann thrombasthenia, alcohol misuse, JIA on high-dose NSAIDS		

GENITOURINARY & RENAL

BALANITIS

INTRODUCTION (ELLEN DUNCAN, MD, PHD, 2/2020)
Balanitis refers to inflammation of the glans penis alone, whereas posthitis refers to inflammation of the foreskin (prepuce) alone. Balanoposthitis refers to the inflammation of both the glans and the foreskin. Inflammation of the foreskin occurs, by definition, in uncircumcised males, but can also occur when a significant amount of foreskin remains following circumcision. Because isolated posthitis is rare, this PEM Guide will focus on balanitis and balanoposthitis and will use the term balanitis to refer to both.

ETIOLOGY
Inadequate personal hygiene in uncircumcised males is the most common cause of balanitis. Moisture between the foreskin and the glans penis promotes skin breakdown and pathogen growth. Prior to toilet training the proximity of stool to the penis in a moist environment contributes to balanitis.

Infection can occur from overgrowth of normal groin flora, from extension of adjacent infections (diaper dermatitis, peri-anal strep) or through sexual contact. Infection with Candida albicans is the most commonly identified infectious cause. Recent antibiotics increase the risk of Candidal Infection. Infection with anaerobic bacteria, group A streptococcus and staphylococcus aureus have also been described. Sexually transmitted infections with Trichomonas vaginalis, HSV, human papilloma virus (HPV), syphilis and Mycoplasma genitalium may also cause balanitis. Diabetes mellitus and chronic dermatologic conditions can predispose to balanitis.

BALANITIS/BALANOPOSTHITIS: CLASSIFICATION	
TYPE	PATHOPHYSIOLOGY
Infectious	Susceptibility to fecal or skin flora, yeast, or sexually transmitted infections owing to skin breakdown from excessive cleaning, presence of significant smegma leading to disruption of protective secretions, or trauma
	Common: Candida, anaerobic bacteria, Group A strep, Staph aureus, Sexual contact: Gonorrhea, chlamydia, trichomonas, tinea, syphilis, HSV
	Pre-toilet training: E Coli Early childhood: Enterococcus Late childhood: Group A strep, Staph aureus Adolescent: Gonorrhea, chlamydia, trichomonas, HSV, syphilis, Gardnerella vaginalis and anaerobic bacteria (Bacteroides)
Irritant	Poor hygiene (most common) Excessive cleaning (especially with harsh soaps) Other irritants such as condom lubricants
Traumatic	In younger children, forceful retraction of the foreskin In older children, injury during masturbation or sexual intercourse Zipper entrapment injuries

COMPLICATIONS
Extension: Urethritis, meatitis, inguinal adenitis
Urinary obstruction
Fournier gangrene (rare): Polymicrobial, necrotizing fasciitis of the perineum. Premature and immunocompromised at highest risk. Can occur in others.
Phimosis: Inability to retract the foreskin*
Paraphimosis: Trapping of the foreskin behind the glans*
*See also PEM Guide: GU-Renal: Phimosis and Paraphimosis

CLINICAL MANIFESTATIONS

Diagnosis of balanitis is based on history and physical examination findings.

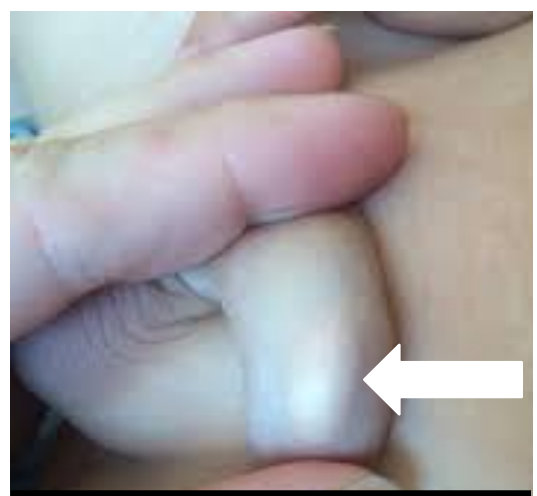
HISTORY: Patients may report a history of pain, redness, swelling, itching, irritation, or discharge. Parents of nonverbal patients may report inconsolable crying. It is important to ask about hygiene (either poor hygiene or excessive cleaning, especially with harsh soaps), exposure to infectious sources or allergens, current or recent medication use and, in sexually active patients, sexual practices (including use of barrier protection, symptoms in sexual partners, and history of sexually transmitted infections).

PHYSICAL EXAMINATION: Patients with balanitis exhibit erythema and swelling of the glans, meatus, and penile shaft. Patients with balanoposthitis will also have inflammation of the prepuce and possibly scarring between the glans and prepuce. Both groups may experience urethral discharge, which may be exudative or transudative and is often foul-smelling, differentiating it from physiologic smegma (see below). The table below lists specific physical exam findings seen in different types of infections.

EXAMINATION FINDINGS BASED ON INFECTIOUS PATHOGEN	
Group A Streptococcus	“Fiery red” skin changes with transudate or exudate under foreskin; seen with GAS infection at another site
Anaerobic bacteria	Erythema, edema, malodorous exudate, superficial erosions
Candida albicans	Erythema and fissures, with thick white discharge
Tinea corporis or cruris	Pruritic, annular lesions
HSV	Necrotizing balanitis

DIFFERENTIAL DIAGNOSIS

Skin conditions, including fixed drug eruptions, psoriasis, eczema, human papilloma virus and scabies, may mimic balanitis. Balanitis should be differentiated from smegma. In infancy and early childhood the foreskin is attached to the glans by adhesions. Smegma is a collection of desquamated epithelial cells under the foreskin as the foreskin lyses from the glans penis. This collection is frequently referred to as smegma “pearls” and is often be mistaken for pus. Smegma is a benign condition that will resolve spontaneously as the foreskin continues to lyse from glans penis



SMEGMA “PEARL”

MANAGEMENT

The management of balanitis depends on the etiology and includes general hygiene and treatment of infections.

GENERAL: All patients should be encouraged to use proper hygiene, including gentle retraction of the foreskin and cleansing with water or saline solution. Avoid the use of harsh soaps which may exacerbate balanitis. Treatment of non-specific balanitis with topical antimicrobials (e.g. Bacitracin, Polysporin, Mupirocin) may prevent secondary bacterial infection. Neosporin, which may cause a contact dermatitis, should be avoided. Hydrocortisone (1% cream, BID x 7 days) can be administered if concomitant infection does not exist.

INFECTIOUS: Treatment of infectious balanitis depends on the causative agent. However, specific pathogens are not often identified. Candida infection can be treated with either topical or oral antifungal medications. If there is no response to topical antifungals consider 1% Hydrocortisone cream BID x 7 days for a nonspecific dermatitis. Anaerobic bacterial infection can be treated with topic or oral Metronidazole depending on the severity. Topic clindamycin or oral Amoxicillin-Clavulanate may be used as alternatives. Group. A strep and staphylococcal infections may be treated with topical mupirocin. Oral antibiotics may such as Cephalexin may be used for more severe disease.

PATHOGEN	TREATMENT
Candida	Clotrimazole (1% cream) or Miconazole (2% cream) BID x 7-14 days >Mild: Fluconazole 150 mg PO OR Topical Imidazole AND Hydrocortisone (1% cream) BID x 7 days Treat female sexual partners to prevent recurrence
Anaerobic bacteria	Mild: Topical Metronidazole (0.75%) BID x 7 days >Mild: Metronidazole PO 7.5 mg/kg (max 500 mg) BID x 7 days Alternatives: Augmentin PO or Clindamycin 1% gel topical
Group A strep, S. aureus	Mild: Mupirocin cream BID-TID x 7-14 days >Mild or if infection at other site (e.g. Strep pharyngitis, perianal) Cephalexin PO 12.5 mg/kg (max 500 mg) QID x 7 days
Sexually transmitted infections	Ceftriaxone 250 mg IM + Azithromycin 1 gm PO x 1 or Doxycycline 100 mg PO BID x 7 days + Metronidazole 500 mg PO BID x 7 days

UROLOGY CONSULTATION IN THE ED
Paraphimosis that cannot be reduced in the ED
Urinary obstruction
Suspected Fournier’s gangrene (necrotizing fasciitis of the perineum)

DISPOSITION

In most cases patients with balanitis and balanoposthitis may be discharged home with instructions to follow up with their primary care physician.

INDICATIONS FOR UROLOGY REFERRAL
Refractory or recurrent balanitis
Non-physiologic phimosis: Inability to fully retract the foreskin at an age where it should be retractable
Balanitis complicated by paraphimosis that has been reduced in the ED

HEMOLYTIC UREMIC SYNDROME

INTRODUCTION (IlYSSA GOODMAN, M.D. 1/2021)
Hemolytic uremic syndrome (HUS) consists of a microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure. It is most often seen in children less than four years of age and is the most common cause of renal failure in healthy children. Infection related HUS peaks seasonally with E. coli infection from June to September.

CLASSIFICATION
Previously, HUS was categorized at D+ HUS (Diarrheal or Endemic Type) or D- HUS (Non-diarrheal or Sporadic Type). Currently, HUS is classified as hereditary (genetic) or acquired. Hereditary HUS is due to complement gene mutations, errors of cobalamin metabolism and diacylglycerol kinase epsilon gene mutations. Acquired HUS is most commonly due to infection but can occur with autoantibodies to complement due to medication toxicity (most commonly chemotherapeutic agents), cancer or organ transplantation. Acquired HUS can rarely be associated with pregnancy or autoimmune disorders such as Lupus. This PEM Guide will focus on the infectious causes of acquired HUS.

The most common cause of acquired infectious HUS in children (90%) Shiga toxin producing bacteria. It occurs in healthy children, usually 6 months to 5 years of age, and mostly during the summer months. Enteritis is usually the prodrome. Shiga Toxin producing E Coli (STEC) is the most common cause. In the U.S., E. Coli O157:H7 is the primary pathogen though other strains of enterohemorrhagic E Coli (EHEC), Shigella and Salmonella may also be responsible. It is typically sporadic but may be associated with outbreaks. Risk factors include: consumption of undercooked ground beef, unpasteurized milk, fruits, and juices, and human-to-human contact with a person with diarrhea (e.g. daycare attendance).

The second most common infectious etiology is Streptococcus pneumonia, particularly with severe infections such as empyema or meningitis. It may be confused with pneumococcal sepsis due to the overlap in symptoms. It is associated with greater morbidity and mortality. A recent case series demonstrated that it is primarily cause by SP strains that were not covered by the initial protein conjugate pneumococcal vaccine (PCV7) but are covered by the more recent vaccine (PCV13).

PATHOPHYSIOLOGY
Toxin from gram negative organism crosses the epithelium of the GI tract, enters the blood, and causes vascular endothelial injury leading to a cascade of events including: activation of coagulation factors, fibrinolytic reactions, and release of inflammatory cytokines resulting in multi-organ injury. Occlusive microvascular thrombi (thrombotic microangiopathy) results in thrombocytopenia, microangiopathic hemolytic anemia, and varying degrees of end-organ damage. It preferentially targets the kidney and can lead to acute renal failure. The pathophysiology of non-diarrheal infections that cause HUS is less clear though complement dysregulation appears to play a role.

CLINICAL MANIFESTATIONS
The diagnosis of HUS is clinical with support from laboratory data. Diarrheal illness occurs typically one week prior to development of HUS. Watery diarrhea can progress to hemorrhagic colitis in some cases. Approximately 50% have bloody stools. Fever and abdominal pain also occur. Imaging is not warranted unless other disease processes are being considered (e.g. intussusception, pneumococcal pneumonia).

CLINICAL MANIFESTATIONS	
Renal	Hematuria, hypertension, anuria/oliguria
Pulmonary	Pulmonary edema due to fluid overload
Hematology	Despite thrombocytopenia, purpura and active hemorrhage are rare
Neurologic	Seizures, depressed mental status, stroke, cortical blindness.
Gastro-intestinal	Hemorrhagic colitis with bowel necrosis/perforation, peritonitis, intussusception, vomiting. Pancreatitis, glucose intolerance
Cardiac	Hypertension, heart failure due to fluid overload. Myocarditis, myocardial ischemia, cardiac tamponade, pericarditis (uremia)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of HUS includes: vasculitis, sepsis, disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP) and leukemia. Appendicitis, ulcerative colitis and other enteric pathogens (Salmonella, Campylobacter, Yersinia, Amebiasis, Clostridioides difficile) should also be considered. TTP usually presents as a pentad with additional features of neurological symptoms and fever. However, children with HUS may have fever during diarrheal illness and 25% of STEC HUS may have neurological signs.

LABORATORY TESTING

Laboratory testing supports the diagnosis of HUS and can exclude other disease in the differential.

LABORATORY FINDINGS IN HEMOLYTIC UREMIC SYNDROME	
CBC	Hemoglobin: Microangiopathic hemolytic anemia with Hb < 8
	Platelets: Mild to moderate thrombocytopenia (typically 40-60,000)
	Blood smear: Schistocytes, helmet cells
	Reticulocyte count: Elevated
BMP	Markedly elevated BUN and creatinine
	Metabolic acidosis (renal failure)
LFT	Elevated indirect bilirubin, LDH, transaminitis, hypoalbuminemia
Haptoglobin	Low (binds free hemoglobin)
Coombs	Normal (Positive in antibody mediated hemolytic anemia)
Coags	Normal (Elevated in DIC)
D-Dimer	Normal
Fibrinogen	Normal (Decreased in DIC)
Urinalysis	Proteinuria, hematuria, or red cell casts
Stool	Culture: Often negative. May detect Shiga-toxin producing E. coli

MANAGEMENT

Emergency department care is mostly supportive and includes treatment of complications due to fluid overload and treatment of electrolyte abnormalities associated with renal failure. There are no interventions that are both safe and efficacious. Consult pediatric nephrology and pediatric hematology early. All patients with HUS should be admitted and many will require ICU level care.

MANAGEMENT OF HEMOLYTIC UREMIC SYNDROME	
Fluids	Balance between dehydration and fluid overload. Fluid Overload: Only replace insensible losses, urine output, stool, and emesis. Consider diuretics for severe hypertension, congestive heart failure Dehydration: Fluid resuscitation with close monitoring for fluid overload
Antihypertensives	Seizures, congestive heart failure
Correct Electrolytes	Hyperkalemia, hyperphosphatemia, metabolic acidosis
Dialysis	60% require dialysis with a mean duration of 1-2 weeks. Indications • Signs/Symptoms of uremia, BUN > 80-100 mg/dl • Fluid overload with cardiopulmonary compromise refractory to medical management • Hyperkalemia, metabolic acidosis refractory to medical management
Hematology	Transfuse only for severe anemia (Hemoglobin < 6 mg/dl) with the goal of a Hb of 8-9 gm/dl. Monitor closely for fluid overload Platelets for significant hemorrhage or planned invasive procedure (rarely required)
Antibiotics	Avoid unless septic. May cause release of more toxins If pneumococcal infection is the cause of HUS, Vancomycin and a 3rd generation cephalosporin should be administered
Anti-Motility Agents	Avoid agents that prolong the duration of toxin in the intestines
Other Treatments	Avoid nephrotoxic medications
	Eculizumab: Monoclonal antibody that blocks complement activation. Primarily indicated in complement mediated HUS but can be given with STEC HUS with coma, seizure or neurologic deficits
	Not recommended: Plasma infusion/exchange, antithrombotic agents. Shiga toxin binding agents

PROGNOSIS

Mortality is approximately 5% in STEC HUS. 50-60% develop severe renal failure requiring dialysis during the initial presentation. 65-85% with STEC HUS recover completely. Most patients (even those who require dialysis) have recovery of renal function. However, some patients slowly progress to end stage renal disease. All patients require close follow up with a pediatric nephrologist.

NEPHROTIC SYNDROME

INTRODUCTION (KRISTY WILLIAMSON, M.D. 1/2014)
Nephrotic syndrome is a constellation of findings including proteinuria, hypoalbuminemia, hyperlipidemia, and edema caused by a variety of glomerular diseases. The glomerular filtration barrier is altered, causing heavy proteinuria and resultant edema. Nephrotic syndrome can occur at any age though most commonly at 18 months to 8 years of age, and is more frequent in boys.

Nephrotic syndrome is a clinical expression of a variety of diseases that can be primary or secondary in nature. Over 75% of cases are primary and caused by minimal change nephropathy (MCN) in which there is no significant glomerular inflammation seen on renal biopsy.

PHYSIOLOGY
Total body water consists of intracellular fluid (2/3) and extracellular fluid (1/3). The extracellular fluid if further divided into intravascular volume (1/4) and interstitial fluid (3/4).

Starling's law governs fluid distribution. Increases in capillary hydrostatic pressure gradient, decreases in the oncotic pressure gradient and increases in capillary permeability can result in edema. Causes of edema can be further divided into those that result in localized edema and those that result in generalized edema.

DIFFERENTIAL DIAGNOSIS OF EDEMA
INCREASED CAPILLARY HYDROSTATIC PRESSURE
Congestive heart failure
Lymphatic obstruction
Venous obstruction/thrombosis
Dependent edema (prolonged standing)
INCREASED CAPILLARY PERMEABILITY
Sepsis, cellulitis
Anaphylaxis, Hereditary angioedema
Pit Viper (crotalid) envenomation
Burns, Frostbite
DECREASED PLASMA ONCOTIC PRESSURE
Proteinuria (Nephrotic syndrome)
Protein losing enteropathy
Liver failure
Malnutrition
Cystic fibrosis
OTHERS
Hypothyroidism (Myxedema)

ETIOLOGY OF NEPHROTIC SYNDROME	
PRIMARY CAUSES	SECONDARY CAUSES
Minimal Change Nephrotic Syndrome	Systemic disease: Diabetes, lupus
Focal Segmental Glomerulosclerosis (FSGS)	Infection: HIV, hepatitis B, hepatitis C
Membranous Nephropathy (MN)	Pre-eclampsia
Membranoproliferative Glomerulonephritis (MPGN)	Certain drugs and toxins
IgA nephropathy	Congenital due to intrauterine infections
Hereditary (Finish-type, Denys-Drash, Frasier)	

CLINICAL MANIFESTATIONS

HISTORY: Swelling is the presenting symptom in 98% of children. The history may include reports of swelling of the face (often confused with allergies), genitals, and lower extremities, and occasionally with refusal to walk. Other common complaints include irritability, fatigue, abdominal pain, and diarrhea. Less common presentations include “foamy” urine and/or hematuria.

PHYSICAL EXAM: Physical examination findings include pitting edema, usually first in areas of lower tissue resistance including periorbital, scrotal/labial, and pretibial areas. Focal swelling can progress to generalized edema with ascites, anasarca, and pleural effusions. Other findings can include hypertension, respiratory symptoms secondary to pleural effusion, abdominal tenderness secondary to peritonitis and ascites or signs of sepsis. The presence of rash, purpura, petechiae, lymphadenopathy, or arthritis suggests a multi-system etiology.

LABORATORY: Initial work-up includes urinalysis, albumin, a lipid panel, and a basic metabolic panel. Other testing can be obtained based on an individual clinical picture.

PRIMARY LABORATORY FINDINGS		
Hypoalbuminemia	< 2.5 gm/dl	
Proteinuria Urinalysis Urine protein/creatinine	> 1+ protein Ratio > 2	UA should not have significant hematuria, RBC casts, or WBCs (suggests nephritis or other renal etiology).
Hyperlipidemia	↑ Cholesterol ↑ LDL ↑ Triglycerides	Increased liver production and decreased catabolism by lipoprotein lipase

ADDITIONAL TESTING		
Antithrombin III, Plasminogen, Protein S	Low	Hypercoagulable
Immunoglobulins	Low	Relatively immunocompromised
BUN/Creatinine	High	Mild elevation reflects volume depletion; Large elevations may signify renal insufficiency and other disease
Total Ca++	Falsely Low	Corrected Ca = [0.8 x (normal albumin - patient's albumin)] + serum Ca level Ionized calcium will be normal
HIV, Hepatitis B or C Serology	Can be positive	Check if history suggestive or atypical features on presentation
Complement: C3/C4	Can be low	Post-infectious nephritis, MPGN, lupus nephritis
Antinuclear antibodies Double stranded DNA	Can be high	If rheumatic cause suggested (e.g. rash, arthritis)
Chest XRAY	Effusion	If shortness of breath, chest pain

RENAL BIOPSY: A renal biopsy is not indicated for a typical presentation. Consider a biopsy in children less than 1 year of age (higher risk of congenital disease), >10 years and if the history, physical exam, or laboratory data indicate a secondary cause of nephrotic syndrome or primary nephrotic syndrome other than minimal change.

MANAGEMENT

The overall mortality of the nephrotic syndrome is low (2-5%), but there is a higher morbidity with chronic, relapsing disease. The majority of patients can be managed as outpatients. A trial of corticosteroids is the first step in treatment of idiopathic nephrotic syndrome. Patients at low risk may be considered for steroid treatment prior to biopsy. Rituxumab a monoclonal anti Cd20 antibody may be indicated, in consultation with a pediatric nephrologist, for steroid refractory or chronic, relapsing disease.

CORTICOSTEROID CRITERIA
Ages 1-10 years
No renal insufficiency
No macroscopic hematuria
No symptoms of systemic disease
No hypertension
Normal C3 levels

INDUCTION: Prednisone 2 mg/kg/day x 6 wks then 1.5 mg/kg every other day x 6 wks
RELAPSE: Prednisone 2 mg/kg/day until proteinuria resolves for ≥ 3 consecutive days

RECOMMENDATIONS
Close follow-up with a Pediatric Nephrologist
Sodium restricted diet while edematous
Pneumococcal vaccination as outpatient
Diuretics for severe edema: Lasix 1-2 mg/kg/day
Albumin infusion for anasarca and signs of intravascular depletion
Antihypertensives for significant hypertension: ACE* inhibitors, ARB*
Statins for persistent hypercholesterolemia
*ACE: Angiotensin Converting Enzyme, ARB: Angiotensin Receptor Blockers

COMPLICATIONS

Patients with nephrotic syndrome are at risk for a number of complications including: thrombotic events, infections and renal failure

FLUID OVERLOAD: The increase in total body water in nephrotic syndrome can result in congestive heart failure, pulmonary edema, pleural effusions and ascites. Because of the shift in fluids from the intravascular volume to the interstitial space patients may be intravascularly depleted while having normal or increased total body water. Traditional signs of dehydration may be absent. An elevated BUN and creatinine may result from decreased intravascular volume or renal insufficiency or failure. Care should be taken in treating with diuretics for fluid overload. An albumin infusion may be required prior to diuresis to avoid exacerbating intravascular depletion.

INFECTION: The loss of immunoglobulins in the urine, impaired synthesis and the use of corticosteroids increase the risk of infection. In addition, pleural effusions and ascites serve as a growth medium for bacteria and may result in pneumonia/empyema and spontaneous bacterial peritonitis respectively. Infections are typically due to encapsulated organism. These include Streptococcal pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae, Neisseria meningitides , Group B streptococcus and Salmonella typhi.

Patients with abdominal pain, fever and peritoneal signs should undergo paracentesis. Beside ultrasonography may be used to guide the procedure. Antibiotics should cover gram positive and enteric pathogens (e.g. E Coli).

Patient with respiratory symptoms such as cough, shortness of breath or chest pain are at risk of pneumonia, pleural effusions/empyema, pulmonary embolism and myocardial infarction. Patients with significant respiratory distress due to a pleural effusion should undergo sonography-guided therapeutic pleurocentesis.

THROMBOSIS: The loss of antithrombin III, plasminogen, and protein S in the urine in addition to a hemoconcentrated state predispose to arterial and venous thrombosis. Renal vein thrombosis should be considered in children with nephrotic syndrome who present to the ED with significant hematuria or signs of renal insufficiency.

Patients with respiratory symptoms (cough, shortness of breath, chest pain) are at risk of pulmonary embolism as well as pneumonia and pleural effusions. A D-dimer may be elevated at baseline and may not be diagnostic of pulmonary embolism or deep vein thrombosis. A spiral chest CT should be obtained if a pulmonary embolism is suspected. Doppler sonography should be obtained deep vein thrombosis is suspected.

Patients with nephrotic syndrome are also at increased risk of myocardial ischemia due to coronary thrombosis. An EKG and troponins should be obtained in those with chest pain. The use of central venous catheters should be avoided. The role of prophylactic anticoagulant therapy is poorly defined and often reserved for very high-risk patients.

NEPHROTIC PATIENT WITH CHEST PAIN
Pulmonary embolism: Chest XRAY, chest CT
Myocardial ischemia: EKG, troponin
Pneumonia: Chest XRAY
Pleural Effusion: Chest XRAY, chest sonography, Chest CT

DISPOSITION

Patients who appear well can be discharged with close follow-up with a pediatric nephrologist. Parents should be instructed to check first morning voids for protein. Parents must be educated to seek medical attention if the child appears ill, is febrile, has abdominal pain (bacterial peritonitis), respiratory symptoms (chest pain, shortness of breath, cough – pneumonia, pleural effusion, pulmonary embolism, myocardial ischemia) or decreased urine output with headache, vomiting or seizure (renal failure).

PHIMOSIS AND PARAPHIMOSIS

INTRODUCTION (ELLEN DUNCAN, MD, PHD, 2/2020)
The foreskin, or prepuce, comprises the redundant skin that protects the urethral meatus and glans penis. Although the foreskin begins to separate from the glans in utero, by birth it has separated completely in only a small percentage of infants. After birth, separation of the foreskin continues through epithelial desquamation. See PEM Guide: GU-Renal: Balanitis, PEM Guide; Trauma: Scrotal and Penile Trauma.

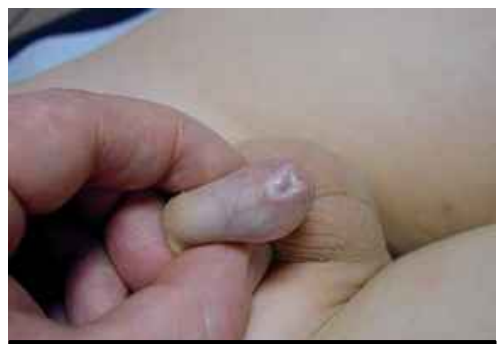
PHIMOSIS

INTRODUCTION
Phimosis is the inability to retract the foreskin. It can be classified as physiologic and pathologic. Physiologic phimosis is found in most newborn males and is due to incomplete separation of the foreskin from the glans. Studies have demonstrated that approximately 50% of 10-year-old and 95-99% of 17-year-old males have fully retractable foreskin. Pathologic phimosis occurs as a result inflammation, infection or trauma that result in scarring which precludes full retraction of the foreskin.

HISTORY
In patients with phimosis, parents may give a history of being unable to fully retract their child's foreskin. It is important to determine whether the child is able to void normally and whether he appears uncomfortable during voiding. Transient ballooning of the foreskin while urinating is normal.

Patients with pathologic phimosis will often have previously retractable foreskin that can no longer be retracted. History may include signs of inflammation from the preputial orifice (discharge, erythema, swelling), painful erections, urinary retention, and recurrent balanoposthitis.

EXAMINATION
On examination in both physiologic and pathologic phimosis, difficulty retracting the foreskin will be observed. Patients with pathologic phimosis will often have a contracted white fibrous ring around the preputial orifice.


PHIMOSIS

MANAGEMENT
Parents should be encouraged to gently wash the penis when giving the child a bath, and to gently retract the foreskin during both baths and diaper changes. They should avoid forceful retraction of the foreskin, which can cause bleeding and scarring.

After the foreskin has been retracted and the glans has been cleaned and dried, the foreskin should be returned to its normal position to avoid paraphimosis. Topical corticosteroids may be used to expedite the retraction process.

Patients with pathologic phimosis should be referred to pediatric urology because of the risk of paraphimosis, urinary tract infections, balanoposthitis, and balanitis xerotica obliterans (an atrophic dermatitis which can lead to scarring and meatal stenosis).

DISPOSITION
Patients with phimosis, either physiologic or pathologic, may be discharged provided that paraphimosis or other complications are not present. Parents should be instructed to wash the penis frequently with water (avoiding the use of harsh irritants) and to avoid forcible retraction. Urology referral is indicated for pathologic phimosis, given the possible complications. A number of foreskin procedures and elective circumcision are possible surgical options.

PARAPHIMOSIS

INTRODUCTION

Paraphimosis occurs when the retracted foreskin becomes entrapped by the coronal sulcus of the glans. Venous and lymphatic congestion of the glans penis results in swelling and inability to release the foreskin. If prolonged, this can cause insufficient arterial supply to the penis with necrosis and gangrene. Urgent intervention is required

PARAPHIMOSIS RISK FACTORS
Trauma
Masturbation
Urethral foreign body
Sexual intercourse,
Infection e.g. severe or recurrent balanitis

PARAPHIMOSIS COMPLICATIONS	
Common	Skin necrosis
Rare	Penile necrosis, glans infarction, gangrene, autoamputation

HISTORY

Patients with paraphimosis will often present with penile swelling or pain. In infants and children, paraphimosis is most often caused by failure to return the foreskin to its normal position after retraction for cleaning or urination. In adolescents, however, paraphimosis may occur after sexual intercourse as well as after cleaning or urination.

DIFFERENTIAL DIAGNOSIS

DIFFERENTIAL DIAGNOSIS	
CONDITION	DISTINGUISHING CHARACTERISTICS
Tourniquet syndrome	Hair or clothing fiber around the penis
Balanoposthitis	Discharge may be present, pain is less common
Insect bites	Asymmetric soft tissue swelling with punctate lesion
Generalized edema	Systemic disease with edema not localized to glans
Angioedema	Painless penile swelling

EXAMINATION

Patient with paraphimosis will usually have swelling and tenderness of the glans penis as well as constriction around the coronal sulcus; the penile shaft will be unaffected. The area should be examined for any object that might be causing constriction, including hair, clothing, rubber bands, piercings, and sexual devices.

PARAPHIMOSIS

MANAGEMENT

The most important step in the management of paraphimosis is the timely reduction of the foreskin in order prevent ischemic complications. Placement of a urinary catheter may be required for urinary obstruction.

PARAPHIMOSIS REDUCTION STEPS	
1	Adequate analgesia: Topical, local, regional, parenteral, procedural sedation
2	Efforts to reduce swelling of the glans and or foreskin (non-invasive vs. invasive)
3	Manual compression or surgical techniques to replace the foreskin over the glans.

UROLOGY CONSULTATION IN THE ED
Urinary Obstruction
Evidence of necrosis
Failed manual reduction

ANALGESIA: Patients should receive adequate pain control, as manual reduction can be quite painful. Effective analgesia can be achieved with topical anesthetics, parenteral analgesics, and regional anesthesia (penile nerve block (see Appendix)). Young children may require procedural sedation.

PAIN CONTROL FOR PARAPHIMOSIS REDUCTION		
TECHNIQUE	ADVANTAGES	DISADVANTAGES
Topical anesthesia: LMX, EMLA[1]	Non-invasive	Can take up to an hour to reach full efficacy.
Local infiltration**:** Lidocaine (No Epinephrine[2])	Rapid onset	Painful, invasive, requires cooperative patient
Dorsal penile nerve block[3]	Full regional anesthesia	Painful, invasive
Oral analgesia	Non-invasive	Efficacy may vary
Parenteral analgesia	Rapid onset	Requires IM or IV administration
Procedural sedation	Analgesia and amnesia: For invasive techniques	Requires significant personnel and resources
1. Contraindicated < 3 months, also G6PD deficiency due to risk of methemoglobinemia 2. Epinephrine should not be used on the penis 3. See appendix		

REDUCTION OF SWELLING: Reduction in swelling facilitates replacement of the foreskin. Several methods may be used to reduce swelling of the glans, foreskin, or both prior to reduction. These include non-invasive and invasive techniques. Invasive techniques require penetration of the glans or foreskin with a needle or an incision made by a scalpel. Invasive techniques have a higher complication rate and are best accomplished in consultation with a urologist.

REDUCTION OF SWELLING TECHNIQUES	
NON-INVASIVE	INVASIVE
Manual compression	Puncture techniques
Compression bandages	Dorsal slit procedure
Application of ice	Glans aspiration
Osmotic agents: Granulated sugar, Gauze soaked with D50 or 20% Mannitol	

MANUAL REDUCTION: Manual reduction with pressure on the glans and simultaneous longitudinal traction on the foreskin is the most commonly used noninvasive reduction technique and associated with the fewest complications. The technique should be preceded by effective analgesia and efforts to reduce swelling as described above.

MANUAL COMPRESSION AND REDUCTION
Circumferential pressure is first applied for several minutes to the distal penis until swelling is lessened.
Water soluble lubricant is then applied to the glans.
Reduction is accomplished by simultaneous applying pressure on the glans, using the thumbs, toward the patient and pulling the foreskin with the second and third fingers over the glans away from the patient.

VIDEO LINK: MANUAL REDUCTION: NEJM (Requires personal or institutional access)

ALTERNATIVE TECHNIQUES: If manual reduction fails, other alternatives include reduction with forceps, puncture techniques to reduce swelling, glans penis aspiration, and dorsal slit reduction. These are beyond the scope of this PEM guide and should be performed by a trained provider and/or in conjunction with a qualified urologic surgeon. Complications of more invasive techniques may include bruising, abrasions, bleeding, infections, scarring, and phimosis

INVASIVE REDUCTION TECHNIQUES
Manual reduction under general anesthesia
The Babcock or Adson clamp technique: Grasp foreskin and pull anteriorly
The dorsal slit procedure: Incision of the constriction band of the foreskin
Puncture techniques: Multiple punctures to foreskin with 25-gauge needle
Hyaluronidase: Hydrolyzes hyaluronic acid; 1 ml of 150 units/ml into the foreskin
Glans aspiration: Tourniquet applied proximally, 3-10 ml of blood aspirated
Urgent circumcision

DISPOSITION

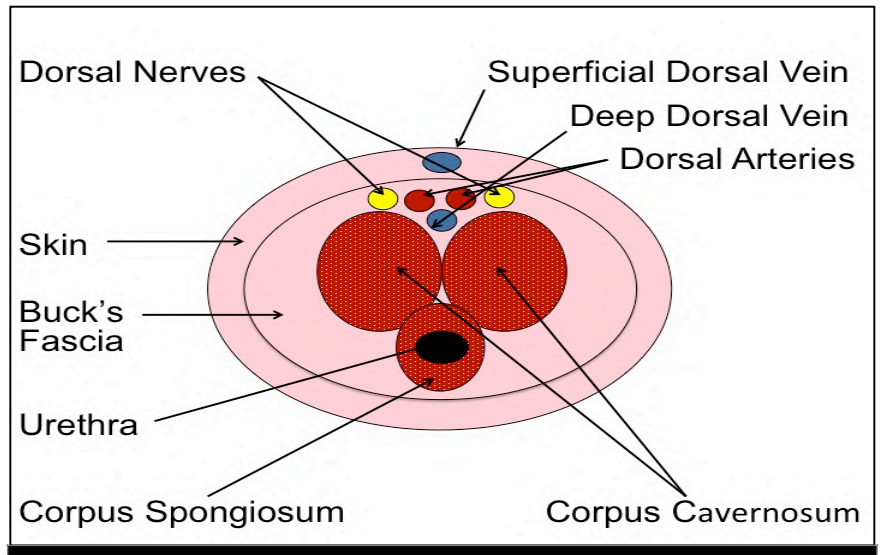
Patients with successfully reduced paraphimosis may be discharged with follow-up with either a primary care provider or a urologist. Patients should be instructed to avoid retraction for one week, as well as to practice proper hygiene, including washing with water and avoiding irritants. Any tears to the foreskin should be treated with topical bacitracin and examined for signs of infection. Patient with paraphimosis related to sexual activity should be instructed to avoid sexual activity for several days.

UROLOGY REFERRAL
Significant trauma during reduction
An invasive reduction technique used
Recurrent paraphimosis
Family prefers an elective circumcision

APPENDIX: DORSAL PENILE NERVE BLOCK

ANATOMY

The penis is innervated by the pudendal nerve (S2-S4). This nerve divides into the right and left dorsal nerves of the penis that pass under the pubis symphysis to travel just below the Buck fascia to supply the sensory innervation to the penis. The penile shaft is composed of 3 erectile columns, the 2 corpora cavernosa and 1 corpus spongiosum. These erectile columns are enveloped by fascial layers, which include nerves, lymphatics, and blood vessels. All are covered by skin.



ANATOMY: CROSS SECTION

INDICATIONS
Dorsal slit procedure for paraphimosis reduction
Paraphimosis Reduction
Repair of penile lacerations
Release of penile skin entrapped in zippers

CONTRAINDICATIONS
Suspected testicular torsion
Skin infection at the site of injection

EQUIPMENT	
1	Antiseptic solution: Povidone-iodine or Chlorhexidine
2	Gauze
3	Sterile drapes
4	Topical anesthetic cream (EMLA or LMX)
5	Local anesthetic: 1% Lidocaine without epinephrine
6	3 or 5 ml syringe
7	16 and 27 gauge needles

PROCEDURE: PATIENT PREPARATION
Obtain informed consent
Parenteral analgesia with or without sedation is recommended
Topical anesthetic cream such as EMLA or LMX is recommended (for 45 minutes)
Apply a generous amount of antiseptic solution to the penis and scrotum
Soak 4 x 4 gauze in antiseptic solution. Clean the glans and shaft of the penis
Create a sterile field with drapes

PROCEDURE: DORSAL PENILE NERVE BLOCK
The right and left dorsal penile nerves are blocked proximally at the base of the penis
Use a 27 gauge needle to raise skin wheals at the 2 o’clock and 10 o'clock positions
Slowly insert the needle through the center of each skin wheal.
Needle is directed toward the center of the shaft, to a depth of about 0.5 cm or until loss of resistance is felt (the needle is within Buck’s fascia)
Aspirate to ensure that the needle is not in a blood vessel
If > 10 kg slowly inject about 2 mL of local anesthetic on each side
If < 10 kg inject 0.2-0.4 mL of 1% Lidocaine using a 30-g needle. Maximum 4.5 mg/kg

COMPLICATIONS
Bleeding: Most bleeding can be easily controlled with direct pressure
Failure to achieve adequate anesthesia
Skin sloughing: More common with distal injections and when epinephrine is used
Infection: Rare. Prophylactic antibiotics are not recommended

POST-INFECTIOUS GLOMERULONEPHRITIS

INTRODUCTION (ELLEN DUNCAN, M.D., PhD., 1/2017)
Post-Infectious Glomerulonephritis (PIGN) can be associated with bacterial, viral, fungal, protozoal, and helminthic infections. The preceding infection may be mild and the time between infection and renal manifestations ranges from days to weeks. Glomerulonephritis generally occurs 1-2 weeks after initial pharyngitis and 3-6 weeks after cutaneous infections.

PATHOGENESIS: POST-INFECTIOUS GLOMERULONEPHRITIS
1. Deposition of bacterial antigens in the glomeruli
2. Production of antibodies that interact *in situ* with the bacterial antigens
3. Circulation of immune complex
4. Deposition in the glomeruli causing immune complex-mediated inflammation

Although this disease is thought to occur mostly in children between the ages of 3 and 12, the epidemiology is changing such that adults are affected in increasing numbers, and the diagnosis should be considered in teens and young adults as well.

CLINICAL MANIFESTATIONS
Disease can vary greatly in severity, from asymptomatic hematuria to florid renal failure and acute nephritic syndrome. Although most patients are asymptomatic, patients may present with periorbital and facial edema, hypertension, and gross hematuria.

Gross or macroscopic hematuria is visible to the naked eye and is characterized by tea-colored or cola-colored urine. Bright red blood in the urine indicates urinary tract bleeding, and is beyond the scope of this chapter.

DIFFERENTIAL DIAGNOSIS: MACROSCOPIC HEMATURIA
Post-infectious glomerulonephritis
Membranoproliferative glomerulonephritis
IgA nephropathy
Henoch-Schonlein purpura
Hemolytic-uremic syndrome
Hematologic causes: Any cause of thrombocytopenia or coagulopathy
Infections: GU tract: pyelonephritis, cystitis
Infections: Non-GU tract: TB, endocarditis
Nephrolithiasis
Sickle cell disease or trait
Malignancy
Trauma

LABORATORY TESTING: In the presence of gross hematuria, microscopy must be performed to assess for the presence of red blood cells. Urine dipsticks are very good for detecting microscopic hematuria (Sensitivity 100%, Specificity 99%). However, false positives can be seen when urine contains hemoglobin, myoglobin, or hypochlorite, with a high specific gravity or in the presence of reducing agents. Glomerular bleeding is characterized by red cell casts and dysmorphic RBCs, although the absence of these does not rule out glomerular disease.

ADDITIONAL TESTING
Comprehensive metabolic panel
Complete blood count
Coagulation profile
Serum C3, C4 levels: ↓ C3, normal C4 in acute phase, normalize 8-10 weeks
Anti-streptolysin O: Elevated. May be normal because many nephritogenic strains are not streptolysin producers and due to non-streptococcal infections
Imaging Studies: Ultrasound, CT scan: Trauma, stones, malignancy
ANCA, ANA for Lupus though may be elevated in severe PIGN
Kidney biopsy is seldom required

MANAGEMENT

There is no specific treatment for PIGN. Volume overload and its associated complications such as hypertension or, less commonly, pulmonary edema should be addressed. This is generally accomplished through water restriction and loop diuretics. If patients develop hypertensive encephalopathy, they require emergent blood pressure control, for example with Nifedipine or Nicardipine (See: PEM Guide: Cardiology: Hypertensive Emergencies). Angiotensin converting enzyme (ACE) inhibitors may cause hyperkalemia and should be avoided. If fluid overload or hypertension is unresponsive to treatment or if the diagnosis is in question, nephrology should be consulted.Patients with recurrent group A streptococcal infection should be treated with antibiotics.

INDICATIONS FOR DIALYSIS
Life-threatening fluid overload refractory to therapy
Hyperkalemia > 6.5
Uremia with BUN 89-100mg/dL

PROGNOSIS

The prognosis for patients with PIGN is generally good, with resolution of hematuria within 3-6 months and slower recovery of proteinuria. If C3 levels do not return to normal by 10 weeks, or if serum creatinine remains elevated or worsens, other causes of hematuria should be considered. Some patients may develop hypertension or renal insufficiency many years or even decades after the initial illness, although these complications are rare.

RENAL STONES

INTRODUCTION: (MICHAEL MOJICA, MD, 9/2019)
Renal stones occur less frequently in pediatrics. However, the pediatric incidence of renal stones has been increasing. There is a paucity of pediatric specific evidence and recommendations for the diagnosis and treatment of renal stones in children are primarily extrapolated from adult data.

The primary goal in the patient with a suspected renal stone is to identify stone related emergencies (infection, obstruction) and exclude important alternative diagnoses. The secondary goal is identifying urolithiasis. Uncomplicated renal stones are almost always managed expectantly.

PATHOPHYSIOLOGY

Nephrolithiasis can be categorized as primary (metabolic) or secondary (urinary tract abnormalities, medical conditions, medications and infections). Children are more likely to have metabolic, genetic and urinary tract abnormalities. These factors increase the likelihood of recurrence and the potential for long-term complications.

Stones form when there is an increase in urinary solute relative to supernatant. This can occur as a result if an increase in solute (e.g. hypercalcuria) or a decrease in supernatant (e.g. dehydration). Stones typically form in the kidney and are propelled into the ureter. Calcium oxalate stones are the most common followed by calcium phosphate and a mix of calcium oxalate and calcium phosphate. Magnesium ammonium phosphate (struvite) stones are the result of a urinary track infection with urea splitting organisms such as Klebsiella, Pseudomonas and Proteus.

CLINICAL MANIFESTATIONS

Severe, colicky, unilateral flank pain is the most common presentation in older children and adolescents. Pain typically originates in the flank and radiates around the abdomen and into the groin. Pain migration follows stone passage through the ureter, bladder and urethra. Stones within the kidney typically do not cause pain. Patients with ureteral colic typically writhe in pain, unable to find a position of comfort. A 2009 case series including 339 pediatric patients (110 with renal stones) found that a history of prior stones, vomiting, and abdominal pain was associated with an increased risk of renal stones on CT (Persaud, Pediatrics 2009, PubMed: 19661055). The presence of fever, dysuria and costovertebral angle tenderness were associated with a decreased risk of renal stones.

Nausea, vomiting and dysuria are common. Approximately one-third of patients present with gross hematuria (with or without abdominal pain). Fever should suggest the possibility of an infected stone. Significant abdominal tenderness is rare. Younger children often have non-specific symptoms including diffuse abdominal pain, vomiting and irritability.

HISTORY	
Symptoms	Pain location/radiation, severity/quality, dysuria, hematuria, fever, vomiting, inguinal/scrotal/pelvic pain, last menstrual period
Medical history	Urinary tract obstruction, vesicoureteral reflux, inflammatory bowel disease, rickets, short gut syndrome, cystic fibrosis, epilepsy, immobilization, bone deformities, recurrent urinary tract infection with urea splitting organisms
Medications	Vitamin D, C, loop diuretics, antiepileptics, antibiotics, steroids, antacids, chemotherapy, carbonic anhydrase inhibitors, uricosurics for gout
Family history	25-75% (though not always genetic in origin)
Diet	Excessive protein intake, ketogenic diet, ↓ fluid intake, ↓ urine output

DIFFERENTIAL DIAGNOSIS
Appendicitis
Cholelithiasis
Ectopic pregnancy
Intussusception
Ovarian torsion
Pelvic inflammatory disease
Renal artery or vein thrombosis
Ruptured ovarian cyst
Testicular torsion
Urinary tract infection: Cystitis, pyelonephritis

LABORATORY EVALUATION

URINE TESTING: The urinalysis is used to support the diagnosis of urolithiasis. Urine should be screened and retrieved stones should sent for analysis. A 24-hour urine collection for: calcium, oxalate, uric acid, citrate, magnesium, phosphorus, sodium and potassium should be initiated in children to identify a potentially modifiable metabolic etiology. A urine culture should be sent on all patients.

URINALYSIS	
Hematuria	70-90% (30-50% gross), absence of hematuria does not exclude stone
Glycosuria, Proteinuria	Tubular dysfunction
pH	> 6 →↑ $CaPO_4$ crystals, > 7 = Urease producing organism
Pyuria	Infection versus inflammation, absence doesn’t exclude UTI
Crystals	Oxalate, Phosphate, Cystine, Xanthine, Dihydroxyadenine

Electrolytes should be sent to assess renal function (creatinine, blood urea nitrogen, potassium, acidosis) as well as potential causes of urolithiasis (calcium, magnesium, phosphorus, uric acid). Additional testing may be indicated based on the serum and urine findings though these seldom direct management in the emergency department. A urine beta HCG should be sent for females of reproductive age.

IMAGING

In adults, imaging can frequency be deferred if the clinical picture is consistent with renal stones, there are no associated signs of complications (fever, intractable pain or vomiting) and a low suspicion of other critical entities in the differential diagnosis. Plain XRAYS are of limited utility due to their low sensitivity and specificity though they are sometimes used to follow stone progression.

NON-CONTRAST CT ABDOMEN/PELVIS: Historically, a non-contrast CT of the abdomen and pelvis has been the study of choice to identify the size and location of a stone as well as signs of obstruction. Hydronephrosis and hydroureter are evidence of obstruction. CT has both a high sensitivity and specificity ((SN: 97%, SP 96%, Smith, AJR Am J Roentgenol. 1996, PubMed ID: 8571915), (SN: 94.1%, SP 94.2%, Pfister, Eur Radiol. 2003, PubMed ID: 12898174).

ULTRASOUND: Ultrasound has been increasing utilized to limit the radiation exposure associated with CT. Ultrasound has a similar ability to identify hydronephrosis though a lesser ability to identify stones when compared to CT. Hydronephrosis on ultrasound is highly predictive of a renal stone on CT though the absence of hydronephrosis does not exclude the presence of a renal stone (Leo, West J Emerg Med. 2017, PubMed ID: 25229916). The absence of hydronephrosis, without other high risk factors, is an indication for expectant management. Ultrasound is the first line study to identify important alternative diagnosis such as cholelithiasis, ovarian torsion, ectopic pregnancy and appendicitis (in pediatric patients).

In a multicenter, clinical trial, 2,759 adults were randomized to radiology ultrasound, point of care ultrasound or CT (Smith-Bindman NEJM 2014, PubMed ID: 25229916). The sensitivity and specificity of the 3 imaging modalities were similar (Range: Sensitivities: 84-86%, Specificity: 50-53%). There was no difference in the rate of missed serious diagnosis, admission to the hospital, unscheduled return visits, average pain score or adverse events. 25% of the patients in the radiology ultrasound group and 40% of the patients in the point of care ultrasound group ultimately received a CT scan.

MANAGEMENT: MEDICAL OBSERVATION

The majority of patients with uncomplicated nephrolithiasis whose pain is adequately controlled can be managed expectantly as outpatients. Spontaneous passage occurs in 30-50% of pediatric renal stones and 40-60% of pediatric ureteral stones. In adults, approximately, 98% of stones less than or equal to 3 mm will pass. The rate of passage decreases as stone size increases: 4 mm (81%), 5 mm (65%), 6 mm (33%) and ≥ 6.5 mm (9%) (Jedenberg, Eur Radiol 2017, PubMed ID: 28593428).

INTRAVENOUS FLUIDS: Traditionally, intravenous fluids have been given to increase renal and ureteral flow in the hope of flushing out the stone. However, there is little evidence to support this practice (Worster, Cochrane Database Syst Rev. 2012, PubMed ID: 22336806). In the patient with an obstructed stone, intravenous fluids may increase ureter spasm and renal colic pain. Fluids may be warranted in the dehydrated patient and antiemetics (e.g. Ondansetron) in the patient who is persistently vomiting.

ANALGESIA: Adult studies have demonstrate that NSAIDS and Acetaminophen are of equal or greater efficacy to narcotics in relieving renal colic pain with fever adverse effects (Pathan, Lancet 2016, PubMed ID: 26993881). The European Association of Urologists recommended NSAIDS as the first line therapy for pain management over opioids (Turk, Eur Urol 2016, PubMed ID: 26318710). Parenteral Ketorolac (Intravenous or Intramuscular) can be used in the patient who cannot tolerate oral medications due to vomiting. Narcotics can be utilized for patients unresponsive to NSAIDS.

MEDICAL EXPULSION THERAPY: $Alpha_1$ antagonists (e.g. Tamsulosin) and calcium channel blockers (e.g. Nifedipine) can relax ureteral smooth muscle, reducing renal colic pain and facilitating stone passage. Passage depends primarily on the stone size and to a lesser degree on the stone location: Small, distal stones will likely pass on their own. Large proximal stones are unlikely to pass with or without medical expulsion therapy.

A Cochrane meta-analysis of high-quality, placebo-controlled trials (5 studies, n = 4,133) suggest that the alpha blockers increase stone clearance (Risk Difference: 6.8%, 95% CI (4.5, 9.8%) (Campschroer, Cochrane Database Syst Rev. 2018, PubMed ID: 29620795). The authors concluded that “for patients with ureteral stones, alpha-blockers likely increase stone clearance but probably also slightly increase the risk of major adverse events. Subgroup analyses suggest that alpha-blockers may be less effective for smaller (5 mm) than for larger stones (> 5 mm).” A meta-analysis of 5 pediatric trials including 406 patients found an increase stone expulsion rate with Tamsulosin for distal ureteral stones (OR 2.70, 95% CI (1.49, 4.91) (Tian, J Pediatr Surg 2017, PubMed ID: 27837990).

INFECTED STONES: Well appearing patients with a suspected infected stone and without evidence of obstruction who are tolerating fluids may be safely discharged with appropriate antibiotics for pyelonephritis and close follow up. All others infected stones should be admitted for parenteral antibiotics. Those with signs and symptoms of sepsis and evidence of obstruction require urgent urology consultation for possible urinary collecting system decompression via a nephrostomy tube or a ureteral stent (Preminger, Nephrolithiasis Guideline Panel. J Urol. 2007, PubMed ID: 17993340).

MANAGEMENT: SURGICAL INTERVENTION

Approximately 20% of pediatric patients with renal stones will require a surgical intervention within 6 months of presentation. Stones greater than 4 mm and with signs of obstruction are less likely to pass without intervention. There has been a shift from open surgical techniques to minimally invasive surgical or endoscopic techniques. However, pediatric appropriate size equipment for these approaches may not be available. An open operative approach is generally only used in those who fail less invasive methodologies.

ADMISSION
Intractable pain
Intractable vomiting
Obstruction: Moderate to Severe (can lead to renal scarring). Controversial
Infected stone: Obstruction, ill appearing or signs of sepsis
History: Single or transplanted kidney, renal insufficiency

Urology should be consulted for patients with large stones with significant obstruction with or without signs of infection to assess the need for acute surgical decompression. Ureteral stents and nephrostomy tubes are equal efficacious.

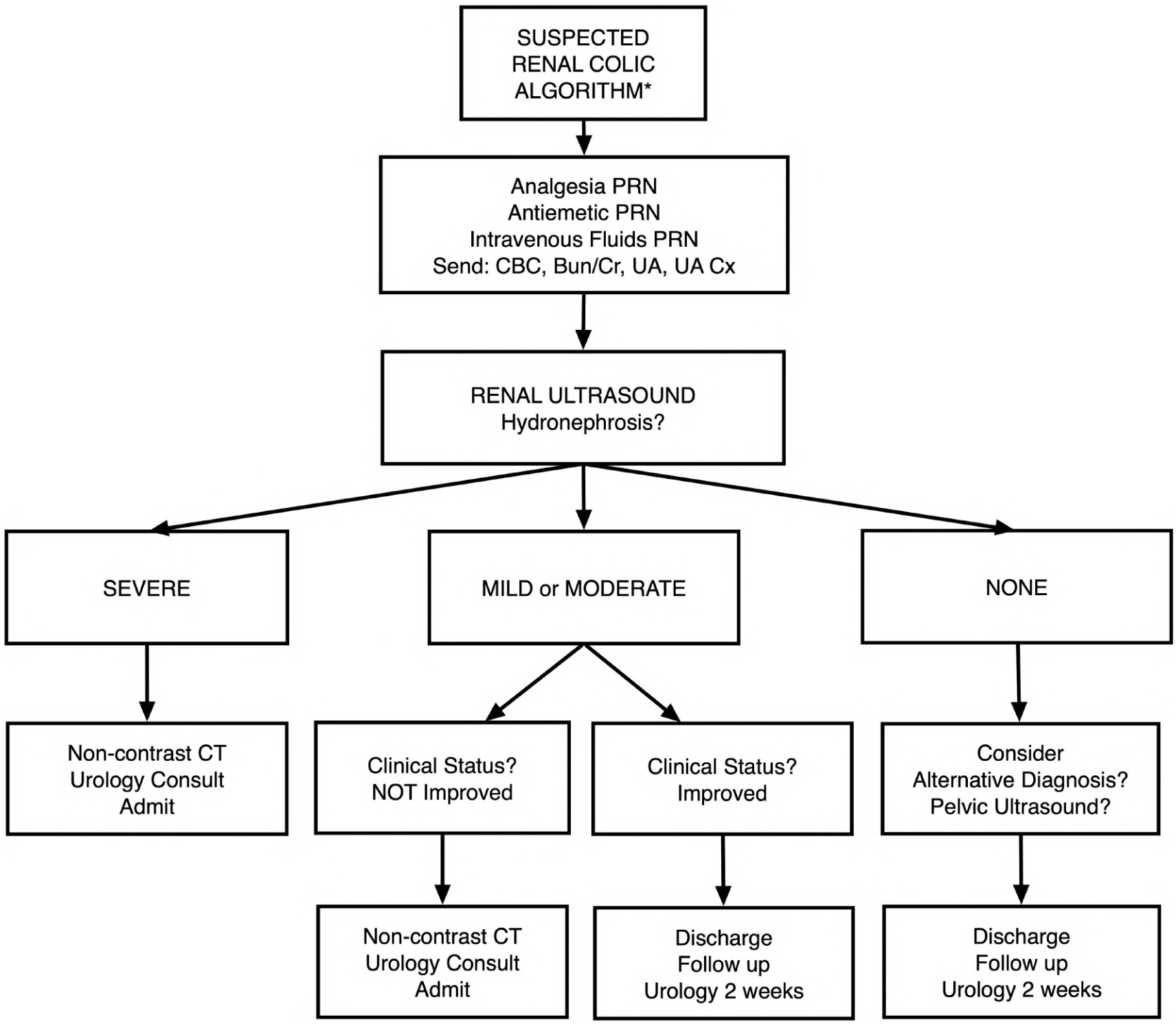
DISPOSITION

The majority of patients who are tolerating fluids can be managed as outpatients with adequate analgesia. Follow up with a pediatric nephrologist and/or urologist is essential.

Most consider a 2 week trial of expectant management before considering surgical options. Increased fluid intake limits urinary supersaturation of precipitants. Discontinue or wean medications associated with kidney stones. Specific dietary and pharmacologic interventions may be initiated when stone composition is known.

SURGICAL OPTIONS	
Small stones	Extracorporeal shock wave lithotripsy
	Ureteroscopy with lithotripsy or stone extraction
Large stones	Percutaneous nephrolithotomy
	Minimally invasive or open pyelolithotomy

APPENDIX: RENAL STONE DECISION ALGORITHM



*Use of the algorithm presumes that:
1. The degree of hydronephrosis correlates with stone size
2. There is no suspicion of an infected stone
3. The patient has normal baseline renal function
4. The patient has no significant co-morbidities

SCROTAL PAIN

INTRODUCTION (CARRIE DANZIGER, M.D. 12/2021)
Children and adolescents presenting to the emergency department with scrotal pain must be evaluated promptly. The most common causes of non-traumatic, scrotal pain are testicular torsion, torsion of the appendix testis, torsion of the appendix epididymis (embryologic remnants), epididymitis and epididymo-orchitis. Fournier's gangrene is a rare but life-threatening necrotizing fasciitis of the perineal, genital and perianal regions that requires urgent surgical intervention.

TESTICULAR TORSION: Testicular torsion occurs due to an embryologic defect in the attachment of the testes to the scrotal wall called a bell-clapper deformity. This allows the testicle to rotate (typically medially) causing torsion of the spermatic cord and decreased blood flow. Testicular torsion can quickly result in loss of the testis. The likelihood of salvaging the testis decreases with the duration of the torsion.

EPIDIDYMITIS: Epididymitis signifies inflammation of the epididymis. Epididymo-orchitis refers to inflammation of both the epididymis and testis. Typically, there is a gradual onset of scrotal pain localized to the epididymis that may then spread to the testes and scrotal wall. The etiology of epididymitis varies with age. Epididymitis is less common in the prepubertal age group. It is thought to be due to reflux of urine into the ejaculatory ducts. The urine may be sterile or infected. In adolescents, it is most commonly due to sexually transmitted infections. Infections with Gonorrhea and Chlamydia are most common. Men who have anal insertive intercourse are also at risk of infection with enteric organisms.

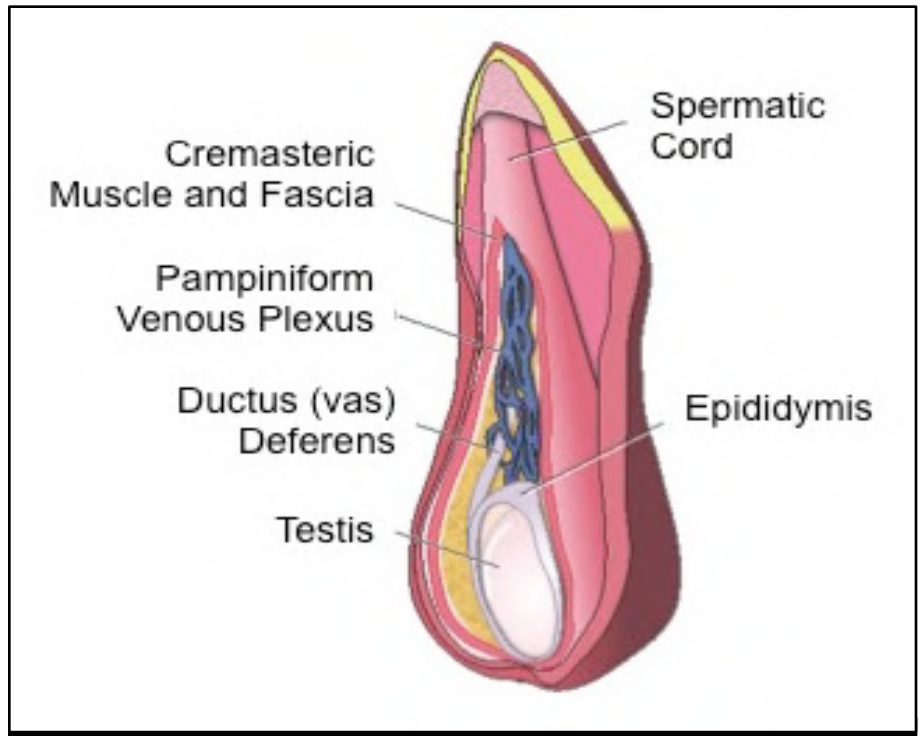
DIFFERENTIAL DIAGNOSIS
The differential diagnosis of scrotal pain also includes trauma, Henoch-Schonlein Purpura (HSP) orchitis, viral orchitis (e.g. mumps) and referred pain from an abdominal source (i.e. retrocecal appendicitis, renal stone, inguinal hernia). A detailed history and physical exam can help narrow the differential and often establish a diagnosis. (See PEM Guide: Scrotal and Penile Trauma).

HISTORY

KEY COMPONENTS OF THE HISTORY
Onset and severity of pain
Prior occurrence of pain (suggestive of intermittent torsion and detorsion)
History of trauma (presence of trauma doesn't rule out other causes of scrotal pain)
Presence or absence of swelling, erythema
Sexual activity, and use of condoms
Presence or absence of urethral discharge
Urinary tract symptoms: Dysuria, urgency, frequency, hematuria

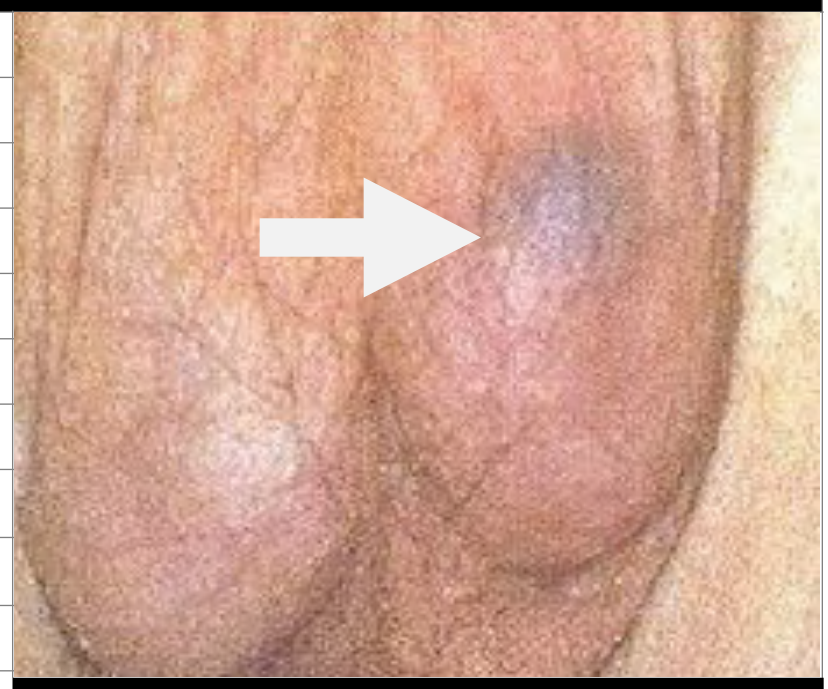
PHYSICAL EXAMINATION

Physical exam should include inspection and palpation of the abdomen, testis, epididymis, scrotum and inguinal region. The genital exam is best when performed in the standing position.



SCROTAL ANATOMY

PHYSICAL EXAMINATION FINDINGS
Position of the testicle
High riding (torsion) or low riding
Transverse lie (torsion) or vertical lie
Swelling and/or erythema, asymmetry
Location of tenderness
Diffuse or localized
Epididymis or testes
Cremasteric reflex[1]
Prehn's sign[2]
Inguinal Hernia
Hydrocele
Blue dot sign (testicular appendage torsion)



BLUE DOT SIGN

1. A normal cremasteric reflex is assessed by stroking the upper thigh and observing a cremasteric contraction with elevation of the ipsilateral testis. It is often absent in testicular torsion (because the testicle is already elevated).
2. Prehn's sign is the relief of pain (epididymitis) or exacerbation of pain (testicular torsion) when the scrotal contents are raised. It is not considered reliable in children

DIAGNOSTIC TESTING

LABORATORY: Urinalysis can help in evaluation of patients with an acute scrotum. Pyuria with or without bacteria is suggestive of infection and is consistent with an epididymitis, a urinary tract infection (cystitis or pyelonephritis) and urethritis. Hematuria without signs of infection is seen is patients with renal stones. Urine amplification test for Gonorrhea and Chlamydia, HIV and syphilis testing should be sent in sexually active males.

IMAGING: If the diagnosis of torsion can be made clinically, and obtaining ultrasound will cause a delay, the patient should go directly for surgical exploration. Color Doppler ultrasound should be obtained in all patients with scrotal pain if torsion cannot be excluded clinically. The sensitivity and specificity of Color Doppler for testicular torsion ranges from 70-100% and 77-100% respectively.

DECISION RULE: A clinical decision rule was derived with the aim of identifying pediatric patients at low risk for testicular torsion (Barbosa, J Urology 2013, PubMed ID: 23103800). The TWIST Rule (Testicular Workup for Ischemia and Suspected Torsion) included 338 pediatric patients of which 51 (15%) had testicular torsion. The rule was able to identify those at low risk of testicular torsion. A score of ≤ 2 had a predictive value of a negative rule of 100%, 95% CI (98-100%) with an area under the receiver operating characteristic curve was 0.98, 95% CI (97-99). The rule has the potential to reduce ultrasound utilization by 80%. There are a number of limitations. There is not an accurate description of the study population. Those assessing the presence of the rule parameters were urologists and some of the clinical predictors were subjective with only moderate inter-rater reliability between urologists and non-urologists.

The rule was assessed using pediatric emergency medicine providers in a population of 258 patients of which 19 (7.4%) had testicular torsion (Frohlich, Acad EM 2017, PubMed ID: 28833896). In this prospective validation, 5 of the 19 patients (26%) with testicular torsion would have been considered low risk by a score of 2 or lower. The area under the receiver operating characteristic was 0.82, 95% CI (0.71, 0.94) and inter-rater reliability for the score was poor (kappa 0.39, 95% CI (0.22, 0.46). The kappa for “hard testicle” was 0.25, 95% CI (-0.20, 0.69) and this predictor had the highest predictive ability of all of the rule components in the regression analysis (Odds ratio 10.86, 95% CI (3.80, 31.04).

TWIST RULE FOR TESTICULAR TORSION			
PARAMETER	POINTS	RISK	MANAGEMENT
Testicular swelling	2	Low: Score ≤ 2	No ultrasound
Hard testis on palpation	2	Intermediate: Score 3-4	Ultrasound
Nausea or emesis	1	High: Score ≥ 5	OR without ultrasound
High riding testis	1		
Absent cremasteric reflex	1		

MANAGEMENT

TESTICULAR TORSION: Urology should be consulted early in the course of suspected torsion for surgical detorsion and orchiopexy. Manual detorsion can be accomplished with external (lateral) rotation of the affected testicle (as the testicle typically twists medially) if operative repair is not readily available.

TESTE VIABILITY	
With 4-6 hours	100%
> 12 hours	20%
> 24 hours	0%

TORSION OF APPENDIX TESTIS OR APPENDIX EPIDIDYMIS: The appendix testicle is typically located at the upper, lateral border of the testicle. Treatment is supportive and may include analgesia, bed rest, and scrotal support. Pain may persist for 5-10 days. Surgical intervention may be an option for patients with persistent, severe pain.

EPIDIDYMITIS/EPIDIDYMO-ORCHITIS: Symptoms typically improve within a few days but can persist for weeks. Supportive care includes non-steroidal anti-inflammatory agents, scrotal support and ice packs as tolerated.

Males who are not sexually active should be tested for a urinary tract infection. If the urinalysis is suggestive of a UTI then they should be treated with appropriate antibiotics based on local sensitivities. This most typically includes a 2nd or 3rd generation cephalosporin for E Coli infection. If the urinalysis does not demonstrate evidence of infection than treatment is supportive. Avoidance of holding urine and treatment of constipation may also be required.

CDC recommendations for the treatment for epididymitis in the sexually active patient are included below. Treatment of the sexual partner should also be discussed with the patient.

EPIDIDYMITIS LIKELY DUE TO AN STI (CDC 2021)
Ceftriaxone 500 mg IM in a single dose (1 gram if > 150 kg) AND
Doxycycline 100 mg PO BID for 10 days OR
Levofloxacin 500 mg PO QD x 10 days (for men who practice insertive anal sex)

Patients with chronic epididymitis or recurrent epididymitis, should follow-up with urology and be evaluated for urinary tract abnormalities.

APPENDIX: DIFFERENTIAL DIAGNOSIS SUMMARY

	TESTICULAR TORSION	TORSION OF APPENDIX TESTIS APPENDIX EPIDIDYMIS	EPIDIDYMITIS EPIDIDYMO-ORCHITIS
Onset	Acute (<12 hours)	Acute to subacute	Subacute
Age	Early puberty	Prepubertal	Adolescence
Tenderness	Diffuse, Severe	Localized to appendix testis, Less severe	Epididymal, Severity varies
Cremasteric	Absent	Present	Present
Prehn’s Sign	Absent	Absent	Present
Other	High riding, transverse lie	Blue dot sign	Urinary symptoms, urethral discharge
Urinalysis	Negative	Negative	Positive or Negative
Doppler Ultrasound	Decreased testicular perfusion	Area of low echogenicity, normal or increased flow	Increased flow to epididymis
Treatment	Surgery Manual detorsion	Bed rest, Analgesia	Antibiotics

URINARY TRACT INFECTION

INTRODUCTION (ADRIANA MANIKIAN, M.D. 1/2023)
Urinary tract infection is the most common serious bacterial infection (SBI) in febrile infants and young children under 2 years of age without an apparent source of fever. The overall incidence of UTI in febrile children less than 2 years of age is approximately 7%. 60% of these patients have evidence of pyelonephritis on renal scans and are at risk for subsequent renal scarring (Hoberman. Pediatrics 1999, PubMed ID: 10390264). (See: PEM Guide: Infections: Febrile Neonate for a review of UTI in patients less than 2 months of age).

DIAGNOSTIC TESTING

URINALYSIS: Young infants may lack pyuria due to a blunted inflammatory response. In addition, high urine flow rates reduce the time for production of nitrites from dietary nitrates (and not all uropathogens produce nitrites). Therefore, the absence of pyuria or nitrites does not exclude UTI in young infants. Bag urine specimens have high contamination rates (up to 85% false positives) and should not be used for culture. If a bag specimen is used for screening UA, then a catheterized or suprapubic aspiration specimen should be sent for a urine culture for children less than 2 years of age. A UA is considered positive in the presence of (+) leukocyte esterase, (+) nitrites, (+) bacteria and/or pyuria (>5 WBC/hpf or 10 WBC/L^2 (enhanced UA using a hemocytometer)).

URINE CULTURE: Diagnosis of UTI requires both a UA suggestive of infection and growth of a single uropathogen obtained by catheterization or suprapubic aspiration (SPA_ in those less than two years of age. Success rate of SPA and catheterization are dependent on urine volume in the bladder. Ultrasound guidance has demonstrated increased catheterization success rates (Witt, Academic EM 2015, PubMed ID: 15805331). A midstream UA or catheterization can be sent for those greater than two years of age.

UTI DIAGNOSIS: CULTURE RESULTS		
Age	Suspicious for UTI[1]	Confirmed UTI[1]
Birth-2 mo[3]	≥ 10,000 CFU/ml +/- Pyuria[2]	≥ 50,000 CFU/ml + Pyuria[2]
2-24 mo[3]	≥ 10,000 CFU/ml + Pyuria[2]	≥ 50,000 CFU/ml + Pyuria[2]
> 24 mo[4]		50,000 CFU/ml + Pyuria[2] (catheter) 100,000 CFU/ml + Pyuria[2] (midstream)
1. Of a single uropathogen 2. Pyuria: ≥ 5 WBC/hpf or ≥ 10 WBC/L^2 (enhanced UA using a hemocytometer) 3. Catheterized or suprapubic aspiration specimen for culture 4. Catheterized or midstream specimen for culture		
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BLOOD CULTURE: UTI and coincident bacteremia have been reported at rates between 4-9%. Several studies have demonstrated that bacteremia associated with UTI is most likely in the youngest infants, particularly in those less than 6 months of age with the highest incidence in those less than 2-3 months of age. Clinical parameters such as appearance, irritability, crying, vomiting, height or duration of fever as well as acute phase reactants such as WBC, ESR and CRP do not reliably distinguish bacteremic from non-bacteremic infants. There is no significant difference in short-term and long-term outcomes of bacteremia with UTI with the exception of prolonged fever. Therefore, obtaining blood culture doesn't appear to have a significant impact on the management of these children, although it may be prudent to obtain a blood culture in infants less than 6 months of age

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WBC, ESR, CRP: Sixty percent of young febrile children with UTI will have evidence of pyelonephritis on DMSA renal scan (Hoberman. Pediatrics 1999, PubMed ID: 10390264). In general, WBC, ESR and CRP are likely to be elevated with pyelonephritis though normal values do not exclude pyelonephritis. As mentioned previously, these tests are also poor discriminators of bacteremia. Recently, procalcitonin has been shown to indicate renal parenchymal involvement and vesicourinary reflux. Its role in the diagnosis and management of UTI has yet to be determined.

ELECTROLYTES: There is no evidence to support or refute the need to obtain a basic metabolic profile. It may be useful to check electrolytes and renal function in children with protracted vomiting and dehydration, ill or septic appearing patients, in infants less than 2-3 months of age and in those with known abnormality of the urinary tract.

LUMBAR PUNCTURE: Meningitis in infants with UTI is rare. In a retrospective study of 354 children less than 2 years of age with UTI, lumbar puncture was performed in 70%. 4% (14/354) had CSF pleocytosis and of these, 1% (4/354) had a positive CSF culture. All patients with a positive CSF culture were less than 1 month of age (Bachur, Pediatric Emerg Care 1995, PubMed ID: 8570449).

COINCIDENCE OF VIRAL INFECTIONS: The presence of a documented viral infection with RSV, influenza, parainfluenza, enteroviruses and other viruses lowers but does not eliminate the risk of UTI. Febrile infants less than 2 months of age with clinical bronchiolitis irrespective of RSV status had a UTI rate at 6.5% (Levine, Pediatrics 2004, PubMed ID: 15173498). Febrile children greater than 2 months of age with bronchiolitis have very low incidence of UTI or bacteremia. 2% of febrile children 2 months-2 years of age with bronchiolitis had UTI, while 12% of those without bronchiolitis had positive urine culture (Kupperman, Arch Dis Adolesc Med 1997, PubMed ID: 9412595).

RISK STRATIFICATION

Shaikh derived and internally validated a number of models to clinically predict the risk of UTI in febrile children less than 2 years of age (Shaikh, JAMA Pediatrics 2018, PubMed ID: 29710324). The models were derived based on the those with a greater than 2% risk require urine testing and if the urinalysis indicates a UTI risk of greater than 5% required empiric antibiotic coverage pending the results of the urine culture.

The clinical model alone had the lowest area under the receiver operating characteristic curve (AUC) and a significantly lower specificity than any of the laboratory models. However, it had a 95% sensitivity in identifying those with a UTI risk of greater than 2%. Each of the laboratory models (which include the clinical model) had a higher area AUC, equivalent sensitivities and higher specificities than the clinical model alone.

The UTI Calc model was tested in a hypothetical cohort of 1,000 febrile children less than 2 years of age with a 7% UTI rate. Compared to the AAP UTI algorithm, UTI Calc would reduce the need for urine sampling by 8.1%, 95% CI (4.2, 12.0%) and reduced the number of missed patients from 3 to 0.

UTI CALC: MODEL TEST CHARACTERISTICS

Model	Derivation AUC (95% CI)	Validation AUC (95% CI)	Derivation		Validation	
			SN	SP	SN	SP
Clinical	0.80 (0.77, 0.82)	0.81 (0.72, 0.89)	95%	35%	100%	34%
Dipstick LE or Nit	0.97 (0.96, 0.98)	0.99 (0.98, >0.99)	95%	92%	96%	95%
Dipstick + Gram	0.98 (0.97, 0.99)	0.99 (0.98, >0.99)	96%	92%	100%	92%
Hemocytometer	0.97 (0.96, 0.98)	0.99 (0.98, >0.99)	93%	91%	100%	95%
Enhance UA	0.98 (0.98, 0.99)	0.99 (0.98, >0.99)	96%	93%	96%	93%

UTI CALC: CLINICAL MODEL RISK FACTORS	
Age < 12 months	*Other fever source can include (but is not limited to): acute otitis media, upper respiratory tract infection (i.e., any cough or congestion), gastroenteritis, pneumonia, meningitis, bronchiolitis, and viral syndrome
Temperature ≥ 39 C (102.2 F)	
History of UTI	
Female or uncircumcised male	
No other fever source*	
Duration of fever ≥ 48 hours	WEB LINK: UTI RISK CALCULATOR

MANAGEMENT

Approximately 90% of pediatric UTI's are caused by E. coli. Additional uropathogens include: Klebsiella, Proteus, Enterobacter, Pseudomonas, Enterococcus, Staph. aureus, and group B streptococcus. Initial empiric antibiotic treatment is chosen to provide coverage for E coli. Previous cultures, when available, should guide antibiotic selection. Further therapy should be guides by the urine culture (organism and sensitivities).

If a screening urinalysis is positive, empiric antibiotics should be started. Those with negative urinalysis can be followed clinically until urine culture result is available. The choice of initial empiric antibiotic treatment depends on the local sensitivities of E. coli as well as the clinical condition of the patient. In the recent years, resistance to commonly used antibiotics has dramatically increased. It appears that the best empiric antibiotic choice is a 3rd generation oral or intravenous cephalosporin. Agents such as Nitrofurantoin which are secreted in the urine but do not achieve therapeutic concentrations in the blood should not be used to treat infants with febrile UTI who predominantly have pyelonephritis and not cystitis. See Appendix: Empiric Antibiotic Selection.

DISPOSITION

In the past, the standard of care for children with UTI was hospitalization for intravenous antibiotics for 3-7 days or until 24 hours after defervescence, followed by oral antibiotics to complete a 14 days course. A large, well designed, randomized clinical trial for treatment of children 1 months - 2 years of age with UTI, compared an oral 3rd generation cephalosporin (Cefixime) for 14 days and parenteral 3rd generation cephalosporin (Cefotaxime) for 3 days or until defervescence followed by oral Cefixime to complete 14 days (Hoberman, Pediatrics 1999, PubMed ID: 10390264). Both short-term (time to defervescence, sterilization of urine at 24 hours) and long-term outcomes (recurrent UTI, renal scarring on DMSA scan at 1 month and 6 months) were comparable in the two groups. Outpatient treatment of well-appearing infants and young children with UTI appears to be a viable option. However, less than 0.5% of patients were 4-7 weeks of age and the proportion of patients less than 3 months of age could not be determined from the data presented.

ADMISSION CRITERIA
Ill or septic appearing child
Age < 1 month
Age 1-2 month and not low risk for adverse events
Dehydration
Inability to tolerate oral liquids
Compliance concerns or other social factors
Oral antibiotic treatment failure at 48 hours
Clinical deterioration after initial discharge

Children should follow up with their primary care provider within 24-48 hours. If still febrile or without clinical improvement the child should be admitted for parenteral antibiotics. A renal ultrasound should be obtained to identify hydronephrosis, obstruction and renal or perinephric abscess. After an initial febrile UTI parents should be advised to seek prompt medical evaluation (within 48 hours) of future febrile illnesses.

RADIOGRAPHIC EVALUATION

The AAP recommends that all children less than 2 years of age undergo radiographic evaluation with renal and bladder sonography to detect hydronephrosis and other urinary tract anomalies following the first episode of UTI. Those with severe illness or are unresponsive to therapy should undergo ultrasonography within 2 days to identify renal or perinephric abscess.

For well infants who are responding to therapy, the timing of ultrasonography is not specified. There is evidence that demonstrates changes related to the acute infection that might not represent baseline and that sonography should be deferred until resolution of the acute infection. Approximately 15% of ultrasounds will demonstrate abnormalities with 1-2% requiring intervention (VCUG, urology consult, surgery).

For patients over 2 years of age, a CT scan may be obtained to exclude a perinephric abscess in patients with pyelonephritis and persistent fever despite appropriate antibiotics.

IMAGING RECOMMENDATIONS		
AGE	ULTRASOUND	VCUG
Birth-1month	With 1st UTI	After Antibiotics Completed[1]
1-2 months	With 1st UTI	After Antibiotics Completed[1]
3-24 months	With 2nd or worsening UTI	After 2nd UTI, abnormal US
>24 months-Puberty	Worsening UTI (48 hrs ABx)	After 2nd UTI, abnormal US[2]
Adolescents	Worsening UTI (48 hrs ABx)	NA[2]

1. Place on prophylactic antibiotics after treatment course pending VCUG
2. Consider CT to identify a perinephric abscess
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PROPHYLACTIC ANTIBIOTICS

Evidence suggests that prophylactic antibiotics reduce the risk of recurrent but not reduce the risk of later renal scarring at the cost of increasing the risk of multi-drug resistant organisms. Prophylactic antibiotics are indicated in infants less than 3 months of age with any grade vesicoureteral reflux (VUR) and for older children with grade V VUR. Circumcision should be discussed with parents of uncircumcised boys with recurrent UTI. Common antibiotics choices include: Amoxicillin, cephalexin, trimethoprim sulfamethoxazole (not in < 2 months due to risk of kernicterus) and nitrofurantoin (not in < 1 months due to risk of hemolytic anemia).

APPENDIX: EMPIRIC ANTIBIOTIC SELECTION

EMPIRIC ANTIBIOTIC SELECTION FOR UTI BY AGE		
AGE	INITIAL ANTIBIOTICS	DURATION
Birth-28 days	IV: Ceftazidime AND Ampicillin	Total 10-14 days (IV → PO)[1]
	PO: Cefdinir AND Amoxicillin	Total 10-14 days (IV → PO)[1]
1-2 months	IV: Ceftriaxone AND Ampicillin (Total Bilirubin ≤ 12)	Total 10-14 days (IV → PO)[1]
	IV: Ceftazidime AND Ampicillin (Total Bilirubin > 12)	Total 10-14 days (IV → PO)[1]
	PO: Cefdinir AND Amoxicillin	7-10 days
2-23 months	IV[3]: Ceftriaxone AND Ampicillin	Total 7-10 days (IV → PO)[2]
	IV[4]: Cefazolin AND Ampicillin	Total 7-10 days (IV → PO)[2]
	PO: Cefdinir OR Cephalexin +/- Amoxicillin[a] (No IV Criteria)	7-10 days
> 24 months-Adolescent	IV[3,]: Ceftriaxone AND Ampicillin	Total 7-10 days (IV → PO)[2]
	IV[4]: Cefazolin AND Ampicillin	Total 7-10 days (IV → PO)[2]
	PO[5]: Nitrofurantoin	7-10 days
	PO[6]: Tablet: Cephalexin OR Cefuroxime +/- Amoxicillin[a]	7-10 days
	PO[6]: Liquid: Cephalexin OR Cefdinir +/- Amoxicillin[a]	7-10 days
Adolescent	IV[3]: Ceftriaxone AND Ampicillin	Total 7 days (IV → PO)[2]
	IV[4]: Cephazolin +/- Ampicillin[a]	Total 7 days (IV → PO)[2]
	PO[5]: Nitrofurantoin	5 days
	PO[6]: Cephalexin OR Cefuroxime +/- Amoxicillin[a]	10-14 days
Severe Penicillin Allergy: Urticaria, anaphylaxis, angioedema, respiratory distress. a. Substitute Levofloxacin for cephalosporin b. Substitute Vancomycin OR Linezolid for Amoxicillin/Clavulanate for enterococcus coverage Non-Severe Penicillin Allergy: Rash only a. Cephalosporins (with the exception of Cephalexin) may still be used b. Substitute Vancomycin OR Linezolid for Amoxicillin/Clavulanate for enterococcus coverage		
a. Enterococcus: Coverage Indications: Add Ampicillin if prior history of enterococcus, urinary catheter or stent in place, recent urinary tract instrumentation, anatomic abnormality		
1. Transition to oral when clinically well, tolerating PO, afebrile ≥ 24 hours, culture/sensitivities resulted 2. Transition to oral when clinically well, tolerating PO, afebrile ≥ 24 hours 3. Indication IV therapy: Septic/Ill appearing, failed PO antibiotics > 48 hours 4. Indication IV therapy: Well appearing, no prior antibiotics, unable to take PO 5. Indication PO therapy: Uncomplicated UTI AND able to swallow whole capsules 6. Indication PO therapy: Complicated UTI/pyelonephritis OR unable to swallow whole capsules		
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HEAD AND NECK INFECTIONS

1. Conjunctivitis	Elise Perlman, MD
2. Mastoiditis	Evan Yanni, MD
3. Otitis Externa	Roshni Patel, MD
4. Otitis Media	Deborah Levine, MD
5. Periorbital and Orbital Cellulitis	Alvira Shah, MD
6. Peritonsillar Abscess	Ellen Duncan, MD, PhD
7. Pharyngitis	Micheal Tunik, MD
8. Retropharyngeal Abscess	Michael Mojica, MD
9. Sinusitis	Brent Rogers, MD
10. Upper Respiratory Infection	Marc Auerbach, M.D. MSc

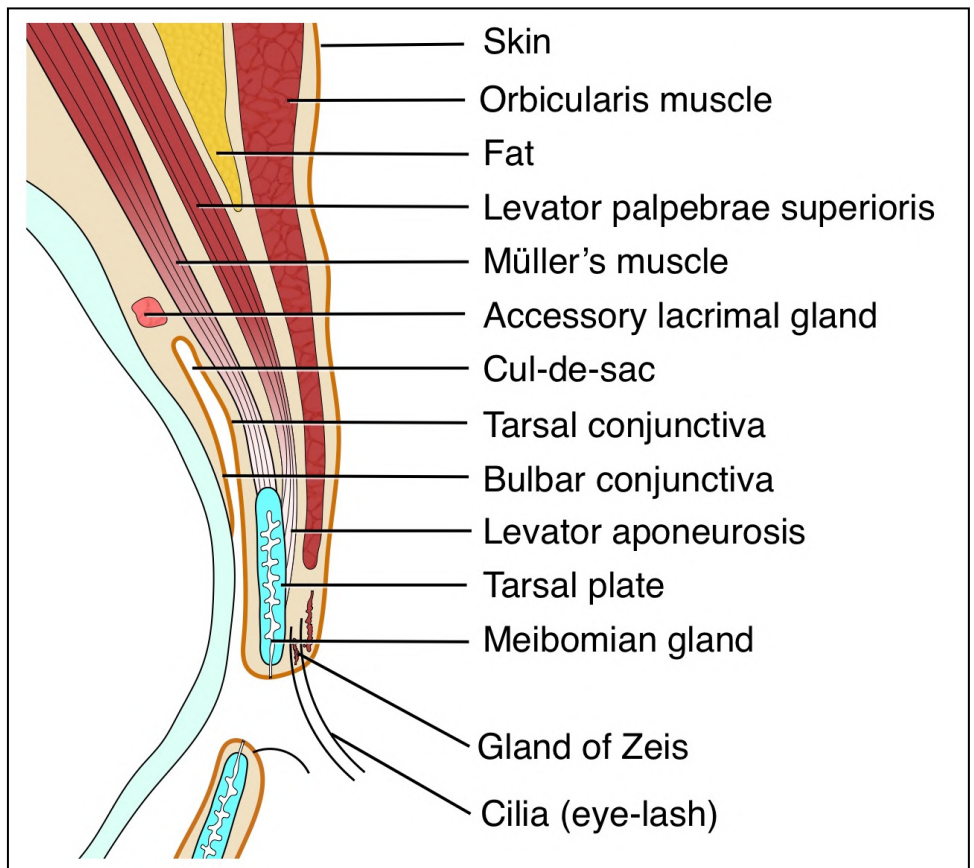
CONJUNCTIVITIS

INTRODUCTION (ELISE PERLMAN, MD. 2/2018)
Conjunctivitis is defined as inflammation or infection of the conjunctiva. In pediatric patients, acute conjunctivitis is usually benign and self-limited or can be easily treated. Causes can be categorized as infectious (viral vs. bacterial) and non-infectious (allergic vs non-allergic). Viral conjunctivitis is more common in adults and school aged children while bacterial conjunctivitis is more common in neonates and infants. The focus of this PEM Guide is on acute infectious conjunctivitis.

ANATOMY

Conjunctiva are the mucus membranes that line the inside surface of the eye lids (tarsal or palpebral conjunctiva) and cover the surface of the globe (bulbar conjunctiva) up to the limbus (the junction of the sclera and the cornea). The conjunctiva are usually transparent, but when inflamed, the vessels dilate, resulting in hyperemia and edema such that they can appear diffusely pink or red. Inflammation of the posterior conjunctival vessels results in diffuse palpebral and bulbar conjunctival injection. Ciliary flush, a ring-shaped erythema at the limbus, is suggestive of keratitis, iritis, or angle closure.

The eyelids contain loose connective tissue and may become swollen with conjunctivitis. The eyelid swelling of conjunctivitis is typically soft and non-tender in contrast to the indurated, warm and tender eyelid swelling that can occur in periorbital and orbital cellulitis (See: PEM Guide: Infections: Periorbital and Orbital Cellulitis).



EYELID ANATOMY

CLINICAL ASSESSMENT

Clinical assessment involves a focused ophthalmologic history and examination as well as an assessment of systemic signs and symptoms. The focus of assessment is determining if infection is limited to the conjunctiva or extends to the cornea and below.

Keratitis is inflammation/infection of the epithelial layer of the cornea. Keratitis can lead to corneal perforation and is sight threatening. Patients at high risk of keratitis include those with contact lenses and those with herpes simplex virus infection. These patients may complain of moderate to severe eye pain, a marked foreign body sensation, photophobia and a decrease in visual acuity. The cornea may appear hazy but pupillary response is preserved in the absence of anterior uveitis. Suspicion of keratitis warrants on ophthalmology consultation. Fluorescein staining, slit lamp examination, ophthalmoscopy, and/or intraocular pressure measurement may be helpful. If there is normal vision and no suspicion of keratitis, iritis or open angle glaucoma (severe headache, nausea), then the focus becomes identifying the etiology of conjunctivitis so that appropriate treatment can be initiated. Patients symptoms and exam findings do not reliably distinguish between viral, bacterial and allergic conjunctivitis.

FOCUSED OPHTHALMOLOGIC ASSESSMENT	
HISTORY	EXAM
Time course	Pupillary reaction to light
Change in visual acuity	Discharge, quality and quantity
Sensation: Pain, foreign body, itching	Unilateral vs Bilateral
Discharge: Quality, quantity	Pattern of redness
Photophobia	Corneal lesions on Fluorescein exam
Trauma	Proptosis, extraocular muscle movements
Contact lens use	Preauricular adenopathy
Ill contacts	Conjunctiva texture e.g. Follicular
Associated systemic symptoms	Visual acuity

VIRAL CONJUNCTIVITIS

Viral conjunctivitis is spread by secretions acquired through direct contact or contact with a contaminated surface. It is highly contagious with an estimated communicability of 10-14 days. Viral conjunctivitis usually begins with unilateral conjunctival injection and a watery discharge with bilateral involvement within 24-48 hours. Patients may also have concurrent URI symptoms or exposure to a sick contact. Patients will often complain of a burning or sandy feeling in one or both eyes. Exam may reveal a follicular appearance on the tarsal conjunctiva and possibly lymphadenopathy. Clinical course follows that of an upper respiratory infection with gradual resolution over several days.

Adenovirus infection is responsible for more than half of viral conjunctivitis. The combination of sudden onset of high fever, non-exudative pharyngitis, bilateral conjunctivitis and preauricular lymph node swelling is characteristic of “pharyngoconjunctival fever” due to adenovirus. Adenovirus epidemic keratoconjunctivitis involves the epithelial layer of the cornea (keratitis). Patient may present with a severe foreign body sensation and photophobia limiting the ability to open the eye. Suspicion of keratitis warrants an ophthalmology consultation.

Viral conjunctivitis is self-limited, and treatment is limited to supportive care. Treatment may include warm compresses, ocular lubricant drops (e.g. artificial tears) and possibly topical antihistamines for symptomatic relief. Topical antibiotics are not indicated. The use of topical antibiotics in a patient with viral conjunctivitis exposes the patient to the risk of antibiotics without an associated benefit. However, some caregivers choose to treat viral conjunctivitis because clinical distinction between viral and bacterial conjunctivitis is unreliable and treatment facilitates return to daycare or school.

HSV AND VARICELLA: Herpes simplex virus conjunctivitis is associated with a high risk of keratitis. Patients present with a unilateral red eye, watery discharge and complain of a foreign body sensation and photophobia. A vesicular rash may be seen on the ipsilateral eyelid or in the distribution of the first and second branches of the trigeminal nerves. Hutchinson’s sign is a vesicle on the tip of the nose (V2). Fluorescein exam reveals a classic dendritic pattern of corneal involvement. It is typically self-limited, though duration can be reduced with topical and/or oral anti-viral agents. These patients require ophthalmology follow up. Corticosteroids should be avoided.

BACTERIAL CONJUNCTIVITIS

Bacterial conjunctivitis, similar to acute otitis media, is most commonly caused by Streptococcal pneumoniae, non-typable H influenza and M catarrhalis in children. In adults, staph aureus is also a common pathogen. Similar to viral conjunctivitis, it is spread by secretions which may be acquired through direct contact or contact with a contaminated surface. Bacterial conjunctivitis is more commonly unilateral though involvement of both eyes can occur. Patients may complain that their eye is “stuck shut” in the morning (matting) and have a thick discharge produced throughout the day. Examination may reveal purulent discharge particularly at the lid margins and corners of the eye that reappears after wiping.

It is estimated that approximately 50% of bacterial conjunctivitis will resolve without antibiotics though antibiotics may decrease symptom duration and increase the rate of clinical and microbiologic cure in patients with culture proven bacterial conjunctivitis. Treatment includes topical antibiotics. Those who wear contact lenses should remove their contacts and discard the lenses and contact lens case. Ointments are typically used for young infants or at bedtime. Ointments are not for patients who need to read or see clearly. A variety of topical antibiotics drops are available for use. Common classes include: fluoroquinolones, macrolides, sulfonamides and combination agents. Fluoroquinolones are preferred for contact lens wearers who are at higher risk for pseudomonas infections. Combination antibiotic and corticosteroid drops should not be used. Steroids may increase the duration of symptoms and transmissibility in adenovirus infection and potentiate corneal involvement in those with bacterial or herpes infection.

All broad-spectrum antibiotics appear to have similar efficacy. A single blinded clinical trial included 144 patients randomized to Polymyxin B-trimethoprim (Polytrim) 4 times a day for 7 days or Moxifloxacin (Vigamox) 3 times a day for 7 days (Williams, J Pediatrics 2013, PubMed ID: 23092529). Clinical cure at 4-6 days was statistically similar between the 2 groups (Polytrim (Trimethoprim/Polymixin B) 72% versus Vigamox (Moxifloxacin) 77%). The authors concluded that “Polymyxin B-trimethoprim continues to be an effective treatment for acute conjunctivitis with a clinical response rate that does not differ from moxifloxacin. Use of Polymyxin B-trimethoprim for the treatment of conjunctivitis would result in significant cost savings compared with fluoroquinolones”.

GONOCOCCAL CONJUNCTIVITIS: Both sexually active adolescents and neonates of mothers with untreated infections are at risk for conjunctivitis in the postnatal period due to Neisseria gonorrhea. Neonatal gonococcal conjunctivitis is rare in developed countries due to routine prophylaxis after delivery. It typically occurs within the first week of life. Patients present with profuse (hyper-acute) purulent discharge. Adolescents may have symptoms of a concurrent urethritis. Examination may reveal chemosis, eyelid swelling with tender preauricular adenopathy. Gram stain of discharge reveals gram negative diplococci. Complications include keratitis and corneal perforation. This is an ocular emergency and patients are treated as an inpatient with both topical and intravenous antibiotics (Ceftriaxone). Adolescents should also be treated for Chlamydia.

CHLAMYDIAL CONJUNCTIVITIS: Inclusion conjunctivitis is caused by chlamydia trachomatis serotypes D to K, and is transmitted perinatally in newborns, or via sexual contact in adolescents/adults. It is characterized by a chronic and indolent conjunctivitis. Patients present more commonly with unilateral conjunctivitis for weeks to months that has failed other treatment including topical antibiotics. Diagnosis is made with Giemsa or direct fluorescent antibody staining of conjunctival smears or by PCR. Conjunctivitis in neonates typically occurs 1-2 weeks after delivery. The conjunctiva is often friable, and discharge may be bloody. Neonates have a high rate of concurrent lung and nasopharyngeal infection. Pneumonia may present from 1-3 weeks with a characteristic paroxysmal staccato cough. Chest XRAY reveals hyperinflation and symmetric interstitial infiltrates. Neonates are admitted. Conjunctivitis is treated with oral antibiotics (Erythromycin or Azithromycin) based on culture/PCR results. Pneumonia is treated based on clinical and/or XRAY findings.

Trachoma is caused by chlamydia trachomatis serotypes A, B, and C. Infection is spread through secretions and is considered the leading infectious cause of blindness worldwide. Active infection is most commonly seen in young children. It is usually mild and self-limited. The major findings on exam are the characteristic follicles on the superior tarsal conjunctiva. The diagnosis is made based on clinical manifestations of infection and the severity is determined according to the simplified world health organization trachoma grading system (WEB LINK: TRACHOMA GRADING) which uses the number of follicles, degree of inflammation, scarring, eyelash rubbing and corneal involvement. Treatment includes a single dose of azithromycin (20 mg/kg) or topical tetracycline (BID x 6 weeks)

INFECTIOUS CONJUNCTIVITIS IN THE NEONATE		
FINDINGS	N. GONORRHOEAE	C. TRACHOMATIS
Transmission	30-40%	20-50%
Presentation	2-5 days after birth	5-14 days after birth
Discharge	Purulent	Watery, may become purulent
Other findings	Swelling of the eyelids	Swelling of the eyelids, chemosis, +/- bloody discharge
Diagnosis	Gram stain, Culture, should also be screen for C. Trachomatis due to high rate of coinfection with gonococcal disease	Culture, PCR
Treatment	Cefotaxime 100 mg/kg x 1 IM/IV	Erythromycin 50 mg/kg/day PO divided QID x 14 days Azithromycin 20 mg/kg/day PO Once x 3 days

PSEUDOMONAS: Pseudomonas infections can occur in individuals who utilize extended-wear contacts. Patients will present with a red eye, mucopurulent discharge and complain of blurred vision, pain and foreign body sensation. Examination may reveal corneal opacities/infiltrates and with a positive fluorescein test. These patients are at risk of ocular perforation and require ophthalmology consultation.

CULTURE INDICATIONS
Neonates
Recurrent conjunctivitis
Recalcitrant to treatment
Severe purulent discharge

ANTIBIOTIC INDICATIONS
Purulent or mucopurulent discharge
Contact lens users
Immunocompromised patients
Significant discomfort
Suspected gonorrhea or chlamydial infection

ADDITIONAL CAUSES OF CONJUNCTIVITIS

Conjunctivitis may represent an upper respiratory tract infection or a sign of a systemic disease. In Kawasaki disease conjunctivitis is bilateral, non-exudative, includes the bulbar injection only and is limbus sparing) (See: PEM Guide: Rheumatology: Kawasaki Disease). Parinaud's oculoglandular syndrome is unilateral granulomatous conjunctivitis, fever and ipsilateral preauricular lymphadenopathy. Most cases are caused by cat-scratch disease. Occasionally it may be caused by other infections such as tularemia. Stevens-Johnson syndrome may involve any mucous membrane including the conjunctiva. Conjunctivitis is a prominent manifestation of measles

INDICATIONS FOR OPHTHALMOLOGY CONSULTATION
Decreased visual acuity
Moderate to severe pain
Corneal involvement
Severe purulent discharge
Photophobia: Uveitis, iritis
Contact lens use (increased risk of keratitis)
Symptoms not improved within 1 week
Eye trauma
Clinical suspicion: Acute angle glaucoma, hypopyon, iritis or infectious keratitis

DISPOSITION

RETURN TO SCHOOL/WORK: Committee on pediatric infectious disease Red Book Recommendations: “Those infected with viral/bacterial conjunctivitis are presumed contagious until symptoms resolve though transmission can be minimized by proper hand hygiene. Infected individuals can return to school/work once indicated therapy is initiated, though should remain at home if there are concurrent signs of systemic infection.” Most day cares and schools required 24 hours of treatment prior to returning.

APPENDIX: CAUSES OF INFECTIOUS CONJUNCTIVITIS

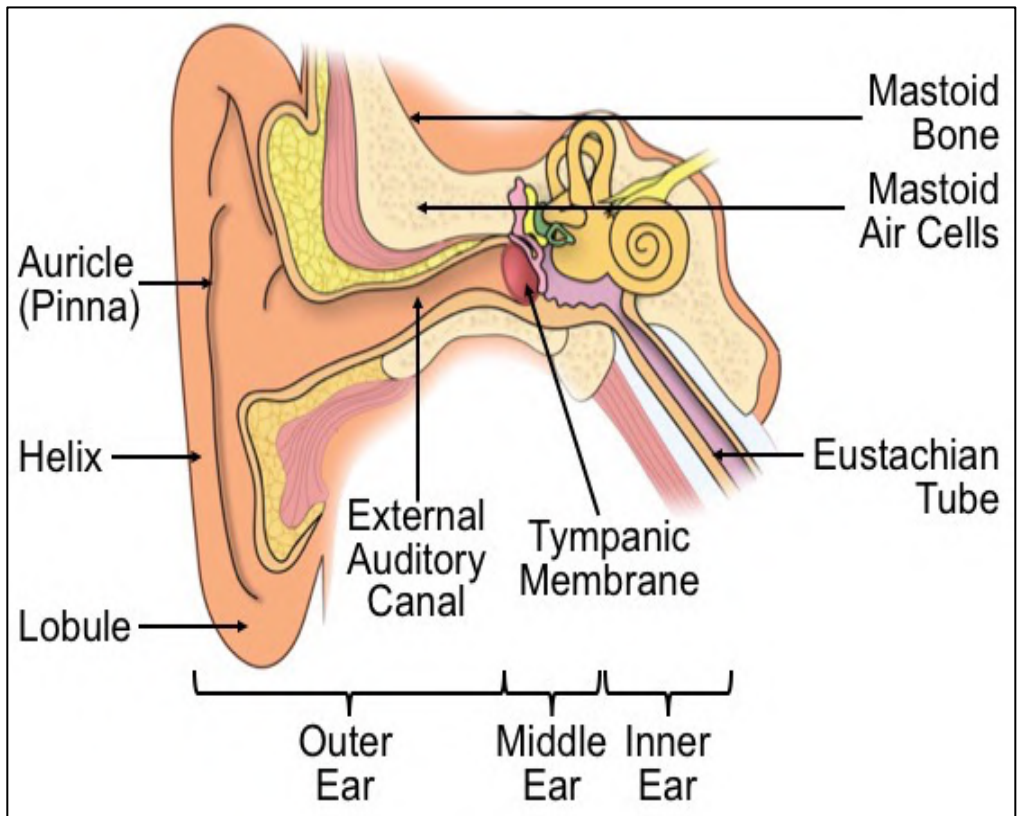
See: PEM Guide: Respiratory: Allergic Conjunctivitis and Rhinitis

OVERVIEW: COMMON CAUSES OF CONJUNCTIVITIS				
FINDINGS	VIRAL	BACTERIAL	ALLERGIC	OTHER
Eye Involvement	Begins unilateral, progresses to bilateral	Unilateral	Bilateral	Usually unilateral
Discharge	Watery	Purulent	Watery	Mucoid
Symptoms	Burning, Gritty, Irritation	Eye “Stuck Shut” in the morning	Pruritus	Known Insult
Timing	Summer	Winter	Seasonal Perennial	N/A
Course	7-10 days	7-10 days	Variable	2-3 days
Treatment	Self-Limiting, supportive treatment, frequent hand washing, avoid contact with eyes	Antibiotics to decrease transmission and spread	Removal of allergen, +/- artificial tears, topical or oral antihistamines	Irrigation, Fluorescein to rule out corneal abrasion +/- antibiotics

MASTOIDITIS

INTRODUCTION (EVAN YANNI, MD., 8/2018)
Mastoiditis is defined as a suppurative infection of the mastoid air cells and is the most common suppurative complication of acute otitis media (AOM). The incidence of acute mastoiditis as a complication of otitis media in children less than or equal to 6 years of age is 37 cases per 100,000 otitis media child-year visits (Marom, JAMA Peds, PubMed ID: 24276262). That is roughly 1 case of acute mastoiditis per 2,700 otitis media visits. This represents a dramatic decrease from rates as high as 1 in 5 cases of acute otitis media in the pre-antibiotic and pre-vaccine era (Nussinovitch, Clin Ped 2004, PubMed ID: 15094950). However, some argue that given increasing antimicrobial resistance and recommendations for withholding antibiotics for AOM, the incidence of mastoiditis has the potential to increase.

PATHOGENESIS
The mastoid air cells are a division of the temporal bone. They are anatomically adjacent to the middle ear and are directly connected to the middle ear via a narrow channel called the aditus ad antrum. When AOM occurs, purulent fluid is able to travel from the middle ear into the mastoid air cells. This results in the nonspecific CT finding of “mastoid air cell opacification” seen in many cases of uncomplicated AOM (Lin, Clin Pedr 2010, PubMed ID: 19734439). This does not constitute mastoiditis.



EAR ANATOMY

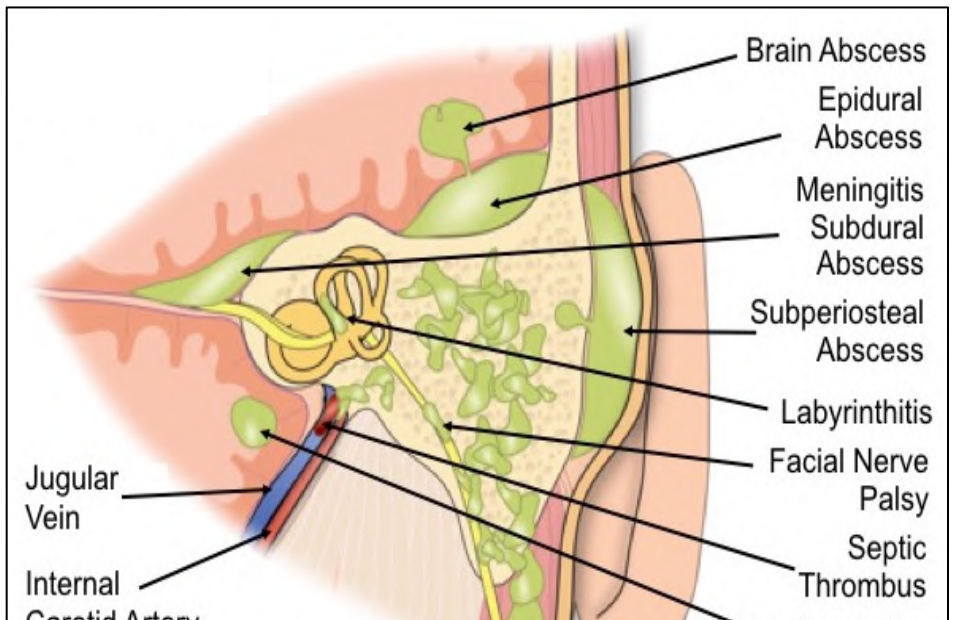
MASTOIDITIS PROGRESSION	
1	Presence of purulent materials in the mastoid air cells as a result of adjacent AOM
2	Mastoiditis with Periostitis: Periosteal inflammation without bone destruction
3	Coalescent Mastoiditis: Abscess formation, destruction of bone septae
4	Extracranial and intracranial spread

Typically, as AOM resolves, the purulent fluid in the mastoid air cells is able to drain. However, in episodes of severe AOM where mucosal edema or inflammatory granulation tissue obstructs the aditus ad antrum, the purulent fluid is unable to drain. This results in further progression of the infection and the development of mastoiditis. The initial (incipient) stage of acute mastoiditis is referred to as acute mastoiditis with periostitis. This occurs when purulent material within the mastoid cavities causes inflammation of the periosteum without destruction of the boney septae. This can progress to acute coalescent mastoiditis where destruction of the boney septae occurs allowing for abscess formation and invasion into adjacent structures. This process is of particular concern given the mastoid’s proximity to critical structures such as the inner ear, facial nerve, jugular vein, carotid artery, meninges, and brain.

MASTOIDITIS COMPLICATIONS	
EXTRACRANIAL	INTRACRANIAL
Subperiosteal abscess (behind pinna)	Meningitis
Facial nerve palsy	Abscess of temporal lobe
Hearing loss	Abscess of the cerebellum
Suppurative labyrinthitis	Epidural abscess
Osteomyelitis: temporal, occipital bones	Subdural abscess
Septic thrombophlebitis (IJ vein, carotid)	Venous sinus thrombosis
Bezold Abscess: Between the insertions of the sternocleidomastoid and digastric muscles	
Gradenigo syndrome: Acute otitis media, eye pain, abducens (cranial nerve 6) nerve palsy	

DIAGNOSIS

The presentation of mastoiditis depends on the patient's age, stage of mastoiditis and path of spread. The classic criteria for diagnosing acute mastoiditis are nonspecific. Evidence of acute otitis media may or may not be present or the tympanic membrane may not be visualized due to canal edema.



MASTOIDITIS COMPLICATIONS

DIAGNOSTIC CRITERIA: MASTOIDITIS
1. Acute otitis media on otoscopy with local inflammatory findings over the mastoid
2. Radiographic or surgical findings of mastoiditis (without signs of AOM)

DIAGNOSTIC CRITERIA: ACUTE OTITIS MEDIA: AAP 2013*		
1	Moderate-Severe bulging of the tympanic membrane	
2	Mild bulging of the tympanic membrane AND	
A	Recent onset (48 hours) of Ear pain (verbal child) OR Holding, tugging, rubbing of the ear (non-verbal child)	
or B	Intense erythema of the tympanic membrane	
3	New onset otorrhea not due to acute otitis externa	
*The diagnosis should not be made in the absence of a middle ear effusion		

ADDITIONAL FINDINGS: MASTOIDITIS			
HISTORY		EXAMINATION	
Fever	76%	Postauricular swelling/fluctuance	85%
Lethargy/malaise	96%	Postauricular erythema	83%
Irritability	71%	Postauricular tenderness	81%
Ear pain	67%	Protrusion of auricle/pinna	79%
Acute otitis media	80%		
Otorrhea	50%		
van den Aardweg, Otol Neurotol 2008 PubMed ID: 18617870			

DIFFERENTIAL DIAGNOSIS	
Postauricular lymphadenopathy	Palpable rubbery moveable lymph node
Otitis Externa	Pain is localized to pinna or tragus
Superficial cellulitis	Absence of involvement of TM
Perichondritis of external ear	Absence of involvement of TM
Tumor	Absence of involvement of TM
Basilar skull fracture	Mastoid and/or periorbital bruising, hemotympanum

LABORATORY FINDINGS

There is no defined role for laboratory testing in the diagnosis of acute mastoiditis. Inflammatory markers such as WBC, ANC, and CRP may or may not be elevated and these markers are nonspecific. (Bilavsky, Int J Pediatr Otorhinolaryngol 2009, PubMed ID: 19539381). However, they may be useful to trend for response to treatment.

RADIOGRAPHY

Imaging can confirm the diagnosis, determine the stage of mastoiditis and identify intracranial and extracranial spread. However, imaging may not be required for all patients. Patients with characteristic findings of uncomplicated mastoiditis can be treated empirically and imaging obtained only if signs and symptoms do not resolve as expected with appropriate antimicrobial therapy.

Contrast-enhanced CT scan is the gold standard for assessment of the mastoid bone for cortex dehiscence, coalescence, and abscess. In mastoiditis with periostitis, imaging will demonstrate soft tissue inflammation and suppurative disease in the absence of radiographic coalescence and bone erosion. In coalescent mastoiditis, imaging may demonstrate findings of rim-enhancing fluid collections, mastoid air cell coalescence, cortical bone erosion and extracranial or intracranial involvement.

INDICATIONS FOR CONTRAST ENHANCED CT*
Suspected extracranial spread
Suspected intracranial spread
Severe illness of toxic appearance
Acute otitis media not responding as expected to antibiotics (masked mastoiditis)
Poor response to parenteral antibiotics in a patient without a prior CT

MANAGEMENT

Treatment of mastoiditis includes the administration of appropriate antimicrobial therapy and ENT consultation for possible surgical drainage. Neurosurgery consultation is indicated for intracranial complications such as CNS abscess or subdural/epidural empyemas.

ANTIBIOTICS: Acute mastoiditis warrants inpatient admission for parenteral antibiotics. The most common pathogens include: Streptococcus pneumoniae, streptococcus pyogenes and staphylococcus aureus. Vancomycin is the preferred antibiotic for these pathogens. Pseudomonas coverage may be indicated in addition to Vancomycin if there is history of recurrent acute otitis media or recent antibiotic use.

ANTIBIOTIC SELECTION	
A	Vancomycin: 15 mg/kg/dose Q6H (maximum dose 1 gram) AND
B	Suspected Pseudomonas: History of recurrent AOM or recent antibiotic use
1. No Penicillin allergy	
Cefepime: 50 mg/kg/dose Q6H (maximum dose 2 grams) OR	
Ceftazidime: 50 mg/kg/dose Q6H (maximum dose 2 grams) OR	
Piperacillin/Tazobactam: 300 mg/kg/day divided Q6H/Q8H (max 16 gm/day)	
2. Non-type 1 hypersensitivity reaction	
Cefepime or Ceftazidime as above	
3. Type 1 hypersensitivity reaction:	
Aztreonam 30 mg/kg/dose Q6H (maximum dose 2 grams)	

SURGERY: Antibiotic therapy may not be sufficient. Surgical management is based on disease progression and sites of involvement. Surgical management typically includes myringotomy with or without tympanostomy tube placement and/or cortical mastoidectomy depending on the stage of illness (Bakhos, Arch Otolaryngol Head Neck Surg 2011, PubMed ID: 21502472). Indications for these procedures vary considerably by center so ENT consultation is essential. Neurosurgical drainage may be required for intracranial complications.

Mastoidectomy is the removal of the mastoid cortical bone and underlying air cells. Simple mastoidectomy opens the aditus ad antrum and promotes external drainage while preserving the posterior portion of the external auditory canal. In radical mastoidectomy, the posterior portion of the external auditory canal is removed as well. Radical mastoidectomy may be indicated if there is no clinical improvement after simple mastoidectomy. Cultures and sensitivities should be obtained during either approach.

DISPOSITION

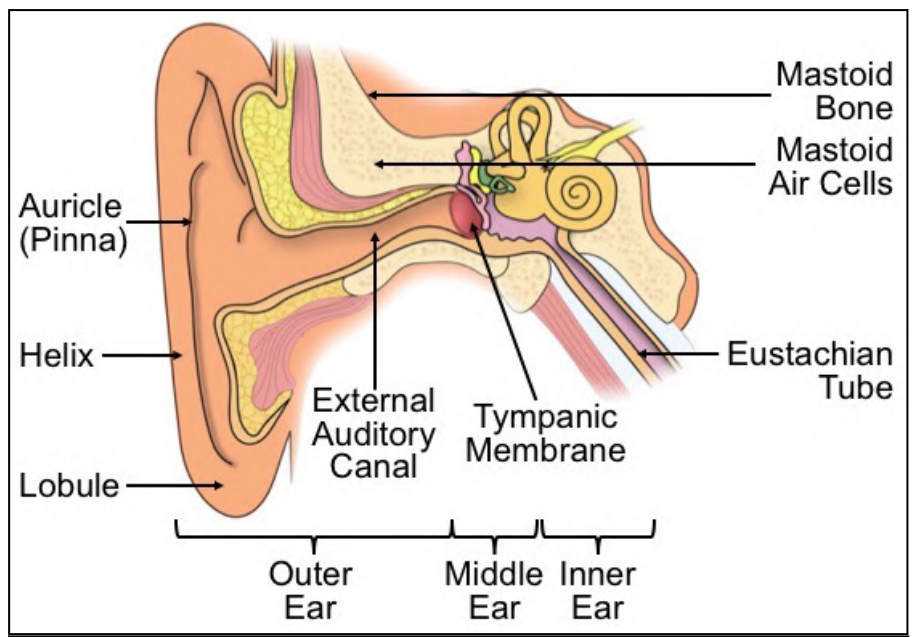
All patients with acute mastoiditis should require inpatient admission. Subsequent discharge from the hospital varies based on complications, appropriate surgical management, and establishment of appropriate antibiotic treatment regimen.

OTITIS EXTERNA

INTRODUCTION (ROSHNI PATEL, MD, 7/2018)
Otitis externa (also known as swimmer's ear or tropical ear) is defined as inflammation of the external auditory canal. The condition can occur at all ages but has a peak prevalence between the ages of 7 and 12 years. About 10% of the population will have acute otitis externa at some point in their lifetime and it is more common in warmer, humid climates. Timely diagnosis and management are key to preventing more serious complications of this common illness. (See Also PEM Guide: Head and Neck Infections: Acute Otitis Media)

BACKGROUND/PATHOPHYSIOLOGY

Pathogenesis of otitis externa starts with moisture or local trauma removing cerumen that protects the skin in the ear canal (Figure). Limited cerumen leads to an increase in pH in the ear canal and this moist, static, alkaline ear becomes conducive to bacterial growth. The skin cells then become edematous leading to pruritis and obstruction. The most common bacterial pathogens are: Pseudomonas Aeruginosa, Staphylococcus Epidermidis, and Staphylococcus Aureus. Aspergillus and Candida are the most common fungal causes but only account for two-ten percent of cases.



EAR ANATOMY

RISK FACTORS: IMPAIR INHERENT DEFENSE MECHANISMS OF EAR CANAL
Swimming
Excessive cleaning/scratching of ear
Hearing Aids, Earphones, Diving Caps
Allergic Contact Dermatitis
Environmental temperature
High humidity

COMPLICATIONS

Untreated or insufficiently treated external otitis can lead to spreading of infection. Periauricular cellulitis presents with erythema and edema in the skin around the auricle leading to mild pain. Malignant otitis externa occurs when the infection spreads from the skin to the adjacent bones. Malignant external otitis is far more common in immunocompromised individuals. Patients present with pain out of proportion to the examination findings. Granulation tissue at the base of the ear canal is apparent on exam and patients may have cranial nerve abnormalities as well.

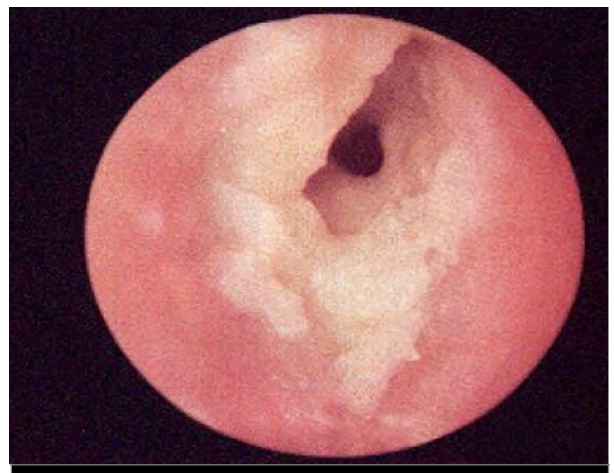
DIFFERENTIAL DIAGNOSIS	
Furunculosis	Contact/Allergic Dermatitis
Foreign Body*	Infected Sebaceous Cyst
Acute Otitis Media with Perforation*	Carcinoma of the ear canal
Mastoiditis*	Brain Abscess
*See separate PEM Guides on these topics	

HISTORY

The diagnosis of acute otitis externa (AOE) is based on history and physical findings. Patients typically present with unilateral ear pain, pruritis, discharge and fullness in the ear/hearing loss. Unlike acute otitis media (AOM), fever is uncommon. History of risk factors such as tympanic membrane perforation, previous ear infections, ear surgery, ear instrumentation and water exposure should be elicited.

PHYSICAL EXAMINATION

Physical exam reveals pain on manipulation of the pinna and tragus. The auricle and tragus should be examined for signs of trauma. On otoscopic exam, the ear canal will be edematous, erythematous and tender. Discharge can be yellow, brown, white or gray. Darker coating is more indicative of Aspergillus and whiter thicker secretions is more likely with Candida. The tympanic membrane may be erythematous if visualized. An air fluid level would indicate a middle ear effusion. A perforated tympanic membrane is likely a middle ear infection with secondary inflammation into the ear canal. Pneumatic otoscope may help with differentiating acute otitis media from acute otitis externa. The tympanic membrane will be mobile with otitis externa



OTITIS EXTERNA

LABORATORY STUDIES

No laboratory evaluation is necessary for first time routine otitis externa. Cultures are necessary in more severe cases before treatment, immunocompromised patients, recurrent otitis, or those who do not respond to initial therapy.

MANAGEMENT

Cleansing of the ear canal followed by oto-topical medications is the mainstay treatment in otitis externa. Analgesia is important in severe pain. Treatment type is dictated by the severity of inflammation. Early otitis externa may simply need acidifying agents and glucocorticoids to restore normal flora in the canal. Mild to moderate disease warrants debridement as well as acidic drops with antibiotics and glucocorticoids. Severe infection with some element of cellulitis will need debridement, antibiotic/ acidifying drops via a wick as well as oral antibiotics. Of note, swimming should be avoided during treatment to promote healing and further damage.

CLEANSING: Cleaning of the ear canal is done via the otoscope with a loop or cotton swab to remove cerumen and debris. If the tympanic membrane can be visualized and is intact, the canal can be rinsed out with a one to one mixture of 3% hydrogen peroxide and water. If the tympanic membrane cannot be visualized, ENT should be consulted for cleaning under binocular vision given the ear will be very tender. Once cleaned, ENT can direct treatment.

ACIDIFYING AGENTS/GLUCOCORTICOIDS: Acidifying agents usually range in pH from 3.0 to 6.0. This inhibits the growth of bacteria but may cause some burning/irritation to the infected site. Topical steroids help reduce inflammation that results in the pain and itching involved in the infection. Acetic acid 2% and hydrocortisone otic has a range of pH from 2.0 to 4.0 and is a reasonable choice.

ANTIBIOTICS: Topical antibiotics should be administered three to four times a day for 7 to 10 days. Course varies depending on the medication given. The most common agents include neomycin, polymyxin B, polymyxin E, and fluoroquinolones. Systemic fluoroquinolones toxicity is very rare when they are applied topically and at appropriate pediatric dosing. If the opening to the ear canal is obscured, ear wicks can be used and stay in place 24-72 hours. Most antibiotics are typically buffered and would need an additional acidifying agent with the exception of Coly-Mycin S, Cortisporin TC (pH 5) or Pred-G (pH 5.4-6.6). In cases of severe otitis externa with swelling preventing access to the ear canal, a wick is indicated. Wicks are made of polyvinyl alcohol and will expand when topical medications are applied. These stay in place in the ear canal for 1-3 days at a time while the swelling persists and allows for more directed medication. Typically wicks are placed by ENT.

OTITIS MEDIA

INTRODUCTION (DEBORAH LEVINE, M.D. 2/2022)
Acute otitis media is the most common bacterial infection in childhood and the most common reason for antibiotic prescription. The peak incidence is from 6-12 months of age. It is estimated that 25% of children will experience an episode of acute otitis media during the first year of life and 60% within the first 5 years. This increased susceptibility is likely due to the younger infant and child's shorter eustachian tube, its horizontal position, their limited prior exposure to both bacterial and viral pathogens, and their limited response to antigens as well as the increased exposure in child care settings.

RISK FACTORS	
ENVIRONMENTAL	PATIENT
Child care attendance	Abnormal anatomy e.g. cleft palate
Not breast fed	Early onset of 1st episode of otitis media
Atopy	Immune deficiency
Absence of pneumococcal vaccine	Family history of acute otitis media
Absence of influenzae vaccine	Cochlear implant
Exposure to tobacco smoke	Male, non-Hispanic white

BACTERIOLOGY
The predominant organisms responsible for acute otitis media are: non-typable *Haemophilus influenzae* *Streptococcus pneumoniae* and *Morexella catarrhalis*. The table below contains data on middle ear infusions obtained by tympanocentesis from 319 patients from 6-36 months of age with 495 middle ear infusions (Kaur, Euro J Clin Microbiol Infect Dis 2021, PubMed ID: 34432166). This was primarily a middle class, suburban population. 90% of pneumococcal disease was from non-vaccine serotypes, serotype 35B was the most common. Unfortunately, the upcoming pneumococcal vaccines from Merck (15 serotypes) and Pfizer (20 serotypes) do not contain many of the dominant serotypes. *Group A beta-hemolytic streptococcus*, *Staphylococcus aureus*, *Pseudomonas aerogenosis*, and respiratory viruses account for the minority of infections.

ACUTE OTITIS MEDIA MICROBIOLOGY (2015-19)		
Organism	Prevalence	Resistance
H. influenzae	34%	49% beta lactamase (+)
Pneumococcus	24%	25% Amoxicillin Resistance
M. Catarrhalis	15%	100% beta lactamase (+)

Prevalence rates of infections due to *Streptococcus pneumoniae* are declining due to widespread use of the pneumococcal (Prevnar 7 and Prevnar 13)) vaccines. *Streptococcus pneumoniae* is often resistant due to penicillin-binding protein alterations. The resistance may be overcome with higher doses of Amoxicillin.

Due to the two pneumococcal vaccines, infection with non-typeable *Haemophilus influenzae* is present in a greater proportion of acute otitis media. *Haemophilus influenzae* and *Morexella catarrhalis* are gram negative organisms that produce beta-lactamase enzyme to inhibit antibiotic activity. Higher doses of Amoxicillin used to combat the penicillin binding protein resistance of *Streptococcus pneumoniae* do not overcome resistance due to beta-lactamase. As the prevalence of strep pneumoniae decreases further, that rate of Amoxicillin resistant acute otitis media can be expected to increase.

COMPLICATIONS

Persistent effusion, relapse, and recurrence of acute otitis media are common, especially in the younger children and those with the most severe presentations. Approximately 50% of children treated for acute otitis media will have a middle ear effusions at 1 month and 10% at 3 months. The presence of effusion is associated with recurrent of acute otitis media. Hearing loss is the most common complication. It can be conductive and/or sensorineural, temporary or permanent and may lead to language delays.

Suppurative sequelae of acute otitis media are rare (approximately 1-2/100,000/year). The incidences of mastoiditis and facial nerve paralysis have decreased significantly since the widespread use of antibiotics but do occur sporadically. Intracranial complications such as meningitis, abscesses and lateral sinus thrombosis are rare but may be life-threatening.

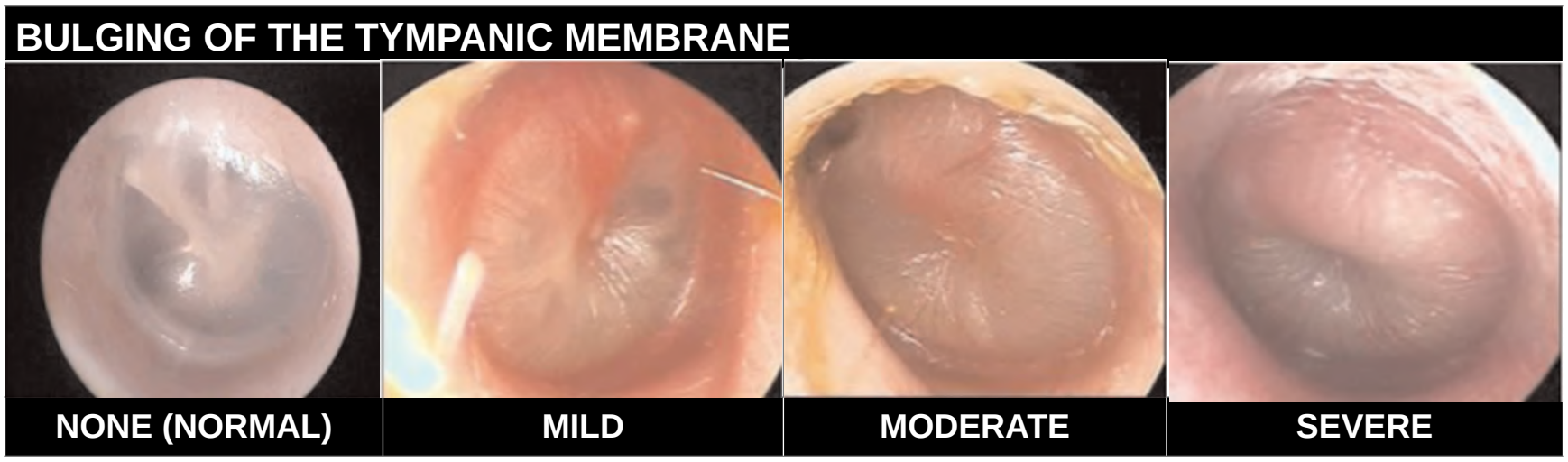
COMPLICATIONS
Tympanic membrane perforation
Facial nerve (cranial nerve 7) palsy
Subperiosteal abscess (temporal bone)
Mastoiditis
Cavernous sinus vein thrombosis
Labyrinthitis
Bacteremia
Meningitis

DIAGNOSIS

The diagnosis of acute otitis media is made clinically. Tympanocentesis is seldom used to confirm the diagnosis outside of research settings. The diagnosis can be challenging especially in the younger patient, whose symptoms may be non-specific, have a concomitant upper respiratory infection, do not cooperate with the examination, or has cerumen obscuring the view. Erythematous tympanic membranes may be due to viral infection, crying, or efforts to remove cerumen. Fever or irritability may or may not be present. Pulling/tugging at the ears has a sensitivity of less than 50% (Rothman, JAMA 2003, PubMed ID: 14506123).

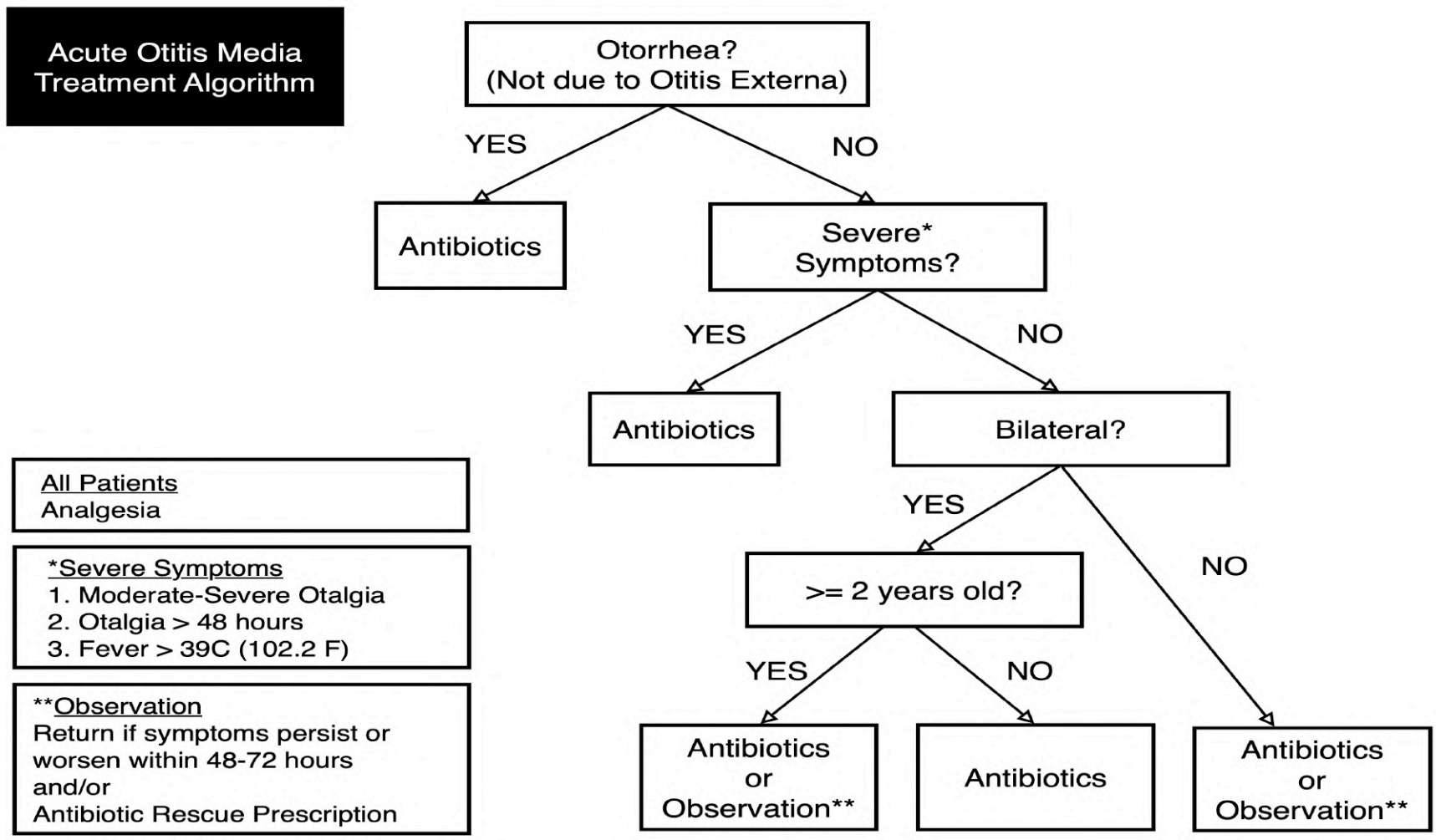
DIAGNOSTIC CRITERIA FOR ACUTE OTITIS MEDIA: AAP 2013*		
1	Moderate-Severe bulging of the tympanic membrane	
2	Mild bulging of the tympanic membrane AND	
	A	Recent onset (48 hours) of Ear pain (verbal child) or Holding, tugging, rubbing of the ear (non-verbal child)
	or B	Intense erythema of the tympanic membrane
3	New onset otorrhea not due to acute otitis externa	
*The diagnosis should not be made in the absence of a middle ear effusion		

Strict adherence to diagnostic criteria will decrease unnecessary antibiotic use reducing the risk of associated adverse effects and the potential to increase bacterial resistance. Diagnosis requires bulging of the tympanic membrane and the presence of tympanitis (inflamed tympanic membrane and opacified fluid behind the membrane). In contrast, a middle ear effusion is characterized clear fluid behind the tympanic membrane with bulging but without signs of inflammation. A middle ear effusion may be the result of an appropriately treated acute otitis media or may occur due to eustachian tube dysfunction as a result of an upper respiratory infection.



MANAGEMENT

In 2013, the American Academy of Pediatrics revised their 2004 otitis media practice guideline (AAP, Pediatrics 2013, PubMed ID: 23439909). Emphasis is placed on appropriately diagnosing of otitis media. A treatment option for an “uncertain” diagnosis is no longer included. The option of expectant management (or “watchful waiting”) has been expanded to younger age groups. Appropriate analgesia should be provided to all patients.



ANTIBIOTICS OR WATCHFUL WAITING: A strategy of “watchful waiting” in which children with acute otitis media are not immediately treated with antibiotic therapy, has been endorsed by the American Academy of Pediatrics. Observation without antibiotics is a widely adopted practice in Western Europe without a significant increase in serious sequelae. When observation is used, a mechanism must be in place to ensure follow-up and begin antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms. Parents may be given a “rescue” prescription to facilitate treatment if symptoms persist or worsen.

The studies on which the observation option has been based have been criticized for lack of stringent diagnostic criteria, small sample sizes and use of antibiotics in suboptimal doses. Two well-designed clinical trials (Hoberman NEJM 2011 PubMed ID: 23439909 and Tähtinen NEJM 2011 PubMed ID: 212265577) collectively randomized approximately 600 children meeting strict diagnostic criteria for acute otitis media to receive Amoxicillin/Clavulanic acid or placebo. These studies demonstrated a significant reduction in symptom burden and clinical failures in those who received antibiotics. The authors conclude that those patients with a clear diagnosis of acute otitis media would benefit from antibiotic therapy. A comparison group treated with Amoxicillin would have been helpful.

ANTIBIOTIC SELECTION: Amoxicillin is the recommended first-line agent to cover the most common bacterial causes of otitis media. Amoxicillin is an attractive option for a number of reasons. It is not broad spectrum, it is associate with few adverse events and is inexpensive. Due to increased prevalence of resistant strains of *streptococcus pneumoniae,* high-doses of Amoxicillin (80-90 mg/kg/day divided BID) are recommended.

If the incidence of strep pneumoniae continues to decline due to vaccination and the proportion due to H. Influenza and M. Catarrhalis increases, then antibiotics with greater activity against beta lactamase producing gram negative organisms should supplant Amoxicillin as the preferred first-line agent. Some authors recommend that Amoxicillin should not be used as a first line agent because up to 50% of infections are currently resistant.

Amoxicillin should not be used if the patient has received Amoxicillin in the past 30 days, has concomitant purulent conjunctivitis (non-typeable Haemophilus influenza) or has a non-type one hypersensitivity reaction to penicillin. In these circumstances, a beta lactamase resistant antibiotic should be used. These include: Amoxicillin clavulanate or 2nd (Cefuroxime) or 3rd generation cephalosporins (Cefdinir, Cefpodoxime). If patients are not able to tolerate parental antibiotics then a single dose of 50 mg/kg of Ceftriaxone can be administered intramuscularly.

Patients with a history of a severe type 1 hypersensitivity reactions to penicillin could be treated with Levofloxacin though it is not FDA approved for this purpose. Macrolides such as Azithromycin and Clarithromycin do not provide coverage for H. Influenza.

DURATION OF THERAPY: A clinical trial randomized 467 patients 6-23 months of age with acute otitis media to either 10 days of Amoxicillin/Clavulanate or 5 days of Amoxicillin/Clavulanate followed by 5 days of placebo in a blinded fashion. Those in the 10 days of antibiotics groups had significantly fewer treatment failures (16% versus 34%, risk difference 18% 95% CI (9, 25%). The authors concluded that a 10-day course of therapy was superior to a 5-day course (Hoberman, NEJM, 2016, PubMed ID: 28002709). The generalizability of these results to patients older than two years of age is unclear.

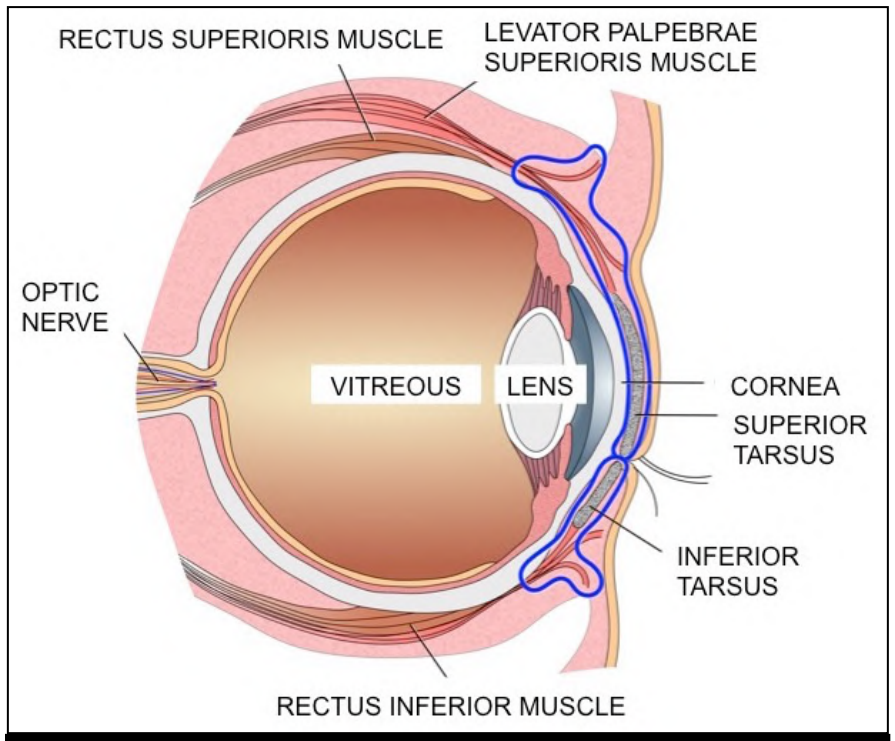
DURATION OF THERAPY: AAP 2013	
10-day course	Children < 2 years of age and children with severe symptoms
7-day course	Children 2 to 5 years with mild or moderate symptoms
5-7 day course	Children ≥ 6 years with mild to moderate symptoms

PERIORBITAL AND ORBITAL CELLULITIS

INTRODUCTION (ALVIRA SHAH, M.D. 10/2021)
Periorbital (preseptal) cellulitis and orbital (postseptal) cellulitis are different disease entities that can be difficult to distinguish. They can both cause ocular pain and eyelid swelling and erythema. It is important to accurately identify them for appropriate treatments. Periorbital cellulitis is a more common and a benign condition when compared to orbital cellulitis, which is a serious ophthalmic emergency. Periorbital cellulitis rarely has complications, but orbital cellulitis can cause loss of vision and even loss of life. Both are more common in children than adults.

ANATOMY

The orbital septum is a fibrous sheath that separates the eyelids from the orbital contents. Periorbital cellulitis is an infection of the eyelid & surrounding skin anterior (preseptal) to the orbital septum. Orbital cellulitis is an infection of the soft tissues (fat & ocular muscles) posterior (postseptal to the septum. Neither infection involves the globe itself. The orbital septum is outlined in blue.



EYE ANATOMY: CROSS SECTION

PATHOGENESIS AND MICROBIOLOGY

Periorbital cellulitis is often caused by contiguous spread of infection from a local skin disruption on or near the eyelid. This includes abrasions, insect or other animal bites, foreign bodies, infected skin lesion (e.g. herpes zoster virus or herpes simplex vesicle), or a hordeolum (stye). It can also be caused by sinusitis, dacryocystitis (infection of the lacrimal gland and duct), or conjunctivitis.

Orbital cellulitis is almost always caused by infection extension from adjacent sinuses, especially the ethmoid sinus (90%). It can also be caused by penetrating trauma or surgery of the orbit, spread of infection from face, ears or upper teeth, or by hematogenous spread. Rarely, it may occur as an extension of periorbital cellulitis, particularly in young children in whom the orbital septum is not fully developed. Intracranial complications include: meningitis, brain abscess and cavernous sinus thrombosis.

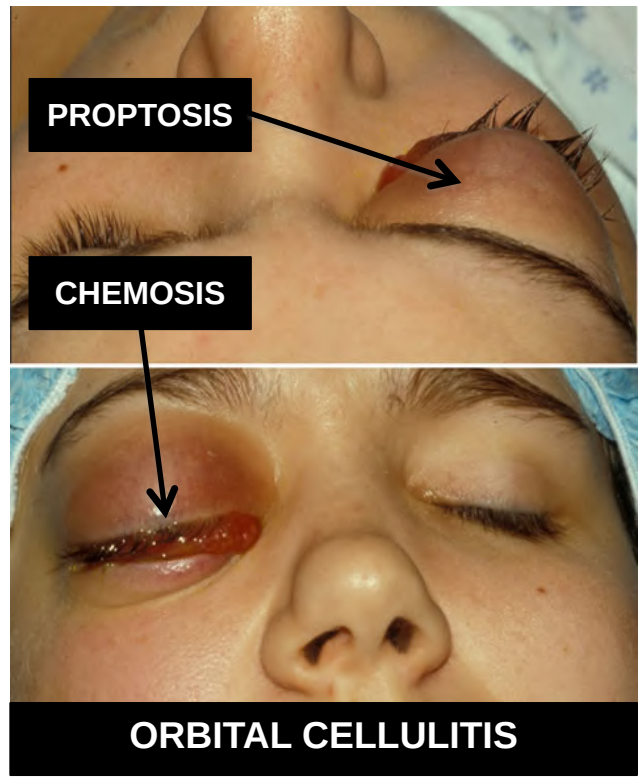
Pathogens vary by etiology and patient age. *S pneumoniae* (most common), *non-typeable H. Influenzae and M. catarrhalis*, are the pathogens associated with sinus infection. Rarely S. aureus and anaerobes are associated with sinusitis. *Staph aureus* and *S. pyogenes* predominate when infection arises from local trauma. Methicillin resistant Staph aureus (MRSA) is an increasingly common cause of infection. H. influenzae type b, once a common cause, has been virtually eliminated due to widespread vaccination. Fungi (e.g. *Mucorales and Aspergillus*) are uncommon pathogens, causing orbital cellulitis in diabetic or immunocompromised patients. Mycobacterium tuberculosis is also a rare cause of orbital cellulitis.

CLINICAL MANIFESTATIONS

PERIORBITAL CELLULITIS: Periorbital cellulitis is characterized by swelling, tenderness, and erythema of the eyelid. There is loose connective tissue in the eyelid and conjunctivitis can also present with eyelid swelling and erythema. The presence of induration, warmth and tenderness is indicative of periorbital cellulitis. Periorbital cellulitis differs from orbital cellulitis in that all the swelling is confined to the eyelid. Once the eyelid is open, examination shows that there is no proptosis, and vision and ocular motility are normal.

PERIORBITAL CELLULITIS

ORBITAL CELLULITIS: Orbital cellulitis may also have eyelid swelling and erythema. Features that can distinguish it from periorbital cellulitis. include pain with eye movements, ophthalmoplegia with diplopia or blurry vision, and or proptosis (bulging of the eye anteriorly out of the orbit). This can often best be seen looking down from the top of the head In addition, patients with orbital cellulitis more commonly have: fever, malaise, headache, purulent eye discharge, and or chemosis (conjunctival swelling). In some cases of orbital cellulitis, eyelid erythema may be absent.



ORBITAL CELLULITIS

IMAGING

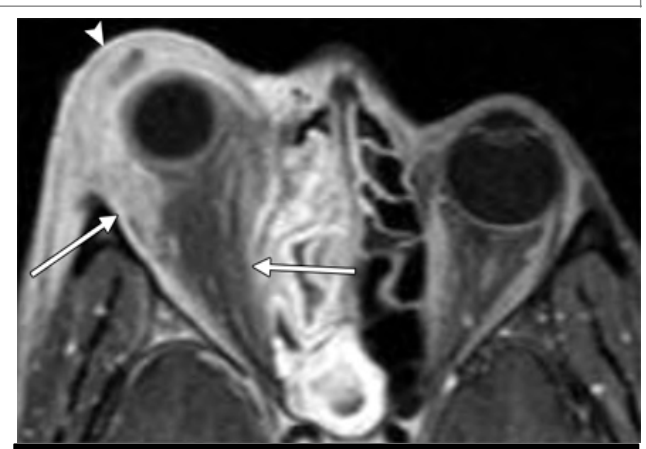
A CT scan with contrast or MRI of the orbits and sinuses is recommended if there are signs or symptoms indicating a diagnosis of orbital cellulitis. This will enable you to localize the source of the infection and identify the presence of complications. Findings of orbital cellulitis may include fat stranding of orbital contents, proptosis, and edema of extraocular muscles. Sinusitis is almost always present. Brain imaging should be included if central nervous system.

INDICATIONS: CT ORBIT/SINUS
Suspected orbital cellulitis
Suspected CNS complication (CT orbits with contrast and CT brain with contrast)
Periorbital cellulitis involving both eyes
Periorbital cellulitis unable to assess eye
Periorbital cellulitis without intravenous antibiotic response in 24-48 hours

LABORATORY EVALUATION

A CBC may show leukocytosis with polymorphonuclear neutrophil dominance for both periorbital and orbital cellulitis. The white blood cell count cannot be used to reliably distinguish between the two. If cerebral or meningeal signs develop, the patient may require a lumbar puncture.

For periorbital cellulitis, blood cultures are almost always negative. Blood culture is recommended prior to giving antibiotics for orbital cellulitis, although there is also low yield. Cultures should be obtained if an orbital abscess is drained surgically.



ETHMOID SINUSITIS AND ORBITAL CELLULITIS

MANAGEMENT: PERIORBITAL CELLULITIS

Adults and children over 1 year of age with mild periorbital cellulitis and no signs of systemic toxicity can generally be treated as outpatients with oral antibiotics, provided that close follow-up can be ensured. Patients who cannot cooperate fully for a thorough examination and patients who are severely ill should generally be admitted to the hospital and managed according to the recommendations for orbital cellulitis. It is important to note that patients with subtle clinical and or radiographic findings suggesting that the orbit is involved should be treated as though they have orbital cellulitis given its serious complications.

Antibiotics are chosen to provide coverage for S. Aureus (including MRSA) and S. Pyogenes. If the patient has not been immunized against *H. influenzae*, one of the combination regimens should be used in order to insure coverage for this organism. Periorbital cellulitis responds rapidly to treatment. If no signs of improvement or continued fevers in 24-48 hours then obtain a CT to identify orbital cellulitis and its complications, and admit for intravenous antibiotics.

PERIORBITAL CELLULITIS: ANTIBIOTIC SELECTION*
OUTPATIENT
Indications: > 1 year, no systemic signs, orbital cellulitis excluded
Amoxicillin/Clavulanate (Augmentin) AND Trimethoprim/Sulfamethoxazole (Bactrim)
Duration: 7 days
INPATIENT
Ampicillin/Sulbactam (Unasyn) AND Vancomycin
Alternative: Clindamycin and Trimethoprim/Sulfamethoxazole (Bactrim)
Duration 7 days
*NYU Pediatric Antibiotic Stewardship 2021

MANAGEMENT: ORBITAL CELLULITIS

Patients with suspected orbital cellulitis should have a CT scan, should be hospitalized and treated and treated with broad-spectrum intravenous antibiotics. Antibiotic selection should be targeted to cover the most common organisms associated with sinusitis including: *S pneumoniae* (most common), *non-typeable H. Influenzae and M. catarrhalis*. ENT and or ophthalmology consultation is recommended. Empiric treatment consists of Intravenous Vancomycin plus an extended spectrum penicillin or a third generation cephalosporin (see table below).

Patients should show improvement after 24-48 hours of antibiotics. If they do not improve consider repeat imaging and possible surgery. Abscesses in older children usually have mixed flora and are more likely to require drainage. A patient with uncomplicated (no abscess or other surgical indication) orbital cellulitis can be switched to oral antibiotics once afebrile and eyelid and orbital symptoms subside, usually in 3 to 5 days.

Antibiotics should be continued until all signs of orbital cellulitis have resolved, and for a total of at least 2-3 weeks. A longer period (at least 4 weeks), is recommended for patients with severe ethmoid sinusitis and bony destruction of the sinus. If a pathogen is identified on blood culture, abscess cultures or sinus aspirates then treatment should be modified accordingly. In particular, if the organism is methicillin sensitive staph aureus (MSSA) and patient is on Vancomycin, they should be changed to Oxacillin or Nafcillin because these are more rapidly bactericidal for MSSA.

ORBITAL CELLULITIS: ANTIBIOTIC SELECTION*
CNS Not Involved: Ampicillin/Sulbactam AND Vancomycin
CNS Involved: Ceftriaxone AND Vancomycin AND Metronidazole
Alternative to Ceftriaxone: Levofloxacin
Alternative to Vancomycin: Linezolid
Duration: 10-14 days after surgical drainage
*NYU Pediatric Antibiotic Stewardship 2021

COMPLICATIONS

Serious complications are rare in periorbital cellulitis, but can occur with orbital cellulitis.

ORBITAL CELLULITIS COMPLICATIONS
Sub-periosteal abscess
Orbital abscess
Cavernous sinus thrombophlebitis and or thrombosis*
Dural sinus thrombosis
Central retinal artery occlusion
Meningitis
Intracranial abscess
Epidural or subdural empyema
*Suspect if orbital inflammation occurs in contralateral eye

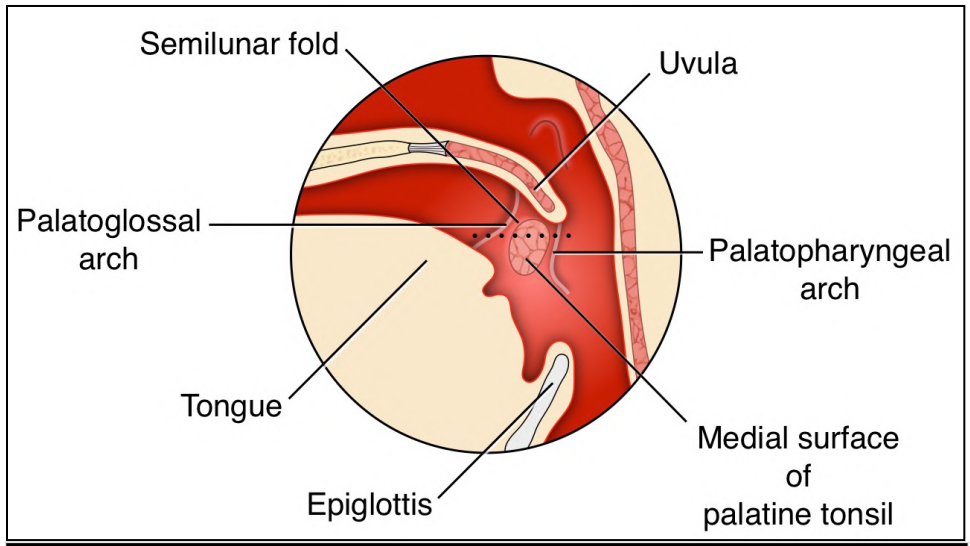
SURGERY

Surgical intervention may be required if there is poor response of orbital cellulitis to an appropriate antibiotics or is a large abscess (generally > 10 mm diameter) is present. A CT scan of the brain should be included if it was not completed initially. Abscesses can develop rapidly; patients need close monitoring of visual acuity and pupillary light reflex to assess for optic nerve dysfunction. Visual changes warrant repeat imaging and likely surgery. Signs of intracranial extension can include: headache, vomiting, altered mental status, and cranial nerve palsies. Vision loss from nerve and vascular ischemia occurs in 3-11% of patients, and death from orbital cellulitis occurs in 1-2% of patients.

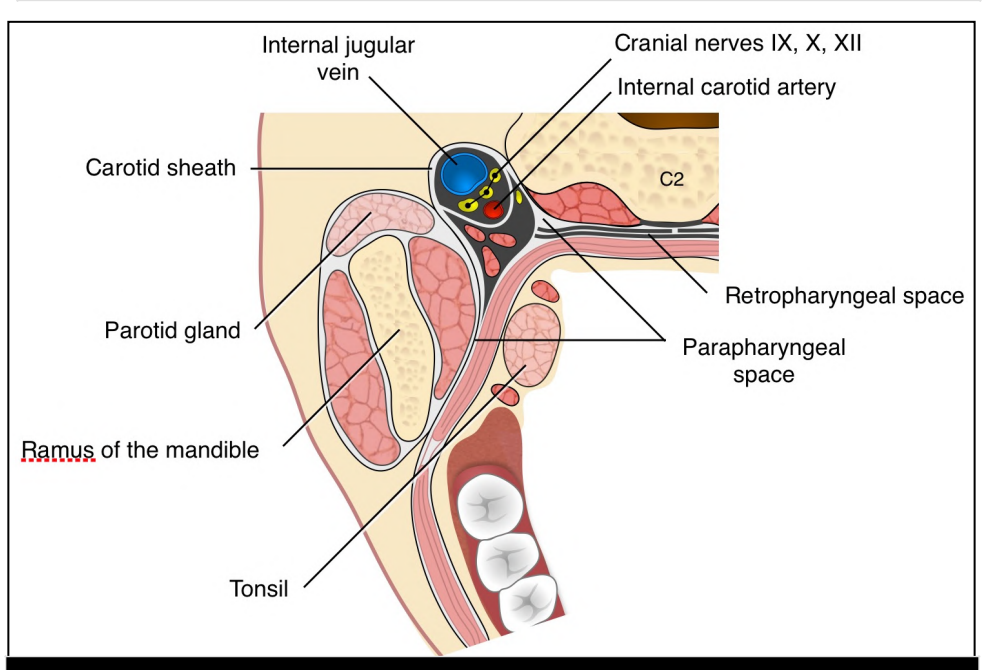
PERITONSILLAR ABSCESS

INTRODUCTION (ELLEN DUNCAN, M.D., PhD, 12/2017)
Peritonsillar abscess (PTA) is the most common deep infection of the neck. It occurs mostly in teenagers and young adults. Because Group A streptococcus is the most common causative organism, incidence of PTA peaks in November to December, and in April to May, when streptococcal pharyngitis is most common. (See also PEM Guide: Pharyngitis and PEM Guide: Retropharyngeal abscess.)

The pathophysiology of PTA is classically thought to involve an acute exudative tonsillitis that develops into a cellulitis and subsequently into an abscess. Pus accumulates between the palatine tonsil capsule and pharyngeal muscles. However, some research suggests that Weber's glands, which sit above the tonsils, may play an important role in development of PTA. This is supported by the fact that abscesses generally form above the superior pole of the tonsil, where the Weber's glands are located (Powell, J Antimicrob Chemother 2013, PubMed ID: 23612569).



PHARYNX ANATOMY: SAGITTAL



PHARYNX ANATOMY: TRANSVERSE

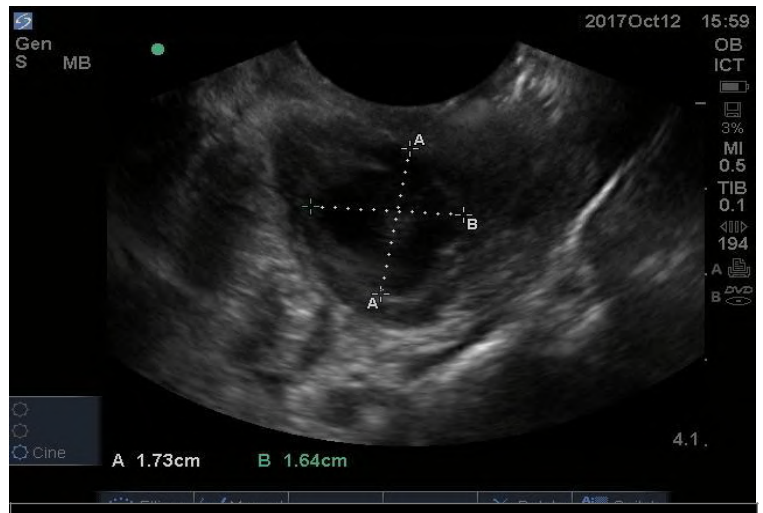
CLINICAL MANIFESTATIONS
Patients with PTA are often ill-appearing. Localizing symptoms include sore throat, dysphonia and dysphagia. Systemic symptoms include fever and malaise. The first priority is to establish the patency of the airway. If epiglottitis is suspected that patient should be left in a position of comfort and manipulation of pharyngeal structures should be avoided. A more complete examination can occur in the operating room.

Physical examination may show tender cervical lymphadenitis and erythema and swelling above the tonsil and overlying soft palate. Patients may also have uvula deviation to the unaffected side. Other exam findings include trismus, muffled ("hot potato") voice, and an inability to swallow secretions (drooling, spitting out secretions). Trismus is a limited ability to open the mouth due to irritation or reflex spasm of the pterygoid muscle and the pain that occurs with stretching of the inflamed pharyngeal tissue. The muffled voice occurs because the patient limits themselves to sounds that don't require movement of the posterior palate. Pain limits oral intake and there may be some degree of dehydration.

COMPLICATIONS
Airway obstruction
Infections: Aspiration pneumonia, mediastinitis, necrotizing fasciitis, sepsis
Vascular: Thrombosis of the internal jugular vein, septic thrombophlebitis of the jugular vein (Lemierre's syndrome), carotid artery rupture or pseudo-aneurysm

DIFFERENTIAL DIAGNOSIS
Peritonsillar cellulitis
Parapharyngeal abscess: AKA pharyngomaxillary or lateral pharyngeal space
Retropharyngeal abscess
Epiglottitis
Severe tonsillopharyngitis: EBV, Coxsackie. Adenovirus, Diphtheria, Lemierre's
Lymphoma

IMAGING: Although diagnosis is generally made based on history and physical examination, point of care intraoral ultrasound can increase the sensitivity and specificity of the diagnosis (Constantino, Acad EM 2012, PubMed ID: 22687177). CT with intravenous contrast MRI/MRA may be useful if the infection has spread beyond the peritonsillar space such as with parapharyngeal abscess, retropharyngeal abscess or Lemierre's syndrome or the diagnosis is unclear. Ensure that the patient can adequately protect their airway in a supine position before sending them for cross sectional imaging.



US: PERITONSILLAR ABSCESS

Ultrasound with an intracavitary probe can be used to distinguish between peritonsillar cellulitis and abscess. A mixture of viscous lidocaine and ultrasound gel can be applied to the tip of the probe and the patient asked to position the probe tip at the most painful location. A PTA will appear as an anechoic or hypoechoic lesion. In addition to localizing the abscess cavity medial and superior to the palatine tonsil, the ultrasound should identify vascular structures and in particular the carotid artery which is posterior and lateral to the abscess cavity. The carotid artery will appear as an anechoic tubular and pulsatile structure with color doppler. The ultrasound sound can also be used directly to guide drainage if trismus is not severe. The abscess location can be re-imaged after the procedure to ensure the adequacy of abscess drainage.

MANAGEMENT

Treatment consists of needle aspiration, incision and drainage, or tonsillectomy. Needle aspiration is the preferred technique in the emergency department. Needle aspiration is less invasive, less painful and less likely to cause bleeding than incision and drainage. A pooled analysis of 10 studies (612) patients found an increased rate of recurrence rate with needle aspiration compared with incision and drainage (RR: 3.74, 95% CI (1.63, 8.59) (Cochrane 2016, PubMed ID: 28009937). However, the authors emphasize that the quality of evidence was low. There is also evidence that there is no difference in treatment success and complication with medical therapy alone (antibiotics, steroids) when compared to medical and surgical therapy (Battaglia, Otolaryngology Head Neck Surg 2017, PubMed ID: 29110574).

Drainage should occur in a setting in which airway complications can be adequately assessed and managed. Adequate systemic and topic analgesia such as atomized benzocaine or lidocaine should be administered. Older and cooperative children can undergo needle aspiration or incision and drainage using topical anesthesia. Younger children or uncooperative patients may need to go to the operating room for surgical management. Tonsillectomy should be considered in patients with impending airway obstruction, failure or aspiration or incision and drainage and in those unable to cooperate with the procedure.

EQUIPMENT
Systemic and topical analgesia Topical Cetacaine spray (Benzocaine 14.0%, Butamben 2.0%, Tetracaine Hydrochloride 2.0%). Maximum 2 sprays (risk of Methemoglobinemia) Lidocaine 1% with Epinephrine to infiltrate tissue overlying abscess.
Ultrasound with intracavitary probe and ultrasound gel
Laryngoscope with a MAC 3 blade can be used as a tongue depressor and a light source to ensure adequate visualization. Use of a video laryngoscope for teaching. The patient can hold it to decrease the risk of gagging
10 ml syringes
Aspiration: Spinal needle (3.5 inch) Distal 1.5 cm of the needle cap cut off limits penetrable distance and puncture of the carotid artery. The longer spinal needle allows aspiration without having to put your hands into the oral cavity that has been narrowed by trismus.
Incision and Drainage: Scalpel
Suction catheter
Emesis basin
Cup of ice water: Patient gargles after the procedure to promote vasoconstriction

PROCEDURE: ABSCESS ASPIRATION
Administer systemic and topical analgesia
Position the patient in a sitting position leaning slight forward and the head angled slight downward to facilitate drainage of fluids and prevent aspiration.
Identify the abscess with ultrasound and an intracavitary probe
Have the patient hold the laryngoscope to improve visualization
Aspirate the abscess under direct ultrasound visualization if not limited by trismus or based on anatomic location previously identified by ultrasound.
Advance the needle into the abscess cavity while providing negative pressure on the syringe plunger Do not advance the needle beyond the cut of needle cap tip to avoid penetrating the carotid artery Most PTAs occur at the superior pole of the tonsil. If aspiration at the superior pole is unsuccessful then aspiration can be attempted at the middle and inferior pole as well.
Re-image to the area of the abscess to ensure the adequacy of drainage.

VIDEO LINK: PERITONSILLAR ABSCESS ASPIRATION

ANTIBIOTIC SELECTION: Infection is typically polymicrobial. The most common causative organisms include Group A strep, S. aureus, H. influenza, Fusobacterium necrophorum, peptostreptococcus, and prevotella. Antibiotics should target Group A streptococcus and oral anaerobes. Appropriate oral antibiotics include Amoxicillin/Clavulanate, a combination of Penicillin VK and Metronidazole or Clindamycin in the penicillin allergic patient. Ampicillin/Sulbactam is the most commonly prescribed intravenous antibiotic choice. Vancomycin, Clindamycin, and Linezolid can be used intravenously if methicillin resistant staph aureus is suspected.

CORTICOSTEROIDS: Steroids (e.g. Dexamethasone 0.6 mg/kg, maximum 10 mg IV) are often prescribed to reduce edema and duration of symptoms though the evidence is limited (Lee, Clin Exp Otolaryngology 2016, PubMed ID: 27090283).

DISPOSITION

Patients with improvement in pain and able to tolerate fluids can be safely discharged with follow up in the next 24-48 hours. If pain does not improve significantly after aspiration then cross-sectional imaging and ENT consultation should be considered.

PHARYNGITIS

INTRODUCTION (MICHAEL TUNIK, M.D. 4/2020)
Sore throat is a very common presenting complaint in children with inflammation and infection of the pharynx (pharyngitis). The most common causes are viral and streptococcal infections. Consider other etiologies to avoid missing serious, treatable, or life-threatening causes. The challenge is to determine if the patient with sore throat has: a self-limited viral illness, a bacterial infection that may be readily identified by testing and treated or a more serious condition.

LIFE-THREATENING CAUSES OF PHARYNGITIS
Abscess: Parapharyngeal, Peritonsillar*, Retropharyngeal*
Epiglottitis
Epstein Barr Virus (severe tonsillar enlargement)*
Diphtheria
Lemierre's syndrome: Septicemia with Fusobacterium nucleatum
Neisseria gonorrhea
Stevens-Johnson Syndrome*
Kawasaki disease*
Pharyngeal foreign body*
Ingestion of caustic substances*
*Reviewed in detail in specific PEM Guides

HISTORY
Age
Temperature
Time of year
Sick contacts
Past frequency and causes of pharyngitis
Vaccination status
Ingestions

PHYSICAL EXAMINATION
Most children with pharyngitis are alert and well hydrated with a normal mental status. Assess: temperature, general appearance, respiratory status, appearance of the pharynx, tonsils, cervical lymph nodes, and other localizing signs of infection.

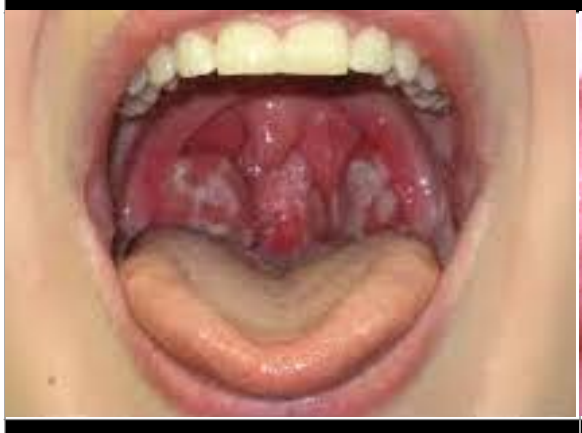
Patients with respiratory distress and/or stridor should be managed urgently. Maintain in a position of comfort, avoid agitation and provide blow by oxygen in a non-threatening manner. Consultation with ENT or anesthesiology may be required for operative evaluation of the oropharynx (e.g. suspected epiglottitis, retropharyngeal abscess). Patients who demonstrate sign of dehydration should be provided with oral or intravenous fluids. Oral fluids should be withheld in patients in patients with a caustic ingestion, foreign body, or respiratory distress.

PHYSICAL EXAMINATION FINDINGS	
ETIOLOGY	FINDING
Viral, Herpetic infection	Stomatitis
Stephens Johnson	
Kawasaki (also strawberry tongue)	
Herpes (anterior pharynx)	Vesicles, Ulcers
Coxsackie (posterior pharynx)	
Behcet's syndrome	
EBV	Cervical adenopathy (post), splenomegaly
Diphtheria	Grey membrane, un-immunized
GAS, non-GAS, gonococcal infection	Thick exudates
Peritonsillar abscess	Unilateral enlarged tonsil, uvula deviated, palatal swelling drooling, trismus,
Retropharyngeal abscess	Posterior pharynx swollen, drooling, stiff neck, history FB penetrating pharynx

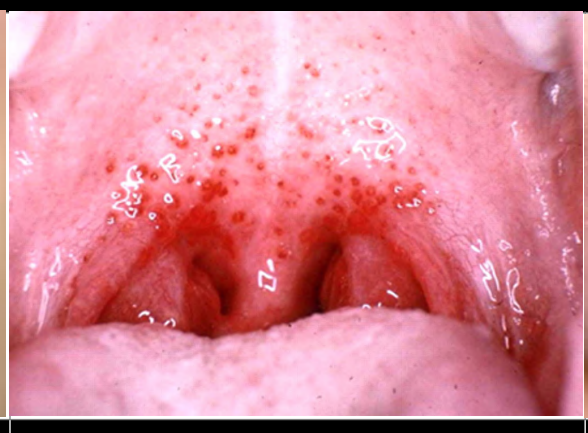
GROUP A STREPTOCOCCAL (GAS) PHARYNGITIS

Oral examination findings suggestive of streptococcal findings include and exudate pharyngitis, glossitis (strawberry tongue) and palatal petechiae. Extra-oral findings include perioral pallor and cervical adenitis, Pastia's lines in the antecubital fossa and a scarlatiniform rash.

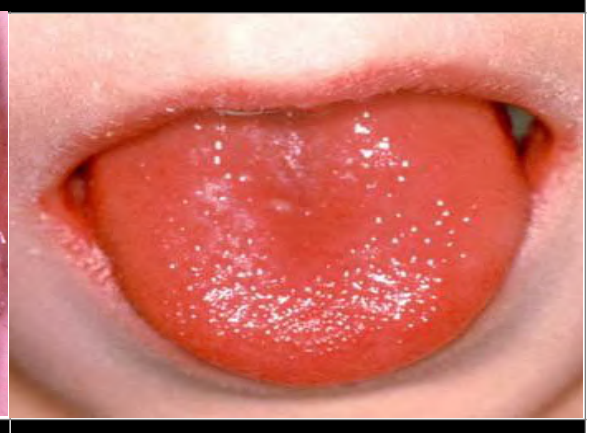
GROUP A STREPTOCOCCUS: PHYSICAL EXAM FINDINGS



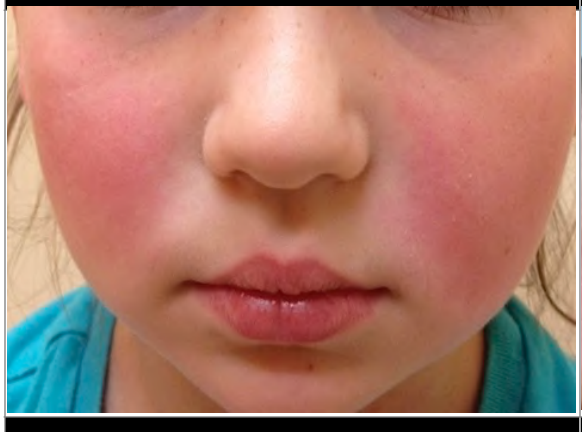
EXUDATIVE TONSILLITIS



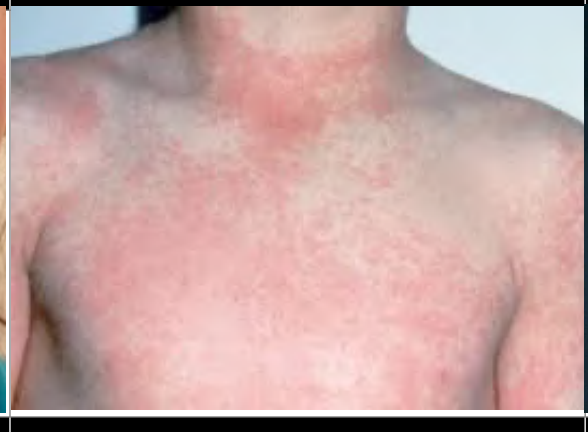
PALATAL PETECHIAE



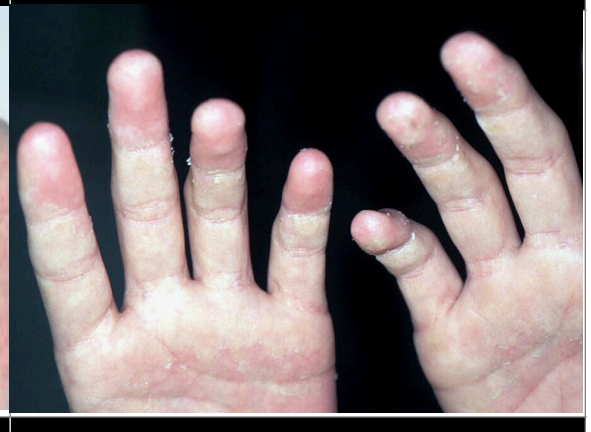
STRAWBERRY TONGUE



PERIORAL PALLOR



SCARLET FEVER



DESQUAMATION (LATE)

COMPLICATIONS OF STREPTOCOCCAL PHARYNGITIS	
Suppurative (Acute)	Non-Suppurative (Sub-Acute 1-3wks)
Peritonsillar abscess*	Acute rheumatic fever*
Retropharyngeal abscess*	Post-streptococcal glomerulonephritis*
Parapharyngeal abscess	
Otitis media*	
Cervical adenitis	
Sinusitis*	
*Reviewed in detail in specific PEM Guides	

SEASONALITY: Strep pharyngitis is most common in the winter. It occurs in 20% of children age 3-18 with a sore throat (Summer: 5%. Fall and Spring: 10%).

SCORING: Scoring Systems to differentiate viral from streptococcal pharyngitis have been developed. They are not accurate enough to differentiate viral pharyngitis from streptococcal in all cases. One example is the Centor score. A score of 4 makes strep pharyngitis very likely, and a score of 0 makes it unlikely. Scores of 1,2,3 have an intermediate risk of strep and frequently other testing is needed. The Centor score can be combined with season to approximate the pre-test probability of strep pharyngitis.

CENTOR SCORE	
CRITERIA	POINTS
Fever	1
Tonsillar exudates or palatal petechiae	1
Tender anterior cervical node(s)	1
Absence of URI Symptoms	1

STREPTOCOCCAL PHARYNGITIS LIKELIHOOD: BY SEASON AND CENTOR			
CENTOR SCORE	SUMMER (5%)	SPRING/FALL(10%)	WINTER (20%)
0	O.64 %	1.3 %	3 %
1	1.7	3.5	7.6
2	4.5	9	18
3	11.4	21	38
4	26	42	62

LABORATORY EVALUATION

The need for laboratory testing should be individualized. Testing for Group A strep is not recommended for children and adults with findings strongly suggestive of a viral syndrome (cough, rhinorrhea) or for children less than 3 years old due to their low risk of strep pharyngitis and subsequent acute rheumatic fever.

RAPID ANTIGEN TESTING OR PCR: In cases that have an intermediate risk of strep based on season and symptoms a rapid antigen test can be used further classify the likelihood of strep. The rapid antigen test will not identify non-Group A strep and will be negative (as will the culture) after one or two doses of antibiotics. Testing of asymptomatic household contacts is not recommended.

CULTURE: Children and adolescent patients with a negative rapid antigen test should have a throat culture sent. This is not recommended in adults due to the low risk of subsequent rheumatic fever.

MANAGEMENT

Strep pharyngitis is treated with antibiotics. Typical treatment is either parenteral (IM) or oral Penicillin VK or Amoxicillin. Treatment with antibiotics has not been proven to significantly reduce the time to symptom resolution. Treatment is aimed at: reducing transmission, reducing suppurative and non-suppurative complications. Recent population-based studies have shown that the risk of acute rheumatic fever has reduced significantly (though accurate estimates are not available). Some have argued that treatment may not be warranted (Number needed to treat approximately 5,000).

ANTIBIOTIC SELECTION: The first line antibiotic is Penicillin. Amoxicillin is commonly substituted. Multiple studies suggest that a single oral dose of Amoxicillin (50 mg/kg, maximum of 1 gram) given once a day for 10 days is efficacious. For children who do not tolerate oral therapy Intramuscular Penicillin (Pen G Benzathine) is an alternative. (See Appendix for Antibiotic Dosing)

Though the in vitro resistance of GABHS to Penicillin has not increased there have been increasing reports of treatment failures with Penicillins. This may be due to the high concentration of beta lactamase producing organisms in the normal oral flora of children that may reduce the effective concentration of Penicillins. For this reason, some experts suggest treatment with a cephalosporin or Amoxicillin/Clavulanate).

For a patient with non-type 1 allergy to penicillin a first-generation cephalosporin such a cephalexin may be substituted for a penicillin. For type 1 Penicillin allergic patients, a macrolide (Clarithromycin or Azithromycin) or Clindamycin may be used. Sulfa drugs and Tetracyclines are not effective alternatives.

ADJUNCTIVE THERAPY: Provide pain relief (acetaminophen, Ibuprofen) and instructions for oral hydration. Severe pain may be treated with topical analgesics: viscous lidocaine swish and spit (risk of overdose when too much is swallowed) or a mixture of diphenhydramine and kaopectate swish and spit. There is evidence that the adjunctive use of oral corticosteroids may hasten symptom resolution. There is little pediatric data to suggest the corticosteroids are more efficacious than Acetaminophen or Ibuprofen and are therefore not recommended.

DISPOSITION

Most children with pharyngitis can be discharged home. They may return to school after 24 hours of antimicrobial therapy. Those who cannot tolerate oral fluids, or who have respiratory distress, altered mental status, or a serious cause of pharyngitis should be managed as inpatients.

APPENDIX: ANTIBIOTIC SELECTION AND DOSING

GROUP A STREPTOCOCCAL PHARYNGITIS: ANTIBIOTIC SELECTION		
Name	Pediatric Dose	Adult Dose
PENICILLINS		
Penicillin V	250mg BID-TID (< 27kg) 500mg BID-TID (> 27kg)	500 mg BID-TID
Amoxicillin	50 mg/kg QD (can also be divided BID or TID)	1 gram PO QD 500 mg BID
PCN G Benzathine (LA Bicillin)	600,000 units IM x 1 (< 27kg) 1.2 million units IM x 1 (> 27kg)	1.2 million units IM x 1 dose
CEPHALOSPORINS		
Cephalexin (1st)	20 mg/kg BID	500 mg BID
Cefadroxil (1st)		1 gram PO QD
Cefuroxime (2nd)	10 mg/kg BID	250 mg BID
Cefpodoxime (3rd)	5 mg/kg BID	100 mg BID x 5-10 days
Cefdinir (3rd)	7 mg/kg BID x 5-10 days 14 mg/kg QD	600 mg 300 mg BID x 5-10 days
Cefixime (3rd)		400 mg QD x 10 days
MACROLIDES		
Azithromycin	12 mg/kg D1, 6 mg/kg D2-5	500 mg D1, 250 mg D2-5 500 mg QD x 3 days
Clarithromycin	7.5 mg/kg BID	250 mg BID
LINCOSAMIDES		
Clindamycin	7 mg/kg TID	300 mg TID
All doses are oral except Benzathine PCN (which is IM) All durations are for 10 days unless otherwise specified All pediatric dose are mg/kg/dose (not mg/kg/day to be divided) Pediatric maximum individual doses are the adult dose		

RETROPHARYNGEAL ABSCESS

I**NTRODUCTION** (MICHAEL MOJICA, M.D., 2/2022)

A retropharyngeal abscess (RPA) is a potentially life-threatening suppurative infection of the deep tissues of the neck (the retropharyngeal space). The retropharyngeal space is a potential space that extends from the base of the skull to the posterior mediastinum. Adjacent infections such as an upper respiratory infection, pharyngitis, otitis media and sinusitis may spread to retropharyngeal lymph nodes. These nodes then become infected and suppurate, develop into an abscess. The nodes are more prominent in young children. RPA typically occurs between 2 and 5 years with 96% prior to 6 years of age when the retropharyngeal nodes typically disappear. RPA is rare after 6 years of age outside the setting of pharyngeal trauma.

RETROPHARYNGEAL ABSCESS: COMPLICATIONS
Airway obstruction
Distal extension: Empyema, mediastinitis, pericarditis, aspiration pneumonia
Vascular involvement: Jugular vein thrombosis, carotid artery rupture
Posterior extension: Osteomyelitis, meningitis
Sepsis
Necrotizing fasciitis

BACTERIOLOGY: TYPICALLY POLYMICROBIAL	
Gram (+)	Group A Strep, Staph aureus (MSSA and MRSA)
Respiratory Anaerobes	Bacteroides, Fusobacterium, and Peptostreptococcus
Rare	Gram (-): Eikenella corrodens, Bartonella hensalae, Mycobacterium Tuberculosis

CLINICAL PRESENTATION

A high index of suspicion is required as history and physical examination findings are often nonspecific. Patients may have a preceding upper respiratory infection, pharyngitis, peritonsillar abscess, parapharyngeal abscess, otitis media or parotitis.
Penetrating trauma from a fall with a foreign body in the mouth or airway procedures (intubation, dental procedures, nasogastric tube placement) may also result in infection.

The child typically presents with fever, a toxic appearance and respiratory distress.
Symptom progression is less acute than epiglottitis. The diagnosis should be considered in a patient with a severe sore throat and/or inability to tolerate oral fluids and a normal pharyngeal exam.

Limited extension of the neck is typically seen in retropharyngeal abscess (extension stretches the prevertebral soft tissues) while neck flexion is unimpaired. In contrast, meningitis causes limitation of neck flexion and unimpaired neck extension. In addition, meningitis is more commonly associated with an altered mental status (irritability, somnolence). Patients with severe symptoms who are at risk for airway obstruction should be examined in the operating room in conjunction with ENT and anesthesia.

SIGNS AND SYMPTOMS	
SYMPTOMS	SIGNS
Fever	Torticollis
Dysphagia/odynophagia	Dysphonia
Neck stiffness (limited extension)	Stridor
Poor oral intake	Drooling
Preference for supine position	Exudative pharyngitis
Chest pain (mediastinitis)	Trismus
Difficulty breathing	Pharyngeal bulging (rare)
Irritability	Cervical lymphadenitis

DIFFERENTIAL DIAGNOSIS: LIFE THREATENING CAUSES OF DYSPHAGIA	
Airway foreign body	Ludwig’s angina
Angioedema/anaphylaxis	Lymphoma
Bacterial tracheitis	Kawasaki disease
Caustic ingestion	Neisseria gonorrhea
Diphtheria	Peritonsillar, retropharyngeal abscess
Epiglottitis	Post tonsillectomy hemorrhage
Epstein Barr Virus (tonsillar enlargement)	Stevens-Johnson Syndrome
Lemierre’s: Septic thrombophlebitis, internal jugular vein, Fusobacterium necrophorum	

LABORATORY TESTING

Laboratory evaluation may reveal nonspecific elevation in the white blood cell count and acute phase reactants. Blood culture yield is low

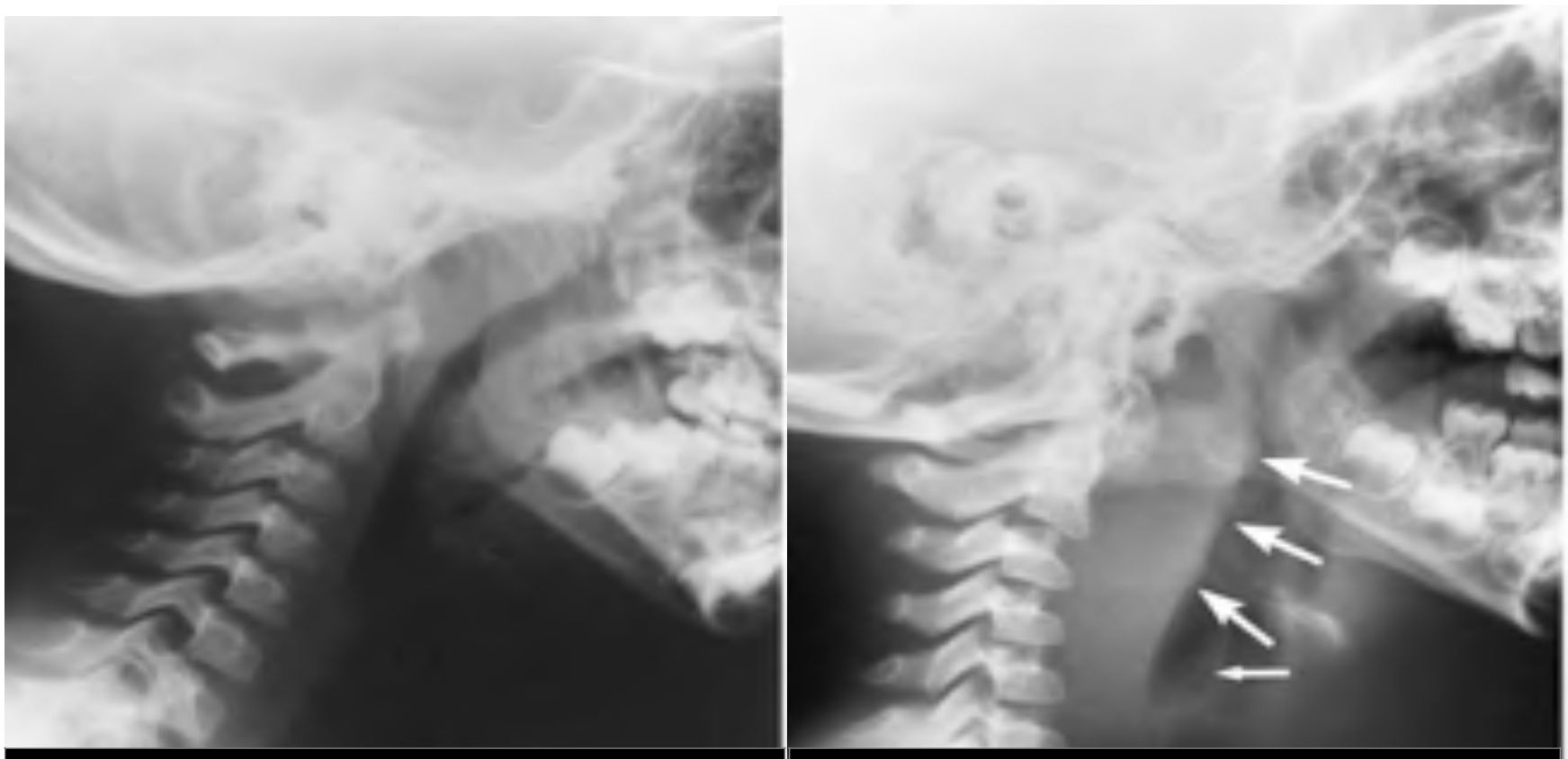
RADIOLOGIC EVALUATION

NECK SOFT TISSUE: A lateral neck soft tissue XRAY may reveal swelling of the prevertebral soft tissues. Typically, the prevertebral thickness is less than 2-thirds of the adjacent vertebra from C2-C3 4 and less than one vertebral width from C5-8. Alternatively, the specific normal criteria of C2 ≤ 7mm, C6 ≤ 14mm (<15yrs) and ≤ 22mm (>15yrs).

The XRAY should be obtained in extension on inspiration. Flexion of the neck, expiration and crying may result in pseudo-enlargement of the prevertebral space.Air or an air fluid level may also be seen in the prevertebral tissue. Normal cervical lordosis may be lost secondary to muscle spasm and inflammation. Epiglottitis and radiopaque foreign bodies may also be identified.

CHEST XRAY: A chest XRAY should be considered to identify pneumonia/empyema and mediastinitis.

CT SCAN: A CAT scan with contrast of the neck will better identify the nature of the infection (cellulitis versus abscess) and the extent of the lesion as well as proximity to vasculature, lateral spread) and will assist in determining the surgical approach. In addition, it may identify a radiolucent foreign body. Care should be taken in sedating the patient with a retropharyngeal abscess. Muscle relaxation may precipitate complete airway obstruction. Appropriate equipment and personnel trained in advanced airway management including surgical airways should be present.



NORMAL PREVERTEBRAL SOFT TISSUE

SWELLING OF THE PREVERTEBRAL SOFT TISSUE (ARROWS)

MANAGEMENT

Supportive care includes airway maintenance/monitoring, hydration and analgesia. The patient should be allowed to stay in a position of comfort (e.g. sitting in their parent's lap). Patients may benefit from a dose of corticosteroids and nebulized Epinephrine to reduce swelling.

SURGERY: ENT should be consulted. Definitive criteria for surgery have not been established. Those with airway compromise, a large abscess (> 2cm) or who fail initial antibiotic therapy are candidates for surgery. Specimens for aerobic and anaerobic culture should be sent at the time of surgical drainage. In general, those without airway compromise and without evidence of a mature abscess may be managed with antibiotics alone initially. Antibiotics early in the disease course may prevent progression and subsequent need for surgery.

ANTIBIOTICS: Infection is typically polymicrobial. Antibiotics that cover Gram positive (Group A Strep, Staph aureus (MSSA and MRSA)) and respiratory anaerobes (Bacteroides, Fusobacterium, and Peptostreptococcus) are required. Gram-negative pathogens are rare. Eikenella corrodens, Bartonella hensalae and Mycobacterium tuberculosis have also been infrequently implicated. These rare organisms should be considered if there is inadequate response to therapy.

Though many different antibiotic regimens have been suggested, no comparative treatment studies for retropharyngeal abscesses have been reported. Empiric therapy should cover Group A Strep, Staph aureus and respiratory anaerobes. Antibiotic coverage may need to be adjusted based on cultures and/or clinical response. Ampicillin/Sulbactam does not cover MRSA. Clindamycin covers MSSA but depending on local resistance does not cover MRSA and some group A Strep.

ANTIBIOTIC SELECTION	
Mild	Ampicillin/Sulbactam OR Clindamycin
Moderate-Severe	Vancomycin OR Linezolid AND Ampicillin/Sulbactam

STEROIDS: The use of steroids in retropharyngeal abscess is highly variable. A study including 46 pediatric tertiary care center found a range of use in these patients of 0-84% of patients (Goenka, Pediatrics. 2021, PubMed ID: 34697219). Surgical drainage occurred less frequently in the steroid group when compared with the non-steroid group (22% vs 51.5%), (Risk Difference: 29.4%, 95% CI (25.1, 33.3%)) with a significantly lower odds of surgery in the steroid group (OR: 0.28, 95% CI 0.22-0.33). This risk difference corresponds to a number need to treat is 3.4 (NNT = 1/ARD = 1/.293 = 3.4) for every 3.4 patients treated with corticosteroids, 1 additional patient would be spared surgery compared to no steroid treatment).

In the steroid group, there was a statistically significant higher rate of more than one CT performed (Risk Difference: 3.4%, 95% CI (0.9, 6.3%)) and ED revisit (Risk Difference: 2.3%, 95% CI (0.8, 4.3%)). Required interventions or number of patients re-admitted from the 7-day ED revisit was not presented. There was a statistically significant lower rate of the use of opioid analgesia (Risk Difference: 9.2%, 4.5, 13.9%)) and health care costs (Risk Difference: $1,039). The clinical significance of these differences is unclear. There was no statistically significant difference between the groups in use of intravenous fluids, intravenous analgesia, hospital length of stay or 30 days re-admission. There results should be considered in the context of the limitations of using a primarily administrative database lacking important clinical data such as whether the lesion was an abscess or phlegmon, the size of the lesions and the dose and duration of steroid treatment.

DISPOSITION

Patients who do not go directly to the OR should be admitted to the intensive care unit for airway monitoring.

SINUSITIS

INTRODUCTION (BRENT ROGERS, M.D. 3/2018)
The normally sterile sinuses can be predisposed to bacterial entry due to changes in their normal physiology, including mechanical obstruction (nasal polyps) or damage to cilia (viral or allergy induced inflammation), increased intra-cavity pressure (sneezing, sniffing, nose blowing), and thickened secretions (cystic fibrosis). The sinuses develop and aerates at varying times. Each sinus is connected to the nasal cavity via a passage or ostia.

SINUS DEVELOPMENT		
LOCATION	DEVELOPMENT	AERATES
Maxillary	Birth	4 months
Ethmoid	Birth	4 months
Sphenoid	3 years	8 years
Frontal	6-8 years	Adolescence

Acute bacterial sinusitis (ABS) or acute bacterial rhinosinusitis (ABRS) is defined as any infection of the paranasal sinuses lasting less than 30 days (subacute is 30-90 days; chronic is > 90 days). In children less than 10 years of age maxillary sinusitis is most common. In the patient with acute respiratory tract symptoms such as nasal congestion, rhinorrhea and cough, it is essential to differentiate between uncomplicated viral infections and sinusitis. An estimated 5-13% of the 6-8 viral upper respiratory tract infections (URI's) that children have each year are complicated by bacterial sinus infection. Correct identification is important to starting antibiotics promptly in order to improve symptoms and avoiding serious complications.

Infection of the paranasal sinuses may result in occasional life-threatening complications. Complication of ABS are due to spread by local extension. Hematogenous spread may occur with frontal sinusitis. Orbital complications are most commonly due to ethmoid sinusitis. CNS complications are most commonly due to frontal sinusitis.

COMPLICATIONS OF SINUSITIS		
ORBITAL	INTRACRANIAL	OSTEOMYELITIS
Periorbital cellulitis*	Cavernous sinus thrombosis	Frontal (Pott's puffy tumor)
Sub-periosteal abscess	Sagittal sinus thrombosis	Maxillary
Orbital abscess*	Epidural empyema	
Orbital cellulitis	Subdural abscess	
Optic neuritis	Meningitis	
	Brain abscess	
*See: PEM Guide: Head and Neck Infections: Periorbital and Orbital Cellulitis		

CLINICAL PRESENTATION

Sinusitis symptoms overlap considerably with those of uncomplicated upper respiratory infections. To differentiate the two, it is essential to understand the typical course of a URI. In a URI, fever typically presents early in the first 24-48 hours. Cough, nasal congestion, coryza, headache, sore throat and muscle aches follow, peaking at 3-6 days. Symptoms then gradually resolve. Most URI's last for 5-7 days but some may persist up to 10 days. Symptoms such as the character of the nasal discharge, headache, facial pain and halitosis do not reliably distinguish between sinusitis and URI.

The physical exam is also of limited value in differentiating sinusitis from rhinitis. Findings such as: mucopurulent discharge, erythematous and boggy nasal mucosa, and sinus tenderness, may be seen in both conditions. Transillumination of the sinuses does not distinguish between sinus congestion and sinus infection. The diagnosis of sinusitis is made on clinical grounds based on the severity and persistent or worsening of symptoms. The Infectious Disease Society of America's pediatric and adult sinusitis guidelines (IDSA 2012, PubMed ID: 22438350) and the American Academy of Pediatrics pediatric sinusitis guideline (AAP: 2013, PubMed ID: 23796742) define presentations as persistent, severe or worsening symptoms.

DIAGNOSIS OF ACUTE SINUSITIS IN CHILDREN: AAP 2013		
PERSISTENT ILLNESS	SEVERE ONSET	WORSENING COURSE
Nasal discharge (of any quality) or daytime cough, or both lasting > 10 days without improvement	Concurrent fever (T ≥ 39°C) and purulent nasal discharge for a least 3 consecutive days	Worsening or new onset of nasal discharge, daytime cough after initial improvement

DIAGNOSIS OF ACUTE SINUSITIS IN CHILDREN AND ADULTS: IDSA 2012		
PERSISTENT SYMPTOMS	SEVERE SYMPTOMS	WORSENING SYMPTOMS
Nasal discharge, cough, or both present > 10 days and not improving	High fever (T ≥ 39° C) and purulent nasal discharge together for > 3-4 days	Resolving URI symptoms (5-6 days) which worsen around illness day 7 with new or recurrent fever, headache and exacerbation of nasal symptoms and/or cough

PERSISTENT: The most common presentation of sinusitis is persistent symptoms of nasal discharge and/or cough lasting 10-30 days without improvement. Most uncomplicated episodes of viral URI resolve within 5-7 days, and even when they last longer they will have peaked in severity and are improving by day 10.

SEVERE: Another presentation of sinusitis is a "cold" that seems more severe with an abrupt onset, persistence of high fever (≥ 39° C / 102.2° F) and purulent, opaque discharge for at least 3-4 consecutive days. Viral URI's commonly have fever early, which resolves within 48 hours, followed by the onset of respiratory symptoms. Viral nasal discharge is also watery initially, becoming thicker and more opaque over days.

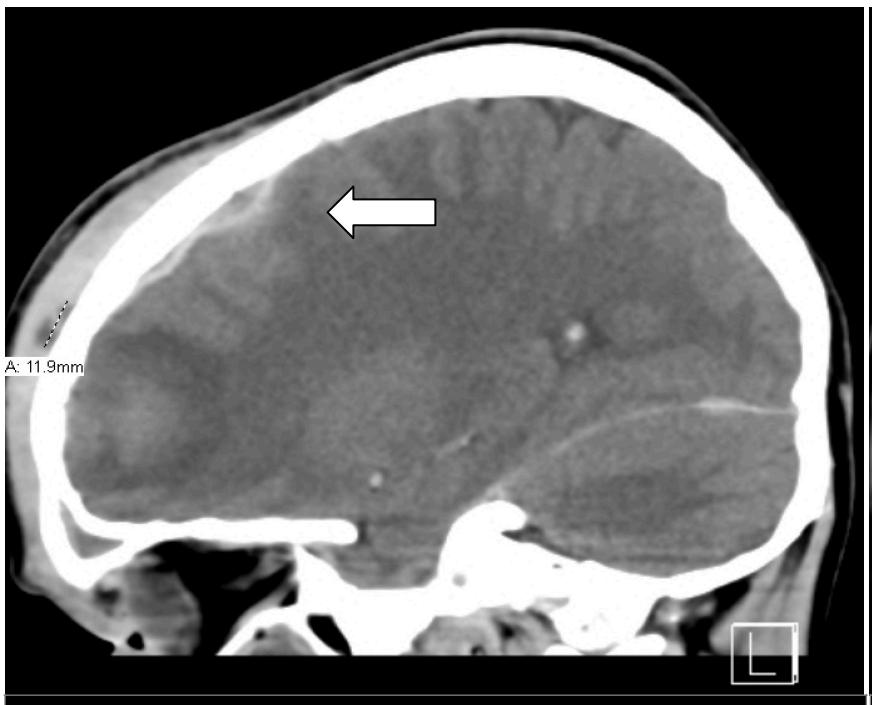
WORSENING: The least common presentation of sinusitis includes a biphasic illness with a seemingly improving uncomplicated viral URI with worsening of symptoms around day 6-7 of illness. This worsening is manifested by the new onset or recurrence of fever and increase in respiratory symptoms.

RADIOLOGIC EVALUATION

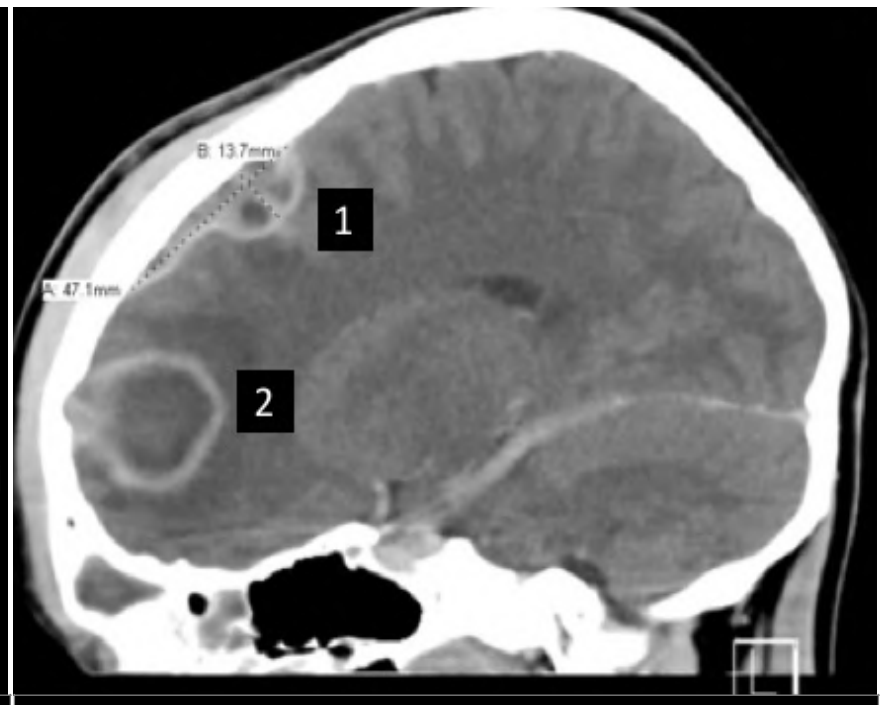
Radiographic imaging (plain XRAY, CT or MRI) should not be used routinely. Correct positioning for plain radiographs is difficult to achieve in young children. Positive findings include diffuse opacification of the sinus, mucosal thickening of ≥ 4mm, or air-fluid levels. Studies indicate that nearly 100% of children with a history of respiratory tract infection in the prior 2 weeks will have soft tissue changes. The presence of soft tissue changes does not distinguish between sinus congestion and sinus infection.

A CT with contrast should be reserved for patients with suspected orbital or central nervous system complication or to establish precise sinus anatomy in those being considered for surgery (significant recurrent or chronic sinusitis).

Indications for CT or MRI include: proptosis, impaired vision, limited extraocular movements, severe facial pain, swelling of the forehead or face, abnormal neurologic exam and toxic appearance. Bilateral symptoms and cranial nerve palsies (III, IV, V1, V2 and V6) are suggestive or intracranial extension such as cavernous sinus thrombosis. A lumbar puncture is indicated if meningitis is suspected (meningeal signs, altered mental status, seizures).



ABSCESS/OSTEOMYELITIS (POTTS PUFFY TUMOR)



1. EPIDURAL EMPYEMA
2. BRAIN ABSCESS

CULTURE: Maxillary sinus aspiration for gram stain and culture (aerobic/anaerobic) by a skilled otolaryngologist is the gold standard of sinusitis diagnosis but is rarely necessary. The procedure is invasive and often requires sedation in children. Aspiration may be indicated when a lack of response to multiple courses of antibiotics, orbital or intracranial complications, or with sinusitis in an immunocompromised patient.

MANAGEMENT

Randomized clinical trials using strict definitions of sinusitis and comparing antibiotics to placebo have demonstrated improvement in symptoms and clinical cure with antibiotics. (Wald, Pediatrics 2009, PubMed ID: 19564277). The IDSA and AAP guidelines agree that children meeting the clinical diagnostic criteria for severe or worsening sinusitis should be treated with antibiotics to achieve a rapid cure and prevent complications. Unlike the IDSA guidelines that recommend treatment for all categories of sinusitis, the AAP guidelines suggest that those meeting criteria for persistent sinusitis may be treated or observed for 72 hours, similar to the approach recommended for acute otitis media. Consultation with ENT, ophthalmology or neurosurgery may be indicated depending on the location of the complication.

MICROBIOLOGY: The bacteriology of sinusitis is similar to that of acute otitis media. There have been no studies of sinusitis bacteriology in the post pneumococcal vaccine eras (Prevnar 7 (2000), Prevnar 13 (2010)). Treatment recommendations are therefore extrapolated from otitis media tympanocentesis studies. The most important bacterial pathogens in sinusitis are *Streptococcus pneumonia (SP)* (30%), non-typeable *Haemophilus influenza (HF)* (20-30%), and *Moraxella catarrhalis* (MC) (10-20%). These are the same pathogens often implicated in acute otitis media and treatment recommendations are therefore similar. There is considerable geographic variation in resistance rates to penicillin – SP (10-50%), HF (10-40%), MC (100%). Sinusitis due to *S. aureus* and respiratory anaerobes is rare.

ANTIBIOTIC INDICATIONS: CLASSIFICATION OF SINUSITIS			
	PERSISTENT	SEVERE	WORSENING
IDSA 2012	Antibiotics	Antibiotics	Antibiotics
AAP 2013	Antibiotics* or Observation: 3 Days	Antibiotics	Antibiotics

*Patients with persistent sinusitis who should be treated with antibiotics include:
1. Treatment with antibiotics in the past month
2. Concurrent bacterial infection such as acute otitis media, streptococcal pharyngitis
3. Actual or suspected orbital or CNS complications of sinusitis
4. Underlying disease such as: asthma, cystic fibrosis, immunodeficiency, prior sinus surgery or anatomic abnormalities of the upper respiratory tract

ANTIBIOTIC SELECTION: The IDSA recommends Amoxicillin/Clavulanate as first line therapy based on the increasing prevalence and antibiotic resistance of H. Influenza infection. High dose Amoxicillin/ Clavulanate (90 mg/kg/day) is indicated for: areas with > 10% Streptococcal pneumoniae resistance, severe symptoms (systemic toxicity, fever), age less than 2 years, day care attendance, antibiotics use within 1 month, recent hospitalization or for patients who are immunocompromised. The duration of therapy is a minimum of 10 days or for 7 days after symptom resolution.

The AAP guidelines recommend Amoxicillin +/- Clavulanate. Amoxicillin should be dosed at regular or high dose depending on local SP resistance rates. Clavulanate should be considered for those with moderate-severe illness, attend child care of have received antibiotics within the past month. The AAP acknowledges that as SP infection becomes less common due to the pneumococcal vaccines and HFlu infection becomes relatively more common than Amoxicillin/Clavulanate may be required as first line therapy.

The guidelines also differ in the recommendations of treatment for penicillin allergic patients. The AAP guideline indicates that the risk of serious allergic reaction to 2nd and 3rd generation cephalosporins is near zero or equal to non-penicillin allergic patients. Macrolides and trimethoprim/sulfamethoxazole are not recommended due to high rates of HF and SP resistance.

ADJUVANT THERAPIES: There is currently insufficient data to support the uses of: saline nasal irrigation, antihistamines, alpha agonist decongestants and mucolytic agents as a supplement to antibiotics. Intranasal corticosteroids may be used primarily for patients with a history of allergic rhinitis.

FOLLOW-UP: Clinical improvement with resolution of fever and reduction of nasal discharge and cough should be evident in 48-72 hours. The initial management strategy should be changed if symptoms fail to improve.

MANAGEMENT AT FOLLOW-UP
Patient with failure to improve* OR worsening infection** and is well appearing AND if there is no clinical suspicion of orbital or CNS complications
Antibiotics should be started if they have not already been initiated
If Amoxicillin was used initially then change to Amoxicillin/Clavulanate
If Amoxicillin/Clavulanate was used initially then change to: Clindamycin and Cefixime OR Clindamycin and Linezolid OR Levofloxacin
Patient with failure to improve* OR worsening infection** and is ill appearing OR if there is clinical suspicion of orbital or CNS complications
Should be hospitalized
Antibiotic coverage with an IV third-generation cephalosporin (Cefotaxime, Ceftriaxone) and possibly Vancomycin (for staph coverage) and/or Metronidazole (for anaerobic coverage)
Imaging: CT with contrast or MRI
Consultation with an otolaryngologist, infectious disease, ophthalmologist, or neurosurgeon may be necessary based on the complication
*Failure to improve: lack of reduction in all clinical symptoms within 72 hours. **Worsening infection: progression of initial symptoms or develops new symptoms

APPENDIX; SINUSITIS ANTIBIOTIC SELECTION

ACUTE BACTERIAL SINUSITIS TREATMENT: AAP 2013	
SYMPTOMS/SITUATION	INTERVENTION
Uncomplicated sinusitis Mild to moderate > 2 years of age No child care attendance No antibiotics past month	Amoxicillin (standard dose) if SP resistance < 10% 45 mg/kg/day divided BID (max 2 grams/dose) Duration: Until 7 days after symptom free
	Amoxicillin (high dose) if SP resistance > 10% 80-90 mg/kg/day divided BID (max 2 grams/dose) Duration: Until 7 days after symptom free
Uncomplicated sinusitis Moderate to severe < 2 years of age Child care attendance Antibiotics in past 4 weeks	Amoxicillin/Clavulanate (high dose) Amoxicillin 80-90 mg/kg/day + Clavulanate 6.4 mg/kg/day divided BID (max Amoxicillin 2 grams) Duration: Until 7 days after symptom free)
Not tolerating oral ABx	Ceftriaxone: 50 mg/kg IV/IM
Penicillin allergy	Child (Type 1, non Type1) Cefdinir, Cefuroxime, Cefpodoxime OR (Clindamycin or Linezolid) and Cefixime OR Levofloxacin
Toxic appearing Complicated sinusitis Persistent symptoms (> 72 hours on Antibiotics)	Hospitalization Sinus CT scan with contrast PRN ENT/Neurosurgery/Ophthalmology consultation PRN Ceftriaxone or Cefotaxime

ACUTE BACTERIAL SINUSITIS TREATMENT: IDSA 2012	
SYMPTOMS/SITUATION	INTERVENTION
First Line therapy	Amoxicillin-Clavulanate (high dose) Child: 90 mg/kg/day divided BID x 10-14 days Adult: 2 grams BID x 5-7 days
Penicillin allergy	Adults: Doxycycline or a respiratory fluoroquinolone (Levofloxacin or Moxifloxacin) Child (Type 1): Levofloxacin Child (nonType1):Clindamycin+3rd Gen Cephalosporin
Persistent symptoms (> 72 hours on Antibiotics) Major complications	Hospitalization Ceftriaxone or Cefotaxime ± Vancomycin, CT scan with contrast ENT consult: Consider sinus aspiration

UPPER RESPIRATORY INFECTIONS

INTRODUCTION (MARC AUERBACH, M.D. 10/2020)
Upper respiratory infections (URI) are acute, self-limited, infections of the upper respiratory tract (nasopharynx, oropharynx). URIs are responsible for 22 million missed school days/year in the US. Younger children will have a longer duration of symptoms. For this reason, the less than 6-year-old child is frequently reported to “always be sick”. It is normal for this age group to experience up to 1 upper respiratory infection per month. See also: PEM Guide: Infections: Enteroviral Infections, PEM Guide: Infections: Infectious Mononucleosis, PEM Guide: Infections: Influenza, PEM Guide: Infections: Measles, PEM Guide: Respiratory: Bronchiolitis and PEM Guide: Respiratory: Croup.

The causative viral agent varies by season. A simple URI can progress to involve the lower respiratory tract and other organ systems. It is important to look for clinical and historical information that suggest that the infection is not confined to the upper respiratory tract or that a secondary bacterial coinfection has occurred (e.g. acute otitis media, sinusitis, pneumonia). Patients with minimal respiratory reserve (co-morbid conditions) must be observed closely for complications.

Causative viruses are easily transmissible through inhalation of aerosols, hand-hand with self-inoculation, and the deposition of large droplets on surfaces (daycare). These viruses can survive up to two hours on a child’s hands and up to 3-5 days on a surface.

SEASONAL DISTRIBUTION: COMMON RESPIRATORY INFECTIONS

	J	F	M	A	M	J	J	A	S[1]	O	N	D
Enterovirus 68												
Rhinovirus[2]												
Adenovirus[3]												
Human parainflu 1,2[4]												
Human parainflu 3												
Influenza A												
Influenza B												
RSV[5]												
Human metapneumo												

BLACK: Peak Months
1. Coincide with start of school year, 2. Pharyngitis, 3. Pharyngitis conjunctivitis
4. Croup, 5. Bronchiolitis

ASSOCIATED ILLNESS	
Bronchiolitis	Respiratory Syncytial Virus, Human Metapneumovirus, Rhino-entero
Croup	Parainfluenza virus, Adenovirus, Measles
Pharyngitis	Adenovirus, Measles, Enterovirus
Conjunctivitis	Adenovirus, Measles, Enterovirus

COMPLICATIONS*	
Asthma exacerbation	Mastoiditis
Acute otitis media	Retropharyngeal abscess
Bacterial pneumonia	Sinusitis
Bacterial tracheitis	Viral pneumonitis/pneumonia
*All reviewed in a separate PEM Guide	

CLINICAL MANIFESTATIONS

The clinical timeline after inoculation can be generalized for the variety of causative agents. Parents should be educated on the typical course. On day one the virus infects non-ciliated cells of the upper tract and causes local inflammation with a cytokine cascade resulting in fever without viremia. Fever typically presents in the first 24-48 hours. Subsequent invasion of polymorphonuclear lymphocytes in the nasal submucosa and epithelium results in rhinorrhea, nasal congestion, sneezing, cough and pharyngitis peaking at 3-6 days. Concurrent cervical lymphadenopathy, conjunctivitis, myalgias and epistaxis are common. An abnormal middle ear exam is apparent in two-thirds of children though acute bacterial otitis media occurs in less than 5%. The nasal discharge and sputum color can be yellow, white, or green (due to enzymatic breakdown of cells) with a simple viral URI. Clear rhinorrhea and pharyngitis are caused by bradykinin increasing vascular permeability. Most URI's last for 5-7 days but some may persist for up to 10 days.

The total duration of symptoms is generally 14 days or less and will peak near 7 days.
Patients with an extended course of illness (> 10-14 days) who are not improving or worsening should be clinically evaluated for secondary bacterial infections. These are most commonly the result of occlusion of air spaces such as: acute otitis media, sinusitis and pneumonia. Symptoms such as the character of the nasal discharge, headache, facial pain and halitosis do not reliably distinguish between a URI from bacterial sinusitis. (See PEM Guide: Infections: Sinusitis)

MANAGEMENT

Supportive care and reassurance are the rule for treating children with a simple URI. Saline drops or spray with nasal suction with a bulb syringe can be considered in infants. Adequate hydration should be maintained.

ANTIPYRETICS: Antipyretics should be administered for fever and comfort. In a randomized clinical trial including 156 patients less than 6 years of age, Ibuprofen and the combination of Ibuprofen with Acetaminophen were superior to Acetaminophen alone in reducing the time without fever in the first 4 hours. The combination of Ibuprofen with Acetaminophen was superior to either antipyretic alone in reducing the time without fever in the first 24 hours. However, the proportion of children considered normal on a distress scale at 24 hours was similar in all treatment groups. It appears that there is a clear benefit of Ibuprofen over Acetaminophen. The combination of both antipyretics may have some benefits but the complexity of giving both with different frequencies may not offset the potential benefits (Hollinghurst, BMJ 2008, PubMed ID: 18782838). (See Appendix: Antipyretics)

COUGH AND COLD MEDICATIONS: Symptoms are not affected by treatment with decongestants, antihistamines, or antibiotics. In 2007, the FDA's advisory concluded that evidence from pediatric studies was insufficient to prove the efficacy of cold and cough medications in children. In 2008, the FDA recommended that over-the-counter cough and cold medications not be used in children under 2 years of age because of the risk of serious, life-threatening adverse events and should be used with caution if at all in those less than 4 years of age (Sharfstein, NEJM 2007, PubMed ID: 18057333). These recommendations are supported by the American Academy of Pediatrics.

PREVENTION: Hand washing and good ventilation decreases transmission. Antibacterial cleansing products have not been reported to decrease transmission. Influenza vaccine should be administered annually. High risk populations should be considered for RSV immune globulin.

APPENDIX: ANTIPYRETICS

INTRODUCTION

Evidence supports both a beneficial and adverse effect of fever on the clinical outcome of an infection. Microbes replicate less efficiently and some immune responses (e.g. leukocyte migration) are enhanced at higher temperatures.

PHYSIOLOGY

Microbes → Secretion of endotoxins and exotoxins
Host → ↑ Pyogenic cytokines
→ ↑ Prostaglandins (requires the enzyme cyclooxygenase)
→ Central: Reset hypothalamic set point → ↑ Core temperature
→ Peripheral: Inflammation → Myalgias, arthralgias, pain

PHARMACOLOGY

Antipyretics are frequently administered to offset the unpleasant effects of fever such as: headache, myalgias and arthralgias. Antipyretics can be classified as NSAIDS (aspirin, ibuprofen, naproxen, ketorolac), acetaminophen and corticosteroids. Most antipyretics reduce fever by inhibiting cyclooxygenase (COX_1, COX_2) enzymes. Inhibition of COX_1 and COX_2 result in a decrease in prostaglandins that promote inflammation, pain and fever. Inhibition of COX_1 also decreases prostaglandins that activate platelets and protect the stomach lining.

ACETAMINOPHEN: Acetaminophen is a poor COX inhibitor but its oxidized form is more effective. It functions primarily through COX inhibition in the CNS. It exhibits little to no antiplatelet or anti-inflammatory effects.

ASPIRIN: Low doses of aspirin (< 100 mg/kg/day) irreversibly inhibit COX_1 resulting in an antithrombotic effect (antiplatelet). Higher doses of aspirin inhibit COX_1 and COX_2 adding antipyretic and analgesic effects. However, aspirin is associated with the development of Reye syndrome in patients with Influenza or varicella and its use if limited in pediatrics.

NSAIDS: Non-salicylate antipyretics such as NSAIDS reversibly inhibits cyclooxygenase. The anti-inflammatory effect of NSAIDS is due to inhibition of COX_2. The adverse effects of NSAIDS are primarily due to inhibition of COX_1. COX_1 stimulated prostaglandins that protect the stomach from acid and activate platelets. Selective CO_2 inhibitors were developed that reduced the risk of gastric effects but increased the risk of cardiovascular adverse events.

GLUCOCORTICOIDS: Glucocorticoids reduce the synthesis of prostaglandin and reduce transcription of genes encoding pyrogenic cytokines

HEMATOLOGY & ONCOLOGY

1.	Febrile Oncology Patient	Vaishali Shah, MD
2.	Hyperbilirubinemia	Michael Mojica, MD
3.	Immune Thrombocytopenia	Ellen Duncan, MD, PhD
4.	Leukemia	Ellen Duncan, MD, PhD Joanna Pierro, DO
5.	Sickle Cell Disease Crises	Eric Weinberg, MD
6.	Tumor Lysis Syndrome	Elise, Perlman, MD

FEBRILE ONCOLOGY PATIENT

INTRODUCTION (VAISHALI SHAH, M.D. 10/2021)
Infection is a major cause of morbidity and mortality in pediatric cancer patients. Febrile episodes occur in one-third of neutropenic episodes in children with chemotherapy-induced neutropenia or after bone marrow transplant. Chemotherapy, in addition to causing neutropenia, disrupts normal barriers to infection including mucosal barriers and skin. The presence of central venous catheters (CVC) also serve as a point of entry to infection. This risk is higher for tunneled e.g. Broviac or Hickman catheters or PICC Lines (peripherally inserted central venous catheters) than it is for indwelling catheters.

The recommendations presented in this PEM Guide are based on institutional guidelines (Reissued 2021) and guidelines from the American Society of Clinical Oncology (J Clin Onc 2017, PubMed ID: 28459614). This PEM Guide focuses on initial management in the emergency department.

DEFINITIONS	
FEVER (oral or axillary)[1]	38.3 C (101 F) OR
	38.0 C (100.4 F) twice in a 12-hour period at least 1 hour apart
NEUTROPENIA	ANC[2] 500 cells/mm^3 OR
	ANC 1,000 cells/mm^3 with a predicted decline to < 500 cells/mm^3 over the next 24-48 hours based on recent chemotherapy
1. No rectal temperatures 2. ANC = (Total WBC count (cells/microL) x (% neutrophils + % bands))/100	

BACTERIOLOGY: Most documented pathogens are bacterial. Aerobic gram-negative bacilli account for 1/3-1/2 of bacteremic episodes. E. Coli, Klebsiella species, Pseudomonas species, Acinetobacter species and Enterobacter species are most commonly isolated. Of the gram-positive pathogens, coagulase negative staphylococci, viridans streptococci, and Staphylococcus aureus are most commonly isolated. Infections with fungi are most common in patients exposed to chronic broad-spectrum antibiotics or in those with prolonged neutropenia.

ORGANISMS	
Gram Negative Bacteria	E Coli, Pseudomonas, Klebsiella
Gram Positive Bacteria	Coagulase negative strep (venous catheter), Staph, Strep
Anaerobic Bacteria	Rare
Fungal	Candida, Aspergillus
Viral	HSV, Varicella, CMV, Adenovirus, EBV, Influenza
Protozoa	Pneumocystis, toxoplasmosis

CLINICAL MANIFESTATIONS
A careful history and physical exam should be performed. The normal inflammatory response is blunted in the neutropenic patient. Induration or erythema of the skin may be mild requiring careful examination.

HISTORY
Chemotherapy agents and timing
Type of indwelling catheter: Implantable, tunneled or PICC Lines
History of bone marrow or stem cell transplantation
History of prior invasive infections or colonization
History of allergies to antibiotics

SPECIFIC PHYSICAL EXAM SITES
Skin-areas surrounding nail beds
Central venous line exit sites and subcutaneous tunnel
Previous procedure sites: lumbar puncture or bone marrow aspiration sites
HEENT: Pharynx, sinuses, teeth and gums
Lungs
Abdomen
Perineum (no rectal exams or rectal temperatures)

DIAGNOSIS

At least one set of blood cultures from each lumen of the central venous catheter should be obtained. Peripheral blood cultures are not required in patients with central access. The additional pain and the possibility of contaminants make obtaining a peripheral a weak recommendation by current guidelines. Peripheral cultures are not routinely recommended at our institution. The microbiology lab should be advised to hold for possible fungal pathogens.

A CBC, CMP, LFT’s and lactate should be obtained. Urine culture may be useful in febrile neutropenic girls. UTI accounted for 11% of documented infections in febrile neutropenic patients, 76% of them in females. Pyuria may not be present in neutropenic patients so a dedicated (not reflexive based on urinalysis) urine culture should be sent. Consult ID for a history of resistant organisms or recent travel outside of US or Canada.

ADDITIONAL TESTING AS CLINICALLY INDICATED
Chest XRAY only if respiratory signs or symptoms are present
Lumbar puncture for altered mental status, meningismus
Stool specimens: (culture, stool pathogen panel), C difficile PCR if diarrhea is present
UA, Urine culture: Allogeneic transplant patients, clean catch, midstream sample can be obtained prior to antibiotics (no catheterization if neutropenic)
Respiratory pathogen panel, throat, sputum, viral swabs as indicated at MD discretion
Any drainage from a site should be cultured
MRSA nasal culture
Abdominal CT if abdominal pain/tenderness, peritonitis (possible typhlitis), lipase

A number of clinical decision models have been validated to risk stratify patients. These rules use a variety of patient history-related, disease-related, clinical findings/status and laboratory results to identify those a low risk. Regional and temporal variation have been demonstrated. In addition, some laboratory predictors may not be available in a timely fashion at all institutions. Guidelines do not recommend a specific decision rule and encourage institutions to choose based on local factors.

RISK CLASSIFICATION		
	LOW RISK	HIGH RISK
Chemotherapy	Non-intensive phase	Intensive phase
Clinical status	Stable	Unstable
Comorbidity	No comorbidity	Comorbidity
Focal Infection	No	Yes
ANC	> 100 mm^3	≤ 100 mm^3
Neutropenia	Anticipated for < 7 days	Anticipated for ≥ 7 days
Other	Malignancy in remission	Mucositis: ↓PO intake or diarrhea
		Presents on antibiotic prophylaxis
RISK	Low Risk = NO high-risk criteria	High Risk = ANY high-risk criteria

MANAGEMENT

Management decisions should be guided by institutional guidelines and hematology-oncology and infectious disease consultation. Rectal temperatures are contraindicated as they can cause mucosal injury leading to infection and bleeding. Tylenol is preferred for temperature control. Patients should be rapidly assessed for signs of cardiopulmonary compromise: hypotension, poor perfusion, altered mental status. See: PEM Guide: Infections: Septic Shock.

ANTIBIOTIC SELECTION

Since gram positive and gram-negative organisms are common pathogens, therapy should be broad-spectrum and bactericidal. The goal is to administer the first dose of antibiotics within 1 hour of ED arrival. Do not delay antibiotics due to difficulty in obtaining blood or urine cultures.

Monotherapy is recommended as first-line therapy. This includes an antipseudomonal b-lactam, a fourth-generation cephalosporin, or a carbapenem. There is no significant differences in failure rates, infection-related mortality, or overall mortality when monotherapy is compared to combination therapy with the addition of an aminoglycoside.

Initial antibiotics selection may be modified by the presence of gastrointestinal symptoms or a history of drug allergy or contraindications. Empiric vancomycin or an aminoglycoside may also be indicated. Antiviral and antifungal coverage may also be warranted. See indications for additional therapy in the tables below.

ANTIBIOTIC SELECTION CONSIDERATIONS
Risk assessment: ANC mild (1000-1500), moderate (500-1000) severe (<500)
Local antibiotic susceptibility patterns
Presence of a central venous catheter
Medication allergies
Clinical status: Signs of cardiopulmonary compromise
Organ dysfunction: Hepatic or renal disease may require dose adjustment
Chemotherapy regimen
Previous invasive infections (susceptibility), colonization

The goal is to provide antimicrobials within 1 hour of sepsis recognition. Obtain appropriate cultures first if this does not delay antimicrobial administration. Obtain IV access x 2 to allow administration of more than one antibiotic simultaneously. Prioritize order of antimicrobial administration to target site of likely source.

INITIAL EMPIRIC ANTIBIOTIC SELECTION: FEVER AND NEUTROPENIA[5]			
60 DAYS: NEUTROPENIC	FIRST	NEXT	LAST
No allergies	Cefepime		
Low-Risk[1] Beta-lactam Allergy	Zosyn[3]		
High-Risk[2] Beta-lactam Allergy	Aztreonam	Vancomycin[4]	
GI Source (Option 1)	Zosyn[3]		
GI Source (Option 2)	Cefepime	Metronidazole	
1. Low-Risk Allergy: Pruritis without rash, remote (>10 years ago), mild rash (self-resolved without treatment),no other symptoms, patient denies allergy but is on record 2. High-Risk Allergy: Any of: Respiratory symptoms, angioedema, cardiovascular symptoms, severe rash requiring treatment (anti-histamines, corticosteroids) without additional symptoms and/or requiring ED visit or hospitalization 3. Zosyn = Piperacillin/Tazobactam 4. Vancomycin Allergy: Substitute Linezolid 5. Ceftriaxone if febrile without neutropenia			
NYU Pediatric Antibiotic Stewardship Guideline: Fever and Neutropenia (2021)			

INDICATIONS FOR ADDITIONAL GRAM (+) AND/OR GRAM (-) COVERAGE
EMPIRIC AMINOGLYCOSIDE INDICATIONS (2nd)
Hypotension or other evidence of hemodynamic instability or respiratory failure
Altered mental status
Disseminated intravascular coagulation
Presence of uncontrolled cancer (in consultation with hematology/oncology consult)
Gentamycin (2nd): Dose 2.5 mg/kg/dose OR Amikacin (2nd): Dose 17.5 mg/kg, maximum dose: 1200 mg
EMPIRIC VANCOMYCIN INDICATIONS (2nd)*
Hemodynamic instability: Fluid refractory hypotension, cardiovascular collapse
Hospitalization within 90 days for a MRSA infection
Patient is ultra-Orthodox from Brooklyn (high prevalence of MRSA carriage)
Receipt of high dose Cytarabine (1 gram/m^2)
Severe mucositis
History of alpha hemolytic Streptococcus infection
Clinically apparent or suspected central catheter infection
Skin or soft tissue infection
Radiographically documented pneumonia
Vancomycin (2nd): Dose 15 mg/kg

ANTIFUNGAL INDICATIONS
Indications: History of prior fungal infection and not on prophylaxis, severe mucositis
Micafungin: Dose 3 mg/kg, maximum dose: 150 mg
Indication: Suspicion of aspergillosis
Voriconazole: Dose 9 mg/kg (< 12 years), 6 mg/kg (> 12 years) OR
Ambisome (Liposomal Amphotericin)

ANTIVIRALS		
Influenza	Oseltamivir	< 15 kg: 30 mg BID x 5 days 15-23 kg: 45 mg BID x 5 days 23-40 kg: 60 mg BID x 5 days > 40 kg: 75 mg BID x 5 days
Meningitis	Acyclovir	10 mg/kg

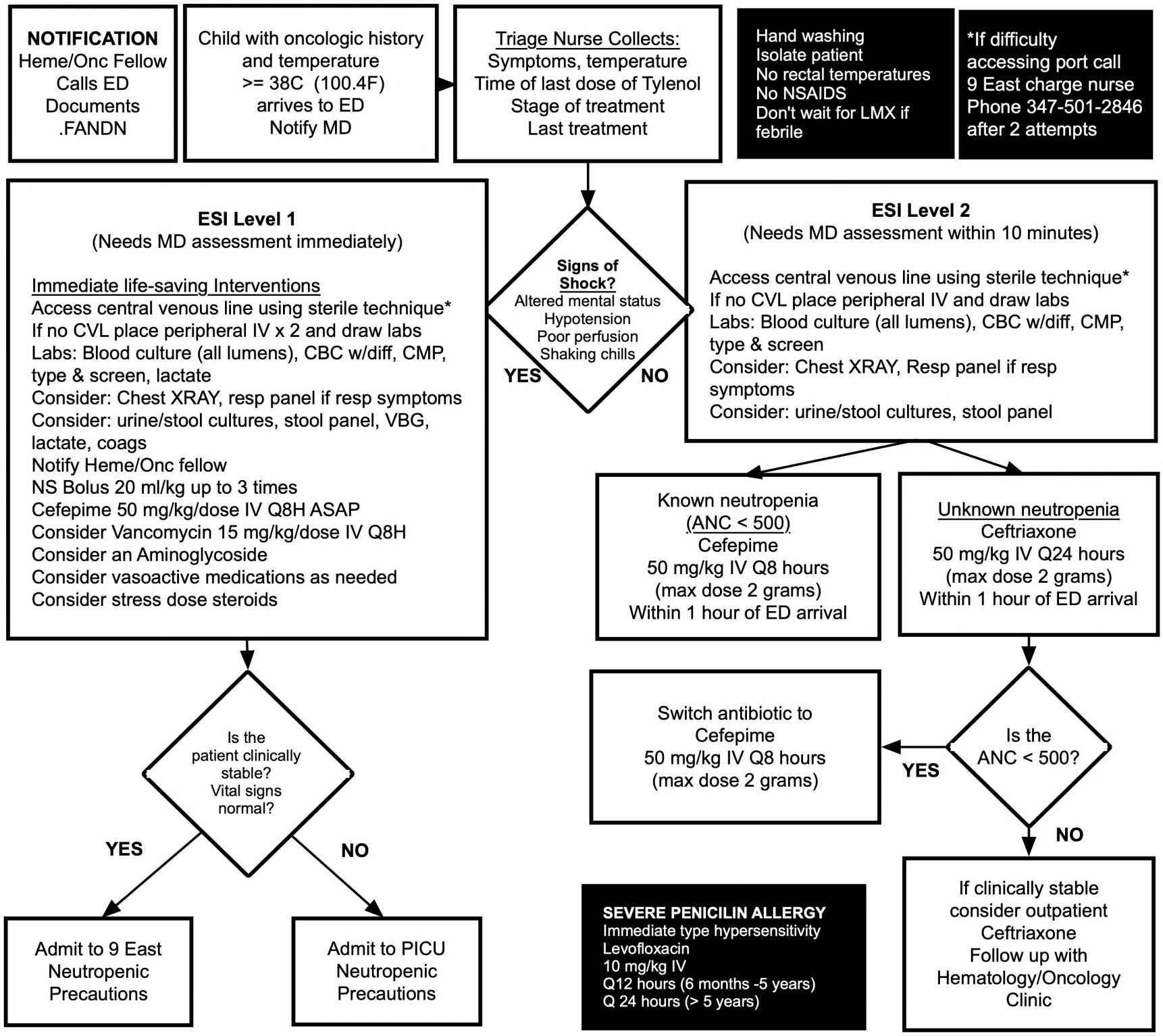
HEMATOPOIETIC GROWTH FACTORS: Colony stimulating factors (CSF) have not been shown to be effective in reducing infection-related mortality rates in patients with established febrile neutropenia. GCSF may be added only in life-threatening situations such as multi-organ failure due to sepsis or infections not responding to antimicrobial therapy.

DISPOSITION

The patient who is clinically ill appearing or those with severe neutropenia are admitted to the floor or ICU on neutropenic precautions to continue antibiotic coverage.

Patients who are well appearing and no do not have severe neutropenia may be treated as outpatients in consultation with pediatric hematology oncology if close follow up is assured. There is an option to withhold further antibiotic therapy pending culture results or start on an oral antibiotic. Oral antibiotic choices include: a fluoroquinolone or a fluoroquinolone and Amoxicillin/Clavulanate or Cefixime.

APPENDIX: FEBRILE ONCOLOGY PATIENT ALGORITHM



NOTE: Contact the pharmacist for dosing modifications for patients with new or existing renal or hepatic dysfunction

APPENDIX: MEDIPORT FLUSH

Mediports should be flushed with Heparin when:
1. They are de-accessed.
2. They are accessed but not in use.

PATIENTS	VOLUME	CONCENTRATION	DOSE
Pediatrics (≤ 10 kg)	3 ml	10 units/ml	30 units
Pediatrics (> 10 kg)	3 ml	100 units/ml	300 units
Adults	5ml	100 units/ml	500 units
Volume x Concentration = Dose			

HYPERBILIRUBINEMIA

INTRODUCTION (MICHAEL MOJICA, M.D., 9/2022)
This PEM Guide focuses on the diagnosis and management of the well-appearing, term (> 37 weeks) and near term (35-36 6/7 weeks) newborn with indirect hyperbilirubinemia in the emergency department. It reflects the revised 2022 AAP Guidelines (PubMed ID: 35927462). Management consists of a thorough history, physical examination and laboratory testing to assess the need for phototherapy and exchange transfusion.

PHYSIOLOGY
The destruction of red blood cells releases hemoglobin that is metabolized by the enzyme heme oxygenase to biliverdin. Biliverdin is converted by the enzyme biliverdin reductase to bilirubin. Unconjugated (indirect) bilirubin is bound to albumin and released into the circulation. Unconjugated bilirubin is not water-soluble, is difficult to excrete and crosses the blood brain barrier at high levels. Unconjugated bilirubin is taken up by the liver and conjugated with glucuronic acid by the enzyme uridine diphosphoglucuronate glucuronosyl transferase 1A1 (UGT1A1). Conjugated bilirubin (direct) is water-soluble and does not cross the blood brain barrier. Conjugated bilirubin is excreted into the biliary and intestinal tract. It is excreted in the stool or converted by beta glucoronidase back to unconjugated bilirubin and reabsorbed by the entero-hepatic circulation.

PATHOPHYSIOLOGY
The etiology of indirect hyperbilirubinemia can be classified as due to increased bilirubin production, decreased bilirubin excretion, increased entero-hepatic circulation or related to breast feeding. Some etiologies combine more than one of these mechanisms.

DIFFERENTIAL DIAGNOSIS: INDIRECT HYPERBILIRUBINEMIA
INCREASED BILIRUBIN PRODUCTION
Hemolytic disease of the newborn (immune mediated blood group incompatibilities)
Rh Isoimmunization
Minor blood group incompatibilities
Inherited red cell membrane defects: Hereditary spherocytosis, elliptocytosis
Inherited RBC enzyme deficiencies: G6PD deficiency, pyruvate kinase deficiency
Hemoglobinopathies
Blood Extravasation: Cephalohematoma, adrenal hemorrhage, polycythemia
Sepsis, disseminated intravascular coagulation
DECREASED EXCRETION
Decreased Bowel Motility: Obstruction, Hirschsprung’s, meconium ileus
Prematurity: Immature liver conjugation system
Inborn Errors of Metabolism: Galactosemia, Tyrosinemia
UGT1A1 Defects: Crigler-Najar, Gilbert syndrome
Congenital Hypothyroidism: Lethargy, poor feeding, constipation
BREAST FEEDING ASSOCIATED
Breast feeding jaundice
Breast milk jaundice

INCREASED PRODUCTION: Increased bilirubin production occurs in hemolytic disease of the newborn also known as immune mediated blood group incompatibilities. This occurs when the mother produces antibodies to major blood group antigens that the neonate has but she does not. For example, a type O mother may produce antibodies to an infant with type B blood. One-third of these patients will have detectable maternal antibodies on the neonate's red blood cells (Direct Antiglobulin Test (DAT)). 20% of DAT positive newborns will have a peak total bilirubin greater than 13 mg/dl. Hyperbilirubinemia typically occurs within the first 24 hours in these patients. The same situation may arise with minor blood group antigen incompatibilities. Rh isoimmunization occurs when an Rh-negative mother produces antibodies to an Rh-positive neonate. This has decreased due to the use of Rh immunoglobulin (Rhogam).

MAJOR BLOOD GROUP ANTIGEN COMBINATIONS					
	NEONATE				
		A	B	AB	O
MOTHER	A	NO	YES	YES	NO
	B	YES	NO	YES	NO
	AB	NO	NO	NO	NO
	O	YES	YES	YES	NO
YES = Major blood group incompatibility					

DECREASED EXCRETION: Decreased excretion through the gastrointestinal tract can occur through a number of mechanisms including any cause of obstruction (mechanical or functional). In addition, decreased excretion can result in an increase in the entero-hepatic circulation.

BREAST FEEDING: Breast-feeding jaundice peaks in the first 3-5 days of life. Inadequate breast-feeding with poor caloric intake results in dehydration and decreased stool output, resulting in increased entero-hepatic circulation. In contrast, breast milk jaundice occurs despite adequate feeding in the first 4-7 days of life, peaks at 2-3 weeks and may last up to 3 months. The etiology is unclear.

CLINICAL PRESENTATION

A careful history and physical examination are required to assess for signs and symptoms of acute bilirubin encephalopathy and risk factors for hyperbilirubinemia. Red flags in the history include lethargy, poor feeding, vomiting and fever. Additional history such as: birth complications, blood type of mother and neonate, time of onset of jaundice, stool pattern, urination, sibling history of hyperbilirubinemia, family history of a hematologic disorder and weight loss since birth are also essential.

A yellow tint to the skin may be seen at total bilirubin levels of greater than 5 mg/dl. This will vary with skin tone. Identification of the degree of jaundice based on examination findings alone is unreliable. A complete physical examination should be included with a focus on: mental status, muscle tone, signs of dehydration and perfusion, signs of infection, presence of bruising or cephalohematoma, abdominal distension and hepatosplenomegaly.
Pathologic jaundice may present in the first 24 hours of life. Physiologic jaundice typically peaks by day 3 in term infants and a day later in preterm neonates. If the onset of jaundice is at day 4-10 then it is typically related to breast-feeding.

ACUTE BILIRUBIN ENCEPHALOPATHY	
EARLY	Sleepy but arousable, decreased suck, mild-mod hypotonia High-pitched cry
INTERMEDIATE	Lethargic with poor suck OR Irritable/jittery with strong suck, shrill cry, difficult to console With or without fever Hypertonia: Retrocolis (backward arching of the neck) and Opisthotonis (backward arching of the trunk) with stimulation
ADVANCED	Stupor/Coma, irritability, shrill cry, fever, cessation of feeding Retrocolis/Opisthotonis at baseline Death from respiratory failure (apnea) or intractable seizures If survives, CNS damage likely irreversible
KERNICTERUS	Athetoid cerebral palsy (chorea, ballismus, tremor, dystonia) Decreased upward gaze, sensorineural hearing loss Intellectual impairment (1/3), enamel dysplasia

RISK FACTORS FOR SIGNIFICANT HYPERBILIRUBINEMIA (AAP 2022)
INFANT HISTORY
Lower gestational age (increases with each week less than 40 weeks)
Down syndrome
Macrosomic infant of a diabetic mother
Exclusive breastfeeding with suboptimal intake
Phototherapy before discharge
INFANT EXAMINATION
Scalp hematoma or significant bruising
Jaundice in the first 24 hours
LABORATORY TESTING
Predischarge transcutaneous bilirubin (TCB) or total serum bilirubin (TSB) close to the phototherapy threshold
Hemolysis from any cause, based on a rapid increase in the TSB or TCB of: >0.3 mg/dL/hour in the first 24 hours OR >0.2 mg/dL/hour after 24 hours.
FAMILY HISTORY
Parent or sibling requiring phototherapy or exchange transfusion
Family history or genetic ancestry suggestive of inherited red blood cell disorders, Glucose-6-phosphate dehydrogenase (G6PD) deficiency one of the most important causes of kernicterus

WEIGHT LOSS: In the first few days after birth, newborns are expected to lose weight. Traditionally, weight loss of less than 10% is not considered worrisome. This proportion is slightly higher in breastfed infants. After initial weight loss, infants should gain approximately 30 grams (1 ounce) per day until three months of age. Most infants re-obtain their birth weight in 10-14 days. A calculator and tracker are available to analyze infant weight loss (LINK: WWW.NEWBORNWEIGHT.ORG).

ASSESSMENT OF FEEDING ADEQUACY	
Intake	150 ml (5 ounces/kg/day), difficult to assess if breast feeding
Weight Gain	After initial weight loss, gain 30 grams (1 ounce/kg/day)
Pre/Post Weight	1 millimeter consumed → 1 gram of weight gain
Infant	Sleeps after feeding
Mother	Notices swallowing during feeding, sensation of breast emptying
Urine Output	1 wet diaper/day in first few days then 6-8 wet diapers/day

LABORATORY TESTING

2022 AAP guidelines recommend that all newborns should have transcutaneous bilirubin (TCB) or total serum bilirubin (TSB) within 24-48 hours of birth or before discharge if that occurs earlier. TCB is non-invasive with results available immediately. TCB provides a good estimate of TSB in the first few days of life (TCB = TSB 3 mg/dl) but tends to underestimate TSB at high levels (> 15 mg/dl). Measure TSB if: TCB is greater than the phototherapy threshold, TCB is less than 3 mg/dL below the phototherapy threshold or TCB is greater than 15 mg/dL. Do not subtract the direct bilirubin from the total bilirubin. Measure a total and direct (conjugated) bilirubin to assess for pathologic cholestasis in breastfed infants jaundiced at 3-4 weeks of age and formula-fed infants jaundiced at 2 weeks of age.

A CBC with reticulocyte count can be obtained as to asses for hemolysis in newborns exceeding the phototherapy threshold within 24 hours, have an increase in TSB >0.3 mg/dL/hour in the first 24 hours or have an increase in TSB >0.2 mg/dL/hour after 24 hours. Infant DAT (Direct Antiglobulin Test) should be obtained for all infants with a maternal antibody screen that is positive or unknown. A false positive infant DAT may be seen in mothers who have received Rh Immune Globulin if the infant DAT is positive only for anti-Rh(D) and mother was not anti-Rh(D) positive prior to Rh Immune globulin.

Additional testing will depend on the clinical assessment. For example, a febrile, ill appearing neonate with poor perfusion will require a complete sepsis workup. This is typically not required for the majority of the infants presenting with hyperbilirubinemia.

LABORATORY TESTING: INFANTS REQUIRING PHOTOTHERAPY	
CBC	CBC with reticulocyte count to assess for anemia, hemolysis
DAT	Mother with positive antibody screen or blood group O regardless of Rh(D) status or whose mother is Rh(D)2.
G6PD	TSB despite intensive phototherapy, suddenly or after initial decline and who requires escalation of care

MANAGEMENT

The combination of clinical risk assessment and laboratory testing will assist in defining the need for additional therapy such as phototherapy or exchange transfusion.

PHOTOTHERAPY: Phototherapy converts bilirubin to a water-soluble isomer that can then be excreted in the urine or stool. Intensive phototherapy includes an overhead radiant light source and a bilirubin-blanket beneath. The efficacy is phototherapy is based on its intensity and the extent of exposed surface area. Phototherapy can increase fluid losses. Breast-feeding should be continued and if necessary supplemented with pumped breast milk or formula. Intravenous fluids may be required for significant dehydration not correctable by enteral feeding. Oral water or dextrose water should not be used to prevent or decrease hyperbilirubinemia.

The combination of: gestational age, postnatal age and the presence of neurotoxicity risk factors define the need for phototherapy for newborns at least 35 weeks gestational age. Thresholds are based on expert opinion rather than strong evidence. Phototherapy thresholds are set far below the level for acute bilirubin neurotoxicity or kernicterus. There is limited evidence for an association between phototherapy and epilepsy. However, phototherapy thresholds have been set at levels at which benefits exceeds risks. In addition, the 2022 thresholds are higher than in the 2004 guidelines. See Appendix: Phototherapy Thresholds.

Gestational age is incorporated into the graphs of phototherapy and exchange transfusion thresholds. If no other neurotoxicity risk factors are present, then use the tables labelled “No Hyperbilirubinemia Neurotoxicity Risk Factors”. Bilitool (http://bilitool.org) is an online resource that facilitates interpretation and decision making. If the newborn meets phototherapy criteria they should also be assessed for the need of an exchange transfusion. See Appendix: Exchange Transfusion Thresholds

NEUROTOXICITY RISK FACTORS (AAP 2022)
Gestational age <38 weeks (increases with the degree of prematurity)
Albumin <3.0 gm/dL (bilirubin not bound to albumin). Testing not routinely recommended. Recommended as part of care escalation
Isoimmune hemolytic disease (positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
Sepsis
Significant clinical instability in the previous 24 hours

CARE ESCALATION: When the bilirubin level reaches the escalation of care threshold (≤ 2 mg/dl below the exchange transfusion level), then care should be escalated to prevent an exchange transfusion or kernicterus. These interventions should be continued until the bilirubin is no longer above the escalation of care threshold.

CARE ESCALATION: INTERVENTIONS
Neonatology consultation
Initiate phototherapy and PO/IV hydration prior to transfer if possible
Stat Labs: Total/Direct bilirubin, TSB Q2 hours, CBC, BMP, Albumin, Type and Cross
Notify blood bank
Intensive phototherapy
Oral AND Intravenous hydration
Consider Intravenous Immune Globulin (IVIG): 0.5-1.0 grams/kg over 2 hours (below)

RESPONSE TO CARE ESCALATION: INTERVENTIONS		
Exchange Threshold	Escalation Threshold	Next Intervention
Above[1]	Above	Exchange Transfusion
Below	Above	Continue care escalation, TSB Q2Hr
Below	Below	Regular phototherapy guidelines
1. or Signs of intermediate or advanced acute bilirubin encephalopathy: Hypertonia, arching, retrocollis, opisthotonos, high-pitched cry, or recurrent apnea.		

EXCHANGE TRANSFUSION: Exchange transfusion is the most rapid method to reduce bilirubin. It replaces 85% of the circulating blood volume. A double volume exchange (160-180 ml/kg) will reduce bilirubin levels 2-3 mg/dl within 4-6 hours. Cross-matched, washed, packed red blood cells that are mixed with thawed adult fresh-frozen plasma to a hematocrit of approximately 40% are preferred. The Bilirubin to Albumin Ratio (Table Below), can be used to determine the need of exchange transfusion.

INTRAVENOUS IMMUNE GLOBULIN (IVIG): It is unclear if IVIG prevents the need for an exchange transfusion and there may be an association between IVIG and necrotizing enterocolitis. Consider the response to phototherapy, the rate of rise of bilirubin and the likelihood of a timely exchange transfusion in deciding on IVIG use. IVIG is administered as a 2-hour infusion of 0.5-1.0 grams/kg and may be repeated in 12 hours. Continue all escalation of care interventions if IVIG is used.

EXCHANGE TRANSFUSION: INDICATIONS
TSB above exchange threshold despite escalation care
Bilirubin to Albumen Ratio above threshold (Table below)
Intermediate or severe acute bilirubin encephalopathy: Hypertonia, arching, retrocollis, opisthotonos, high-pitched cry, or recurrent apnea.

BILIRUBIN TO ALBUMIN RATIO[1]		
B/A Ratio Threshold	Gestational Age	Neurotoxicity Risk Factors[2]
≥ 8.0	≥ 38 weeks	None
≥ 7.2	≥ 38 weeks	≥ 1
≥ 7.2	35-37 weeks	None
> 6.8	35-37 week	≥ 1
1. Bilirubin to Albumin Ratio = TSB (mg/dl) divided by serum Albumin (grams/dl) 2. Excluding gestational age		

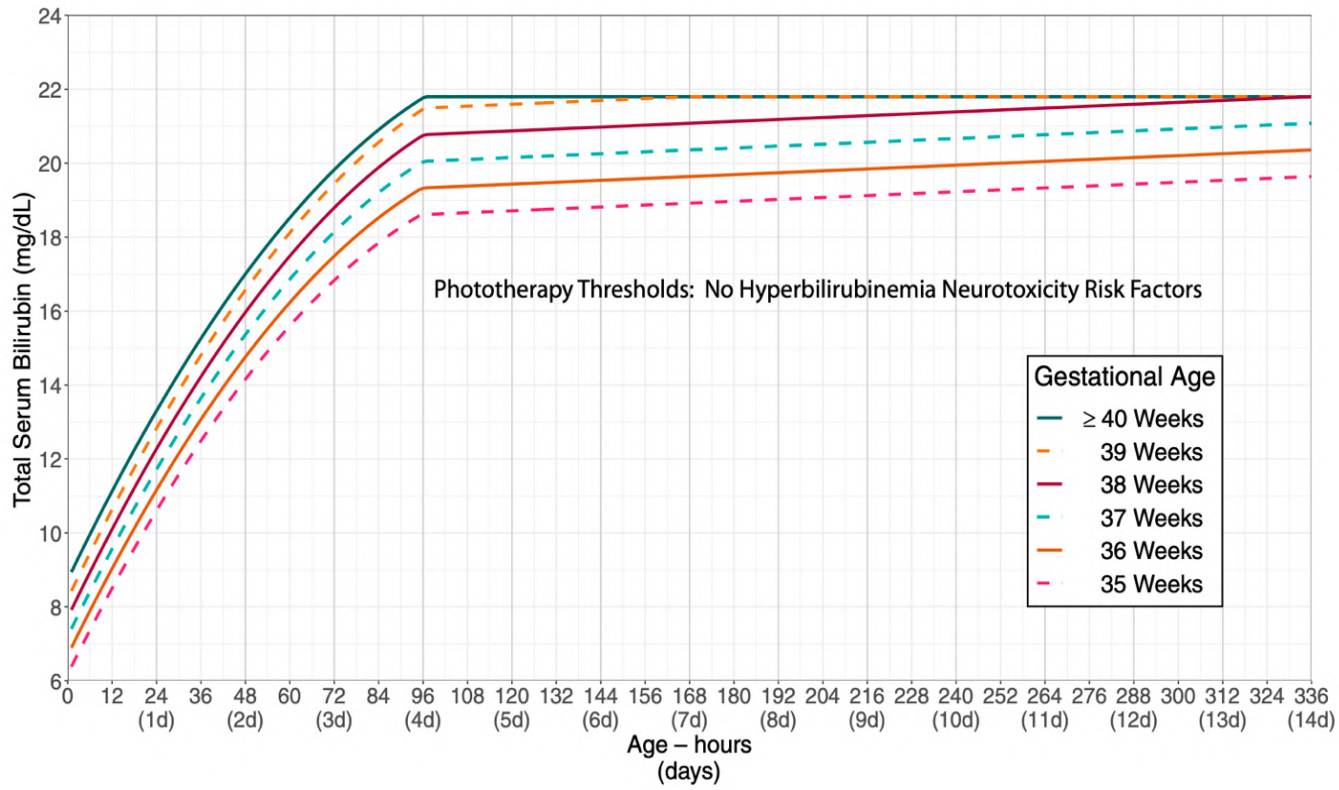
DISPOSITION

The current guidelines recommend using the difference between the current TSB level and the phototherapy threshold, gestational age and the presence of neurotoxicity risk factors to determine when follow-up should occur and the need for follow-up testing. The presence of other hyperbilirubinemia risk factors should also be considered. Unfortunately, this recommendation applies only to patients being discharged from their initial birth hospitalization.

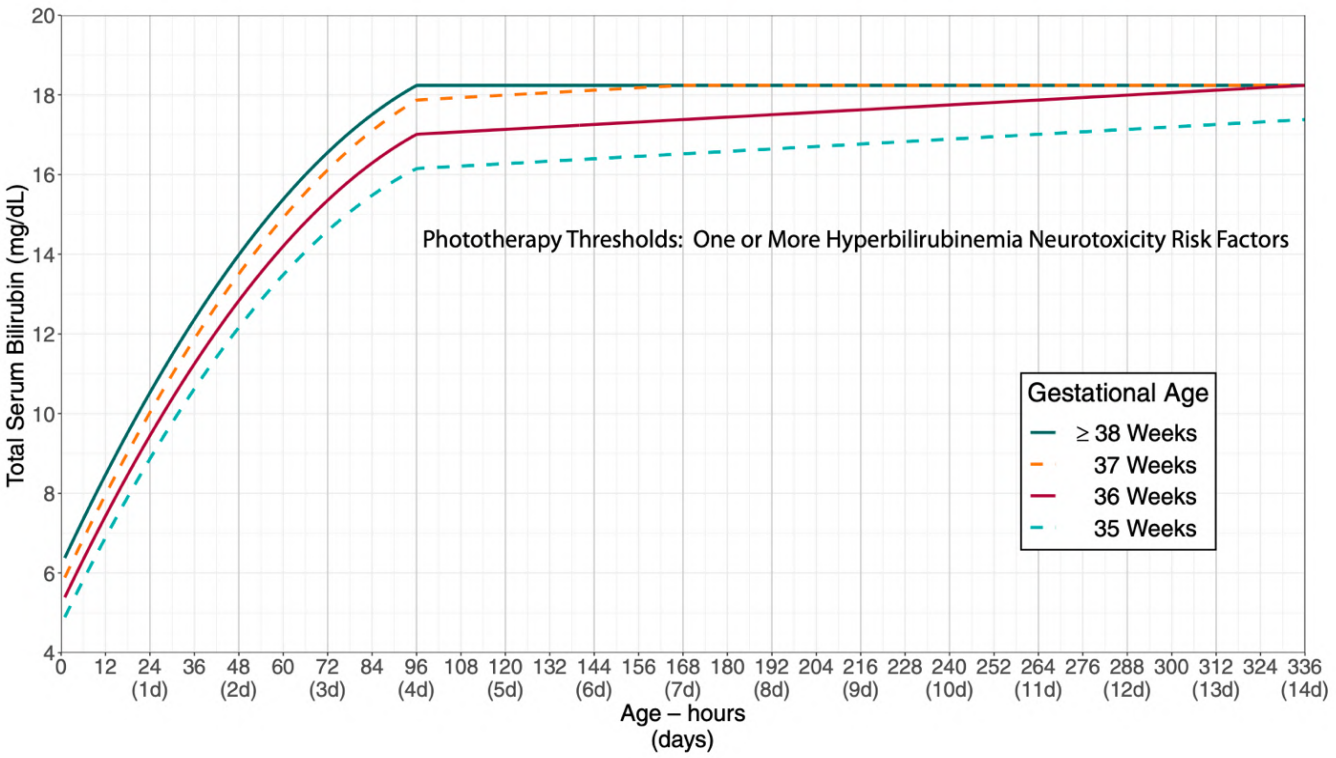
No follow-up recommendation are made for patients seen in the ED after discharge from their birth hospitalization. It is prudent to discuss follow-up of these patients with their primary care provider. Patients who are close to the phototherapy threshold, with significant risk factors for rebound hyperbilirubinemia or for whom follow-up is not likely, should be admitted for phototherapy. Patients not meeting these criteria can follow-up with their primary care provider or the ED in 24 hours. Patients with a repeat bilirubin in the ED that is down trending may not require follow-up id there are no other clinical concerns. Parents should be educated about the signs of acute bilirubin encephalopathy.

APPENDIX: PHOTOTHERAPY THRESHOLDS (AAP 2022)

A. **NEUROTOXICITY RISK FACTORS: 0 (NONE)**

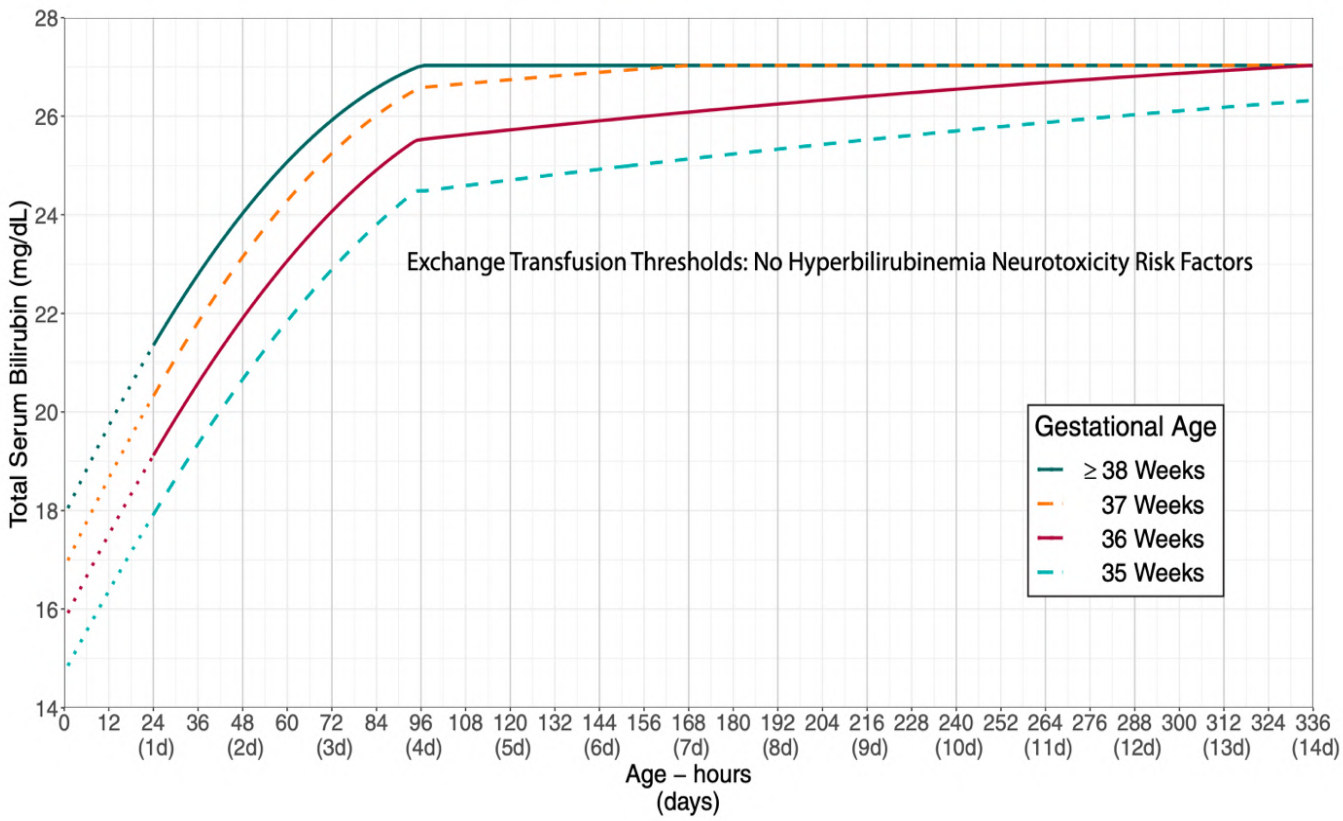


B. **NEUROTOXICITY RISK FACTORS: ≥ 1**

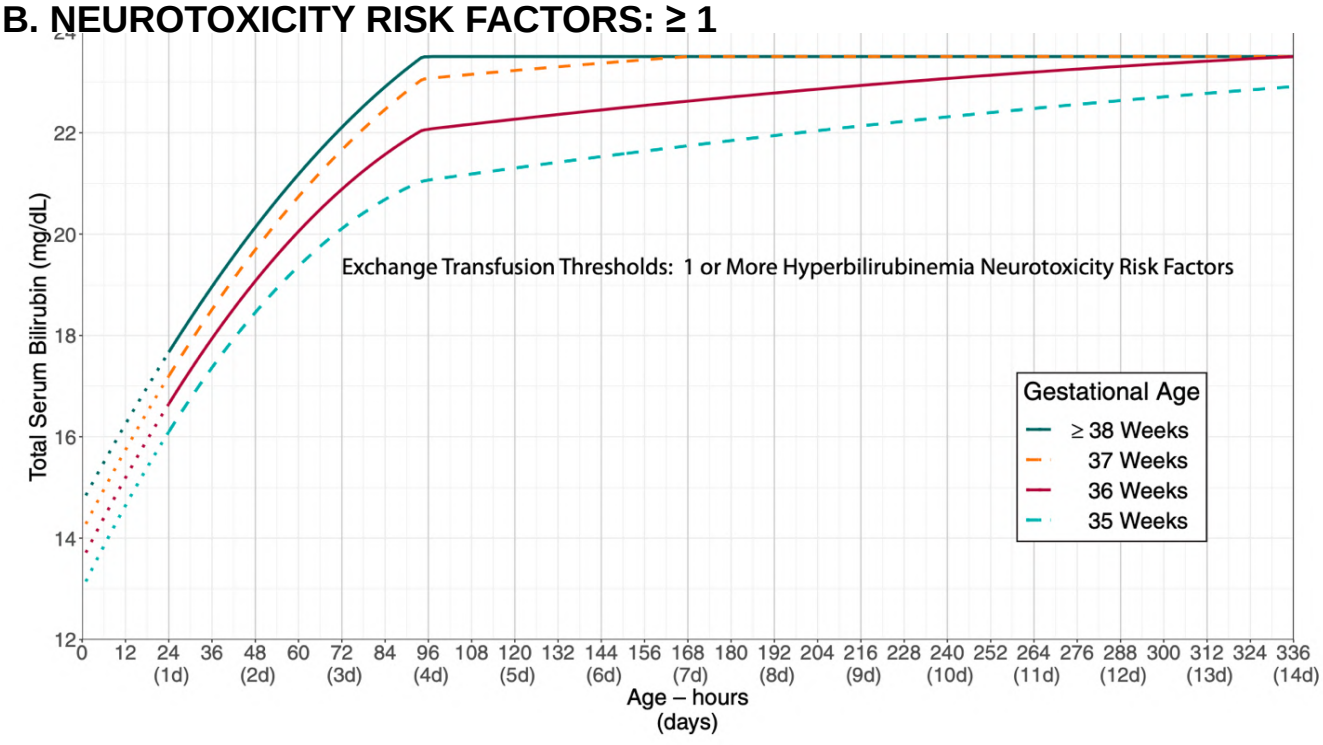


NEUROTOXICITY RISK FACTORS (AAP 2022)[1]
Albumin <3.0 gm/dL (bilirubin not bound to albumin). Testing not routinely recommended. Recommended as part of care escalation
Isoimmune hemolytic disease (positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
Sepsis
Significant clinical instability in the previous 24 hours
1. Gestational age <38 weeks is incorporated into the tables above. If no risk factors other than gestation age, use table labelled “Neurotoxicity Risk Factors: 0 (none)”

APPENDIX: EXCHANGE TRANSFUSION THRESHOLDS (AAP 2020)



B. NEUROTOXICITY RISK FACTORS: ≥ 1



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Isoimmune hemolytic disease (positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
Sepsis
Significant clinical instability in the previous 24 hours
1. Gestational age <38 weeks is incorporated into the tables above. If no risk factors other than gestation age, use table labelled “Neurotoxicity Risk Factors: 0 (none)”

IMMUNE THROMBOCYTOPENIA

INTRODUCTION (ELLEN DUNCAN, MD, PHD, 2/2020)
Immune thrombocytopenia (ITP) (formerly known as immune or idiopathic thrombocytopenic purpura) is caused by autoantibodies to platelet membrane antigens, which accelerate clearance and limit production of platelets. ITP can be either primary or secondary to other factors, such as medications, systemic illness or infection. Isolated thrombocytopenia is the hallmark of immune thrombocytopenia. Although the primary peak is in early childhood (2-5 years), there is a smaller peak in adolescence as well. Primary ITP is divided into three phases: newly diagnosed (< 3 months from onset); persistent, ongoing disease (3-12 months); and chronic disease (> 12 months).

WEB LINK: GUIDELINE: IMMUNE THROMBOCYTOPENIA: AMER SOC HEMATOLOGY 2019

HISTORY
Patients with ITP usually present without constitutional symptoms and appear well on presentation. Because ITP can be caused by infection, it is important to ask about preceding systemic illnesses. History should elicit exposure to drugs known to induce thrombocytopenia (see the “Drug-induced thrombocytopenia” section of the Differential Diagnosis table below), as well as recent vaccinations, as an MMR vaccination within the past 6 weeks has been associated with a slightly increased risk of ITP.

Bleeding is common in patients with ITP, although it may be absent. It is crucial to determine the timing, location, and severity of bleeding.

BLEEDING MANIFESTATIONS	
TYPE	CHARACTERISTICS
“Dry” Bleeding (86%)	Cutaneous bleeding only Petechiae, purpura, and ecchymoses
“Wet” Bleeding (40%)	Mucosal bleeding: Buccal, gingival, and nasal mucosa most common GI, GU, GYN sites may be involved as well.
Severe Bleeding (3%)	Bleeding requiring transfusion and/or hospitalization Severe thrombocytopenia: Platelet count < 10,000-20,0000/microL, Epistaxis > 5-15 minutes, GI bleeding, mucosal bleeding, trauma (especially head injury)
Intracranial Bleeding (0.5-1%)	Characterized by signs of increased intracranial pressure (ICP) Risk factors include head injury, severe thrombocytopenia, excessive bleeding especially at mucosal sites
Antiplatelet (Aspirin, NSAIDS) and anticoagulant medications may exacerbate bleeding	

EXAMINATION
Findings of splenomegaly, hepatomegaly, or lymphadenopathy are uncommon in ITP, and indicate the possibility of an alternative diagnosis. However, splenomegaly can be seen in up to 10% of patients.

LABORATORY FINDINGS
ITP is a diagnosis of exclusion. A patient without systemic systems (fever, weight loss, bone pain), a normal examination with the exception of bruising or petechiae (no generalized adenopathy or hepatosplenomegaly), laboratory tests with isolated thrombocytopenia and excluding alternative diagnosis (see table below) are likely to have ITP.

Thrombocytopenia, defined as a platelet count of < 100,000/microL, is usually the only finding on a complete blood count. The platelet count is usually < 30,000/microL. The remainder of the CBC, including white blood count, differential, and hemoglobin, as well as reticulocyte count, are typically normal. However, the hemoglobin may be low if there is significant bleeding. A peripheral blood smear will show fewer normal platelets as well as an increased in mean platelet volume due to larger, younger platelets (megakaryocytes).

Bone marrow aspiration is not required unless there are atypical features. Testing for anti-platelet antibodies is not necessary (approximately 40% are negative)

LABORATORY TESTING TO EXCLUDE ALTERNATIVE DIAGNOSES
CBC, reticulocyte count, and smear
Coagulation profile (PT/aPTT) with fibrinogen
Basic metabolic profile
Liver function tests
LDH
D-dimer
Blood type and Direct antiglobulin test (Coombs)
Immunoglobulins
Indicated viral testing (e.g. EBV, HIV, Hepatitis C)

DIFFERENTIAL DIAGNOSIS	
CONDITION	DISTINGUISHING FEATURES
Hemolytic uremic syndrome	Microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and acute kidney injury, with preceding diarrheal illness
Thrombotic thrombocytopenic purpura	Severe MAHA, thrombocytopenia, and neurologic impairment, ± renal impairment, hematuria, high LDH
Disseminated intravascular coagulation	Ill-appearing; thrombocytopenia, hemorrhage, and thrombosis leading to end-organ damage; ↑PT/aPTT, ↓fibrinogen, and ↑d-dimer
Leukemia (e.g. ALL)	Concurrent systemic symptoms, hepatosplenomegaly, lymphadenopathy, leukocytosis, anemia, mild-moderate thrombocytopenia, blast cells on smear
Viral infection	Systemic symptoms with positive viral serology (e.g. EBV, CMV, hepatitis C, HIV)
Autoimmune hemolytic anemia ↓ Platelets (Evan's)	Hemolysis, thrombocytopenia, with anemia, jaundice, reticulocytosis; smear showing polychromasia and spherocytes, direct antibody test (+)
Autoimmune disease	Features of underlying disease (e.g. Lupus, autoimmune lymphoproliferative syndrome (ALPS)
Immunodeficiency syndromes	Dependent on underlying condition (e.g.combined variable immune deficiency, Wiskott-Aldrich, DiGeorge)
Inherited ↓ Platelets	Dependent on underlying disease
Drug-induced ↓ Platelets	Heparin, Quinidine, Phenytoin, Sulfa drugs, Valproate and Vancomycin
Bone marrow failure	Many cell lines affected, possibly with pancytopenia

MANAGEMENT

Management decisions should be made in consultation with a pediatric hematologist. Management includes activity restriction to decrease the risk of trauma, and avoidance of medications that might worsen bleeding (e.g. antiplatelet medications, including aspirin and NSAIDs, and anticoagulant agents). Additional therapy is based on the degree of bleeding. Hormonal therapy may be required to control menstrual bleeding.

Target platelet count is generally > 20,000-30,000/microL, though it is often higher for life-threatening bleeding or before surgical procedures. Management of chronic ITP may include splenectomy, Rituximab, high-dose steroids, chronic immune suppression or thrombopoietin receptor agonists (TPO-RAs). Emergency splenectomy may be considered in those with life-threatening bleeding who are refractory to medical therapy.

BLEEDING MANAGEMENT	
Low-risk bleeding	Watchful waiting
Moderate-High risk Bleeding	IVIG or anti-D immune globulin[1] if significant bleeding or if rapid rise in platelet count is needed (e.g. for surgery or procedure).
	Oral glucocorticoids if rapid rise in platelet count is not needed (no signs of severe bleeding and no upcoming procedure)
Severe, Non-life-threatening Bleeding	Platelet transfusion if needed Combination of methylprednisolone, IVIG and/or anti-D immune globulin[1] for up to 4 days Possible role for thrombopoietin receptor agonist (e.g. Romiplostim) or antifibrinolytic agents (e.g. Tranexamic Acid)
Life-threatening Bleeding	Platelet transfusion with frequent post-transfusion checks, Methylprednisolone x 3-4 days, IVIG x 1-3 days Limited support for anti-D immune globulin, recombinant human factor VIIa, Vincristine, Tranexamic Acid, splenectomy
Surgical Procedures	Combination: Glucocorticoids, IVIG, anti-D, platelet transfusion
1. Anti-D may cause severe hemolysis, Use only if Rh (+) AND DAT (-)	

TREATMENT	DOSING REGIMEN
Methylprednisolone	IV 30 mg/kg (max 1gram/day) daily for 3-4 days[1]
Dexamethasone	PO 24 mg/m^2/day (max 40 mg/day) daily for 4 days[1]
Prednisone	PO 4 mg/kg/day (max 240 mg/day) for 7 days[2] OR PO 1-2 mg/kg daily (qAM) for 7-21 days[2]
Platelet transfusion	10-30mL/kg, bolus then continuous infusion x 1-3 days
IVIG	Intravenous Immune Globulin: 1 gram/kg/day
Anti-D Immune Globulin	Only If Rh (+) & Direct Antiglobulin Test (-): 75 mcg/kg x 1
1. No taper required, 2. Taper required	

DISPOSITION

Patients with low-risk ITP may be discharged home with frequent follow-up visits for clinical and laboratory assessments, beginning weekly and then at increasing intervals until platelet count is > 150,000/microL. Patients with moderate-high risk bleeding, or with severe bleeding with or without hemodynamic instability, should be admitted for further management, in the latter case to the pediatric intensive care unit.

PROGNOSIS

Bleeding complications can occur, but mortality is rare. In most children, ITP resolves within 6 months. 30-50% of patients with ITP may relapse. Up to 20% of patients may develop chronic ITP even with early intervention; however, up to 50% of these patients will experience spontaneous remission. Chronic ITP refractory to secondary treatments is rare in pediatric patients.

LEUKEMIA

INTRODUCTION: (ELLEN DUNCAN, MD, PHD, JOANNA PIERRO, DO, 12/2020)
Leukemia accounts for approximately 30% of pediatric cancer, making it the most common pediatric malignancy. The most common types of leukemia in childhood are acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). ALL is approximately five times more common than AML. The primary subtypes of ALL include T-cell and B-cell ALL. Both genetic and environmental factors have been associated with the development of pediatric leukemias. This PEM Guide will focus on identifying and managing new-onset leukemia and its complications in the emergency department. See: PEM Guide: Hematology-Oncology: The Febrile Oncology Patient and PEM Guide: Hematology-Oncology: Tumor Lysis Syndrome.

PRIMARY PEDIATRIC LEUKEMIAS		
	ALL	AML
Age	2-5 years	Biphasic peaks in infancy and adolescence
Ethnic predilection	Caucasian, Hispanic	Caucasian
Gender	Boys > Girls	N/A
Incidence	80% of pediatric leukemia	13% of ped leukemia <10 years 36% of ped leukemia 15-19 years
Subtypes	B-ALL (85%) T-ALL (10-15%)	Many subtypes, initial management similar except for acute promyelocytic leukemia

CLINICAL MANIFESTATIONS

Symptoms of both ALL and AML can be nonspecific and may include fever, fatigue, and anorexia, making them difficult to distinguish from many self-limited pediatric illnesses. Diagnosis requires a high index of suspicion. Fever can be due to concomitant infection or due to the disease itself. More specific indicators of leukemia include splenomegaly, hepatomegaly, generalized lymphadenopathy, pallor, ecchymoses, or petechiae.

Marrow infiltration leads to expansion of the marrow cavity, which can present as bone pain or refusal to bear weight. Cytopenias can present with pallor, fatigue, bleeding, bruising, and infection. Half of children may have hepatosplenomegaly and/or lymphadenopathy. DIC is a common presenting feature of acute promyelocytic leukemia (APML) and can be rapidly fatal.

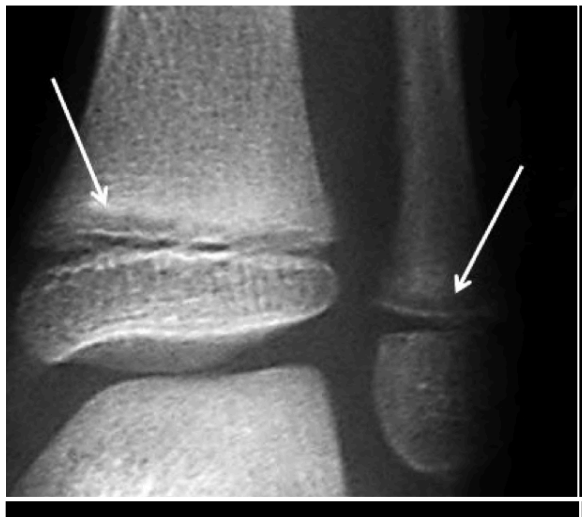
More than half of patients with T-ALL present with mediastinal mass, which can lead to complications such as superior vena cava (SVC) syndrome and respiratory distress if there is concomitant compression of the trachea. Chloromas are extramedullary solid tumors comprised of leukemia cells, and can present with mass effects and, in rare cases, lead to oncologic emergencies such as spinal cord compression.

Extramedullary involvement may be characterized by CNS (headache, vomiting, lethargy, cranial nerve abnormalities) or testicular (pain, swelling) symptoms.

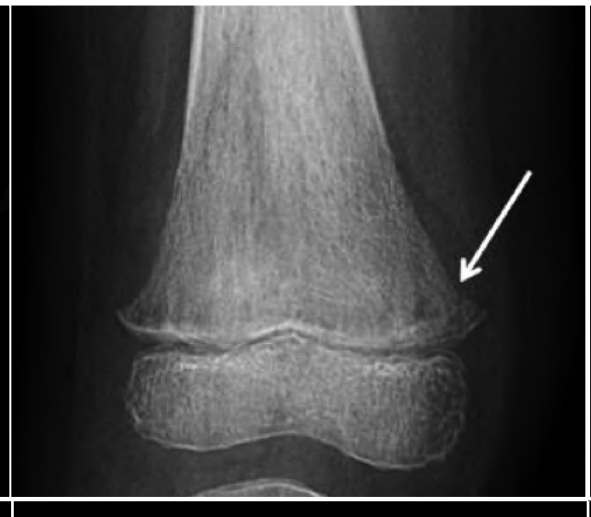
DIFFERENTIAL DIAGNOSIS		
	DISEASE	DISTINGUISHING FEATURES
Malignant Conditions	Burkitt lymphoma	“Starry sky” appearance on histology Commonly presents with a RLQ mass mimicking appendicitis Spontaneous tumor lysis syndrome
	Aplastic anemia	Pancytopenia with reticulocytopenia Hypocellular bone marrow with fatty infiltration into marrow space
	Small round blue cell tumors (e.g. Ewing sarcoma)	Small round blue cells on histology
Non-malignant Conditions	Immune thrombocytopenia*	Isolated thrombocytopenia Occasionally with concomitant hemolytic anemia (Evans Syndrome)
	B12/Folate deficiency	Ranges from isolated macrocytic anemia to pancytopenia with macrocytosis
	Infection (e.g. HIV, infectious mononucleosis*, tuberculosis)	Varies depending on infection
	Medications (chemotherapeutic drugs, valproic acid, mycophenolate mofetil)	Associated with use of offending drug
*Covered in detail in a separate PEM Guide		

RADIOGRAPHIC FINDINGS

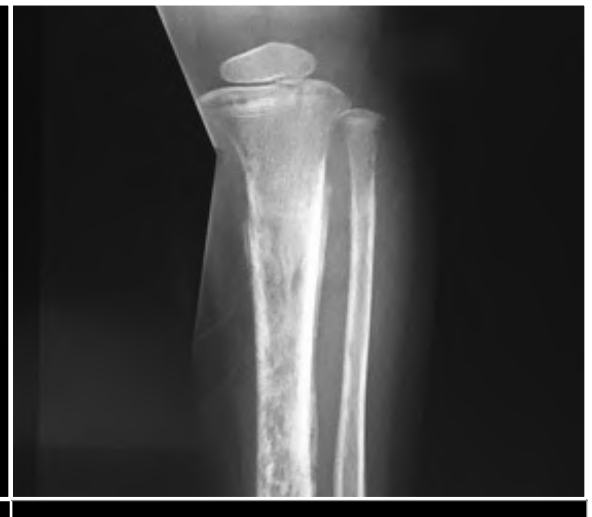
Chest radiography, with plain films and CT, are useful when symptoms of mediastinal mass (plethora, respiratory distress) are present. If chest radiograph is negative, a CT scan is usually not needed. Brain imaging is indicated if physical exam is concerning for intracranial involvement. Bone radiographs may reveal metaphyseal radiolucent bands, subperiosteal new bone formation, and osteolytic lesion of the cortex and medullary cavity (see below).



METAPHYSEAL LUCENT BANDS



DIFFUSE OSTEOPENIA



LYTIC BONE LESIONS

LABORATORY FINDINGS

Laboratory studies in the Emergency Department should include the following:

LABORATORY STUDIES	
TEST	IMPORTANT FEATURES
CBC	WBC: Low, normal, or high in B-ALL, AML. Often >100K in T-ALL Hb/HCT: Normocytic anemia Platelet: Mild-severe thrombocytopenia with risk of spontaneous hemorrhage. Thrombocytosis rare, should prompt further workup.
Differential, Peripheral smear	Circulating blasts. Difficult to differentiate lymphoblasts from myeloblasts except in rare cases where Auer rods are visualized ALL: Lymphoblast count of 25% diagnostic AML: Myeloid blasts diagnostic
Reticulocytes	Low: Myelosuppression due to marrow infiltration by leukemia cells
Basic Metabolic	Tumor lysis syndrome*: Elevated potassium, phosphorus, and creatinine, decreased calcium
Hepatic	Transaminitis or hyperbilirubinemia: Due to hepatic infiltration
Uric acid, LDH	Elevated in tumor lysis syndrome*
Coagulation (+ fibrinogen)	AML, specifically APML, can present with disseminated intravascular coagulation
Blood culture	In febrile patients, prior to starting broad spectrum antibiotics
Peripheral blood flow cytometry	Should be sent in all patients with high suspicion for leukemia as soon as possible in consultation with the heme/onc team
CSF studies	Lumbar puncture should be performed by the heme/onc team as chemotherapy is administered simultaneously once the diagnosis has been established
*Covered in detail in a separate PEM Guide	

MANAGEMENT

Emergency department management includes treatment of electrolyte abnormalities associated with tumor lysis, arranging plasmapheresis or exchange transfusion for symptomatic leukostasis, and management of bleeding abnormalities and severe cytopenia with blood products. Broad-spectrum antibiotic coverage is indicated in the febrile, neutropenic patient with newly diagnosed leukemia (See PEM Guide: Hematology-Oncology: Febrile Oncology Patient).

Emergency physicians are often called upon to tell the parents of the suspicion for leukemia. This is a difficult conversation and should be done sitting down in a private space with the parents. Many parents do not want a younger child to be told the diagnosis at this time. It is important to ascertain the parent’s wishes before having the conversation. Questions about definitive diagnosis, therapy, and prognosis should be deferred to the hematologist/oncologist.

Pediatric hematology/oncology should be consulted in patients with concern for leukemia. Patients with ALL require risk-stratified, multiagent chemotherapy with CNS prophylaxis depending on biological and clinical features of their tumor. AML requires intensive, severely myelosuppressive therapy, which is often delivered inpatient for the course of their treatment. Survival rates for ALL are approximately 90% whereas AML outcomes remain lower at ~70%.

COMPLICATIONS		
COMPLICATIONS	DESCRIPTION	MANAGEMENT
Leukostasis	Hyperleukocytosis may lead to leukostasis, an oncologic emergency that can lead to both hemorrhagic and thromboembolic events Hyperleukocytosis is defined as a WBC count >100K in AML and >300K in ALL	Emergent initiation of chemotherapy Leukapheresis indicated for symptomatic leukostasis
Tumor lysis syndrome[1]	↑ Phosph, K, Uric acid, LDH ↓ Calcium (due to ↑ Phos) Renal failure	Hyperhydration without potassium, Allopurinol: Normal uric acid Rasburicase: Elevated uric acid
Disseminated Intravascular Coagulation (AML)	↑ D-dimer, PT, PTT ↓ Fibrinogen, platelets	Treat underlying leukemia (All-trans retinoic acid if APML[3]) Support with blood products PRN (e.g. FFP, platelets, pRBCs[2])
Febrile Neutropenia[1]	Fever in a neutropenic patient	Broad spectrum antibiotics with pseudomonal coverage +/- vancomycin in certain situations
1. Discussed in detail in a separate PEM Guide 2. pRBCs should be leuko-reduced and irradiated for all patients with suspected malignancy; CMV-negative products are also preferred, however, leuko-reduced products are considered CMV-safe and can be used in emergent situations while workup is pursued 3. APML: Acute Promyelocytic Leukemia		

RISK STRATIFICATION (ALL)	
Standard Risk	Age 1* through <10 year AND initial WBC < 50,000/μL
High Risk	Age ≥ 10 years OR initial WBC ≥ 50,000/μL, regardless of age
*ALL in patients < 1 year of age is a distinct entity characterized by poor outcomes	

DISPOSITION

Pediatric patients with high suspicion of leukemia should be admitted for further evaluation and management.

APPENDIX: CHEMOTHERAPY SIDE EFFECTS

CHEMOTHERAPY SIDE EFFECTS		
MEDICATION	SIDE EFFECT	TREATMENT/RESCUE
Methotrexate	Transaminitis, renal tubular injury (IV) Headache, dizziness, blurry vision, ***stroke-like syndrome*** (intrathecal)	Leucovorin, glucarpidase in certain situations (please consult your oncology providers to determine if these therapies are indicated, as treatment is often supportive care only)
PEG L-asparaginase	Pancreatitis, hyperbilirubinemia, transaminitis, thromboembolic complications (most often cerebral sinus venous thrombosis)	Supportive care
Anthracyclines (doxorubicin, daunorubicin)	Cardiotoxicity (late effect)	Screening echocardiograms throughout life to assess for development of cardiomyopathy
Vincristine	Peripheral neuropathy, hyponatremia	Supportive care, dose modifications if needed

SICKLE CELL DISEASE CRISES

INTRODUCTION (ERIC WEINBERG, M.D. 11/2021)
Sickle Cell Disease (SCD) is a recessive, inherited disorder of hemoglobin synthesis. African Americans (1/500) and Hispanic populations (1/1,400) have a higher prevalence of the disease. SCD is caused by a single amino acid substitution in position 6 of the beta-globin chain of hemoglobin, resulting in deformed sickle-shaped red blood cells. The clinical signs and symptoms of SCD result from the abnormal behavior of these sickle cells.

Sickle cells are more fragile and have a decreased survival time compared to normal red blood cells, resulting in chronic anemia. In addition, these cells can obstruct the microcirculation, leading to vasoocclusion. It is helpful to remember that vasoocclusion can affect almost any organ system resulting in severe, life-threatening disease. Organ system dysfunction can occur at any time and is commonly referred to as a sickle cell “crisis”. These crises can be categorized as: vaso-occlusive, anemic and infectious crises though elements of more than one crisis can occur (eg. Acute chest crises combined infection and vaso-occlusion, splenic sequestration combines vasoocclusion and anemia).

SICKLE CELL CRISES
VASO-OCCLUSIVE CRISES
Musculoskeletal Pain
Acute Chest Syndrome (ACS)
Stroke
Dactylitis
Priapism
Aseptic necrosis
ANEMIC CRISES
Aplastic Crisis
Splenic Sequestration Crisis
Hyper-hemolytic Crisis
INFECTIOUS CRISES
Bacteremia/Sepsis
Pneumonia (+/-) Acute Chest
Osteomyelitis

VASO-OCCLUSIVE CRISES

VASO-OCCLUSIVE PAIN CRISIS: Vasoocclusive crisis is the most common presenting symptom of sickle cell disease. A vasoocclusive crisis may be caused by a precipitating event (most commonly dehydration, infection and hypoxia) that leads to increased sickling and vaso-occlusion. Vaso-occlusion is thought to cause tissue ischemia, resulting in pain.

A vasoocclusive crisis can affect any area of the body including the chest, abdomen, and extremities. In infants vasoocclusive crisis can cause dactylitis, a painful swelling of the hands and feet. The primary treatment of vasoocclusive crisis is analgesics (See Appendix: Analgesics) Guidelines recommend a standardized protocol with the goals of assessment and treatment within 1 hour of ED arrival and reassessment every 30-60 minutes (Amer Soc Heme, Blood Adv 2020, PubMed ID: 32559294).

Ideally, an individual care plan would be available in the electronic medical record. Medication selection should be based on baseline opioid therapy and previously effective therapy. The use of the intranasal or subcutaneous route can rapidly deliver therapy prior to obtaining intravenous access. A non-steroidal anti-inflammatory agent is recommended in addition to initial opioid therapy in patients without renal disease, peptic ulcer disease or the use of anticoagulants. Patients refractory to opioid therapy should be admitted.

ANALGESIA IN VASOOCCLUSIVE CRISIS (SEE APPENDIX FOR DOSING)		
CATEGORY	DRUG	COMMENTS
NSAIDS	Ketorolac, Ibuprofen	Small studies support use in mild crisis May be used in conjunction with opiates Contraindicated in renal disease
Opiates: Oral	Norco, Vicodin,	Recommended for mild crisis
Opiates: Intranasal	Fentanyl	Rapid administration and onset
Opiates: Intravenous	Morphine, Hydromorphone	Recommended for moderate to severe crisis Titrate to effect (begin with smaller dose) Patient controlled analgesia is recommended if admitting to hospital Hydromorphone reserved for severe crisis

ADDITIONAL MANAGEMENT OF VASO-OCCLUSIVE CRISIS	
Intravenous Fluids	Cochrane review[1]: “there are no randomized controlled trials that have assessed the safety and efficacy of different routes, types or quantities of fluid” Administer intravenous fluids at maintenance Bolus fluids only if clinically dehydrated Do not over-hydrate. May precipitate acute chest syndrome Encourage oral intake if tolerated
Oxygen	No evidence supporting use Recommended only if O_2Sat < 95%
1. Cochrane Database of Systematic Review 2017, PubMed ID: 28759112	

ACUTE CHEST SYNDROME: Acute Chest Syndrome (ACS) is diagnosed in patients with SCD that meet two criteria: 1. Presents with signs and symptoms of respiratory disease (chest pain, fever, tachypnea, wheezing or cough) and 2. Chest XRAY with a new pulmonary infiltrate. ACS is the most common cause of death from sickle cell disease (respiratory failure 15%, mortality 2-4%). The peak age for presentation of ACS is 2-4 years. Risk factors include a history of prior acute chest or asthma. Because of the serious sequelae of this disease, any patient with SCD who presents with respiratory symptoms or signs should have a chest XRAY.

The pathophysiology of ACS includes elements of infection, pulmonary infarction, airway hyperreactivity, ventilation/perfusion mismatch and pulmonary edema. The most common the cause is infection from atypical bacteria such as: Chlamydia or Mycoplasma pneumoniae, or bacterial infection typically with Staphylococcal or Streptococcal species.

Chest XRAY findings may lag behind symptoms and signs and symptoms have poor accuracy in diagnosing ACS. Lung ultrasound is painless, radiation free, can be easily repeated, takes less than 10 minutes and may be available at the point of care in locations where radiography is unavailable. Consolidation on lung ultrasound demonstrated a higher sensitivity (100%, 95% CI (84, 100%) and higher predictive value of a negative test (100%, 95% CI (92, 100%) than chest XRAY (Preto-Zamperlini, Pediatr Blood Cancer 2022, PubMed ID: 34931750).

It can be used to rule out ACS if the lung ultrasound is negative and to rule in ACS in order to initiate therapy in the patient with a high clinical suspicion of ACS and a negative chest XRAY. Two pediatric studies conducted in the US with a similar rate of ACS demonstrated lower sensitivities of 81-87% and higher specificities 91-94%, 95% CI (88, 97%) (Daswani, Acad EM 2018, PubMed ID: 27155438), (Cohen, Annals EM 2020, PubMed ID: 32928462). The later studies differed in that the ultrasonographers were blinded to history and physical examination findings.

The management of ACS involves treating the most common causes of infection with antibiotics, and providing respiratory monitoring and support. The usual antibiotic regimen is oral Azithromycin (Chlamydia/Mycoplasma coverage) and intravenous Ceftriaxone (typical bacterial coverage). Vancomycin is reserved for patients with severe disease to cover resistant Staphylococcal and Streptococcal species. These patients should only be given maintenance fluids, and bolus fluids should be avoided unless there are signs of dehydration. Overhydration will put them at risk for worsening disease and respiratory failure. Oxygen and non-invasive ventilation may be required. Indications for simple or exchange transfusion include severe anemia, refractory hypoxemia and clinical or radiographic evidence of severe or worsening disease.

MANAGEMENT OF ACUTE CHEST SYNDROME	
CATEGORY	COMMENTS
Antibiotics	Azithromycin: Chlamydia and mycoplasma pneumoniae Ceftriaxone: Bacterial coverage Vancomycin: indicated for severe infection or if not responding to initial coverage, concern for Staphylococcus, Penicillin-resistant pneumococcus
Bronchodilators	Limited evidence for routine use Recommended if wheezing or asthma history
Incentive Spirometry	Evidence supports usage in all patients
Transfusion	Evidence supports usage in: Moderate/severe disease Decreased hemoglobin (> 1 gm/dl below baseline) Consider partial exchange transfusion in severe disease
BiPAP	Small studies show benefit with respiratory distress
Nitric Oxide	Case reports of improvement in critical patients
Steroids	Not recommended (risk outweighs benefits)
Intravenous Fluids	Maintenance Fluids unless dehydrated, Avoid hypervolemia and hypovolemia as both can worsen outcomes.

STROKE: Cerebrovascular accident (CVA) is a rare though life-threatening sequelae of SCD. The likelihood of having a CVA increases with age, peaking at 24% by age 45. CVA associated with SCD can result from infarction (occlusion, embolic) as well as hemorrhage. Presenting symptoms of infarction include hemiparesis, dysphasia, gait disturbance, altered mental status and headache. Hemorrhage stroke may present with symptoms of increase intracranial pressure such as severe headache, vomiting, stiff neck, coma, and seizures. Any patient with SCD who presents with a neurologic sign or symptom must undergo immediate non-contrast CT scan. CT will readily identify hemorrhagic lesions, although infarcts may not appear on imaging until 6 hours following the event. A CT angiogram or CT perfusion can demonstrate ischemic stroke earlier. Treatment includes exchange transfusion and neurologic and neurosurgical consultation. There is limited evidence for thrombolytic therapy.

PRIAPISM: Priapism is a persistent painful erection that is not related to sexual simulation. Priapism can be categorized as ischemic or non-ischemic. In general, the patient's medical and medication history as well as the physical exam. can distinguish between the two types. Doppler ultrasonography or cavernosa blood case analysis (Ischemia → acidosis, hypercarbia) can confirm the etiology.

PRIAPISM CLASSIFICATION[1]		
	ISCHEMIC	NON-ISCHEMIC
Prevalence	Common	Rare
Blood Flow	↓ or No cavernosa flow	↑ Abnormal arterial flow
Etiology	Sickle Cell Malignancy, Medications[2]	Trauma
Pain	Severe	Mild
Firmness	Severe	Mild-Moderate
Long Term Damage	Yes	No
Management	Emergent	Elective, Operative

1. A 3rd category of "stuttering" priapism is defined as unwanted, painful erections that are often self-limiting but may precede ischemic priapism
2. Antihypertensives, Anticoagulants, Antidepressants, Cocaine, Methylphenidate, Intracavernous injection for erectile dysfunction (Alprostadil, Papaverine, Prostaglandin E1)

In sickle cells disease, ischemic priapism it is a result of vaso-occlusion. It should be managed as a medical emergency as it can cause permanent damage (fibrosis) and lifelong disability (erectile dysfunction). Early hydration, pain control and urologic consultation is essential but no systemic treatment has demonstrated efficacy.

Intracavernous treatment is warranted for priapism lasting more than 4 hours with a goal of detumescence (American Urologic Association Guideline: J Urol 2003 (Validity Confirmed 2010), PubMed ID: 14501756). Some patients can be managed with parental analgesia and a dorsal penile nerve block. Others may require procedural sedation.

The first step is aspiration of each corpus cavernosum of blood with an 18-20 gauge needle and irrigation with saline. The initial aspirate can be sent for blood gas analysis. If the penis remains erect, a sympathomimetic agent (most commonly phenylephrine: an $alpha_1$ agonist vasoconstrictor) is injected. Phenylephrine should be diluted to a concentration of 500 mcg/ml (0.5 ml of 10mg/ml Phenylephrine and 9.5 ml of normal saline). 1 ml is injected every 5 minutes for 3 injections. A lower concentration and volume of Phenylephrine should be considered for pediatric patients. Patients should be monitored for systemic effects (hypertension, headache, reflex bradycardia or tachycardia, arrhythmias). A surgical shunt may be indicated for patients not responsive to Intercavernous treatment. The role of exchange transfusion is controversial.

WEB LINK: PRIAPISM INTRACAVERNOUS PROCEDURE

ANEMIC CRISES

Anemia in sickle cell patients may occur chronically due to increased red cell destruction or acutely by a number of mechanisms. While chronic anemia is generally well tolerated acute anemic crises may result in a severe symptomatology. Chronic hemolysis increases the risk of bilirubin (pigment) gall stone cholelithiasis and cholecystitis. See also: PEM Guide: Gastrointestinal: Cholelithiasis and Cholecystitis.

ACUTE ANEMIC CRISES				
	MECHANISM	HEMOGLOBIN	RETICS	SPLEEN
Aplastic	↓ Production	↓	↓↓	No
Hyperhemolytic	↑ Breakdown	↓	↑↑↑	No
Splenic Sequestration	↓ Circulating RBCs	↓	↑	Yes

APLASTIC CRISIS: Aplastic crisis is a life-threatening sequelae of sickle cell disease. The etiology of aplastic crisis is thought to arise from Parvovirus B19 infection destroying erythroid precursor cells. Patients commonly present with pallor, petechiae, and weakness following a viral prodrome. Treatment is predominantly symptomatic, involving packed red blood cells (PRBC) and platelet transfusion and isolation, and treatment of infection if febrile. If properly treated, patients often recover in 5-10 days.

SPLENIC SEQUESTRATION: Acute splenic sequestration (ASSC) is the most common cause of an acute exacerbation of anemia (anemic crises) in patients with sickle cell disease and is associated with significant morbidity and mortality (10-15%). It can be fatal within a few hours of onset. ASSC is caused by intrasplenic trapping of red cells which causes a precipitous fall in hemoglobin level and the potential for hypovolemic, hemorrhagic shock. It is often associated with viral or bacterial infections. 50% of those who survive the first episode have a recurrence.

It is most common in children with SCD-SS from 3 months - 5 years of age. In patients with non-SS sickle cell disease it can occur at later ages as splenic fibrosis due to auto-infarction occurs over a longer time frame. For example, the mean age of ASSC in patients with SCD-SC is approximately 9 years. Splenic sequestration can also occur in adults with SCD-SC disease and SCD-S beta-thalassemia. Patients present with sudden signs of shock (weakness, pallor, tachycardia, tachypnea hypotension) and left sided abdominal pain/distention.

ACUTE SPLENIC SEQUESTRATION DEFINITION
Hemoglobin > 2 g/dL from baseline AND
Erythropoiesis: Reticulocyte count AND
An acutely enlarging spleen on examination
Thrombocytopenia due to splenic platelet sequestration can also occur

The primary, emergency treatment is the correction of hypovolemia with red blood cell transfusion. After transfusion, red cells sequestered in the spleen are remobilized, splenomegaly regresses, and the hemoglobin level increases, often to a level greater than predicted on the basis of the volume of red cells administered.

Prevention strategies for disease recurrence include: observation only, chronic transfusion, and splenectomy. Indications for these approaches are not clearly defined because of insufficient or conflicting evidence. Some recommend chronic transfusion in those less than 2 years of age due to their increased risk of infection with splenectomy until a splenectomy can be considered after 2 years of age.

HYPER-HEMOLYTIC CRISIS: Hyper-hemolytic crisis is a sudden severe hemolytic anemia accompanied by reticulocytosis. The etiology is poorly understood, and is thought to overlap with the other sickle cell crises (splenic sequestration, aplastic crisis, painful crisis). It can also be precipitated by drugs and infection. Treatment is supportive, involving partial exchange transfusion if severe.

INFECTIOUS CRISES

Fever is a common ED presenting complaint in patients with SCD. Infection and in particular sepsis in patients with SCD is the most common cause of mortality in pediatric sickle cell patients. Patients with SCD are considered immunocompromised due to splenic dysfunction and atrophy, leaving them susceptible to encapsulated organisms (Strep Pneumoniae, Salmonella, Pseudomonas, Klebsiella). They should be evaluated quickly and thoroughly. There is a low threshold for the use of empiric antibiotics. Laboratory evaluation may include: CBC, urinalysis, chest XRAY and oxygen saturation and cultures of blood (all patients) and urine and throat as indicated. A lumbar puncture should be performed for toxic appearing children and those with clinical signs of meningitis.

HIGH RISK CRITERIA: SICKLE CELL DISEASE AND FEVER	
History	Prior sepsis
Toxic appearance	Altered Mental Status Respiratory Distress (ACS) Poor Perfusion Dehydration
Severe Pain	Vaso-occlusive Crisis
Temperature	> 40º Celsius
CBC	WBC < 5,000 or > 30,000 Hemoglobin < 5 grams/dl Platelets < 100,000
Family	History of poor compliance History of allergy to beta-lactam antibiotics No telephone (cannot be reached for follow up)
Infection Requiring Admission	Meningitis Pneumonia with or without acute chest syndrome or ↓ oxygen saturation Osteomyelitis, Cellulitis or Abscess Pyelonephritis
WEB LINK: NIH: NATIONAL HEART, LUNG AND BLOOD INSTITUTE (2014)	

Patients should be treated for possible streptococcal infection with Ceftriaxone. For the treatment of lower respiratory tract infections, Azithromycin should be added to include coverage of mycoplasma and chlamydia pneumoniae. Staphylococcal and salmonella coverage should be included for bone (osteomyelitis) or joint (septic arthritis) infections. If a urinary tract infection is possible then coverage for E. Coli and other gram negative pathogens should be added.

There have been several studies on how to risk-stratify patients with SCD who present with fever. Patients can be treated with intramuscular or intravenous ceftriaxone and discharged with 24-hour followup if they do not meet high-risk criteria and remain clinically stable for 3 hours after antibiotic administration. If patients are classified as high risk, they should be hospitalized and treated with Ceftriaxone. Vancomycin should be reserved for patients with symptoms of sepsis or meningitis.

APPENDIX: SYSTEMIC ANALGESIA

Systemic pain relievers can be categorized as opioid or non-opioid. When systemic analgesia is required, consider all possible adverse effects. Consider placing the patient on cardiorespiratory monitoring if indicated, have airway supplies handy in the event of unintentional over-sedation, and know your reversal agents.

1. NON-OPIOID ANALGESIA

ACETAMINOPHEN (TYLENOL)	
Routes	IV, PO, PR
Pharmacology	Inhibition of prostaglandin production
Dose	10-15 mg/kg (maximum dose 1 gram)
Onset	PO: < 1 hour, IV: 5-10 minutes
Duration	4-6 hours
Indications	Mild pain, antipyretic

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)	
Examples	Ibuprofen (PO), Naproxen (PO), Toradol (IV/IM)
Pharmacology	COX enzyme inhibition, decreasing downstream production of prostaglandin
Dose	Ibuprofen: 10 mg/kg, maximum dose 600-800 mg Naproxen: 5-6 mg/kg, maximum dose 500 mg Toradol: 0.5 mg/kg/dose (maximum dose 15 mg < 17 years, 30 mg > 17 years
Onset	Ibuprofen: 30-60 minutes Naproxen: 30-60 minutes Toradol: 30 minutes
Duration	Ibuprofen: 6 hours Naproxen: < 12 hours Toradol: 4-6 hours
Adverse Effects	Gastrointestinal irritation, inhibited platelet function

KETAMINE: Ketamine is a non-opioid medication that is more popular in ED settings for procedural sedation or induction of anesthesia, though it is less popular for pure analgesia. It is touted for its abilities to provide different effects at different doses. In low doses, it can provide analgesia. Due to attempts to decrease opioid usage, analgesic dose ketamine has become more common. At higher doses it produces dissociative effects, resulting in analgesia and amnesia.

Ketamine is available in PO, IV, IM, and intranasal formulations. However, PO formulations have very low bioavailability and are rarely used. Ketamine can cause hallucinations and other emergence phenomena. Adverse reactions include laryngospasm, increased oral secretions (therefore one may also consider pre-medication with atropine).

KETAMINE	
Class	Phencyclidine derivative, dissociative agent
Pharmacology	NMDA receptor antagonist
Dose (analgesia only)	0.1-0.15 mg/kg IV 1-2 mg/kg IM
Onset	IV: 1-2 minutes, IM: 5 minutes
Duration	IV: 15-60 minutes, IM: 15-60 minutes
Indications	Painful procedures that may benefit from amnestic effects
Adverse Effects	Respiratory depression < 3 months of age Laryngospasm Increased airway secretions Prolonged emergence/emergence reactions (hallucinations) Significant increases in intraocular and intracranial pressure have not be demonstrated with Ketamine

2. OPIOID ANALGESIA

CODEINE: In 2013 after multiple high profiled mortalities, the FDA issued a black box warning stating that codeine should not be used in children less than16 years of age. Codeine is a prodrug. It has no intrinsic analgesic properties. It is metabolized in the liver by CYP2D6 enzyme, ultimately producing morphine and morphine-6-glucuronide, which have analgesic properties. There is considerable variation among individuals in the efficacy of codeine as a result of the CYP2D6 enzyme, which exhibits genetic polymorphism. This ultimately means that following a normal dose of Codeine, rapid metabolizers may produce very high concentrations of morphine and poor metabolizers may produce no active metabolites at all.

OPIOID COMPARISON		
	ONSET	DURATION
Morphine	5-15 minutes	3-4 hours
Fentanyl	IV: 1-2 minutes IN: 10 minutes IM: 7-15 minutes	IV: 30-60 minutes IN: 60 minutes IM: 1-2 hours
Hydromorphone	IV: Almost immediately PO: 30 minutes	IV: 2-4 hours PO: 4-5 hours

MORPHINE	
Pharmacology	Mu opioid receptor agonist
Dose	IV: 0.05 to 0.1 mg/kg PO: 0.2-0.5 mg/kg
Onset	IV: 5 minutes, PO: 30 minutes
Duration	4 hours
Indications	Severe pain
Adverse Effects	Respiratory depression, pruritus, constipation

OXYCODONE	
Pharmacology	Mu opioid receptor agonist
Dose	PO: 0.1 to 0.2 mg/kg If ≥ 50 kg 5 to 10 mg
Onset	10-15 minutes
Duration	4 hours
Indications	Moderate to severe pain
Adverse Effects	Respiratory depression, constipation

NORCO*	
Pharmacology	Mu opioid receptor agonist
Dose	PO: Hydrocodone 0.1-0.2 mg/kg ≥ 50 kg: Hydrocodone 5-10 mg
Onset	10-20 minutes
Duration	4-8 hours
Indications	Moderate to severe pain
Adverse Effects	Risk of acetaminophen overdose if combining with other acetaminophen containing products for pain control
*Hydrocodone (5.0. 7.5 or 10 mg) + Acetaminophen (325 mg)	

FENTANYL	
Pharmacology	Mu opioid receptor agonist
Dose	IV 1-2 mcg/kg (If ≥ 50kg give 25-50 mcg) slow push IN 1.5 mcg/kg once
Onset	IV: Immediate IM: 7-8 minutes IN: 5-10 minutes
Duration	IV: 30-60 minutes IM: 1-2 hours IN: variable – can re dose up to 0.5 mcg/kg every 5 minutes, up to 3 mcg/kg
Indications	Short acting but strong pain control
Adverse Effects	Rapid infusion may cause chest wall rigidity Respiratory depression

HYDROMORPHONE	
Pharmacology	Mu opioid receptor agonist
Dose	PO: 0.03 to 0.08 mg/kg IV: 0.015 mg/kg If ≥ 50 kg: PO 1-2 mg/kg, IV: 0.2-0.6 mg/kg
Onset	PO 15-30 minutes, IV 5 minutes
Duration	PO 3-4 hours, IV 3-6 hours
Indications	Has longer duration of action compared to other opioid meds, especially if using XR formulations which can last 12 hours
Adverse Effects	Respiratory depression, constipation

APPENDIX: SICKLE CELL DISEASE RBC TRANSFUSIONS

TRANSFUSION: TYPES	
Simple	Transfusion RBCs without removal of the patient's blood.
Exchange*	Transfusion RBCs with removal of the patient's blood.
*Manual or via an automated apheresis with an extracorporeal continuous flow device Both can be therapeutic or preventative/prophylaxis (prevent complications) Exchange transfusion does not increase iron stores/iron overload	

TRANSFUSION: GOALS
↑ Hb (addition) → ↑ Oxygen carrying capacity (CaO_2), ↑ Perfusion
Exchange: ↓ %HbSS (dilution, suppress production) → ↓ Viscosity → ↓ Vasoocclusion
Exchange transfusion more effective in ↓ %HbSS). Typically target HbSS < 30% No evidence that transfusion improves vasoocclusive painful crisis

TRANSFUSION: ACUTE THERAPEUTIC INDICATIONS	
Vasoocclusive	Stroke, Acute chest syndrome[1]
Anemic	Acute/Symptomatic: aplastic, hyper-hemolytic, splenic sequestration[2]
Infectious	Sepsis with multiorgan failure and Hb < 7 mg/dl
Cardiovascular	Any above with hemodynamic compromise
The decision to perform an acute simple vs exchange transfusion should be made in conjunction with the patients hematologist 1. Exchange transfusion typically recommended in severe vasoocclusive complication 2. Simple transfusion typically recommended in severe, acute, symptomatic anemia	

SIMPLE TRANSFUSION: INDICATIONS
1. Hgb < 2 g/dL below patient's baseline AND new signs or symptoms*
2. Progressive ↓ Hb over several days without a compensatory ↑ Reticulocyte count
*Symptoms: Tachycardia, postural hypotension, dizziness, mental status change, dyspnea, or congestive heart failure

TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD (TACO)
Symptom occurrence, signs of acute pulmonary edema within 6 hours of transfusion
Risk factors: Chronic renal failure, history of heart failure, hemorrhagic shock increased number of blood products transfused and fluid balance per hour
Monitor for fluids overload: 1/2 way through, immediately after, several hours after

BLOOD TRANSFUSION VOLUMES
Children**:** 10 mL/kg PRBC → ↑ Hgb by 2.5-3.0 g/dL and ↑ HCT by 7-9%
Adults**:** 1 unit PRBC → ↑ Hgb by 1 g/dL and ↑ HCT by 3%

TRANSFUSION: FORMULAS AND SAMPLE CALCULATIONS	
SIMPLE TRANSFUSION	FORMULA
Volume to Transfuse (ml) =	((desired HCT – current HCT) x TBV) / prbc HCT
Volume to Transfuse (ml) =	((30% – 20%) x 1,600 ml) / 60% = 266 ml
MANUAL PARTIAL EXCHANGE TRANSFUSION	FORMULA
Volume to Transfuse (ml) =	((desired HCT – current HCT) x TBV) / (prbc HCT - [(current HCT + desired HCT) ÷ 2])
Volume to Transfuse (ml) =	((30% – 20%) x 1,600 ml) / (60% - [(20% + 30%) ÷ 2]) = 458 ml
1. Normal Saline: 500 ml 2. Phlebotomize: 458 ml (maximum amount phlebotomized = 500 ml) 3. Transfuse 458 ml PRBC (maximum amount transfused = 2 units)	
SAMPLE CALCULATIONS: 20 kg child Desired HCT = 30%, current HCT = 20%, prbc HCT = 60% TBV = 80 ml/kg x 20 kg = 1,600 ml	
Children: Do not round the volume up or down to the nearest PRBC unit Adults: May round up or down to nearest number of PRBC units	

FORMULAS DEFINITIONS	
Total Blood Volume (TBV)	Infants: 100 mg/kg, Children: 80 ml/kg Adult (Men): 70 ml/kg, Adult (women): 60 ml/kg
Hematocrit (HCT)	Expressed as a percent e.g. HCT 30%
PRBC Hematocrit	Typically HCT = 55-60%
PRBC Volume	Variable, typically volume = 300-400 ml

TUMOR LYSIS SYNDROME

INTRODUCTION (ELISE PERLMAN, MD 12/2020)
Tumor Lysis Syndrome (TLS) is an oncologic emergency that is caused by the rapid breakdown of tumor cells resulting in the release of intracellular contents into the bloodstream. Intracellular content release results in hyperkalemia, hyperphosphatemia, hyperuricemia and secondary hypocalcemia. Clinical toxicity can include acute renal insufficiency, cardiac arrhythmias, seizures and multiorgan failure leading to death.

PATHOPHYSIOLOGY

TLS most often occurs after the initiation of cytotoxic therapy (chemotherapy, cytolytic antibody therapy, radiation therapy and glucocorticoid therapy) in patients with acute lymphoblastic leukemia and highly aggressive lymphoma (specifically Non-Hodgkin's lymphoma (Burkitt's subtype)). However, it can also occur spontaneously prior to treatment. The improvement in the number and types of highly effective therapies has increased the likelihood of tumor lysis syndrome.

HIGH-RISK INTRINSIC TUMOR-RELATED FACTORS
High tumor cell proliferation rate
Chemosensitivity of the malignancy
Large tumor burden: Bulky disease >10 cm in diameter, WBC >100K
Pre-treatment LDH >2x upper limit of normal
Organ infiltration or bone marrow involvement

NUCLEIC ACIDS: Tumor lysis leads to hyperuricemia. The purine nucleic acids adenosine and guanosine are metabolized into hypoxanthine and xanthine respectively. These, in turn, are metabolized into uric acid by the enzyme xanthene oxidase. Uric acid is poorly water soluble leading to the crystal precipitation of in the renal tubules and ultimately leading to renal insufficiency. The use of Allopurinol, which competitively inhibits xanthine oxidase can result in the accumulation of xanthine which cans also precipitate in the renal tubes.

POTASSIUM: Large quantities of potassium are released from tumor cell lysis. In addition, hyperkalemia can be exacerbated in the setting of acute kidney injury. Potassium depolarizes cell membranes, slows conduction and increases myocardial excitability.

PHOSPHATE: Tumor cells have a 4-fold higher phosphate concentration than normal cells. Rapid lysis of tumor cells leads to hyperphosphatemia when homeostatic mechanisms are overwhelmed. Hyperphosphatemia can be exacerbated in the setting of acute kidney injury. Hyperphosphatemia causes calcium-phosphate precipitation in the renal tubules contributing to acute kidney injury and the development of secondary hypocalcemia. In addition, calcium phosphate can precipitate in cardiac tissues leading to arrhythmias.

CALCIUM: Secondary hypocalcemia occurs due to hyperphosphatemia which causes calcium-phosphate precipitation in tissues.

RENAL INJURY: Renal tubule injury can result from deposition of uric acid, calcium phosphate and xanthine (increased with Allopurinol treatment). A decrease in renal function further exacerbates hyperkalemia and hyperphosphatemia leading to a cascade of worsening renal function.

MULTI-ORGAN FAILURE: Tumor Lysis leads to the release of cytokines that cause a systemic inflammatory response syndrome that can cause multi-organ failure.

CLINICAL MANIFESTATIONS

A high index of suspicion is required in patients presenting with any newly diagnosed oncologic process especially in the setting of recent initiation of treatment. It is also possible for electrolyte disturbances and kidney injury to be present prior to formal diagnoses due to high level of tumor turnover. Case reports suggest that TLS in children may also be triggered by infections including urinary tract infections and pneumonia. The signs and symptoms associated with TLS are due to the associated metabolic abnormalities.

CLINICAL MANIFESTATIONS	
Cardiac	Heart failure, arrhythmia, syncope
GI	Vomiting, diarrhea, anorexia
Musculoskeletal	Muscle cramps, tetany
Neurologic	Lethargy, seizures
Renal	Hematuria, flank pain

HYPERKALEMIA: Hyperkalemia is the most dangerous component of TLS due to the risk of arrhythmia and sudden death. Signs and symptoms of hyperkalemia may be nonspecific. Patients may complain of fatigue, muscle weakness or cramps, paralysis or paresthesias, palpitations, nausea and vomiting. Clinical signs may include: altered mental status, dysrhythmias, weakness/paralysis and decreased deep tendon reflexes. EKG changes progress from peak T waves to a sine wave QRS pattern and asystole.

HYPOCALCEMIA: Hypocalcemia can cause arrhythmias, hypotension, heart failure, sudden death, seizure and neuromuscular irritability. Signs of neuromuscular irritability may include tetany, paresthesia, muscle twitching, carpopedal spasms, Trousseau’s sign, Chvostek’s sign, laryngospasm and bronchospasm.

DIAGNOSIS

Tumor Lysis is defined by both laboratory and clinical features. In Laboratory TLS two or more metabolic abnormalities must be present during the same 24-hour period either 3 days before or 7 days after the initiation of therapy. Clinical TLS requires the presence of laboratory TLS plus at least one of the following: increased creatinine level (as a marker of renal insufficiency), seizures, cardiac arrhythmias or death.

DIAGNOSTIC TESTING	
LABS	PRN
CBC	Chest XRAY (? Mediastinal mass)
BMP, magnesium, phosphorus, VBG	EKG (K^{+}, Ca^{++} changes)
Uric Acid	Infection evaluation (? Precipitant)
LFT’s, LDH	G6PD (Contraindication to Rasburicase)
Urinalysis (blood, crystals)	Beta HCG

TUMOR LYSIS SYNDROME: LABORATORY CRITERIA (CAIRO-BISHOP)	
≥ 2 below within 3 days before or 7 days post cytotoxic therapy	
↑ Uric Acid	8.0 mg/dl (476 mmol/L) or ↑ > 25% from baseline
↑ Potassium	6.0 meq/L (6.0 mmol/L) or ↑ > 25% from baseline
↑ Phosphorus	Children:6.5 mg/dl (2.1 mmol/L) or ↑ > 25% from baseline Adult: 4.5 mg/dl (1.45 mmol/L) or ↑ > 25% from baseline
↓ Calcium	≤ 7 mg/dl (≤ 1.75 or mmol/L) or ↓ >25% from baseline

TUMOR LYSIS SYNDROME: CLINICAL CRITERIA
Lab Criteria for TLS + ≥ 1 of following not attributable to therapy
Acute kidney injury: ↑ Creatinine 0.3 mg/dL or 1.5 times upper limit of normal or Oliguria: Average urine output < 0.5 ml/kg/hour for 6 hours
Cardiac arrhythmias
Seizure
Sudden death

MANAGEMENT

Treatment may be preventative if TLS is anticipated or in response to existing TLS. Prevention of TLS is dependent on the risk of TLS (tumor burden, therapy to be used) and typically involves intravenous hydration with or without hypouricemic agents. Management of existing TLS is based on TLS severity (Appendix: TLS Severity) and includes include hydration, hypouricemic agents and the correction of electrolyte abnormalities, focusing on the prevention of dysrhythmias and neuromuscular irritability and the preservation of renal function. Hematology-oncology should be involved early in the care of both new and existing patients. Renal consultation is essential if renal replacement therapy is anticipated (See: Guideline, Journal Clin Onc 2008, PubMed ID: 18509186). Patients require cardiac monitoring and frequent electrolyte assessment.

MANAGEMENT GOALS	
1	Treatment of symptomatic hyperkalemia
2	Treatment of hyperphosphatemia
3	Treatment of symptomatic hypocalcemia
4	Hydration to promote renal flow
5	Reduce uric acid production with Allopurinol or Febuxostat
6	Increase uric acid degradation with Rasburicase
7	Renal replacement therapy

TREAT SYMPTOMATIC HYPERKALEMIA: The management of symptomatic hyperkalemia is dependent on the etiology, degree of hyperkalemia and clinical manifestations.

Three methods are used to treat hyperkalemia
1. Antagonize the membrane effects of potassium: Calcium gluconate
2. Drive extracellular potassium into cells: Beta agonists, glucose/insulin, $NaHCO_3$
3. Remove excess potassium from the body: Diuretics, exchange resins, dialysis

The first two methods above provide only transient decreases in serum potassium but do not decrease total body potassium. Hemodialysis is favored in renal failure, arrhythmia related to hyperkalemia or expected ongoing cell lysis. Asymptomatic hyperkalemia can be treated with sodium polystyrene sulfonate. See Appendix: Medication for Hyperkalemia

2. TREAT HYPERPHOSPHATEMIA: Treatment of hyperphosphatemia includes reduction of phosphate intake, adequate hydration and the use of phosphate binders. Calcium containing phosphate binders (e.g. calcium carbonate) are preferred in patients with both hyperphosphatemia and hypocalcemia. Severe refractory hyperphosphatemia may require dialysis.

3. TREAT SYMPTOMATIC HYPOCALCEMIA: Symptomatic hypocalcemia is treated with calcium at the lowest dose required to relieve symptoms as to avoid further increase in the production of calcium-phosphate, the rate of crystallization and obstructive uropathy. Asymptomatic hypoglycemia is not treated due to calcium phosphate deposition. Calcium will also antagonize the membrane effects of hyperkalemia. Unless, severely symptomatic (tetany, arrhythmias), calcium should be delayed until hypophosphatemia is corrected.

HYPOCALCEMIA: IV/IO			
	Pediatric	Adult	Indication
Calcium Chloride (10%)	0.2 ml/kg (20 mg/kg)	1.0 gram	Arrest, CVL
Calcium Gluconate (10%)	0.6 ml/kg (20 mg/kg)	3.0 grams	Non-arrest, PIV
While both preparations are labelled 10% (1 gram/10ml), calcium chloride has 3 times the amount of elemental calcium Slow infusion over 3-5 minutes while on a cardiac monitor, Ca Gluconate preferred Do not give in same IV with $NaHCO_3$ ($CaCO_3$ precipitates)			

4. HYDRATION: Administer intravenous crystalloid at 2-3 liters/m^2/day (200 ml/kg/day if < 10 kg) to prevent uric acid and calcium phosphate deposition in the renal tubules and promote excretion. Fluids are titrated to achieve a urine output 2 ml/kg/hour (4-6 ml/kg/hour in patients less than 10 kg) and urine specific gravity of 1.010. The choice of fluids depends on the clinical context. Some experts prefer hypotonic fluids (e.g. D5 1/4 Normal Saline), as excess sodium in the setting of hyperuricemia may lead to formation of poorly soluble uric acid compounds and sodium retention may occur if treated with corticosteroids. Isotonic saline should be administered to patients who are hyponatremic or volume depleted.

Patient with underlying renal or cardiac disease should be monitored for signs of fluid overload. Diuretics may be required to maintain urine output. Diuretics should be avoided in patients with obstructive uropathy or volume depletion. Loop diuretics (e.g. Furosemide) which promote potassium excretion are preferred.

5. **REDUCE URIC ACID PRODUCTION:** Allopurinol is a xanthine analog and functions to competitively inhibit the xanthine oxidase enzyme. This prevents the metabolism of xanthine and hypoxanthine to uric acid. Allopurinol prevents the production of new uric acid but does not facilitate the degradation or excretion of pre-existing uric acid and therefore may take several days for uric acid to normalize.

There are several impediments to the use of allopurinol. There are a number of interactions with other medications (chemotherapy agents, antibiotics, diuretics and antiepileptics), severe cutaneous reactions can occur in Asian patients with certain HLA alleles and Allopurinol requires dosing adjustment in renal insufficiency. In addition, allopurinol leads to the accumulation of the precursor, xanthine, which is less soluble than uric acid and may precipitate in the renal tubules and cause xanthine nephropathy.

ALLOPURINOL DOSING	
Oral	Adult: 100 mg/m^2 PO Q8H (maximum 800 mg/day)
	Children: 50-100 mg/m^2 PO Q8H (maximum 300 mg/m^2/day) or 10 mg/kg/day divided Q8H (maximum 800 mg/day)
Intravenous	200-400 mg/m^2/day divided QD to TID IV (maximum 600 mg/day)
*Renal dosing adjustment required	

Febuxostat is a selective inhibitor of xanthine oxidase. It is indicated in patients who do not tolerate Allopurinol or for whom Rasburicase is unavailable or contraindicated. It can be used in patients with mild-moderate renal insufficiency and has fewer interactions with other medications when compared to Allopurinol. Evidence of Febuxostat's safety and efficacy in the pediatric population, is limited.

Previously, alkalinization with sodium bicarbonate was recommended to enhance excretion of uric acid. However, alkalinization also decreases the excretion of phosphorus which can lead to calcium phosphate precipitation in the renal tubules and decreases the solubility of xanthine and hypoxanthine leading to xanthine uropathy.

6. INCREASE URIC ACID DEGRADATION: Rasburicase is a recombinant urate oxidase enzyme, an enzyme found in some mammalian species but absent in humans. This enzyme enhances the degradation of uric acid into allantoin, a more soluble and readily excreted metabolite. By preventing both xanthine and uric acid accumulation, Rasburicase is more effective than allopurinol for the prevention and treatment of existing hyperuricemia. Rasburicase is preferred in those with existing hyperuricemia, renal or cardiac involvement or Asian patients requiring urgent chemotherapy before HLA alleles testing is available. Rasburicase is contraindicated in patients with G6PD deficiency. Serious adverse effects include hemolysis, hemoglobinuria, methemoglobinemia, anaphylaxis, neutropenia, mucositis and sepsis.

There have been several controlled and observational studies in children with hyperuricemia secondary to TLS, that have demonstrated a rapid reduction of uric acid after the initiation of Rasburicase. However, the use of Rasburicase is controversial and not standardized and remains at the discretion of the oncology service.

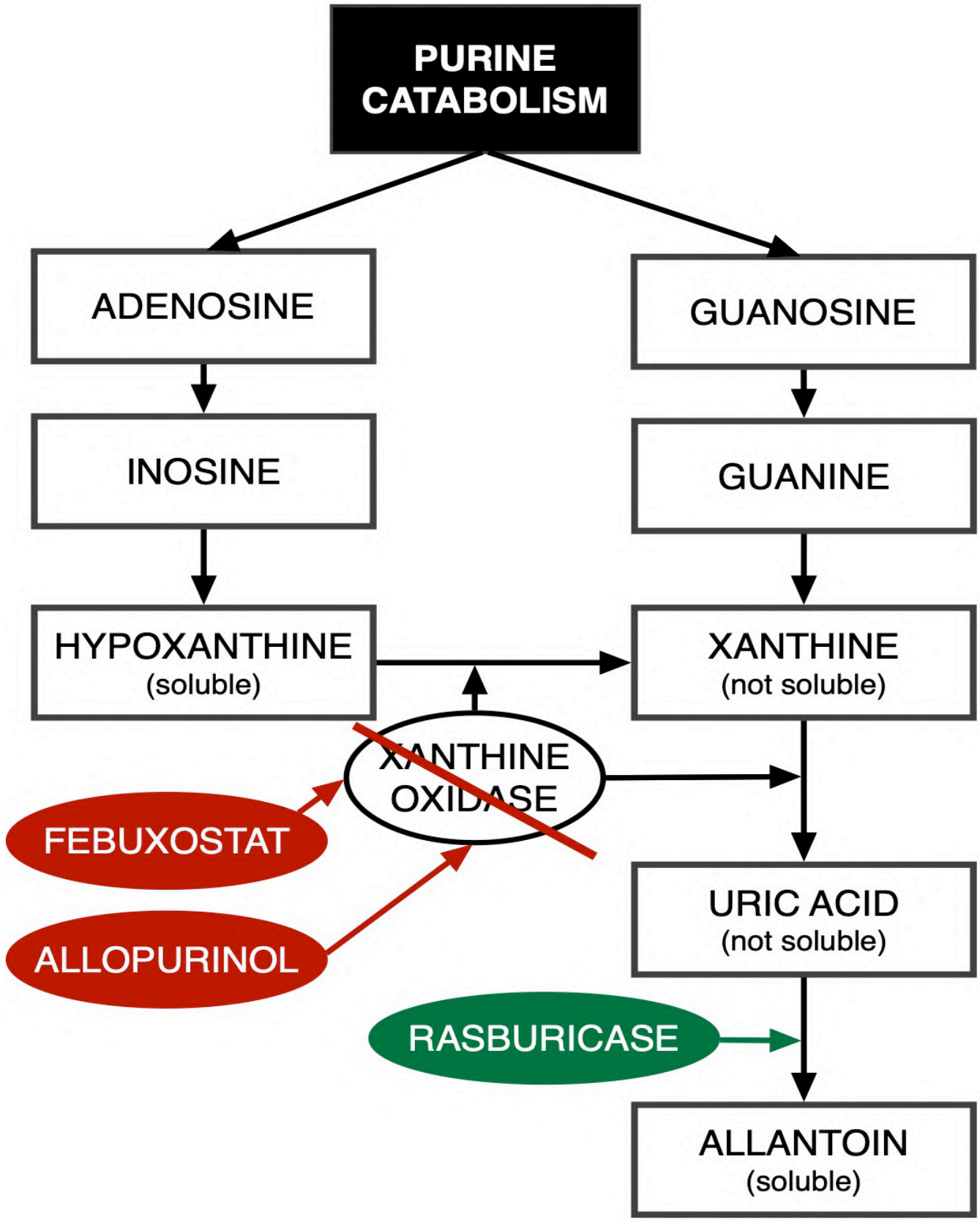
RASBURICASE DOSING	
0.2 mg/kg IV daily x 5-7 days	High risk of TLS or uric acid ≥ 8 mg/dl
0.15 mg/kg IV daily x 5-7 days	Intermediate risk of TLS and uric acid < 8 mg/dl
*Avoid with G6PD deficiency	

7. RENAL REPLACEMENT THERAPY: Severe hyperkalemia with acute kidney injury or cardiac arrhythmia is an indication for renal replacement.

INDICATIONS FOR RENAL REPLACEMENT THERAPY
Severe oliguria or anuria
Severe acidosis
Fluid overload refractory to diuretics
Persistent hyperkalemia
Uremia
Severe hyperphosphatemia
Symptomatic hypocalcemia

DISPOSITION
Patients with TLS should be admitted to the Pediatric Intensive Care Unit for continuous telemetry and frequent electrolyte monitoring.

APPENDIX: PURINE CATABOLISM



ALLOPURINOL inhibits the enzyme xanthine oxidase thereby preventing formation of uric acid. It does not reduce the uric acid that has already been formed. In addition, it increases the amount of xanthine which can also precipitate in the renal tubule.

FEBUXOSTAT inhibits the enzyme xanthine oxidase thereby preventing formation of the uric acid.

RASBURICASE is a recombinant urate oxidase enzyme that converts uric acid to a more water soluble metabolite, allantoin, that can then be excreted.

APPENDIX: TUMOR LYSIS SYNDROME: SEVERITY GRADING

TUMOR LYSIS SYNDROME: SEVERITY GRADING			
	Creatinine	Cardiac Arrhythmia	Seizure
0	< 1.5 x ULN	None	None
1	1.5 x ULN	No intervention indicated	None
2	1.5-3.0 x ULN	Non-urgent intervention	One brief, generalized Controlled by antiepileptic or Infrequent focal motor seizure not interfering with ADL
3	3.0-6.0 x ULN	Symptomatic, incompletely controlled medically or Controlled with Device	Seizure with altered consciousness or Poorly controlled with breakthrough generalized seizure despite medical intervention
4	> 6.0 x ULN	Life-threatening e.g. arrhythmia with heart failure, shock, hypotension or syncope	Seizure of any kind which are prolonged, repetitive or difficult to control (e.g., status epilepticus, intractable epilepsy)
5	Death	Death	Death
Abnormality not directly or probably attributable to a therapeutic agent			
ULN: Upper Limit of Normal, if ULN not available use the table below			
	> 1 to < 12 years	> 12 to 16 years	≥ 16 years
Male	> 0.7 mg/dl	> 1.0 mg/dl	> 1.3 mg/dl
Female	> 0.7 mg/dl	> 1.0 mg/dl	> 1.2 mg/dl

APPENDIX: MEDICATIONS FOR HYPERKALEMIA

CALCIUM	
Mechanism	Stabilizes cardiac cell membranes to effect of hyperkalemia
Indications	Prolonged QRS
Timing	Onset: 2-3 minutes, duration 30-60 minutes
Calcium Chloride	Calcium Chloride 10% (1 gram/10ml) (13.6 meq elemental Ca+/10ml) Child: 0.2 ml/kg (20 mg/kg), maximum dose 1 gram (10 ml) Adult:10 ml (1 gram) More rapid dissociation in the blood stream than Calcium Gluconate Risk of tissue necrosis with extravasation use CVL or large PVL
Calcium Gluconate (preferred)	Calcium Gluconate 10% (1 gram/10ml) (4.6 meg elemental Ca+/10ml) Child: 0.6 ml/kg (60 mg/kg), maximum dose 3 grams (30 ml) Adult: 30 ml (3 grams) Requires hepatic metabolism → Slower onset than Calcium Chloride Avoid in liver failure, shock
Frequency	Repeat Q5 minutes if EKG changes persist or recur
Caveat	Slow infusion on cardiac monitor over 3-5 minutes Do not give in same IV with $NaHCO_3$ ($CaCO_3$ precipitates) Contraindicated in digoxin toxicity

INSULIN/GLUCOSE	
Mechanism	Enhances activity of Na-K-ATPase pumps Shifts K+ from extracellular to intracellular space
Indications	EKG changes, K+ > 6.5
Timing	Onset 10-20 minutes, peak at 30-60 minutes, duration 4-6 hours
Indications	EKG changes or K+ > 6.5-7.0 meq/l
Adult Dosing	Glucose: 25 grams (50 ml of D50) Regular Insulin: 10 units
Child Dosing	Glucose:1 gram/kg D10 = 10 ml/kg, D25 = 4 ml/kg, D50 = 2 ml/kg) Regular Insulin: 0.2 units per gram of glucose
Caveats	Provide glucose infusion to avoid hypoglycemia Monitor bedside glucose closely

$NaHCO_3$	
Mechanism	Increase H+ ion out of cell to buffer HCO_3. K+ into cell in exchange for H+
Dose	Adult: 150 meq $NaHCO_3$ in 1 liter D5W at 250 ml/hour Do not give hyperosmolar concentration (e.g. 50 meg/50ml)
Caveat	Limited efficacy. Do not give with Ca++ ($CaCO_3$ precipitates) Not indicated in the absence of metabolic acidosis

BETA AGONISTS	
Mechanism	Decrease potassium release from cells,
Albuterol	10-20 mg/4ml via nebulizer over 10 minutes, duration 2 hours Note: This is 4-8 times the typical asthma dose of 2.5-5.0 mg

SODIUM POLYSTYRENE SULFONATE (KAEXOLATE)	
Mechanism	Binds potassium in GI tract, releases Na+ in exchange
Timing	Onset: 1-2 hours
Dose	Adult: 15-30 grams PO Child: 1 gm/kg PO
	May also be given as a retention enema (50 gm in 250 ml D5W)
	May repeat dose in 4-6 hours based on repeat K+
Caveat	Do not use with sorbitol. May cause intestinal necrosis
	Do not use in post-op or renal transplant patients
	DO not use rectal route in neutropenic patients

FUROSEMIDE (LASIX)	
Mechanism	Loop diuretic. Enhances excretion of K+
Dose	Adult: 20-40 mg IV Child: 1-2 mg/kg IV
Caveat	Higher dose may be required in renal insufficiency
	Limited short term efficacy
	Replace fluid losses (unless the patient is volume overloaded)

INFECTIONS

1. Cat Scratch Disease	Alexandra Van Oyen, DO
2. Enteroviral Infections	Ellen Duncan, MD, PhD
2. Febrile Infant and Child	James Tsung, MD
3. Febrile Neonate	James Tsung, MD
4. Infectious Mononucleosis	Michael Mojica, MD
5. Influenza	Carrie Danziger, MD
6. Lyme Disease	David Kessler, MD MSc
7. Measles	Shweta Iyer, MD
8. Mycoplasma Pneumoniae	Giovanna Varuzza Baye, MD
9. Poliomyelitis	Michael Mojica, MD
10. Rocky Mountain Spotted Fever	Michael Mojica, MD
11. Sepsis and Septic Shock	Michael Mojica, MD

CAT SCRATCH DISEASE

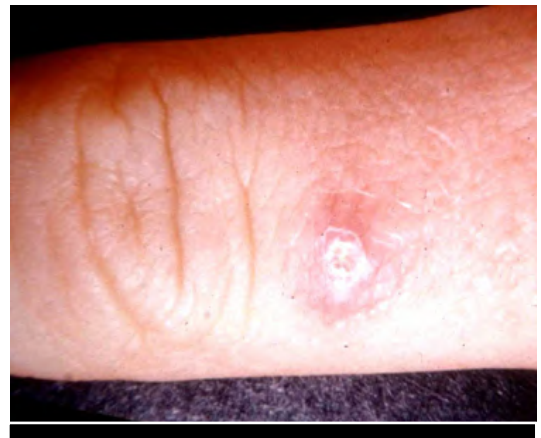
INTRODUCTION (ALEXANDRA VAN OYEN, DO 4/2023)
Cat scratch disease is caused by *Bartonella* species and is typically characterized by fever and self-limited regional lymphadenopathy though disseminated disease can occur. More than half of cases occur in children less than 18 years of age with a highest incidence in those 5-9 years of age. There are an estimated 22,000 new cases of cat scratch disease per year in the United States. In northern temperate zones, cat scratch disease occurs more often in the late summer through early fall.

MICROBIOLOGY
Bartonella henselae is an intracellular, gram negative rod. Arthropods (flees) serve as the vector for cats and cats serve as the vector for transmission to humans. Domestic cats have a 30-40% seroprevalence. B henselae is found in feline erythrocytes, which can contaminate saliva and then can be introduced into humans through cat bites or scratches as well as through contact with cat saliva in non-intact skin. The cat may be bacteremic though is typically asymptomatic. Kittens, cats adopted from shelters and strays are approximately 5 times more likely to be bacteremic than older, domesticated cats.

CLINICAL MANIFESTATIONS
Cat scratch disease is typically mild in the immunocompetent host consisting of self-limited regional adenopathy in the majority of patients. Constitutional symptoms occur in a third of patients and can include fever, myalgias, headache, nausea and abdominal pain. Clinicians should maintain a high index of suspicion for cat scratch disease in those with less common presentations. Bacillary angiomatosis and bacillary peliosis are reported in those immunocompromised with HIV infection.

PRESENTING SIGNS AND SYMPTOMS	
Fever	46.4%
Chills	3.1%
Night Sweats	3.8%
Weight Loss	2.1%
Headache	12.6%
Abdominal Pain	10.6%
Lymphadenopathy	
Neck	52.0%
Axillary	28.3%
Inguinal	13.9%
Other	28.3%
Splenomegaly	8.5%
Hepatomegaly	3.2%
Amin, Open Forum Peds ID 2022, PubMed ID: 36072697 Retrospective Case Series: 304 Children (1/2010-12/2018)	

CUTANEOUS: After contact with an infected cat, patients can develop a primary skin lesion at the inoculation site after 3 to 12 days. The lesion is often papular or pustular, but can be vesicular or nodular. It persists for 1-3 weeks but can last for months. Patients may also present with a maculopapular rash, erythema multiforme, erythema nodosum or thrombocytopenic purpura. The skin papule typically precedes lymphadenopathy by 1-2 weeks.



SKIN PAPULE

LYMPHADENOPATHY: Regional lymphadenopathy is the hallmark of cat scratch disease and develops one to two weeks after the cutaneous manifestations. Lymphadenopathy is typically unilateral and localized to the nodes draining the area inoculation site. The most common locations are the axillary, epitrochlear, cervical, supraclavicular, and submandibular lymph nodes. Younger children tend for have cervical adenopathy while adolescents tend to have groin or axillary adenopathy. The nodes are often tender with overlying erythema, induration and warmth and can range in size from 1-8 cm. Approximately 10% suppurate. Lymphadenopathy can persist for several months.

OCULAR: Ocular involvement occurs in 5-10% and is the most common atypical manifestation. Ocular disease can include Parinaud oculoglandular syndrome (most common), panuveitis, neuroretinitis, papillitis, optic neuritis, focal retinochoroiditis as well as retinal artery or vein occlusion. Parinaud's oculoglandular syndrome (POGS) consists of unilateral, follicular conjunctivitis (the site of inoculation) and ipsilateral facial lymphadenopathy (preauricular, upper anterior cervical, submandibular). The conjunctivitis is severe and can last several weeks. Neuroretinitis can manifest as an abrupt, painless, unilateral (though rarely bilateral) loss of vision.

VISCERAL INVOLVEMENT: Disease can disseminate to the liver and spleen. Patients may also have fever, myalgias, arthralgias, arthritis, hepatosplenomegaly and abdominal pain.

CENTRAL NERVOUS SYSTEM: Children typically present with aseptic meningitis or encephalitis. Complications can include seizures, ataxia and cranial nerve palsies.

OTHER: Less common manifestations include endocarditis, osteolytic lesions, glomerulonephritis, pneumonia, erythema nodosum and thrombocytopenic purpura. It is estimated that cat scratch disease may be etiologic in one-third of pediatric cases of fever of unknown origin.

DIFFERENTIAL DIAGNOSIS

Cat scratch disease should be considered in the differential diagnosis of any acute, subacute or chronic lymphadenopathy.

DIFFERENTIAL DIAGNOSIS
Cytomegalovirus lymphadenopathy
Epstein-Barr virus lymphadenopathy
Group A streptococcal adenitis
Human immunodeficiency virus lymphadenopathy
Malignancy (lymphoma, leukemia)
Nontuberculous mycobacterial lymphadenitis
Staphylococcus aureus adenitis
Toxoplasmosis lymphadenopathy

DIAGNOSTIC TESTING

Recent exposure to cats and characteristic physical examination findings can lead to a presumptive diagnosis of cat scratch disease. However, nearly a quarter of those with cat scratch disease report no exposure to cats. B. henselae is difficult to culture but is detectable by PCR and serologic testing. Both enzyme immunoassays (EIA) and indirect immunofluorescence antibody (IFA) detection of IgM and IgG antibodies are available. Serologic testing can confirm but not exclude the diagnosis. False negative and false positive IgM can occur. IgG most commonly reflects past exposure.
PCR for blood or tissue is highly specific and fairly sensitive.

Lymph node biopsy with silver staining can be considered if the diagnosis is unclear. Though the stain does not distinguish B henselae from other Bartonella species. Lymph node excision and abscess incision and drainage are typically not recommended due to the concern for fistula development. Testing and/or treatment of cats is not recommended .

Laboratory abnormalities are non-specific and include leukocytosis, elevated acute phase reactants and transaminitis.

DIAGNOSTIC TESTING	
Serology	Enzyme immunoassay (EIA) or indirect fluorescence assay (IFA)
	IgG titers < 1:64**:** No acute infection
	IgG titers of 1:64 to 1:256: Acute or Past infection (repeat in 2-4 weeks)
	IgG titers ≥ 1:256: Active or recent infection
	IgM (+): Acute infection, but production of IgM is usually brief and false positive and negative results can occur
Culture	Culture not routinely recommended: Fastidious, slow-growing (> 10 days),
PCR	Should not be routinely obtained: Sensitivity less than 20%
Lymph Node Biopsy	Not routinely recommended. In specific circumstances, including a delayed resolution of systemic symptoms or if an alternative diagnosis is suspected, providers may consider obtaining a biopsy

MANAGEMENT

In the majority of cases there is spontaneous resolution within 2-4 months. In mild cases, supportive care including antipyretics, anti-inflammatory and warm compresses to the inoculation site may be all that is required (Committee on Pediatric Infectious Disease 2021). Painful suppurative nodes can be treated with needle aspiration for symptoms relief. In most cases, antibiotics are unnecessary as they have not been proven to increase the cure rate or prevent disease progression. However, there is little high quality evidence to guide treatment recommendations.

For severe disease or disease in immunocompromised patients, several antibiotics have in vitro activity against B henselae. These include macrolides (azithromycin, clarithromycin), fluoroquinolones (ciprofloxacin), doxycycline, ceftriaxone, rifampin. trimethoprim/sulfamethoxazole and gentamycin. Azithromycin is most commonly recommended in immunocompetent patients with mild to moderate disease. It has been demonstrated to relieve pain but not to reduce the duration of symptoms. Pediatric infectious disease consultation is prudent in these patients. Consult ophthalmology for ocular involvement.

ANTIBIOTIC SELECTION	
Lymphadenitis: Single-Drug Therapy	
Azithromycin	≤ 45.5 kg: 10 mg/kg PO on day 1, 5 mg/kg PO on days 2-5
	> 45.5 kg: 500 mg PO on day 1, 250 mg PO on days 2-5
Clarithromycin	≤ 45.5 kg: 15-20 mg/kg/day PO divided BID x 7-10 days
	> 45.5 kg: 500 mg/kg PO BID x 7-10 days
Rifampin	Pediatric: 10 mg/kg (max dose 300 mg) PO BID x 7-10 days
	Adult: 300 mg PO BID x 7-10 days
Trimethoprim-sulfamethoxazole	Pediatric: 4 mg/kg (of TMP, max 80 mg TMP) PO BID x 7-10 days
	Adult: 1 double strength (800 mg/160 mg) PO BID x 7-10 days
Adjunctive Therapy: Two-Drug Therapy (above plus …): Severe or Refractory Cases	
Adults and Peds ≥ 8 years	Doxycycline (dose below) AND Rifampin (dose above) x 10-14 days (visceral involvement), x 4-6 weeks (neuroretinitis)
	≤ 45 kg: 2.2 mg/kg (max 100 mg) PO/IV BID
	> 45 kg: 100 mg PO/IV BID
Peds < 8 years	Rifampin AND (Azithromycin OR Trimethoprim-Sulfamethoxazole)
	Dosing as above
	x 10-14 days (visceral involvement), x 4-6 weeks (neuroretinitis)
Severe or Refractory Disease: In addition to antibiotics above	
Corticosteroids	Prednisone: 1 mg/kg (max 80 mg) PO QD x 5-7 days then taper over the subsequent 10-14 days. Consider for neuroretinitis in conjunction with ophthalmology consultation

DISPOSITION

Patients should be followed closely by their primary care physician and/or pediatric infectious disease and be provided anticipatory guidance regarding evolution including visceral or neurologic involvement.

ENTEROVIRAL INFECTIONS

INTRODUCTION: (ELLEN DUNCAN, MD, PHD, 10/2020)
Enteroviruses are the most common cause of non-specific viral illness resulting in fever and malaise in infants and young children and headache and myalgias in older children. Upper respiratory tract symptoms are typically accompanied by mild to moderate gastrointestinal symptoms such as anorexia, nausea, vomiting, and diarrhea. Enteroviral infections are most common in the spring, summer and fall, but can occur year-round. While manifestations are typically benign and self-limited, enteroviruses can occasionally cause severe focal and/or systemic viral illnesses (encephalitis, myocarditis) and can be complicated by bacterial superinfection.

ENTEROVIRUSES
Coxsackieviruses (A, B)
Echoviruses
Numbered enteroviruses (e.g. D68)(new classification scheme since 1970)
Polioviruses
>100 serotypes

DISEASE PROGRESSION	
1	Fecal-oral transmission, some respiratory
2	Colonization of the respiratory and gastrointestinal tracts
3	Accumulation in lymph nodes
4	Systemic viremia (Day 3)
5	Focal/systemic infection (Day 4-6)

ENTEROVIRAL INFECTIONS BY SYSTEM*	
Cardiac	Myopericarditis
Dermatologic	Hand, foot, mouth disease, nonspecific viral exanthem
Generalized	Sepsis
Neurologic	Meningitis; encephalitis; acute flaccid myelitis
Ocular	Hemorrhagic conjunctivitis
Oropharynx	Herpangina
Respiratory	Pleurodynia; pneumonitis
*Typically, present 4-6 days post exposure	

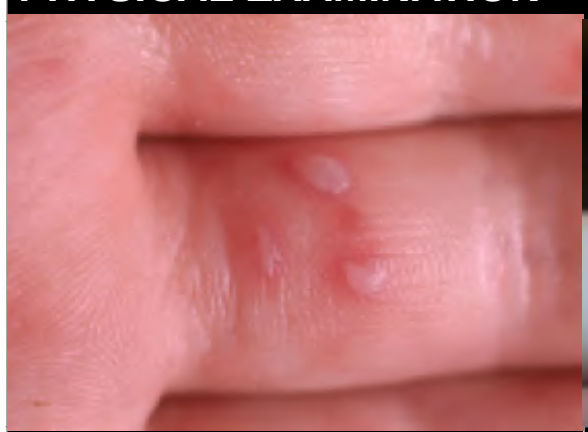
CLINICAL MANIFESTATIONS

The most recognizable enterovirus infection is Hand, foot, and mouth disease (HFMD). Because HFMD is spread through both direct contact and droplets, it is common in the pediatric population, especially those younger than 10 years of age. HFMD and herpangina (oral lesions only) are caused by a number of enteroviruses. These include coxsackie A and B viruses, echoviruses, and enterovirus A71. Many cases are caused by coxsackievirus A16 and enterovirus A71.

Patients with HFMD may have general viral symptoms, including fever, decreased oral intake, odynophagia, and general malaise. Fever is usually moderately high (38.3-40C) and typically last 2-4 days. HFMD caused by enterovirus D71 can be associated with brainstem myelitis, pulmonary edema/ hemorrhage and heart failure. A variant of HFMD, caused by coxsackie A6, can cause a more widely distributed vesiculobullous rash.

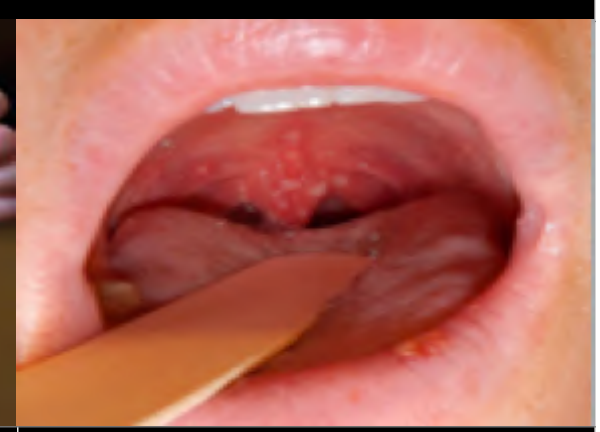
DIFFERENTIAL DIAGNOSIS	
DISEASE	DISTINGUISHING FEATURES
Other viral pharyngitis	Pharyngitis without vesicles
Herpetic gingivostomatitis	Lip and gingival lesions; severe pain
Aphthous stomatitis	Mucosal ulcers, not associated with viral symptoms
Varicella zoster	Cutaneous lesions at different stages of healing
Kawasaki disease*	Prolonged fever, conjunctivitis, adenopathy, hand/foot changes, and cracked lips/strawberry tongue
Henoch-Schoenlein purpura*	Non-blanching rash; primarily on buttocks and legs
Measles*	Ill appearing; rash with cephalocaudal spread; preceded by cough, coryza, conjunctivitis (3C's)
Erythema multiforme	Targetoid rash more common
Stevens-Johnson/TEN*	Ill-appearing; skin and mucous membrane involvement
*Covered in detail in a separate PEM Guide See: PEM Guide: Dermatology: Febrile Rashes.	

PHYSICAL EXAMINATION



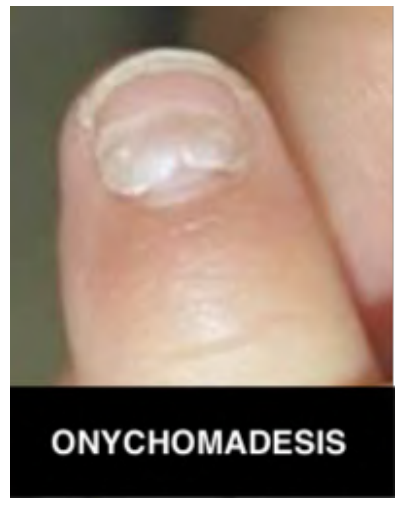
HAND

FOOT



MOUTH

DERMATOLOGIC: Many coxsackie virus and echovirus infection may cause non-specific, erythematous, maculopapular viral exanthems. In contrast, hand-foot-mouth disease lesions may be macular, papular, pustular, or vesicular. They can be present on the hands and feet only (hence the name); in the diaper area, elbows, and knees; or throughout the body. In the latter case, they can be mistaken for conditions such as varicella. Mild, painful swelling of the hands and feet can occur and may present with limp and/or refusal to walk. Echovirus 9 and coxsackie A29 can cause petechiae and purpura.


ONYCHOMADESIS

Eczema coxsackium is the accentuation of the coxsackie rash in previously affected areas of atopic dermatitis. Beau lines (deep, horizontal grooves in the nails) and nail shedding may occur.

OROPHARYNX: Herpangina is characterized by vesiculo-papular lesions on the posterior pharynx that erode, leaving shallow, painful blisters that then ulcerate. Lesions are localized to the anterior tonsillar pillars, soft palate, tonsils and pharyngeal walls. Lesions are not present in the anterior mouth (tongue, gingiva), which distinguishes it from HSV stomatitis.

NEUROLOGIC: In rare cases, enteroviruses can cause CNS manifestations such as encephalitis, aseptic meningitis, acute transverse myelitis, acute flaccid myelitis and Guillain-Barré syndrome. Meningitis is the most common CNS manifestation followed by generalized or focal encephalitis. Encephalitis is associated with altered mental status and seizures. Enteroviruses are responsible for more than 90% of aseptic (viral) meningitis in infants. In general, enteroviral encephalitis is associated with better outcomes than other causes of viral encephalitis (e.g. HSV encephalitis)

Clinical decision rules can assist in distinguishing viral from bacterial meningitis. The most accurate rule, derived in a pre-Prevnar 7 population, is the Bacterial Meningitis Score (Nigrovic, Pediatrics. 2002, PubMed ID: 12359784). One point is assigned for each parameter (see table below). A score of ≥1 predicts bacterial meningitis with a sensitivity of 97.6% 95% CI (91.5, 99.3%) and a specificity of 70.4%, 95% CI(65.5, 74.9%). If patients less than 2 months are excluded the sensitivity improves to 100%, 95% CI (96.9,100%). Though the score was derived in the pre-Prevnar 7 population, it was validated in a post-Prevnar 7 cohort (Nigrovic, JAMA. 2007, PubMed ID: 17200475). See PEM Guide: Neurology: Meningitis

BACTERIAL MENINGITIS SCORE
Positive CSF Gram Stain
CSF ANC ≥1000 cells/μL
CSF Protein ≥ 80 mg/dL
Peripheral ANC ≥10,000 cells/μL
H/O seizure before or at the time of presentation

Enterovirus D68 has also been associated with acute flaccid myelitis (AFM) in the US, occurring during peaks of respiratory illnesses due to enterovirus. Symptoms include acute focal limb weakness with or without cranial nerve abnormalities. CSF analysis reveals a lymphocytic pleocytosis and MRI reveals non-enhancing gray matter spinal cord lesions.

RESPIRATORY: Enterovirus D68 is associated with both upper and lower respiratory tract disease. It is most common in the summer months and in patients with asthma. It typically presents with cough and coryza without fever. Over the following 1-2 days, lower respiratory tract symptoms develop, which are similar to bronchiolitis and asthma. Patients have been treated with bronchodilators and corticosteroids, though the efficacy of these interventions has not been conclusively established.

Pleurodynia is characterized by painful, paroxysms of the chest and abdominal wall musculature. Adolescent and adults have more severe disease. Illness lasts for 4-6 days. It can be confused with pneumonia, pulmonary embolism, myocardial infarction and an acute abdomen.

CARDIAC: Coxsackie B viruses are most commonly associated with myopericarditis. Typically, either clinical signs of pericarditis or myocarditis predominate. Disease can range from asymptomatic to cardiogenic shock and cardiopulmonary arrest (See PEM Guide: Cardiology: Myocarditis, PEM Guide: Cardiology: Pericarditis.

DIAGNOSIS

The majority of enteroviral disease is self-limited and is diagnosed clinically. Rapid PCR testing of the nasopharynx and CSF is typically reserved for those with severe illness and those for which identification of enterovirus could influence clinical decision making (extent of laboratory evaluation, disposition). However, these rapid test do not distinguish between enteroviruses and rhinoviruses.

MANAGEMENT

For the majority of patients, treatment is supportive. NSAIDs and Acetaminophen are useful for the treatment of pain and fever. Oral or intravenous hydration may be required**.** Magic mouthwash (a combination of a 1:1:1 ratio of liquid Benadryl, Maalox/Mylanta, with or without viscous lidocaine) can be helpful for herpangina. Intravenous immune globulin is not supported by evidence but is often administered to those with life-threatening myocarditis. CNS disease and those who are immunocompromised. Consultation with pediatric infectious disease is recommended in these situations.

DISPOSITION

Most patients can be discharged with supportive care. Those with CNS manifestations should be admitted for further management. Patients with coxsackievirus may experience onychomadesis, or separation of the proximal nail plate from the nail matrix. Although this is a benign finding, it can be distressing to parents, and they should be warned in advance.

FEBRILE INFANT AND CHILD

INTRODUCTION (JAMES TSUNG, M.D. 7/2019)
Fever is the most common presenting complaint of infants and children in the emergency department. Fever is generally defined as a rectal temperature greater than 38C (100.4 F). Fever may be the presenting sign of the body's response to a benign process, such as a viral infection, or to a potentially life-threatening bacterial infection, such as sepsis or meningitis. While fever usually signifies an infectious process, on rare occasions it may indicate other processes, such as: poisoning (aspirin), collagen vascular disease or malignancy. The challenge for physicians who care for infants and children with fever is differentiating the vast majority of patients presenting who will have a self-limited viral illness from the few who will have life-threatening infections.

DIFFERENTIAL DIAGNOSIS: NON-INFECTIOUS CAUSES OF FEVER	
Rheumatology	Kawasaki*, system onset juvenile immune arthritis, acute rheumatic fever, inflammatory bowel disease
Endocrine	Hyperthyroid crisis*
Oncology	Leukemia, Ewing's tumor, osteoid osteoma, pheochromocytoma
Neurology	Hypothalamic dysfunction, familial dysautonomia,
Environmental	Heat related illness e.g. heat stroke*
Toxicology	Sympathomimetics (e.g. Cocaine)*, salicylates*, tricyclics*, anticholinergics*, MAOI, hyperpyrexia syndromes (malignant hyperthermia, neurologic malignant syndrome, serotonin syndrome*)
*Covered in detail in a separate PEM Guide	

This PEM Guide will focus on the general approach to the infant greater than 3 months of age with fever. See: PEM Guide: Infections: Febrile Neonate for an approach to the care of infants younger than 3 months of age. See specific PEM Guides for a discussion of serious bacterial infections (PEM Guide: Renal-GU: Urinary Tract Infections, PEM Guide: Respiratory: Pneumonia, PEM Guide: Neurology: Meningitis, PEM Guide: Orthopedics: Septic Arthritis, PEM Guide: Infections: Septic Shock).

The evaluation of the febrile infant and child is one of the most controversial topics in pediatric emergency medicine. It is well documented that a small percentage of these children are at risk for serious bacterial infections. The extent of the evaluation necessary to identify the minority of infants and children with these infections is unclear. Classically, these patients are divided into the "rule out sepsis" age group (0-3 months) and the "rule out bacteremia" age groups (3-36 months) reflecting the different level of serious bacterial infection risk and epidemiology in these groups. Over time, the approach to these groups has evolved due to changes in the epidemiology due to new vaccines and the interpretation of the risk and benefits of evaluation and treatment involved.

OCCULT INFECTIONS

URINARY TRACT INFECTIONS: In infants and children with a fever without an apparent source, urinary tract infection is the most common bacterial infection. Approximately 16% of girls less than 2 years of age and 8% of uncircumcised boys less than 1 year of age with fever without a source will have a UTI. The rate of UTI in circumcised males is significantly lower. It is important to differentiate between lower urinary tract infection (cystitis) and upper urinary tract infection (pyelonephritis). Approximately 60% of febrile infants with a urinary infection will have evidence of pyelonephritis on renal scan. (See: PEM Guide: Infections: Urinary Tract Infection).

BACTEREMIA: The evaluation of nontoxic appearing febrile young children from 3 to 36 months for 'occult' bacteremia has been the subject of considerable study and debate. The introduction of the Haemophilus Influenzae type b (HIB) vaccine in the early 1990's reduced the incidence of H. influenza meningitis by 99%. The current prevalence of occult bacteremia among febrile children aged 3 to 36 months is approximately 1%. After the introduction of the HIB vaccine, pneumococcal infections represented approximately 90% of bacteremia. The remaining 10% consist of N. Meningitis, Salmonella sp, Staph aureus, and Group A beta hemolytic Step. Of children aged 3 to 36 months with fever without a source, 0.3% will develop significant sequelae (pneumonia, septic arthritis, osteomyelitis, meningitis, sepsis). Only 0.03% of febrile children without a source will develop sepsis or meningitis. The introduction of the heptavalent pneumococcal conjugate vaccine has decreased the prevalence of pneumococcal infection significantly. Recent data suggest significant reductions in the incidence of invasive pneumococcal disease in those who have received their primary series of vaccinations (2,4 and 6 months) as well as reductions in non-vaccinated individuals (i.e. herd immunity). Multidrug resistant strains off pneumococcus (for example strain 19A) emerged after the introduction of the heptavalent vaccine. A new 13-serotype vaccine was introduced to account for emerging invasive serotypes (including serotype 19A). In NYC, after the introduction of Prevnar 13, the incidence of invasive pneumococcal infection decreased by 70% with an 83% decrease in the serotypes included in the vaccine. (Farnham, JAMA Pediatrics 2015, PubMed ID: 25938798).

EVALUATION

Evaluation of the febrile child includes a thorough history (including age, maximum temperature, underlying medical condition, past infections and vaccination status) and physical examination (including careful assessment of general appearance and localizing signs of infection). The need for laboratory and/or radiologic evaluation should be individualized. See Appendix: Approach to Febrile Infant/Child who is Unvaccinated or Under-vaccinated.

GENERAL APPEARANCE: Observation and clinical impression are key components in the evaluation of febrile infants and young children. Indicators such as a child's alertness, playfulness, interaction with the environment, color, state of hydration, quality of cry and the ability to be consoled have been included in a scoring system known as the Acute Illness or Yale Observation Score. The older the patient, the more reliable the clinical impression becomes in predicting serious bacterial illness (defined as urinary tract infection/pyelonephritis, bacteremia and meningitis).

PHYSICAL EXAMINATION

On physical examination, an infant may appear pale or mottled, tachypneic, tachycardic, have a weak cry, or have grunting respirations. Meningeal signs may be absent despite the presence of meningitis. An infant with a urinary tract infection may have only fever with or without vomiting or diarrhea. In older infants and children clinical impression becomes increasingly more accurate in identifying serious bacterial illness, such as meningitis or pneumonia. An older child (toddler age) with meningitis usually has nuchal rigidity and positive Kernig's and/or Brudzinski's signs. (See: PEM Guide: Infection: Meningitis)

A retrospective, multicenter study attempted to answer the following question: In pediatric patients 1 month to 5 years of age who present with meningitis or septicemia within 5 days of an ED what are the characteristics of the patients on initial presentation and what are the consequences of a delay in identification (Vaillancourt, Annals of Emergency Medicine, 2015, PubMed ID: 25458981). 25% of patients with septicemia and or meningitis had an emergency department visit within the past 5 days. The median time to return was 24 hours. Those with septicemia or meningitis were more likely to: present to a community emergency department without a pediatric consultant, were older and had a lower triage score on initial presentation. There was no significant difference in length of stay, proportion requiring a pediatric ICU stay or mortality between those who did or did not have a prior ED visit. Though this study has some limitations (use of an administrative database, no measure of morbidity and prior non-ED visits not captured), some regard this as evidence that "sick kids look sick" and emphasize that timely follow up is essential.

LABORATORY EVALUATION: URINALYSIS AND URINE CULTURE
Urine should be obtained sterilely (via catheterization or suprapubic aspiration) for urinalysis and culture in uncircumcised boys up to 1 year of age (6 months for circumcised boys) and girls up to 2 years of age. Bedside ultrasonography has been shown to increase the yield of successful catheterizations. (See PEM Guide: Infections: Urinary Tract Infection).

Shaikh derived and internally validated a number of models to clinically predict the risk of UTI in febrile children less than 2 years of age (Shaikh, JAMA Pediatrics 2018, PubMed ID: 29710324). The models were derived based on the those with a greater than 2% risk require urine testing and if the urinalysis indicates a UTI risk of greater than 5% required empiric antibiotic coverage pending the results of the urine culture.

UTI CALC CLINICAL MODEL RISK FACTORS	
Age < 12 months	*Signs and/or symptoms within 24 hours of the ED visit could include acute otitis media, upper respiratory tract infection (any cough or congestion) gastroenteritis, pneumonia, meningitis, bronchiolitis or viral syndrome.
Temperature ≥ 39 C (102.2 F)	
Non-black race	
Female or uncircumcised male	
No other fever source*	

The UTI Calc model was tested in a hypothetical cohort of 1,000 febrile children less than 2 years of age with a 7% UTI rate. Compared to the AAP UTI algorithm, UTI Calc would reduce the need for urine sampling by 8.1%, 95% CI (4.2, 12.0%) and reduced the number of missed patients from 3 to 0.

WEB LINK: UTI RISK CALCULATOR

LABORATORY EVALUATION: CBC AND BLOOD CULTURE
A number of decision analyses have concluded that routine laboratory screening and empiric antibiotic therapy may no longer be cost effective when the incidence of occult pneumococcal bacteremia reaches 0.5%. In addition, studies of parent preference generally indicate a desire for a less invasive approach to management.

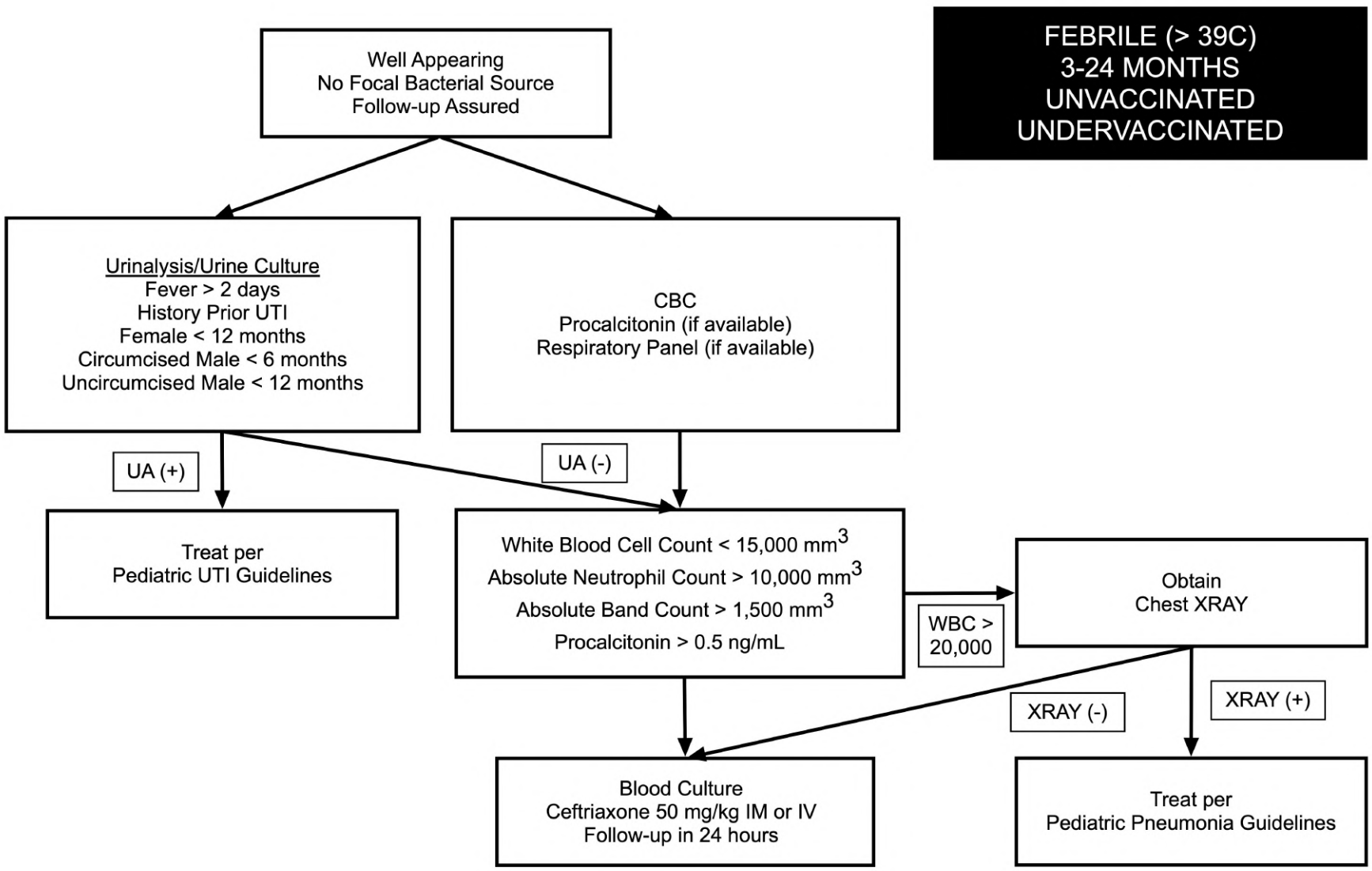
LABORATORY EVALUATION: STOOL CULTURE
A stool culture should be sent if the patient has bloody diarrhea or greater than 5 WBC per high powered field in a stool smear. Antibiotic therapy should be started in infants less than 3 months. Older children with salmonella enteritis rarely need antibiotic therapy

RADIOLOGIC EVALUATION: CHEST XRAY
A chest radiograph may be obtained if there are signs of lower respiratory tract disease, especially tachypnea. A WBC greater than 20 has also been shown to be a predictor of lobar infiltrate on chest radiograph (Rutman, Pediatr Emerg Care. 2009, PubMed ID: 19116501). (See PEM Guide: Infections: Pneumonia)

TREATMENT
Patients who are febrile with a positive urinalysis are presumed to have pyelonephritis. Outpatient management is an option in those infants who are well appearing, are tolerating oral fluids and in whom close follow up can be assured. Antibiotic selection should be based on community-based resistance rates to E Coli the most common pathogen.

DISPOSITION
Patients who appear toxic (alteration in mental status, respiratory distress, poor perfusion) are treated as inpatients. Children who are well appearing are often discharged. The most important aspects of care are careful and frequent follow-up.

APPENDIX: FEBRILE UNVACCINATED INFANT/TODDLER ALGORITHM



FEBRILE NEONATE

INTRODUCTION (JAMES TSUNG, M.D, MICHAEL MOJICA. 4/2022)
Fever is the most common emergency department presenting complaint in neonates. It is defined as a rectal temperature greater than or equal to 38C (100.4 F). Fever may be the presenting sign of the body's response to a benign process, such as a viral infection, or of a potentially life-threatening bacterial infection, such as sepsis or meningitis. While fever usually signifies an infectious process, on rare occasions it may indicate other processes, such as: poisoning (e.g. salicylates), collagen vascular disease (e.g. JIA) or malignancy (e.g. leukemia)). The challenge for physicians who care for neonates is differentiating most patients presenting with fever who will have a benign, self-limited illness from the few who will have a life-threatening illness.

MICROBIOLOGY

The approach to the evaluation and management of serious bacterial infection in a febrile infant should be based on the current epidemiology. This has changed considerably in the past few decades. In the early 1990's the H. influenza type B vaccine was introduced and virtually eliminated this very invasive pathogen as a consideration. In 2002, the first pneumococcal protein conjugate vaccine (Prevnar 7) was introduced and in 2010 the follow-up Prevnar 13 was approved. The practice of treating pregnant women with group B strep and the vaccination of adolescents against Neisseria meningitides has also decreased this incidence of these infections.

SERIOUS BACTERIAL INFECTION (SBI): Approximately 10% of febrile infants less than 2 months of age will have a serious bacterial infection. Serious bacterial infection (SBI) is defined as the isolation of a bacterial pathogen in a typically sterile location. SBI's include: UTI (pyelonephritis), bacteremia, meningitis, pneumonia, bacterial enteritis, septic arthritis and osteomyelitis. The most common serious bacterial infection is UTI (pyelonephritis)(8%). The term "rule out sepsis" is no longer recommended.

INVASIVE BACTERIAL INFECTION (IBI): The term invasive bacterial infection (IBI) refers to bacteremia and meningitis. A PECARN, multicenter study included 4,313 febrile infants less than 60 days for which blood cultures were obtained. 2.3% (1 in 44 patients) had an IBI. The rate of bacteremia was 2% (1 in 50 patients). The rate of meningitis was 0.6% (1 in 167 patients). E Coli was the leading cause of isolated bacteremia and isolated meningitis. Overall, E Coli accounted for 37% and group B streptococcus accounted for 24% of invasive bacterial infections (Cruz (PECARN), JAMA Pediatrics 2017 (PubMed ID: 28892537)

INVASIVE BACTERIAL INFECTION (IBI): MICROBIOLOGY			
	E COLI	GBS	OTHER
Isolated Bacteremia	43.8%	19.2%	Staph Aureus 15.1%
Isolated Meningitis	23.1%	23.1%	Enterococcus 23.1%
Bacteremia + Meningitis	9.1%	54.6%	4 others with 9.1%[1]
	36 (37%)	23 (24%)	
1. Enterobacter cloacae, Klebsiella, Neisseria meningitides, Strep pneumonia			

URINARY TRACT INFECTIONS: UTI is the most common serious bacterial infection. UTI is also responsible for a significant proportion of bacteremia and meningitis. Approximately 60% of febrile infants with a UTI will have evidence of pyelonephritis on a renal scan (Hoberman. Pediatrics 1999, PubMed ID: 10390264).

In a multicenter cohort of 1,842 febrile infants age 30-60 days with a UTI, E. Coli (86%), Klebsiella sp. (5.7%), Enterobacter (2.8%) and Enterococcus sp (1.9%) accounted for most isolates (Schnadower, Pediatrics 2010, PubMed ID: 21098155). 99.2% of isolates were sensitive to Ceftriaxone. 6.5% (1 in 15), 95% CI (5.5-7.7) of those with a UTI were bacteremic and 0.1 % (1 in 1,000), 95% CI (0.0-0.4%) met criteria for meningitis.

URINALYSIS: A case-control study (Schroeder, Pediatrics 2015, PubMed ID: 26009628) analyzed the diagnostic accuracy of the urinalysis in infants less than 0-90 days. To calculate sensitivity, the reference standard was infants with both a positive urine culture (AAP definition of growth of a single pathogen > 50,000 CFU/ml) and a positive blood culture with the same pathogen. This was done to decrease the likelihood of including patients with asymptomatic bacteriuria. The authors suggest that previous studies demonstrating poor test characteristics of urinalysis in this age group may be the result of the inclusion of patients with asymptomatic bacteriuria. Specificity was calculated in a control group of infants with a negative urine culture. With an aggregate definition of a “positive” urinalysis of pyuria (> 3 WBC/HPF) with or without any positive leukocyte esterase, the sensitivity was 99.5%, 95% CI (94.5, 99.2%) and specificity was 87.8%, 96% CI (80.4, 93.2%). The test characteristics did not change significantly if infants less than 30 days of age were compared to those 31-90 days of age or if bagged urine specimens were excluded. The primary concern with this study is that of spectrum bias, which is the urinalysis test characteristics may be better in those with both a positive urine culture and a positive blood culture when compared to those with only a positive urine culture. (See also PEM Guide: Infections: Urinary Tract Infection)

UTI AND MENINGITIS: A study analyzed 1,737 febrile infants less than or equal to 60 days of age with a urinary tract infection to determine the rate of concomitant bacterial meningitis. Meningitis was rare, but more common in infants 0-28 days (0.9%, 95% CI: 0.4-1.9%, 1 in 111 patients) than in infants 29-60 days (0.2%, 95% CI: 0-0.8%, 1 in 500 patients). The clinical appearance of the 9 infants with concomitant UTI and bacterial meningitis was not presented. All infants with concomitant UTI and meningitis were also bacteremic. The authors conclude that: “Our findings suggest that a selective, rather than universal, approach to lumbar puncture in infants with UTI may be appropriate, especially in well appearing infants 29-60 days of age (Thomson, Ped ID, 2017, PubMed ID: 28472006).

BACTEREMIA: Greenhow et al (Pediatrics 2012, PubMed ID: 22371459) retrospectively studied the incidence of bacteremia of infants 1-90 days of age, full term, previously healthy neonates. 18.6% of those for which physical examination findings were available were described as “ill appearing”. 2% (92/4,255) of blood cultures were positive. 56% of these patients had a concomitant UTI and 11% had meningitis. 56% had E. Coli bacteremia and 98% of these had a UTI. Group B Strep (21%) and Staph aureus (8%) accounted for most other bacteremia cases. There were no cases of Listeria monocytogenes or Neisseria meningitides.

SBI RISK: CONCOMITANT VIRAL ILLNESS: A multicenter study analyzed the rate of SBI in 1,169 febrile infants less than 2 months of age with and without RSV (Levine, Pediatrics 2004, PubMed ID: 15173498) and with and without influenza (Krief, Pediatrics 2009, PubMed ID: 19564280). Both authors concluded that the rate of SBI is lower in patients with RSV or influenza. However, the rate of UTI remains appreciable. Conclusions regarding bacteremia and meningitis could not be made.

A recent analysis of any viral infection and the risk of SBI drew similar conclusions to the RSV and Influenza studies “Febrile infants ≤ 60 days of age with viral infections are at significantly lower, but non-negligible risk for SBIs, including bacteremia and bacterial meningitis.” (Mahajan (PECARN), J Pediatr 2018, PubMed ID: 30195552).

RISK OF SBI WITH/WITHOUT VIRAL INFECTION			
	Virus Negative (n=1,745)	Virus Positive (n= 1,200)	Relative Risk (95%CI)
UTI	10.7% (9.2, 12.2%)	2.8% (1.9, 3.5%)	3.9 (2.7, 5.6)
Bacteremia	2.9% (2.1, 3.8%)	0.8% (0.3, 1.4%)	3.8 (1.9, 7.7)
Meningitis	0.8% (0.4, 1.3%)	0.4% (0.1, 1.0%)	1.9 (0.7, 5.3)
Any SBI	12.7% (11.2, 14.4%)	3.7% (2.7, 4.9%)	3.5 (2.5, 4.8)
GREEN = Statistically significant, RED = Not statistically significant			

SBI RISK: RECENT VACCINATIONS: Wolff (Academic EM 2009, PubMed ID: 20053249) determined the rate of serious bacterial infection in a population of febrile neonates from 30-90 days of age. Overall, 6.6% (5.5-7.7) of 1,978 infants had a serious bacterial infection. Those without a vaccination within 72 hours had an SBI rate of 7.0%, 95% CI (5.9, 8.3%). Those with a vaccination within 72 hours had an SBI rate of 2.8%, 95% CI (0.6, 5.1%) while those with a vaccination within 24 hours had an SBI rate of 0.6%, 95% CI (0.0,1.9%). The authors concluded that evaluation for a UTI should be considered for those with a vaccination within 24 hours but those with a vaccination between 24 and 72 hours should be managed as if they did not have a vaccination.

SBI RISK: FEVER AT HOME ONLY: Utilizing a PECARN data set with 1,233 patients, the rate of SBI in patients with fever at home only was 8.8% compared to 12.8% in patients with fever in the ED as well (RR 0.68, 95% CI (0.56, 0.84) (Rangopal, J Peds 2019, PubMed ID: 31345996). The authors concluded the that the “risk of SBI in infants presenting afebrile to the ED with only a history of fever was two-thirds the risk of infants with fever in the ED. Nevertheless, this represents a not-insignificant risk”.

MANAGEMENT

Management decisions include the extent of laboratory evaluation required (e.g. LP, HSV testing) initiation of empiric antimicrobials (antibiotics and/or antivirals) as well as a determination of disposition (admission or home). Decision making should be shared with parents and the patient’s primary care provider when possible.

CLINICAL DECISION-MAKING PROCESS		
1	Clinical assessment	A focused history and full physical examination
2	Laboratory assessment	Basic labs and whether to perform a lumbar puncture
3	Risk assessment	Based on clinical and laboratory findings
4	Antimicrobials	Indications for antibiotics and/or acyclovir
5	Disposition	Decision to observe as an inpatient or an outpatient

AAP FEBRILE INFANT CRITERIA: The 2021 AAP clinical practice guideline provides recommendations on the diagnosis and management of the well-appearing, febrile infant from 8-60 days without an apparent bacterial source based on current evidence and expert consensus opinion. This included input from primary care pediatricians, pediatric emergency physicians, pediatric hospitalists and pediatric infectious disease physicians (AAP, Pediatrics 2021, PubMed ID: 34281996). AAP Pathway inclusion and exclusion criteria are included in the tables below.

NYU ALGORITHMS: This PEM Guide reviews the NYU/Bellevue implementation of the AAP guidelines which differ slightly from the AAP guideline (See Appendix: NYU Algorithms). There are three algorithms based on risk of SBI for 0-21 days (AAP uses 8-21 days), 22-28 days and 29-60 days. Importantly, while the NYU pathways are preferred, physician clinical judgement may dictate final workup, treatment and disposition.

The 8-21-day group is a new addition and recognizes that this group is at intermediate risk for SBI. In the past, all of these infants would have received antibiotics and been admitted. There are now options to admit this age group without antibiotics or discharge them with antibiotics under certain conditions.

PATHWAY INCLUSION CRITERIA (AAP 2021)	
Gestation	≥ 37 weeks and < 42 weeks
Fever	38C (100.4 F) at home or clinical setting within the past 24 hours
Source	No bacterial source of infection (except of acute otitis media)
Respiratory	Upper respiratory tract symptoms or respiratory symptoms not diagnostic of bronchiolitis should not exclude infants from pathway
Diarrhea	Suspected bacterial pathogens should have stool specimens. If studies for bacteria are negative, infants may then enter the decision tree pathway. Loose stools do not exclude infants from the pathway.
Otitis media	Otitis media does not preclude their entry into the pathway.
Antimicrobials	Current/Recent in infants < 2 weeks of age requires individualized interpretation for febrile infants who enter the pathway
Positive viral test results	Rapid respiratory molecular testing for a variety of viruses is increasing, outpacing evidence for how such testing should be used.

PATHWAY EXCLUSION CRITERIA (AAP 2021)
Preterm infants (< 37 weeks)
< 2 weeks with perinatal courses with maternal fever, infection or antimicrobial use
High suspicion of herpes simplex virus (HSV) infection (e.g. vesicles)
Focal bacterial infection (e.g. cellulitis, omphalitis, septic arthritis, osteomyelitis)
Clinical bronchiolitis, with or without respiratory syncytial virus
Documented or suspected immune compromise
Neonatal course complicated by surgery or infection
Congenital or chromosomal abnormalities
Requiring some form of technology or ongoing therapeutic intervention to sustain life
Received immunizations within the last 48 hours

1. CLINICAL ASSESSMENT

Evaluation of the febrile infant includes a thorough history. This includes prenatal and antenatal history, age, temperature, underlying medical conditions and recent symptoms. The physical examination should include a careful assessment of general appearance as well as localizing signs of infection.

In the well appearing febrile neonate it is not possible to clinically distinguish between those with and without with a serious bacterial infection (SBI) or invasive bacterial infection (IBI). In a population of 4,591 neonates less than 60 days of which 9.7% had a SBI and 2.1% IBI, a Yale Observation score of ≤ 10 had a sensitivity of 11.6%, 95% CI (8.8, 15.0%) for SBI and 24.2%, 95% CI (16.0, 34.1%) for IBI. Patients who clinicians assessed as having a less than 1% risk of infection had an SBI rate of 6.4% and IBI rate of 1.0%. The authors conclude that “neither the Yale Observation Score nor unstructured clinician suspicion reliably identified those with invasive bacterial infections.” (Nigrovic, Pediatrics 2017, PubMed ID: PubMed ID: 28759413).

2. LABORATORY ASSESSMENT

The degree of laboratory testing required is based on the age of the infant as well as risk factor for HSV and bacterial infection. All children should have a urinalysis, urine culture, CBC, blood culture and inflammatory markers. Indications for further testing and lumbar puncture are included in the below.

LABORATORY TESTING (NYU 2022): ALL
Urinalysis, Urine culture (catheterized)
CBC with differential, Blood culture, BMP, Hepatic function tests
Procalcitonin available (0-21 days): PCT, ANC and CRP
Procalcitonin available (22-28 days and 29-60 days): PCT and ANC
Procalcitonin not available: ANC and CRP and a Temperature > 38.5C
Respiratory pathogen panel with COVID (if available)
0-21 days: Serum HSV PCR

LABORATORY TESTING (NYU 2022): AS INDICATED
HSV Risk (+): Serum HSV PCR
Vesicles: Surface HSV NAAT: Single swab: Conjunctiva Nose Mouth Anus
Lumbar Puncture: CSF culture, gram stain, cell counts, glucose, protein
CSF Meningitis/Encephalitis panel including HSV (if available)
Stool culture, stool pathogen panel: Diarrhea (particularly bloody diarrhea)
Chest XRAY: Signs of lower respiratory tract illness not attributable to bronchiolitis

LUMBAR PUNCTURE INDICATIONS (NYU 2022)	
0-21 days	All
22-28 days	Any Bacterial or HSV risk factor
	No Bacterial or HSV risk factor (shared decision making)[1]
29-60 days	Any Bacterial or HSV risk factor
1. This is an important decision node. Infants in this age group with a normal LP can be discharged with antibiotics. Infants who do not have an LP are admitted with antibiotics (Urinalysis (+)) or without antibiotics (Urinalysis (-))	

URINALYSIS POSITIVE (IF ANY OF THE BELOW) (AAP 2021)	
Leukocyte Esterase (LE)	Any Positive
Pyuria	> 5 WBC/HPF (centrifuged)
Pyuria (enhanced UA)	> 10 WBC/mm^3 (uncentrifuged with hemocytometer)

INFLAMMATORY MARKERS: ABNORMAL VALUES (AAP 2021)
PCT > 0.5 ng/ml (Use temperature > 38.5 C if procalcitonin is not available)
CRP > 20 mg/L
ANC > 4,000/mm^3

CSF STUDIES (NORMAL VALUES (RANGE))[1](AAP 2021)		
	1-28 days	29-60 days
Cell Count (WBC)	0-18	0-8.5
Cell Count (RBC)	0-236	0-64.5
Gram Stain	Negative	Negative
Glucose	30-61	20.6-65.5
Protein	15.8-131.0	5.5-105.5
Bacterial Culture	Negative	Negative
Entero-viral PCR	Negative	Negative
1. Byington, J Peds 2011, PubMed ID: 20801462		

3. RISK ASSESSMENT

Several evaluation tools that combine history, clinical findings and laboratory parameters have been developed to aid in identifying those infants at low risk for SBI. These criteria vary with: age, definition of previously healthy, extent of laboratory evaluation, criteria of individual labs, use of empiric antibiotics and disposition. These criteria were developed from the late 1980's to early 1990's and there has been a significant change in the epidemiology of disease since that time. The most common criteria sited are the Rochester (Dagan, J Pediatrics 1985, PubMed ID: 4067741), Boston (Baskin, J Pediatrics 1992, PubMed ID: 1731019), and Philadelphia Criteria (Baker, NEJM 1993, PubMed ID: 8413453).

A systematic review (Huppler, Pediatrics 2010, PubMed ID: 20083517) of low risk criteria demonstrated a rate of serious bacterial infection for those who were considered low risk of 2.2% in all studies and 0.67% in prospective studies. Diagnostic accuracy was similar in all of the low risk criteria with a negative predictive value of 94-100%. Each of the original decision rules have been modified and a number of new rules have been derived. The PECARN decision rule divided a group of patients with a 9% risk of SBI into a high-risk group with an SBI rate of 21.0% (PPV) if the rule was positive and a low-risk group with an SBI rate of 0.2% (1-NPV) if the rule was negative (PECARN, JAMA Pediatrics 2019, PubMed ID: 30776077). The PECARN rule require further validation.

PECARN FEBRILE NEONATE DECISION RULE: LOW RISK CRITERIA*
UA = (-) Leukocyte Esterase AND (-) Nitrite, AND No Pyuria (5 WBC/HPF)
ANC ≥ 4,090 per microL (to convert to $\times 10^9$ per liter, multiply by 0.001)
PCT ≥ 1.7 ng/ml
Similar sensitivity, lower specificity with rounded values of ANC ≥ 4,000, PCT ≥ 1.5

High risk factors for bacterial infection include elements of the history and laboratory tests (Table below). These risk factors are used to determine the need for lumbar puncture and antimicrobials in the 22-28-day and 29-60-day age groups. High risk factors are not delineated for neonates 0-21 days as a lumbar puncture and antimicrobials are indicated in all of these patient.

BACTERIAL INFECTIONS: HIGHER RISK FACTORS (NYU 2022)	
History	< 37 weeks' gestation
	Antibiotic use within prior 48 hours
	Complicated course: Infection, unplanned surgery, immunocompromised
Laboratory	PCT available (22-60 days): ANC > 4,000 or PCT > 0.5 ng/ml
	PCT not available: ANC > 4,000 or CRP > 20 mg/ml or Temp > 38.5C

4. ANTIMICROBIALS

ANTIBIOTIC COVERAGE: Antibiotic coverage should be targeted to the most likely pathogen. In the absence of a specific infection, empiric coverage may be initiated. Targeted antibiotic regimens should be used if a UTI or meningitis are identified or if specific organism (e.g. enterococcus, Listeria) are suspected. Empiric coverage includes E Coli coverage with a third-generation cephalosporin. Importantly, antibiotic selection should be guided by local sensitivities.

The inclusion of empiric coverage for Listeria is somewhat controversial, as the rate of Listeria has decreased significantly. Ampicillin is generally added to cover Listeria monocytogenes in infants less than 4-6 weeks of age, if the gram stain of urine is gram positive (enterococcus sp.) or the CSF gram stain is gram positive (Group B strep) However, Ampicillin resistance has been increasing.

ANTIMICROBIALS: INDICATIONS
0-21 days: Antibiotics and Acyclovir
Toxic Appearing: Altered mental status, poor perfusion, respiratory distress/failure
Positive bacterial risk factors (See table in risk assessment section above)
Positive HSV risk factors (See table in antiviral section below)
UA consistent with UTI (See table in lab assessment section above)
CSF consistent with meningitis (option if CSF enterovirus PCR (+))(See table in lab assessment)

ANTIBIOTIC INDICATIONS					
Bacterial Risk (+)	LP Performed	CSF[1]	UA	Disposition	Antibiotics
0-21 DAYS					
YES	YES	+/-	+/-	Admit	YES
NO	YES	+/-	+/-	Admit	YES
22-28 DAYS					
YES	YES	+/-	+/-	Admit	YES
NO	YES[2]	-	+	Admit	YES
NO	YES[2]	+	-	Admit	YES
NO	YES[2]	-	-	Admit	NO[2]
NO	YES[2]	-	-	Discharge	YES[2]
NO	NO[2]	NA	+	Admit	YES
NO	NO[2]	NA	-	Admit	NO
29-60 DAYS					
YES	YES	+/-	+/-	Admit	YES
NO	NO	NA	+	Discharge	YES[2]
NO	NO	NA	-	Discharge	NO[2]

1. CSF (+): CSF profile abnormal/uninterpretable or meningitis-encephalitis panel (+)
   Option to withhold or administer antibiotics if CSF enterovirus PCR (+)
2. Opportunity for shared decision making on LP, antimicrobials and disposition

ANTIMICROBIAL SELECTION: EMPIRIC AND TARGETED (NYU 2022)		
0-21 DAYS		
Admit: Empiric	Ceftazidime	50 mg/kg IV Q8 hours
	+ Ampicillin	75 mg/kg IV Q6 hours
	+ Acyclovir	20 mg/kg Q8 hours
22-28 DAYS		
Admit: Empiric	Ceftriaxone[1]	50 mg/kg IV Q24 hours
Admit: UTI	Ceftazidime	50 mg/kg IV Q8 hours
	+ Ampicillin	50 mg/kg IV Q6 hours
Admit: Meningitis	Ceftazidime	50 mg/kg IV Q8 hours
	+ Ampicillin	75 mg/kg IV Q6 hours
Discharge	Ceftriaxone	50 mg/kg IV Q 24 hours
HSV Risk (+)	Acyclovir	20 mg/kg Q8 hours
29-60 DAYS		
Admit Empiric	Ceftriaxone	50 mg/kg IV Q12 hours
Enterococcus concern[2]	+ Ampicillin	50 mg/kg IV Q6 hours
Admit: UTI	Ceftazidime	50 mg/kg IV Q8 hours
	+ Ampicillin	50 mg/kg IV Q6 hours
Admit: Meningitis	Ceftriaxone	100 mg/kg IV Q24 hours
	+ Vancomycin	15 mg/kg IV Q6 hours
Discharge: UTI	Amoxicillin	25 mg/kg PO BID x 10-14 days
	+ Cephalexin	25 mg/kg PO Q6 hours x 10-14 days
HSV Risk (+)	Acyclovir	20 mg/kg Q8 hours
1. If total Bilirubin >12, substitute Ceftazidime 50 mg/kg IV Q8 hours for Ceftriaxone 2. Previous infection, vesicoureteral reflux, prior GU surgery		

ANTIVIRAL COVERAGE: Antiviral therapy is most commonly indicated for HSV (Acyclovir) and influenza (Oseltamivir). HSV infection is potentially life-threatening in the neonate. Risk of transmission of HSV to a neonate is higher when the mother acquires primary genital HSV near the time of delivery (25-60%) than compared to reactivation of longstanding HSV or HSV acquired in the first half of pregnancy (2%). However, 60-80% of neonates with HSV are born to mothers without a history of HSV. A rash may not be present in a high proportion at presentation but may develop later.

NEONATAL HSV PATTERNS
SKIN-EYE-MOUTH (SEM) DISEASE: 45% (15-20% without rash, eye/mouth only)
Well-appearing infants
Lesions not present at birth. Develop between 7-14 days of age
Clusters of vesicular or rarely pustular lesions on an erythematous base.
Older lesions may be crusted papules.
Often on the face, scalp. (Breech presentations more common on buttocks)
CNS DISEASE: 30% (30-40% without rash)
2nd-3rd week of age
Symptomatic: Fever, fussiness, lethargy, poor feeding, seizures, bulging fontanelle.
DISSEMINATED DISEASE: 25% (20% without rash)
Presenting 1st-2nd weeks with sepsis like illness
Liver: Hepatitis
Lung: Pneumonitis, respiratory failure
Adrenal: Hypotension, temperature instability (hypothermia)
Neurologic: Seizures, altered mental status

HERPES SIMPLEX VIRUS (HSV): HIGHER RISK FACTORS (AAP 2021)	
History	Maternal history of HSV during delivery
	Maternal fever 48 hours before or after delivery
	Exposure to close contact with HSV
	Seizure activity
Examination	Hypothermia
	Vesicular skin or mucosal lesions
	Petechial rash
Laboratory	Thrombocytopenia
	Elevated ALT (alanine aminotransferase)
	CSF pleocytosis with a negative gram stain

ACYCLOVIR: INDICATIONS AND DOSING	
0-21 Days	All infants 0-28 days (pending laboratory confirmation)
22-28 Days	HSV risk factors (see table above)
29-60 Days	HSV risk factors (see table above)
Acyclovir 20 mg/kg IV Q8 hours	

5. DISPOSITION

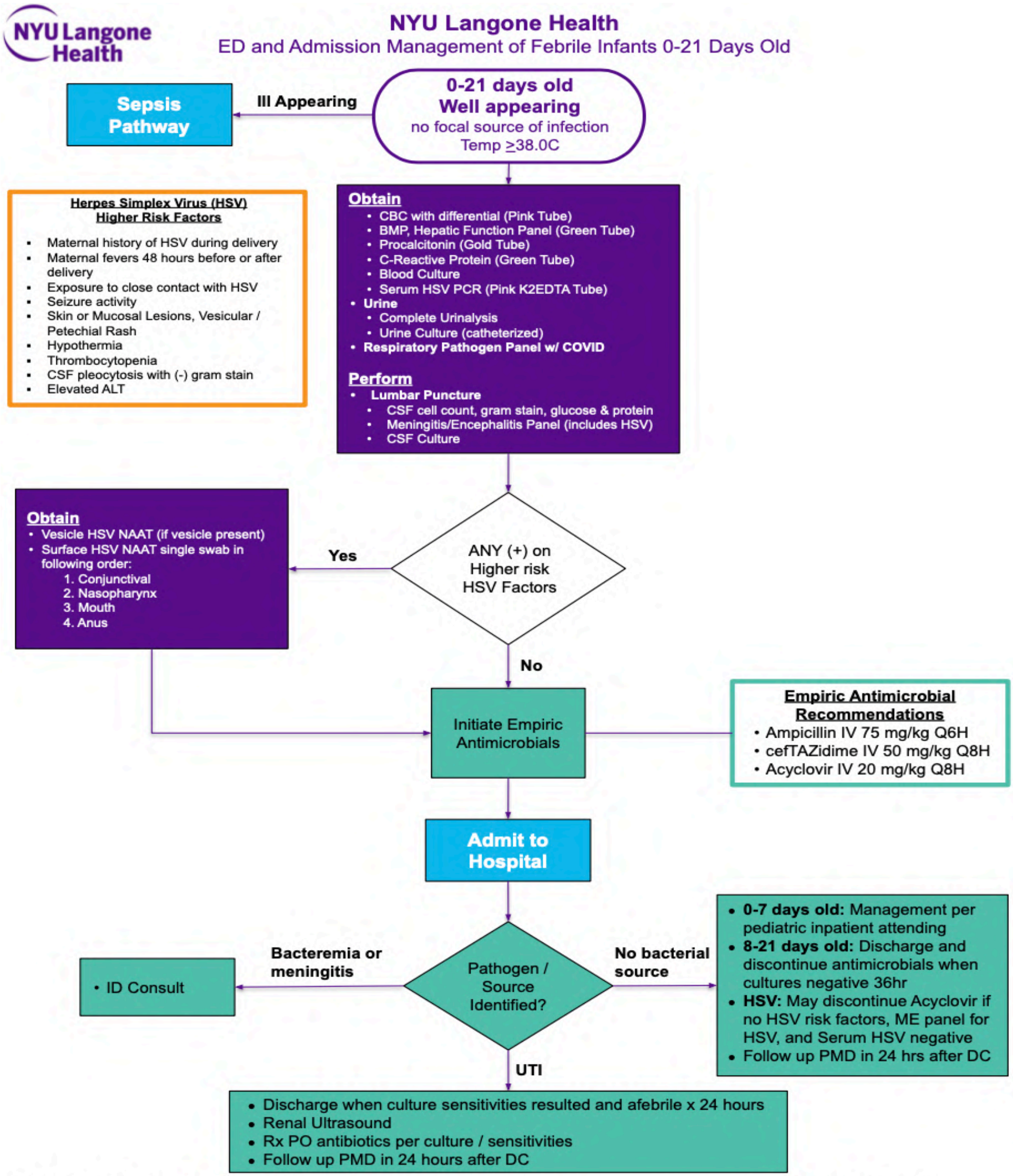
Admission to the hospital for observation and/or treatment may be the “conservative approach” but is not without risk. Infants are at risk of nosocomial infections, antibiotic adverse events, intravenous infiltrates and cessation of breast-feeding. The stress of admission on parents should not be underestimated. The table below indicates the conditions under which a febrile neonate can be safely discharged. All patients not meeting these conditions should be admitted. Only patients without bacterial or HSV risk factors can potentially be discharged.

For those who are managed as outpatients, instructions on signs and symptoms to return for and follow up within 24 hours are essential. The patients contact information should be obtained and a mechanism must be in place to monitor pending cultures.

ADMISSION: ALL NOT MEETING DISCHARGE CONDITIONS (ABOVE)					
Age	Bacterial or HSV Risk (+)	LP Performed	CSF[1]	UA	Antibiotics
0-21 days	YES	YES	+/-	+/-	YES
	NO	YES	+/-	+/-	YES
22-28 days	YES	YES	+/-	+/-	YES
	NO	YES[2]	-	+	YES
	NO	YES[2]	+	-	YES
	NO	YES[2]	-	-	NO
	NO	NO[2]	NA	+	YES
	NO	NO[2]	NA	-	NO
29-60 days	YES	YES	+/-	+/-	YES
1. CSF (+): CSF profile abnormal/uninterpretable or ME panel (+) (except enterovirus)					

DISCHARGE					
Age	Bacterial or HSV Risk (+)	LP Performed	CSF[1]	UA	Antibiotics
22-29 days	NO	YES	-	-	YES
29-60 days	NO	NO	NA	+	YES
29-60 days	NO	NO	NA	-	NO
1. CSF (+): CSF profile abnormal/uninterpretable or ME panel (+) (except enterovirus)					

ALGORITHM: FEBRILE NEONATE 0-21 DAYS



* These are the preferred pathways. However, physician clinical judgement may dictate final workup, treatment, and disposition. Last Updated: February 2022

ALGORITHM: FEBRILE NEONATE 22-28 DAYS

NYU Langone Health

ED and Admission Management of Febrile Infants 22-28 Days Old

22-28 days old
Well appearing
No focal source of infection,
Temp ≥38.0C

Sepsis Pathway ← **Ill Appearing**

Herpes Simplex Virus (HSV) Higher Risk Factors
- Maternal history of HSV during delivery
- Maternal fevers 48 hours before or after delivery
- Exposure to close contact with HSV
- Seizure activity
- Skin or Mucosal Lesions, Vesicular / Petechial Rash
- Hypothermia
- Thrombocytopenia
- CSF pleocytosis with (-) gram stain
- Elevated ALT

Obtain
- **Bloodwork**
  - CBC with differential - Pink Tube
  - BMP, Hepatic Function Panel - Green Tube
  - Procalcitonin (PCT) - Gold Tube - Only available at Tisch/Brooklyn/Long Island
  - C-Reactive Protein (CRP) - Green Tube - Send **only** if PCT unavailable (Cobble Hill)
  - Blood Culture
- **Urine**
  - Complete urinalysis
  - Urine culture (catheterized)
- **Respiratory Pathogen Panel w/ COVID**

Bacterial Infection Higher Risk Factors
- <37 weeks gestation
- Antibiotic use within prior 48 hours
- Complicated neonatal course (infection, unplanned surgery, immunocompromised)

Inflammatory Markers:
- ANC >4000
- PCT elevated >0.5 ng/ml
- CRP >20 mg/L
- Temperature >38.5C (101.3F) - this is a risk factor ONLY if PCT unavailable

ANY (+) Bacterial or HSV Risk Factors

Yes → **Perform LP**
- CSF cell count, gram stain, glucose, protein Meningitis-Encephalitis (ME) Panel (includes HSV)
- CSF Culture

No → **Use shared decision making on whether to perform LP**

Document SDM using smartphrase .REVISESDMCSF

Performed LP → •CSF pleocytosis or uninterpretable? •ME panel abnormal (except enterovirus+)? •UA with +LE, +Nitrites or >5 WBC?

Abnormal / uninterpretable CSF or positive UA

No LP → UA with +LE, +Nitrites or >5 WBC?

No → **Admit**
- No empiric antibiotics needed. Discuss with PHM[2]

Yes → **Admit**
- Initiate empiric antimicrobials for UTI[3]

All labs normal, or ME panel (+) *only* for enterovirus

Use shared decision making regarding observation at home vs inpatient

Document SDM using smartphrase .REVISESDMDISPO

For (+) HSV Risk
- Vesicle HSV NAAT (if vesicle present)
- Surface HSV NAAT single swab in following order:
  1. Conjunctival
  2. Nasopharynx
  3. Mouth
  4. Anus
- Serum HSV PCR (Pink K2EDTA)

Admit
- Initiate empiric antimicrobials [4,5]

Discharge
- Administer antimicrobials[1]
- Follow up in 24 hours

Bacteremia / meningitis ← Pathogen / Source Identified? → **UTI**

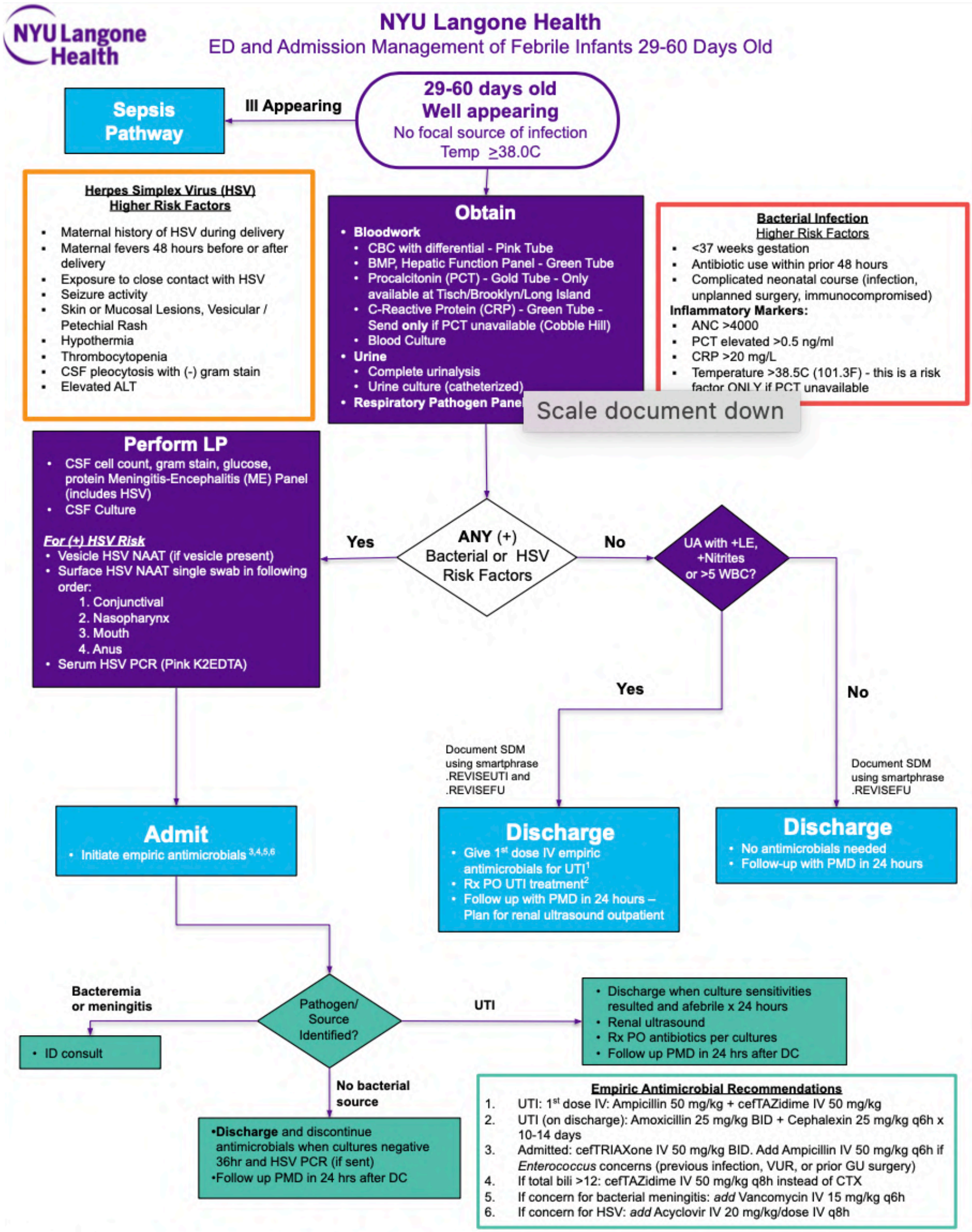
No bacterial source

- •ID consult
- •**Discharge** and discontinue antimicrobials when cultures negative 36hr and HSV PCR neg (if sent) •Follow up PMD in 24 hrs after DC
- •Discharge when culture sensitivities resulted and afebrile x 24 hours •Renal ultrasound •Rx PO antibiotics per cultures •Follow up PMD in 24 hrs after DC

Empiric Antimicrobial Recommendations
1. Discharge: cefTRIAXone IV 50 mg/kg x1 dose
2. Admitted (no source and clinical decision to give abx): cefTRIAXone IV 50 mg/kg q24hr. If total bili>12, use cefTAZidime IV 50 mg/kg q8h instead
3. UTI: Ampicillin IV 50 mg/kg q6h + cefTAZidime IV 50 mg/kg q8h
4. Concern for meningitis: Ampicillin IV 75 mg/kg q6h + cefTAZidime IV 50 mg/kg q8h
5. (+) HSV Risk – add Acyclovir 20 mg/kg IV q8h

* These are the preferred pathways. However, physician clinical judgement may dictate final workup, treatment, and disposition. Last Updated: February 2022

ALGORITHM: FEBRILE NEONATE 29-60 DAYS



* These are the preferred pathways. However, physician clinical judgement may dictate final workup, treatment, and disposition. Last Updated: February 2022

INFECTIOUS MONONUCLEOSIS

INTRODUCTION (MICHAEL MOJICA, MD, 2/2019)
Epstein-Barr virus (EBV) is a herpes virus (HV4). Infection of B cells is responsible for distribution throughout the reticular system. Like other herpes viruses, it remains latent in cells. More than 90-95% of adults have serologic evidence of EBV exposure. Reactivation is generally not an issue with the exception of transplant recipients who can develop a lymphoproliferative disorder. EBV has also been associated with development of certain cancers including: Burkitt's, Hodgkin's, B and T cell lymphomas, leiomyosarcomas and nasopharyngeal carcinoma.

CLINICAL MANIFESTATIONS

Infectious mononucleosis (IM) is the most common manifestation of acute EBV infection and EBV is responsible for more than 90% of infectious mononucleosis. The peak incidence is between 15 and 24 years of age. The disease spectrum ranges from asymptomatic to fatal. It is generally mild in children and more severe in adults. The majority of primary infections are subclinical. In early childhood, less than 10% developed clinical infection. Genetic factors may influence who develops clinically apparent disease.

The virus is spread by close personal contact with a patient with active infection or with those who are asymptomatic EBV shedders. The virus is viable in saliva outside of the body for more than several hours. Oral shedding can persist for up to 6 months after onset but may extend to 18 months and occurs intermittently throughout life. The incubation period is estimated to be between 30 and 50 days.

Infectious mononucleosis consists of a nonspecific early phase which includes malaise, headache and fever. A more specific later phase includes a triad of pharyngitis, cervical lymphadenitis and high-grade fever. Acute symptoms typically last for 1-2 weeks while fatigue may persist for months. EBV infection is not related to chronic fatigue syndrome.

Infection in infants and young children is frequently asymptomatic. Clinical manifestation in infants can include acute otitis media, diarrhea, abdominal pain and upper respiratory tract findings. Respiratory symptoms are particularly common in young infants.

INFECTIOUS MONONUCLEOSIS: CLINICAL FEATURES	
COMMON	LESS COMMON
Cervical lymphadenitis (Posterior > Anterior)	Palatal petechiae
Generalized lymphadenopathy	Peritonsillar abscess
Tonsillar exudates (white, grey, necrotic)	Periorbital edema
Fever	Palpebral (eyelid) edema
Severe fatigue	Maculopapular rash
Nausea, vomiting, anorexia	Morbilliform rash
Mild hepatitis, jaundice, hepatomegaly	Pneumonitis
Splenomegaly	Bradycardia

INFECTIOUS MONONUCLEOSIS: SUBFORMS	
Classic	Prominent pharyngeal involvement
Typhoidal	Glandular enlargement greater than pharyngeal involvement
Systemic	Fever, fatigue without prominent pharyngeal or glandular findings
GI	Hepatitis without other typical symptoms

INFECTIOUS MONONUCLEOSIS: OTHER MANIFESTATIONS		
HEMATOLOGIC	NEUROLOGIC	OTHER
Aplastic anemia	Aseptic meningitis	Genital ulceration
DIC[1]	Facial nerve palsy	Glomerulonephritis
Hemolytic anemia	Guillain-Barre syndrome	Mesenteric Adenitis
Hemolytic uremic syndrome	Meningoencephalitis	Myocarditis
Thrombocytopenia	Optic neuritis	Myositis
TTP[2]	Peripheral neuritis	Pancreatitis, cholecystitis
	Transverse myelitis	Pneumonia, effusions
1. Disseminated intravascular coagulation, 2. Thrombotic thrombocytopenic purpura		

INFECTIOUS MONONUCLEOSIS: ACUTE COMPLICATIONS
Rash: More common with Amoxicillin/Ampicillin than Penicillin (not a true drug allergy) Maculopapular, urticarial, petechial and rarely erythema nodosum
Airway obstruction: Due to lymphoid hyperplasia and mucosal edema
Splenic rupture: 1-2/1,000, most commonly 4-21 days, not correlated with IM severity
Lymphoproliferative disorders: X-linked, post-transplantation
Other potentially life-threatening: Fulminant hepatitis, meningoencephalitis, severe thrombocytopenia, hemolytic anemia
Oral hairy leukoplakia: White, painless plaques of lingual squamous epithelium Lateral tongue most common. Can occur floor of the mouth, palate, buccal mucosa Primarily in immunosuppressed patients

DIAGNOSTIC TESTING

The diagnosis of infectious mononucleosis is based on clinical manifestations, supportive evidence from the peripheral blood smear (atypical lymphocytosis) and EBV antibody titers. PCR for EBV viral load can be considered for transplant recipients with suspected lymphoproliferative disease. Testing for streptococcal infection should be obtained.

CBC: The most common CBC finding is lymphocytosis. Lymphocytosis may be absolute (absolute lymphocyte count of > 4,500/microL) or relative (> 50% lymphocytes). An atypical lymphocytosis (>10% of lymphocytes) can also be seen but is a nonspecific finding. The total WBC count is typically in the range of 12-18,000 but may be higher.

Mild neutropenia and thrombocytopenia may also be present. The smear should be reviewed manually if an automated differential identifies atypical lymphocytes to exclude blasts and other abnormal cells. Rare hematologic findings are included in the “Other Manifestations” table above.

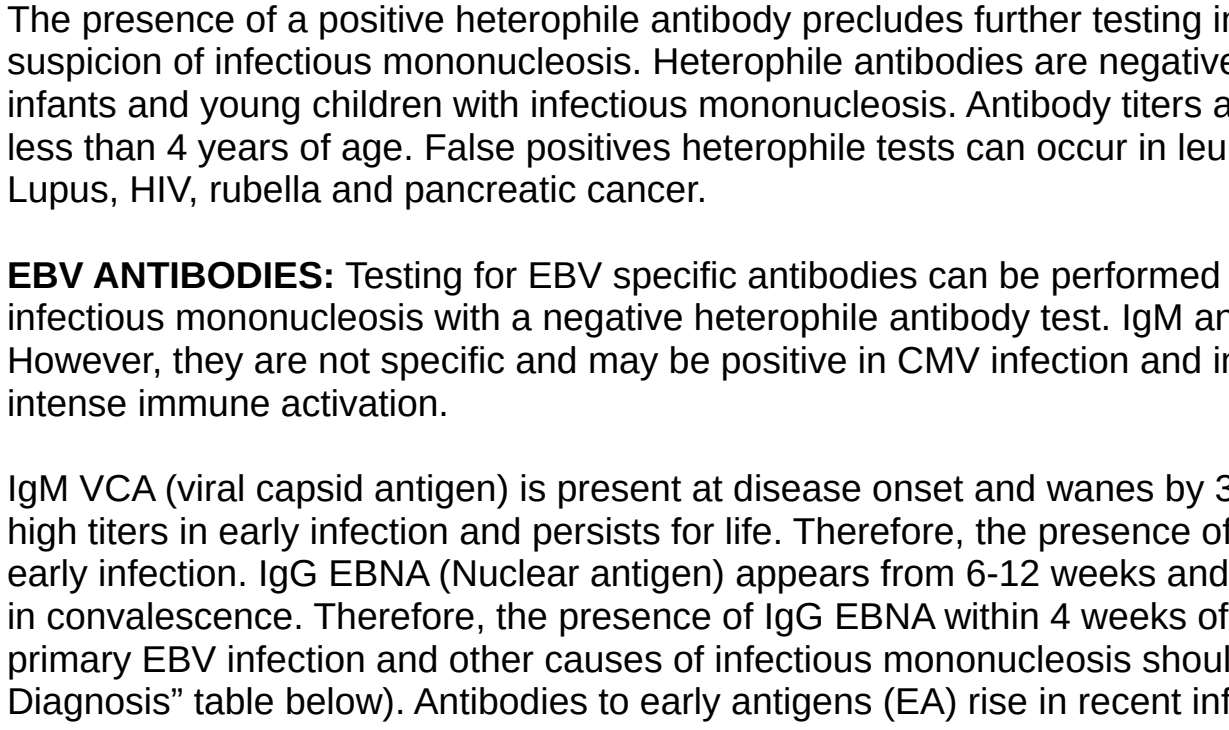
HETEROPHILE ANTIBODIES: EBV infection results in circulating antibodies against EBV and unrelated antigens. Heterophile antibodies (primarily IgM) can found on horse (Monospot) and sheep (Paul-Brunnell) red cells. Heterophile antibodies are present in the 1st week (75%), 2nd week (90-95%) and 3rd week (>95%) of illness. These gradually disappear over a 6 months period.

The presence of a positive heterophile antibody precludes further testing in a patient with a high clinical suspicion of infectious mononucleosis. Heterophile antibodies are negative in approximately 75% of infants and young children with infectious mononucleosis. Antibody titers are recommended for those less than 4 years of age. False positives heterophile tests can occur in leukemia, CMV, lymphoma, Lupus, HIV, rubella and pancreatic cancer.

EBV ANTIBODIES: Testing for EBV specific antibodies can be performed in patients with suspected infectious mononucleosis with a negative heterophile antibody test. IgM and IgG are highly sensitive. However, they are not specific and may be positive in CMV infection and in illnesses associated with intense immune activation.

IgM VCA (viral capsid antigen) is present at disease onset and wanes by 3 months. IgG VCA occurs in high titers in early infection and persists for life. Therefore, the presence of IgM VCA is most specific for early infection. IgG EBNA (Nuclear antigen) appears from 6-12 weeks and persists throughout life rising in convalescence. Therefore, the presence of IgG EBNA within 4 weeks of symptom onset excludes primary EBV infection and other causes of infectious mononucleosis should be sought (see “Differential Diagnosis” table below). Antibodies to early antigens (EA) rise in recent infection, are undetectable by 3-4 months and, may reappear with reactivation.

EBV ANTIGEN TITER INTERPRETATION				
INFECTION	Viral Capsid Ag (VCA IgM)	Viral Capsid Ag (VCA IgG)	Early Ag (EA)	Nuclear Ag (EBNA)
None prior	-	-	-	-
Acute	+	+	+/-	-
Recent	+/-	+	+/-	+/-
Past	-	+	+/-	+
AAP Red Book on Pediatric Infectious Disease: 2018				



EBV TITERS

DIFFERENTIAL DIAGNOSIS: EBV NEGATIVE INFECTIOUS MONONUCLEOSIS	
Bacterial	Streptococcal pharyngitis, Diphtheria, Tularemia
Viral	CMV, acute HIV, human herpes virus 6, 7, hepatitis A, B, adenovirus
Parasitic	Toxoplasmosis
Antiepileptics	Phenytoin, Carbamazepine
Antibiotics	Minocycline, Isoniazid
Approximately 10% of infectious mononucleosis is not caused by EBV	

MANAGEMENT

Treatment of infectious mononucleosis is primarily supportive. Acetaminophen or NSAIDs are recommended for fever, odynophagia and malaise. Adequate hydration is essential. Acyclovir temporarily reduces viral shedding has not been proven to improve symptoms or prevent or improve complications.

CORTICOSTEROIDS: Corticosteroids have not been shown to improve symptoms or prevent complications. In addition, there is a theoretical concern for immunosuppression. Corticosteroids are typically used for impending airway obstruction though data on their efficacy is limited. Corticosteroids may also be considered in patients with massive splenomegaly, myocarditis, hemolytic anemia, severe thrombocytopenia and hemophagocytic lymphohistiocytosis. Prednisone 1-2 mg//kg/day for 5-7 days is most commonly recommended.

RETURN TO PHYSICAL ACTIVITY: Splenomegaly is seen in 50-60% of patients and typically recedes by the third week. Splenic rupture is rare (1-2/1,000) with the majority of cases occurring in males and most commonly occurring 4-21 days after disease onset. Splenic rupture may be spontaneous or traumatic. Non-operative management is preferred though splenectomy is sometimes required.

Data on which to make recommendations on return to sports is limited. Athletic activity should be restricted during the acute illness. Strenuous activity and contact sports should be avoided for 3 weeks after disease onset. After 3 weeks limited, non-contact activity may be initiated if overt splenomegaly is absent. Clearance to full participate in sports is appropriate after 4-6 weeks if overt splenomegaly is absent. (AAP, Red Book of Pediatric Infectious Disease, 2018).

INFLUENZA

INTRODUCTION (CARRIE DANZIGER, M.D. 11/2021)
Influenza virus is a respiratory tract pathogen. Outbreaks of the influenza virus occur because the virus has a high propensity for antigenic change of the envelope glycoproteins (hemagglutinin and neuraminidase). These changes can be minor and lead to local epidemics such as annual seasonal outbreaks. The changes may also be major leading to the occurrence of worldwide pandemics. While minor outbreaks may occur every 2-3 years, pandemics are estimated to occur every 10-20 years. The most recent is the H1N1 pandemic of 2009. Influenza has a high degree of transmissibility. It is transmitted via respiratory secretions (cough/sneeze) or via contaminated surfaces. Once infected, viral shedding peaks at 24-48 hours, and continues for 5-10 days.

In the 2019-20 Influenza season, there were 182 pediatric deaths with a median age of 6.1 years. 57.5% did not have medical comorbidities. Bacterial coinfection was present in 46% of those who died. Of those who were vaccine eligible (> 6 months of age), 74% were unvaccinated and an additional 4.9% were incompletely vaccinated.

VACCINATION: Influenza vaccination is targeted to the most likely strains predicted for the coming year. Mutation in the prior year's strains and emergence of new strains can make vaccination less effective. Immunity after vaccination decreases approximately 50% within 6-12 months so annual vaccination is recommended. Vaccination is recommended for those older than 6 months. The number of dose required is based on age, time of the first administered dose and vaccine history (WEBLINK: CDC).

CLINICAL PRESENTATION
Symptoms typically start 1-4 days after exposure as an acute, febrile respiratory illness. Patients' symptoms may include high fever, chills, malaise, headache, myalgias, fatigue, sore throat, nasal congestion, cough, and conjunctivitis. Younger children are more likely to have gastrointestinal tract symptoms including vomiting and diarrhea. Illness is usually mild and self-limited though it can lead to exacerbations of underlying chronic medical conditions as well as respiratory and non-respiratory complications.

Rates of serious illness and death are highest among children < 2 years (and in particular those < 6 months), adults > 65 years, and those with underlying medical conditions. However, approximately half of pediatric deaths and admissions occur in those without high-risk medical conditions.

INFLUENZA COMPLICATIONS	
Upper respiratory tract disease	Sinusitis, otitis media, croup
Lower respiratory tract disease	Bronchiolitis, pneumonia, asthma exacerbation
Cardiac disease	Myocarditis, pericarditis
Musculoskeletal disease	Myositis, rhabdomyolysis
Neurologic disease	Acute and post-infectious encephalopathy, encephalitis, febrile seizures, status epilepticus
Systemic disease	Staph toxic shock syndrome, sepsis

RISK FACTORS FOR INFLUENZA COMPLICATIONS: CDC/AAP 2021-2022	
1	Children < 5 years, especially those < 2 years
2	Adults ≥ 50 years, especially those ≥ 65 years
3	Co-morbidities
	a. Respiratory
	1. Chronic respiratory diseases: Asthma, cystic fibrosis
	2. Compromised function, secretion handling: Tracheostomy, mechanical vent
	b. Cardiac: Hemodynamically significant: Except for isolated hypertension
	c. Hematologic: Sickle cell disease, other hemoglobinopathies
	d. Metabolic: Diabetes mellitus
	e. Neurodevelopmental: Brain, spinal cord, peripheral nerve, muscle
	1. Epilepsy, cerebral palsy, stroke
	2. Neuromuscular disorders: Muscular dystrophy, spinal cord injury
	3. Moderate to severe developmental delay
	g. Immunodeficiency/Immunosuppression: HIV, medications
	h. Pregnant or post-partum during influenza season
	f. Other: Renal, hepatic, obesity (BMI 40)
4	Long term aspirin (< 19 years): Kawasaki, other rheum due to Reye syndrome
5	American Indians or Alaskan natives
6	Residents of chronic care facilities and nursing homes
Guideline: AAP: PubMed ID: 34493538, Guideline: CDC: PubMed ID: 32820746	

LABORATORY TESTING

Rapid influenza diagnostic tests (RIDT) are known to have poor sensitivity (10-70%) but high specificities (71-83%). A negative rapid test does not rule out infection and should not be used to determine the need for treatment. Definitive testing is available using real time reverse transcriptase tests (rRT-PCR) or cell culture. A point of care rapid influenza PCR test (Roche) has a sensitivity of 97.7% and specificity of 93.3%.

INFLUENZA TESTING RECOMMENDATIONS: AAP 2021-22
All patients admitted with an acute febrile respiratory illness
When testing will influence management decisions: Test results would: 1. Influence the decision to treatment with an antiviral 2. Limit further diagnostic testing to to identify another etiology of infection
As a basis for additional infection control measures: e.g. Cohorting of admissions
A family member with high risk of influenza complications

MANAGEMENT: ANTIVIRAL MEDICATIONS

Three classes of medications are available to treat influenza. The neuraminidase inhibiters (Oseltamivir, Zanamivir, Peramivir) interfere with the release of virus from the cell and are effective against all influenza strains. The amantadines (Amantadine and Rimantadine) interfere with viral uncoating inside the cell. They are effective against influenza A but not influenza B and are associated with more adverse effects. Recent high levels of influenza A resistance have made the amantadines less effective and therefore not recommended. A new class of agents selectively inhibit of influenza cap-dependent endonuclease (Baloxavir).

RECOMMENDED MEDICATIONS: The neuraminidase inhibitors and selective inhibiters of influenza cap-dependent endonuclease are currently recommended for antiviral treatment. Oral oseltamivir is the current drug of choice. Inhaled Zanamivir is an acceptable alternative in those without chronic respiratory disease but is more difficult to administer. Intravenous Peramivir was approved in 2017 for acute, uncomplicated influenza in non-hospitalized children at least 2 years of age with symptoms for less than or equal to 2 days. Its efficacy in serious influenza requiring hospitalization has not been established. Baloxavir was approved in 2018 for uncomplicated influenza in non-hospitalized children at least 12 years of age with symptoms for less than or equal 2 days. Only a single dose is required.

EFFICACY: A 2014 Cochrane review (Jefferson, Cochrane DSR 2014, PubMed ID: 24718923), including previously unpublished studies, demonstrated a 16.8-hour reduction (from 7.0 – 6.3 days) in the duration of symptoms if antivirals are given within 48 hours of symptoms onset. There was no difference in the rate of influenza complications or admissions. Inclusion of subjects with a clinical diagnosis without laboratory confirmation of influenza may have decreased the apparent efficacy of antivirals. A meta-analysis of 5 pediatric randomized trials (n=1,598) with laboratory confirmation of influenza demonstrated a -17.6-hour, 95% CI (-34.7, - 0.62) reduction in the duration of symptoms (-29.9 hours, 95% CI (-53.9, -5.8) in those without asthma) and a decrease in otitis media. (Malosh, Clin Infect Dis 2018, PubMed ID: 29186364)

Based on the available evidence, the AAP, CDC, WHO and Infectious Disease Society of America recommend the use of antivirals. Randomized trials have demonstrated a reduction in symptom duration in children. Observational studies suggest that treatment may decrease the risks of certain complications including hospitalization and death in children. However, this benefit has not been evaluated in randomized clinical trials in admitted patients or in children with co-morbid conditions.

ANTIVIRAL TREATMENT RECOMMENDATIONS: AAP 2021-2
Treatment should be offered as early as possible for influenza[1] regardless of influenza immunization status or time from the duration of symptoms to:
Any hospitalized child
Any inpatient or outpatient child with severe, complicated or progressive illness
Any child at high risk of complications
Treatment may be considered for influenza[1] to:
Any previously healthy child without risk factors for complications and with uncomplicated influenza if treatment can be initiated within 48 hours of onset[2]
Children whose siblings or household contacts who are younger than 6 months of age or with risk factors for influenza complications
1. Laboratory confirmed OR presumed if influenza is circulating in the community 2. Antiviral therapy should still be considered beyond 48 hours of symptom onset in children with severe disease or those at high risk of complications

Potential downsides of therapy include: a cost of over $100 for an adult course of Oseltamivir, the potential for increasing antiviral resistance and common adverse events. The most common adverse effect is nausea and vomiting (5%). Neuro-psychiatric events have been demonstrated primarily in Japanese children less than 16 years of ago and include: confusion, hallucinations, self-injurious behavior and seizures. The etiology of these neuropsychiatric events are unknown and a link between Oseltamivir and neurologic or psychiatric events has not been established.

MEDICATION DOSING: TREATMENT AAP/CDC 2021-22		
OSELTAMIVIR (Tamiflu) 30, 45, 75 mg capsules, 6 mg/ml suspension		
Preterm Infants		
< 38 weeks postmenstrual age[1]		1.0 mg/kg/dose PO BID x 5 days
38-40 weeks postmenstrual age[1]		1.5 mg/kg/dose PO BID x 5 days
> 40 weeks postmenstrual age[1]		3.0 mg/kg/dose PO BID x 5 days
Term Infants: 0[2]-8 months		3.0 mg/kg/dose PO BID x 5 days
Infants: 9-11 months		3.5 mg/kg/dose PO BID x 5 days
Children ≥ 12 months	15 kg	30 mg PO BID x 5 days
	15-23 kg	45 mg PO BID x 5 days
	23-40 kg	60 mg PO BID x 5 days
	> 40 kg	75 mg PO BID x 5 days
Adults		75 mg PO BID x 5 days
See dosing adjustment recommendations for those with impaired renal function		
ZANAMIVIR (Relenza): Inhaled Powder (2 inhalations = 10 mg) contraindicated in those with chronic respiratory disease (e.g. asthma)		
Adults		10 mg (2 inhalations) BID x 5 days
Children (≥ 7 years)		10 mg (2 inhalations) BID x 5 days
PERAMIVIR		
Children 2-12 years		12 mg/kg (max 600 mg) IV over 15-30 min
Children 13-17 years		600 mg IV over 15-30 min
Adults		600 mg IV over 15-30 min
BALOXAVIR		
≥ 12 years: 40-80 kg		40 mg PO x 1
≥ 12 years: ≥ 80 kg		80 mg PO x 1
1. Postmenstrual age = Gestational age + Chronological age 2. Oseltamivir: FDA approved 2012 for > 2 Weeks of age. AAP recommends use < 2 weeks of age in both term and preterm infants because the likely benefits outweigh the potential harms.		

PROPHYLAXIS

Contacts who are at high risk of influenza complication should be advised to see their physician to obtain prophylactic antivirals. Chemoprophylaxis is given at the same dose in the table above but at a frequency of once a day for 7-10 days. It is not recommended for infants less than 3 months of age due to limited safety data

ANTIVIRAL PROPHYLAXIS SHOULD BE CONSIDERED FOR
Children at high-risk of influenza complications for whom vaccine is contraindicated
Children at high-risk during the 2 weeks post influenza vaccination
Unvaccinated family members or health care providers who ongoing close exposure 1. Unimmunized children at high risk 2. Unimmunized infants and children < 2 years
As a supplement to vaccination in those who are high-risk or immune-compromised
Control of influenza outbreaks for unimmunized staff and children in a closed institutional setting with children at high-risk (e.g. extended care facilities)
Household or other close contacts of patients with confirmed, probable, or suspected influenza, who are high risk for complications
Children at high risk as well as family members, closed contacts and health care providers when the circulating virus strain is not matched to influenza vaccine strains

MEDICATION DOSING[4]: PROPHYLAXIS AAP/CDC 2021-22		
OSELTAMIVIR (Tamiflu) 30, 45, 75 mg capsules, 6 mg/ml suspension		
Preterm Infants		
< 38 weeks postmenstrual age[1]		Not Provided
38-40 weeks postmenstrual age[1]		Not Provided
> 40 weeks postmenstrual age[1]		Not Provided
Term Infants: 3-8 months[2]		3.0 mg/kg/dose PO QD x 7-10 days[3]
Infants: 9-11 months		3.5 mg/kg/dose PO QD x 7-10 days[3]
Children ≥ 12 months	15 kg	30 mg PO QD x 7-10 days[3]
	15-23 kg	45 mg PO QD x 7-10 days[3]
	23-40 kg	60 mg PO QD x 7-10 days[3]
	> 40 kg	75 mg PO QD x 7-10 days[3]
Adults		75 mg PO QD x 7-10 days[3]
* See dosing adjustment recommendations for those with impaired renal function		
ZANAMIVIR (Relenza): Inhaled Powder (2 inhalations = 10 mg) contraindicated in those with chronic respiratory disease (e.g. asthma)		
Adults		10 mg (2 inhalations) QD x 7 -10 days[3]
Children (≥ 5 years)		10 mg (2 inhalations) QD x 7-10 days[3]
BALOXAVIR		
≥ 12 years: 40-80 kg		40 mg PO x 1
≥ 12 years: ≥ 80 kg		80 mg PO x 1
1. Postmenstrual age = gestational age + chronological age 2. Not recommended < 3 months due to limited efficacy/safety data 3. 10 days as part of an institutional outbreak 4. Peramivir not recommended as prophylaxis		

DISPOSITION

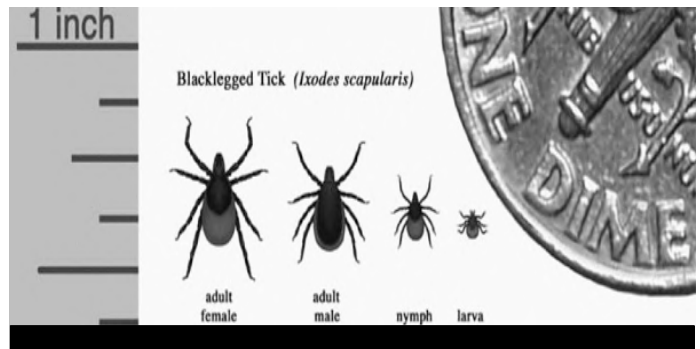
Outpatient management includes supportive care such as rest, hydration and analgesics, avoiding aspirin. Patients whose symptoms resolve and then reoccur should be advised to return for signs and symptoms of secondary bacterial infections.

Patients and parents should be educated on how to limit spread by hand washing and covering up during sneezing and coughing. Patients should be advised to remain home for 24 hours after the fever resolves.

LYME DISEASE

INTRODUCTION (DAVID KESSLER, M.D. 4/2021)
Lyme disease is caused by the spirochete Borrelia Burgdorferi, which is harbored in the Ixodes tick. Clinical manifestations most commonly include: rash (erythema migrans), peripheral facial nerve palsy, arthritis, carditis and meningitis. Nonspecific systemic symptoms such as fever, fatigue, headache and arthralgias may also be present. See also: Guideline, ISDA, Amer Coll of Rheum, Amer Acad Neuro, Clinical ID 2021, PubMed ID: 33251716.

Lyme disease is the most common tick born infection in the US. It is most common in Northeast (Virginia to eastern Canada) (Ixodes scapularis tick). It is present but with a lower frequency in the upper Midwest (Michigan, Minnesota) (Ixodes scapularis tick). It is less commonly seen in northern California and Oregon (Ixodes pacificus tick). Most cases occur from April to October with 50% of cases in July and August. Lyme ticks are usually small. Larger dog ticks do not transmit Lyme.



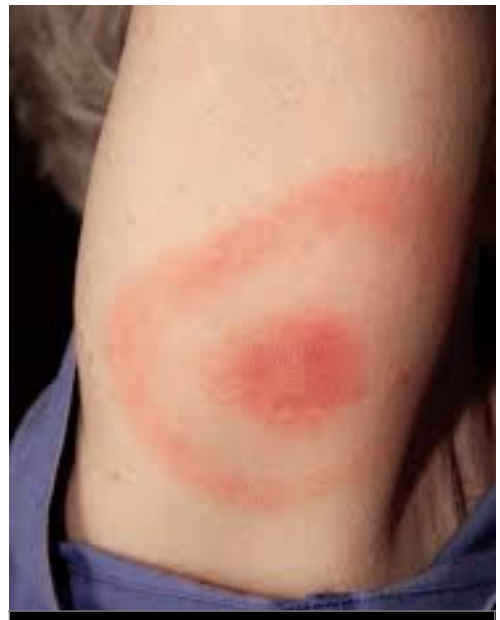
TIC SIZE

STAGES OF LYME DISEASE	
EARLY LOCALIZED (1-2 weeks post tick bite)	
Cutaneous	Erythema Migrans: Initial red macule at the site of tick bite, central clearing in 10%, develops into an annular lesion with serpiginous border over time. Typically, painless and non-pruritic. If untreated may expands to > 5 cm
Systemic	Fever, malaise, headache, mild neck stiffness, myalgia or arthralgias
EARLY DISSEMINATED (3-5 weeks post tick bite)	
Cutaneous	Multiple erythema migrans (15%): 2° lesions 3-5 weeks post bite by hematogenous spread
Musculoskeletal	Arthritis (50%), arthralgias
Neurologic	Cranial nerve palsies (especially peripheral facial nerve (VII) Lymphocytic meningitis
Cardiac	Conduction system: Heart blocks, atrial and ventricular arrhythmias Myocarditis, pericarditis
Systemic	Myalgia, headache, fatigue
LATE DISEASE (Months to years post tick bite)	
Musculoskeletal	Recurrent arthritis (monoarticular), large joints (knee > 90% of cases)
Neurologic	CNS disease or peripheral neuropathy (rare)

CO-INFECTION: Ixodes scapularis also transmits Anaplasma phagocytophilum (previously known as Ehrlichiosis) which causes human granulocytic anaplasmosis and Babesia microti which causes babesiosis. These infections may occur simultaneously with Lyme disease.

Patients with persistent fever after treatment with antibiotics for Lyme or laboratory abnormalities should be investigated for these pathogens. Thrombocytopenia, leukopenia, neutropenia, and/or anemia are consistent with both anaplasmosis and babesiosis. Evidence of hemolysis (indirect bilirubinemia level and elevated lactate dehydrogenase) is more commonly seen with of babesiosis.

CLINICAL MANIFESTATIONS



ERYTHEMA MIGRANS

EARLY LOCALIZED: ERYTHEMA MIGRANS: A characteristic erythema migrans rash is often the presenting symptom of Lyme disease. The rash develops at the site of the tick bite The time from tick bite to erythema migrans rash is typically 7-14 days with a range of 3-30 days.

The diagnosis of early Lyme disease can be made clinically in the setting of erythema migrans. A clear history of a prior tick bite is not present in most cases of Lyme disease. The appearance of the erythema migrans rash is variable. It can occur as the classic target lesion (see image) but can also be uniformly red or red-blue or have a central blister. Systemic signs and symptoms such as fever, fatigue, headache and arthralgia are common.

Antibodies are not detectable in most patients within the first few weeks after infection when localized erythema migrans is most commonly identified. Consider serum testing for atypical lesions convalescent serum antibodies in 2-3 weeks if acute phase serum antibodies are negative.

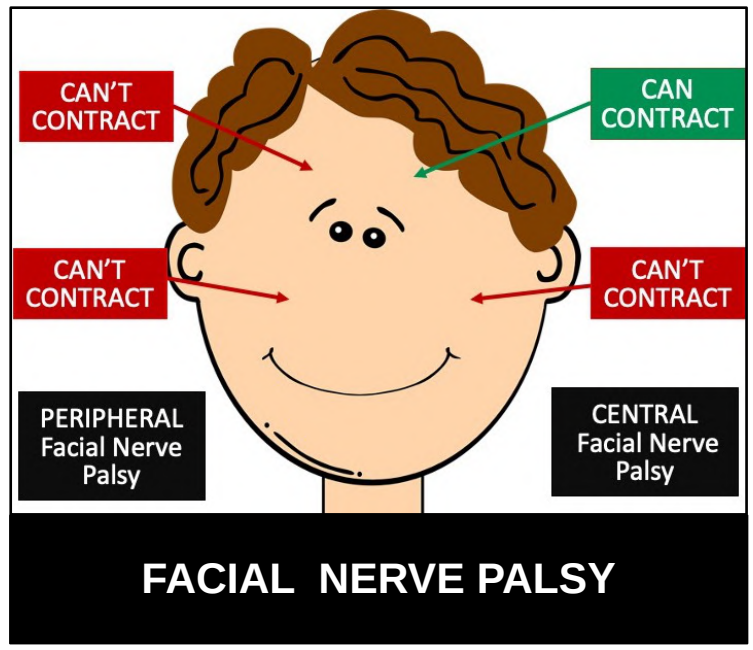
Erythema migrans will resolve spontaneously. However, treatment will lead to faster resolution of the rash and associated symptoms and prevent later developing manifestations. If untreated, patients may develop early disseminated or late manifestation of Lyme disease (arthritis, meningitis, cranial nerve palsies (most commonly peripheral facial nerve palsy) and carditis).

DIFFERENTIAL DIAGNOSIS: ERYTHEMA MIGRANS	
Tick Bite Hypersensitivity Reaction	Time of tick bite: 2 days after, resolve 1-2
Southern Tick Associated Rash Illness	Southeast U.S.
Nummular Eczema	Pruritic, scaly
Tinea Corporis	Pruritic, scaly, red raised border
Cellulitis	Erythema, tenderness, induration, warmth
Granuloma Annulare	Papules/pustules, circular configuration
Brown Recluse Spider Bites, Ecthyma	Necrotic center
Erythema Multiforme	Target lesions +/- mucous membranes

EARLY DISSEMINATED: ERYTHEMA MIGRANS: Secondary erythema migrans from hematogenous spread may appear three to five weeks after the tick bite. Lesions are rounder and smaller than primary erythema migrans lesions.

EARLY DISSEMINATED: FACIAL NERVE PALSY: Lyme disease is the most common cause of peripheral facial nerve palsy (lower motor neuron) in children. Of note, the term Bell's palsy is typically applied to peripheral facial nerve palsy of unknown etiology, though the terms are often used interchangeably. Lyme disease can be differentiated from other causes of facial nerve palsy by the presence of fever and headache, onset from June to October and the absence of herpetic lesions. (See also: Guideline: Baugh, ENT Surg 2013), PubMed ID: 24189771)

The anatomy of the facial nerve is complex. Patients typically present with unilateral facial paralysis. Physical examination findings may include: decreased forehead movement, sagging of the eyebrow, inability to close the eye, and the absence of the nasolabial fold. Decreased tearing, hyperacusis, and loss of taste on the anterior two-thirds of the tongue may also be present.



It is essential to differentiate between involvement of the central facial nerve from the peripheral facial nerve. Sparing of the forehead muscles is suggestive of a central (upper motor neuron) lesion due to bilateral innervation.

Corticosteroids are not indicated in Lyme peripheral facial nerve palsy. Corticosteroids may be indicated in patients 16 years of age or older without objective clinical or serologic evidence of Lyme within 72 hours of facial weakness onset. Artificial tears during the day and eye ointment at night should be provided to prevent corneal abrasions.

The necessity for a lumbar puncture (LP) in patients with a peripheral facial nerve palsy is controversial. Though these patients may have CSF abnormalities, the significance of these abnormalities is unknown. The American Academy of Neurology (AAN, Neurology and the Infectious Disease Society of America (IDSA, Clinical ID, 2006, PubMed ID: 17029130) recommend that an LP may be deferred in the absence of fever, severe headache, meningeal signs, seizures and papilledema.

EARLY DISSEMINATED: MENINGITIS (NEUROBORRELIOSIS): The season and presentation of Lyme meningitis is similar to that of aseptic meningitis. A history of erythema migrans, cranial nerve palsy, and papilledema make Lyme meningitis more likely. Lyme meningitis is characterized by a lymphocyte pleocytosis (generally < 10% neutrophils). Typically, glucose is normal and protein is elevated.

A clinical decision rule was derived and validated in a Lyme endemic area to identify those at low risk of Lyme meningitis. (Cohn, Pediatrics 2011, PubMed ID: 22184651). The multicenter, validation phase included 117 patients with Lyme meningitis and 306 with aseptic meningitis and no patients with bacterial meningitis. Three parameters ("rule of sevens") were identified as low risk for Lyme meningitis. The rule had a sensitivity of 96%, 95% CI (90, 99%) and specificity of 41%, 95% CI (36, 47%). In the 390 children without erythema migrans, 3 of the 127 low-risk patients had Lyme meningitis (2% 95% CI: 0.0, 7%). The authors conclude that: "Patients classified as low risk by using the Rule of 7's were unlikely to have Lyme meningitis and could be managed as outpatients while awaiting results of Lyme serology tests."

LYME MENINGITIS DECISION RULE: RULE OF 7s
< 7 days of headache
< 70% CSF mononuclear cells
Absence of 7th or other cranial nerve palsy.

EARLY DISSEMINATED: ARTHRITIS: Arthritis is typically monoarticular, involving the large joints. The knee is involved in over 90% of cases. Pain, limp, fever and erythema are less common than with bacterial arthritis. The synovial fluid white blood cell (WBC) count ranges from 20,000-60,000 cells/microL but it can exceed 100,000 cells/microL. A retrospective cohort study in a Lyme endemic area concluded that synovial fluid findings alone do not reliably distinguish between Lyme from bacterial septic arthritis (Deanehan, Pediatri Emerg Care 2014, PubMed ID: 24365728).

A knee, monoarthritis decision rule underwent multicenter validation in 8 pediatric emergency departments in Lyme endemic areas. No patients with septic arthritis were misidentified by the rule. Rule characteristics were nearly identical to those of the derivation cohort. Both the external validation cohort and derivation cohort had a higher specificity than the Kocher rule. In the validation cohort,

66.3% (303/457) of patients had a negative rule and would be classified as low risk. In low risk patients, use of the rule would decrease the rate of arthrocentesis by 17.2%, operative joint washout by 5.3% and admission by 17.8%.

KNEE MONOARTHRITIS DECISION RULE			
	Validation[1]	Derivation[2]	Kocher[2]
Prevalence	2.6% (1.5, 4.4%)	3.1% (1.8, 5.3%)	3.2% (1.9, 5.5)
Sensitivity	100% (75.8, 100%)	100% (77.2, 100%)	100% (77.2, 100%)
Specificity	68.1% (63.6, 72.3%)	62.4% (57.6, 67.0%)	26.5% (22.3, 31.1%)
PV (+) Rule	7.8% (4.5, 13.1%)	7.9% (4.7, 13.1%)	4.3% (2.6, 7.3%)
PV (-) Rule	100% (98.8, 100%)	100% (98.5, 100%)	100% (96.4, 100%)
LR (+) Rule	3.1 (2.7, 3.6)	2.7 (2.3, 3.0)	1.4 (1.3, 1.4)
LR (-) Rule	(0 in calculation)	(0 in calculation)	(0 in calculation)
% (-) Rule	66.3% (61.8, 70.5%)	60.5% (55.7, 65.1%)	25.6% (21.6, 30.1%)
1. Grant, Pediatr Emerg Care. 2021 May 13., PubMed ID: 34160185 2. Deanehan, Pediatrics, 2013., PubMed ID: 23420916			

EARLY DISSEMINATED: CARDITIS: Carditis is a rare finding occurring in approximately 1% of patients with Lyme disease. It can present from days to months with an average of 3 weeks. Involvement of the atrioventricular node is most common, resulting in varying degrees of heart block. Involvement of the atrial and ventricular conducting system can lead to atrial and ventricular arrhythmias. Myocarditis and pericarditis can also occur.

Routine EKG testing is not recommended. EKG is indicated in patients with chest pain, shortness of breath, palpitations, exercise intolerance, dizziness or syncope. An echocardiogram for identification of pericardial effusion and cardiac contractility and troponin testing for evidence of myocarditis is indicated in patients with signs and symptoms of carditis. The presence of second- or third-degree heart block may require temporary cardiac pacing (See: PEM Guide: Cardiology: Cardiac Pacing for Bradycardia). Admit patients with significant PR prolongation, high grade heart blocks, arrhythmias and clinical manifestation or myopericarditis. In adults, a PR interval of > 300 msec is associated with higher grade blocks requiring cardiac pacing.

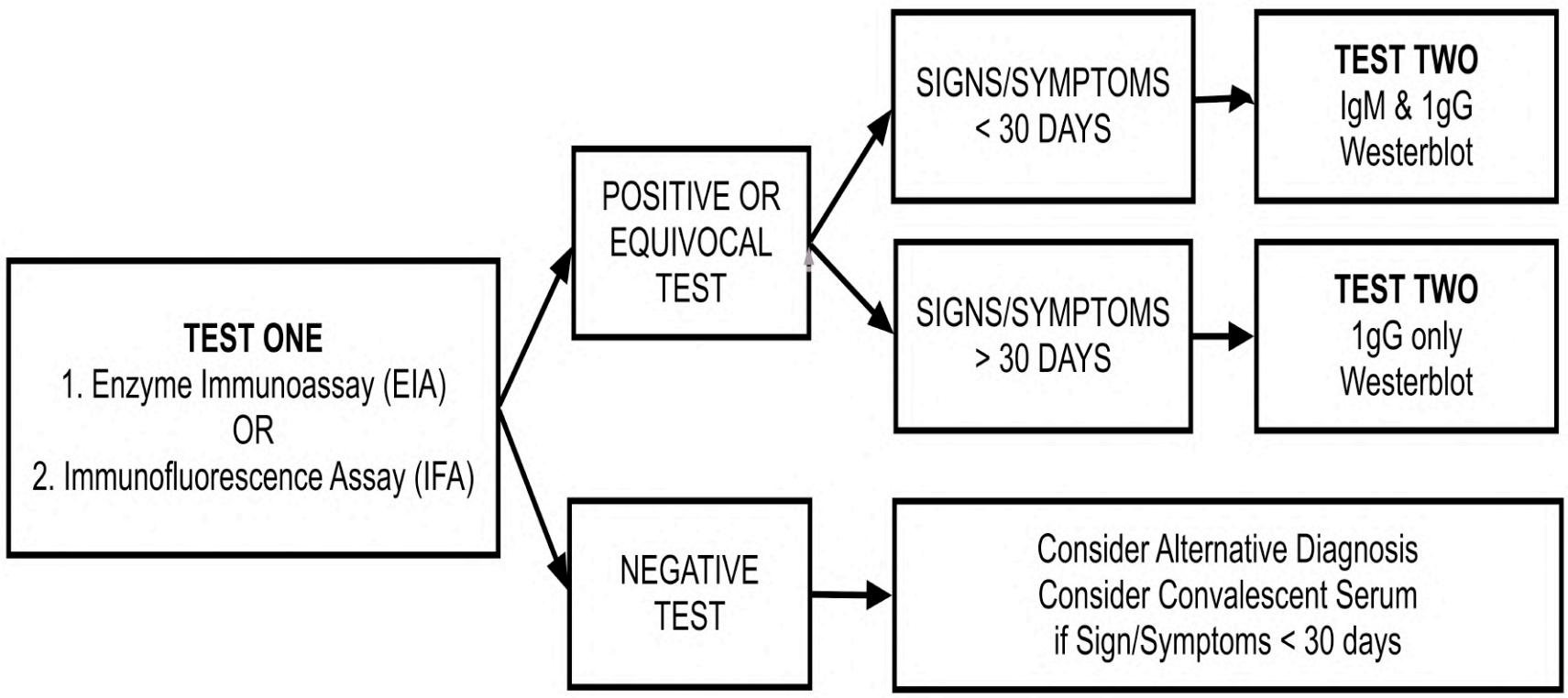
LATE: PROLONGED LYME DISEASE: Longitudinal studies have demonstrated persistent and often debilitating symptoms including fatigue, musculoskeletal and neurocognitive symptoms in 10-20% of appropriately diagnosed and treated Lyme disease patients at 1 year. However, prospective controlled trials have demonstrated the same frequency of these symptoms in healthy controls. While these symptoms can potentially be attributed to immunologic changes in response to Lyme disease, there is no evidence that infection persists or that these symptoms are amenable to antibiotic therapy.

LABORATORY DIAGNOSIS

The diagnosis of early, localized Lyme disease is made on the basis of the characteristic appearance of the erythema migrans rash. The diagnosis of extracutaneous manifestations of early disseminated and late Lyme disease is made on the basis of both clinical and serologic evidence.

Antibodies are usually not detectable for 4 weeks so that antibody testing will be negative in early localized erythema migrans. If treated in this stage most will not develop antibodies. Antibody testing is very sensitive in patients with later developing, non-cutaneous Lyme disease manifestations. For peripheral nervous system (facial nerves palsy) or central nervous system (meningitis) manifestation of Lyme disease, serum antibody testing is preferred over CSF or blood PCR or culture. In patients with arthritis, serum antibodies are preferred over PCR or culture of blood or synovial fluid.

Initial screening tests for serum antibodies (Enzyme Immunoassay (EIA) and Immunofluorescence antibody assay (IFA)) are sensitive but with false positives.
False positive results may occur with syphilis, leptospirosis, EBV, varicella and lupus.
Further confirmation is required for positive or equivocal results. The Western blot test is specific. IgM peaks at 3-6 weeks and IgG peaks in weeks to months. Lyme IgM may be elevated for months to years making it difficult to distinguish new infection in those with a previous history of Lyme disease. Two-tiered testing improves specificity.



MANAGEMENT

The goals of treatment are the resolution of signs and symptoms and the prevention of other manifestation or relapse. In most cases, oral therapy is equivalent to intravenous therapy at lower cost and with fewer adverse events. In general, patients sick enough to require admission should be administered intravenous therapy. Patients may have a transient increase in symptoms with or without fever in the first 24 hours of treatment. This is likely related to bacterial antigen release.

TREATMENT: ANTIBIOTIC REGIMENS AND DURATION OF TREATMENT	
Early Localized Erythema Migrans (EM)	
Doxycycline x 10 days (Doxycycline use < 8 years of age should be individualized)[1]	
Amoxicillin x 14 days	
Cefuroxime x 14 days	
Azithromycin x 7: 2nd Line. Less effective, if can't use any of the above. Only for EM	
Early Disseminated and Late	
Disseminated EM	Same antibiotic regimens as above
Isolated facial nerve palsy	Doxycycline x 14-21 days
Arthritis	Doxycycline, Amoxicillin or Cefuroxime x 28 days
Arthritis: Recurrent, refractory arthritis	PO: Doxycycline, Amoxicillin or Cefuroxime x 28 days IV: Ceftriaxone x 14 days (may be extended to 28 days if without improvement)
Meningitis, cranial neuropathy, radiculopathy, other peripheral nervous system manifestations	IV Ceftriaxone x 14-21 days Alternatives: IV Cefotaxime or Penicillin G (IV preferred for parenchymal CNS or spinal cord involvement, can be transitioned to oral for a total 14-21d) PO Doxycycline x 14-21 days
Carditis	Admitted: IV Ceftriaxone until clinical improvement then PO Antibiotics to a total of 14-21 days Outpatient: Doxycycline, Amoxicillin, Cefuroxime x 14-21d
Recent evidence demonstrates that Doxycycline does not cause dental staining as does Tetracycline Cross, Expert Opinion Drug Safety 2016, PubMed ID: 26680308 Doxycycline also treats anaplasmosis. Amoxicillin does not	

TREATMENT: ANTIBIOTIC DOSING		
	ADULTS	PEDIATRICS
Doxycycline	100 mg TID or 200 mg PO QD	4.4 mg/kg/day PO divided BID1
Amoxicillin	500 mg PO TID	50 mg/kg/day PO divided TID[2]
Cefuroxime	500 mg PO BID	30 mg/kg/day PO divided BID[1]
Azithromycin[3]	500 mg PO QD	10 mg/kg PO QD[1]
Ceftriaxone	2,000 mg IV QD	50-75 mg/kg IV QD[1]
Cefotaxime	2,000 mg IV TID	150-200 mg/kg divided IV TID or QID[2]
Penicillin G	18-24 million units IV Q4H	200,000-400,000 units/kg IV Q4H[2]
1. Maximum per dose in pediatric patients is the adult dose (200 mg for Doxycycline) 2. Maximum daily dose in pediatric patients is the adult dose 3. Only indicated for erythema migrans and if cannot take any other PO antibiotics 4. A second course of treatment may be required for objective signs of relapse		

TICK REMOVAL: Remove the tick by grasping the head near the skin surface and pulling gently upward with forceps. Remaining mouthparts are not infectious. Methods that cause the tick distress (suffocation with ointments, burning and squeezing of the body of the tick) increase the extrusion of infectious material. Testing of ticks for Lyme is not recommended though the tick may be submitted for species identification.

TICK BITE PROPHYLAXIS: Antibiotic prophylaxis for tick bites is not recommended. Doxycycline may be offered if all four of the criteria in the table below are met. A watch and wait approach is recommended if the tick cannot be definitively identified.

ANTIBIOTIC PROPHYLAXIS FOR TICK BITE: IDSA* 2020
Tick reliably identified as an adult or nymphal Ixodes. scapularis (larva not infectious)
Attached for ≥ 36 hours on the basis of the degree of engorgement of the tick with blood or a certain time of exposure
Prophylaxis can be started within 72 hours of the time that the tick was removed
Local rate of tick infection with B. burgdorferi is ≥ 20% Northeast, Mid-Atlantic, parts of Minnesota and Wisconsin (Not Northern California)
Doxycycline treatment is not contraindicated: Single dose 4.4 mg/kg (max 200 mg)
*Infectious Disease Society of America

PREVENTION
Protective clothing: Light colored, long sleeves/pant legs. Tucked into socks
Tick repellant: N,N-Diethyl-meta-toluamide (DEET), picaridin, ethyl-3-(N-n-butyl-N-acetyl), aminopropionate (IR3535), oil of lemon eucalyptus (OLE), p-methane-3,8-diol (PMD), 2-undecanone. Permethrin only for application to clothing and/or gear
Fully body check after potential exposure
Prompt removal of attached ticks

MEASLES

INTRODUCTION (SHWETA IYER, MD, 11/2018)
Measles (rubeola) is a highly contagious viral respiratory illness. It is estimated that 90% of those susceptible with close contact to a patient with measles will develop measles. The virus is transmitted by direct contact with infectious droplets or via airborne spread when an infected person breaths, coughs, or sneezes. The virus can remain in the air for up to two hours. Patients are considered contagious from 4 days before until 4 days after the appearance of the rash.

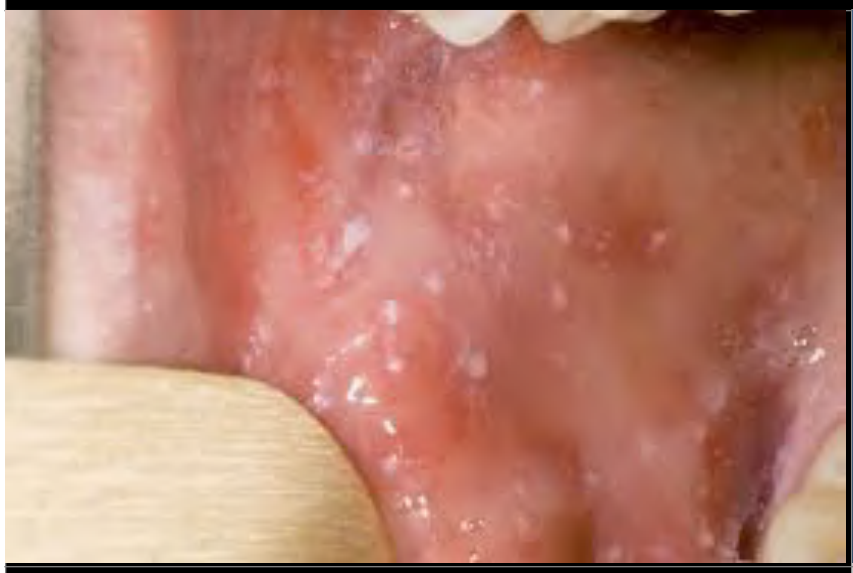
WEB LINK: CDC MEASLES

Approximately 30% of measles patients will sustain a complication, and 25% will require hospitalization. One out of every 1,000 patients will develop encephalitis and 1-2 of every thousand will die from respiratory or neurologic complications in the U.S. 4-10% of patients in developing countries may die. People at high risk for complications include the immunocompromised (e.g., AIDS, malignancy), children less than 5 years of age, people with poor nutrition or vitamin A deficiency, pregnant women, and adults.

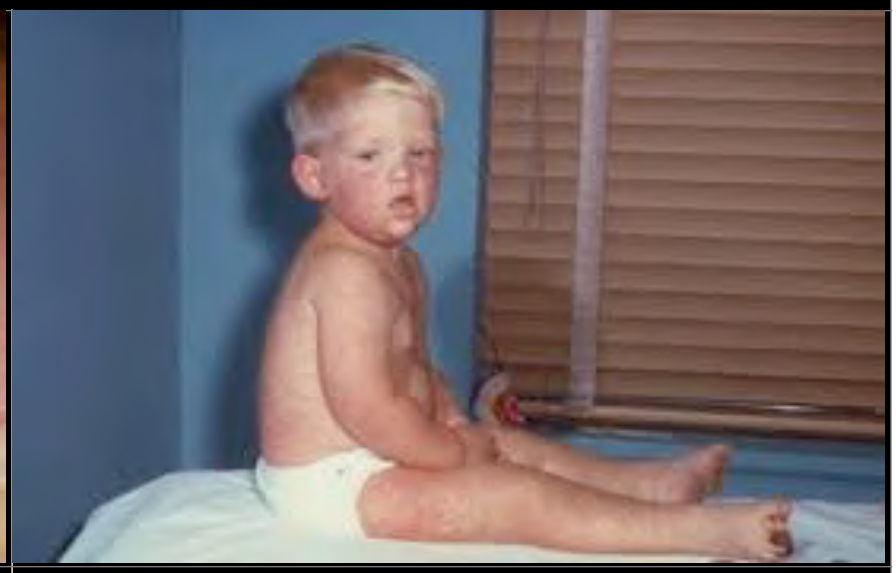
CLINICAL MANIFESTATIONS
The diagnosis of measles is primarily clinical. Consider the diagnosis of measles in patients with a high fever, malaise, cough, coryza, and conjunctivitis (the 3 C's) followed by an exanthem, especially if they are not immunized, have been exposed to measles, and/or are coming from an area with high measles prevalence.

DISEASE COURSE		
PHASE	TIMING	SIGNS/SYMPTOMS
Incubation	7-21 days (average: 14d)	Typically asymptomatic. +/- Transient respiratory symptoms, rash or fever
Prodrome	2-4 days (as long as 8d)	Signs/Symptoms: Fever, malaise, anorexia, followed by conjunctivitis, coryza, and cough (the 3 C's). Symptoms typically intensify before the exanthem
		Enanthem: Koplik spots: Pathognomonic if present. 1-3 mm white, grey or bluish lesions on an erythematous base in the oropharynx. May coalesce. Last 1-3 days. Slough when exanthem appears.
Exanthem	2-4 days after fever onset (2 week after exposure)	Signs/Symptoms: High fever, lymphadenopathy, pharyngitis, non-purulent conjunctivitis.
		Exanthem: Erythematous, maculopapular, blanching rash +/- petechiae, rarely palms/soles Cranial to caudal: Begins on face/neck, becomes confluent on the face, spreads to trunk/extremities. Lasts 6-7 days. Darkens to brown, fades, desquamates in severe areas Rash severity correlates with illness severity.
Recovery	1-2 weeks post infection	Typically improve in 3-4 days after rash onset Cough may persist from 2-4 weeks Fever for > 3-4 days suggests complications

MEASLES: MUCOSAL/SKIN MANIFESTATIONS



ENANTHEM: KOPLIK SPOTS



EXANTHEM

COMPLICATIONS

Gastrointestinal	Diarrhea (most common, 8%), stomatitis, gingival stomatitis, mesenteric adenitis, appendicitis
Respiratory	Pneumonia (6%): # 1 cause of pediatric measles-associated death
	Acute otitis media (5-10%), laryngotracheal bronchitis, bronchiolitis
Ophthalmologic	Conjunctivitis, Keratitis (may lead to blindness), corneal ulceration
Neurologic	Encephalitis Approximately 1/1,000 measles cases Typically within 5 days of exanthem onset Fever, headache, neck stiffness, seizures, mental status changes CSF: Lymphocytic pleocytosis, elevated protein 25% with neurodevelopmental sequelae 15% rapidly progressive and fatal
	ADEM (Acute Demyelinating Encephalo-Myelitis) Approximately 1/1,000 measles cases Post-infectious autoimmune response During recovery phase (within two weeks of the exanthem) Symptoms: Fever, headache, neck stiffness, seizures, mental status changes, ataxia, myoclonus, choreoathetosis, myelitis (paraplegia, quadriplegia, sensory loss, loss of bladder/bowel control, back pain) CSF: Lymphocytic pleocytosis, elevated protein
	SSPE (Subacute Sclerosing Pan-Encephalitis) Fatal, progressive. degenerative disease of the CNS Occurs 7 to 10 years after measles virus infection < 1 year of age = 1 in 600, < 5 years of age = 1 in 1,400 Pathogenesis not well understood 4 stages of SSPE which evolve from neurologic symptoms (seizures, myoclonus, dementia, neurologic deterioration) to death

DIFFERENTIAL DIAGNOSIS: FEBRILE ILLNESS WITH EXANTHEM
Erythema infectiosum (parvovirus B19)
Infectious mononucleosis (EBV)
Juvenile Immune Arthritis (JIA): Systemic onset
Kawasaki disease
Meningococcemia
Mycoplasma pneumoniae with rash
Rocky mountain spotted fever
Roseola (human herpes virus 6)
Rubella (German measles)
Streptococcal infection: Scarlet fever, toxic shock syndrome
Varicella

LABORATORY TESTING

A complete blood count may reveal leukopenia and thrombocytopenia. Chest radiography may reveal an interstitial pneumonitis, pneumonia, or bronchiectasis.

LABORATORY CONFIRMATION OF MEASLES (ANY ONE)	
IgM Antibody	Detectable 3-30 days after exanthem onset May be absent or elevated only transiently if previously vaccinated
IgG Antibody	Detectable 7 days after exanthem onset. Peaks 14 days Paired acute/convalescent sera (>10 days apart): ≥ 4X ↑ in IgG
Viral Culture**	Blood, respiratory secretions, conjunctival swabs, or urine
Viral RNA PCR	Detectable 3 days after exanthem onset Blood, throat or nasopharyngeal aspirates and urine**
*Report to NYC DOH for rapid testing through the NYS Wadsworth Center Laboratory **Requires > 2 weeks but may be helpful for monitoring genetic characteristics	

MANAGEMENT

There is no specific measles antiviral therapy. The treatment of measles is supportive. Supportive therapy includes antipyretics, fluid replacement, and treatment of bacterial superinfections such as bacterial pneumonia and otitis media. Respiratory support may be required for those with severe measles laryngotracheal bronchitis and pneumonia. Adjunctive treatment with Vitamin A and/or Ribavirin may also be indicated (see tables below). Suspected measles cases should be reported to the local health department within 24 hours (NYC DOH Provider Access Line: (866) 692-3641).

VITAMIN A
Vitamin A deficiency contributes to delayed recovery and measles complications Measles infection may precipitate acute vitamin A deficiency and xerophthalmia
Administer to all children with severe measles (such as children who are hospitalized) May reduced overall and pneumonia-specific mortality*
Administer (IV or PO) on diagnosis and repeat the next day for 2 total doses < 6 months: 50,000 IU, 6-11 months: 100,000 IU, ≥ 12 months: 200,000 IU
D'Souza, Cochrane Database Sys Rev, 2002, PubMed ID: 11869601

RIBAVIRIN
Some experts recommend Ribavirin in specific cases: 1. Measles pneumonia in patients <12 months 2. Patients ≥ 12 months with pneumonia requiring ventilatory support 3. Patients who are severely immunocompromised
Not licensed by the FDA for measles Dosing: 15 to 20 mg/kg per day IV or aerosol in two divided doses x 5-7days Optimal duration of therapy is unknown

INFECTION CONTROL

Measles is highly contagious. It is spread through direct contact and through the air. Measles virus can remain suspended in the air for up to two hours; therefore, the room should not be used for two hours after the patient's departure. Patients are considered contagious from 4 days before until 4 days after the rash appears.

Airborne transmission precautions are indicated for 4 days after the onset of rash in otherwise healthy patients, and for the duration of illness in immunocompromised patients. Patients and staff should wear appropriate masks/respirators in patient rooms even if immune, and suspected measles patients should be in an airborne isolation negative pressure rooms. Exposed susceptible individuals without immunity should be excluded from outbreak areas until 21 days after onset of measles rash. Healthcare providers should be excluded from work from day 5 after first exposure to day 21 after last exposure, if not immune, to prevent spread.

EVIDENCE OF IMMUNITY
Written or electronic documentation of measles vaccine: 2 doses: School aged (K-12) children, adults at high risk 1 dose: Preschool children, adults not at high risk
Laboratory evidence of immunity: e.g. (+) measles IgG
Laboratory confirmation of measles: (+) measles IgM, PCR or culture
Born prior to 1957

ISOLATION: TIME FROM EXPOSURE	
Immune: Measles IgG(+), proof of 2 MMR, born prior to 1957	None
Non-immune: 1 prior MMR, measles testing sent	Until test results
Non-immune: No post exposure prophylaxis received	21 days
Non-immune: Received MMR within 3 days of exposure	21 days
Non-immune: Received Immune Globulin within 6 days	28 days

POST EXPOSURE PROPHYLAXIS

Post exposure prophylaxis with measles vaccine or immune globulin in susceptible patients may modify the clinical course of measles infection. Recommendation vary based on the patient’s age, time of exposure and contraindications to measles vaccine.

POST-EXPOSURE PROPHYLAXIS					
Time Since Exposure[1]	0-5 months	6-11 months	≥ 12 months (0 MMR)	≥ 12 months (1 MMR)	MMR Contraindicated[5]
0-3 days	IG	MMR[2]	MMR	MMR[3]	IG
4-6 days	IG	IG	None	Test or MMR[4]	IG
> 6 days	None	None	None	Test or MMR[4]	None

1. Infectious from 4 days before rash until 4 days after rash appearance
2. Should subsequently receive 2 doses of MMR as per vaccine schedule
3. Can receive a 2nd MMR if > 28 days since the first
4. Household contact: Blood test for Measles IgG, stay home until test result
   Non-household contact: ≥ 4 years. Attend/work in childcare, healthcare, airport?
   Yes: Blood test for Measles IgG, stay home until test result
   No: MMR
5. See contraindications and precautions table below

POST EXPOSURE PROPHYLAXIS: MMR VACCINE	
Indications	> 6 months who have not received 2 prior doses on MMR
Timing	Within 3 days of exposure
Isolation	21 days post exposure
Comment	A 2nd MMR can be given at least 28 days later.

POST EXPOSURE PROPHYLAXIS: IMMUNE GLOBULIN	
Indications	Those at risk for severe measles or complications of measles: < 6 months 6-12 months presenting after 3 and before 6 days of exposure Pregnant patients without evidence of immunity Immunocompromised regardless of immunologic or vaccination status
Timing	Within 6 days of exposure if MMR vaccine not indicated
Dosing	Intramuscular: 0.5 ml/kg (maximum of 15 ml) Intravenous: 400 mg/kg (Pregnant without evidence of immunity, severely immune-compromised, contraindication to measles vaccine)
Isolation	28 days post exposure

PREVENTION

The MMR (Measles-Mumps-Rubella) vaccine or MMRV (Measles-Mumps-Rubella-Varicella) vaccine is administered routinely in childhood for prevention. The first dose is administered between 12 and 15 months of age, and the 2nd dose is administered between ages 4 and 6 years of age, or at least 28 days following the first dose. The measles vaccine is estimated to be 93% (1 dose) and 97% (2 doses) effective. Those who get measles after vaccination typically have a less severe course and are less likely to transmit the disease.

Measles outbreaks still occur every year in the United States because measles is still commonly transmitted in many parts of the world, including countries in Europe, Asia, the Pacific, and Africa. Sporadic outbreaks occur in the U.S., primarily in unvaccinated populations. Herd immunity greater than 95% is required to prevent broad transmission.

MEASLES VACCINE CONTRAINDICATIONS AND PRECAUTIONS
CONTRAINDICATIONS
Severe allergic reaction after a previous dose or to a vaccine component
Pregnancy or possibility of pregnancy within 4 weeks
Immunosuppression
Primary or acquired immunodeficiency
Blood dyscrasia, leukemia, lymphoma, bone marrow/lymphatic system neoplasms
Long-term immunosuppressive therapy
Congenital or hereditary immunodeficiency in a parent/sibling
PRECAUTIONS
Receipt of antibody-containing blood product within past 3-11 months
History of thrombocytopenia or thrombocytopenic purpura
Need for tuberculosis testing
Moderate or severe illness with/without fever (more severe than URI, AOM, AGE)
MMRV only: Personal history of seizures or seizures in sibling or parent

MYCOPLASMA PNEUMONIA

INTRODUCTION (GIOVANNA VARUZZA BAYE, MD, 4/2022)
Mycoplasma pneumoniae is an “atypical” bacteria. It is both aerobic and anaerobic, has no cell wall, and is rod shaped. Out of all of the mycoplasma species,

Mycoplasma pneumoniae is by far the most common cause of human illness, specifically respiratory tract infections. This is because the bacteria are specifically attracted to human respiratory epithelium. In addition, *Mycoplasma pneumoniae* is also known to cause several different extrapulmonary clinical presentations. This is thought to be secondary to the host’s immune response which creates antibodies against *Mycoplasma pneumoniae* glycolipid antigens which then act as autoantibodies, specifically targeting red blood cells and brain cells. Thus, *Mycoplasma pneumoniae* causes symptoms due to the bacteria itself as well as immune-mediated responses.

PATHOGENESIS
Mycoplasma pneumoniae attach to and attack respiratory epithelial cells via transmembrane proteins. This adherence makes it difficult for the host to clear the infection. After adherence the bacteria create superoxide and hydrogen peroxide which destroys the host cell. Though primarily extracellular, there are some strains that have evolved to invade and live inside the host cell, avoiding the immune system and thus explaining the potential for long-term asymptomatic carriage (Yavlovich, FEMS Microbiol Let 2004, PubMed ID 15063492).

EPIDEMIOLOGY
Mycoplasma pneumoniae commonly causes community acquired pneumonia (CAP). Pneumonia caused by *Mycoplasma pneumoniae* is referred to as “walking pneumonia” due to its typically mild course. It is also referred to as “atypical pneumonia” due to the fact that the bacteria itself are difficult to detect by standard microbiology methods.

The CDC estimates that there are about 2 million cases of *Mycoplasma pneumoniae* infections per year, most occurring during the summer and fall. A population-based study found that *Mycoplasma pneumoniae* was the most frequently detected bacteria in children hospitalized for CAP. They determined that 7 years old was the median age of a child hospitalized with *Mycoplasma pneumoniae* CAP and that co-infections with viruses were common (Kutty, Clin Infect Dis 2019, PubMed ID: 29788037).

TRANSMISSION
Mycoplasma pneumoniae is transmitted via respiratory droplets. Transmission usually requires prolonged exposure. The typical outbreak occurs where people are living together in close contact, such as on college campuses and on military bases. The incubation period ranges from 1 to 4 weeks.

CLINICAL MANIFESTATIONS
The clinical manifestations of *Mycoplasma pneumoniae* vary in severity from an asymptomatic carriage, to an isolated respiratory tract illness, to an illness involving additional systems. *Mycoplasma pneumoniae* infection also varies widely depending on the host’s immune competence.

The most common presentation of *Mycoplasma pneumoniae* is pneumonia. Symptoms typically begin with headache, sore throat, and fever. Around day 2 of illness, a non-productive cough usually develops. This cough may last for weeks to months. 75% of cases have abnormal lung exams, specifically rales and decreased breath sounds.

Mycoplasma pneumoniae infection in children is often mild. Some children, especially those under the age of 5, may never develop pneumonia and instead will exhibit typical upper respiratory illness (URI) symptoms such as runny nose, cough, and sometimes otitis media. In these mild cases the child usually remains afebrile. Auscultation of wheezing on lung exam is common, even in children without a history of asthma. Additionally, gastrointestinal symptoms such as vomiting and diarrhea can develop.

In children over 5 years of age, *Mycoplasma pneumoniae* usually results in pneumonia. When pneumonia does develop, it is usually mild in nature and lasts 1to 2 weeks on average. Symptoms typically include fatigue, cough, fever, chills, and shortness of breath. Severe pneumonia may require intensive care for monitoring and treatment of sequelae such as pleural effusions.

EXTRAPULMONARY SYMPTOMS: About a quarter of children who have *Mycoplasma pneumoniae* develop extrapulmonary manifestations. The extrapulmonary symptoms usually occur in conjunction with respiratory symptoms but it is also possible to only have extrapulmonary symptoms. Some of these extrapulmonary symptoms are secondary to direct infection and some are due to immune-mediated responses, many of which are not clearly understood (Gordon, Pediatric Infect Dis J 2019, PubMed ID: 30985519).

EXTRAPULMONARY MANIFESTATIONS	
Hematologic	Hemolysis
Mucocutaneous	Mild maculopapular rash MIRM (Mycoplasma pneumoniae-induced rash and mucositis, similar to Stevens Johnson syndrome)
Central Nervous System	Meningoencephalitis, ADEM, transverse myelitis, cerebellar ataxia, Guillain-Barre syndrome, infarcts, neuropathy
Gastrointestinal	Vomiting, diarrhea, intussusception, hepatitis, pancreatitis
Cardiac	Heart failure, pericardial effusion, myocarditis
Renal	Glomerulonephritis
Musculoskeletal	Arthritis/arthralgias

DIAGNOSIS TESTING

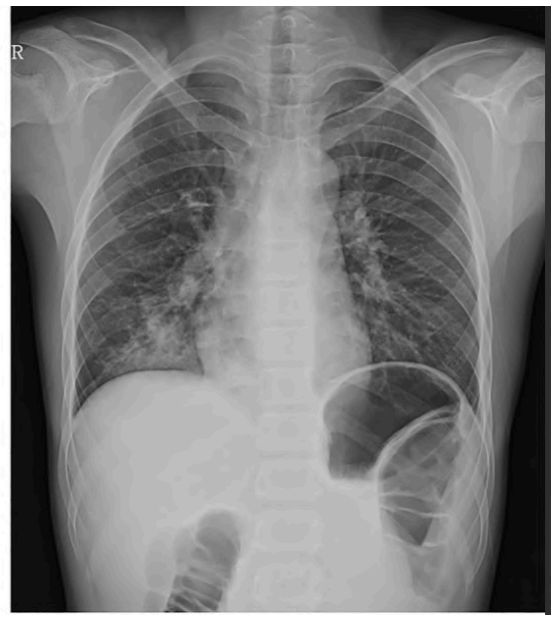
Confirmation of *Mycoplasma pneumoniae* is often not required and is only indicated if it will change clinical management. In patients who are being treated for outpatient CAP, the recommendation is not to test since empiric treatment is usually successful.

In patients hospitalized for CAP, testing is usually done. To confirm infection, *Mycoplasma pneumoniae* or antibodies against Mycoplasma pneumoniae need to be detected. A PCR test, a type of nucleic acid amplification test (NAAT), is the typical method used to detect *Mycoplasma pneumoniae*. Serology can also be done to detect *Mycoplasma pneumoniae* IgM and IgG. Antigen testing is possible but it has become obsolete in most countries. Culture is also possible but it is rarely done as the bacteria takes a long time to grow and it requires a specialized media.

PCR testing is sensitive, specific, and results quickly. Though it is unable to distinguish between acute *Mycoplasma pneumoniae* infection and asymptomatic *Mycoplasma pneumoniae* carriage. This can get confusing if a patient has asymptomatic carriage of Mycoplasma pneumoniae but is experiencing symptoms due to an additional pathogen.

Serology is able to distinguish between acute and asymptomatic carriage, however there are limitations. There is a window period of about 1 week at the start of an acute infection where both IgM and IgG are negative. IgM antibodies increase initially, about a week into the infection and persist for months. IgG antibodies increase about 2 weeks after IgM titers and can persist for years. Serology testing is often used in addition to PCR testing.

RADIOGRAPHIC FINDINGS



Classically, the chest x-ray findings of atypical pneumonia are described as bilateral interstitial infiltrates and patchy reticulonodular opacification. However, several studies have demonstrated that consolidation can also be a common finding in *Mycoplasma pneumoniae* CAP.

A study published in 2019 explored the most common chest x-ray findings in pediatric patients with confirmed *Mycoplasma pneumoniae* CAP. The authors found that consolidation (lobar or segmental) was the most common chest x-ray finding accounting for over 35% of chest x-ray findings. Patchy infiltration was actually the least common chest x-ray finding, accounting for only 15% of the cases. Children with consolidation on x-ray tended to be 5 years or older and had more severe illness such as pleural effusions. Thus, even though a chest x-ray may be helpful in the work-up of possible *Mycoplasma pneumoniae* CAP, it is usually not diagnostic as there is no specific pathognomonic finding (Cho, PLOS one 2019, PubMed ID: 31461462).

LABORATORY FINDINGS

Children with *Mycoplasma pneumoniae* infection can have an elevation in white blood cells, neutrophils, and platelets. In addition, C-reactive protein and erythrocyte sedimentation rate may also be increased.

MANAGEMENT: EMPIRIC

Treatment of *Mycoplasma pneumoniae* CAP is usually empiric if a patient is being treated outpatient or in the emergency department. In these cases, it is unlikely that there will be confirmation of diagnosis.

Empiric treatment of CAP is administered based on clinical judgment, age, symptoms, and radiographic features. Empiric treatment is likely failing if there is no symptomatic improvement within 2 to 3 days of therapy.

Empiric treatment for *Mycoplasma pneumoniae* CAP is considered in children 5 years and older with specific clinical features (usually milder symptoms compared to typical bacterial pneumonia) and radiographic findings as described above. In children that are well enough to be treated outpatient, *Mycoplasma pneumoniae* is a highly likely pathogen. Antibiotics of choice are macrolides, tetracyclines, or fluoroquinolones (see doses below).

In children who are less than 5, typical bacterial pneumonia is much more common. Though the chance of developing *Mycoplasma pneumoniae* CAP is low, covering for atypical bacteria should be considered if there is treatment failure (usually amoxicillin) for typical pneumonia (*S. pneumoniae*) after 2 to 3 days.

A prospective cohort study assessed the efficacy of empiric combination beta lactam and macrolide therapy (n=1,019) compared to beta lactam alone (n=399). Propensity scoring was used to account for differences in potential confounders (n=280 pairs). Atypical infection was identified in 8.8% of patients (<5 years: 3%, 5 years: 19%). There was no significant difference in hospital length of stay, ICU admission within 24 hours, recovery, and rehospitalization between empiric β-lactam monotherapy and β-lactam therapy in combination with a macrolide. Importantly, there was no difference in patients with confirmed atypical bacterial infection and those a greater risk of atypical bacterial infection based on age (Williams, JAMA Pediatrics. 2017., PubMed ID: 29084336). The use of nasopharyngeal PCR testing could be used to target macrolide therapy to those with identified atypical bacterial infection though the test does not distinguish between infection and carriage.

MANAGEMENT: CONFIRMED

Patients who have a confirmed *Mycoplasma pneumoniae* infection resulting in URI symptoms but do not have pneumonia are not treated with antibiotics, instead supportive treatment is provided.

If a patient has a confirmed diagnosis of *Mycoplasma pneumoniae* CAP, it is recommended that a child be treated with either a macrolide, a tetracycline, or a fluoroquinolone antibiotic. Given the fact that *Mycoplasma pneumoniae* lacks a cell wall, it is not susceptible to antibiotics that inhibit cell wall synthesis such as beta-lactams.

Note: If a macrolide is started in a child with confirmed *Mycoplasma pneumoniae* CAP and the child does not improve, the possibility of resistance to the macrolide must be considered. A study in several hospitals found a more than 7% rate of resistance of *Mycoplasma pneumoniae* to macrolides. If this is suspected, consider transitioning to Doxycycline, Tetracycline (if over 8 years), or a fluoroquinolone (Waites, J Clin Microbiol 2019, PubMed ID: 31484701).

COMMON ANTIBIOTIC REGIMENS
IMMUNOCOMPETENT CHILDREN
Azithromycin: 10 mg/kg once (max 500 mg/dose) PO or IV on day 1 followed by four days of 5mg/kg (max 250 mg/dose)
Clarithromycin: 15 mg/kg per day PO divided BID (max 1 gram daily) for 7-10 days
Doxycycline 2-4 mg/kg daily PO or IV (max 200 mg daily dose) for 7 days
Considered a safe tetracycline for children of all ages
Tetracycline 25-50 mg/kg per day PO divided in 4 doses (max 2 grams daily) for 7-10 days for children over 8 years old
IMMUNOCOMPROMISED CHILDREN
Levofloxacin: Can consider a fluoroquinolone if the patient has been treated with a macrolide in the past (as resistance can occur), though there is a higher risk of side effects compared to the options listed above
6mo-5yrs: 8-10 mg/kg per dose PO or IV BID (max 750 mg/day daily dose) x 7-10d
>5 years: 10 mg/kg per dose once daily PO or IV (max 750 mg/kg daily dose) x 7-10d

DISPOSITION

Criteria for hospital admission for a child with *Mycoplasma pneumoniae* infection is based on provider judgment. Many factors may be considered when deciding upon admission such as age, severity of illness, underlying medical conditions, and social situation. Reasons to admit a child with *Mycoplasma pneumoniae* infection include, but are not limited to: hypoxemia, respiratory distress, dehydration, inability to tolerate feeds, and failure to improve within 2 to 3 days of outpatient treatment.

POLIOMYELITIS

INTRODUCTION (MICHAEL MOJICA, MD 9/2022)
Poliovirus is a neurotropic enterovirus. Three subtypes of the poliovirus cause neuromuscular disease (poliomyelitis). The naturally occurring or wild subtype remains present in Pakistan and Afghanistan. Oral vaccine-related disease can also occur. Vaccine-derived poliomyelitis (VDPV) occurs due to circulation and mutation of the virus in areas with low immunization rates. Epidemics of VDPV continue to occur periodically in Asia and Africa. Vaccine-associated paralytic poliomyelitis (VAPP) is due to reversion of a vaccine strain to a neurovirulent form in the patient receiving the vaccine. This is rare but more common in the immunocompromised. Poliomyelitis occurs when the virus affects the motor neurons of the spine cord and brainstem and may be life-threatening. See also: PEM Guide: Neurology: Weakness

Wild type polio had been eliminated in the US in 1979. In the summer of 2022, an unvaccinated, adult resident of New York State without a history if travel was hospitalized with acute, flaccid lower limb weakness and was found to have revertant Sabin vaccine Type II polio virus (VDPV). The detection of polio virus in the communities wastewater (and subsequently in New York City wastewater) indicates that the origin from a source outside of the US where oral poliovirus vaccine is still used. The oral polio vaccine was replaced by an inactivated polio vaccine (IPV) injection since 2000 in the US.

Poliovirus is transmitted by the fecal-oral, respiratory, or oral-oral route. It is highly infectious and is transmissible for up to 2 week prior to and after symptom onset. Virus is present in the oropharynx for 1-2 weeks and fecal shedding can last for several weeks. The best way to protect against polio is by maintaining a high degree of immunity in the community through vaccination and rapid identification and isolation of suspected polio cases.

CLINICAL MANIFESTATIONS
The incubation period is 3-6 days for non-paralytic poliomyelitis and 7-21 days for paralytic poliomyelitis. Approximately 1 in 4 to 1 in 10 of the infected are asymptomatic. The remainder develop a non-specific febrile illness with fever, headache, nausea, vomiting, sore throat and malaise that lasts from 2-5 days. 1 in 20 to 1 in 100 will develop symptoms of viral meningitis (headache, fever, vomiting, stiff neck). 1 in 200 to 1 in 2,000 will develop acute flaccid myelitis.

Acute flaccid myelitis is the result of polio virus infection of the anterior horn cells and typically occurs with the onset of viral meningitis symptoms. Paralysis can involve isolated muscles, muscle groups or quadriplegia. Involvement of cranial nerves occurs in up to one-third of patients and can lead to difficulty swallowing and involvement of the brainstem (dysphagia, dysarthria, difficulty handling secretions) and thoracic musculature weakness leading to respiratory failure.

CDC CASE DEFINITION: ACUTE FLACCID MYELITIS
Acute onset flaccid paralysis or ≥ 1 limb
Decreased or absent tendon reflexes in the affected limb(s)
Without sensory or cognitive loss
Without other apparent cause

POLIOMYELITIS: EXAMINATION FINDINGS
Muscle pain, spasms followed by rapid progression of weakness
Asymmetric loss of muscle tone (flaccid) and strength (weakness)
Weakness: Legs > Arms
Weakness: Proximal > Distal
Deep-tendon reflexes may be decreased or absent
Intact sensation (though may complain or paresthesias)
Bulbar paralysis can lead to respiratory failure

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of weakness is extensive. Poliomyelitis can be confused with other causes of acute flaccid myelitis (enterovirus D68, adenovirus, West Nile Virus, botulism), transverse myelitis and Guillain-Barre. In addition, central nerve system (CNS) signs due to meningitis, encephalitis (primarily in infants) and brain stem involvement may be present, suggesting a CNS cause of weakness.

WEAKNESS: DIFFERENTIAL DIAGNOSIS (PARTIAL)			
Cerebral Cortex	Hemorrhage	Peripheral Nerve	Guillain-Barre
	Migraine		Toxins
	Seizure (post)		Trauma
	Stroke	Neuromuscular Junction	Botulism
	Tumor		Myasthenia Gravis
Spinal Cord	Discitis		Organophosphates
	Epidural Abscess		Snake Envenomation
	Poliomyelitis		Tic paralysis
	Transverse Myelitis	Muscle	Electrolyte Abnormalities
	Trauma		Myositis
	Tumor		Periodic Paralysis
			Rhabdomyolysis

DIAGNOSTIC TESTING

The diagnosis of poliomyelitis of typically made clinically based on the presence of aseptic meningitis and acute flaccid weakness in those in an area in which wild-type or vaccine-derived polioviruses circulate. CSF analysis and MRI are frequently used to further identify poliomyelitis and other diagnoses in the differential. Pediatric neurology and pediatric infectious disease should be consulted early in the care of these patients to identify specific testing and imaging requirements.

Cerebral spinal fluid (CSF) analysis is consistent with a viral (aseptic) meningitis with early neutrophil pleocytosis progressing to lymphocyte predominance. CSF protein is elevated. CSF polio virus culture or PCR identifies poliovirus in less than a third of patients.

The gold standard for polio virus testing is stool testing. The specific polio virus isolated can also be typed to determine its origin. Throat testing can also be used in the first week. In New York State, polio virus testing is conducted at the Wadworth Center (WEB LINK: WADWORTH CENTER). Alternatively, local state departments of health or the CDC should contacted for specimen submission (WEB LINK: CDC Submission Form)

SPECIMEN COLLECTION (NEW YORK STATE)
Nasopharyngeal swab in viral transport media
Oropharyngeal swab in viral transport media
CSF: If available, 2-3 ml in a sterile container
Serum (acute, convalescent), prior to IVIG, 2-3 ml in a red or speckled-top tube
Two stool quarter-sized specimen in a sterile wide-mouth container, 24 hours apart
Stored refrigerated and shipped on frozen gel packs WEB LINK: WADWORTH Center Infectious Disease Requisition Form

IMAGING: MRI of the spine with and without contrast demonstrates hyperintense lesions of the ventral motor tracts (anterior horn cells). An MRI of the brain, should be obtained as well if there is bulbar involvement.

MANAGEMENT

The management of poliomyelitis is primarily supportive. There are no polio virus targeted antivirals available. There is insufficient evidence to support the use of immune modulating therapies such as intravenous immune globulin and corticosteroids. Pain management may be required. Standard and contact precautions should be instituted. Cases should be reported to local and state health departments as soon as possible.

Ventilatory support may be required. Measurement of negative inspiratory flows and serial monitoring of quantitative end-tidal CO_2 can guide the decision to institute mechanical ventilation. Patients with bulbar involvement require cardiopulmonary monitoring due to the risk of autonomic dysfunction.

VACCINATION: A 4 dose regimen of inactivated polio vaccine is recommended in the US (2 months, 4 months, 6-18 months and 4-6 years). It is estimated that a 2 dose regimen is at least 90% effective and a 3 dose regimen 99% effective.

Patients who are unvaccinated or of unknown vaccination status should receive an outbreak dose of IPV. This should be followed by a second dose 1-2 months after the first dose and a third dose 6-12 months after the second dose. (WEB LINK: CDC Catch up Polio Vaccination). Patients who are vaccinated, who are at high risk of community exposure or have close personal contact with a patient with poliomyelitis, can receive at booster dose of IPV.

PROGNOSIS

Approximated two-thirds of patients with acute flaccid poliomyelitis do not regain full strength. Patients are at risk for chronic symptoms such pain, contracture, depression, fatigue and are at risk for post-polio syndrome. This is defined as the new or progressive weakness occurring up to decades after the initial infection.

ROCKY MOUNTAIN SPOTTED FEVER

INTRODUCTION (MICHAEL MOJICA, MD, 8/2019)
Rocky mountain spotted fever (RMSF) is a rapidly progressing, potentially fatal systemic small vessel vasculitis caused by Rickettsia Rickettsii. Rickettsia Rickettsii is a small, gram-negative, obligate intracellular coccobacillus that is transmitted by a tick vector. RMSF is part of the group of Rickettsial infections called “spotted fever rickettsiosis” that also include infection with R. Parkeri and R. Philips.

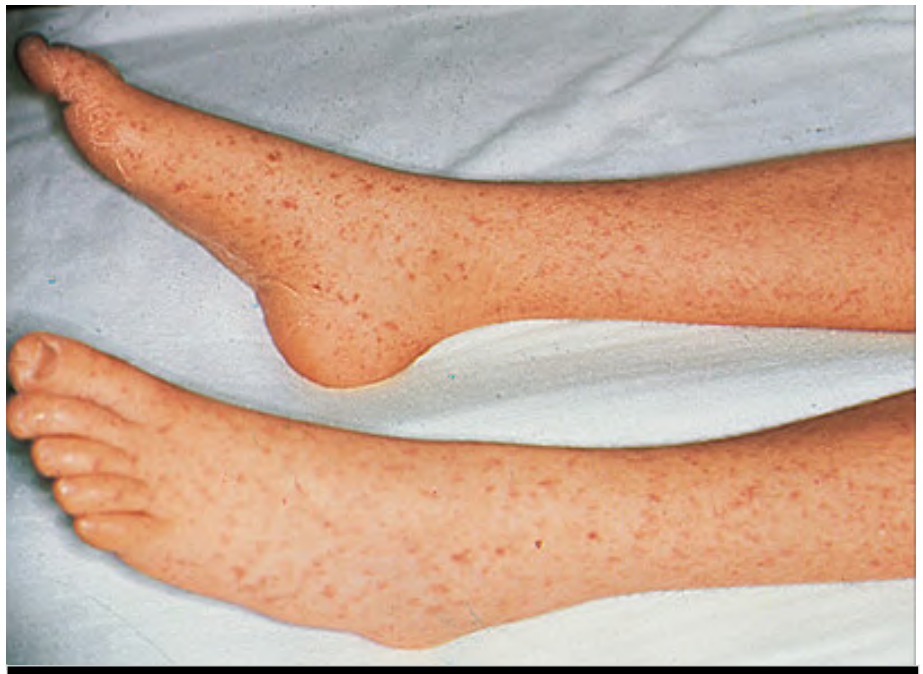
RMSF is the most common Rickettsial infection in the United states and most commonly seen in the south-eastern and south-central United States (NC, TN, MO, OK and AR account for 60% of cases). RMSF also occurs in Canada, Mexico, Central America and parts of South America (Bolivia, Argentina, Brazil and Columbia). Despite its name, it is uncommon in the Rocky Mountains. Its occurrence parallels that of increased outdoor and tick activity (Spring and early Summer in the US).

Two-thirds of cases occur in those less than 15 years of age and the incidence has been increasing. The case fatality rate (< 0.5%) has been decreasing, likely in response to early recognition and treatment. Mortality is approximately 25% for untreated disease. Mortality is greatest in those less than 10 years or age, greater than 50 years of age and those with a delay in diagnosis and treatment of more than 5 days from symptom onset. Most deaths occur within 8 days of symptoms onset highlighting the need for early recognition and treatment.

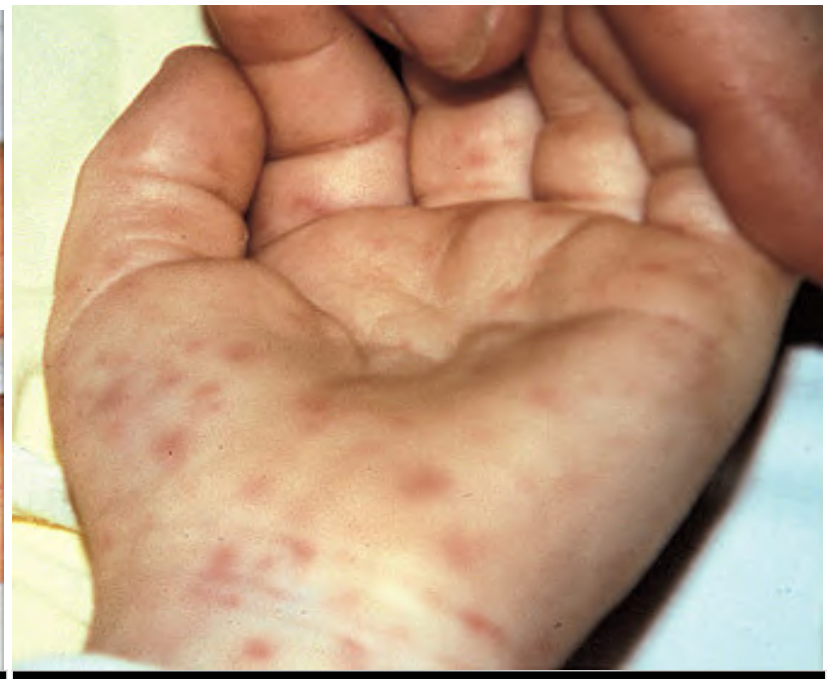
PATHOPHYSIOLOGY
The tick vector responsible for transmission varies by region and country. Animal hosts for the tick include deer, dogs and livestock. The bite may be overlooked because it is generally painless and can be obscured in hairy areas or skin folds. Rickettsia are released from the tick’s salivary glands after 4-6 hours. Rickettsia infect the vascular endothelium resulting in a systemic small vessel vasculitis. An increase in prostaglandin release results in increased vascular permeability and activation of clotting factors. Hypovolemia and decreased tissue perfusion result in an increase in antidiuretic hormone and hyponatremia. Host immune responses to the infection can lead to generalized inflammation.

CLINICAL MANIFESTATIONS
Systemic manifestations are due to vasculitis and inflammation. Onset of signs and symptoms occurs within 2-14 days of a tick bite with an average of 7 days. However, more than half of those with disease do not report a tick bite. Initial symptoms are non-specific and mimic many common viral illnesses. Signs and symptoms are highly variable. Less than 3% of patients have the classic triad of fever, headache and rash within the first three days. The rash may be absent, may skip the macular stage and does not always involve the palms and soles. Symptoms may progress more rapidly in children

RASH: The characteristic rash of RMSF typically begins as erythematous macules (though it may skip the macular stage) and progresses to petechiae. The rash begins in ankles and wrists and then extends to the trunk. Involvement of the palms and soles is a late finding. Lesions may become confluent and then necrose. The rash appears in 3-5 days in approximately 90% of patients though less than 50% of patients will develop the rash within the first 72 hours. Do not wait for the rash to begin treatment. A late onset rash is associated with higher mortality. An eschar may develop at the tick bite site.



DISTAL EXTREMITY PETECHIAE



PALMER PETECHIAE

SIGNS AND SYMPTOMS	
1-2 days	Abrupt onset: high fever, headache, malaise, myalgias, arthralgias, cough, nausea, vomiting and photophobia
2-4 days	Macular rash begins on the wrists, forearms, ankles and spreads centrally
	Abdominal pain nausea and vomiting and periorbital and peripheral edema are more common in children
5-7 days	Rash becomes petechial and more widespread, involving the palms/soles
	Persistence/progression of earlier symptoms
	Worsening respiratory status and abdominal pain
7-9 days	Rash becomes diffuse and confluent, forms purpura, necrotic areas
	Multi-organ damage and failure, death (See Table: Complications below)

WEBLINK: CDC: RMSF SIGNS AND SYMPTOMS POSTER

LATE COMPLICATIONS	
Cardiac	Myocarditis, arrhythmias, heart failure
Cutaneous	Skin necrosis, gangrene, mucosal ulceration
GI	Hepatitis, hepatomegaly, jaundice
Hematologic	Coagulopathy: e.g. gastrointestinal hemorrhage, DIC
Infectious	Septic shock
Muscle	Rhabdomyolysis
Ocular	Conjunctivitis, cortical blindness, retinal artery occlusion, hemorrhage
Renal	Acute tubular necrosis, acute renal failure
Respiratory	Acute Respiratory Distress Syndrome (ARDS), pulmonary edema
Neurologic	Meningoencephalitis, seizures, cerebral edema, cranial nerve palsy

DIFFERENTIAL DIAGNOSIS	
Fever and Headache	Meningitis: Lyme, Neisseria Meningitides
	Encephalitis: West Nile, enterovirus, HSV
	Other: Syphilis, TB
Fever and Rash*	Petechial: Meningococcemia, Ehrlichiosis, Anaplasmosis, Leptospirosis
	Maculopapular: EBV, Strep, 1°HIV, 2°syphilis, Parvo, Roseola, Kawasaki
*See PEM Guide: Dermatology: Febrile Rashes	

DIAGNOSTIC TESTING

RMSF is a clinical diagnosis but laboratory testing can support the diagnosis.
Serologic confirmation is of limited value as results are available after treatment should be initiated. In addition, there is cross reactivity with other Rickettsial infections. IgG is not positive until 3-4 weeks after symptom onset A 4-fold rise in IgG from baseline to convalescent titers obtained 2-4 weeks apart is diagnostic of acute infection. A negative IgG does not exclude infection and a positive IgG may represent prior exposure. IgM is not positive until 1-2 weeks after symptom onset. PCR testing is also used but none are currently FDA approved in the US. Because rickettsia circulates in low numbers a negative PCR in the first few days of illness does not exclude infection.

LABORATORY TESTING[1] AND IMAGING	
WBC	Typically, normal, may be mildly elevated late in disease
Hb/HCT	Decreased
Platelets	Progressive ↓ over time due to consumption
Fibrinogen	Decreased
Fibrin split	Increased
PT/PTT	Increased
Sodium	Decreased. More common with CNS involvement
BUN/Cr	↑ Early: Hypovolemia, Late: Acute tubular necrosis → Renal failure
LFT's	Mild transaminitis, ↑ bilirubin, progressive increase over time
CPK	Increased due to rhabdomyolysis
UA	Coarse granular casts
CSF WBC	Initial Segmented → Monocytic, Typically < 100 WBC/HPF
CSF Protein	Increased
Chest XRAY	Non-cardiogenic pulmonary edema, interstitial pneumonia, ARDS
1. Lab tests are generally normal day 1-2, mild changes days 2-4, progress over time	

MANAGEMENT

Treatment before 5 days of symptoms is more effective in preventing morbidity and mortality. Empiric treatment should be initiated based on a clinical diagnosis, appropriate exposure and severity of disease. Do not wait for the petechial rash or laboratory testing for confirmation to begin treatment.

ANTIBIOTICS: Doxycycline is the drug of choice for all ages including children and pregnant patients. There is no concern for pediatric teeth staining with Doxycycline at recommended dosage and duration of treatment. Alternative medication for the patient with a Doxycycline allergy include: Azithromycin, Clarithromycin and Chloramphenicol. Broad spectrum antibiotics should be administered to the critically ill patient to cover for other potential etiologies (e.g. meningococcal sepsis).

SEPSIS AND SEPTIC SHOCK

INTRODUCTION (MICHAEL MOJICA, M.D., 7/2022)
Shock is defined as inadequate blood flow and oxygen delivery to meet tissue metabolic demands. Shock must be rapidly identified, since as it progresses, it will become more refractory to treatment. Management of shock will be governed by both the etiology and degree of cardiovascular impairment. The goal is to maximize tissue oxygen delivery by optimizing cardiac output, systemic vascular resistance and arterial oxygen content and by minimizing oxygen utilization. The 2020 pediatric sepsis guidelines, were unable to make recommendations for many clinical questions due lack of evidence and when recommendations were made, they were often weak recommendations based on very low quality evidence. This PEM Guide will focus on the early recognition and management of septic shock in the emergency department.

SEPSIS DEFINITIONS: PEDIATRIC	
Sepsis Associated Organ Dysfunction	Severe infection leading to cardiovascular and/or non-cardiovascular organ dysfunction.
Septic Shock	Severe infection leading to cardiovascular dysfunction
	Include: Hypotension, vasoactive medication, impaired perfusion
Pediatric Surviving Sepsis: Pediatric Critical Care Med 2020, PubMed ID: 32032273	

SEPSIS DEFINITIONS: ADULT	
Sepsis	Life-threatening organ dysfunction, dysregulated host response to infection
	In adults, this is indicated by an increase of ≥ 2 in the Sequential Sepsis-related Organ Failure Assessment (SOFA) (WEB LINK: MDCALC: SOFA)
Septic Shock	A subset of sepsis with profound circulatory, cellular, and metabolic abnormalities associated with a greater risk of mortality than sepsis alone.
	Identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and lactate ≥ 2 mmol/L in the absence of hypovolemia.
International Sepsis 3 Consensus Definitions: JAMA 2016, PubMed ID: 26903338	

GOAL DIRECTED THERAPY: In 2001, a landmark trial conducted at a single center and including 263 patients demonstrated the efficacy of early goal directed therapy (EGDT) for adult sepsis (Rivers, NEJM 2001, PubMed ID: 11794169). This strategy is based on the prevention of global tissue hypoxia leading to multi-organ system failure. The manipulation of cardiac preload, afterload, and contractility is used to achieve balance between oxygen delivery and oxygen consumption. Intravenous fluids, infusion of vasoactive medications and the treatment of underlying causes (antibiotics, source control) form the basis of treatment of septic shock. EGDT can be divided into discrete steps. Collectively, these steps are referred to as the sepsis bundle.

Several adult trials published in the NEJM in 2014 (PROCESS Trial PubMed ID: 24635773, PROMISE Trial PubMed ID: 25776532, and ARISE Trial PubMed ID: 25272316) did not demonstrate the same efficacy of early goal directed therapy as the original Rivers trial. A meta-analysis of the three 2014 trials including 3,723 patients from 138 hospitals in seven countries concluded that early goal directed therapy did not result in better outcomes than “usual care” and was associated with higher hospitalization costs. (PRISM Investigators, NEJM 2017, PubMed ID: 28320242). Proponents of EGDT argue that “usual care” in the more recent trials has improved since 2001 because of a heightened awareness of sepsis and “usual care” management strategies include many of the components of EGDT.

SEPSIS MANAGEMENT	
1	Initial assessment and diagnosis
2	Treatment of underlying infection and source control
3	Fluid resuscitation, correction of electrolyte abnormalities
4	Management of fluid-refractory shock with vasoactive medications
5	Management of vasoactive medication-refractory shock
6	Potential additional therapies: Corticosteroids, PRBC transfusion

MANAGEMENT: OVERVIEW
Begin high flow, heated and humidified oxygen via nasal cannula
Consider intubation with a sedative (avoid Etomidate) and a paralytic
Continuous monitoring
Establish IV/IO access
Obtain relevant labs to detect organ dysfunction including lactate and bedside glucose
Obtain relevant studies for identifying infection: Blood cultures, urine culture, CXR
Initiate rapid fluid resuscitation with crystalloid or colloid
Rapid antibiotic administration: Ideally after cultures and within 1 hour of recognition
Fluid refractory shock: Initiate vasoactive medications
Catecholamine refractory shock: Additional vasoactive infusions, consider ECMO
Consider Hydrocortisone: Adrenal suppression, catecholamine resistant shock
Consider RBC transfusion to increase O_2 carrying capacity if hemoglobin < 7 gm/dl

MANAGEMENT: GOALS
Normal mental status
Threshold heart rates (including improvement in both tachycardia and bradycardia)
Normal pulses with equality of central and peripheral pulses
Normal blood pressure: Adults: MAP > 65 mmHg, See Appendix: Pediatric MAP
Capillary Refill ≤ 2 seconds
Adequate urine output: Adults: > 0.5 ml/kg/hour, Pediatrics: > 1.0 ml/kg/hour
Correct electrolytes: Glycemic control: Glucose < 180 mg/dl, Normal ionized calcium

1. INITIAL ASSESSMENT AND DIAGNOSIS

Septic shock should be considered in any patient with a suspected infection manifested by hyper or hypothermia and clinical signs of inadequate tissue perfusion. Septic shock may begin with a “warm” phase in which the patient appears well perfused due to vasodilation. Subsequently, a “cold” phase develops in which peripheral perfusion is impaired.

Pediatric patients who are immunocompromised (e.g. neonates, chemotherapy, HIV, sickle cell disease, those on immunosuppressive medications (e.g. Lupus, nephrotic syndrome) and those with indwelling devices (e.g. VP shunt, central line, cochlear implant) are at high risk of sepsis. However, approximately 50% of pediatric patients who develop sepsis have no underlying risk factors.

CIRCULATORY STATUS: CLINICAL ASSESSMENT	
CENTRAL CIRCULATION	Mental Status
	Blood Pressure
	Central Pulses: Rate and Quality
	Signs of CHF: Rales, Hepatomegaly, Heart Murmur, Gallop
PERIPHERAL CIRCULATION	Skin Color
	Skin Temperature
	Peripheral Pulses: Rate and Quality
	Capillary Refill

CARDIOVASCULAR FINDINGS: SEPTIC SHOCK		
	COLD SHOCK	WARM SHOCK
Capillary Refill	> 2 seconds	Flash refill
Peripheral Pulses	Diminished	Bounding[1]
Pulse Pressure[2]	Normal	Increased
Skin	Mottled, cool	Pink, warm
1. Bounding pulses are an indicator of increased pulse pressure 2. Pulse Pressure: Normal = Diastolic BP > ½(Systolic BP)		

PEDIATRIC SUSPECTED SEPSIS: CLINICAL DIAGNOSIS
Suspected Infection: Fever or hypothermia
History: High-risk comorbid disease, immunosuppression
Clinical signs of inadequate perfusion
Altered Mental Status: Depressed or agitated
Blood Pressure: Hypotension*, widened pulse pressure (Diastolic < ½(Systolic))
Pulses: Diminished (cold) or bounding (warm)
Skin color/temperature: Mottled, cool extremities (cold), flushed, pink (warm)
Capillary refill > 2 seconds (cold) or Flash capillary refill (warm)
Urine Output: < 1 ml/kg/hour

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS) CRITERIA: A combination of abnormal vital signs, physical exam findings, patient characteristics and laboratory parameters were previously recommended to identify those with sepsis. However, SIRS vital signs were found to be neither sensitive nor specific in children (Scott, Academic EM 2015, PubMed ID: 25778743). The study analyzed the prevalence and test characteristics of SIRS vital signs in children presenting to a children's hospital ED. SIRS vital signs were defined as a fever with elevation of at least one other vital sign. 15% of non-trauma patients met SIRS vital signs criteria while only 0.25% required a critical care intervention (intubation or vasoactive infusion within 24 hours). 82% of those with SIRS vital signs were discharged from the ED. More importantly, SIRS vital signs identified only 23% (16-33%) of those requiring a critical care intervention.

SEQUENTIAL SEPSIS-RELATED ORGAN FAILURE ASSESSMENT (SOFA). qSOFA (q for quick) is a variant of the SOFA score that can be applied rapidly be at the bedside and includes: respiratory rate, blood pressure and mental status (Glasgow Coma Scale). A pediatric, age-adjusted qSOFA score was assessed in 864 patients less than 18 years of age, admitted for suspected bacterial infection and treated with antibiotics within 24 hours of ED entry (van Nassau, Front Pediatr., PubMed ID: 30327759). The reference standard was a composite of: transfer to academic center pediatric ICU due to cardiorespiratory or neurologic failure or mortality within 30 days. The area under the receiver operating characteristics curve was adequate at 0.72, 95% CI (0.57, 0.86). Of the score components, altered mental status was the most predictive. The age-adjusted qSOFA had a higher area under the curve when compared to age-adjusted qSOFA plus lactate and the Quick Pediatric Logistic Organ Dysfunction score but not SIRS criteria.

SEPSIS IDENTIFICATION: Given the limitations of prior screening practices, the 2020 pediatric surviving sepsis guidelines acknowledge that there is insufficient evidence to endorse a specific sepsis trigger tool and recommend that each institution develop their own sepsis recognition bundle tailored to patient population, resources and local procedures. (Amer College Critical Care, Critical Care Medicine 2020, PubMed ID: 28509730) (See Appendix A: AAP Triage Tool, Appendix B: NYU Sepsis Trigger). The guideline could not make any recommendation on the use of lactate for risk stratification though trends in lactate level may be used to assess the efficacy of care.

OXYGENATION AND VENTILATION: Up to 40% of cardiac output can be utilized for work of breathing. Intubation with sedation and paralysis can reduce oxygen utilization. Patients should be placed on oxygen via a face-mask and high flow nasal cannula for persistent respiratory distress or hypoxia. If possible, avoid intubation and mechanical ventilation until after fluid resuscitation and vasoactive infusions as mechanical ventilation may reduce systemic vascular return and worsen cardiac output. It is advisable to have crystalloid and vasoactive infusion available during or immediately after intubation. Noninvasive ventilation with CPAP or BPAP is recommended in those who do not have a clear indication for intubation who are responding to treatment (See PEM Guide: Airway Procedures: Noninvasive Ventilation). Atropine as a premedication and Ketamine as a sedative are preferred. Etomidate should be avoided in septic shock due to adrenal suppression though considerable debate exists.

2. TREATMENT OF UNDERLYING INFECTION

ANTIBIOTIC ADMINISTRATION: If possible, blood cultures should be obtained prior to antibiotic administration but antibiotics should not be delayed. Guidelines recommend broad-spectrum antibiotics as soon as possible but ideally within 1 hour of sepsis recognition for patients in septic shock and within 3 hours in patients with sepsis related organ dysfunction without shock. Selection should be guided by the likely pathogen. (See Appendix C: NYU Antibiotic Stewardship: Sepsis Antibiotic Selection Guidelines)

SOURCE CONTROL: Identify the infection source and implement source control as soon as possible. Examples include: surgical wound debridement, (e.g. necrotizing fasciitis), abscess drainage and removal of potentially infected central venous catheters.

3. RAPID FLUID RESUSCITATION

CRYSTALLOID ADMINISTRATION: In health care settings with available intensive care, initiate rapid fluid resuscitation with 10-20 ml/kg crystalloid via push or pressure bag. Repeat boluses of up to and beyond 40-60 ml/kg may be required in the first hour. Balance/buffered crystalloid is recommended over normal saline (weak recommendation, based on low quality evidence). Fluids are titrated to reverse signs of hypoperfusion. Patient should be assessed after each bolus for signs of fluid overload such as rales, respiratory distress or hepatomegaly.

The FEAST Trial (Maitland, NEJM 2011, PubMed ID: 21615299) demonstrated that intravenous fluid may be harmful in pediatric septic shock in resource poor settings. Restricting fluids resulted in improved survival at 2 days and 4 weeks.This difference remained significant when subgroups with and without malaria, a hemoglobin < 5 mg/dl or a lactate > 5 were analyzed. The 2015 recommendation as result of this trial is: when caring for children with severe febrile illness in setting with limited critical care resources (e.g. mechanical ventilation) administration of bolus intravenous fluids should be undertaken with extreme caution because it may be harmful. In health care setting without intensive care, the 2020 recommendation is to administer maintenance fluids in those without hypotension amd a fluid bolus of 10-20 ml/kg in those with hypotension with frequent reassessment for effectiveness and signs of fluid overload.

A retrospective, cohort study using a multicenter, pediatric sepsis, quality improvement collaborative database included patients younger than 18 years old presenting to the ED with suspected sepsis and hypotension who received a fluid bolus within the first hour of ED arrival and were admitted (Eisenberg, Ann Emerg Med. 2022, PubMed ID: 35641356). There was no statistically significant difference between patients receiving greater than or equal to 30 ml/kg compared to patients receiving less than 30 ml/kg in sepsis-attributed mortality at 30 days (Risk Difference: 0.2%, 95% CI (-2.1, 2.4%)), ICU free days (Median Difference: 0.0 days, 95% CI (-1.1, 1.1)), use of mechanical ventilation (Risk Difference: 5.6%, 95% CI (-1.0, 12.1%)) or in ventilator free days (Median Difference: 0.0 days, 95% CI (-0.4, 16.0)). This study will likely alleviate some of the concerns with fluid administration in the first hour that has occurred due to the FEAST trial (a randomized clinical trial in a resource poor setting).

ELECTROLYTES: Hypoglycemia and hypocalcemia should be corrected.

ELECTROLYTE CORRECTION					
HYPOGLYCEMIA			HYPOCALCEMIA		
	0.5 mg/kg	1.0 mg/kg	20 mg/kg IV/IO	ml/kg	Indication
Infant: D10	5 ml/kg	10 ml/kg	Ca^{++}Chloride (10%)	0.2	Arrest, CVL
Child: D25	2 ml/kg	4 ml/kg	Ca^{++}Gluconate (10%)	0.6	Non-arrest, PIV
Adult: D50	1 ml/kg	2 ml/kg			

BLOOD PRODUCTS: An adult study concluded that a more liberal transfusion cutoff (< hemoglobin < 7 mg/dl vs < 9 mg/dl) resulted in equivalent outcomes. (Holst NEJM 2014, PubMed ID: 25270275). Consider transfusion of 10 ml/kg of PRBCs to increase oxygen carrying capacity for a hemoglobin less than 7 mg/dl in unstable pediatric patients. Adults should receive 1 unit of PRBC for a hemoglobin of less the < 7 mg/dl. Consider fresh frozen plasma and/or platelet transfusion in patients with active bleeding or for a planned invasive procedure.

4. MANAGEMENT OF FLUID REFRACTORY SHOCK

The treatment of fluid refractory shock involves the administration of vasoactive medications. As a group, these agents are often referred to a “pressors” or “vasopressors”. Ongoing therapy should be guided by monitoring of the patient’s fluid and cardiovascular parameters. Invasive monitoring of central venous pressure and $ScvO_2$ may be indicated to guide further therapy and delivers mediation directly to the heart for distribution. See PEM Guide: Resuscitation: Vasoactive Medications for Shock

VASOPRESSOR SELECTION: In general, vasoactive infusions should be targeted to the underlying pathophysiology. For example, in distributive shock, an agent with vasoconstrictive properties may be considered while in cardiogenic shock due to poor contractility, an agent with inotropic and/or afterload reducing properties may be considered. In septic shock, elements of hypovolemic, cardiogenic and distributive shock can coexist. In pediatric patients, vasoactive infusions may be administered through a peripheral intravenous or intraosseous until central access is available. Obtaining central access in children in the emergency department in a timely manner is difficult and could lead to a delay in initiating vasoactive infusions. A delay in administration of inotropes is associated with significant increase in mortality risk.

Pediatric sepsis 3 guidelines recommend both Epinephrine and Norepinephrine over Dopamine. A single center, clinical trial (Ventura, Critical Care Med 2015, PubMed ID: 26323041) randomized pediatric patients with fluid refractory septic shock to receive either Dopamine or Epinephrine Infusions. The Epinephrine group had 13% less all-cause mortality at 28 days. Dopamine is only indicated if both Epinephrine and Norepinephrine are not available. In addition, Dopamine stimulates the release of Epinephrine and Norepinephrine and patients in a catecholamine depleted state may not respond or worsen with Dopamine. There is insufficient evidence to recommend Epinephrine over Norepinephrine.

1. EPINEPHRINE: Epinephrine has potent $beta_1$ and moderate $beta_2$ and $alpha_1$ activity. Epinephrine's response is dose dependent. At low doses, the $beta_1$ activity predominates increasing cardiac output. $Alpha_1$ (vasoconstriction) and $beta_2$ (vasodilation) have offsetting effects on systemic vascular resistance at low doses. At high doses, $alpha_1$ activity (vasoconstriction) predominates increasing systemic vascular resistance. Splanchnic vasoconstriction is more common with Epinephrine than with Norepinephrine or Dopamine

2. NOREPINEPHRINE: Norepinephrine has potent $alpha_1$ activity and modest $beta_1$ activity. Alpha induced vasoconstriction can cause a reflex bradycardia that can offset the tachycardia due to $beta_1$ activity. Norepinephrine does not increase heart rate to the same extent as Epinephrine and Dopamine. Norepinephrine is indicated in normal/high cardiac output states with low systemic vascular resistance (distributive shock).

5. CATECHOLAMINE RESISTANT SHOCK

Patients with catecholamine resistant shock require invasive monitoring, ideally, in the intensive care unit. Perfusion pressure (MAP-CVP), $ScvO_2$ (Central venous oxygen saturation < 70% indicates hypoperfusion) and cardiac index can be used to guide therapy. Further titration of catecholamines or the addition of vasopressin is recommended when high doses of catecholamines are ineffective at restoring adequate perfusion.

6. CONSIDER ADDITIONAL THERAPIES

CORTICOSTEROIDS: Hydrocortisone is indicated in patients with adrenal insufficiency or risk of hypothalamic-pituitary axis failure (purpura fulminans, congenital adrenal hyperplasia, prior steroid exposure or other hypothalamic/pituitary abnormalities). It may also be considered in the patient in septic shock who is refractory to both fluid and vasoactive agents. The Hydrocortisone dose is 2 mg/kg (max 100 mg). A study of adults with severe sepsis concluded that a continuous infusion of hydrocortisone for 5 days did not reduce progression to septic shock or mortality (HYPRESS Trial, JAMA 2016, PubMed ID: 27695824).

ADDITIONAL THERAPIES: Identify and correct potential underlying causes such as: pericardial effusion, pleural effusion and pneumothorax. If persistently resistant to therapy consider extracorporeal membrane oxygenation.

APPENDIX A: AAP SEPSIS IDENTIFICATION TOOL (WEB LINK)

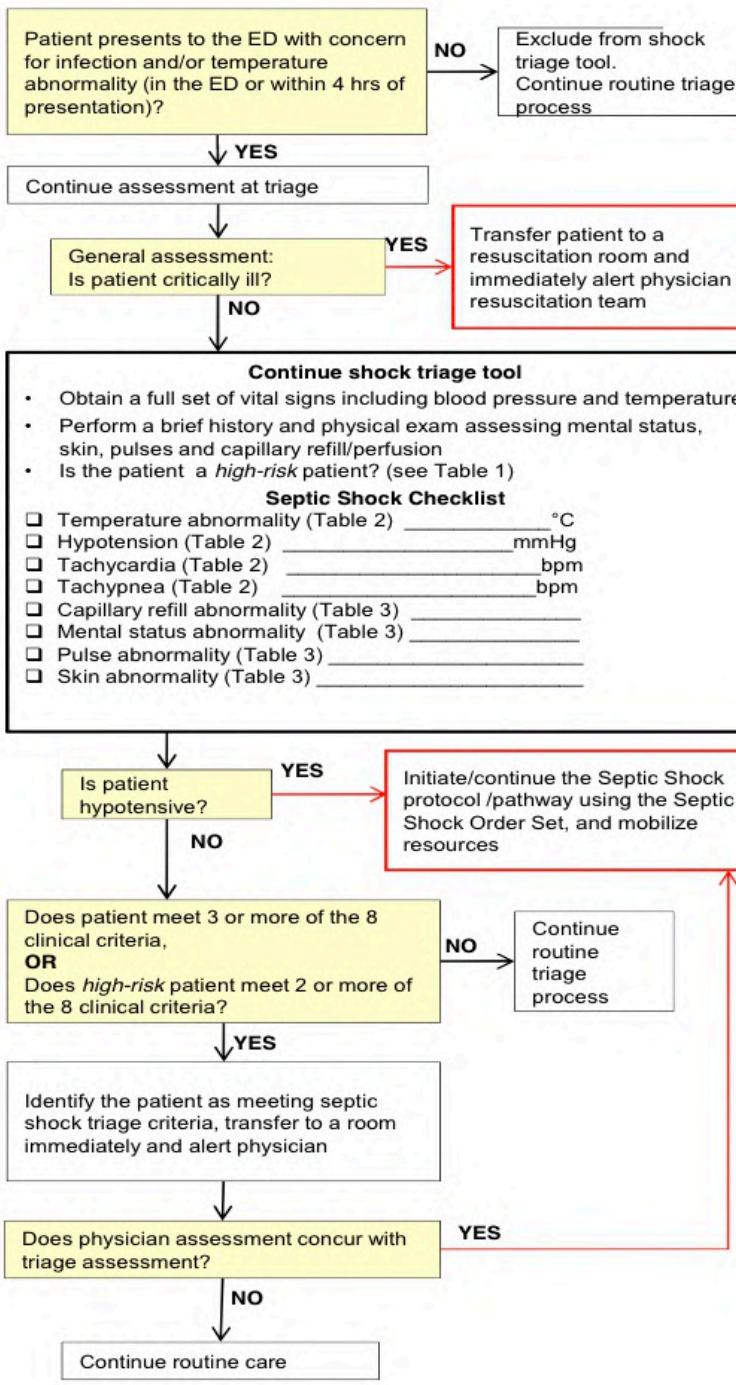


Table 1. High Risk Conditions

- Malignancy
- Asplenia (including SCD)
- Bone marrow transplant
- Central or indwelling line/catheter
- Solid organ transplant
- Severe MR/CP
- Immunodeficiency, immunocompromise or immunosuppression

Table 2. Vital Signs (PALS)

Age	Heart Rate	Resp Rate	Systolic BP	Temp (°C)
0 d – 1 m	> 205	> 60	< 60	<36 or >38
≥ 1 m - 3 m	> 205	> 60	< 70	<36 or >38
≥ 3 m - 1 r	> 190	> 60	< 70	<36 or >38.5
≥ 1 y - 2 y	> 190	> 40	< 70 + (age in yr × 2)	<36 or >38.5
≥ 2 y - 4 y	> 140	> 40	< 70 + (age in yr × 2)	<36 or >38.5
≥ 4 y - 6 y	> 140	> 34	< 70 + (age in yr × 2)	<36 or >38.5
≥6 y- 10 y	> 140	> 30	< 70 + (age in yr × 2)	<36 or >38.5
≥ 10 y - 13 y	> 100	> 30	< 90	<36 or >38.5
> 13 y	> 100	>16	< 90	<36 or >38.5

Table 3. Exam Abnormalities

	Cold Shock	Warm Shock	Non-specific
Pulses (central vs. peripheral)	Decreased or weak	Bounding	
Capillary refill (central vs. peripheral)	≥ 3 sec	Flash (< 1 sec)	
Skin	Mottled, cool	Flushed, ruddy, erythroderma (other than face)	Petechiae below the nipple, any purpura
Mental status			Decreased, irritability, confusion, inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtunded

APPENDIX B: SEPSIS TRIGGER: NYU

SEPSIS HUDDLE: BASED ON VITAL SIGN ALERT OR CLINICAL CONCERN
1. Enter full set of vital signs, allergies and weight into EPIC
2. Review of high-risk conditions (see table below)
3. Huddle Decision
a. Not on sepsis protocol
b. Not on sepsis protocol (concern for possible sepsis) → Cardiac monitor, consider indications for fluids and/or antibiotics
c. On sepsis protocol: All metrics must be completed prior to movement from ED
1. Document time of activation of protocol
2. Use EPIC order panel

TACHYCARDIA: AGE AND TEMPERATURE ADJUSTED				
TEMPERATURE	0-1 years	2-5 years	6-12 years	≥ 13 years
< 100F or 37.8C	> 180	> 140	> 130	> 110
101F or 38.3C	> 185	> 145	> 135	> 115
102F or 38.9C	> 190	> 150	> 140	> 120
103F or 39.4C	> 195	> 155	> 145	> 125
104F or 40C	> 200	> 160	> 150	> 130
105F or 40.6C	> 205	> 165	> 155	> 135
106F or 41.1C	> 210	> 170	> 160	> 140
ALERT: Fever (>100.4 F or >38 C) OR Hypothermia <96 F or <36 C) AND Tachycardia?				

HYPOTENSION: AGE ADJUSTED	
AGE	SYSTOLIC BP (mmHg)
< 1 month	< 60
1 month – 1 year	< 70
1 year	< 72
2 years	< 74
3 years	< 76
4 years	< 78
5 years	< 80
6 years	< 84
7 years	< 86
8 years	< 88
9 years	< 88
10-18 years	< 90
>1 year of age the lower limit of normal systolic BP = 70 + 2(age in years)	

HIGH RISK CONDITION CHECKLIST		
CRITERIA	PRESENT	ABSENT
PAST MEDICAL HISTORY		
≤ 56 days old		
Asplenia		
Chronic neurologic disability		
Invasive line or catheter		
Malignancy		
Neutropenia or Immunodeficiency		
Recent (< 14 days) operative procedure		
Stem cell Transplant		
Tech dependent (trach, G-tube, VP shunt)		
VITAL SIGNS		
Age adjusted hypotension (see Table)		
CURRENT HISTORY/EXAMINATION		
Altered mental status or LOC		
Decreased urine output		
Delayed capillary refill (> 2 seconds)		
Petechiae or purpura or erythroderma		
LABORATORY DATA		
Lactate > 4		
OTHER		
Physician Concern		
POSITIVE = Any above = PRESENT		
NEGATIVE = All above = ABSENT		

APPENDIX C: ANTIBIOTIC SELECTION

SEPSIS: INITIAL EMPIRIC ANTIBIOTIC SELECTION: NON-NEUTROPENIC			
0-28 DAYS	FIRST	NEXT	LAST
	Ceftazidime	Ampicillin	+/- Acyclovir[1]
28-60 DAYS			
	Ceftriaxone[4]	Ampicillin	+/- Acyclovir[1]
60 DAYS: NON-NEUTROPENIC	FIRST	NEXT	LAST
No Beta-lactam Allergy	Zosyn[2]	Vancomycin[3]	
Septic Shock	Zosyn[2]	Vancomycin[3]	Gentamycin
Toxin-mediated (Toxic Shock)	Zosyn[2]	Linezolid	
Mild Beta-lactam Allergy	Cefepime	Vancomycin[3]	
Septic Shock	Cefepime	Vancomycin[3]	Gentamycin
Severe Beta-lactam Allergy	Aztreonam	Vancomycin[3]	Gentamycin
60 DAYS: NON-NEUTROPENIC	FIRST	NEXT	LAST
CNS Source	Ceftriaxone	Vancomycin[3]	
Sinus or Dental Source	Ceftriaxone	Metronidazole	Vancomycin[3]
Bone Source	Vancomycin[3]	Add Ceftriaxone (< 4 years old)	
Urinary Tract Infection	Ceftazidime	Ampicillin	
Fungal Infection	Add Amphotericin B Liposomal (Ambisome)		
Tickborne Illness	Add Doxycycline		

1. Acyclovir: Ill appearing, HR > 160, RR > 60, O_2 required, hypothermic, seizures, vesicles
2. Zosyn = Piperacillin/Tazobactam
3. Vancomycin Allergy: Substitute Linezolid
4. If total bilirubin > 12, then switch to Ceftazidime

The goal is to provide antimicrobials within 1 hour of sepsis recognition
Obtain appropriate cultures first if this does not delay antimicrobial administration
Obtain IV access x 2 to allow administration of more than one antibiotic simultaneously
Prioritize order of antimicrobial administration to target site of likely source

*NYU PEDIATRIC ANTIBIOTIC STEWARDSHIP GUIDELINE: PEDIATRIC SEPSIS (2022)

SEPSIS: INITIAL EMPIRIC ANTIBIOTIC SELECTION: NEUTROPENIC			
60 DAYS: NEUTROPENIC	FIRST	NEXT	LAST
No allergies	Cefepime	Vancomycin	
Low-Risk[1] Beta-lactam Allergy	Zosyn[2]		
High-Risk[1] Beta-lactam Allergy	Aztreonam	Vancomycin[3]	
GI Source (Option 1)	Zosyn[2]	+/-Vancomycin	
GI Source (Option 2)	Cefepime	Metronidazole	

1. Low-Risk: Pruritis without rash, remote (>10 years ago), mild rash (self-resolved without treatment), no other symptoms, patients denies allergy but is on record
1. High-Risk: Any of: Respiratory symptoms, angioedema, cardiovascular symptoms, severe rash requiring treatment (anti-histamines, corticosteroids) without additional symptoms and/or requiring ED visit or hospitalization

2. Zosyn = Piperacillin/Tazobactam
3. Vancomycin Allergy: Substitute Linezolid

The goal is to provide antimicrobials within 1 hour of sepsis recognition
Obtain appropriate cultures first if this does not delay antimicrobial administration
Obtain IV access x 2 to allow administration of more than one antibiotic simultaneously
Prioritize order of antimicrobial administration to target site of likely source

INDICATIONS FOR ADDITIONAL GRAM(+) AND/OR GRAM (-) COVERAGE
EMPIRIC AMINOGLYCOSIDE INDICATIONS (2nd)
Hypotension or other evidence of hemodynamic instability
Altered mental status
Disseminated intravascular coagulation
Presence of uncontrolled cancer (in consultation with hematology/oncology consult)
Gentamycin (2nd): Dose 2.5 mg/kg/dose OR Amikacin (2nd): Dose 17.5 mg/kg, maximum dose: 1200 mg
EMPIRIC VANCOMYCIN INDICATIONS (2nd)*
Hemodynamic instability: Fluid refractory hypotension, cardiovascular collapse
Hospitalization within 90 days for a MRSA infection
Patient is ultra-Orthodox from Brooklyn (high prevalence of MRSA carriage)
Receipt of high dose Cytarabine (1 gram/m^2)
Severe mucositis
History of alpha hemolytic Streptococcus infection
Clinically apparent or suspected central catheter infection
Skin or soft tissue infection
Radiographically documented pneumonia
Vancomycin (2nd): Dose 15 mg/kg
*NYU PEDIATRIC ANTIBIOTIC STEWARDSHIP GUIDELINE: PEDIATRIC SEPSIS (2022)

APPENDIX D: PEDIATRIC MEAN ARTERIAL PRESURE

PEDIATRIC MEAN ARTERIAL PRESSURE (BY PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
1	5th	30	35	33	37	34	37	36	39	37	40
	50th	49	53	52	54	53	55	54	57	56	58
	95th	69	71	70	72	72	73	73	74	74	76
2	5th	35	39	38	41	39	42	40	42	41	44
	50th	54	57	56	58	57	59	59	60	60	62
	95th	73	75	75	76	76	77	77	78	79	80
3	5th	39	42	41	44	42	44	44	46	45	47
	50th	58	60	60	61	61	62	62	64	64	65
	95th	77	78	78	79	80	80	81	81	82	83
4	5th	42	45	43	46	46	47	47	47	48	49
	50th	61	63	63	65	64	65	66	65	67	67
	95th	79	80	82	82	83	83	84	84	86	85
5	5th	45	46	47	48	49	49	49	50	51	52
	50th	63	64	66	66	67	67	68	68	69	69
	95th	82	82	84	83	85	85	87	86	88	87
6	5th	47	49	49	50	50	51	52	52	53	54
	50th	66	66	67	68	69	69	70	67	71	71
	95th	84	84	86	85	87	86	88	87	90	89
7	5th	51	50	50	51	52	52	53	53	54	55
	50th	67	68	69	69	70	70	72	71	73	72
	95th	83	85	88	87	89	88	90	89	92	90
8	5th	50	52	53	52	54	54	55	55	56	56
	50th	69	70	71	70	72	71	73	72	75	74
	95th	87	81	89	88	91	89	92	90	93	91
9	5th	51	53	53	54	55	55	56	56	58	57
	50th	70	71	72	71	73	73	75	74	76	75
	95th	88	89	91	89	92	90	93	91	94	93
10	5th	52	54	55	55	56	56	56	57	59	59
	50th	71	72	73	73	75	74	75	75	77	76
	95th	90	90	92	90	93	92	94	93	96	94

PEDIATRIC MEAN ARTERIAL PRESSURE (BY PERCENTILE OF HEIGHT)

Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
11	5th	54	55	57	56	57	57	58	59	59	60
	50th	72	73	74	74	75	75	76	76	78	78
	95th	91	91	92	92	94	93	95	94	96	95
12	5th	54	57	57	58	58	58	60	60	61	61
	50th	73	75	75	75	77	76	78	78	79	79
	95th	92	92	94	93	95	94	96	95	98	97
13	5th	56	58	57	59	59	60	60	61	61	62
	50th	75	76	76	77	77	78	79	71	80	80
	95th	93	94	95	94	96	95	97	97	99	98
14	5th	59	60	59	60	61	61	62	62	63	64
	50th	75	77	78	78	79	79	80	80	82	81
	95th	91	95	96	96	97	97	99	98	100	99
15	5th	58	61	61	61	62	62	63	63	64	64
	50th	77	78	79	79	80	80	82	81	83	82
	95th	96	91	98	97	99	98	100	99	102	100
16	5th	90	61	62	62	63	63	65	63	66	66
	50th	79	79	81	90	82	81	83	82	85	84
	95th	98	96	99	98	101	99	102	100	104	101
17	5th	63	61	63	62	65	63	67	65	69	66
	50th	81	79	83	80	84	81	85	82	87	84
	95th	100	96	102	98	103	99	104	100	106	101

Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40
Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55

Haque IU, Zaritsky AL.
Analysis of the Evidence for The Lower Limit of Systolic and Mean Arterial Pressure in Children
Pediatr Crit Care Med. 2007 Mar;8(2):138-44., PubMed ID: 17273118

NEUROLOGY

ALTERED MENTAL STATUS

INTRODUCTION (LOUIS SPINA, M.D., 9/2016)
A patient's mental status is based on their level of interactions with their environment. It is important to acknowledge that mental status is a continuum from totally unresponsive on the "depressed" mental status side of the continuum to extreme agitation and psychosis on the "upper" side of the continuum: with "normal" appearing somewhere in the middle. A number of terms, such as lethargy, obtundation, stupor, coma, delirious and agitated are used to describe different degrees of altered mental status. These terms are ambiguous and their interpretations often differ from provider to provider. The AVPU system, and the Glasgow Coma scale are attempts to objectify the assessment of mental status. There measures are most useful when used to serially assess a patient's mental status. More detailed assessment tools such as the mini mental status exam can be used with a patient who is closer to "normal" mental status when finer distinctions are required. WEB LINK: MINI MENTAL STATUS EXAMINATION

AVPU CLASSIFICATION	
A	Alert
V	Responds to Voice Stimuli
P	Responds to Painful Stimuli
U	Unresponsive to all Stimuli

PEDIATRIC GLASGOW COMA SCALE				
	< 1 YEAR	>1 YEAR		
Eye Opening	Spontaneous	Spontaneous		4
	To Verbal Command	To Shout		3
	To Painful	To Painful		2
	No Response	No Response		1
Motor Response	Spontaneous	Obeys Commands		6
	Localizes Pain	Localizes Pain		5
	Withdraws to Pain	Withdraws to Pain		4
	Flexion-Decorticate	Flexion-Decorticate		3
	Extension-Decerebrate	Extension-Decerebrate		2
	No Response	No Response		1
	< 2 YEARS	2-5 YEARS	> 5 YEARS	
Verbal	Smile/Coos Appropriately	Appropriate Words/Phrases	Oriented	5
	Cries and is Consolable	Inappropriate Words	Confused / Disoriented	4
	Persistent Inappropriate crying and/or screaming	Persistent Cries, Screams	Inappropriate Words	3
	Grunts, Agitated or Restless	Grunts	Incomprehensible Sounds	2
	No Response	No Response	No Response	1

DIFFERENTIAL DIAGNOSIS

Altered mental status can be divided into two etiologic groups, structural and medical (toxic-metabolic/ infectious). Structural problems usually cause compression or dysfunction in the area of the brain normally called the sleep center, or the ascending reticular activating system. Medical etiologies usually lead to problems from general dysfunction of both cerebral hemispheres. There are exceptions to this classification scheme (see table next page). It is important to make a rapid assessment of the patient with altered mental status to rule out the possibility of a structural etiology since these may require operative management.

ALTERED MENTAL STATUS: COMMON CAUSES BY AGE		
INFANT	CHILD	ADOLESCENT
Infection	Toxin	Toxin
Metabolic	Infection	Trauma
Inborn Errors of Metabolism	Seizures	Psychiatric
Congenital Abnormalities	Trauma	Infection
Seizure	Intussusception	Seizure
Abuse	Abuse	

The list of possible causes of altered mental status is extensive and therefore, the mnemonic **AEIOU TIPS** (“Tips from the vowels”) may be used to organize the diagnostic possibilities. Abuse, intussusception and inborn errors of metabolism are diagnoses that are not typically included in the mnemonic and are specific to the pediatric population. This PEM Guide will focus on those diagnoses, that if identified early, have effective therapies.

ALTERED MENTAL STATUS: DIFFERENTIAL DIAGNOSIS	
A	Alcohol, Abuse
E	Encephalitis, Electrolytes, Endocrine
I	Insulin, Intussusception, Inborn errors of metabolism
O	Overdose, oxygen deficiency (hypoxia)
U	Uremia
T	Trauma, tumor (CNS)
I	Infection
P	Poisoning, psychogenic
S	Seizures, shock, stroke, space occupying lesion

STRUCTURAL CAUSES
Trauma: intracranial and extracranial hemorrhage, diffuse cerebral edema
Cerebral vascular accident
Cerebral venous thrombosis
Subdural empyema, CNS abscess
Intra-cerebral tumor

ALCOHOL: Although alcohol is more commonly seen as a cause in adolescents it is important to consider it in younger children. Children may have an accidental ingestion, especially if they were unsupervised at a party. Young children may have an altered mental status with a blood alcohol level less than 100 mg/dL. Hypoglycemia is complication of alcohol ingestion in the child due to limited glycogen stores and inhibition of gluconeogenesis by alcohol. See: PEM Guide: Toxicology: Sedative-Hypnotics

ABUSE: Abuse should be considered when a child is presenting in a coma, or if the physical exam findings are not consistent with the history that is given. Physical findings, such as bruising and retinal hemorrhages should be identified. See: PEM Guide: Child Protection: Child Abuse and Neglect

ENCEPHALOPATHY: Lead encephalopathy, although less common today, should be considered in children, especially for those living in older buildings where lead paint may have been used. Reye's Syndrome should be considered in children presenting after a flu-like illness or varicella infection, especially if the child was treated with aspirin.

ELECTROLYTES: Any condition that can lead to abnormalities in serum glucose, sodium, potassium, calcium, or magnesium can cause altered mental status. See: PEM Guide: Endocrine-Metabolic: Hyponatremia, PEM Guide: Endocrine-Metabolic: Hyperkalemia

INSULIN: Changes in mental status can be directly linked to hypoglycemia. At times, this is secondary to excess exogenous insulin, which may be from accidental overdose or accidental ingestion of diabetic medications. It may also be due to an inappropriate response to prolonged fasting. These patients respond quickly to the administration of glucose. Assessment of bedside glucose should occur in every patient with an altered mental status. Glucose should be given in a dose of 0.5 to 1.0 grams/kg

INTUSSUSCEPTION: Intussusception can present with mental status changes prior to the development of abdominal signs. Classically, patients have alternating periods of irritability and lethargy. The diagnosis of intussusception should be considered in any child who under the age of three with altered consciousness and a history of vomiting, abdominal pain or bloody stools. See: PEM Guide: Surgery: Intussusception

INBORN ERRORS OF METABOLISM: These disorders should be entertained in the neonate and infant Signs are often nonspecific include vomiting, seizures, hypoglycemia and acidosis. See: PEM Guide: Endocrine-Metabolic: Inborn Errors of Metabolism

OVERDOSE: The accidental or intentional ingestion of medications or illicit drugs is a common cause of altered levels of consciousness. A careful history of medications available in the household should be obtained from caregivers. Some ingestions leading to a decrease in mental status include barbiturates, benzodiazepines, carbon monoxide, ethanol, gamma hydroxybutyrate and opiates. Some examples of ingestions leading to an increase in mental status include anticholinergics, cocaine, phencyclidine (PCP), salicylates and selective serotonin reuptake inhibitors (SSRIs), Naloxone should be administered to reverse a narcotic induced change in mental status. See Appendix: Toxidromes,
See: PEM Guide: Toxicology: Approach to the Poisoned Patient

UREMIA: Uremic encephalopathy is most commonly caused by hemolytic uremic syndrome (HUS) in pediatrics. However any cause of acute or an exacerbation of chronic renal impairment can lead uremia. HUS is characterized by a prodromal upper respiratory infection or gastroenteritis with subsequent acute renal failure, thrombocytopenia and hemolytic anemia.
See: PEM Guide: GU-Renal: Hemolytic Uremic Syndrome

TRAUMA: Trauma is the leading cause of death in children under the age of four. Injuries to the head, chest or other injuries causing shock or hypoxia may lead to an altered mental status. In non-accidental trauma the history may be misleading or absent. Head trauma may lead to intracranial hemorrhage (subdural or epidural hematomas), intraparenchymal bleeding or cerebral edema leading to increased intracranial pressure and herniation. See: PEM Guide: Trauma: Head Trauma

INFECTION: The most common types of infection leading to an altered mental status are meningitis and encephalitis. Though any infection leading to abscess can lead to cerebral hypoperfusion and an alteration in consciousness. See: PEM Guide: Infections: Meningitis

PSYCHIATRIC: Alterations in mental status are not always related to an organic etiology. A careful physical exam and history may reveal a psychogenic cause. Psychiatric causes of altered mental status should be considered only as a diagnosis of exclusion. See: PEM Guide: Psychiatry: The Agitated Child

SEIZURE: A child presenting during a seizure and in a post ictal state after a seizure will have altered levels of consciousness. Seizures may be subclinical. See: PEM Guide: Neurology: Status Epilepticus

SHUNT: Any patient with a known ventriculo-peritoneal presenting with altered levels of consciousness should have the shunt evaluated to determine if shunt malfunction or shunt infection is present. See PEM Guide: Neurology: CSF Ventricular Shunt Complications

STROKE: Although less common in children, both ischemic and hemorrhagic stroke must be considered for those who have underlying disorders which would predispose them to cerebrovascular accidents. These include those with congenital heart disease and a right to left shunt, those with abnormalities of cerebral vessel (arteriovenous malformations, MoyaMoya disease) and those with a hypercoagulable state. The latter group can include those with sickle cell disease as well as those with inborn errors of metabolism such as homocystinuria. See: PEM Guide: Hematology-Oncology: Sickle Cell Anemia Crises, PEM Guide: Neurology: Subarachnoid Hemorrhage

EVALUATION

When evaluating a child with altered mental status, it is important to pay attention to the patient's respiratory pattern, size and reactivity of the pupils, induced eye movements, motor responses and vital signs. These can give clues to the nature of the disease process, the rate of progression and the functional level of involvement of the brain. A constellation of signs and symptoms called a toxidrome may aid in the identification of a toxin or class of toxin. See Appendix: Toxidromes

MANAGEMENT

When managing a patient with altered mental status, one should remember to begin with the ABC's. Abnormalities in oxygenation and ventilation should be assessed and treated. The patient should be placed on a cardiovascular monitor and have intravenous access. Blood should be sent for appropriate laboratory evaluation and a bedside blood glucose level should be obtained. Specific therapy should be begun based on a likely differential diagnosis and not delayed pending a definitive diagnosis.

CLINICAL FINDINGS		
	STRUCTURAL	MEDICAL
Pathology	Compress Brain Stem	Both Cerebral Hemispheres
Pupils	Unequal, unreactive, sluggish	Equal and reactive +/- sluggish
Exam	Focal neurologic findings	Non-focal neurologic findings

If a structural cause of an altered mental status is suspected urgent neuroimaging and neurosurgery consultation is essential. Methods to medical maintain cerebral perfusion pressure are indicated in the table below. Surgical management may be required.

EXCEPTIONS	
NON-FOCAL STRUCTURAL DISEASE	FOCAL METABOLIC DISEASE
Acute bilateral cerebrovascular disease	Hyperglycemia / Hypoglycemia
Cardiac emboli	Hepatic encephalopathy
Bilateral subdural hematomas	Uremia
Early acute hydrocephalus	Hypercalcemia
	Post-ictal state with Todd’s paralysis
	Drugs: sympathomimetics

ANCILLARY TESTING
Bedside glucose
Complete blood count: anemia, signs of infection
Electrolytes (calculate anion gap), lactate
Arterial/Venous blood gas, co-oximetry panel (carbon monoxide, methemoglobin)
Toxicology screening – serum osmolarity, drug levels
Cultures PRN
Ammonia, transaminases (? inborn errors of metabolism)
EKG: arrhythmias, electrolyte changes
Non-contrast Head CT
Abdominal ultrasound for intussusception
Lumbar puncture

DEXTROSE DOSING			
	CONCENTRATION	0.5 GRAMS/KG	1.0 GRAMS/KG
Neonate/Infant	D10	5 ml/kg	10 ml/kg
Child	D25	2 ml/kg	4 ml/kg
Adolescent/Adult	D50	1 ml/kg	2 ml/kg
Rule of 50’s: Example D10 x 5 ml/kg = 50. Provides 0.5 grams/kg of glucose Rule of 100’s: Example D10 x 10 ml/kg = 100. Provides 1.0 grams/kg of glucose			

MEDICAL INTERVENTIONS
Support vital signs
Correct acid-base abnormalities
Correct electrolyte abnormalities
Intravenous antibiotics, Acyclovir if febrile (defer lumbar puncture if unstable),
Activated charcoal, enhanced elimination, antidotes for specific ingestion

APPENDIX: MANAGEMENT OF INCREASED INTRACRANIAL PRESSURE

MANAGEMENT: INCREASED INTRACRANIAL PRESSURE	
Positioning	Head of bed up to 30 degrees. Neutral head/neck position. (maximizes cerebral venous return)
Temperature	Avoid hyperthermia: Antipyretics, cooling blanket, Cerebral metabolic demand ↑ 5% for each ↑ 1°C Recent evidence suggests that cooling is ineffective
Sedation and Analgesia	Balanced to maintain blood pressure and ability to assess neurologic status
Systolic Blood Pressure	Maintain mean arterial pressure > 5% for age Do not restrict fluids if poor perfusion or hypotension PRBC > Crystalloid for poor perfusion Consider vasoconstrictor for neurogenic shock
Controlled Hyperventilation	Consider brief periods hyperventilation (PCO_2 30-35) for signs of herniation. Otherwise normal PCO_2
Mannitol (20%)*	Dose: 0.5-1.0 grams/kg over 10-20 minutes Avoid in the hypotensive patient: Diuretic effect may decrease intravascular volume
Hypertonic Saline (3%)	Bolus Dose: 5 ml/kg over 20 minutes Infusion Dose: 0.1-1.0 ml/kg/hour Benefit of increasing intravascular volume
Anticonvulsants	Keppra (Levetiracetam): 20 mg/kg IV Indications: >1 seizure, seizure > 1 hour post injury or severe intraparenchymal brain injury
Neurosurgery	Decompressive craniectomy
*"Although mannitol is commonly used in the management of raised ICP in pediatric TBI, no studies meeting inclusion criteria were identified for use as evidence for this topic." Mannitol has not been subjected to contemporary controlled clinical trials versus placebo, other osmolar agents, or other therapies in children". Brain Trauma Foundation Guidelines, Pediatr Crit Care Med. 2019, PubMed ID: 30830015)	

APPENDIX: TOXIDROMES

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET
*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size					

BREATH HOLDING SPELLS

INTRODUCTION (ELLEN DUNCAN MD, PHD, 2/2020)
Although frightening for parents, breath-holding spells are typically benign events. The incidence of breath-holding spells is approximately 0.1-4.6% in healthy children. Such spells usually occur between the ages of 6 months and 6 years, although the first episode usually occurs before 18 months of age. A positive family history for breath-holding spells is seen in 20-35% of patients.

PATHOPHYSIOLOGY
While the etiology of breath-holding spells is not entirely understood, they are thought to be due to some combination of dysregulation of the autonomic nervous system, vagally-mediated cardiac inhibition, delayed brain stem myelination, and iron deficiency. Breath-holding spells may represent a variant of vasovagal (neurocardiogenic) syncope. The connection between iron deficiency (both with and without anemia) is two-fold: patients with iron deficiency may be more easily provoked, and they have a lower oxygen-carrying capacity.

HISTORY
There are two types of breath-holding spells: pallid and cyanotic. Patients can exhibit both types but typically one predominates. Episodes of both types typically last from 10-60 seconds; characteristics are listed in the table below. In addition to color change (cyanosis or pallor), the sequence of events can be used to distinguish the two types. Breath holding/apnea precedes loss of tone/consciousness in cyanotic breath holding spells. In contrast, loss of loss of tone/consciousness precedes breath holding/apnea in pallid breath holding spells.

BREATH HOLDING SPELLS

TYPE	TRIGGER	CHARACTERISTICS	OTHER
Cyanotic (~75%)	Anger or frustration after even a trivial reprimand; can be caused by laughter	Loud, brief cry → Breath holding in forced expiration → 1. Apnea 2. Cyanosis (faster than typical with breath holding) 3. Loss of tone and consciousness	Cyanosis resolves rapidly with normal breathing Prolonged apnea → 1. Posturing and/or 2. Generalized seizure → Prolonged LOC
Pallid (~25%)	Pain or fear; for example, after a minor fall or injury (up to 30 seconds after traumatic event)	Loss of tone and consciousness → 1. Briefer apnea 2. Pallor 3. Diaphoresis	Can be confused or sleepy afterwards If > few seconds → 1. Increased tone 2. Incontinence 3. Clonus

DIFFERENTIAL DIAGNOSIS
Breath holding spells are most commonly confused with seizures. Distinguishing features are included in the table below. A video EEG may be required to distinguish the two if the diagnosis is in question.

DIFFERENTIAL DIAGNOSIS	
DIAGNOSIS	DISTINGUISHING CHARACTERISTICS
Seizures	Less common: Lack precipitating emotional factors, usually lack of crying. Less prominent pallor, cyanosis. Not elicited by oculo-cardiac reflex. More common: Tongue-biting, incontinence, post-ictal period, tachycardia, occurs during sleep.
Sepsis	Accompanied by clinical signs and symptoms of infection Fever, poor perfusion, altered mental status
Sudden breath-holding during sleep	Abrupt awakening from sleep, often with choking episodes DDx: Obstructive sleep apnea, parasomnia, sleep-related laryngospasm, gastroesophageal reflux, frontal lobe epilepsy
Cardiac syncope	Tachyarrhythmias: WPW, prolonged QT, Brugada Bradyarrhythmias: Heart blocks Structural: Severe aortic stenosis, hypertrophic cardiomyopathy, myocarditis, arrhythmogenic right ventricular dysplasia
Hyperekplexia	Also known as stiff baby syndrome or startle disease Rare genetic disorder characterized by stiffness during waking periods, sometimes an exaggerated startle response, or amplified head retraction after tapping on nose or forehead
Shuddering attacks	Sometimes precipitated by emotions No color change
Congenital laryngeal stridor	Inspiratory stridor without other signs of breath-holding spell Exacerbated by agitation, upper respiratory infection
Laryngospasm	Characterized by high-pitched inspiratory crowing sound with possible subsequent apnea, often occurring during sleep DDx: Submersion, GE reflux, ↓ Ca++, sedation with Ketamine.
Pertussis	Cyanosis usually accompanied by characteristic paroxysms of cough, inspiratory strider (whoop), fever and nasal discharge

EVALUATION

If a patient experiences a breath-holding spell while in the emergency department, telemetry may show a respiratory sinus arrhythmia. In addition, patients with a pallid breath-holding spell may be bradycardic. Pallid breath-holding spells are caused by cardiac bradycardia and may be elicited by 10 seconds of ocular pressure (which triggers the oculo-cardiac reflex). A positive oculo-cardiac reflex (asystole ≥ 2 seconds) is indicative of breath-holding rather than seizure activity but is no longer recommended due to the possibility of retinal detachment.

If other more serious conditions can be excluded based on history and physical exam, additional laboratory studies are usually unnecessary. However, if iron deficiency anemia is suspected a CBC and iron studies may be obtained.

An EKG may be useful to rule out cardiac causes of syncope including long QT syndrome (though it is unclear whether these two conditions are related), Brugada syndrome, supraventricular tachycardia (Wolf-Parkinson-White), hypertrophic cardiomyopathy, and arrhythmogenic right ventricular dysplasia.
See: PEM Guide: Neurology: Syncope.

MANAGEMENT

A 2010 Cochrane systematic review on the efficacy of iron supplementation for breath holding spells concluded that “Iron supplementation appears to be useful in reducing the frequency and severity of breath-holding attacks. Supplementation is of particular benefit in children with iron deficiency anemia, responses correlating with the improvements in hemoglobin values. Iron may still be of assistance in children who are not anemic or who have low, normal hemoglobin levels.” (Zehetner, Cochrane Database Syst Rev. 2010, PubMed ID: 20464763). A typical dose of Ferrous Sulphate is 5-6 mg/kg/day of elemental Fe divided TID.

Patients with pallid spells may benefit from medications such as Atropine, Glycopyrrolate, Theophylline, or Duloxetine. However, such treatment is beyond the scope of this discussion. Anticonvulsants are not useful in reducing these spells. Cardiac pacing may be required in rare patients with prolonged bradycardia or asystole during pallid breath-holding spells.

DISPOSITION

Patients with prolonged bradycardia or asystole should be admitted to a monitored setting for further evaluation and management. Patients with unclear or atypical features or severe episodes way warrant consultation with a pediatric cardiologist and/or pediatric neurologist. The majority of children with breath-holding spells can generally be safely discharged from the ED with good return precautions.

PROGNOSIS

There are no long-term neurodevelopmental sequelae. The median age of remission is 4 years of age with most resolving spontaneously by 8 years of age. However, because of the significant distress that parents of children with breath-holding spells can experience, it is important to thoroughly educate and support parents. Additionally, parents should be encouraged to reduce stressors, such as premature potty training. It is crucial to inform parents that breath-holding spells are involuntary.

FEBRILE SEIZURES

INTRODUCTION (DENNIS HEON, M.D., 4/2021)
Febrile seizures are a common childhood neurologic condition with a prevalence of 2-4%. The peak age is 18-24 months, but can be seen from 6 months to 6 years. They are defined as a seizure with temperature ≥ 38 C without a central nervous system infection. Febrile seizures can be classified as simple or complex**.** They are frightening to parents to the extent that some parents think their child is dying.

CLASSIFICATION OF FEBRILE SEIZURES		
	SIMPLE	COMPLEX
Percentage	80 %	20%
Duration	< 15 minutes	> 15 minutes
Frequency	Once in 24 hours	More than once in 24 hours
Seizure Type	Generalized Tonic Clonic	Focal
Neurologic Deficits	Absent	Present

It is difficult to predict which children will have febrile seizures. A history of febrile seizures in a first or second degree relative, day care attendance, neonatal discharge greater than 28 days, and slow neurological development have all been associated with increased risk. Any one of these factors increased the risk from 2-4% to 6-10%. With 2 risk factors the incidence increases to 28%, however, less than 3% of the population has 2 or more risk factors (Bethune, Am J Dis Child 1993, PubMed ID: 7678187).

CLINICAL EVALUATION

The diagnostic evaluation for children that have had a febrile seizure should be directed at establishing the cause of the fever rather than the seizure. A clinical practice guideline for neurodiagnostic evaluation of the child with a simple febrile seizure has been published by the American Academy of Pediatrics (AAP, 2011, PubMed ID: 21285335). The guidelines apply to neurologically healthy children 6 to 60 months presenting within 12 hours of a simple febrile seizure.

AAP: NEURODIAGNOSTIC EVALUATION OF SIMPLE FEBRILE SEIZURE (2011)	
Lumbar Puncture	A lumbar puncture should be performed a. Meningeal signs and symptoms (stiff neck, Kernig, Brudzinski) b. History or examination suggests the presence of meningitis or intracranial infection
	A lumbar puncture is an option a. 6-12 months has not received HfluB or Strep pneumo vaccines b. 6-12 months when immunization status cannot be determined c. Pretreated with antibiotics (can mask signs and symptoms)
EEG	An EEG should not be performed in a neurologically healthy child
Laboratory Testing	The following tests should not be ordered for the purpose of identifying the cause of the seizure: a. Electrolytes, Ca, P, Mg, Glucose, CBC
Neuroimaging	A CT or MRI should not be performed as a routine evaluation

LABORATORY EVALUATION

Patients with a simple febrile seizure do not have an increased incidence of bacteremia or urinary tract infection. Evaluation for a urinary tract infection, bacteremia or pneumonia would be based on the same criteria for those patients with a fever but without a febrile seizure.

LUMBAR PUNCTURE: Meningitis should be considered in the differential diagnosis of all infants presenting with a febrile seizure. A lumbar puncture should only be done if meningitis is suspected clinically. Many clinicians will wait a short period of time to see if the patient's mental status normalizes before progressing to a lumbar puncture. In most studies, everyone with meningitis was clinically ill appearing or had obvious meningeal signs. A study of 503 meningitis patients determined that 23% (115) had a seizure prior to diagnosis. 105/115 (91.3%) were obtunded or comatose. Of the remaining 10 patients, 8 had irritability and nuchal rigidity and 2 had complex febrile seizures. (Green, Pediatrics 1993, PubMed ID: 8414822).

In the past, it has been recommended that a lumbar puncture should be considered in patients with a complex febrile seizure. A 2017 study included 2,839 patients presenting with a complex febrile seizure of which 31% had a lumbar puncture (Guedj, Annals EM 2017, PubMed ID: 28259480). The rate of bacterial meningitis in those with seizures was 0.7%, 95% CI (0.2, 1.6%). The rate of bacterial meningitis in patients without an examination suggestive of meningitis was 0.0%, 95% CI (0.0, 0.6%). The authors concluded that "in children with a complex febrile seizure, bacterial meningitis and herpes meningoencephalitis are unexpected events when the clinical examination after complex febrile seizure is not suggestive of meningitis or encephalitis".

NEUROIMAGING: There is no role for a head CT or MRI in simple febrile seizures. If the patient had a complex seizure, a head CT or MRI may be considered. The incidence of a significant finding in this group 5-10%.

MANAGEMENT

Supportive care such as antipyretics for fever or antibiotics for an identified bacterial infection are generally the only treatment needed.

ANTIPYRETICS: Many clinicians recommend the use of "around the clock" alternating antipyretics such as Acetaminophen or Ibuprofen. Empirically, it makes sense that you cannot have a febrile seizure if you do not have a fever, however, no study has been able to prove this. (Schnaiderman, Eur J Peds 1993, PubMed ID: 8223808). A randomized clinical trial of 231 European children who had had a first febrile seizure were randomized to receive Diclofenac (a non-steroidal anti-inflammatory agent) or placebo during 851 subsequent febrile episodes. 23.4% had a recurrent febrile seizure. There was no difference in the rate of recurrent in those receiving antipyretic agents (23.4%) compared to those receiving placebo (23.5%) (risk difference, 0.2; 95% CI (-12.8, 17.6), (Strengell, Archive Pediatr Adolesc Med 2009, PubMed ID: 19736332).

ANTIEPILEPTICS: Phenobarbital (Camfield, J Peds 1980, PubMed ID: 7381637) and Sodium Valproate (Mamelle, Neuropediatrics 1984, PubMed ID: 6424041) may decrease the incidence of future febrile seizures. They are not routinely prescribed because of their long-term cognitive effects. Rectal diazepam is sometimes prescribed for those with recurrent febrile seizures. Knudson showed that for patients with 2 or more risk factors for recurrence, giving rectal Diazepam at the onset of fever decreases the risk of recurrence to 12% (Knudson, Arch Dis Childhood 1985, PubMed ID: 8660037). The problem is many patients may present with an altered mental status due to the Diazepam making the evaluation of the need for a lumbar puncture difficult.

DISPOSITION

Simple febrile seizures can be safely discharged after the parents have been counseled. Complex febrile seizures may require a more extensive evaluation and a neurology consult. Admission should be considered in this group.

PROGNOSIS

RECURRENCE RISK: The primary risk of simple febrile seizures is recurrence in approximately 1/3 of patients (14% at 6 months, 25% at 12 months and 30% at 24 months (Berg, Arch Pediatr Adol Med 1997, PubMed ID: 9111436).

The lower the temperature that the patient has their febrile seizure at, the greater the chance or recurrence. Berg found that the incidence of recurrence if the febrile seizure occurs at 101 degrees is 35% and decreases in a linear fashion to 13% for a temperature of greater than 105 degrees (Berg, NEJM 1992, PubMed ID: 1528207).

There is data to support that the seizure occurs early on in the febrile event. Often, the first sign the patient is ill is when they have a seizure. There is no data to support the commonly held belief that a high rate of rise in temperature causes febrile seizures. This was based on animal studies using hyperthermia as a mechanism. The only human study did not show any association with rate of rise in temperature and febrile seizures.

RISK FACTORS FOR RECURRENCE
Age < 15 months
Family History of Epilepsy
First Degree Relative with Febrile Seizure
Complex Febrile Seizure
Day Care Attendance < 20 hours/week

	% With	RISK
0	25%	12%
1	40%	25%
2	25%	50%
3	8%	80%
4	1%	100%
5	1%	100%

EPILEPSY RISK: A common question is “Will my child develop epilepsy?” The risk of epilepsy after a simple febrile seizure (1-2%) has been shown to be only slightly greater than the risk in the general population (0.5%). This risk increased in those with a family history of epilepsy, recurrence of febrile seizures and complex febrile seizures (Pavlidou, Epilepsia 2013, PubMed ID: 24304433).

COGNITIVE EFFECTS: There have been 2 large studies that have assessed future intellectual ability and both have shown no effect as a result of having had a febrile seizure (Verity, NEJM 1998, PubMed ID: 9624192, Ellenberg, Arch Neurol 1978, PubMed ID: 619868).

APPENDIX: SPEAKING TO PARENT ABOUT FEBRILE SEIZURES

ADVICE TO PARENTS AFTER A FEBRILE SEIZURE	
Definition	Febrile seizures, also commonly known as febrile convulsions, are epileptic seizures that occur in association with increased temperature.
	They are not epilepsy. They are due to the increased sensitivity of the child's immature brain to fever.
Validate Feelings	Febrile seizures might appear frightening to observer but are generally harmless.
Frequency	Febrile seizures are common, up to 2-5% of children in the USA and Western Europe, and 6-9% of infants and children in Japan, will have experienced at least one febrile seizure, simple or complex, by the age of 5 years.
Recurrence	Not all illness and episodes of fever will provoke a febrile seizure
In case of seizure	Keep calm, secure site that child cannot harm itself during the seizure, apply stable side position, do not apply anything into mouth or between teeth, note time and character of seizure.
	Most febrile seizures spontaneously terminate within 2–3 minutes, not requiring any treatment.
Call Emergency Medical Services for:	A febrile seizure that lasts longer than 5 minutes
	Rectal diazepam has been applied
	Focal symptoms, postictal paresis, general clinical condition is impaired or symptoms prolonged.
Diagnosis	Diagnosis is based on history taking and physical examination. Laboratory tests, EEG, neuroimaging as a routine diagnostic procedure being not recommended.
Follow up	No specialized follow-up is necessary. A consultation with your physician is recommended to talk about this event
Prognosis	The number of simple febrile seizures does not correlate with the risk of epilepsy nor with the risk of developing cognitive disorders;
	Therefore, neither prophylaxis nor intermittent strategies with benzodiazepines nor continuous antiepileptic drugs are usually recommended.
Prevention	Using antipyretic medication can make child feel better when unwell with fever but should not be seen as useful for "preventing" febrile seizures.
	Parents should avoid co-sleeping, which is dangerous for their child and will not prevent a febrile seizure
Loussouarn, European J Peds 2021, PubMed ID: 33866403	

HEADACHE

INTRODUCTION (MARC AUERBACH M.D., 4/2021)
Headaches occur frequently in children. Population based studies reveal that 50% of children have experienced a headache by six years of age and 80% by 15 years of age. Recurrent headaches occur in 2.5% of school age children and 15% of adolescents. Males predominate in the less than 7 years of age. There is no gender difference in the 7-11 years age group. Over 11 years of age, girls have a three-fold rate of migraine headache. Suicide ideation is increased in adolescents with migraine with aura or high frequency headaches independent of depression symptoms. (See PEM Guide: Trauma: Head Trauma and PEM Guide: Neurology: Subarachnoid Hemorrhage)

DIAGNOSIS
The International Headache Society (HIS) classifies pediatric headaches into the primary headaches (migraine, tension and cluster headaches) and secondary headaches (benign or life threatening). The 3rd category includes cranial neuralgias, central and primary facial pain and other headaches. Twenty-five percent are primary headaches. Sixty percent of headaches are secondary and due to a benign cause, 5% are secondary and are due to a life-threatening cause and 10% are unclassified. The priority in the emergency department is to identify those patients with a life-threatening cause of secondary headaches and symptomatic treatment of primary headaches.

To make the diagnosis providers should characterize the time frame, quality, location, and impact on life of the headache. A thorough examination including a complete neurologic and fundoscopic exam should be completed. The focus should be the identification of focal neurologic findings and/or signs of increased intracranial pressure. The examination should be normal for most primary headaches.

ETIOLOGY OF SECONDARY HEADACHES	
Intracranial	Meningitis, encephalitis, abscess, tumor, hydrocephalus, Arnold chiari, AV malformation, pseudotumor cerebri, post LP, post trauma, subdural, intracerebral hematoma, subarachnoid
Extracranial	Otitis, sinusitis, dental, ocular, c-spine
Systemic	Viral, fever, hypoglycemia, anemia, fever, hypoxia, hypertension, hypercapnia, intoxication, medications, caffeine, constipation, allergy, depression

MIGRAINE HEADACHES
Migraine headache is the most common primary headache in pediatric patients and can occur at any age. Migraines are characterized as with or without an aura. Migraine with aura accounts for approximately 15-30% of pediatric migraine headaches.

Children may characterize their migraines as bilateral or unilateral, without throbbing and shorter duration when compared to adults. Pain is often relieved by sleep and a family history of migraines is frequency elicited. Transient neurologic symptoms may occur in Migraine with aura.

MIGRAINE VARIANTS: There are a number of rare migraine with aura variants including: familial hemiplegic migraine, basilar artery migraine, retinal migraine and acute confusional migraine. It may be difficult to distinguish these from stroke or other neurologic emergencies on their first presentation. A stroke alert is warranted for the first presentation of these migraine variants associated with focal neurologic defects. In addition, there are a number of non-headache migraine equivalents such as cyclic vomiting and abdominal migraine.

PRIMARY HEADACHE CLASSIFICATION: IHS[1]2018 (3rd EDITION)	
Migraine without Aura (previously "common" migraine)	A. ≥ 5 headaches fulfilling features B,C and D below B. Headache lasting 4-72 hours (when untreated or unsuccessfully treated) (Pediatric: 2-72 hours) C. At least 2 of the 4 following features 1. Unilateral location (frontal/temporal) (Pediatric: more bilateral, adult unilaterality more common in late adolescence) 2. Pulsating quality 3. Moderate to severe pain intensity 4. Aggravated by or causing avoidance of routine physical activity D. At least one of the following during the headache 1. Nausea and/or vomiting 2. Photophobia and phonophobia (inferred by behavior in young) E. Not better accounted for by another ICHD-3 diagnosis
Migraine with Aura (previously "classic" migraine)	A. ≥ 2 headache fulfilling criteria B and C B. ≥ 1 fully reversible aura symptoms: visual, sensory, speech and/or language, motor (up to 72 hours), brainstem, retinal C. ≥ 3 of the 6 following characteristics 1. ≥ 1 aura symptom spreads gradually over ≥ 5 minutes 2. ≥ 2 or more symptoms occur in succession 3. Each aura symptom last 5-60 minutes 4. ≥ 1 aura symptom is unilateral 5. ≥ 1 aura symptom is positive (scintillations, pins and needles) 6. Headache accompanies or follows aura within 60 minutes D. Not better accounted for by another ICHD-3 diagnosis
Migraine Variants	Hemiplegic migraine: More common in children then adults Basilar migraine: Dizzy, weak, ataxic (more common in female) Cyclic vomiting and recurrent abdominal pain are migraine variants
Tension Headache	Band-like sensation around the head Associated with neck and/or shoulder pain Worse as the day progresses and can last for days. Associated with stressful events at home or school May be temporarily relieved by sleep
Cluster Headaches	AKA histamine headache, uncommon before 20 years of age Neurovascular origin: Pathophysiology incompletely understood Clusters: Episodic (> 1mo h/a free interval), Chronic (< 1mo h/a free) Severe, unilateral pain (orbital, supraorbital, or temporal pain), 15-180 minutes, every other day to 8 times a day ≥ 1(all ipsilateral): conjunctival injection, lacrimation, miosis, ptosis nasal congestion, rhinorrhea, forehead/facial sweating, eyelid edema
1. IHS: International Headache Society (Cephalgia 2018, PubMed ID: 29368949	

NEUROIMAGING

The need for neuroimaging should be individualized based on the patient's signs and symptoms and underlying risk for a serious secondary headache etiology. The vast majority of patients with headache do not require neuroimaging in the emergency department. A good neurologic exam including fundoscopy, and visual acuity is the first step. MRI is costly, may require sedation, and is often not available on a 24/7 basis. However, it is the best method to identify serious etiologies located in the posterior fossa. CT without contrast is of use to evaluate for bleeding, non-cerebellar mass lesions and signs of increased intracranial pressure.

SERIOUS SECONDARY HEADACHE: PREDICTORS	
Pre-school age	Abrupt altered mental status
Occipital location	Papilledema
Thunderclap onset, first/worst headache	Focal neurologic deficit
Increasing severity or frequency	Persistent fever, bradycardia, high BP
Sharp change in headache quality	Rash: petechial, ash-leaf, café au lait
Sleep arousal, exclusive AM or late night	Nuchal rigidity, meningismus
Severe vomiting, (particularly AM)	Seizure
Associated with straining during valsalva	Lack of improvement with therapy

LIFE-THREATENING SECONDARY HEADACHES: HIGH RISK POPULATIONS	
Sickle cell disease	Stroke
Rheumatologic disease	Stroke, Cerebritis
Prior central nervous system surgery	Hemorrhage
Ventriculoperitoneal shunts	Obstruction, Infection
Immunodeficiency, immunosuppression	Infection
Trauma	Hemorrhage, Herniation

MANAGEMENT (FOCUS ON MIGRAINES)

There are few large, randomized clinical trials of pediatric migraine treatment so recommendations are often based on adult studies.

GENERAL MIGRAINE TREATMENT PRINCIPLES
Provide abortive medication as soon as possible of symptom onset
Create a low stimulation environment (quiet room, lights off), damp towel to forehead
Administer intravenous fluids and antiemetics as needed
Avoid benzodiazepines and opiates (due to rebound effect)

MEDICATION SELECTION: Medication recommendations are made based on the American Academy or Neurology's 2019 Pediatric Migraine Guideline, PubMed ID: 31413171. These guidelines do not focus primarily on ED management.

Treatment should target one of the three mechanisms that cause pediatric headaches: inflammation, 5-hydoxytryptamine metabolism, and/or dopaminergic hypersensitivity. In addition, medication selection, dosing and route should be based on the patients age, weight, ability to swallow pills, associated symptoms of nausea and vomiting and response to previous medications. For example, intranasal medications have a short time to onset are not effected by vomiting and can be given to children who cannot swallow pills. Oral dissolving tables may also be effective in patients with nausea or vomiting. Effective migraine medication classes include analgesics, triptans, antidopaminergic medications. These medication can be administered individually or in combination. Antiemetics medications are often warranted. Intravenous fluid bolus and hydration is often recommended though clear evidence of efficacy is limited.

ANALGESICS: Analgesics include Acetaminophen and nonsteroidal anti-inflammatory drugs (Ibuprofen, Naproxen, Ketorolac) that inhibit cyclooxygenase and decrease prostaglandin and thromboxane synthesis

ANALGESICS		
	CHILD	ADULT
Ibuprofen (Motrin)	10 mg/kg PO	800 mg PO
Ketorolac (Toradol)	0.5 mg/kg IV/IM	30 mg IV/IM
Naproxen (Naprosyn)	5 mg/kg PO	250-500 mg PO
Acetaminophen (Tylenol)	15 mg/kg PO	1000 mg PO

TRIPTANS: Triptans are 5HT serotonin receptor agonists that result in vasoconstriction and are most effective if used within one hour of headache onset but may still be effective outside of that time interval. The lack of response to one Triptan does not preclude response to another. If there is an initial response and then recurrence, an additional dose may be administered. Triptans contraindicated in patients who are pregnant, have a history of stroke, uncontrolled hypertension, cardiovascular disease, hemiplegic migraine and accessory cardiac conduction pathways.

TRIPTANS		
	6-10 years and < 50 kg	> 10 years and < 50 kg
Almotriptan	6.25 mg PO	12.5 mg PO
Rizatriptan	2.5 mg PO, ODT	5 mg PO, ODT
Sumatriptan PO	25 mg PO	50 mg PO
Sumatriptan IN	5 mg IN	10 mg IN
Sumatriptan SQ	3-6 mg SQ	3-6 mg SQ
Zolmitriptan	2.5 mg PO, ODT, IN	5 mg PO, ODT, IN

DOPAMINE RECEPTOR ANTAGONISTS: (Prochlorperazine. Metoclopramide) treat pain and nausea but have anticholinergic and antihistaminic effects. Extrapyramidal adverse effects such as akathisia and dystonia may occur. Patients can be pretreated with diphenhydramine. Chlorpromazine has proven to be poorly effective in children.

DOPAMINERGIC ANTAGONISTS		
	CHILD	ADULT
Prochlorperazine[1] (Compazine)	0.1-0.15 mg/kg IV/IM	5-10 mg IV/IM
Metoclopramide (Reglan)	0.1-0.2 mg/kg PO/IV	10 mg PO/IV
Dihydroergotamine (DHE)	0.1-0.2 mg IV	0.5-1.0 mg IV
1. Only > 2 years of age, may prolong the QT interval,		

COMBINATION REGIMENS: If a single dose of one class of medications is infective, then a combination of agents is utilized (e.g. Ketorolac and Metoclopramide). The decision to administer oral versus parenteral medication is based on the severity of the headache and the degree of nausea and vomiting.

REFRACTORY MEDICATIONS: There are a number of adult therapies that have not been extensively studied in children. These include: magnesium, valproate, corticosteroids, intranasal ketamine and Aspirin/Acetaminophen/Caffeine combinations.

Dihydroergotamine is an ergot alkaloid and serotonin agonist that functions as a vasoconstrictor. The contraindications to Triptans (see above) also apply to dihydroergotamine. Nausea, anxiety and dyskinesia may occur.

DIHYDROERGOTAMINE		
	< 25 kg or 9 years	10 years
Dihydroergotamine (DHE) IV	0.5 mg IV Q8H	1.0 mg IV Q8H
Administer an antiemetic 20 minutes before Administer DHE over 3 minutes For first time administration, give a test dose of 1/2 the recommended dose		

REFRACTORY MIGRAINE MEDICATIONS		
	CHILD	ADULT
Dexamethasone (Decadron)	0.6 mg/kg IV	10 mg IV
Valproic Acid (Depakene)	5-10 mg/kg IV	500-1000 mg IV
Magnesium Sulfate	25-50 mg/kg IV	1-2 grams IV
Propofol (Dripivan)	0.5 mg/kg IV	50 mg IV
Ketamine (Ketalar)	0.5 mg/kg IN	25 mg IN

DISPOSITION

Reassurance of the benign nature of headache is essential if serious secondary causes of headache have been excluded. Patients and their families are frequently concerned about having a brain tumor or an intracranial injury.

Follow-up should be encouraged after an ED for headache and families should be encouraged to keep a headache diary to help the pediatrician or neurologist diagnose the headache disorder. The diary will also help identify precipitants such as dehydration, caffeine, bad sleeping habits, and food additives, headache characteristics and medication effectiveness.

To avoid medical overuse headaches, patients should be counseled to limit analgesic use to less than 14 days a month and triptans to less than 9 days a month.

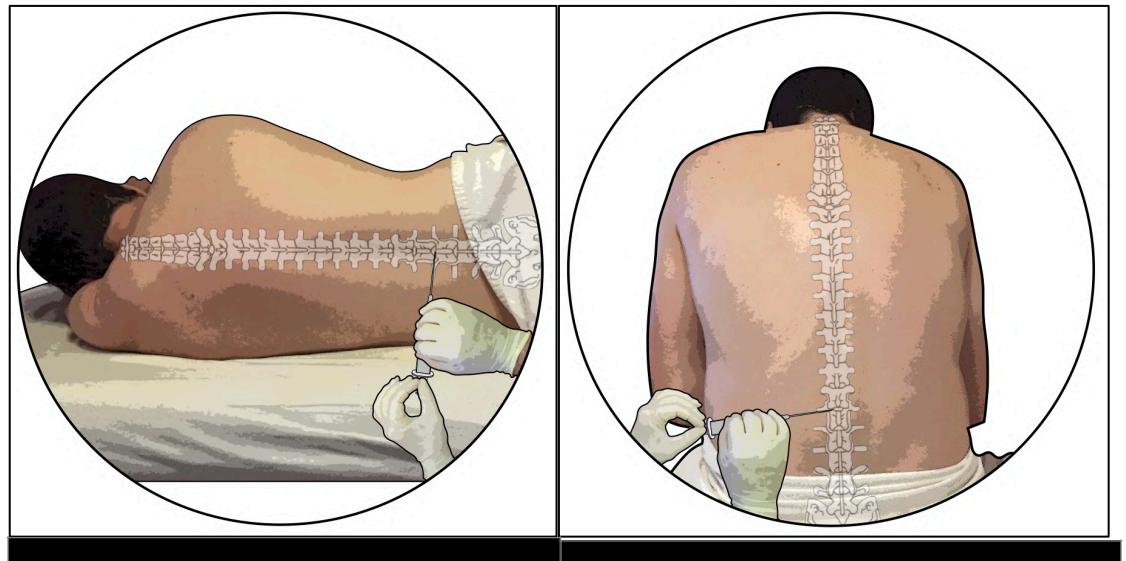
LUMBAR PUNCTURE

INDICATIONS (ZACHARY BINDER M.D., 11/2019)
Lumbar puncture (LP) is a procedure that provides access to a patient's subarachnoid space, which contains cerebrospinal fluid (CSF). It can be utilized either diagnostically or therapeutically. Diagnostic indications for performing a lumbar puncture include assessment for infectious disease (meningitis, encephalitis) inflammatory disease (Multiple Sclerosis, Guillain-Barre syndrome), subarachnoid hemorrhage, oncologic disease, or metabolic disease. Therapeutic indications for lumbar puncture include: the administration of anesthetic agents, administration of antibiotic agents, administration of chemotherapy/methotrexate in the treatment of leukemias/lymphomas, or the relief of increased intracranial pressure by the removal of CSF in idiopathic intracranial hypertension (pseudotumor cerebri).

CONTRAINDICATIONS
ABSOLUTE CONTRAINDICATIONS
Infected skin over the needle entry site
Cardiopulmonary compromise (given the required positioning of procedure)
Pressure gradient between the supratentorial and infratentorial compartments CT findings concerning for pressure gradient such as midline shift, loss of suprachiasmatic/basilar cisterns, posterior fossa mass, loss if superior cerebellar cistern, loss of quadrigeminal plate cistern (See Complications – Herniation)
RELATIVE CONTRAINDICATIONS
Increased intracranial pressure
Coagulopathy increases the risk of spinal hematoma (INR >1.4 suggested criteria)
Thrombocytopenia (platelets < 50-suggested criteria)
Brain Abscess

POSITIONING

Patients must assume either a lateral recumbent or sitting position. Lateral recumbent position allows for the accurate measure of opening pressure, and is thought to reduce post-LP headache. From either position, the patient should adopt the fetal position, with back flexed (in an arched position), in order to widen the space between spinous processes. If in the lateral recumbent position, the patient's lumbar spine should be parallel to the table. If in the sitting position the patient's lumbar spine should be perpendicular to the table. In younger children who required positioning and restraint care should be taken to avoid airway compromise.



HORIZONTAL (LYING) | VERTICAL (SITTING)

PREDICTORS OF LP SUCCESS

A large, prospective, cohort study found the factors listed in the table below to significantly increase the risk of a traumatic (>10,000 RBC) or unsuccessful LP (failure to obtain CSF for cell count after first LP attempt) (Nigrovic, Ann Emerg Med. 2007, PubMed ID: 17321005). Potentially modifiable procedure parameters include the use of local anesthetic and use of the stylet out technique.

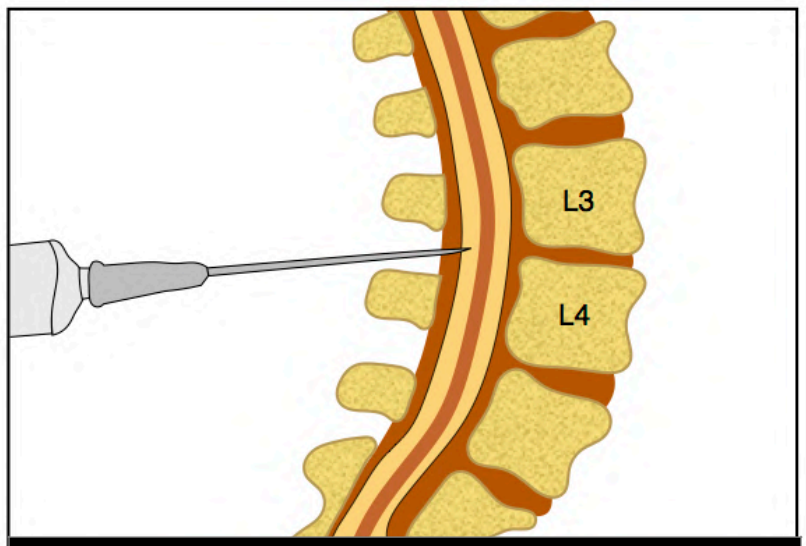
Patient characteristics such as obesity, osteoarthritis, ankylosing spondylitis, kyphoscoliosis or prior lumbar surgery may also result increase the likelihood of failure. These patients may require consultation with an anesthesiologist or interventional radiologist. These patients may also benefit from utilization of ultrasound guided LP.

PREDICTORS OF TRAUMATIC OR UNSUCCESSFUL LUMBAR PUNCTURE		
Predictor	Traumatic > 10,000 RBC/mm^3 or Unsuccessful LP[1]	Traumatic > 500 RBC/mm^3 or Unsuccessful LP[1]
Age 3 months	2.1 (1.9, 2.9)	2.2 (1.6, 3.1)
Black Race	0.9 (0.6, 1.2)	0.8 (0.6, 1.1)
Parental Presence	0.9 (0.7, 1.3)	1.0 (0.8, 1.4)
Presentation 8p-8a	0.9 (0.7, 1.1)	0.9 (1.7, 1.1)
Difficult Spine: Visualize	1.8 (1.3, 2.3)	1.9 (1.5, 2.5)
Difficult Spine: Palpation	3.1 (2.1, 4.4)	2.7 (1.9, 3.9)
Less MD Experience	1.08 (1.01, 1.15)[2]	1.06 (1.0, 1.13)[2]
No Local Anesthetic	1.6 (1.1, 2.2)	1.6 (1.2, 2.3)
Procedural Sedation	0.9 (0.6, 1.3)	0.8 (0.6, 1.1)
Stylet in Advancement	1.3, (1.04, 1.7)	1.4 (1.1, 1.9)
Sitting Position	1.2 (0.6, 2.3)	1.4 (0.7, 2.7)
Patient Movement	2.1 (1.6, 2.6)	2.4 (1.9, 1.3)
GREEN = Statistically Significant, RED = Not Statistically Significant 1. Adjusted Odds Ratio (95% CI) 2. Difference in statistical significance between the primary secondary outcome		

EQUIPMENT
Sterile drapes
Skin antiseptic agent (iodine or chlorhexidine based)
Spinal needle with stylet, typically 22-gauge:1.5 inches (infants), 2.5 inches (children), 3.5 inches (adult)
Collection tubes for CSF
Adhesive bandage
Additional supplies include: Lidocaine with epinephrine, injection needle, manometer, 3 way stop cock, sterile marker
Ultrasound-assisted technique: linear ultrasound transducer, sterile ultrasound transducer, gel

ANATOMIC LANDMARKS

Traditional palpation technique: Palpate the superior aspects of the iliac crests bilaterally. Draw a line (visually or with a skin marking pen), connecting these two points. This line will intersect the spinal column at the L4 spinous process. The L3 and L5 vertebrae can then be palpated just above and just below this spinous process respectively. (See Appendix for ultrasound guided landmark identification)



ANATOMIC LANDMARKS

CSF TESTS BASED ON INDICATION	
TUBE	PROPOSED SAMPLE LABELING
1	Glucose, Protein, Oligoclonal banding, Myelin basic protein
2	Micro/Serology: Gram Stain, Culture (bacterial, viral, fungal, mycobacterial), HSV PCR
3	Cell Count (with differential), flow cytometry
4	Special Tests: e.g. Encephalitis/Meningitis

COMPLICATIONS	
Headache	Most common complication in first 48 hours after LP. Caused by leakage of CSF through puncture site. Increased incidence correlated with larger spinal needle size. An epidural “blood patch” may relieve symptoms. Reduced in the lying position and with the needle bevel in the sagittal plain
Herniation	Most serious complication of LP. Occurs as a result of large pressure gradient between cranial and lumbar compartments. History, funduscopic exam, neurologic exam, and head CT findings can all be used to evaluate potential risk prior to LP though a normal exam and head CT do not eliminate the possibility of herniation
Hemorrhage	Can result in spinal cord compression. Most likely to occur in patients with coagulopathy
Subarachnoid epidermal cyst	Can develop as a result of introducing a skin plug into subarachnoid space. Avoided through use of stylet while passing needle through skin and subcutaneous tissue.

LUMBAR PUNCTURE PROCEDURE	
1	Palpate and identify landmarks
2	Gown and glove in sterile fashion
3	Clean the overlying skin with antiseptic in widening concentric circles
4	Cover field with sterile drapes, leaving lower lumbar spine exposed.
5	Inject local anesthetic subcutaneously to puncture site (if time allows anesthetic cream such as EMLA or LMX can be applied to skin prior to cleaning/draping)
6	Re-palpate landmarks (while carefully ensuring maintenance of sterility)
7	Insert the needle with stylet firmly in place at the superior aspect of the inferior spinous process, in midline, at 15 degrees cephalad aiming for patient umbilicus. Ensure that needle bevel is in sagittal plane (pointing toward the ceiling in the lying position and toward the patients side in the sitting position so as to spread rather than cut the nerve fibers in the dural sac running parallel to spinal.
8a	Stylet-In Technique: Withdraw stylet in 2 mm intervals to access for CSF flow (once in the arachnoid space, CSF should flow)
8b	Stylet-Out Technique: Withdraw the stylet after the needle passes through the skin and subcutaneous tissue. Advance the needle slowly until CSF is obtained.
9	Needle will ideally pass through the following layers: skin, subcutaneous tissue, supraspinous ligament, interspinous ligament, ligamentum flavum, epidural sac, internal vertebral venous plexus, dura, arachnoid and into the subarachnoid space).
9a	As the needle passes through the ligamentum flavum you may appreciate a “pop or popping sensation” though this is less common in infants
9b	If flow is poor, rotate the needle 90 degrees orienting the bevel toward the head (in an attempt to alleviate possible nerve root obstruction)
9c	If unsuccessful, and bone encountered, withdraw needle to subcutaneous tissue, without exiting the skin and redirect the needle.
10	If unsuccessful, and bone encountered, withdraw needle to subcutaneous tissue, without exiting the skin and redirect the needle.
11	Allow CSF to drip into collection tubes (typically 3-4 ml). Collect fluid from manometer by rotating 3-way stopcock, before extracting additional CSF from patient. Never aspirate CSF, as generation of negative pressure can cause a hemorrhage.
12	Allow CSF to drip into collection tubes (typically 3-4 ml). Collect fluid from manometer by rotating 3-way stopcock, before extracting additional CSF from patient. Never aspirate CSF, as generation of negative pressure can cause a hemorrhage.

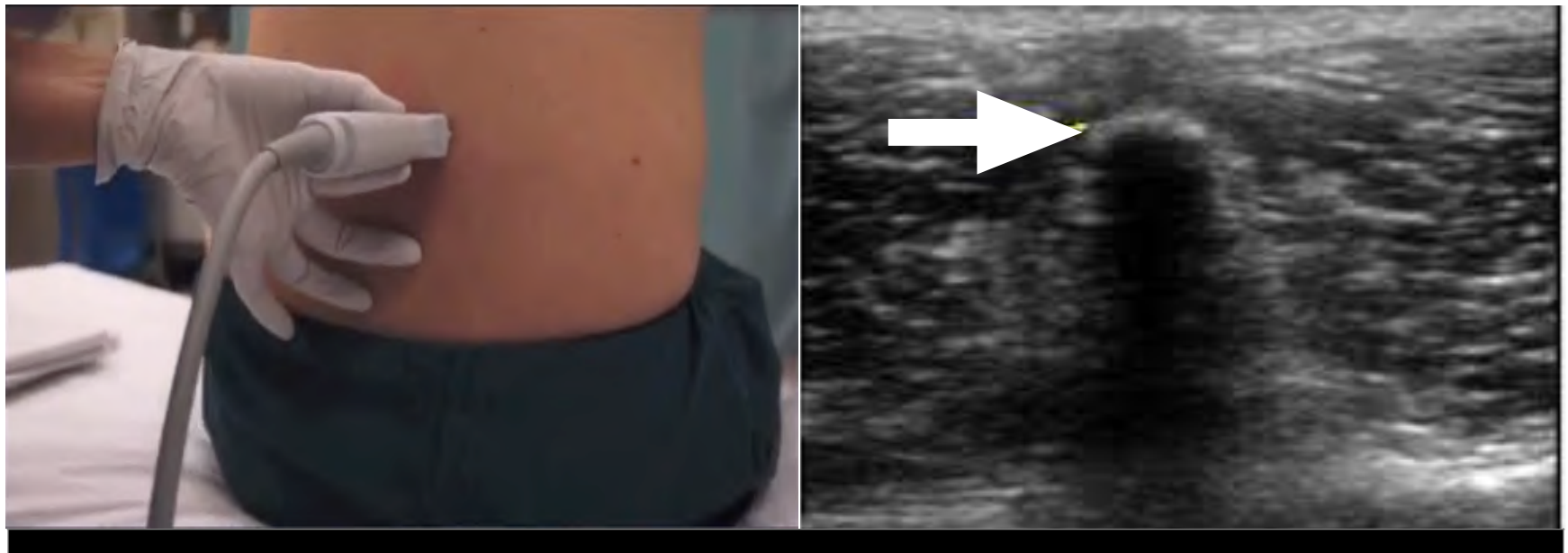
STYLET-OUT TECHNIQUE: The stylet out technique is the removal of the stylet before advancement of the catheter into the subarachnoid space, and after the needle has traversed the skin and subcutaneous tissue. “Stylet out” allows for continuous and direct monitoring for penetration into the subarachnoid space, by looking continuously for CSF return as the needle is advanced a millimeter at a time. The “stylet out” technique has not been associated with increase in epidermal cell spinal tumors as long as the stylet is in place during skin penetration.

APPENDIX: ULTRASOUND ASSISTED LUMBAR PUNCTURE

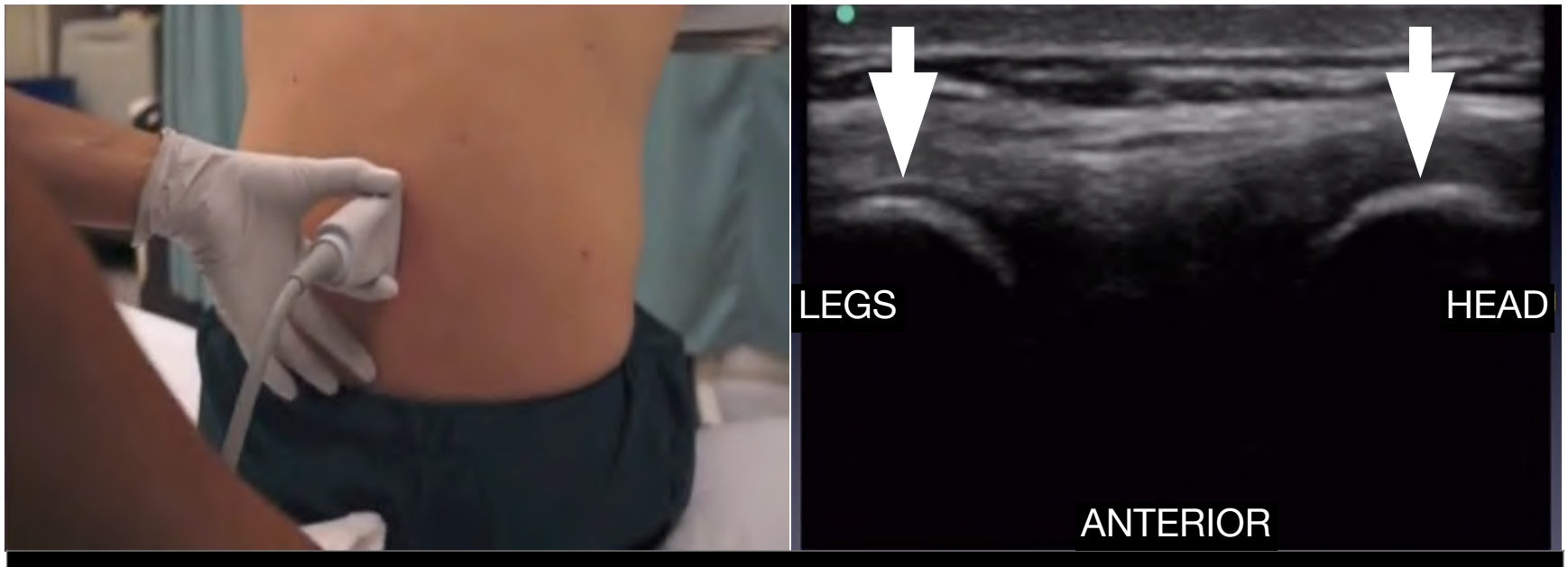
ULTRASOUND CONSIDERATIONS

Ultrasound can be used with LP's in a static (US-assisted) or dynamic (US-guided) fashion (limited by space, and need for a trained assistant). Higher resolution ultrasound may allow for the identification of the ligamentum flavum (as a bright, white, hyperechoic structure deep to level of spinous processes). This can allow for an estimate of the distance to be traversed by spinal needle. In a randomized trial of 80 infants less than 3 months of age, point of care ultrasound did not improve LP

ULTRASOUND GUIDED LP: LANDMARK IDENTIFICATION	
1	May be performed in either lateral decubitus or sitting position.
2	Place high frequency 13-5 MHz linear array transducer in a transverse fashion with the marker dot to the left of the patient, perpendicular to the long axis of the spine, along the midline, at level of iliac crests.
3	Scan until a bright white hyperechoic spinous process is identified (will see a large, far-field shadow,) will appear between the paraspinal muscles. The patient's midline is then identified when the spinous process is centered in the middle of the ultrasound screen. Mark this location with a sterile marker.
4	Use ultrasound to further identify 2 additional spinous processes in a similar fashion. A line connecting these 3 points follows the long axis of the spine, along the midline
5	Rotate the transducer 90 degrees so that it now sits parallel to the long axis of the spine and the marker dot is oriented cephalad. Scanning along the previously identified line reveals spinous processes that now appear as hyperechoic curves casting dark, far-field shadows. Interspinous spaces are then visualized between two adjacent spinous processes.
6	Scan along the long axis of the spine, until an interspinous space is centered on the screen, with an identifiable spinous process on either side. Draw a line at this spot, perpendicular to previously identified midline.
7	Scan along the long axis of the spine, until an interspinous space is centered on the screen, with an identifiable spinous process on either side. Draw a line at this spot, perpendicular to previously identified midline.
8	The intersection of these lines identifies the optimal point of entry for the spinal needle.



IDENTIFICATION OF SPINOUS PROCESSES: TRANSVERSE AXIS



IDENTIFICATION OF SPINOUS PROCESSES: LONGITUDINAL AXIS

MENINGITIS

INTRODUCTION (RACHEL KOWLASKY, MD, MPH, 11/2018)
Meningitis is an infection-mediated inflammation of the meninges. It can be caused by infectious agents such as: bacteria, viruses, and fungi, or can be caused by noninfectious agents such as toxins, granulomatous disease, and autoimmune disease.

Viral meningitis is the most common. Suspected bacterial meningitis is a medical emergency. It is associated with significant morbidity (neurologic sequelae) and mortality (approximately 4% with ideal treatment).

MICROBIOLOGY
Vaccination has changed the microbiology of bacterial meningitis. The prevalence of meningitis due to H. influenzae type B has decreased 97% since vaccination was initiated in 1985. Prevnar vaccination, which protects against the seven most common pneumococcal serotypes, was introduced in 2000 and decreased the incidence of pneumococcal meningitis by 60%. However, there was an increase of non-vaccine S pneumonia strains such as serotype 19A, a multidrug resistant strain currently responsible for approximately 60% of invasive disease. Prevnar 13 initiated in 2010 includes an additional 6 serotypes including 19A.

In a population of 4,313 neonates less than 60 days, bacterial meningitis was present in 0.6% or 1 in every 167 patients (Cruz, JAMA Pediatric 2017, PubMed ID: 28892537). The most common pathogens in patients with isolated meningitis were: Group B Streptococcus (23%), Escherichia coli (23%) and Enterococcus (23%). The most common pathogens in patients with concomitant meningitis and bacteremia were: Group B Streptococcus (54%) and 5 other organisms each accounting for 9.3% (Escherichia coli, Enterobacter cloacae, Klebsiella, Neisseria meningitides and Streptococcus pneumonia).

CLINICAL EVALUATION
Most patients with bacterial meningitis present with fever and symptoms of meningeal inflammation such as neck stiffness, nausea, vomiting, irritability, lethargy, photophobia, and headache. Infants may present with hypothermia, jaundice, poor feeding, or a bulging fontanel.

The physical exam may reveal signs of shock, altered mental status, cranial nerve palsies, papilledema, petechiae, or purpura. Nuchal rigidity can be assessed using the Kernig's sign (supine patient, with the hip flexed to 90 degrees, is unable to extend the knee more than 135 degrees) and Brudzinski's sign (the patient, while in the supine position, flexes the lower extremities during attempted passive flexion of the neck). These signs are unreliable under 2 years of age. Individual history and physical exam parameters have poor diagnostic accuracy.

LABORATORY EVALUATION
A CBC, blood culture, basic metabolic panel, coagulation studies and lumbar puncture should be performed. CSF should be sent for cell count, protein, glucose, gram stain, and culture.

There is significant overlap of CSF findings between viral and bacterial meningitis. Care should be taken in the interpretation of CSF findings in the patient who has received antibiotics prior to presentation. The CSF culture may be negative over 50% of the time in pretreated patients. The CSF WBC and neutrophil count are less likely to normalize with pretreatment.

CSF NORMAL VALUES				
	WBC (WBC/MM^3)	GLUCOSE (MG/DL)	CSF/BLOOD GLUCOSE (%)	PROTEIN (MG/DL)
Preterm	0-25	24-63	55-105	65-150
Term	0-22	34-119	44-128	20-170
Child	0-7	40-48	50	5-40

CSF PATTERNS			
	GLUCOSE	PROTEIN	WBC COUNT (CELLS/μL)
Bacterial	↓	↑	5-1000
Viral	Nl	Nl	5-100
TB	↓	↑	5-100

CSF PCR testing is now routinely available in a time frame to influence emergency decision making. PCR testing should be obtained patient pretreated with antibiotics and those with suspected HSV encephalitis. It may be possible to discharge a well appearing patient with CSF pleocytosis and a positive enteroviral PCR.

MENINGITIS-ENCEPHALITIS PANEL (NYU CSF PCR)
Escherichia coli k1
Haemophilus influenzae
Listeria monocytogenes
Neisseria meningitidis
Streptococcus agalactiae (Group B Streptococcus)
Streptococcus pneumoniae
Cytomegalovirus
Enterovirus
Herpes simplex virus 1
Herpes simplex virus 2
Human herpes virus 6
Human parechovirus
Varicella zoster virus
Cryptococcus neoformans/gattii

IMAGING

Controversy exists over the need for a CT scan prior to lumbar puncture. There is some evidence to suggest a temporal relationship exists between lumbar puncture and herniation. Evidence also indicates that herniation can occur despite a normal head CT.

HEAD CT INDICATIONS (PRIOR TO LP)
Immunocompromised
Ventriculoperitoneal shunt
Hydrocephalus, CNS tumor, prior neurosurgery
Focal neurologic deficits
Focal seizure
Signs of increased ICP
Pupillary changes: Dilation, unresponsive
Papilledema
Cushing's triad
Hypertension (with widened pulse pressure)
Bradycardia
Irregular respiration (irregular deep)

CLINICAL DECISION RULES

Clinical decision rules can assist in distinguishing viral from bacterial meningitis. The most accurate rule, derived in a pre-Prevnar 7 population is the bacterial meningitis score (Nigrovic, Pediatrics. 2002, PubMed ID: 12359784). One point is assigned for each parameter. A score of ≥1 predicts bacterial meningitis with a sensitivity of 97.6% 95% CI (91.5, 99.3%) and a specificity of 70.4%, 95% CI(65.5, 74.9%). If patients less than 2 months are excluded the sensitivity improves to 100%, 95% CI (96.9,100%). The score was validated in a post-Prevnar 7 cohort (Nigrovic, JAMA. 2007, PubMed ID: 17200475).

BACTERIAL MENINGITIS SCORE
Positive CSF Gram Stain
CSF ANC ≥1000 cells/μL
CSF Protein ≥ 80 mg/dL
Peripheral ANC ≥10,000 cells/μL
H/O seizure before or at the time of presentation

MANAGEMENT

Suspected bacterial meningitis is a medical emergency and requires timely therapy. The patient should be placed on a monitor and intravenous access should be established.

ANTIBIOTIC COVERAGE: Antibiotic therapy should be initiated immediately after obtaining blood cultures and before any further studies are done, including CT or LP. Selection should be based on adequate bactericidal activity against the likely organisms and ability to cross the blood brain barrier in significant concentration.

Infants less than 4 weeks of age are at risk for neonatally transmitted infections *(*group B Streptococcus, Listeria Monocytogenes, E. Coli). Recommended antibiotics include Ampicillin with a 3rd generation cephalosporin (Cefotaxime) or an aminoglycoside (Gentamycin). Cefotaxime is preferred because Ceftriaxone can result in hyperbilirubinemia.

In children older than 1-month of age S. pneumoniae and N. meningitidis predominate. Treatment consists of a third generation cephalosporin (Ceftriaxone or Cefotaxime). Vancomycin is added to cover resistant pneumococcus and Staphylococcal aureus. This regimen will also cover H influenzae in the unvaccinated patient.

PATHOGEN TARGETED ANTIBIOTIC SELECTION	
S. pneumoniae	Vancomycin and a 3rd generation cephalosporin
S. aureus	Vancomycin
N. meningitides	3rd generation cephalosporin
L. monocytogenes	Ampicillin
S. agalactiae (GBS)	Ampicillin
H. influenzae (type B)	3rd generation cephalosporin
E. coli	3rd generation cephalosporin

Antibiotic selection should be tailored in children with special circumstances such as: immune deficiency, recent neurosurgery, penetrating head trauma, basilar skull fracture and VP shunt). Infectious disease consultation should be considered.

ANTIBIOTIC SELECTION: SPECIAL CIRCUMSTANCES		
Basilar skull fracture	S. pneumonia (gram (+)) S. pyogenes (gram (+))	Vancomycin and a third generation cephalosporin
Penetrating skull trauma or recent neurosurgery	S. aureus (gram (+)) S. epidermidis (gram (+)) P. Aeruginosa (gram (-))	Vancomycin and (Cefepime, Ceftazidime or Meropenem)
VP shunt	S. epidermidis (gram(+)) P. Aeruginosa (gram (-)) Propionobacter acnes (gram (+)	Vancomycin. If Gram (-) add (Cefepime, Ceftazidime or Meropenem)

FLUID RESUSCITATION: Intravenous fluid should be given as necessary to treat shock. In the past patients were fluid restricted due to the concern for SIADH and hyponatremia. Recent evidence suggests the maintenance fluids result in improved clinical outcomes. Moderate fluid restriction may be considered in the setting of hyponatremia with normal perfusion.

CORTICOSTEROIDS: The evidence for the use of corticosteroids in bacterial meningitis is conflicting. Theoretically, corticosteroids may reduce the inflammation associated with infection and antibiotic administration. Dexamethasone therapy (0.15 mg/kg Q6 hrs x 2-4 days) may reduce hearing loss in children with meningitis, particularly that is caused by Haemophilus influenza type B, if given before or at the same time as the first dose of antibiotics. Reduction in mortality is unclear. A Cochrane review in children (Brouwer, Cochrane Database 2013, PubMed ID: 23733364) showed no decrease in hearing loss of mortality, in those patients with non-haemophilus organisms.

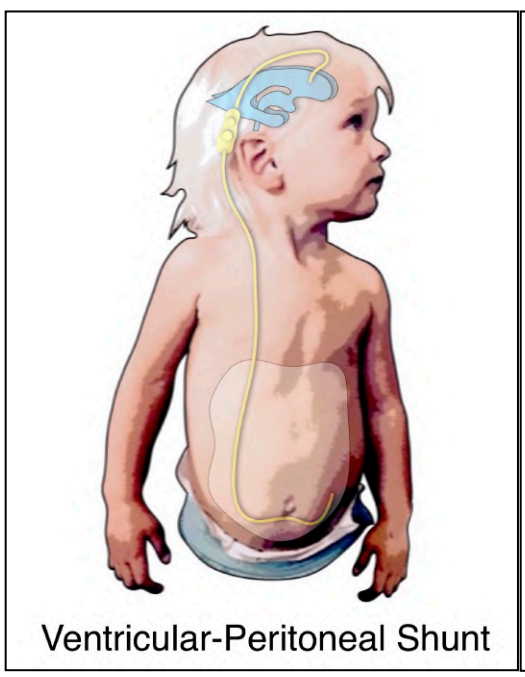
For pneumococcal meningitis, the AAP recommends that “adjunctive therapy with dexamethasone may be considered after weighing the potential benefits and risks. If used, dexamethasone should be administered before or concurrently with the first dose of antimicrobial agents.” (AAP Committee on Infectious Disease 2018-21).

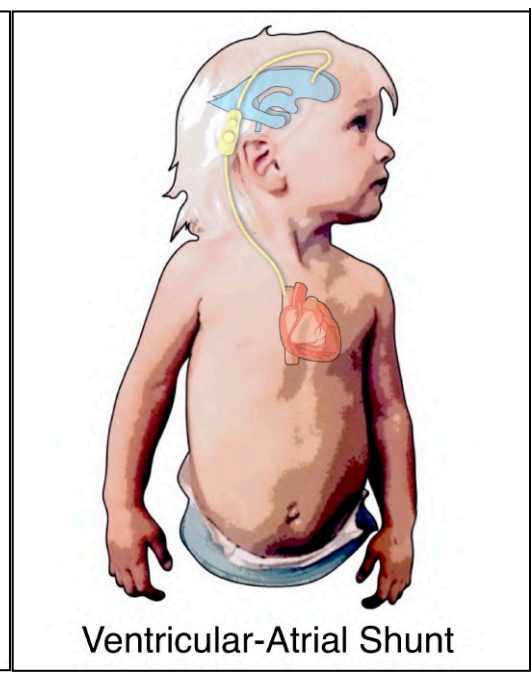
ANTIVIRALS (ACYCLOVIR): Herpes simplex virus (HSV) encephalitis should be considered in patients with a: vesicular rash, maternal history of (HSV) infection, seizures, ill appearance, elevated transaminases or a mononuclear CSF pleocytosis. Unfortunately, the absence of these factors does not preclude HSV infection. HSV polymerase chain reaction is the most reliable with a sensitivity of 75-100%. Serologic testing is unreliable due to the presence of maternal IgG. There is no consensus on whether all infants with CSF pleocytosis should be treated with Acyclovir.

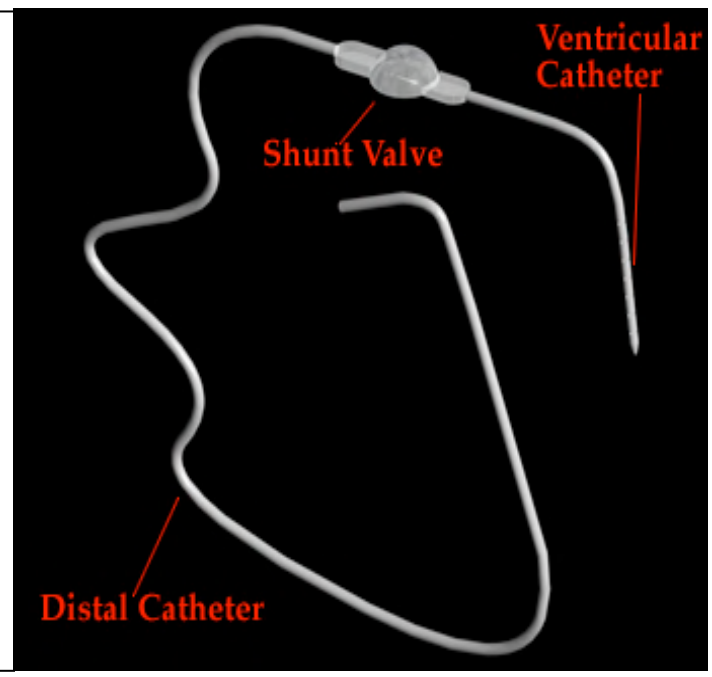
SHUNT COMPLICATIONS

INTRODUCTION (SHERI-ANN WYNTER, MD 4/2018)
Hydrocephalus is the accumulation of excess cerebrospinal fluid. It may be secondary to increased production, poor absorption or poor drainage of CSF. Obstruction to CSF circulation is the most common cause of hydrocephalus in pediatric patients. This is termed obstructive or non-communicating hydrocephalus. Intracranial volume is made up of blood, CSF, and brain. This volume is relatively fixed. The Monro-Kellie Doctrine states than an increase in any component results in an increased intracranial pressure. An accumulation of CSF results in ventricular dilation and compression of adjacent brain tissue and blood volume and eventually cerebral herniation.

Cerebrospinal shunts play an important role in the management of hydrocephalus in the pediatric patient. Placement of a CSF shunt leads to the diversion of the excess CSF to the peritoneum (Ventriculoperitoneal), the vasculature (ventriculoatrial) or pleural cavity (ventriculopleural). Ventriculoperitoneal shunts are more commonly used in children. These devices are subject to several complications. Shunt obstruction and shunt infection are the most common complications. It is important to be able to rapidly assess and manage these complications as a delay in diagnosis and appropriate interventions may result in significant morbidity and possibly death.


Ventricular-Peritoneal Shunt


Ventricular-Atrial Shunt



A cerebrospinal shunt system consists of a proximal catheter, which is placed in the ventricle through a burr hole. The proximal catheter is attached to a valve reservoir, which provides unidirectional flow and regulates pressure for CSF flow. These may operate at a fixed pressure or are programmable. The distal tubing is directed to the specific area of drainage (peritoneal, atrial, pleural). There may be connectors between each portion of the device or the entire device may be continuous.

Additional components of a shunt may include a Rickham reservoir and an anti-siphon device. A Rickman reservoir is placed between the ventricular catheter and the valve. It is a dome-shaped and can be accessed to sample CSF. An anti-siphon device regulates pressure reducing the risk of over drainage It can be part of the valve or placed between the valve and the distal catheter.

CSF SHUNT OBSTRUCTION

INTRODUCTION

Shunt malfunction is most commonly due to mechanical failure. The median survival of shunt placed before two years of age is 2 years and 8-10 years for those placed after 2 years of age. Approximately one third of shunt malfunctions are proximal, and one third are distal obstructions. Proximal obstructions may be the result of catheter migration, tissue debris or choroid plexus blockage. Distal obstructions may be secondary to kinking, clogging, thrombosis or venous occlusion. Shunt obstruction may occur at any point during the lifetime of the shunt.

CLINICAL EVALUATION

Symptoms of a shunt obstruction are often nonspecific with considerable overlap with other childhood illnesses. Symptoms associated with increased intracranial pressure include: headache, nausea, vomiting, lethargy, seizures, ataxia, and changes in behavior. The child must be evaluated for signs of increased intracranial pressure, including bulging fontanelle, upward gaze palsy, papilledema and Cushing's triad (hypertension, bradycardia and irregular respirations). In a study of 755 ED visits, shunt obstruction was identified in 146 visits (19.3%). Headache, nausea or vomiting, bradycardia and mental status changes were more common in those with obstruction (Boyle, Ped Emerg Care 2017, PubMed ID: 28099293).

Bowel obstruction may also be a presenting sign in patients with ventriculoperitoneal shunts. Ventriculoatrial shunt obstructions or migrations can result in cardiac-specific signs such as an arrhythmia, vascular damage and pericardial tamponade.

Compression of the valve reservoir has been used to evaluate for a suspected shunt obstruction though the utility of this technique is questionable. Compression of the reservoir results in CSF flow to the peritoneum (distal). An inability to compress the reservoir indicates at distal obstruction. Refilling of the reservoir occurs due to CSF flow form the ventricles (proximal). Poor reservoir refill indicates a proximal obstruction.

SHUNT COMPRESSION ASSESSMENT		
	COMPRESSION	REFILL
Normal	YES	YES
Proximal Obstruction	YES	NO
Distal Obstruction	NO	YES

IMAGING

Plain radiographs of the shunt ("shunt series") can be diagnostic of disconnections or migrations of the shunt system. Nuclear imaging ("shunt-o-gram") can also be used to determine the integrity of the shunt. These techniques are not ordered routinely at NYU and Bellevue but may be requested by neurosurgery.

A CT scans or rapid MRI should be obtained to determine if there has been interval increase in ventricle size to suggest shunt obstruction. Rapid MRI has the benefit of lack of radiation exposure and a short time of procedure that typically obviates the need for procedural sedation. However, it is not adequate to assess brain tissue. It is essential that electronic shunts be reprogramed after an MRI. A pseudocyst may form at the distal end of a VP shunt and cause obstruction. Ultrasound is the imaging modality of choice to identify a pseudocyst.

MANAGEMENT

Neurosurgery will need to perform a shunt revision to definitively manage an obstructed shunt. There are however medical interventions than can be used in the emergency department to mitigate increased intracranial pressure until surgery can be performed (See Appendix: Management of Increased ICP).

In the event of impending herniation an urgent shunt tap may be required. Inability to withdraw CSF from the reservoir is diagnostic of a proximal obstruction. Proximal shunt obstruction requires operative management (See Appendix: Emergency Shunt Tap).

CSF SHUNT INFECTION

INTRODUCTION

Another common complication of CSF shunts is infection. Shunt infection occurs in 5-15% of shunts. 80% of shunt infections occur within the first 6 months of shunt placement (most commonly in the first month). Infection may occur by hematogenous spread, colonization at the time of placement, or by retrograde spread. Common organisms responsible for shunt infections are listed below.

ORGANISMS	
Gram Positive: Staphylococcus epidermis	50%
Gram Positive: Staphylococcus aureus	25-30%
Gram Negatives and Anaerobes: Klebsiella, E. Coli, Proteus, Pseudomonas	5-10%

CLINICAL EVALUATION

Shunt infections may present with few symptoms and It may be difficult to distinguish VP shunt infection from other routine childhood febrile illnesses. More than half of patients with shunt infection may present afebrile. A shunt obstruction may be the only sign of infection. In addition, patients may lack meningeal symptoms due to the absence of connection between the ventricles and the meninges. Swelling and redness over the shunt tract may rarely be seen in shunt infections.

Ventriculoperitoneal shunt infections may present with peritonitis, fever, and abdominal pain if the infection is localized to the distal portion. Ventriculoatrial shunt infections may present with bacteremia, endocarditis, or septic emboli.

Percutaneous aspiration of the shunt reservoir (See Appendix: Shunt Tap) for CSF analysis is the preferred diagnostic study. A lumbar puncture for CSF analysis may be obtained, but the is usually not positive. Elevated CSF leukocyte count (with neutrophil predominance) and protein are typically seen, but there is usually less inflammation than is seen with typical bacterial meningitis. Blood culture should also be obtained and has been shown in at least one study, to be of higher yield in ventricular atrial shunt infection. In patients with a VP shunt and gastrointestinal signs or symptoms an abdominal ultrasound should be obtained to identify a pseudocyst. CBC and BMP may also be obtained for additional information. Imaging should also be obtained to look for shunt obstruction.

MANAGEMENT

All patients must be admitted with neurosurgery consultation. Shunt removal with external drainage and parenteral antibiotics is the preferred treatment. Alternatively, intraventricular antibiotics may be administered when shunt removal is not possible. However intraventricular antibiotics can be toxic and there are currently no antibiotics approved for this use.

Parenteral vancomycin is a typical first-line agent in children due to its effect against gram-positive *staphylococcal* species (MRSA in particular), although it has lower penetration of the blood-brain barrier than Nafcillin. A third generation cephalosporin, such as Ceftriaxone, with activity against gram-negative organisms, should also be initiated. Cefepime can be used if pseudomonas coverage is required.

EMPIRIC ANTIBIOTIC THERAPY		
	DOSE[1]	COVERAGE
Vancomycin	15 mg/kg q6h	Staph, esp. MRSA
Ceftriaxone	75 mg/kg q6h	Gram negative
Meropenem	40 mg/kg q8h	Resistant Gram negative
Linezolid	10 mg/kg q8h	Vancomycin allergic[2]
1. Assuming normal kidney function, 2. Inconsistent CSF concentration		

APPENDIX: MANAGEMENT OF INCREASED ICP

EMERGENCY MANAGEMENT OF CEREBRAL PERFUSION PRESSURE	
Positioning	Elevate the bead of bed up to 30 degrees. Neutral head/neck position. (Maximizes cerebral venous return)
Temperature	Antipyretics, avoid hyperthermia Cerebral metabolic demand ↑ 5% for each ↑ 1°C Recent evidence suggests that cooling is ineffective
Sedation and Analgesia	Balanced to maintain blood pressure and ability to assess neurologic status
Systolic blood pressure	Maintain mean arterial pressure > 5% for age Do not restrict fluids if poor perfusion or hypotension Crystalloid bolus: 20 ml/kg for poor perfusion Consider vasoconstrictor for neurogenic shock
Controlled hyperventilation	Consider brief periods hyperventilation (PCO_2 30-35) for signs of herniation only. Otherwise maintain a normal PCO_2
Mannitol (20%)	Dose: 0.25 - 1.0 grams/kg over 10-20 min Diuretic effect may decrease intravascular volume
Hypertonic Saline (3%)	Dose: 5 ml/kg over 20 minutes (dosed to maintain ICP < 20 mm/hg and Serum osmolality < 360 mOsm/L) Benefit of increasing intravascular volume
Anticonvulsants	Keppra (Levetiracetam): 50 mg/kg/day divided Q12 hours IV Indications: > 1 seizure, Seizure > 1 hour post injury
Diuretics	Acetazolamide 25 mg/kg/day Furosemide 1 mg/kg/day Decreases CSF production by up to 60%; relatively fast onset of action (~30 mins). However, this can also cause dehydration. Acetazolamide may also cause cerebral acidosis → cerebral vasodilation that can ↑ ICP.
Intravenous hydration at maintenance	The combination of vomiting from shunt obstruction and osmotic agents and diuretics can worsen dehydration. Patient should be made NPO in anticipation of operative repair

APPENDIX: EMERGENCY SHUNT TAP

EMERGENCY VENTRICULAR SHUNT TAP			
INDICATIONS	Emergency situations in which increased ICP results in impending herniation (altered mental status, hypertension, bradycardia, dilated, poorly reactive pupils) a shunt tap may prevent catastrophe. This should be done in conjunction with neurosurgery but time may be insufficient to allow the consultant to arrive. This is not effective in proximal shunt obstruction. Proximal shunt obstruction requires operative management.		
CONTRAINDICATIONS	Overlying infection (absolute), Coagulopathy (relative)		
EQUIPMENT	Personal protective equipment: Sterile gloves, mask, gown Sterilizing solution: Povidone iodine or chlorhexidine Sterile drapes Butterfly needle (≤ 23 gauge) 3 ml syringe, 3-way stopcock Manometer (the one used for lumbar punctures) CSF Collection tubes, Sterile gauze and tape		
PROCEDURE STEPS	1	Patient is positioned so that the shunt reservoir (usually located on the right) is positioned at the highest point. (Generally lying on their left side with right side up)	
	2	Apply personal protection equipment	
	3	Clean the area with Povidone iodine or chlorhexidine	
	4	Drape the area	
	5	Connect the syringe to the 3-way stopcock and then to the end of butterfly needle	
	6	Insert the needle superiorly and perpendicularly into the shunt reservoir. Apply gentle pressure to the syringe	
	7	Attach the manometer, position at the level of the patient’s ear and measure ICP	
		a	Adults: (supine): 7-15 mm Hg, >15 mm Hg abnormal
		b	Children: Normal (supine) < 15 mm Hg
		c	Infants: Normal 5-10 mm Hg
		d	Newborns: Normal subatmospheric pressures
	8	Remove the needle, hold pressure for 2 minutes	
PROCEDURE RESULTS	An opening pressure > 25 cm H20 is present in 90% of distal obstructions. Free flow of CSF indicates that the proximal shunt is functioning. CSF is slowly withdrawn until intracranial pressure is less than 15 mmHg in children and adults or in the normal range for infants and newborns		
	Poor flow is associated with proximal obstructions. If there is no free flow the patient needs an operation urgently. Consider other therapies to lower ICP		
COMPLICATIONS	Occlusion of the catheter with the choroid plexus, Intraventricular hemorrhage and shunt infection		

VIDEO LINK: SHUNT TAP

STATUS EPILEPTICUS

INTRODUCTION (GEORGE KRISTINSSON, M.D. 11/2022)
SE represents a medical emergency with a high rate of morbidity and mortality and has to be treated aggressively. Prolonged febrile seizures are the most common cause of status epilepticus (SE) in children (See: PEM Guide: Neurology: Febrile Seizures). SE is categorized as convulsive or non-convulsive. Convulsive SE includes: tonic-clonic movements and an altered mental status and may include focal neurologic deficits in the post-ictal period (e.g. Todd's paralysis). Non-convulsive SE is seizure activity noted on an EEG without clinical findings consistent with convulsive SE. The most common scenario of non-convulsive SE is an acutely ill patient with a severely impaired mental status with or without motor movements. Refractory status epilepticus is SE refractory to both urgent (phase1) and emergent therapy (phase2).

Seizures that do not terminate spontaneously before arrival to the ED are unlikely to terminate within 20-30 minutes. A child that is transported by EMS, and at arrival is still seizing despite therapy, is likely to meet the criteria for SE and require therapy.

STATUS EPILEPTICUS: DEFINITION
5 minutes of continuous clinical or electrographic seizure activity OR
Recurrent seizure activity without an interim return to baseline mental status

STATUS EPILEPTICUS: COMPLICATIONS	
Cardiac dysrhythmia	Hypoxia
Metabolic abnormalities	Acidosis
Altered autonomic function	Rhabdomyolysis
Neurogenic pulmonary edema	Pulmonary aspiration
Hyperthermia	Permanent neurological damage

DIAGNOSIS

LABORATORY: Laboratory testing is generally of low yield unless indicated by history or physical exam findings. Infants less than 6 months of age should have a set of electrolytes and a bedside glucose. A bedside dextrose and oxygen saturation and blood pressure will help to identify some of the rapidly treatable causes of status epilepticus. Antiepileptic drug (AED) levels should be considered when a child with treated epilepsy develops status epilepticus. Toxicology studies may be considered in children when there are indicators of poisoning. In these cases, a specific serum toxicology level is required, rather than urine toxicology screening. An EKG may identify arrhythmias, toxins and electrolyte abnormalities (e.g. prolonged QT corrected interval).

LUMBAR PUNCTURE: There is insufficient data to support or refute recommendations as to whether a lumbar puncture should be done on a routine basis in patients with new onset status epilepticus. A lumbar puncture may be considered in the febrile child with signs of meningitis or localizing neurologic findings once the patient has been stabilized.

NEUROIMAGING: Should be considered after the patient with SE has been stabilized. In a patient that returns to baseline mental status with a normal neurologic examination neuroimaging may be deferred until outpatient follow up with a neurologist.

EMERGENT NEUROIMAGING INDICATIONS
New onset of focal neurologic deficits
Persistent altered mental status with localizing neurologic findings
Signs of increased intracranial pressure (Cushing's triad, pupillary changes)
Fever with meningeal signs (Meningitis/Encephalitis, cavernous sinus thrombosis)
Recent head trauma (Intracranial hemorrhage, fracture)
Hydrocephalus and/or ventriculoperitoneal shunt (Obstruction)
History of sickle cell disease (Stroke)
History of cancer (Hemorrhage)
History of bleeding disorder or anticoagulation (Hemorrhage)

NEONATES: Neonates are at high risk of developing seizures related to CNS abnormalities and metabolic disease. Classically, it has been taught that Phenobarbital has greater efficacy than Phenytoin in this age group. Randomized trials have shown them to have equal efficacy (45%) when used alone (60% when both are used). However, when transitioned from intravenous to oral medication, phenobarbital is preferred because phenytoin had limited gastrointestinal absorption. Pyridoxine deficiency (Pyridoxine 100 mg IV) and Folinic acid deficiency (Leucovorin 2.5 mg IV) should be considered for refractory status epilepticus in the neonate.

NEONATAL SEIZURES: COMMON ETIOLOGIES	
CNS	Perinatal asphyxia, intracranial hemorrhage, hydrocephalus
Metabolic	Electrolytes: ↓ Na, ↓ Glucose, ↓ Ca^{++}
	Pyridoxine dependence, inborn errors of metabolism, mitochondrial disorders
Infection	Meningitis/Encephalitis,
	TORCH: Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus, and Herpes)

TOXINS THAT CAUSE SEIZURES	
P	Pesticides, Propranolol, Phencyclidine (PCP)
L	Lead, Lithium, Lidocaine, Lindane
A	Alcohols, Amphetamines
S	Sugar (hypoglycemics), Salicylates, Sympathomimetics
T	Tricyclic antidepressants, Theophylline
I	Isoniazid, Iron, Insulin
C	Cocaine, Camphor, Caffeine

MANAGEMENT

Supportive care should be provided for all patients with SE. This includes airway protection with oxygenation and ventilation as required as well as continuous cardiopulmonary monitoring. Fluid therapy and vasopressor support may be required. Underlying causes of seizures should be identified and treated appropriately. The management of SE is divided into: Phase 1: Emergent Initial Therapy, Phase 2: Urgent Control Therapy and Phase 3: Treatment of Refractory Status Epilepticus

The goal is to obtain cessation of seizure activity within 60 minutes of treatment. If therapy at any stage is unsuccessful then rapidly move to the next phase of therapy. If therapy at any stage is successful then maintenance therapy should be provided.

TREATABLE CAUSE OF SEIZURES	
CAUSE	TREATMENT
Alcohols: Methanol, Ethylene Glycol	Fomepizole
Hypoxia	Oxygen, Ventilation
Hypoglycemia	Dextrose 0.5-1.0 gm/kg
Hyponatremia	3% Normal Saline 10-12 ml/kg
Hypocalcemia	Calcium Chloride (10%): 20 mg/kg (0.2 ml/kg)
Hypertensive Crisis	Labetalol, Nitroprusside
Increased Intracranial Pressure	Mannitol, Hypertonic Saline
Iron	Deferoxamine
Isoniazid, Pyridoxine Deficiency	Pyridoxine
Propranolol (Beta Blocker)	Glucagon
Pesticides (Cholinergic)	Atropine, Pralidoxime
Salicylates	Sodium Bicarbonate, Dialysis
Sulfonylurea Hypoglycemics	Octreotide, Dextrose
Tricyclic Antidepressants, Cocaine	Sodium Bicarbonate

PHASE 1:INITIAL THERAPY

Benzodiazepines (BZD) should be used as first line therapy for SE. A randomized clinical trial compared the efficacy and safety or intravenous Lorazepam (Ativan) and intravenous Diazepam (Valium) in pediatric patients with status epilepticus from a variety of causes. The study did not demonstrate the superiority of one BZD over another for both efficacy and safety outcomes (PECARN JAMA 2014, PubMed ID: 24756515). From an efficacy standpoint, approximately 60% in each group had seizure cessation within 5 minutes and an additional 30% required an additional dose of the same benzodiazepine. Approximately 15% required Phenytoin or Fosphenytoin. From a safety standpoint, approximately 40% had some respiratory depression while 15% required assisted ventilation.

Midazolam (Versed) is the preferred antiepileptic for intramuscular administration and may be delivered intranasally and buccally as well. Diazepam (Valium) is the preferred agent for rectal administration. Approximately two-thirds of patients will respond to initial therapy.

STATUS EPILEPTICUS: PHASE 1: INITIAL THERAPY			
MEDICATION	DOSE	MAX	RATE
Lorazepam	0.1 mg/kg IV	4 mg	< 2 mg/min
	0.1 mg/kg IM	4 mg	NA
Midazolam	0.1 mg/kg IV	6 mg	< 2 mg/min
	0.2 mg/kg IM (>40kg)	10 mg	NA
	0.2 mg/kg IM (13-40kg)	5 mg	NA
	0.2 mg/kg Intranasal	10 mg	NA
	0.5 mg/kg Buccal	10 mg	NA
Diazepam	0.15 mg/kg IV	10 mg	< 2 mg/min
	2-5 years: 0.5 mg/kg PR	10 mg	NA
	6-12 years: 0.3 mg/kg PR	10 mg	NA
	12 years: 0.2 mg/kg PR	10 mg	NA

PHASE 2: SECONDARY THERAPY

Second line therapy Is required in all patients with SE refractory to initial benzodiazepines unless a specific underlying cause of SE has been identified and corrected. For patients who respond to initial therapy with benzodiazepines the goal is to rapidly attain therapeutic levels of an AED that can later be used for maintenance therapy. There is no consensus on which AED is the preferred agent though the most commonly considered AED's include fosphenytoin (Cerebyx), phenytoin (Dilantin), Valproate (Depakene), phenobarbital, levetiracetam (Keppra) and a continuous infusion of midazolam (Versed). Fosphenytoin has better safety profile than phenytoin, can be administered relatively quickly (3 mg/kg/min) and can be administered intramuscularly. Valproate may be preferred for children with a history of primary generalized epilepsy. For a patient with epilepsy currently taking an AED a dose of that medication may be considered.

Two international network studies did not find Levetiracetam (40 mg/kg) to be superior to Phenytoin (20 mg/kg) as second line therapy. (PREDICT, Lancet. 2019, PubMed ID: 31005386, PERUKI, Lancet. 2019, PubMed ID: 31005385). In the PREDICT study approximately 50% of the patients were still seizing after the first study drug and 25% after the second alternative study drug. This makes it essential to anticipate the need for addition antiepileptic medications and prepare equipment and medications for rapid sequence intubation.

400 pediatric and adult patients were randomized to receive Fosphenytoin: 20 mg/kilogram (Maximum: 1,500 mg), Valproate: 40 mg/kilogram (Maximum: 3,000 mg) or Levetiracetam: 60 mg/kilogram (Maximum: 4,500 mg) as a 10-minute infusion (Kapur, N Engl J Med. 2019., PubMed ID: 31774955). Approximately, 50% of patients with benzodiazepine refractory status epilepticus were successfully treated with one of the trial second-line antiepileptics. There was no statistically significant difference among the three anticonvulsants in treatment success defined as seizure cessation and improving responsiveness without the need for additional anticonvulsants within 60 minutes. There was no statistically significant difference in the secondary efficacy outcomes of ICU admission, ICU or hospital length of stay and median time from the start of the trial-drug to termination of seizures. Form a safety standpoint. there was no statistically significant difference in life-threatening hypotension or cardiac arrhythmia within 60 minutes. In addition, there was no statistically significant difference in the rates intubation, seizure recurrence, anaphylaxis, respiratory depression, increase in hepatic transaminase or ammonia, purple glove syndrome or death. Approximately 1 in 5 patients were intubated

STATUS EPILEPTICUS: PHASE 2: SECONDARY THERAPY				
MEDICATION	DOSE	MAX DOSE	ADDITIONAL BOLUS	RATE
Phenytoin*	20 mg/kg IV	1.5 gm	5-10 mg/kg	< 1 mg/kg/min
Fosphenytoin	15-20 mg/kg IV	1.5 gm	5 mg/kg	< 3 mg/kg/min
	15-20 mg/kg IM	1.5 gm	5 mg/kg	NA
Phenobarbital	20 mg/kg IV	1 gm	5-10 mg/kg	< 1 mg/kg/min
Valproate	40 mg/kg	3 gm	20 mg/kg	3-6 mg/kg/min
Levetiracetam	60 mg/kg	4.5 gm		2-5 mg/kg/min
Midazolam	0.2 mg/kg at 2 mg/min (loading dose)			0.05-2 mg/kg/hour
*Phenytoin is only compatible with normal saline				

PHASE 3: REFRACTORY THERAPY

If SE is refractory to emergent initial therapy and urgent control therapy then the choice is to repeat a bolus of the urgent control AED or initiate another AED as a continuous infusion. The AEDs most commonly recommended for refractory therapy are continuous infusion of midazolam, propofol and pentobarbital. Pentobarbital appears to have a higher rate of seizure control but may have more adverse effects. Midazolam may cause less hypotension. Continuous EEG monitoring will be required. Alternative therapies for refractory SE are not well studied but may include: Ketamine, corticosteroids, inhaled anesthetics and immunomodulation (IVIG). Non-pharmacologic options may include: vagus nerve stimulation, a ketogenic diet, hypothermia, electroconvulsive therapy, transcranial magnetic stimulation and surgical management.

STATUS EPILEPTICUS: PHASE 3: REFRACTORY THERAPY			
MEDICATION	LOADING	INFUSION	BREAKTHROUGH
Midazolam	0.2 mg/kg, 2 mg/min	0.05 - 2 mg/kg/hr	↑ 0.05-0.1 mg/kg/hr Q3-4 hrs
Propofol	1-2 mg/kg	20 mcg/kg/min	↑ 5-10 mcg/kg/min Q5 min
Pentobarbital*	5-15 mg/kg, < 1mg/kg/min	0.5 - 5 mg/kg/hr	↑ 0.5-1.0 mg/kg/hr Q12 hrs
*Will require mechanical ventilation			

THERAPY WITHOUT INTRAVENOUS ACCESS

Emergent initial therapy can be provided by Lorazepam intramuscularly, Midazolam via the intramuscular, intranasal or buccal route and Diazepam rectally. Fosphenytoin can be delivered intramuscularly for urgent control therapy. If another agent is preferred for urgent control therapy or if refractory therapy is warranted than intraosseous access should be obtained if vascular access is not possible.

NON-INTRAVENOUS THERAPY				
	INTRAMUSCULAR	INTRANASAL	BUCCAL	RECTAL
Lorazepam	YES			
Midazolam	YES	YES	YES	
Diazepam				YES
Fosphenytoin	YES			

APPENDIX: STATUS EPILEPTICUS MANAGEMENT ALGORITHM

Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, Jagoda A, Lowenstein D, Pellock J, Riviello J, Sloan E, Treiman DM.
Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society
Epilepsy Curr. 2016 Jan-Feb;16(1):48-61., PubMed ID: 26900382

STATUS EPILEPTICUS ALGORITHM

1. Stabilize Patient: Airway, Breathing, Circulation, Disability
2. Time seizure from onset
3. Assess Oxygenation: Provide supplemental O2, BVM/Intubate PRN
4. Cardiac Monitor
5. Bedside Glucose (< 60 mg/dl)
   Adult: 50 ml D50, Thiamine 100mg
   Child: 2 ml/kg D25 (>= 2 years), 4 ml/kg D10 (< 2 years)
6. IV/IO access, BMP, CBC, Tox screen/Drug levels PRN
7. Treat Underlying Causes: Toxin, electrolyte etc.

0-5 MINUTES
STABILIZATION
(PHASE 0)

↓

Phase1: First Line Agents (Equivalent, Chose 1)
Midazolam IM: 5 mg (13-40 kg), 10 mg (> 40 kg), single dose OR
Lorazepam IV: 0.1 mg/kg (max dose 4 mg), may repeat x 1 OR
Diazepam IV: 0.15-0.20 mg/kg (max dose 10 mg), may repeat x 1

Phase1: Second Line Agents (If none of the 3 above are available)
Midazolam IN: 0.2 mg/kg, (max dose 10 mg) OR
Midazolam Buccal: 0.5 mg/kg (max dose 10 mg) OR
Phenobarbital IV: 15 mg/kg, single dose OR
Diazepam PR: 0.2-0.5 mg/kg (max 20 mg), single dose

5-20 MINUTES
INITIAL THERAPY
(PHASE 1)

↓

Phase2: First Line Agents (No clear evidence, chose 1)
Fosphenytoin/Phenytoin IV: 20 mg/kg (max dose 1500 mg), single dose
OR
Valproic Acid IV: 40 mg/kg (max dose 3000 mg), single dose OR
Levetiracetam IV: 60 mg/kg (max dose 4500 mg), sigle dose OR

Phase2: Second Line Agent (none of the 3 above available)
Phenobarbital IV: 15 mg/kg, single dose

20-40 MINUTES
SECONDARY THERAPY
(PHASE 2)

↓

Phase 3: No clear evidence
Repeat Phase 2 (Urgent Initial Therapy) OR
Anesthetic infusion doses of: Propofol, Midazolam, Pentobarbital

40-60 MINUTES
REFRACTORY THERAPY
(PHASE 3)

SUBARACHNOID HEMORRHAGE

INTRODUCTION (NICOLE GERBER, M.D., 1/2018)
Subarachnoid hemorrhage (SAH), a type of hemorrhagic stroke, accounts for 10-20% of strokes and is the most common cause of death from stroke. SAH has an approximately 50% mortality rate and 30% of survivors have severe disability. SAH is defined as bleeding within the subarachnoid space between the arachnoid and pia mater. The majority of SAHs, are caused by ruptured intracranial aneurysms (ICAs). In children, unlike adults, approximately 50% of strokes are hemorrhagic, with intra-parenchymal hemorrhage more common than SAH.

In the pediatric population, ICAs are more common in males. The estimated incidence is about 0.05-0.09 per 100,000 person-years in children less than 15 years and 0.5 per 100,000 person years in children between 15-19 years. This is a 35 times lower incidence of aneurysmal hemorrhage than in the adult population.

Adults with SAH typically have saccular aneurysms (80%). In contrast children often have dissecting or fusiform aneurysms. Traumatic aneurysms account for about 5-10% and mycotic aneurysms caused by infection (most commonly S. aureus and S. viridans) account for up to 15%. Other causes of non-traumatic SAH include: arteriovenous malformations, neoplasms, coagulopathy and extension from a traumatic intra-parenchymal hematoma.

The most common site of ICA in children is the internal carotid artery, compared to the anterior communicating artery in adults. Overall, around 20% of pediatric aneurysms are in the posterior circulation, which is approximately 3 times higher incidence than in adults.

NON-ANEURISMAL CAUSES OF INTRACRANIAL HEMORRHAGE	
Peri-mesencephalic non-aneurismal SAH	Blood isolated to the peri-mesencephalic cisterns anterior to the brainstem which has a more benign course
Vascular malformations	Intracranial (arteriovenous malformation (AVM)) or Spinal (dural arteriovenous fistulae)
Intracranial arterial dissection	Associated with collagen disorders e.g. and Fibromuscular dysplasia
Sickle cell disease	Typically, from fragile collateral vessels. Risk factors: recent transfusion, treatment with corticosteroids
Other	Cerebral venous thrombosis, bleeding disorders anticoagulation, pituitary apoplexy, traumatic, cocaine abuse, reversible vasoconstriction syndromes, cerebral vasculitis

RISK FACTORS

In children, about 10% of ICAs are seen in patients with co-morbidities. In the adult population, hypertension, cigarette smoking and moderate to heavy alcohol consumption increase the risk if ICA rupture.

PEDIATRIC RISK FACTORS	
Sickle cell anemia	Marfan Syndrome
Coarctation of the aorta	Fibromuscular dysplasia
Tuberous sclerosis	Hereditary hemorrhagic telangiectasias
Kawasaki disease	Klippel-Trenaunay-Weber syndrome
Ehlers-Danlos syndrome	Alpha-1-antitrypsin deficiency
Neurofibromatosis type 1	Polycystic kidney disease.
Takayasu's disease	

COMPLICATIONS	
Re-bleeding	Typically, within first 24 hours. Adults: 1-2% per day for 1st month. Children: More common and occurs in 50%
Increased ICP	Multiple factors: hemorrhage volume, hydrocephalus, reactive hyperemia, and distal cerebral arteriolar vasodilation.
Hydrocephalus	Obstruction of CSF acutely or later reduction of CSF absorption at the arachnoid granulations occurs in about 15% of adults. Two-thirds of patients will develop chronic shunt-dependent hydrocephalus.
Ischemic stroke	Vasospasm leading to regional cerebral hypoperfusion and delayed cerebral ischemia and infarction. Adults 40-60%. Children 10%.
Seizures	May occur in 6-18%.
Hyponatremia	Secondary to SIADH. Cannot be managed with fluid restriction due to the need to maintain euvolemia.
Other	Cardiac arrhythmias 35%, Pulmonary edema 23%

CLINICAL PRESENTATION

The classic history in adults is the sudden onset (95%) of a severe headache (e.g.. "thunder-clap" headache). It is often described as the "worst headache of my life" and may be lateralized in a third of patients. This may occur after physical exertion (50%). About 30-50% will report a sentinel headache, a warning headache or "leak" that occurred 1-3 weeks before.

SAH may also be accompanied by a transient loss of consciousness, nausea and vomiting. Persistent altered mental status and focal neurologic findings typically indicate larger hemorrhages. Meningismus and lower back pain are typically late symptoms, occurring several hours after the bleeding when breakdown of the blood products leads to an aseptic meningitis. About 10% present with seizures, which is a poor prognostic factor. A complete neurologic exam should be performed though the neurologic exam may be normal. A funduscopic exam may reveal retinal hemorrhages. The presence of vitreous hemorrhage is associated with a poor prognosis.

The derivation of the Ottawa Subarachnoid Hemorrhage Rule (Perry, JAMA 2013, PubMed ID: 24065011) was a multicenter study enrolling 2,131 patients (6.2% with SAH) with a headache peaking within 1 hour and no neurologic deficits. The sensitivity of 100% (95% CI, 97.2%-100.0%) and 15.3% specificity of (95% CI, 13.8%-16.9%). A prospective, multicenter validation of the rule in a population of 1,153 patients of which 67 (5.8%) had a subarachnoid hemorrhage demonstrated a sensitivity of 100%, 95% CI (94.6, 100%) with a specificity of 13.6%, 95% CI (13.1, 15.8%). The neuroimaging rate remained similar (87%). (Perry, CMAJ 2017. PubMed ID: 29133539).

OTTAWA SUBARACHNOID HEMORRHAGE RULE
Age > 40 years
“Thunderclap headache"
Onset during exertion
Witnessed loss of consciousness
Neck pain or stiffness
Limited neck flexion on examination
The absence of all 6 of the above factors indicates a low risk of SAH

DIAGNOSTIC TESTING: IDENTIFY SAH

Traditionally, a negative head CT and LP within a few days of onset essentially preclude the diagnosis of SAH. More recently data suggests that an LP may not significantly change the post-test probability of SAH when a negative non-contrast head CT is performed within 6 hours of symptom onset (Carpenter, Academic EM, 2016, PubMed ID: 27306497) or that a CT angiogram may replace the LP with a post-test probability of SAH of less than 1% (McCormack, Academic EM, 2010, PubMed ID: 20370785).

NON-CONTRAST HEAD CT (NCHCT): Obtain a non-contrast CT with thin cuts through the base of the brain to increase sensitivity to small amounts of blood if SAH is suspected. If performed within 6-12 hours of the bleed, sensitivity is near 100% and declines after 6 hours. By day 5, sensitivity decreases to around 60%.

LUMBAR PUNCTURE (LP): Traditionally, an LP is performed if the non-contrast head CT is negative. Findings of SAH include an elevated opening pressure and an elevated RBC count. RBC count should be measured in tubes 1 and 4 to assess for clearance.

The presence of less than 2000×10^6/L red blood cells and the absence of xanthochromia excluded the diagnosis of aneurysmal subarachnoid hemorrhage, with a sensitivity of 100%, 95% CI (74.7-100%) and specificity of 91.2%, 95% CI (88.6, 93.3%) (Perry, BMJ 2015, PubMed ID: 25694274). Xanthochromia, a pink/yellow tint to the CSF, is a result of hemoglobin degradation products and is typically seen in the CSF within 2 hours of symptoms onset and may be present for up to 2 weeks. It can be assessed by visual inspection. A sample of CSF is compared to a CSF tube containing water against a white background in good lighting. Spectrophotometry may not be superior to visual inspection and is not typically available in the U.S. (Chu, Annals of EM, 2014, PubMed ID: 24635988).

MRI: Although not considered the standard care, proton density and FLAIR sequences may be as sensitive as NCHCT in identifying SAH.

DIAGNOSTIC TESTING: IDENTIFY CAUSE AND LOCATION OF SAH

CT/MR ANGIOGRAPHY: Non-invasive for identification of aneurysms. The downside is that aneurysms less than 3-5 mm may be missed. Overall, 14-22% will not have a cause identified on initial angiography and will require follow up in 4-14 days. Additionally, the prevalence of asymptomatic aneurysms increases with age so that an aneurysm may be identified that is not the cause of hemorrhage.

DIGITAL SUBTRACTION ANGIOGRAPHY: This is the gold standard for identifying the aneurysm. The test involves injecting dye into the bilateral vertebral, internal carotid arteries, external carotid circulation and deep cervical branches.

MANAGEMENT

Neurosurgical consultation should occur soon after diagnosis. Continuous hemodynamic monitoring is essential. Consider early intubation for airway protection with head of the bed elevation to 30 degrees to reduce intracranial pressure.

Management goals include: avoidance of hypoxemia, hypercapnia, metabolic acidosis, blood pressure instability, hyperglycemia, fever, and anemia. Minimize hemodynamic fluctuations to reduce re-bleeding. This Includes: bed rest, stool softeners and analgesia.

Seizure prophylaxis is controversial. Phenytoin use should be avoided as it has been associated with adverse outcomes. Anticoagulation should be reversed until definitive repair. Reversal of intracranial hemorrhage associated with antiplatelet therapy with platelet transfusion has been associated with worse outcomes (Baharoglu, PATCH Trial, Lancet 2016, PubMed ID: 27178479).

AIRWAY MANAGEMENT: Consider early Intubation for GCS < 8, elevated Intracranial Pressure (ICP), poor oxygenation or hypoventilation and hemodynamic instability.

MANAGEMENT OF INCREASED INTRACRANIAL PRESSURE: Initially management is with osmotic therapy. Avoid hyperventilation as it may precipitate or exacerbate vasospasm. Obtain emergent consultation for ventriculostomy in patients with hydrocephalus and signs of increased intracranial pressure. Elevate the head of the bed to 30 degrees.

BLOOD PRESSURE CONTROL: Multiple studies have shown no benefit to aggressive lowering off systolic blood pressure to less than 140 mm Hg. The recent AATACH-2 trial concluded that efforts to maintain blood pressure less than 140 mm/hg did not improve death or disability compared to standard therapy aim at maintaining systolic blood pressure less than 180 mm Hg (Quershi, NEJM 2016, PubMed ID: 27276234).

It is important to avoid vasodilators like nitroprusside or nitroglycerin, which act by increasing cerebral blood volume and thus ICP. Labetalol, and Nicardipine, are preferred. Management of hypertension must be closely balanced with the risk of hypotension which can lead to infarction (Cerebral Perfusion Pressure = Mean Arterial Pressure – Intracranial Pressure).

NIMODIPINE: In adults, this calcium channel blocker has been shown to improve outcomes, although the mechanism is unknown. It is hypothesized to reduce rates of vasospasm and subsequent ischemia stroke. The adult dosing is 60 mg PO Q4 hours for 21 days. Initiation requires careful monitoring of blood pressure.

INTRAVENOUS FLUIDS: Goal is euvolemia with monitoring for hyponatremia.

ANTIFIBRINOLYTIC THERAPY: Tranexamic acid and epsilon aminocaproic acid may be useful if definitive treatment of the aneurysm is delayed. They have been shown to reduce the incidence of re-bleeding but not to affect outcomes.

DEFINITIVE THERAPY

Definitive treatment is by aneurysm repair, which can be done either by surgical clipping (neurosurgery) or endovascular coiling or embolization (interventional neuroradiology).

PROGNOSIS

Long term morbidity may include neurocognitive dysfunction, epilepsy, and other focal neurologic deficits. In adults, 1/3 of patients have a good outcome, while 25% die within 24 hours and 45% within 30 days. The most important prognostic factors are level of consciousness on admission, patient age, and amount of blood on initial head CT. In the pediatric population, the clinical status on presentation appears to correlate most strongly with outcome.

HUNT AND HESS SCALE: SUBARACHNOID HEMORRHAGE GRADING		
CRITERIA	GRADE	MORTALITY
Mild headache, alert, oriented, minimal (if any) nuchal rigidity	I	30%
Full nuchal rigidity, moderate-severe headache, alert and oriented, no neurologic deficit (besides CN palsy)	II	40%
Lethargy or confusion, mild focal neurological deficits	III	50%
Stuporous, More severe focal neurologic deficit	IV	80%
Comatose, signs severe neurological impairment: posturing	V	90%

SYNCOPE

INTRODUCTION (KELLY CLEARY, M.D., 2/2020)
Syncope is defined as the temporary loss of consciousness and postural tone followed by spontaneous recovery. Syncope is the result of a transient disturbance of cerebral function due to inadequate delivery of oxygen or glucose to the brain. It is estimated that by the completion of adolescence, up to 50% of children will have had a syncopal event.

CAUSES OF SYNCOPE

While most causes of pediatric syncope are vasomotor in nature, life-threatening causes (typically cardiac in origin) must be excluded. All syncope associated with exertion or exercise should be considered dangerous.

DIFFERENTIAL DIAGNOSIS
AUTONOMIC
Vasovagal syncope (neurocardiogenic)
Volume depletion (orthostatic)
Reflex: Breath-holding, situational (cough, micturition)
Pregnancy
CARDIOVASCULAR
Structural heart disease: Tetralogy of Fallot, Hypertrophic cardiomyopathy, aortic stenosis, pulmonary hypertension, cardiac tamponade, arrhythmogenic R ventricular dysplasia
Tachyarrhythmias: Prolonged QT, Brugada, supraventricular tachycardia, WPW
Bradyarrhythmias: Atrioventricular blocks, sinus node dysfunction
METABOLIC
Transient hypoglycemia, hypoxia, carbon monoxide poisoning
OTHER
Drug/toxin, anemia, dehydration, hemorrhage (e.g. ectopic pregnancy)

VASOVAGAL SYNCOPE is also known as neurocardiogenic, reflex, or situational syncope and is the most common type of syncope. It is caused by an exaggerated Bezold-Jarisch reflex. Typically, vasovagal syncope occurs in the context of a patient with prolonged standing or sudden change from lying to standing. It begins with a decrease in systemic venous return and decreased preload. This, in turn, enhances sympathetic activity which increases left ventricular contractility. A negative feedback loop results in augmented vagal tone and sympathetic withdrawal.

Precipitating factors often include prolonged standing or stress and may include reflex responses to swallowing or micturition. Patients often describe a prodrome such as dizziness, lightheadedness, visual changes, weakness, nausea, pallor, facial flushing or diaphoresis.A full syncopal event can be avoided if the patient recognizes the prodrome and assumes a supine or Trendelenburg position.

ORTHOSTATIC SYNCOPE is a result of postural changes that may precipitate drops in blood pressure often in the setting of dehydration, anemia, pregnancy, or certain medications (diuretics, beta blockers, calcium channel blockers).

BREATH HOLDING SPELLS typically occur in children 6 months to 2 years and are benign in nature. Children may experience either pallid or cyanotic spells. A cyanotic spell occurs when the child holds his/her breath, becomes cyanotic, and then may have a brief loss of consciousness. Prolonged crying due to anger or frustration usually precedes cyanotic spells. Cyanotic spells result from a combination of hyperventilation with expiratory apnea and valsalva. Pallid spells result from vagally mediated cardiac inhibition typically after pain. In pallid spells, the loss of consciousness may precede the breath holding. Either may be associated with a short period of posturing or tonic-clonic activity. In contrast to seizures, incontinence and a post-ictal phase are not seen. See: PEM Guide: Neurology: Breath-Holding Spells.

TOXIC INGESTIONS should be considered in a patient with syncope. Intoxication may present as syncope from either a decrease in cardiac output or loss of consciousness. Carbon monoxide exposure can also cause syncope as a result of QT prolongation.

HYPOGLYCEMIA is a rare cause of syncope in patients without insulin dependent diabetes, but should be considered and evaluated by a bedside dextrose test.

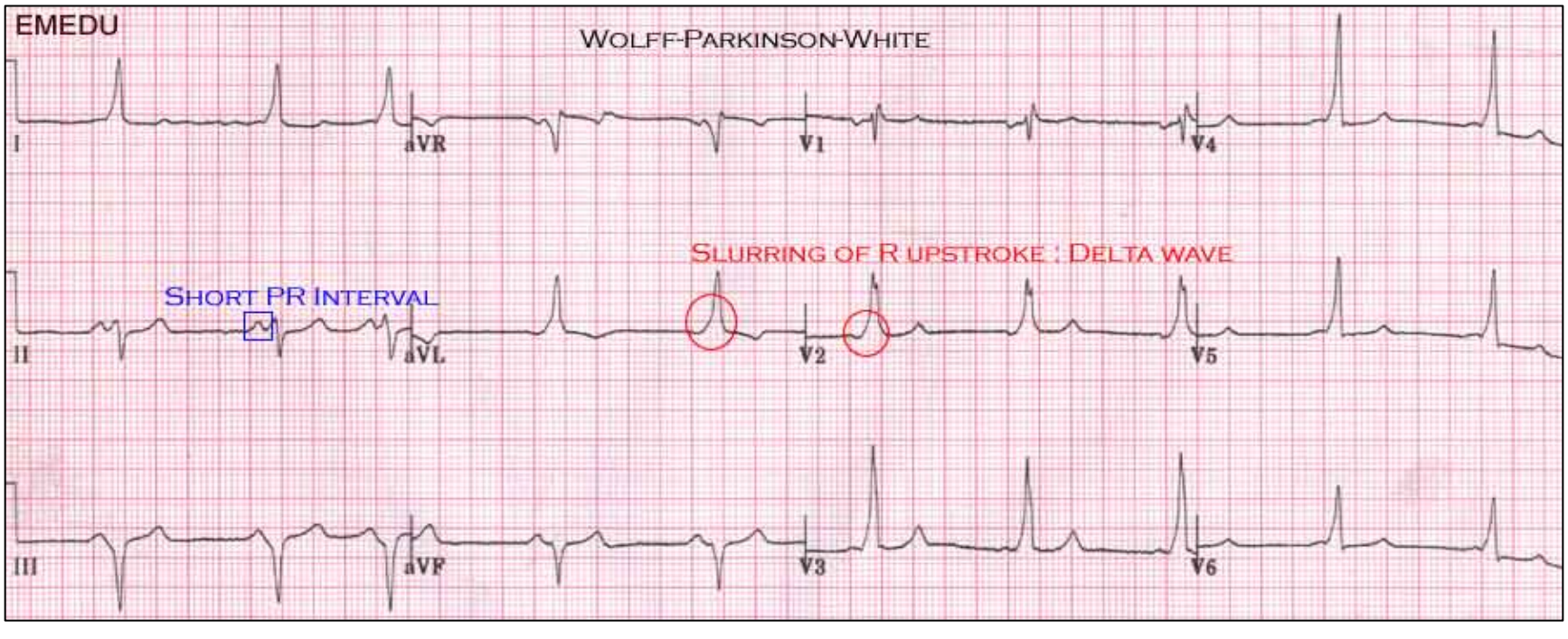
CARDIAC CAUSES OF SYNCOPE

Although less common that autonomic syncope, cardiac causes of syncope should be considered when syncope is associated with known heart disease, exertion, family history of early cardiac or unexplained death, an abnormal ECG or cardiac examination.

In a cohort study of 2,293 pediatric patients with a first episode of syncope, 9 (0.39%) had a cardiac etiology (Gupta, Clin Pediatr 2019, PubMed ID: 31709814). The presence of 1 of 4 screening questions identified all patients with a cardiac etiology of syncope with a sensitivity of 100%, 95% CI (70.1, 100%) and specificity of 86.3%, 95% CI (84.9, 87.7%). These included: 1. Past cardiac history, 2. Chest pain, 3. Syncope with exercise and 4. Absence of a prodrome prior to syncope.

WPW SYNDROME (WOLFF-PARKINSON WHITE) is a type of supraventricular tachycardia (SVT). EKG changes suggestive of WPW include a shortened PR interval and a slurring of the R wave upstroke (delta wave). A “pseudo-wide” QRS can also be found due to the delta wave.

WEB LINK: LITF EKG LIBRARY: WPW

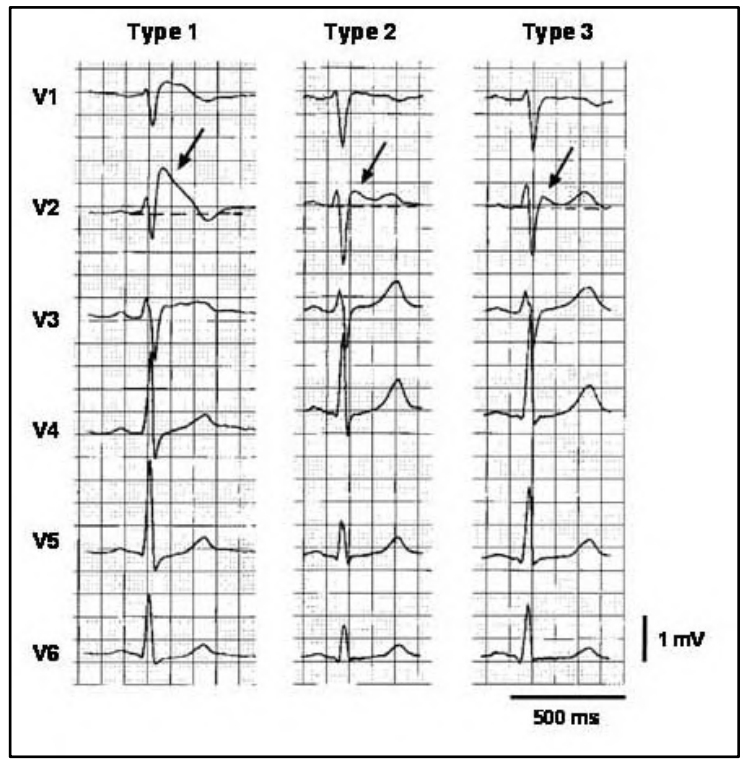


LONG QT SYNDROME may be responsible for 3,000 unexplained pediatric and adolescent deaths per year. Diagnosis is made by documenting a prolongation of the QT interval (generally greater than 0.45 seconds) determined by Bazett's formula (MD CALC). It is a disorder of myocardial repolarization that increases the risk of torsade de pointes (a polymorphic form of ventricular tachycardia).

WEB LINK: LITF EKG LIBRARY: QTC

It may be inherited or acquired. Two of the more common causes of inherited prolonged QT syndrome include Romano-Ward syndrome (purely cardiac, autosomal dominant) and Jervell and Lange-Nielsen syndrome (associated with sensorineural hearing loss, autosomal recessive). Acquired QT prolongation may result from electrolyte disturbances (hypokalemia, hypocalcemia). Numerous medications including some antiarrhythmics, antihistamines and psychotropic drugs may prolong the QT interval.

BRUGADA SYNDROME is a genetic defect in cardiac sodium channels. Patients have a characteristic pattern on EKG (pseudo-right bundle branch block and ST elevations in leads V1-V3). Brugada syndrome is associated with increased likelihood of sudden cardiac death from ventricular dysrhythmias.



WEB LINK: LITF EKG LIBRARY: BRUGADA

TYPE 1: Pronounced levation of the J point, a coved-type ST segment, and an inverted T wave in V1 and V2.
(The type 1 pattern is diagnostic of Brugada)

Type 2: Saddleback ST-segment elevated by >1 mm.

Type 3: ST segment is elevated <1 mm

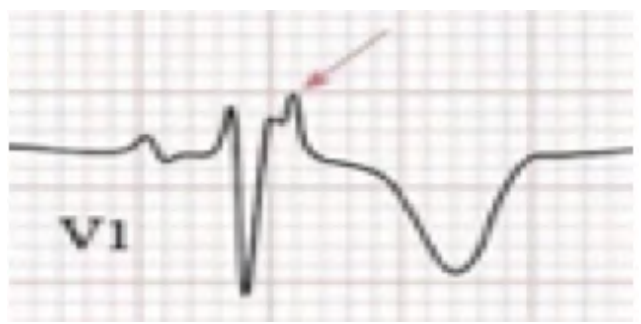
HYPERTROPHIC CARDIOMYOPATHY (HCM) is an autosomal dominant disorder that results in asymmetric hypertrophy of the left ventricle, which causes subaortic stenosis impeding left ventricular outflow. HCM patients are also at risk for a variety of atrial and ventricular dysrhythmias (ventricular tachycardia is the cause of death in 80%). Patients may experience exertional syncope. They may also present with palpitations, chest pain and signs of congestive heart failure. EKG changes may include signs of left ventricular hypertrophy, left axis deviation, prominent Q waves (due to septal hypertrophy) and deep T wave inversions in the inferior or lateral leads.

WEB LINK: LITF EKG LIBRARY: HCM

ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA (ARVD) is an inherited disorder characterized by fibrosis and fatty replacement of the right ventricle leading to ventricular dysrhythmias. It is the second leading cause of early cardiac death after HCM. The diagnosis is based on clinical, EKG and echocardiographic features. Symptoms include palpitations, syncope or cardiac arrest preceded by exercise. There is often a family history of early cardiac death. EKG findings are detailed in the table below. An epsilon wave is most specific (see in 50%). Visualization of epsilon waves can be enhanced with the use of Fontaine leads (RA→Manubrium, LA→Xiphoid, LL→V4). An echocardiogram, CT with RV contrast angiography or MRI will demonstrate the anatomy of the dysplastic right ventricle.

WEB: LITFL EKG LIBRARY: ARVD

EKG CHARACTERISTICS: ARVD
Epsilon wave: Small (+) deflection in end of QRS V1-4*
T wave inversion in V1-V3
S wave upstroke > 55 msec in V1-V3
QRS width > 110 msec in V1-V3
Ventricular tachycardia with LBBB morphology (RV)
*Also seen in posterior or RV MI, sarcoidosis,



EPSILON WAVE

CONDITIONS THAT MIMIC SYNCOPE

SEIZURES may often mimic syncope. Careful attention to history including prolonged tonic-clonic activity, incontinence, post-ictal state, may help in differentiating the two. See: PEM Guide: Neurology: Status Epilepticus

MIGRAINE HEADACHES, particularly basilar and vestibular migraines may also mimic syncope including loss of consciousness, vertigo, and ataxia. Patients will generally have additional symptoms including headache and nausea.

HYPERVENTILATION/ANXIETY often associated with emotional stress can occur more frequently in adolescent patients. Patients frequently describe chest pain, shortness of breath, along with the usual prodromal symptoms for vasovagal syncope. See:: PEM Guide: Neurology: Breath Holding Spells

CLINICAL EVALUATION

A thorough history assessment of potential inciting factors should be completed. A complete physical examination with an emphasis on the cardiovascular and neurologic exam is essential. Trauma related to the fall (if any) should be evaluated.

HISTORY
Associated with: Exertion?
Associated with: Chest pain, palpitations, shortness of breath?
Associated with: Prolonged loss of consciousness, tonic-clonic movements?
Family history of unexplained death, early cardiac death or arrhythmias?
Symptoms induced by standing up?
Pregnant?
Recent medications, drugs, toxic exposures?
Proceeded by dizziness, weakness, sweating, nausea?
Anxiety? stressors?

CARDIAC EVALUATION: The patient should be placed on continuous cardiac monitoring with pulse oximetry. An EKG should be performed on all initial evaluations of syncope. If structural heart disease is suspected (HCM, ARVD, severe aortic stenosis) an echocardiogram and cardiology consultation would be useful.

LABORATORY TESTING: A bedside glucose determination and pregnancy test should be performed. Consider CBC, electrolytes, carboxyhemoglobin level, and toxicology screen based on the patient's history and exam.

DISPOSITION

Therapy is guided by the etiology of the patient's syncope. If vasovagal syncope or breaths holding spells are suspected, reassurance of the benign nature should be given. It is important for patients/ parents to recognize the prodromal signs to avoid further episodes. If symptomatically orthostatic, fluids should be initiated. If a seizure is suspected, an EEG and neuroimaging may be useful. Children with recurrent, unexplained syncope may be referred for outpatient tilt-table testing.

Findings on cardiac exam and/or EKG warrant cardiac consultation. A history concerning for cardiac etiology (e.g. family history of early sudden death, syncope with exertion) also warrant cardiac consultation, though may be done as an outpatient if EKG and cardiac exam are within normal limits.

INDICATIONS FOR SUBSPECIALTY* CONSULTATION
Syncope associated with exertion
Recurrent, unexplained syncope
Syncope associated with chest pain, palpitation, arrhythmia
Syncope associated with abnormal cardiac history, exam or EKG
Syncope associated with a history of early cardiac or unexplained death in the family
Suspected seizure: Post-ictal period, tonic-clonic movements, incontinence(Neurology)
Abnormal neurologic examination (Neurology)
Acute toxic ingestion (Toxicology)
*Cardiology unless otherwise specified

WEAKNESS

INTRODUCTION (MICHAEL MOJICA, M.D. 4/2021)
Weakness refers to the loss of ability to move muscles against resistance. In contrast, tone refers to the resting state of muscle without patient effort. Weakness may be generalized or localized to a specific area of the body. Weakness may result from lesions to brain, spinal cord, peripheral nerves, neuromuscular junction or muscle.

GRADING MOTOR STRENGTH	
0/5	No muscle movement
1/5	Visible muscle movement, but no movement at the joint
2/5	Movement at the joint, but not against gravity
3/5	Movement against gravity, but not against added resistance
4/5	Movement against resistance, but less than normal
5/5	Normal strength

WEAKNESS: DIFFERENTIAL DIAGNOSIS (PARTIAL)			
Cerebral Cortex	Hemorrhage	Peripheral Nerve	Guillain-Barre
	Stroke		Toxins
	Tumor		Trauma
	Seizure (post)	Neuromuscular Junction	Botulism
	Migraine		Myasthenia gravis
Spinal Cord	Trauma		Organophosphates
	Tumor		Snake envenomation
	Abscess		Tic paralysis
	Discitis	Muscle	Rhabdomyolysis
	Transverse myelitis		Myositis
	Poliomyelitis		Periodic paralysis
			Electrolyte abnormalities

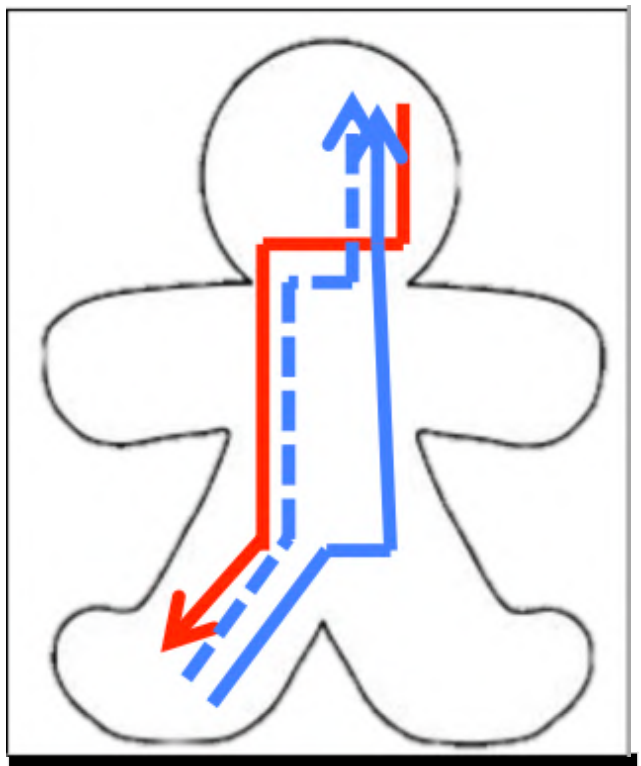
ANATOMIC LOCALIZATION (SEE APPENDIX)
The goal of assessment is to localize and identify the source of weakness. Localization of the lesion and identification of its cause will allow for prompt diagnostic imaging and targeted therapy. Emergency therapy is indicated for a spinal cord or brain lesion requiring surgical decompression and for those patients whose weakness results in respiratory compromise. Anatomic localization requires knowledge of the major motor and sensory pathways and where they cross in the central nervous syndrome.

PRIMARY MOTOR AND SENSORY PATHWAYS		
TRACT	DEFICIT	CROSSES
Corticospinal	Motor	Medulla
Spinothalamic	Sensory (Solid): Pain, Temp, Crude Touch	Spinal Cord
Dorsal Columns	Sensory (Dashed): Proprioception, Vibration. Light Touch	Medulla

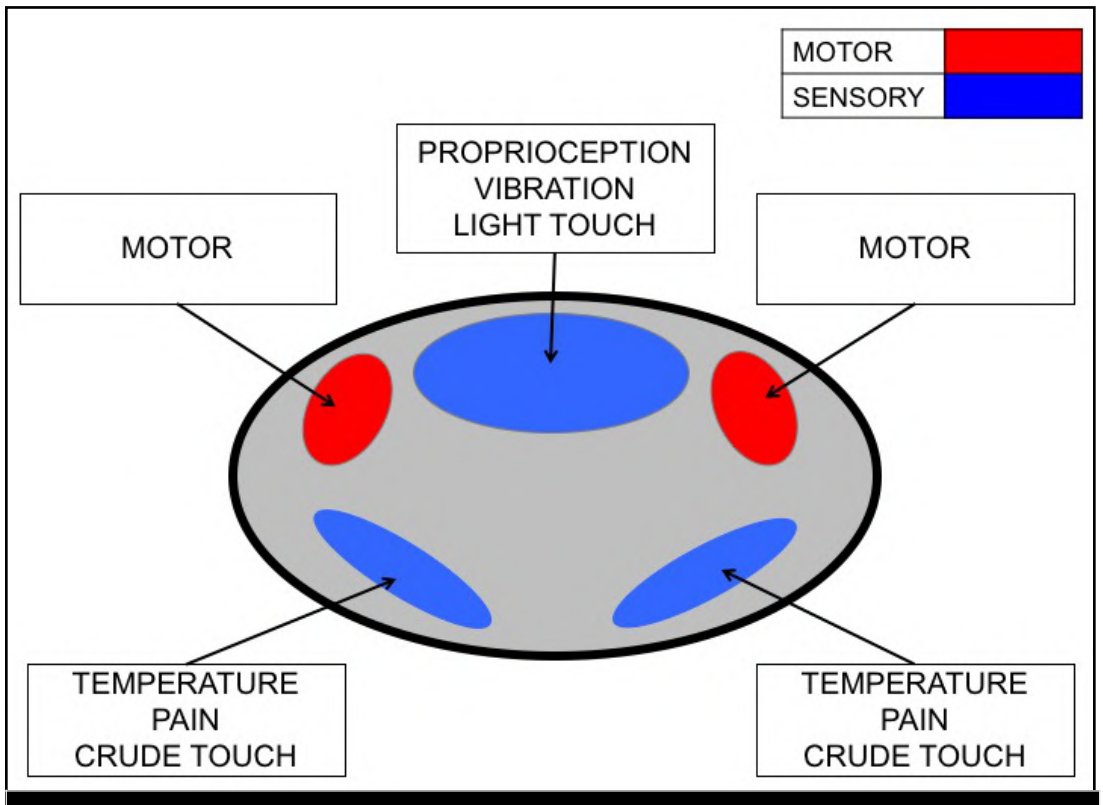
BRAIN
Bilateral lesions of the brain results in complete loss of function below the lesion. A unilateral lesion to the brain (stroke, intracranial hemorrhage) will results in contralateral loss of motor and sensory function. CNS lesions are typically associated with altered mental status and cranial nerve deficits.

SPINAL CORD
The spinal cord is divided into a number of pathways with specific functions. Motor tracts (corticospinal) are descending and cross in the medulla. Sensory tracts are ascending and cross in the medulla (dorsal columns) or the spinal cord (spinothalamic). Patterns of sensory and motor loss aid in localizing a lesion

Complete spinal cord injury results in complete bilateral loss of motor and sensory function below the level of the lesion. A sensory level is indicative of a spinal cord lesion. Incomplete spinal cord injury results in a variable pattern of sensory and motor loss that depends on the location of the lesion.

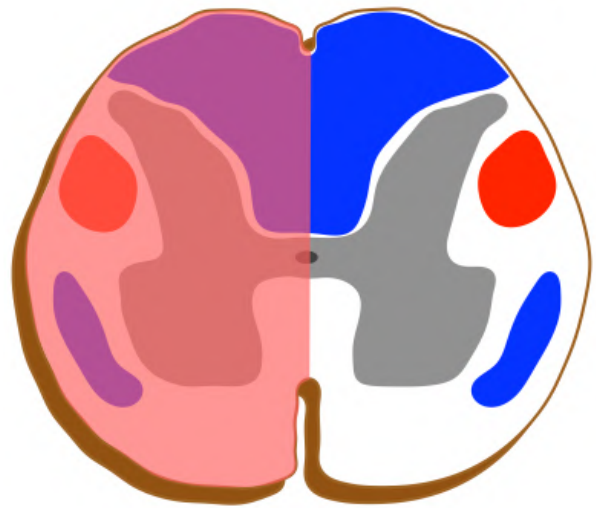


PRIMARY TRACTS



SPINAL CORD TRACTS

LATERAL CORD (BROWN-SEQUARD

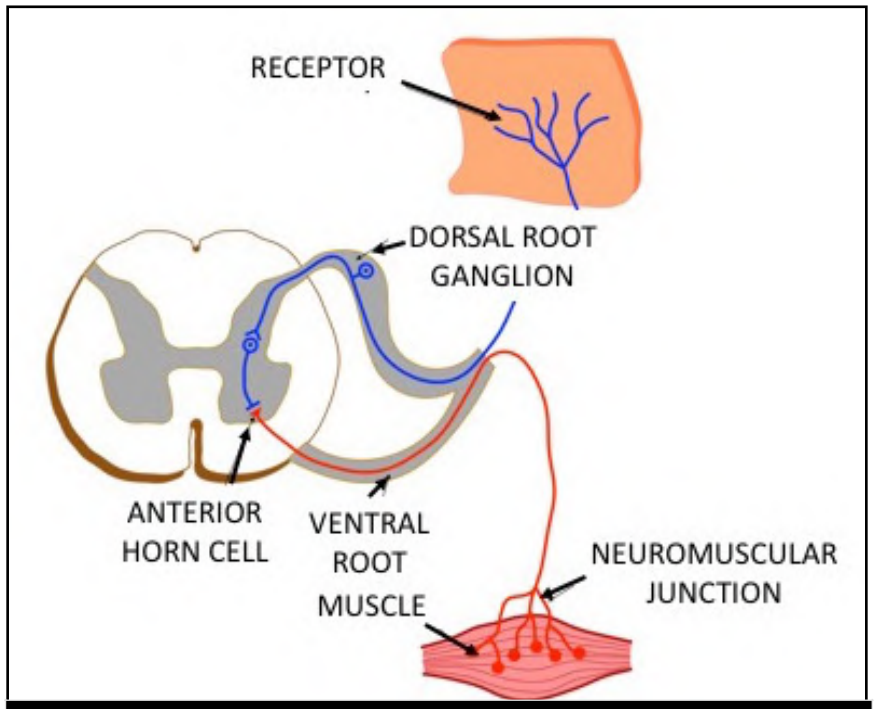


	IPSA-LATERAL	CONTRA-LATERAL
Motor	X	Y
Pain Temperature	Y	X
Proprioception Vibration	X	Y

INCOMPLETE SPINAL CORD SYNDROMES	
Anterior cord	Bilateral loss: Motor
	Bilateral loss: Pain, Temperature
	Preservation: Proprioception and Vibration
Posterior cord	Bilateral loss: Motor
	Bilateral loss: Proprioception, Vibration
	Preservation: Pain, Temperature
Brown-Sequard (Lateral Hemisection: R or L)	Ipsilateral loss: Motor function
	Ipsilateral loss: Proprioception, vibration
	Contralateral loss: Pain and Temperature
Central cord (central to peripheral = Cervical → Thoracic → Lumbar → Sacral)	Bilateral motor weakness: Upper > Lower extremities
	Bilateral motor weakness: Distal > Proximal
	Sensory loss variable, sacral sensory sparing
	Pain, Temperature sensation > proprioception, vibration.

MOTOR NEURONS

Upper motor neurons from the brain synapse with lower motor neurons in the spinal cord. Lower motor neurons exit the ventral spinal cord to join with the sensory nerve to form the peripheral nerve. Lower motor neurons (LMN) are excitatory resulting in increased activity. LMN lesions result in decreased activity (hypotonia, absent DTR's). These are classified according to the location of the lesion.



UMN → LMN → PERIPHERAL NERVE

LOCATION	EXAMPLE
Anterior (ventral) horn cell	Poliomyelitis, Werdnig Hoffman, Acute flaccid myelitis
Peripheral nerve	Guillain-Barre, Radiculopathy
Neuromuscular junction	Myasthenia, Tic paralysis, botulism, organophosphates
Muscle (i.e. myopathy)	Muscular dystrophies, Myopathies

UPPER MOTOR DISEASE	
Hemiplegia (one side)	Brain Infarction
	Brain Hemorrhage
Paraplegia (lower half)	Spinal Cord Compression
	Spinal Artery Occlusion
	Transverse Myelitis

	UPPER MOTOR NEURON	LOWER MOTOR NEURON
Weakness	Asymmetric	Symmetric
Muscle Tone	Increased	Decreased
DTR’s	Increased	Decreased
Babinski	Up	Down
Muscle Atrophy	No	Yes
Fasciculations	No	Yes

TRANSVERSE MYELITIS (SPINAL CORD)

Transverse myelitis is caused by inflammation across both sides of one level, or segment, of the spinal cord (transverse: across the width of the spinal cord). Spinal cord inflammation (myelitis) can damage or destroy myelin. Transverse myelitis has a number of etiologies including: para-infectious (autoimmune response to a viral of bacterial infections), a systemic autoimmune response (Lupus, Multiple sclerosis), para-neoplastic and vascular (thrombus, AVM). Ataxia may be present as well. The disease may rapidly progress (45% worsen in 24 hours). Though the diagnosis is primarily clinical, an MRI may be helpful in identifying the etiology.

PRESENTATION
Weakness of the legs and arms
Radicular back or neck pain
Sensory alteration (paresthesias)
Bowel and bladder dysfunction.

MANAGEMENT: The management of transverse myelitis is primarily supportive. Treatment with corticosteroids is typically initiated though the data do not suggest an improvement in outcome.

ACUTE FLACCID MYELITIS (SPINAL CORD)

AFM is an acquired disorder of the anterior horn cells in the grey matter of the spinal cord. Disease is similar to that of poliovirus. Recently, enterovirus D68 outbreaks have been most commonly implicates though other virus and immune mediated disorders can also be etiologic. An upper respiratory tract infection commonly precedes the development of weakness of one or more extremities. Sensation is typically intact. Altered mental status and cranial nerve involvement may also occur. Diagnosis is made by identification of spinal cord lesion on MRI with and without contrast. The cervical cord is most commonly involved. CSF analysis demonstrated a lymphocytic pleocytosis and a mildly elevated protein. Virus has not been identified in the CSF.

MANAGEMENT: Ventilatory support may be required. Immune modulating therapies include intravenous immune globulin and corticosteroids.

ACUTE POLYNEURITIS (GUILLAIN-BARRE) (PERIPHERAL NERVE)

Acute polyneuritis is an acute demyelinating polyneuropathy often preceded by upper respiratory or gastrointestinal symptoms 1-2 weeks prior to onset. Presentation includes symmetric lower extremity weakness progressing proximally (ascending paralysis) with absent deep tendon reflexes. Cranial nerve involvement is common. Autonomic dysfunction (labile blood pressure and urinary/bladder incontinence) may be seen.

Up to 85% of patients achieve recovery within 6-12 months. The Miller-Fisher Variant includes ataxia, ophthalmoplegia (usually diplopia) and areflexia with or without motor weakness. Thoracic involvement is most common though other levels may occur as well. The level involved will result in different patterns of presentation. A lesion at one level will results in symptoms below the level of the lesion. For example, thoracic involvement will result in deficits at the lumbar and sacral levels as well.

LEVEL OF LESION	
Cervical	Neck, arms, hands, diaphragm
Thoracic	Torso, some part of the arms
Lumbar	Hips, legs
Sacral	Groin, toes, some parts of the legs

DIAGNOSTIC TESTING: CSF analysis may reveal albuminocytologic dissociation. This is an elevated or rising protein level on serial lumbar punctures and 10 or fewer mononuclear cells/mm^3. However, normal CSF protein level does not exclude GBS. Early in the disease course CSF protein may be normal in 10% of patients.

Laboratory screening includes electrolyte levels; liver function tests, erythrocyte sedimentation rate and a stool culture for Campylobacter jejuni. Additional testing may include: antiganglioside antibodies; and antibodies to C jejuni, cytomegalovirus, Epstein-Barr virus, herpes simplex virus, HIV, and Mycoplasma pneumoniae. An EKG may reveal first, second-degree or third-degree heart blocks, T-wave abnormalities, ST depression, QRS widening, and a variety of rhythm disturbances.

MANAGEMENT: Intravenous immune serum globulin (IVIG) and plasma exchange have proven effective in shortening recovery time. IVIG is easier to administer and has fewer complications than plasma exchange. Combining of the two therapies does not improve outcomes. Corticosteroids are ineffective as monotherapy. In combination with IVIG, intravenous methylprednisolone may hasten recovery without affecting the long-term outcome.

GUILLAIN-BARRE: ED MANAGEMENT
ABC’s, O_2, Intravenous access
Monitor respiratory status: Negative inspiratory flow, early intubation for distress
EKG: Monitor for dysrhythmias
Atropine for symptomatic bradycardia
External pacing for 2^{nd}, 3^{rd} degree heart blocks
Treat hypotension with intravenous fluids, positioning
Treat hypertension with short acting antihypertensives
Intravenous immune globulin (IVIG): 0.4 grams/kg/day x 5 days

	TRANSVERSE MYELITIS	ACUTE POLYNEURITIS
BACK PAIN	YES	NO
LESION	Upper motor neuron Brisk DTR's	Lower motor neuron Absent DTR's
SENSORY LEVEL	YES	NO
CSF DISSOCIATION	NO	YES

TICK PARALYSIS (NEUROMUSCULAR JUNCTION)

A toxin is released from dog and wood tics that blocks acetylcholine release. Generalized paralysis occurs within 12-48 hours. There are decreased or absent deep tendon reflexes. There is no sensory loss or increased CSF protein. Removal of the tic is curative.

MYASTHENIA GRAVIS (NEUROMUSCULAR JUNCTION)

Myasthenia gravis is the result of blocked acetylcholine receptors at the neuromuscular junction. It may occur in the neonate due to maternal antibodies. It may also be caused in neonates due to autoimmune disease or congenitally (genetic). In juveniles, is it caused by autoimmune disease. The juvenile form has a mean onset of 8 years with a female to male preponderance of 4:1. Onset may be acute or insidious. Presentations include: ptosis, diplopia or blurred vision (EOM weakness) and generalized weakness. The hallmark of illness is weakness that progresses with continued activity. Deep tendon reflexes are intact. Patients should be monitored closed due to the risk of respiratory compromise from respiratory muscle fatigue.

Serologic antibody testing has replaced the use of Tensilon (Edrophonium), a short acting acetylcholine esterase inhibitor, for the diagnosis of myasthenia gravis. Anti-acetylcholine receptor antibodies are present in 85% of patients with generalized disease and 98-100% with thymoma.

Treatment of myasthenia involves the use of anticholinesterase agents such pyridostigmine (Mestinon). Severe cases may require immunosuppressant agents, plasmaphoresis or thymectomy.

BOTULISM (NEUROMUSCULAR JUNCTION)

Botulism results from toxin release from the spores of Clostridium botulinum. The toxin inhibits release of acetylcholine at terminal nerve fibers. The three forms of botulism are wound, food-born and infant.

Infant botulism is caused by GI tract colonization with botulinum spores. It has been commonly associated with contaminated honey in the past but has become less common due to parental education. It is recommended that infants less than 1 year not consume honey. Infants present with constipation, difficulty sucking and hypotonia. A descending symmetric paralysis with cranial nerve involvement may ensue. The primary clinical concern is to provide respiratory support. The toxin may be isolated from stool. Intravenous botulism immunoglobulin is efficacious at reducing length of stay but should be given early in the disease course. It can be obtained from the CDC. Antibiotics are not recommended for infant botulism as cell lysis may result in more toxin release.

Food-born botulism results from improperly canned foods. Vomiting and diarrhea precede neurologic symptoms. Cranial nerve findings (blurred vision, diplopia, dysarthria) are classic and are often followed by generalized weakness.

Wound botulism results from a contaminated wound. Clinically it is difficult to distinguish from food-born botulism. Treatment includes antibiotics (Penicillin G or Metronidazole) and debridement. Antitoxin may be useful.

PERIODIC PARALYSIS (MUSCLE)

Periodic paralysis is due to a metabolic myopathy. The three primary etiologies are hypokalemia, hyperkalemia and normokalemia.

Hypokalemic paralysis has an onset between 10-20 years. Paralysis begins proximally and extends distally. Treatment with potassium is beneficial

Hyperkalemic paralysis occurs intermittently between 10-20 years. Rest followed by heavy activity may provoke episodes. The respiratory muscles are typically spared.
Normokalemic paralysis can be caused by exposure to alcohol, cold and activity. Treatment with sodium may improve weakness.

APPENDIX: LESION LOCALIZATION

CLINICAL APPROACH

Where is the lesion?

CNS, Spinal Cord, Peripheral nerve, Neuromuscular junction, Muscle
Allows for targeted neuroimaging, differential diagnosis

What is the cause of the lesion?

Does the lesion need to be surgically decompressed?
Does the weakness affect the patient's respiratory effort?
Are there medical therapies that can improve prognosis?

LESION ANATOMIC LOCALIZATION: GENERAL RULES				
LOCATION	MOTOR	SENSORY	REFLEXES	OTHER
Brain	Contralateral	Contralateral	Increased	Altered mental status Cranial nerves involved
Spinal cord	Ipsilateral	Contralateral	Increased or Decreased	Sensory level Bowel, bladder dysfunction
Peripheral Nerve	Distal > Proximal	Glove, Stocking	Decreased	
Neuromuscular Junction	Generalized	Normal	Decreased	
Muscle	Proximal > Distal	Normal	Normal or Decreased	Muscle pain, tenderness

BRAIN

Bilateral CNS lesions result in complete deficits in motor and sensation
Unilateral CNS lesions result in contralateral deficits in motor and sensation

SPINAL CORD

A sensory level is indicative of a spinal cord injury

Hyporeflexia occurs initially due to spinal shock then hyperreflexia occurs

A complete spinal cord injury results in bilateral motor and sensory deficits and autonomic dysfunction (bowel, bladder) below the level of the lesion

Incomplete spinal cord lesions will present with varying motor and sensory deficits depending on which area of the spinal cord is involved

Know the 3 primary spinal cord tracts/columns
Where they are located in the cord
Whether they are sensory or motor
Where they cross

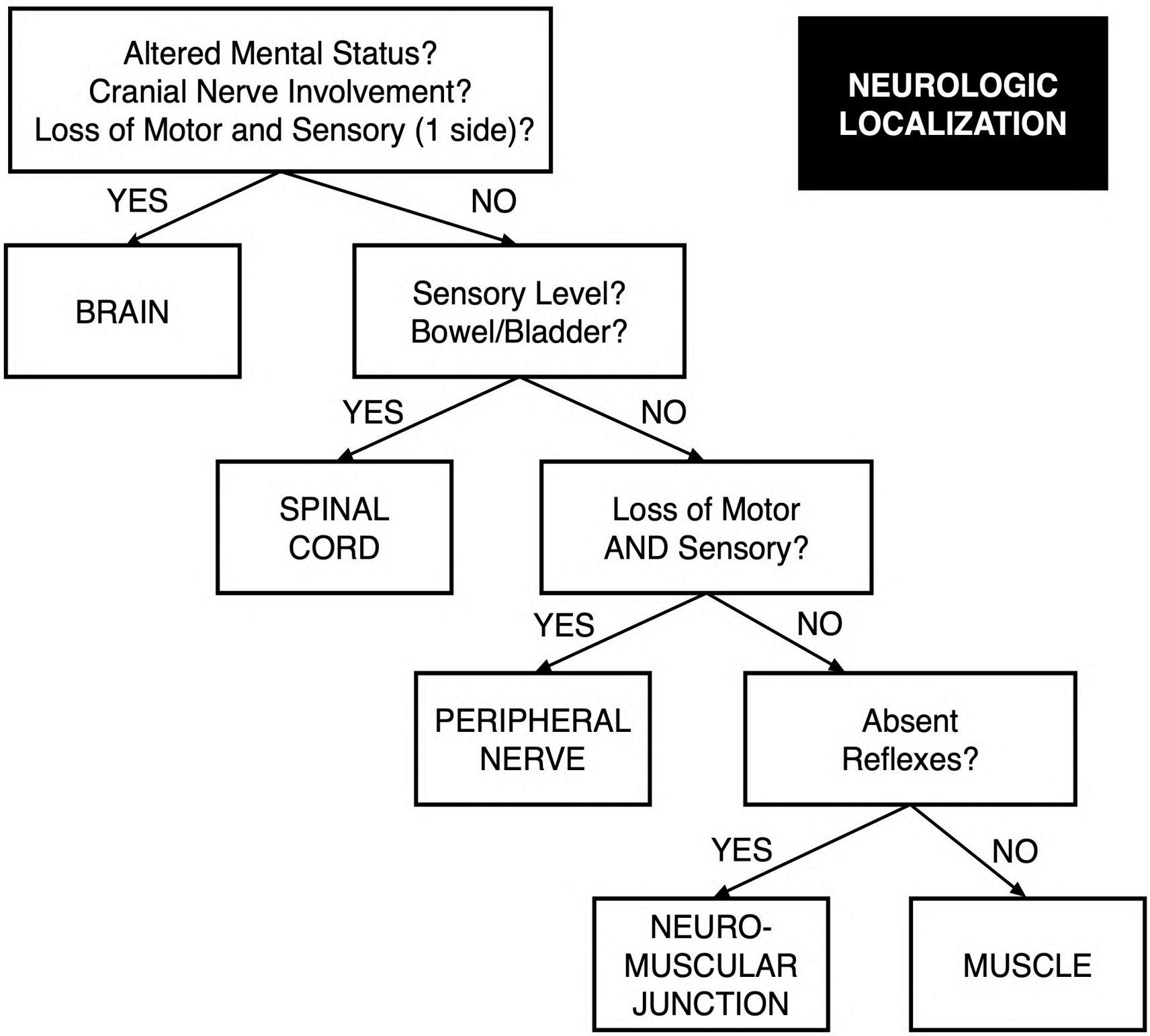
1. Dorsal Cord: Dorsal Columns: Ascending Light Touch, vibration and proprioception
2. Posterior Lateral Cord: Corticospinal Tract: Descending motor
3. Anterior Lateral Cord: Spinothalamic Tract: Ascending Crude touch, pain, temperature

PERIPHERAL NERVE vs NEUROMUSCULAR JUNCTION vs MUSCLE

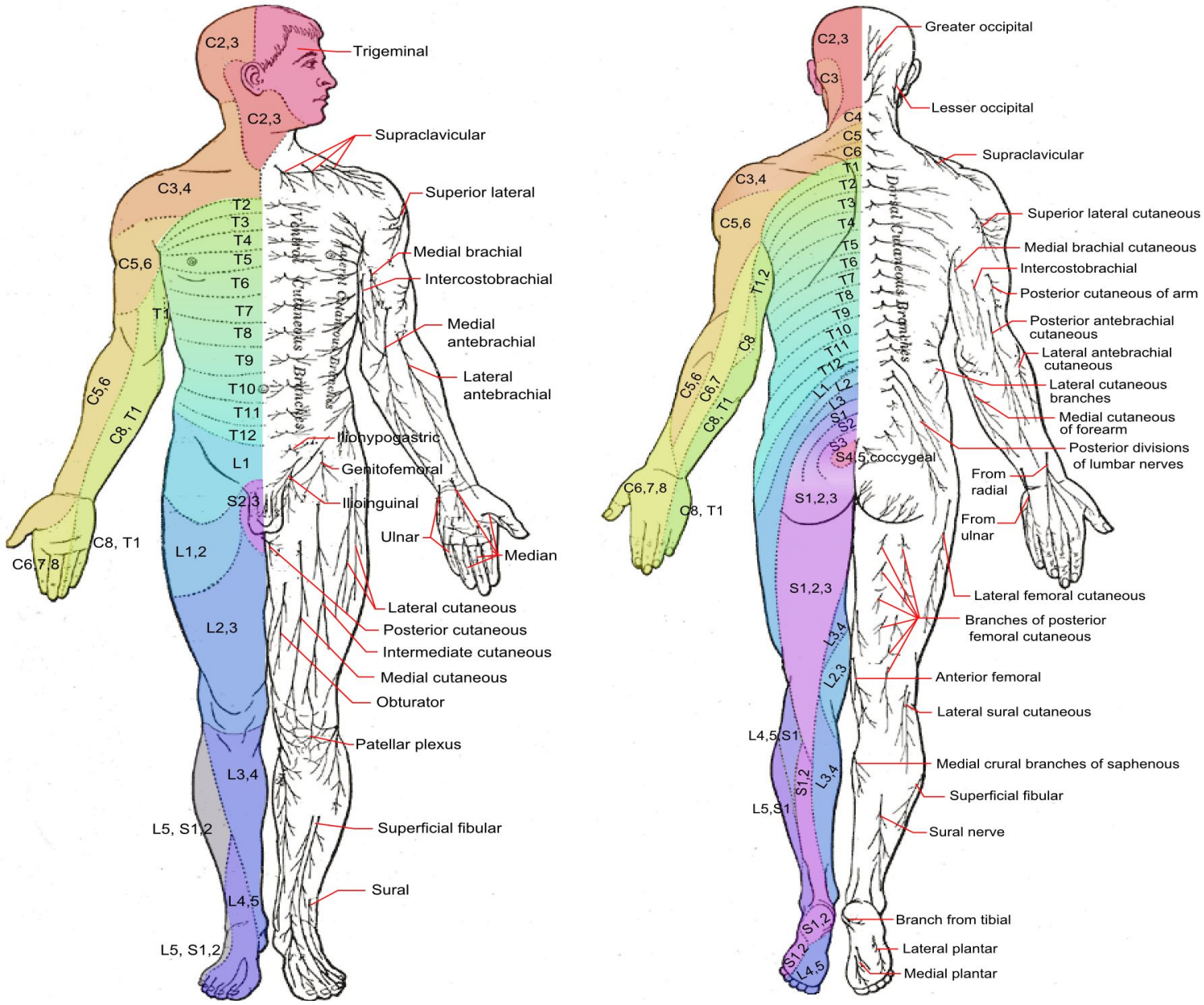
1. A sensory deficit can distinguish between a peripheral nerve lesion and lesions at the neuromuscular junction and muscle lesions
   a. Peripheral nerve lesions are associated with a sensory deficit
   b. Neuromuscular junction and muscle lesions are not associated with a sensory deficit

2. Reflexes can be used to distinguish between upper and lower motor neuron lesions
   a. Lesions at the neuromuscular junction result in the absence of reflexes
   b. Muscle lesions are associated with normal reflexes (unless the myopathy is severe enough that the muscle can't contract)

3. Whether weakness if greatest proximally or distally can distinguish between peripheral nerve and muscle lesions.
   a. Weakness is greatest distally for a peripheral nerve lesion
   b. Weakness is greatest proximally for a muscle lesion



APPENDIX: DERMATOMES, MYOTOMES AND REFLEXES



MYOTOMES			
UPPER LIMBS		LOWER LIMBS	
C5	Elbow flexors	L2	Hip flexors
C6	Wrist extensors	L3	Knee extensors
C7	Elbow extensors	L4	Ankle dorsiflexion
C8	Finger flexors	L5	First toe extensor
C9	Finger abductor	S1	Ankle plantar flexor

REFLEXES		
MUSCLE	NERVE	SPINAL NERVE
Biceps	Musculoskeletal	C5-6
Brachioradialis	Radial	C5-6
Triceps	Radial	C7-8
Patella	Femoral	L2-4
Hamstring	Sciatic	L5, S1-2
Ankle	Tibial	S1-2

OBSTETRICS & GYNECOLOGY

ANORMAL UTERINE BLEEDING

INTRODUCTION (AMANDA SCHNEIDER, M.D., CHANELLE COBLE, M.D., 2/2022)
Abnormal uterine bleeding (AUB) affects up to 40% of adolescents and is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency, or duration. Importantly, it refers to bleeding that occurs in the absence of pregnancy. The terminology can be confusing and therefore the American Congress of Obstetricians and Gynecologists has endorsed the term “Abnormal Uterine Bleeding” which can be divided into heavy menstrual bleeding (HMB) and inter-menstrual bleeding. HMB is defined by ACOG as greater than or equal to 80 ml of total blood loss or 7 days of bleeding. They emphasize that this interferes with “a women’s physical, social, emotional and material quality of life”. Normal menstrual cycles in adolescents and young women can occur at intervals of 21–45 days, with a duration of bleeding of up to 7 days, and normal flow as requiring 3–6 menstrual pads or tampons per day.

DEFINITIONS: PREVIOUSLY USED TERMS	
Dysfunctional Uterine Bleeding (DUB)	Irregular, painless bleeding of endometrial origin that is prolonged, un-patterned, and excessive; it may be due to physiologic or pathologic anovulation
Dysmenorrhea	Painful menstruation
Menorrhagia	Heavy or prolonged uterine bleeding
Menometrorrhagia	Irregular and prolonged bleeding
Oligomenorrhea	Infrequent and irregular bleeding

DIFFERENTIAL DIAGNOSIS

The mnemonic PALM-COEIN can be used to review the differential diagnosis of abnormal uterine bleeding. In adolescents, ovulatory dysfunction and coagulation disorders make up the majority of cases.

DIFFERENTIAL DIAGNOSIS: ABNORMAL UTERINE BLEEDING	
STRUCTURAL: PALM	
Polyp, Adenomyosis, Leiomyoma, Malignancy	
NON-STRUCTURAL: COEIN (common in adolescence)	
Coagulopathy	von Willebrand disease, platelet dysfunction/thrombocytopenia, factor deficiency
Ovulatory dysfunction	Hypothalamic-pituitary-ovarian axis: Anovulation Endocrine: Polycystic ovary syndrome, Hyperprolactinemia, thyroid dysfunction
Endometrial	Sexually transmitted infections
Iatrogenic	Intrauterine devices, hormonal contraceptives
Not	Not otherwise classified

Anovulation is due to the immaturity of the hypothalamus-pituitary-ovarian axis. The endometrial lining gets thicker than usual and there is heavy bleeding when a period does occur. The majority of patients with anovulation do not meet the definition of heavy menstrual bleeding.

Up to 20% of adolescent girls with heavy menstrual bleeding have an underlying bleeding disorder and heavy menstrual bleeding is often the first sign of a bleeding disorder in patients without prior surgery or dental extraction. The most common bleeding disorders include von Willebrand disease, thrombocytopenia or platelet function defects and clotting factor deficiencies.

CLINICAL PRESENTATION

Vital signs and orthostatics should be assessed to establish hemodynamically stability. Those with long standing bleeding may be significantly anemic without a reduction in circulating plasma volume. Patients should be at least Tanner stage III to have menstrual bleeding. Trauma should be expected and an external vaginal exam should be completed if Tanner III stage has not been attained.

A complete history including the focused questions in the table below and a complete physical examination including a pelvic examination should be performed on every patient. Initial history is aimed at distinguishing between focal gynecologic bleeding and more systemic causes of bleeding. It is important to differentiate uterine from vaginal and gastrointestinal causes of bleeding. Non-uterine causes of bleeding can include vaginal trauma, urethral prolapse and hemorrhoids.

The volume of blood loss can be estimated by the frequency of use of absorbent devices. Alternatively, two questions can be asked. Have you absorbed through a pad or tampon in less than 1-2 hours? and have you soaked through bedding?

FOCUSED HISTORY	
MENSTRUAL	Age of menarche Gynecological age = Current age – Age of Menarche Length of cycle, days of menstrual bleeding Last menstrual period (LMP) Associated symptoms
SEXUAL	Age at first intercourse (Coitarche) Date of last intercourse, contraception used at last intercourse History current and past contraception History STI, last STI/HIV testing History pregnancy Number of partners History of trauma, abuse
MEDICAL	Epistaxis, gingival bleeding, easy bruising History of transfusions, iron deficiency, symptomatic anemia Prolonged bleeding after procedures (e.g. dental, surgical) Family history of bleeding or endocrine disorders

DIAGNOSIS

The first consideration in any patient with vaginal bleeding is to determine if the cause is pregnancy related. In early pregnancy, the primary concerns are ectopic pregnancy and spontaneous abortion (See PEM Guide: Obstetrics and Gynecology: First Trimester Vaginal Bleeding). After excluding pregnancy, laboratory evaluation should focus on assessing for anemia, coagulopathy and endocrine disorders.

QUANTIFYING MENSTRUAL BLEEDING: ABSORBENCY			
Tampon	6-9 ml	Menstrual cup	30 ml
Disposable sanitary napkin	5-10 ml	Period pants	10 ml
Night-time sanitary napkin	15 ml	Cloth sanitary towel	5-10 ml

DIAGNOSTIC EVALUATION
ALL PATIENTS
CBC, Iron studies (ferritin, iron)
Type and Screen
Beta HCG: Quantitative if suspect pregnancy
Screen for HIV, Gonorrhea, Chlamydia if sexually active
BLEEDING DISORDER
Coagulation profile (PT, PTT), fibrinogen
von Willebrand Disease panel: vWF activity and antigen
Factor VIII
ANOVULATION/ENDOCRINE DISORDER
Thyroid function tests (TSH and fT4)
Prolactin, LH, FSH, free and total testosterone, androstenedione, DHEA-S
CONSIDER PELVIC ULTRASOUND
Positive pregnancy test with vaginal bleeding or abdominal/flank/back pain
Unexplained pain (ovarian cyst rupture, ovarian torsion)
Suspicion of pelvic inflammatory disease with a tubo-ovarian abscess
Pelvic mass palpable
Abnormality on the gynecologic exam
Suspected polycystic ovarian syndrome

MANAGEMENT

The management options discussed below are predicated on the fact that the patient is not pregnant and interventions are guided by the patient's hemodynamic status. The goals of care are to address the underlying cause of bleeding and replete iron stores. Gynecology, hematology, endocrine, adolescent medicine or child protection consultation may be indicated depending on the cause of bleeding. In the absence of estrogen contraindications (see table below), a combination oral contraceptive pill with 30-50 mcg of ethinyl estradiol every 6-8 hours until bleeding stops and then a taper. Antiemetics should be prescribed to combat the nausea due to high dose estrogen. If estrogen is contraindicated, substitute progesterone in the form of Medroxyprogesterone 10 mg Q4-6 hours or Norethindrone 20 mg Q8 hours to control bleeding and then taper. All patients should be started on iron supplementation and a stool softener.

NOT ACTIVELY BLEEDING (ONE OF THE FOLLOWING OPTIONS)	
Monophasic Oral Contraceptive Pills	Estrogen <u>not</u> contraindicated (table below): • Norgestrel 0.3 mg/Ethinyl Estradiol 30 mcg • Levonorgestrel 0.15 mg/Ethinyl Estradiol 30 mcg • Norgestimate 0.25/Ethinyl Estradiol 35 mcg
Progesterone Therapy	Estrogen contraindicated (table below): • Medroxyprogesterone 10 mg PO daily x 10-12 days • Norethindrone acetate 5-10 mg PO daily
Tranexamic Acid	1,300 mg PO TID for up to 5 days during menses

ACTIVELY BLEEDING		
ANEMIA	INTERVENTION	DISPOSITION
MILD: Hemoglobin > 11 mg/dl	Reassurance Multivitamin with iron	Menstrual calendar PCP follow up in 1 week with Adolescent or Gynecology Clinic
MODERATE: Hemoglobin 9-11 mg/dl No profuse bleeding (soaked pad q3-4 hours)	<u>No Estrogen Contraindications:</u> Monophasic combined OCP 35 mg of ethinyl estradiol 1 pill BID until follow up within 1 week <u>Estrogen Contraindications</u> Medroxyprogesterone acetate (Provera) 10 mg PO daily First dose in ED. Follow up within 1 week.	Fe Gluconate or Sulfate 325 mg BID Colace 100 mg BID If bleeding > 2 days, call Adolescent Clinic Adolescent or GYN follow up within 1 week
SEVERE; Hemoglobin < 9 mg/dl *Profuse bleeding* Hemodynamic instability	Admit Fluid resuscitation, consider transfusion of PRBCs <u>No Estrogen Contraindications</u>: Monophasic combined OCP 1 tab QID. Give the first dose STAT May consider using conjugated estrogen (Premarin) 25mg IV QID (up to 4 doses total); First dose STAT <u>Estrogen Contraindications:</u> Medroxyprogesterone acetate (Provera) 10 mg PO Norethindrone (Aygestin) 5 mg PO Tranexamic acid 1300mg PO TID First dose STAT	ADMIT Consult Adolescent Medicine and gynecology

CONTRAINDICATIONS TO ESTROGEN IN ADOLESCENTS
Untreated hypertension
Migraine with aura
Inherited thrombophilia
History of thrombosis or risk factors: Antiphospholipid Antibodies, factor V Leiden mutation or protein C, protein S, or antithrombin III deficiencies
History of cardiovascular disease, stroke, deep vein thrombosis
Active breast or liver cancer

WEB LINK: MEDICAL ELIGIBILITY CRITERIA FOR CONTRACEPTIVE USE (CDC 2016)

DISPOSITION

The majority of patients can be discharged home with appropriate and timely outpatient follow up. Indications for admission are included in the table below.

ADMISSION
Active, profuse heavy bleeding: > 1 pad/hour for > 2 hours
Hypovolemia, orthostatic hypotension
Hemoglobin < 8 mg/dl (HCT < 25%)

FIRST TRIMESTER VAGINAL BLEEDING

INTRODUCTION (KAREN FRANCO, M.D., 8/2018)
There are several complications that can arise in the first trimester of pregnancy. First trimester vaginal bleeding occurs in up to 25% of pregnancies pregnancy where half of these pregnancies are lost.

DIFFERENTIAL DIAGNOSIS
Spontaneous abortion*
Ectopic pregnancy*
Vaginal trauma
Cervical neoplasms
Molar pregnancy
*Focus of this PEM Guide

DIAGNOSIS
Evaluation of vaginal bleeding in the first trimester includes a thorough history, evaluation of hemodynamic status, physical examination including pelvic examination, laboratory testing and ultrasonography.

LABORATORY TESTING
Quantitative beta HCG
CBC
Coagulation profile
Type and screen (including Rh status)
Urinalysis and Urine culture (urinary tract infection may serve as a precipitant)

SPONTANEOUS ABORTIONS

CLASSIFICATION OF SPONTANEOUS ABORTIONS			
TYPE	VAGINAL BLEEDING	OS	ULTRASOUND
Threatened	+	Closed	Viable Intrauterine Pregnancy (IUP)
Inevitable	+	Open	+/- Viable IUP
Incomplete	+	Closed	Products of conception
Complete	+	Closed	No IUP, Consider ectopic pregnancy

TRANSVAGINAL ULTRASOUND: TIMELINE			
STRUCTURE	GESTATIONAL WEEKS	SIZE	DISCRIMINATORY HCG
Gestational Sac	4-5		1,500
Yolk Sac	5-5.5	GS 8-10 mm	2,500
Fetal Pole	5-6	GS 18 mm	5,000
Fetal Cardiac Activity	6-7	FP 5 mm	15,000
Amnion	6-7		
IUP = Gestational Sac + Yolk Sac in 2 planes (5.5 weeks) in the uterine stripe Definitive IUP = Gestational Sac + Yolk Sac + Fetal Pole (6 weeks) in the uterine stripe			

MANAGEMENT OF SPONTANEOUS ABORTIONS	
Threatened	Reassurance. No treatment necessary 79% have a good outcome if HCG is normal Follow up with obstetrics in 2-3 days to repeat ß-HCG
Inevitable	OB consult to remove products of conception at os to hasten completion
Incomplete	OB consult for urgent D&C
Complete	OB consult. Must r/o ectopic pregnancy if (+) beta and no IUP
Missed	Missed abortion refers to an intrauterine pregnancy that is no longer developing normally. The gestation is termed a missed abortion only if the diagnosis of incomplete abortion or inevitable abortion is excluded (i.e., the cervical os is closed). Before widespread use of ultrasonography, the term missed abortion was applied to pregnancies with no uterine growth over a prolonged period of time, typically 6 weeks

Young women without a history of spontaneous abortion and with definitive IUP with a normal fetal heart rate on ultrasound have an approximately 5% miscarriage rate. Sub chorionic hemorrhage of less than 50% of the gestation sac circumference are also associated with a good prognosis.

RH ISOIMMUNIZATION: Rhesus (Rh)-D-negative mothers who are exposed to the blood of a Rh-D-positive fetus are at risk of developing Rh-D-positive antibodies. The use of Anti-D-Rh-positive immune globulin (e.g. Rhogam) has substantially reduced but not eliminated the risk of Rh isoimmunization. The mechanism of action of Rhogam is unclear.

In the U.S. the American College of Obstetrics and Gynecology recommends that any Rh-D-negative women should be treated when a risk of feto-maternal hemorrhage exists as long as they have not been previously treated (ACOG, OBS & GYN 2017, PubMed ID: 28742673). The risk of Rh isoimmunization is low in patients with spontaneous (1.5-2.0%) and induced abortions (4-5%). Rhogam is recommended for those who are Rh-negative with clinically significant bleeding. There is considerable controversy regarding the necessity of Rhogam in those with a threatened abortion with spotting who are less than 12 weeks of gestation.

RHOGAM	300 micrograms intramuscularly

ECTOPIC PREGNANCY

Extrauterine pregnancies include pregnancy in the in the uterine wall (interstitial) or cervix, the fallopian tubes and intra-abdominal pregnancies. 95% occur within the fallopian tube in the fallopian ampulla. Approximately 7% of women in the first trimester who present to the emergency department with abdominal/pelvic pain and/or vaginal bleeding will have an ectopic pregnancy. Ectopic pregnancy is misdiagnosed in 40% of patients on initial ED visit and is a leading cause of emergency medicine malpractice lawsuits. Heterotopic pregnancy (an intrauterine and extrauterine pregnancy at the same time) may be found in 1 of every 7,000 pregnancies. This risk increases in women receiving infertility treatments (1 in 100). Adolescents are at increased risk of ectopic pregnancy due to Chlamydia infection, pelvic inflammatory disease and intrauterine device use.

PHYSICAL EXAMINATION

Peritoneal signs, cervical motion tenderness, abdominal or pelvic tenderness increase likelihood of ectopic pregnancy. However, 30% of ectopic pregnancies do not have vaginal bleeding, only 10% will have an abnormal pelvic exam and 10% will have an adnexal mass.

BETA-HCG
A single quantitative level does not reliably distinguish between ectopic pregnancy and spontaneous abortions
10% of ectopic pregnancies with levels < 100 mIU/mL were ruptured
7% ruptured ectopic pregnancies had levels <100 mIU/mL
10% of ectopic pregnancies will have an intrauterine pseudo-gestational sac
Serial levels are recommended every 48 hours
Rise > 66% is normal, although this occurs in 15% of ectopic pregnancies
Rise < 66% is strongly suggestive of abnormal pregnancy. Occurs in 85% of ectopic pregnancies and in 15% normal intrauterine pregnancies
Declining levels indicate of a nonviable pregnancy (IUP & ectopic)

ULTRASOUND (See: PEM Guide: OB-GYN: Transvaginal Ultrasound)

Definitive sonographic findings of ectopic pregnancy include an extrauterine gestational sac with a yolk sac, fetal pole or fetal heart rate. This is found only 15% of the time.

Free fluid may be physiologic or represent both rupture and unruptured ectopic pregnancies. The likelihood of ectopic pregnancy increases as the volume of fluid increases. Free fluid in the hepatorenal space (RUQ) without an intrauterine pregnancy is virtually diagnostic of ectopic pregnancy in the first trimester. (Moore, Academic EM, 2007, PubMed ID: 17554008)

SONOGRAPHIC FINDINGS SUGGESTIVE OF ECTOPIC PREGNANCY
Extrauterine pregnancy with gestational sac, yolk sac, fetal pole or fetal heart rate
Pregnancy located within the interstitium (cornua) or cervix
ß-hCG level above discriminatory zone without an intrauterine pregnancy
Pseudogestational sac
Tubal ring (“ring of fire”)
Complex adnexal mass other than a simple cyst that is separate from the ovary
Any echogenic fluid in the cul-de-sac (clotted blood) or fluid in right upper quadrant
Moderate to large amount of anechoic fluid in the cul-de sac >10 mm in diameter

MANAGEMENT

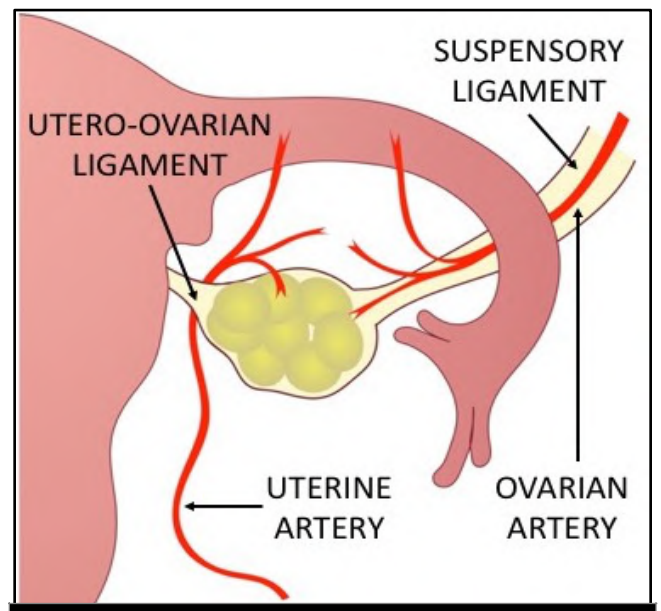
Requires early consultation with obstetrics. Early ectopic pregnancies are often treated with methotrexate. Late ectopic pregnancies require operative intervention.

OVARIAN TORSION

INTRODUCTION (NISHA NARAYANAN, MD, 6/2019)
Ovarian torsion refers to a complete or partial rotation of the ovary on its ligamentous supports. This can result in ischemia of the ovary and is thus a surgical emergency. Torsion which involves both the ovary and fallopian tube are called adnexal torsions and are more common than isolated torsion of either organ. Symptoms may be nonspecific and can occur in women of all ages. Early diagnosis and surgery are essential to protect ovarian and tubal function.

ANATOMY

The ovary is generally positioned laterally or posteriorly to the uterus. It is attached to the pelvic sidewall laterally by the suspensory ligament (infundibulo-pelvic ligament) and is attached to the uterus medially by the utero-ovarian ligament. The fallopian tubes are attached to the broad ligaments with connective tissue called the mesosalpinx. The ovarian artery and vein travel along the suspensory ligament and the uterine artery travels along the utero-ovarian ligament to supply blood to the ovary. Because adnexal tissue is not fixed, twisting can be induced by a lead point such as a cyst or a growth.



OVARIAN VASCULATURE

PATHOGENESIS

Ovarian torsion occurs when the ovary rotates around both the suspensory and utero-ovarian ligaments. The right ovary is more likely to torse than the left. This is likely because the right utero-ovarian ligament is longer than the left utero-ovarian ligament. In addition, the sigmoid colon may prevent torsion on the left.

Ovarian injury occurs when the twisting of the suspensory ligament compresses the ovarian vessels. Venous drainage becomes obstructed first as the muscular arterial walls are less compressible than venous walls. Continued arterial perfusion with blocked outflow leads to ovarian edema, enlargement, and further vascular compression. Ischemia of the ovary can result in ovarian necrosis, infarction, and hemorrhage.

RISK FACTORS FOR TORSION	
Ovarian masses/cysts (most common)	Pregnancy
Reproductive age	<15 years old
Benign and malignant masses	Prior ovarian torsion
Induction of ovulation	Ovarian size (>5 cm)

OVARIAN MASSES: In adults, torsion usually occurs due to an ovarian cyst or mass. The likelihood that the ovary will rotate and become fixed in a torsed position increases as the mass size increases until the mass becomes large enough to be fixed in place in the pelvis. The risk of torsion is highest when masses are 5 to 9 cm. Masses which are greater than 9 cm or those that are fixed in place due to adhesions or malignancy are less likely to torse. Many masses are associated with reproductive hormones thus the risk of torsion is increased in pregnant women (10-22% of torsion cases), women of reproductive age, and in women who are undergoing fertility treatments.

NORMAL OVARIES: The mechanism of ovarian torsion in normal ovaries which are not enlarged and without ovarian masses is unclear. Premenarchal girls are at greatest risk of torsion. A suggested mechanism is that they have elongated suspensory ligaments which permit increased ovarian movement. The ligament shortens with maturation to puberty. Torsion may also occur after a sudden increase in abdominal pressure or after strenuous exercise.

CLINICAL PRESENTATION

Clinical presentation varies significantly by age. The most common symptoms are sudden-onset, acute lower abdominal pain followed by nausea and vomiting, both of which can occur in waves. The pain may radiate to the groin or flank and there may be several waves of pain over the course of hours, days, or weeks.

A systematic review of the pediatric literature on ovarian torsion was limited by varying study definitions and the quality of the literature (retrospective case series in specific sub-populations). The authors were unable to assess the reliability of predictive signs or develop a diagnostic algorithm. They concluded that "acute abdominal pain remains the major presenting symptom of adnexal torsion but is nonspecific and a common complaint in the ED. The diagnosis of adnexal torsion should be considered in any female pediatric patient presenting to the ED with sudden onset lower abdominal pain." (Gasser, Pediatric Emerg Care 2016, PubMed ID: 26855342).

PRESENTATION: OVARIAN TORSION BY AGE	
Infants	Feeding intolerance, vomiting, abdominal distention, fussiness/ irritability
Premenarchal women	Diffuse lower abdominal pain, fever, restlessness, palpable pelvic mass, longer duration of symptoms before presentation than in adults
Adolescent/Adult	Moderate to severe pelvic pain, nausea/vomiting, low-grade fever, adnexal mass
Pregnant patients	Lower abdominal pain, nausea, vomiting, low-grade fever, leukocytosis, palpable mass

DIFFERENTIAL DIAGNOSIS: OVARIAN TORSION	
Ruptured ovarian cyst	Ectopic pregnancy
Urinary tract infection	Appendicitis
Tubo-ovarian abscess/PID	Kidney stone

HISTORY: History should include questions about recurrent abdominal pain, low-grade fever, prior ovarian cysts or masses, prior ovarian torsion, current pregnancy (corpus luteum cyst), and recent vigorous activity as an inciting event for the pain.

PHYSICAL EXAM: Vital sign changes may include low-grade fever or slightly elevated heart rate and/or blood pressure due to pain. Two-thirds of patients have pelvic and/or abdominal tenderness on exam which may either be diffuse or localized to the side of the adnexal mass. Peritoneal signs may signify that adnexal necrosis is occurring.

LABORATORY TESTING

There are no laboratory studies that are definitive for the diagnosis of ovarian or adnexal torsion but they may help to exclude other diagnoses. For example, a high white blood cell count may favor a tubo-ovarian abscess or appendicitis, hematuria may favor a kidney stone, and bacteriuria and pyuria may favor a urinary tract infection.

LABORATORY TESTING
CBC, BMP
Urinalysis
Urine, Serum HCG
Preoperative: Type and Screen, coagulation profile

IMAGING

Transvaginal ultrasound of the ovaries with doppler is the study of choice. Ultrasound identifies ovarian anatomy and assesses ovarian blood flow. Both transvaginal and transabdominal ultrasound may be needed to visualize the abdomen and pelvis. Ultrasound is highly specific but is poorly sensitive. Ultrasounds sensitivity ranges from 46-75% and is user-dependent. Normal doppler flow does not exclude torsion. Some studies suggest that the difference in ovarian size may be a more accurate predictor of ovarian torsion than doppler flow.

If ultrasound findings are equivocal, MRI or CT can help to diagnose an ovarian torsion and can give a more detailed picture of an ovarian mass. Neither of these techniques can assess ovarian flow. However, they can exclude other intra-abdominal pathologies that may present similarly.

NORMAL OVARIAN VOLUMES FOR AGE	
Age	Mean Ovarian Volume (ml)
Birth-12 months	1.05-1.06
1-5 years	0.6-0.9
6-8 years	1.1-1.3
9-11 years	2.0-2.5
12 years	3.8
13 years	4.2
Menstruating	9.8
Garel, Radiographics 2001, PubMed ID: 11706212	

SONOGRAPHIC FINDINGS: OVARIAN TORSION	
Rounder, larger ovary	Torsed ovary may be rounder or larger than the contralateral ovary due to vascular and lymphatic engorgement
Heterogeneous ovarian stroma	Torsed ovary may have heterogeneous-appearing stroma due to edema and hemorrhage
“String of pearls” follicles	Multiple small peripheral follicles can be present due to their displacement by edema (similar finding as in PCOS)
Ovarian mass with tenderness	Pain on same side as mass and tenderness upon scanning with endocavitary probe makes torsion more likely
Abnormal ovarian location	Ovaries may be located anterior to the uterus in torsion instead of posterior or lateral to the uterus
“Whirlpool” sign in ovarian vessels	On Doppler there is a round hyperechoic mass with concentric hypoechoic stripes or internal heterogeneous echoes which is likely a twisted vascular pedicle
Decreased or absent Doppler flow in ovary	Flow can be present even in torsion due to the dual blood supply of ovary. Arterial flow in systole without flow in diastole is evidence for outflow obstruction. Venous flow with torsion is associated with ovarian viability

MANAGEMENT

The only definitive way to confirm and to treat a torsion is surgery. Surgical management may include: detorsion, ovarian cystectomy, and oophorectomy. Most surgeries (even in pregnant patients) are performed laparoscopically. Laparotomy is the approach of choice if malignancy of the ovary or fallopian tube is suspected. Analgesics and antiemetics may be required.

Early detorsion is associated with preserved ovarian function. Postoperative studies suggest that over 80% of patients have normal follicular development after detorsion. While dark and enlarged ovaries with hemorrhagic lesions may appear nonviable, many studies suggest that they may retain function after detorsion. This may be due to the fact that total arterial occlusion may not occur in a torsed ovary despite significant lymphatic and venous congestion. Thus, assessing ovarian viability and preserving function in premenopausal women is usually recommended.

In post-menopausal women or in women with necrotic, gelatinous, or dead tissue that is definitely not viable, oophorectomy or salpingo-oophorectomy can be performed. If a benign mass is present, ovarian cystectomy is usually performed.

There is a risk of recurrence after detorsion but the incidence and causes are unknown. Oophoropexy and the suppression of ovarian cysts by oral contraceptives are two approaches that can be used to decrease this risk but both lack long term follow-up.

PELVIC INFLAMMATORY DISEASE

INTRODUCTION (VAISHALI SHAH, M.D., 3/2023)
Pelvic Inflammatory disease (PID) comprises a spectrum of inflammatory disorders of the upper female genital tract, including endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. PID affects 8% of US women during reproductive years with more than 1 million US women having an episode of PID per year. Long term sequelae, if untreated, can include ectopic pregnancy, chronic pelvic pain and infertility. Early identification and treatment are essential. The diagnosis and management of PID is made difficult by lack of clear criteria or reference standard, a wide spectrum of disease (from subclinical to abscess with peritonitis) and an extensive differential diagnosis (appendicitis, ectopic pregnancy, ovarian cyst rupture and ovarian torsion).

The pathogenesis of PID is a complex and incompletely understood process involving interactions between genetic, immunologic, and bacterial virulence factors. Micro-organisms spread from the lower (vagina, cervix) to the upper genital tract (uterus, fallopian tubes). PID is a poly-microbial infection most commonly caused by sexually transmitted infections (85%). Sexually active women younger than 25 years old are most at risk because of an immature cervix. A higher risk of developing PID is also associated with a higher number of sexual partners.

PID is polymicrobial. N gonorrhea and C trachomatis are identified in a third to half of cases and antibiotic regimens are typically targeted to these agents. However, in approximately 70% of patients no causative organism is identified. The fact that there is a high rate of treatment resistance indicates the potential for other pathogens not covered by current regimens. The 2021 CDC guidelines add Metronidazole to cover anaerobes. Other studies, have implicated Mycoplasma genitalium as a causative agent that is not targeted by currently recommended antibiotic regimens (Haggerty, Sex Transm Infect. 2008, PubMed ID: 18445635).

MICROBIOLOGY	
Common	N. gonorrhoeae, C. trachomatis
Vaginal flora	Anaerobes, G. vaginalis, H. influenzae, enteric Gram-negative rods, Steptococcus agalactiae
Other	CMV, M. hominis, U. urealyticum and M. genitalium

CLINICAL MANIFESTATIONS
Symptoms can range from asymptomatic (sub-clinical) to severe**.** Lower abdominal pain is the most common presentation. However, fever, abnormal vaginal discharge, dyspareunia, dysuria, and dysfunctional uterine bleeding can also be seen. Right upper quadrant pain consistent with peri-hepatitis (Fitz-Hugh-Curtis syndrome) may be seen secondary to liver capsule inflammation**.** Maintain a high index of suspicion and a low threshold for treatment, particularly if an alternative diagnosis cannot be definitively established.

DIAGNOSIS
The CDC diagnostic criteria for PID are intended to lower the threshold for treatment. The diagnostic and treatment options discussed in this PEM Guide are based of the 2021 CDC Guidelines (WEB LINK: CDC STD GUIDELINES: 2021). The CDC STD treatment phone app is available at the above link for both apple and android phones.

Unfortunately, no historical, physical examination or laboratory finding is both sensitive and specific for PID. This makes PID a clinical diagnosis. The absence of a clear reference standard makes diagnsostic and treatment studies difficult to assess. All women with PID should also be tested for HIV, syphilis, GC and chlamydia. Saline microscopy of vaginal fluid (i.e. a wet prep) can identify white blood cells suggestive of PID as well as concomitant infection with Gardnerella vaginalis (bacterial vaginosis) and trichomoniasis. Mycoplasma genitalium PCR with Azithromycin resistance testing should be sent if available.

PID DIAGNOSTIC CRITERIA: CDC 2021
Presumptive treatment is indicated in a sexually active women with pelvic or lower abdominal pain if no other cause for illness is identified
MINIMUM CRITERIA (One or more)
Cervical Motion Tenderness OR Uterine tenderness OR Adnexal tenderness
ADDITIONAL CRITERIA (Presence increases specificity)
Oral temperature > 101 F (38.3 C)
Abnormal cervical mucopurulent discharge or cervical friability
Presence of abundant numbers of WBC's on saline microscopy of vaginal fluid
Elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
Laboratory evidence of cervical infection with *N. gonorrhoeae* and *C. trachomatis*

DEFINITIVE DIAGNOSIS OF PID	
Endometrial biopsy	Histopathologic evidence of endometritis
Transvaginal sonography or MRI	Thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex or abscess, or Doppler studies suggesting pelvic infection (tubal hyperemia)
Laparoscopy	Abnormalities consistent with PID

MANAGEMENT

Treatment should take into consideration availability, cost, and patient acceptance. Anti-microbial coverage should also include coverage of anaerobes, gram-negative organisms, and streptococci. All treatment regimens should be effective against *N. gonorrhoeae* and *C. trachomatis* because negative endocervical screening for these organisms does not rule out an upper reproductive tract infection.

There is limited data to support specific regimens and in particular their impact on long term complications. In women with mild-moderate PID, oral and parenteral therapies appear to be equivalent. Suggested criteria for inpatient therapy are presented in the table below.

The 2021 guidelines emphasize the importance of anaerobic coverage. Metronidazole is recommended whereas in past guidelines Metronidazole has been optional. Metronidazole had the added benefit of treating bacterial vaginosis and trichomonas. Fluoroquinolones are no longer recommend due to emergence of quinolone-resistant GC.

A clinical trial randomized 233 women, 14-40 years of age, meeting clinical criteria for PID to Ceftriaxone and Doxycycline with and without Metronidazole (Wiesenfeld, Clin Infect Dis. 2021., PubMed ID: 32052831). There was no difference in any of the clinical efficacy outcomes. Benefits were limited to a reduction in some anaerobic organisms at 30 days. It could be argued that there is no harm to adding Metronidazole given the lack of difference in tolerability and adverse events between the two study groups.

ANTIBIOTIC REGIMENS FOR PID: CDC (2021)	
PARENTERAL REGIMENS (Until clinical improvement then transition to oral)	
Regimen A	1. Ceftriaxone[1] 1-gram IV Q24 hours x AND 2. Doxycycline[2] 100 mg PO/IV* Q12 hours AND 3. Metronidazole[2] 500 mg PO/IV* Q12 hours days
Regimen B	1. Cefotetan[1] 2 grams IV Q12 hours AND 2. Doxycycline[2] 100 mg PO/IV* Q12 hours
Regimen C	1. Cefoxitin[1] 2 grams IV Q6 hours AND 2. Doxycycline[2] 100 mg PO/IV* Q12 hours
Alternative A	1. Ampicillin/Sulbactam 3 grams IV Q6 hours AND 2. Doxycycline[2] 100 mg PO/IV Q12 hours
Alternative B[3]	1. Clindamycin 900 mg IV Q8 hours AND 2. Gentamycin IV/IM a. Loading 2 mg/kg, Maintenance 1.5 mg/kg Q8 hours OR b. Loading 2 mg/kg, Maintenance 3.0-5.0 mg/kg Daily
INTRAMUSCULAR/ORAL REGIMENS	
Regimen A	1. Ceftriaxone[1] 500[2] mg IM (1,000 mg if 150 kg) AND 2. Doxycycline 100 mg PO BID for 14 days AND 3. Metronidazole 500 mg PO BID a day for 14 days
Regimen B	1. Cefoxitin 2 grams IM AND 2. Probenecid 1-gram PO (concurrent with Cefoxitin) AND 3. Doxycycline 100 mg PO BID x 14 days AND 4. Metronidazole 500 mg PO BID x 14 days
Regimen C	1. Other 3rd gen cephalosporin: Ceftizoxime OR Cefotaxime IM AND 2. Doxycycline 100 mg PO BID for 14 days AND 3. Metronidazole 500 mg PO BID a day for 14 days
Alternative[5]	1a. Levofloxacin 500 mg PO QD x 14 days OR 1b. Moxifloxacin 400 mg PO QD x 14 days AND 2. Metronidazole 500 mg PO BID x 14 days
	1. Azithromycin 500 mg IV QD x 1-2 days followed by 250 mg PO QD to complete a 14 day course 2. Metronidazole 500 mg PO BID x 14 days

1. Ceftriaxone has limited anaerobic coverage. Requires addition of Metronidazole. Cefoxitin and Cefotetan have better. anaerobic coverage
2. Doxycycline and Metronidazole have the same bioavailability IV/IO. Doxycycline IV is painful, IV Metronidazole for severe PID, TOA
3. The cross reactivity of penicillin and cephalosporin allergy is less than 2.5%. Risk is highest for 1st generation. Negligible for most 2nd and all 3rd generation. If severe allergy to cephalosporin (anaphylaxis, Steven's Johnson) use Alternative Regimen B for parenteral administration or the Alternative intramuscular/oral regimen
4. If Ceftriaxone not available or for expedited partner therapy (if state allows)
5. Cephalosporin allergic AND low community and personal risk of GC AND follow-up likely

DISPOSITION

Patients should demonstrate improvement within 72 hours of treatment onset. If without improvement, they should undergo additional testing (e.g. imaging, laparoscopy), evaluation for alternative diagnoses and admission for a parenteral regimen.

Patient should refrain from sexual intercourse until treatment is completed, symptoms have resolved and sex partner(s) has been treated. All patients who have positive tests for GC and chlamydia should be retested 3 months after treatment even if their partners have been treated.

All contraceptive methods can be continued during treatment.

Partners who have had sexual contact with the patient during the 60 days before symptoms occurred should be treated empirically for *N. gonorrhoeae* and *C. trachomatis* regardless of the organism isolated. Male partners are typically asymptomatic. Male partners should be advised to refrain from sexual intercourse until completion of their treatment or until symptoms resolve whichever is longer. Expedited partner therapy is an alternative approach to treating partners. WEB LINK: CDC: EPT

Prevent PID by screening high-risk women, treating any suspected PID, avoiding douching, treating bacterial vaginosis (because of the association with PID) and promoting condom use.

CRITERIA FOR HOSPITALIZATION
Pregnancy
Failure to improve with oral therapy within 72 hours
Failure to follow up or tolerate an outpatient oral regimen
Severe illness including nausea, vomiting, or high fever
Presence of a tubo-ovarian abscess
Inability to exclude a surgical abdomen such as appendicitis

PRECIPITOUS VAGINAL DELIVERY

INTRODUCTION (ELISE PERLMAN, MD, 2/2022)
A precipitous delivery is defined as a labor that lasts no more than three hours from onset of regular contractions to delivery. A precipitous delivery may occur in the Emergency Room either by a patient, a relative or other visitor. These deliveries are often higher risk than those that occur on the labor floor. As an emergency room provider, it is imperative to know how to safely facilitate delivery while expecting and being prepared for potential complications including; nuchal cord, shoulder dystocia, and postpartum hemorrhage. This PEM Guide focuses on delivery of the newborn and care of the mother. See also: PEM Guide: Resuscitation: Neonatal Resuscitation.

CLINICAL PRESENTATION

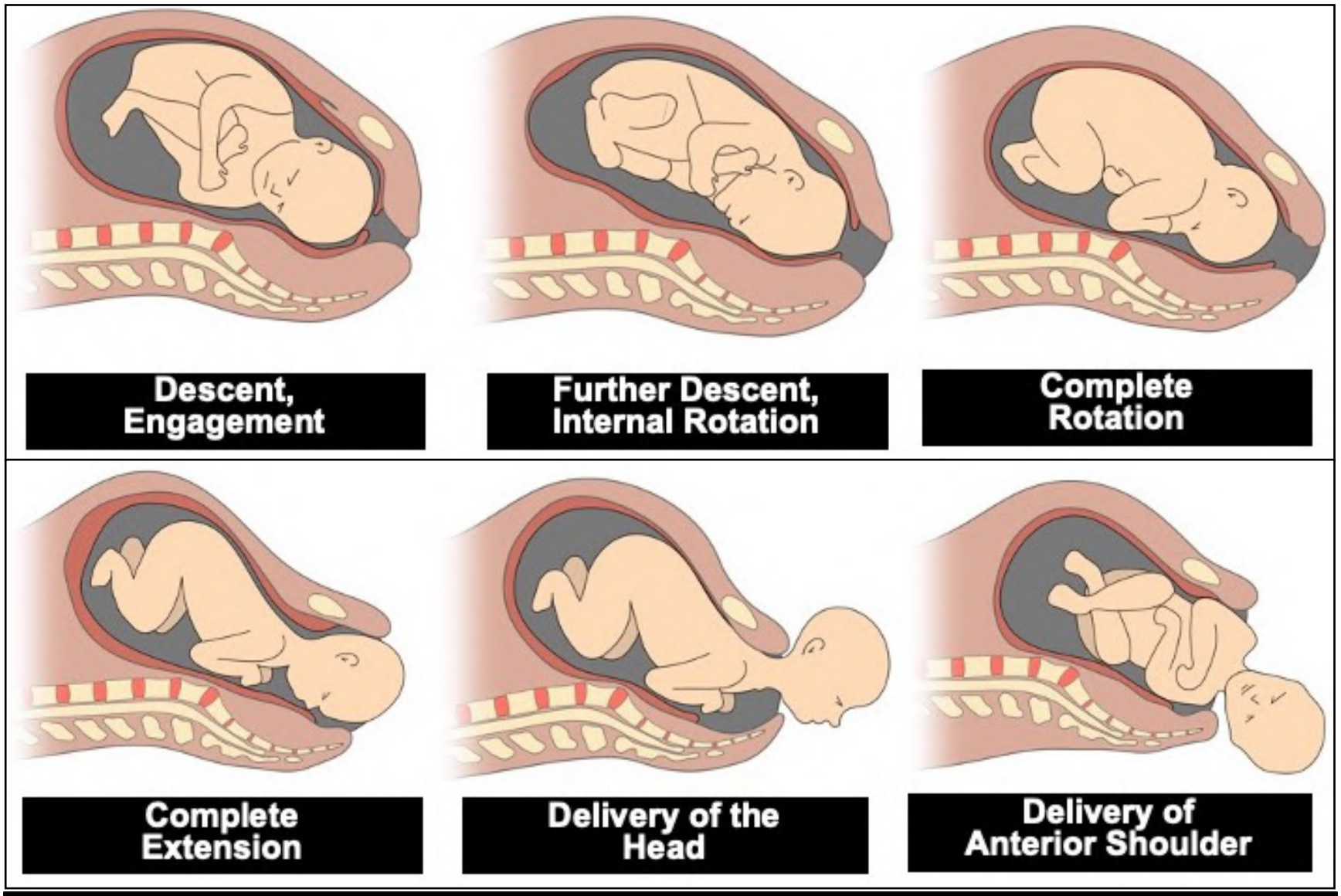
When a patient presents with concern for imminent delivery, it is imperative to perform a rapid obstetrical assessment. Management in the ED always begins with an assessment of Airway, Breathing and Circulation, placing the patient on the monitor, assessing vitals for hemodynamic stability/instability and obtaining the appropriate access and sending laboratory studies as needed. A rapid obstetrical history will identify risk factors and resource needs.

RAPID OBSTETRICAL HISTORY	
Gravity and Parity	The number of prior pregnancies and the number of births respectively. Women with prior vaginal deliveries tend to have more rapid labors
Gestation Age	Usually known by the patient, but can also be estimated by the height of the fundus, this may be affected by twin gestation and factors affecting uterine (e.g. polyhydramnios)
Pregnancy Course and Complications	Routine prenatal care, known anomalies, prior pregnancy complications, previous C-section, gestational diabetes, hypertensive disorders (chronic or gestational).
Medical Problems	Comorbidities, allergies.
Rupture of Membranes	Timing and color.

A brief pelvic exam will help determine whether delivery is imminent or not. With hips flexed/abducted and knees flexed the assessment is done looking for three things:

RAPID OBSTETRICAL EXAMINATION: IS DELIVERY IMMINENT?	
Is the amniotic sac intact?	If yes, there is time
Is the fetus visible at rest?	If yes, delivery is imminent
Is the fetus vertex down?	If yes, proceed with delivery If no (other presenting part), delay delivery, proceed to OR

DELIVERY PROCESS
Head floating pre-engagement Descends to engage in pelvis Rotates Posteriorly
Initial flexion of the head Beginning Extension Complete Extension
Delivery of head Head externally rotates to align with shoulders (restitution)
Delivery of the anterior shoulder Delivery of the posterior shoulder



STAGES OF DELIVERY

EQUIPMENT: VAGINAL DELIVERY	
Mother	Intravenous access, Gown, Pillows, Sheets Medications: Oxytocin, Methergine, Hemabate, Tranexamic Acid Fluids, pRBC (active type and screen) Other: balloon tamponade, 3-0 Vicryl for vaginal laceration
Provider	Sterile Gloves, Gown
Delivery	Lubricant, Gauze, Container for Placenta
Neonate	Sterile Cord Clamps x 2, Sterile Scissors, Bulb Suction Infant warmer with neonatal resuscitation equipment

PROCEDURE: VAGINAL DELIVERY	
1	Call for help as early as possible. Ideally, have the obstetrical team and neonatal team present to help facilitate delivery and resuscitate as necessary. You are now preparing to have two patients and both have the potential to be critically ill.
2	Position the mother with hips flexed/abducted and knees flexed. Blankets or pillows may be placed under the hips to raise the perineum.
3	If the fetus is not yet visible at rest, instruct the patient to push for 10 seconds with each contraction for a total of 3 sets. Keep in mind this is a Valsalva maneuver and in order to achieve maximum strength the patient must “push with her bottom” and not “with her face”. They should be instructed to breath normally in between contractions to regain strength and energy.
4	If the fetal head is crowning (at the vaginal introitus), the delivery is imminent. Control fetal expulsion and prevent trauma by holding gauze at the posterior perineum over where the fetal face is located. The other hand is placed on the crowning portion of the fetal head and light pressure is applied in the flexed position guiding the head “down” without pulling on the head.
5	As the infant’s head is delivered it will rotate to one side (restitution of the head). Feel for an umbilical cord around the baby’s neck. If present, slip it over the head. If unable to easily remove the cord, consider using two clamps to clamp the cord and cut in between to facilitate removal and delivery.
6	Once the neck has been cleared, guide the baby’s head with gentle downward traction to deliver the anterior shoulder, careful not to “pull” with traction. Then guide the head upward to deliver the posterior shoulder.
7	Once both shoulders are delivered, the rest of the baby easily follows. Be sure to secure the baby holding onto the head and buttocks. Clamp the umbilical cord with both clamps/hemostats and then cut clamps. Be sure to cut in between the clamps to prevent unnecessary hemorrhage.
8	If the situation allows, you can place the baby on mother for quick skin to skin where it can be warmed, dried, and stimulated, though a precipitous delivery by default is high risk and therefore you should consider bring the baby directly to the infant warmer for exam and resuscitation.
9	To deliver the placenta, pull gently on the clamped cord in a rotating motion using the clamp as leverage. Separation usually occurs naturally within 5 minutes and can be noted by lengthening cord, a gush of blood and change in shape of the fundus. To help facilitate delivery, have the patient bear down while gently pulling traction on the cord. Advance the clamp higher on the cord as placental separation occurs to maximize control. To prevent uterine inversion, place firm pressure on the mother’s abdomen, above the pubic symphysis during traction.
10	Oxytocin can then be started to stimulate uterine contractions and reduce maternal blood loss. Alternatively, the fundus can be massaged to help it contract into a firm, more globular mass (See section below on post-partum hemorrhage).
11	Inspect the perineum for lacerations. The vaginal mucosa heals rapidly and therefore superficial lacerations do not always require repair. For a deep laceration that is still bleeding, place firm pressure to slow the bleed and repair with 3-0 Vicryl sutures.

VIDEO LINK: VAGINAL DELIVERY (ANIMATION)

VIDEO LINK: VAGINAL DELIVERY (MANIKIN)

COMPLICATIONS:
During precipitous deliveries it is imperative to be prepared for potential complications that can place bother the fetus and mother at risk. While there are many complications including breech presentation and umbilical cord prolapse. This PEM Guide will focus on shoulder dystocia and postpartum hemorrhage.

SHOULDER DYSTOCIA: Shoulder dystocia occurs when gentle traction cannot deliver the fetal shoulders and occurs in 0.2-3% of all births. Most commonly, the anterior shoulder is stuck behind the pubic symphysis. It is impossible to predict which deliveries will be complicated by shoulder dystocia and therefore the emergency medicine provider should always be prepared. Complications to the fetus include: nerve injury, asphyxia, acidemia and clavicular fractures. Complications to mother include; postpartum hemorrhage, uterine rupture and deep perineal lacerations.

As soon as a shoulder dystocia is recognized, often by retraction of the head referred to as the “turtle sign”, the patient should be instructed to stop pushing. Ensure adequate access and maximize oxygen delivered to fetus by providing oxygen to the mother. Optimize her positioning by having her buttocks flush with the edge of the bed. Place a foley catheter to decompress the bladder and remove potential obstruction. Have two people hold each leg in hyperflexion, prepare the neonatal warmer and have a team prepared for neonatal resuscitation.

There are several maneuvers to relieve shoulder dystocia. The HELPERR mnemonic can be used to help remember the management steps for shoulder dystocia. The most common is McRoberts maneuver with a 42% success rate (Gherman, Amer J OB GYN 1997, PubMed: 9077624). The maneuver includes hyperflexion of the legs with knees pulled towards the mother’s chest thereby increasing the AP diameter. If this does not work try again with simultaneous application of suprapubic pressure with a palm or fist.

HELPERR MNEMONIC: SHOULDER DYSTOCIA		
H	Help	Call OB/NICU
E	Empty Bladder	Place a foley catheter
L	Legs Flexed	McRoberts Maneuver
P	Pressure	Suprapubic Pressure to dislodge the anterior shoulder
E	Enter the Vagina	Rubin or Woods corkscrew Maneuver
R	Remove posterior arm	Barnum Maneuver
R	Roll on all fours	Gaskin Maneuver

VIDEO LINK: HELPERR MNEMONIC

POST-PARTUM HEMORRHAGE (PPH): PPH is often defined as at least 500 ml of blood loss following a vaginal delivery. Following complete delivery, any vital sign abnormality should raise concern for PPH. The major causes are referred to as the “Four T’s” 1. Tone 2. Trauma 3. Tissue 4. Thrombin.

PHYSICAL EXAMINATION: SOURCE OF HEMORRHAGE	
Uterus	Identify: Atony (boggy uterus)
Vaginal	Identify: Lacerations, uterine inversion
Placenta	Identify: “Missing pieces” (concerning for retained products)
IV Sites	Identify: Oozing which would be concerning for DIC

MANAGEMENT OF POST-PARTUM HEMORRHAGE: OVERVIEW
Supportive care: IV, Oxygen, Foley catheter to drain bladder
Basic uterine massage: Firm massage of the uterine fundus through abdominal wall
Advanced uterine massage: The external hand compresses and massages the uterus. Place the other hand in a fist internally to massage the anterior uterus,
Uterotonic (tone) medications: Concurrent to uterine massage (See Table below)
Manually sweep uterus of clots/products of conception. Antibiotics: Prevent endometritis
PRBC transfusion, Tranexamic acid, massive transfusion protocol as indicated
Internal uterine balloon tamponade.

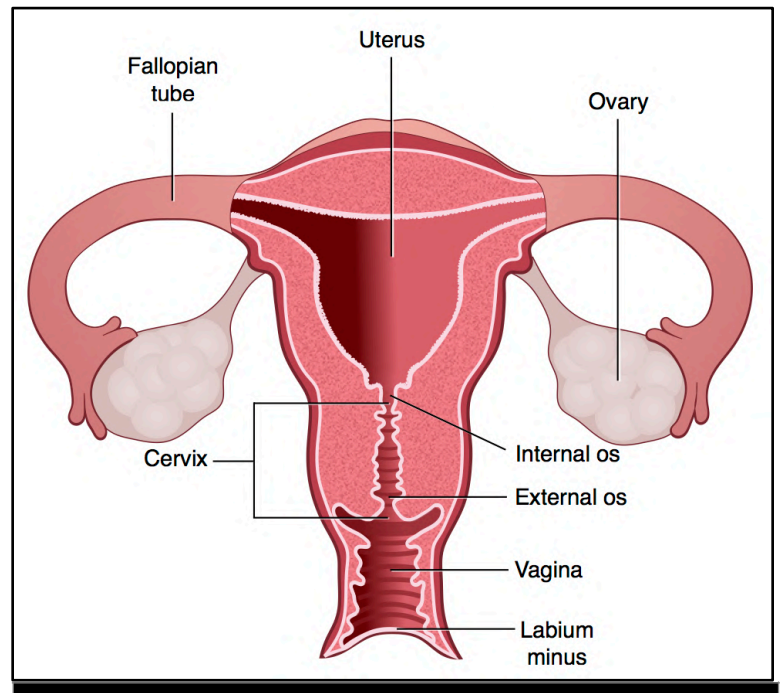
MANAGEMENT OF POST-PARTUM HEMORRHAGE: SPECIFIC INTERVENTIONS	
MANAGEMENT	DOSE (NOTES)
Degree of Blood Loss	> 0.5-1.5 liters
Oxytocin (Pitocin)[1]	IV: 20-40 Units in 1 Liter crystalloid at 200-500 ml/hour IM: 10 Units
Methergine[1]	IM: 0.2 mg q2-4hour (Contraindicated: Hypertension)
Hemabate[1]	IM 250 μg q15min max 8 doses (Contraindicated: Asthma)
Misoprostol (Cytotec) [1]	PR:1000 μg
Degree of Blood Loss	>1.5-2.0 liters (vital signs may be normal)
Tranexamic Acid	IV: 1 gram over 10 minutes
pRBC[2]	IV: 2 units
Balloon Tamponade	Bakri Balloon Consider Blakemore tube (cut the distal tip off if no other balloon tamponade available)
Degree of Blood Loss	Continued bleeding with abnormal vital signs
Massive Transfusion Protocol: PRBC: FFP: Platelets (1:1:1)	
1. Uterotonics: Uterine smooth muscle tone/contraction 2. WOMEN Trial Collaborators, Lancet 2017, PubMed ID: 28456509	

TRANSVAGINAL ULTRASOUND

INTRODUCTION (MICHAEL MOJICA, M.D., 10/2018)
Adolescents and young adult women frequently present to the emergency department with complaints of lower abdominal pain and/or vaginal bleeding. If these symptoms occur in the pregnant patient a transvaginal ultrasound can be utilized to:
1. Determine if the pregnancy is intrauterine (most important)
2. Date the pregnancy (crown-rump length)
3. Assess the viability of the embryo (fetal heart rate)
See: PEM Guide: Obstetrics and Gynecology: First Trimester Vaginal Bleeding

ANATOMY

The uterus is made up of the body (fundus) and neck (cervix). The uterus lies between the bladder anteriorly and the sigmoid colon posteriorly. It is typically 8cm (long) x 5cm (wide) x 3cm (deep). The uterus can be anteverted (tipped anteriorly toward the abdominal wall) or retroverted (tipped posteriorly toward the spine). The fallopian tubes are typically 10cm in length and can be divided in 4 segments from proximal to distal: the interstitial cornua, the isthmus, the ampulla and the infundibulum. The ovaries are elliptical in shape and measure 4cm (length) x 3 cm (width) x 2cm (height). Their location is variable. They may be found anterior to the iliac artery though the best method to localize them is to follow the fallopian tube distally from the uterus.



UTERINE ANATOMY

ULTRASOUND PROCEDURE

Both trans-abdominal and transvaginal approaches may be utilized. Utilize the ultrasounds obstetrics preset. A bimanual exam should be performed first to localize the cervix. External hand pressure during the ultrasound can facilitate visualization of the ovaries.

PROBE SELECTION		
	TRANSABDOMINAL	TRANSVAGINAL
Probe	Curvilinear or Phase Array	Endocavitary
Location	Just above the Pubic Symphysis	Against the Cervix
Bladder	Full*	Empty
Views	Longitudinal (Sagittal) Short (Transverse) Hepatorenal (RUQ)	Longitudinal (Sagittal) Shorts (Transverse) Hepatorenal (RUQ)
*Serves as an acoustic window and displaces overlying bowel		

VIDEO LINK: TRANSVAGINAL ULTRASOUND (MANIKIN)

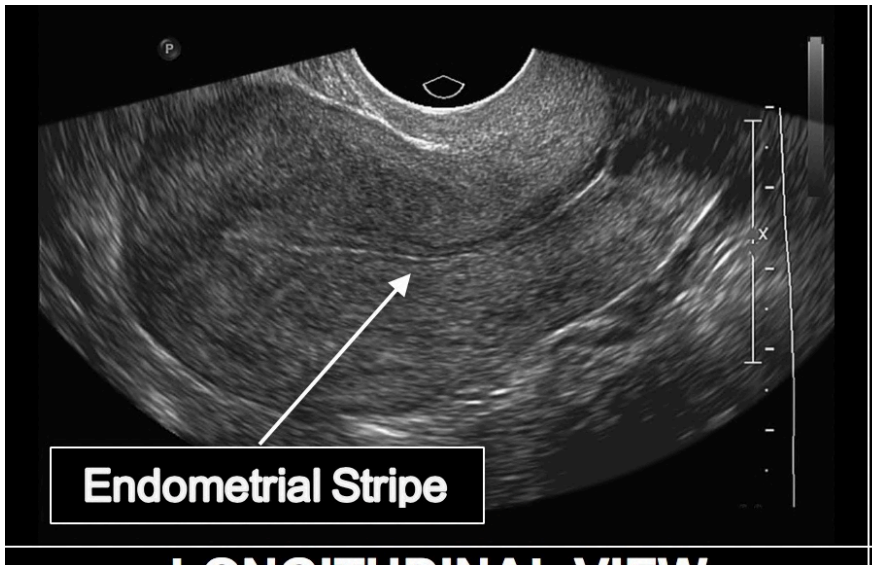
PREPARATION: The transvaginal probe should be coated with ultrasound gel and then placed in a condom sheath. Any air bubbles should be expressed from the tip. The condom tip should also be coated with ultrasound gel. Proper procedures for disinfecting the probe should be followed after each use.

INTRAUTERINE PREGNANCY: SONOGRAPHIC FINDINGS

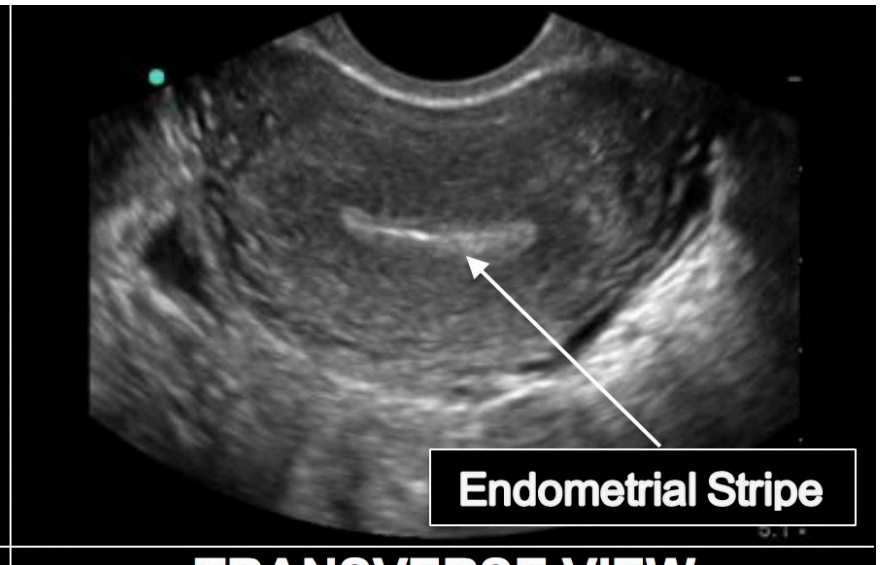
CORRELATION WITH BETA HCG: A quantitative beta HCG may help to determine which findings may be present at a given gestational age. A discriminatory zone of 1,000-2,000 for transvaginal ultrasound is often used for this purpose. It would be expected that evidence of an intrauterine gestation would be found above this level. For example, if a beta HCG is 4,000 and no intrauterine findings are noted than an ectopic pregnancy or pregnancy loss is likely. If a beta HCG is 700 there may not be any intrauterine findings of pregnancy. In a patient with abdominal pain or vaginal bleeding with a BHCG below the discriminatory level an ectopic pregnancy cannot be excluded and typically serial quantitative beta HCG's are followed. A pregnancy should always be localized in two planes to ensure proper localization within the uterus.

LONGITUDINAL VIEW
The tip of the probe is placed at the cervix and the marker dot at 12 o'clock
The uterus can be identified by the endometrial stripe
Scan through the uterus from cervix to fundus
For an anteverted uterus scan from ventrally (fundus) to dorsally (cervix)
For a retroverted uterus scan from ventrally (cervix) to dorsally (fundus)

TRANSVERSE VIEW
The tip of the probe at the cervix and the probe rotated 90 degrees counterclockwise from the longitudinal position so that the marker dot is located at 9 o'clock (toward the patient's right side)
The uterus can be identified by the endometrial stripe.
Scan through the uterus from cervix to fundus
Scan laterally (left and right) following fallopian tube to ovary
Scan through each ovary



LONGITUDINAL VIEW



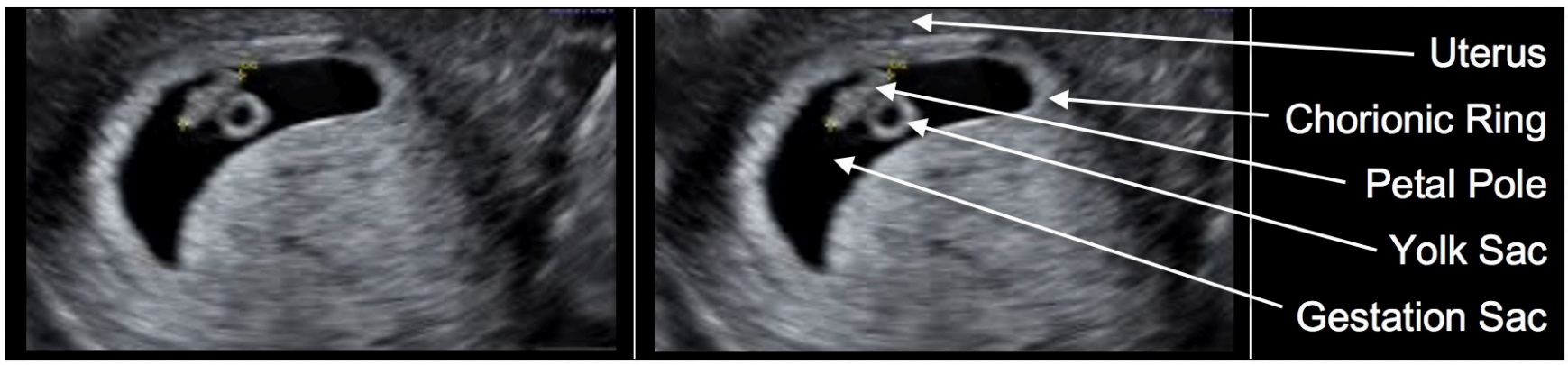
TRANSVERSE VIEW

TRANSVAGINAL ULTRASOUND: TIMELINE			
STRUCTURE	GESTATIONAL WEEKS	SIZE	DISCRIMINATORY HCG*
Gestational Sac	4-5		1,500
Yolk Sac	5-5.5	GS 8-10 mm	2,500
Fetal Pole	5-6	GS 18 mm	5,000
Fetal Cardiac Activity	6-7	FP 5 mm	15,000
Amnion	6-7		
Provisional IUP = GS + YS in 2 planes (5.5 gestational weeks) in the endometrial stripe Definitive IUP = GS + YS + FP (6 gestational weeks) in the endometrial stripe *Add 5,000 for a transabdominal ultrasound			

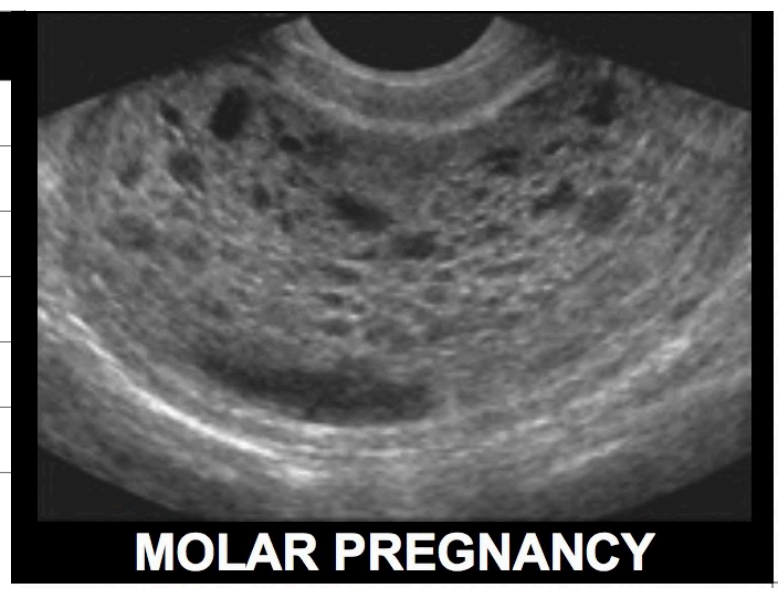
WEEK 4: The earliest finding consistent with pregnancy is seen at 4 weeks is a gestation sac. It is an round, anechoic sac without a distinct chorionic ring. I contrast, a pseudo-gestational sac, seen in ectopic pregnancy, can mimic a normal gestational sac has an irregular shape and is surrounded by echogenic uterine lining.

WEEK 5: The first ultrasonographic signs of intrauterine pregnancy appear at the 5th week. The provisional diagnosis of an IUP can be made with the presence of an intrauterine gestational scan and yolk sac in two plains. The addition of fetal pole is definitive evidence of an IUP. A crown rump length can be measured when a fetal pole is seen to estimate the approximate gestational age.

WEEK 6: By the 6th week, a fetal heart may be identified within the fetal pole. M-mode (a low energy mode, m is for motion) may be used to measure the fetal heart rate (Early first trimester FHR = 90-120 BPM, later first trimester FHR = 120-160 BPM). Fetal heart rates < 90 BPM are associated with a high risk of fetal demise. Spectral doppler (a high energy mode) causes thermal exposure to the fetus and should <u>not</u> be used. In the 7th week a fetal head and extremities may be identified.



ABNORMAL INTRAUTERINE PREGNANCIES
Gestational sac > 10 mm in diameter without a yolk sac
Gestational sac > 18 mm in diameter without a fetal pole
Fetal Pole ≥ 5 mm and no cardiac activity
Fetal heart rate < 90 beats per minute
Molar pregnancy
Pregnancy identified within the cervix



EXTRAUTERINE PREGNANCY: SONOGRAPHIC FINDINGS

HETEROTOPIC PREGNANCY

A heterotopic pregnancy is the presence of an intrauterine and extrauterine pregnancy at the same time and may be found in 1 of every 7,000 pregnancies. This risk increases in women receiving infertility treatments (1 in 100). An accomplished sonographer should complete a thorough scan of the adnexa and ovaries.

ECTOPIC PREGNANCY

Extrauterine pregnancies include pregnancy in the fallopian tubes, intra-abdominal pregnancies and pregnancy in the cervix. 95% occur within the fallopian tube with the fallopian ampula the most common site. Cervical and interstitial ectopic pregnancies have the highest risk of significant bleeding. Approximately 7% of women in the first trimester who present to the emergency department with abdominal/pelvic pain and/or vaginal bleeding will have an ectopic pregnancy.

A single quantitative BHCG level does not distinguish between ectopic and intrauterine pregnancies. Typically, a discriminatory zone of 1,000-2,000 is used to determine when findings of pregnancy may be seen. Unfortunately, there is considerable overlap between intrauterine and extrauterine pregnancies.

SERIAL BETA HCG LEVELS (RECOMMENDED EVERY 48 HOURS)
A rise > 66% is normal, though this occurs in 15% of ectopic pregnancies
A rise < 66% is suggestive of ectopic pregnancy but will occur in 15% of IUPs
A declining level indicates a nonviable pregnancy (intrauterine or ectopic)

ECTOPIC PREGNANCY: SONOGRAPHIC FINDINGS

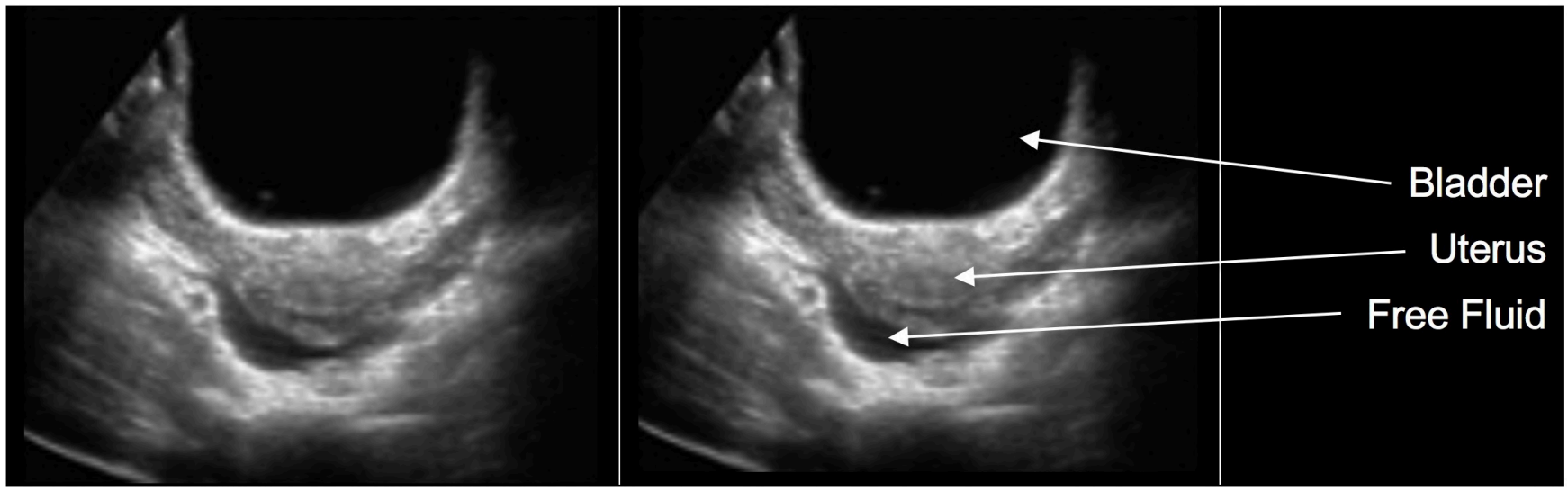
Definitive sonographic findings of ectopic pregnancy include an extrauterine gestational sac with a yolk sac, fetal pole or fetal heart rate. This is found only 15% of the time.

SONOGRAPHIC FINDINGS SUGGESTIVE OF ECTOPIC PREGNANCY
Extrauterine pregnancy with gestational sac, yolk sac, fetal pole or fetal heart rate
Pregnancy located within the cornua or cervix of the uterus
ß-hCG level above discriminatory zone without an intrauterine pregnancy
Pseudogestational sac
Tubal ring (“ring of fire”)
Complex adnexal mass other than a simple cyst that is separate from the ovary
Any echogenic fluid in the cul-de-sac (clotted blood) or fluid in right upper quadrant
Moderate to large amount of anechoic fluid in the cul-de sac >10 mm in diameter

PSEUDOGESTATIONAL SAC: A pseudo-gestational sac may represent an early intrauterine pregnancy or an ectopic pregnancy. In an ectopic pregnancy, the hormonal environment generates an intrauterine gestation sac similar to that of an intrauterine pregnancy. A true gestational sac will appear centrally within the uterus, is oval in shape and have a thick chorionic ring.

COMPLEX ADNEXAL MASS: A heterogeneous adnexal mass may represent: an early ectopic pregnancy prior to gestational sac formation, a failed ectopic pregnancy, a ruptured ectopic pregnancy or a corpus luteal cyst. An ectopic and a corpus luteal cyst will show enhancement of flow (“ring of fire”) with doppler ultrasonography. Pressure with the hand on the effected side may help to separate the mass from the ovary. If the mass can be separated from the ovary then it is likely an ectopic pregnancy.

FREE FLUID: Free fluid may be physiologic or represent both rupture and unruptured ectopic pregnancies. The likelihood of ectopic pregnancy increases as the volume of fluid increases. Free fluid in the hepatorenal space (RUQ) without an intrauterine pregnancy is virtually diagnostic of ectopic pregnancy in the first trimester. (Moore, Academic EM, 2007, PubMed ID: 17554008)



PREGNANCY OF UNKNOWN LOCATION

PREGNANCY OF UNKNOWN LOCATION
Positive BHCG without sonographic findings intra or extrauterine pregnancy
An early viable intrauterine pregnancy (BHCG below discriminatory level)
An ectopic pregnancy ((BHCG above discriminatory level)
A failing intra or extrauterine pregnancy

APPENDIX

PREGNANCY NUMBERS		
GRAVITY	G	Pregnancies regardless of outcome (T + P + A)
PARITY	P	Pregnancies to a viable gestational age (T + P)
	T	Term births (37-40 weeks)
	P	Pre-term births (20-36 weeks)
	A	Abortions: Spontaneous and Elective (< 20 weeks)
	L	Living children

VAGINAL DISCHARGE

INTRODUCTION (SABINA KHAN, MD, CHANELLE COBLE-SADAPHAL, MD, 11/2021)
Vaginal discharge, odor, pruritus and discomfort are common presenting symptoms of adolescents. “Vaginitis” is the general term for disorders caused by infection, inflammation or changes in the normal vaginal flora. Bacterial vaginosis, candida vulvovaginitis and trichomoniasis account for over 90% of infectious vaginitis.

PATHOPHYSIOLOGY

Not all vaginal discharge is pathologic. In reproductive aged women, normal (physiologic) vaginal discharge consists of 1-4 ml fluid/24 hours. Discharge is white or transparent, thick or thin and mostly odorless. Normal vaginal discharge (leukorrhea) should not be accompanied by pruritus, pain, burning or significant irritation, erythema, local erosions, or cervical or vaginal friability.

PREMENARCHAL: Vaginal discharge in prepubertal girls may be the result of hygienic practices, infection, foreign body, dermatologic conditions, and trauma. Vulvovaginal complaints in these girls can sometime be misinterpreted as urinary or bowel symptoms. The factors that contribute to vulvovaginitis at this age includes: a more alkaline vaginal (pH 7), poorly estrogenized vaginal mucosa, lack of labial development, poor hygiene, foreign bodies, obesity, and occlusive clothing. As estrogen levels increasing during puberty, the amount of physiologic vaginal discharge also increases, and there is often more discharge in the 6-12 months prior to menarche. Additionally, frequent rubbing of the vulva, seen in chronic masturbation and sexual abuse, can cause nonspecific vulvovaginitis. Although it occurs infrequently, it is important to always consider child abuse when evaluating a prepubertal girl with vaginal discharge.

POSTMENARCHAL: Premenopausal women have a non-keratinized stratified squamous epithelium of their vaginas, that is rich in glycogen and helps create and maintain an acidic vaginal environment (pH 4.0 to 4.5). Disruption of the vaginal ecosystem by the menstrual phase, sexual activity, contraception, pregnancy, foreign bodies, sexually transmitted infections, or antibiotics can lead to vaginitis.

CLINICAL MANIFESTATIONS

HISTORY	
Discharge	Symptoms: quality, color, consistency, odor, duration
Symptoms	Pruritus, burning, irritation, dyspareunia, spotting, dysuria. Severity of pruritus and soreness correlates with extent of inflammation
Sexual History	Number/gender of partners, date/route of last intercourse Prior sexually transmitted infections Women who have sex with women (WSW) are at high risk for discharge due to Bacterial vaginosis and candida. They should be tested for GC and chlamydia as they may also have sex with men but not disclose this.
Exposures	New hygiene practices, potential irritants (spermicides, soaps, condoms)

PHYSICAL EXAM	
External Genitalia	Inflammatory changes of the vulva: erythema, edema, fissure In pre-adolescents, examination of vaginal vault for foreign bodies can be facilitated by the knee-chest position
Speculum	Identify a foreign body within the vaginal vault, as well as discharge or bleeding within the vault.
Cervix	An erythematous, friable discharge is associated with cervicitis, and not vaginitis, “strawberry cervix” associated with trichomonas
Bimanual	Pelvic or cervical motion tenderness, suggestive of pelvic inflammatory disease or pelvic muscle spasm

DIAGNOSTIC STUDIES	
Vaginal pH	Vaginal pH: Apply a pH test stick/strip for a few seconds to the vaginal sidewall. Normal vaginal pH is 4.0-4.5. Elevated pH suggestive of bacterial vaginosis or trichomoniasis
Wet Mount	Wet mounts: Use a cotton-tipped swab to sample the vaginal discharge. Mix with 1-2 ml of 0.9% saline on a glass slide, view under a microscope.
KOH	KOH may be used in place of normal saline if candidiasis is suspected
Culture Or PCR	Obtain cervical GC/Chlamydia swab during speculum exam. If exam is deferred, can obtain urine GC/Chlamydia

DIFFERENTIAL DIAGNOSES: VAGINAL DISCHARGE

Diagnosis	Discharge*	Symptoms	Vulva Involved	pH	Saline Wet Mount	KOH Wet Mount
Foreign body	Non-specific	Odor	NO	4.0-4.5	NA	NA
Bacterial Vaginosis (BV)	Thin, gray, homo-geneous, “fishy smelling”	Discharge	NO	>4.5	Clue cells	+whiff test (fishy odor with KOH)
Tricho-moniasis (TV)	Purulent, frothy, green, malodorous	Pruritus, dysuria, frequency	NO	5-6	Excess PMNs, Motile trichomonads	Negative
Candida	Thick, white odorless	Pruritus, soreness	YES	4.0-4.5	Pseudo-hyphae	Buds or pseudo-hyphae
*Appearance of discharge alone is never a basis for diagnosis						

MANAGEMENT

Management includes removal of foreign bodies, treatment of infections, reassurance for physiologic discharge and appropriate hygiene measures. Child protection should be consulted if sexual abuse is considered.

Gonorrhea and Chlamydia doses are provided for vaginitis and cervicitis See also: PEM Guide: OB-GYN: Pelvic Inflammatory Disease for regimens for upper gynecologic track disease.

WEBLINK: CDC STD TREATMENT GUIDE 2021

NEISSERIA GONORRHEA: CERVIX, URETHRA, RECTUM	
Primary	Ceftriaxone 500 mg IM (1,000 mg if 150 kg)
Allergy	Risk of cross-reaction between penicillin and 3rd generation cephalosporin is negligible.
	If severe cephalosporin allergy (anaphylaxis, Steve's-Johnson): Gentamycin 240 mg IM x 1 PLUS Azithromycin 2 grams PO x 1
Alternate	Ceftriaxone not available or expedited partner therapy: Cefixime 800 mg PO x 1

CHLAMYDIA TRACHOMATIS	
Primary	Doxycycline 100 mg PO BID x 7 days
Alternate	Azithromycin 1-gram PO OR Levofloxacin 500 mg PO QD x 7days
Pregnant	Azithromycin 1-gram PO OR Amoxicillin 500 mg PO TID x 7days

TRICHOMONIASIS	
Primary	Metronidazole 500 mg PO BID x 7 days
Alternate	Tinidazole 2 grams PO x 1 dose
Pregnant	Metronidazole 2 grams PO x 1 OR Metronidazole 500 mg BID x 5-7 days (fewer GI side effects)
HIV (+)	Metronidazole 500 mg PO BID x 7 days

BACTERIAL VAGINOSIS	
Primary	Metronidazole 500 mg BID x 7 days OR
	Metronidazole gel (0.75%): 1 full applicator (5 grams) intravaginally QD x 5 days
	Clindamycin cream (2%): 1 full applicator (5 grams) intravaginally QHS x 7 days
Alternate	Clindamycin 300 mg PO BID x 7 days
	Clindamycin ovules 100 mg intravaginally QHS x 3 days[1]
	Secnidazole oral granules 2 grams PO x 1[2]
	Tinidazole 2 grams PO QD x 2 days
	Tinidazole 1 gram PO QD x 5 days
1. May weaken rubber/latex (condoms, diaphragms). Do not use these within 72 hrs 2. Sprinkle of unsweetened apple sauce, yogurt, pudding.	

VAGINAL CANDIDIASIS
OVER-THE-COUNTER INTRAVAGINAL AGENTS
Clotrimazole 1% cream 5 g intravaginally daily for 7–14 days
Clotrimazole 2% cream 5 g intravaginally daily for 3 days
Miconazole 2% cream 5 g intravaginally daily for 7 days
Miconazole 4% cream 5 g intravaginally daily for 3 days
Miconazole 100 mg vaginal suppository one suppository daily for 7 days
Miconazole 200 mg vaginal suppository one suppository for 3 days
Miconazole 1,200 mg vaginal suppository one suppository for 1 day
Tioconazole 6.5% ointment 5 g intravaginally in a single application
PRESCRIPTION INTRAVAGINAL AGENTS
Butoconazole 2% cream 5 g intravaginally x 1 (single-dose bio-adhesive product)
Terconazole 0.4% cream 5 g intravaginally daily for 7 days
Terconazole 0.8% cream 5 g intravaginally daily for 3 days
Terconazole 80 mg vaginal suppository one suppository daily for 3 days
PRESCRIPTION ORAL AGENT
Fluconazole 150 mg orally in a single dose

EXPEDITED PARTNER THERAPY

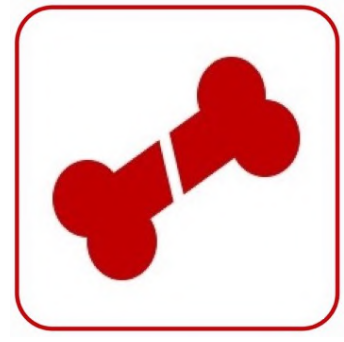
Expedited partner therapy (EPT) should be considered to avoid reinfection in states that allow for EPT. EDT is indicated for eligible partners who are unlikely to seek prompt clinical care. All sexual partners exposed within the 60 days prior to the patient's first reported symptoms or receiving diagnostic test results (whichever occurs earlier) are eligible for EPT. If no sex partners from within the past 60 days are identified, EPT may be offered for the most recent sex partner. EPT should not be provided if the patient is co-infected with gonorrhea, HIV or syphilis. EPT is not indicated in cases of sexual abuse or assault and if the patient's safety is jeopardized.

New York State currently only allows for expedited partner therapy (EPT) for Chlamydia. The recommended therapy is Azithromycin 1 gram orally for 1 dose. EPT is exempt from the requirement for electronic prescription. A paper prescription (write "EPT" in the body of the of the prescription) or the dose of Azithromycin can be provided to the patient for the partner(s).

WEB LINK: NYS DOH EPT POLICY

WEB LINK: STATE EPT POLICIES

ORTHOPEDICS



1. Acromioclavicular Joint Separation	Stephanie Kramer, DO
2. Ankle Injuries	Kevin Ching, MD
3. Arthrocentesis	Rebecca Burton, MD
4. Clavicle Fractures	Stephanie Kramer, DO
5. Elbow Dislocation	Svetlana Dani, MD
6. Elbow Fractures	Janienne Kondrich, MD
7. Finger Injuries	Kelsey Fawcett, MD
8. Forearm Fractures	George Kristinsson, MD
9. Hand Fractures	Nicholas Delacruz, MD
10. Knee Injuries	Kevin Ching, MD
11. Radial Head Subluxation	Janienne Kondrich, MD
12. Rotator Cuff Injuries	Stephanie Kramer, DO
13. Septic Arthritis	Vaishali Shah. MD
14. Shoulder Dislocation	Eric Weinberg, MD
15. Slipped Capital Femoral Epiphysis	Michael Mojica, MD
16. Splinting	Louis Spina, MD

ACROMIOCLAVICULAR JOINT SEPARATION

INTRODUCTION: (STEPHANIE KRAMER, D.O. 3/2017)
The shoulder is a “ball and socket” joint. The anatomy that allows for its extensive range of motion also makes it an inherently unstable joint. It is this instability that makes it susceptible to injury. In the pediatric population, shoulder pain is more likely to occur acutely because of trauma such as falls, although repetitive motions such as those in overhead sports can cause subacute or chronic complaints. Pediatric acromioclavicular joint injuries are typically physeal injuries and not ligamentous. They are referred to as pseudo dislocations. The distal clavicle physes ossifies around 18 years of age.

ANATOMY
The shoulder consists of three bones: the proximal humerus, the clavicle and the scapula (coracoid and acromion processes). These bones articulate at 4 joints: the humeral head with the relatively shallow glenoid fossa, the sternoclavicular joint, the acromioclavicular joint and the scapulothoracic joint. The shoulder is stabilized by a combination of static and dynamic soft tissue structures that include: the glenoid labrum, the glenohumeral ligament complex that make up the joint capsule and the rotator cuff tendons (supraspinatus, infraspinatus, subscapularis, and teres minor muscles).

The acromioclavicular joint is the articulation of the distal clavicle with the acromion process of the scapula. The acromioclavicular joint is supported by the acromioclavicular joint capsule and ligament as well as the coracoclavicular (CC) ligament. The CC ligament is made up of two smaller “V” shaped ligaments attached to the coracoid process inferiorly and clavicle superiorly. The trapezoid ligament inserts 3 cm and the conoid ligament inserts 4.5 cm from end of clavicle on the posterior border.

HISTORY
In an acute traumatic injury, the mechanism of injury often increases the likelihood of specific diagnoses. It is important to determine the exact site of pain, the position of the shoulder at the time of injury and preceding activities. In a patient presenting with chronic shoulder pain, the positions or activities that exacerbate the pain should be explored, as well as training schedules and activities in the athletic population. Acromioclavicular (AC) joint sprains (often called joint separations) typically occur because of a fall or trauma to the superior or lateral aspect of the shoulder with the arm adducted.

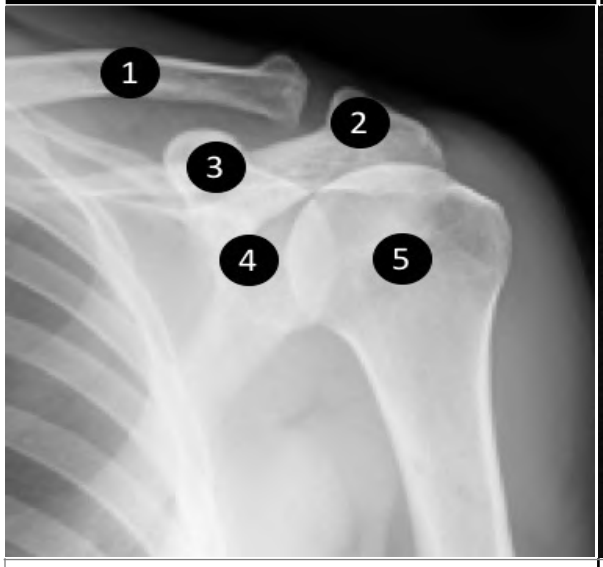
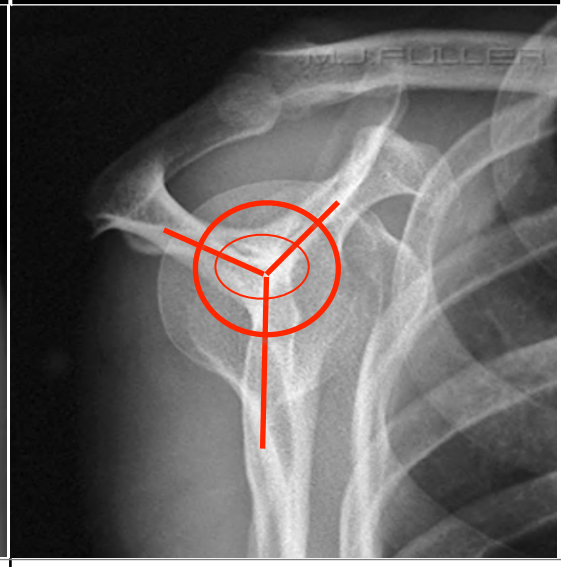
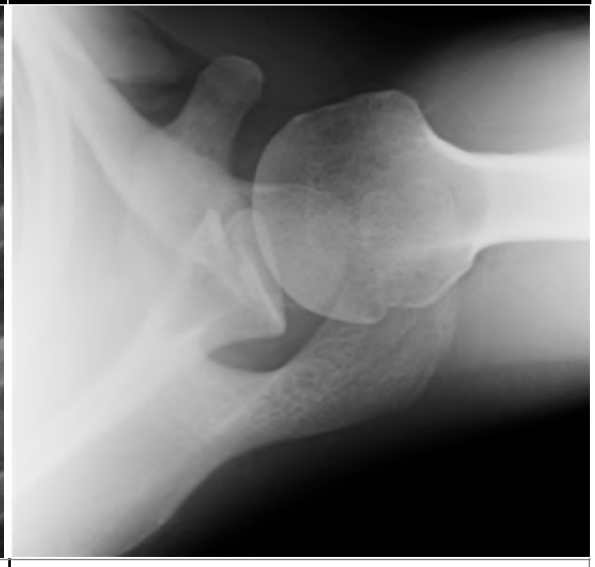
PHYSICAL EXAMINATION
Have the patient remove clothing to visualize visible deformities or asymmetries, the skin for bruising or subtle tenting of the skin, such as that seen with a clavicle fracture. Evaluate neurovascular integrity by palpating distal pulses and assessing strength and sensation distally. Starting at the sternoclavicular joint, palpate along the clavicle to evaluate tenderness, step offs or crepitus. Continue to the acromioclavicular joint and along the spine of the scapula. Palpate the long head of the biceps, and assess symmetry of muscular atrophy. Assess the cervical spine with active range of motion as well as compression/distraction for referred pain. Assess the range of motion of the shoulder both actively (by the patient) and passively (by the examiner). The range of motion is typically described in 3 planes: flexion (forward), extension (backward), abduction (away from the body) and adduction (toward the body) and internal rotation (medial) and external (lateral) rotation. Compare the range of motion of the affected side to the contralateral shoulder. Also assess for symmetry of scapular motion. The scapula should rotate laterally and superiorly with flexion and abduction. Test the biceps with resisted flexion and supination with the elbow at 90° (VIDEO LINK: YERGASON’S TEST), or with the arm flexed to 90° and fully supinated with a straight elbow resisting a downward force (VIDEO LINK: SPEED’S TEST) General Approach to the Shoulder Examination (VIDEO LINK: SHOULDER EXAM).

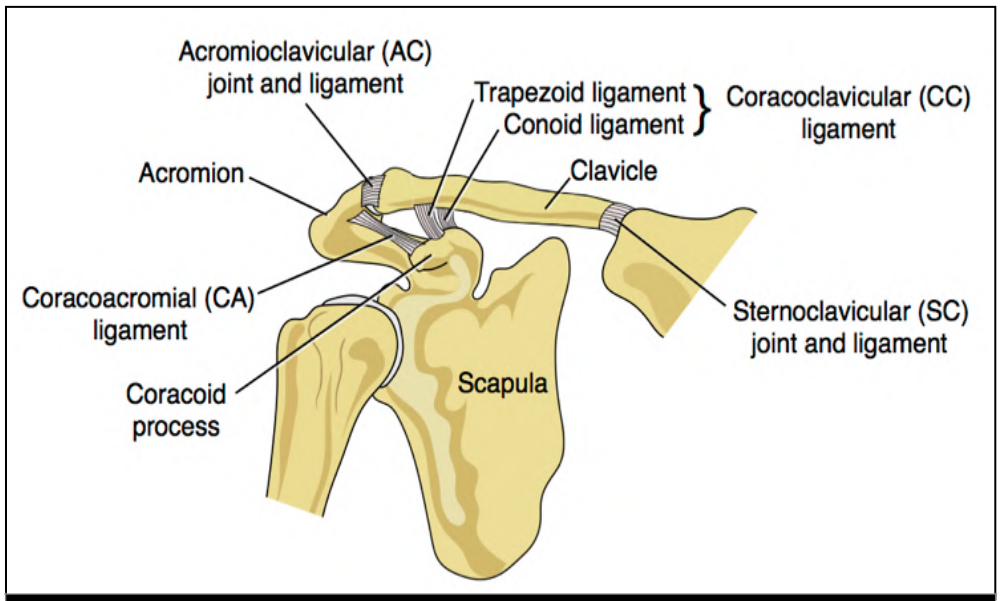
There is typically tenderness over the AC joint without tenderness elsewhere in the shoulder. Tears of the CC ligament result in focal tenderness. The degree of swelling and deformity varies with the type of AC joint injury. Displacement may be in the superior/inferior plane or the anterior posterior plane. Special tests for evaluation of the acromioclavicular joint include the compression test (**V**IDEO LINK: COMPRESSION TEST), performed with one hand on the spine of the scapula and the other on the clavicle, gently squeezing the hands together to provoke pain and/or movement. Another test often used is the scarf test VIDEO LINK: SCARF TEST which is performed with the affected arm raised to 90°. It is then passively adducted across the body. Pain at the acromioclavicular joint is a positive test result increasing the suspicion for an acromioclavicular joint injury.

IMAGING

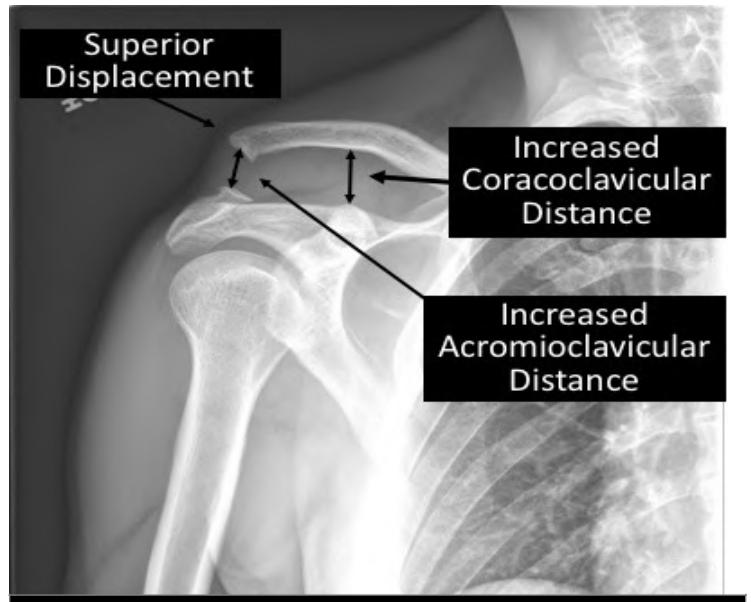
Radiographic evaluation of the shoulder includes upright Anterior-Posterior (AP) XRAYS, as well as specialized views depending on clinical suspicion of diagnosis.

AC joint injuries are classified by the position of the distal clavicle relative to the acromion and coracoid processes. If concerned for AC joint separation, obtain a Zanca (cephalic oblique angled 10-15°) view to isolate the AC joint in addition to an upright AP view. Both shoulders should be imaged separately for comparison of the distance between the lateral border of the distal clavicle and the medial border of the acromion process as well as the distance between the inferior border of the distal clavicle and superior border of the coracoid process. The acromion should be at the level with the clavicle. More than 2-5 mm difference in symmetry may indicate pathology. If the radiographs are normal but clinical suspicion is high, having the patient hold a small weight (stress views) in the affected arm may reveal joint widening, though stress views are obtained less frequently than in the past. Obtain an axillary view if a coracoid fracture is suspected or to determine is anterior or posterior dislocation is present.

AP VIEW	SCAPULA Y VIEW	AXILLARY VIEW
		
1. Clavicle 2. Acromion 3. Coracoid process 4. Glenoid fossa 5. Humeral head	Blade of the Scapula: Anterior and inferior Y Scapula Spine: Posterior Y Glenoid Fossa: Sits at the juncture of the Y (small circle) Head of Humerus: sits in glenoid fossa (large circle)	Coracoid process: Projects anteriorly (upward in this image)



AC JOINT ANATOMY

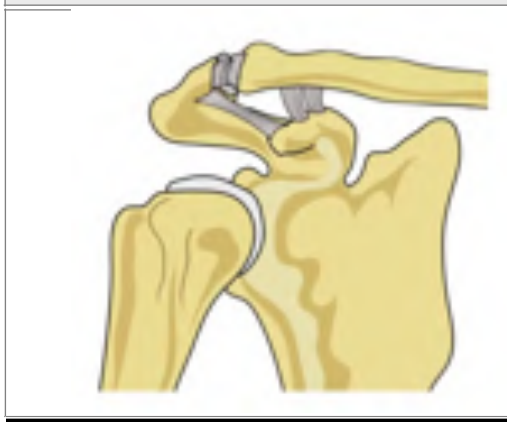


TYPE III AC JOINT SEPARATION

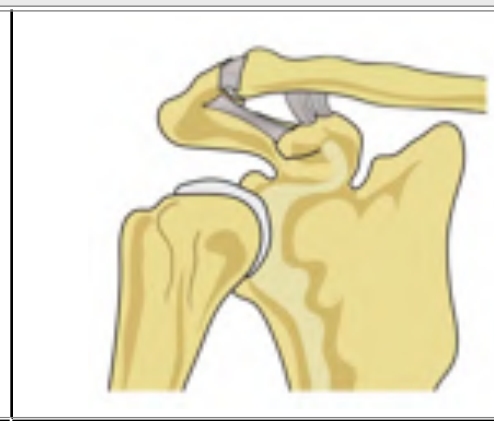
ROCKWOOD CLASSIFICATION: ACROMIOCLAVICULAR JOINT SEPARATION

	Acromioclavicular*	Coracoclavicular*	Exam/XRAY Findings
I	Partial tear	Intact	Tender AC joint, No deformity
II	Complete tear	Partial tear	Superior dislocation: Mild elevation distal clavicle (inferior clavicle not above superior border of acromion)
III	Complete tear	Complete tear	Superior dislocation: Major elevation of distal clavicle (Inferior clavicle above superior border of acromion) Increased CC distance.
IV	Complete tear	Complete tear	Posterior dislocation: Distal clavicle into or through the trapezius muscle +/- sternoclavicular dislocation
V**	Complete tear	Complete tear	Superior dislocation. 1-3x clavicle width. Disruption of muscle attachments of distal clavicle Shoulder droop
VI**	Complete disruption ligaments/muscles	Complete disruption ligaments/muscles	Inferior dislocation. Distal clavicle forced behind biceps, coracobrachialis tendons

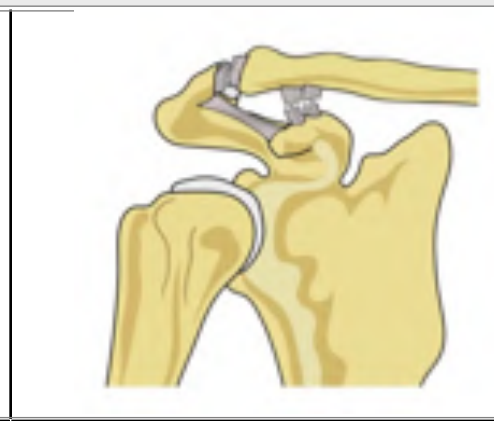
*Coracoclavicular Ligament: Consists of Trapezoid laterally, Conoid medially
**May be associated with neurovascular, cervical spine and thoracic injury



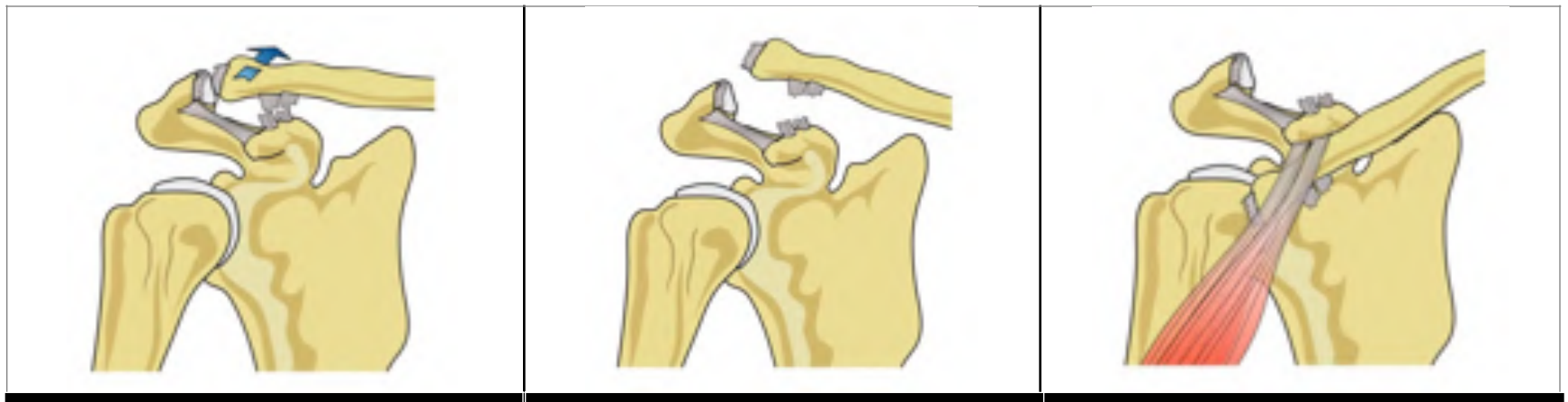
TYPE I



TYPE II



TYPE III



TYPE IV	TYPE V	TYPE VI

MANAGEMENT

Pain control is usually sufficient with non-steroidal anti-inflammatory drugs (NSAIDS). For acute injuries, the patient may apply ice for 20 minutes every 2 hours for the first 48 hours after the incident. Most injuries are immobilized with a sling initially. For injuries that are managed non-operatively, range of motion and shoulder strengthening exercises are indicated when feasible. Management of specific injuries is discussed below.

AC joint separation grades IV-VI require orthopedic consultation for operative management. Urgent reduction may be required for grade VI injuries. Grade III injuries are typically managed non-operatively. Operative management may be considered for grade III AC separations that do not respond to conservative treatment or in population that require significant shoulder strength and mobility (e.g. laborers, elite athletes). Supportive treatment is indicated for grades I and II AC joint injuries. This includes a sling to support the arm for a few days or several weeks, though early mobilization improves outcomes. Range of motion and shoulder strengthening exercises should be encouraged as tolerated.

ANKLE INJURIES

INTRODUCTION: (KEVIN CHING, MD, 5/2015)
Sports related injuries are a common cause of acute ankle injures in children and adolescents. The prevalence is highest among children who play basketball, soccer, and those who ice skate. A working knowledge of the ankle's basic anatomy is essential to understanding the clinical features of foot and ankle pain.

HISTORY
The mechanism of injury may suggest specific injury patterns. Any appreciable sensations or noises (i.e. pops or cracks) may be clues to the underlying problem. Note the onset, location, intensity, and radiation of pain and swelling. Athletes should be asked about their training routine and type of running surface.

Localization of the pain can indicate the likelihood of a specific injury. This may be difficult in younger children who may report non-localized lower leg or foot pain.

INJURY LOCALIZATION	
Talar pain	Acute osteochondral fracture, chronic osteochondritis dissecans, stress fracture.
Lateral ankle pain	Anterior talofibular ligament (ATFL) sprains, sinus tarsi syndrome, distal fibular fractures.
Medial ankle pain	Tendonitis (flexor hallucis longus or Achilles), distal tibial fractures
Anterior ankle pain	Anterior tibialis tendonitis, navicular stress fractures
Posterior ankle pain	Achilles tendonitis, calcaneal fracture

PHYSICAL EXAMINATION
Inspection of the foot and ankle should begin with the child in a seated position. Begin by palpating the distal pulses; vascular compromise may be associated with a posterior ankle dislocation. Evaluate peroneal nerve function by checking ankle dorsiflexion, and test the extensor hallucis longus by opposing dorsiflexion of the first toe. Sensation should be evaluated by testing the space between the 1st and 2nd toes.

Examine the foot and ankle for any obvious deformities, swelling, or ecchymoses. If any gross deformity is found, further manipulation of the foot and ankle should be limited, and careful re-assessment of neurovascular integrity is essential.

Palpate the bones of the ankle first by tracing the tibia, fibula, and talus, paying especially close attention to areas of point tenderness corresponding to an underlying physis. Then palpate the bones of the foot, including the dome of the talus and along each metatarsal. Proceed by palpating along each of the ligaments, including the laterally located anterior talofibular ligament (ATFL), the medially located deltoid ligament, and the tibiofibular syndesmotic ligaments.

Assess passive and active range of motion in plantar-flexion, dorsi-flexion, inversion, and eversion at the ankle, as well as flexion and extension of each toe. The anterior drawer test assesses the stability of the ATFL, and is abnormal if there is a difference in anterior displacement of more than 4 mm when compared to the contralateral ankle. The talar tilt test (inversion stress test) evaluates the stability of both the ATFL and calcaneofibular ligament. A difference of 10 degrees more inversion compared to the contralateral ankle is considered abnormal. The Thompson test can be used to demonstrate rupture of the Achilles tendon if the foot does not plantar-flex.

VIDEO LINK: ANKLE EXAMINATION

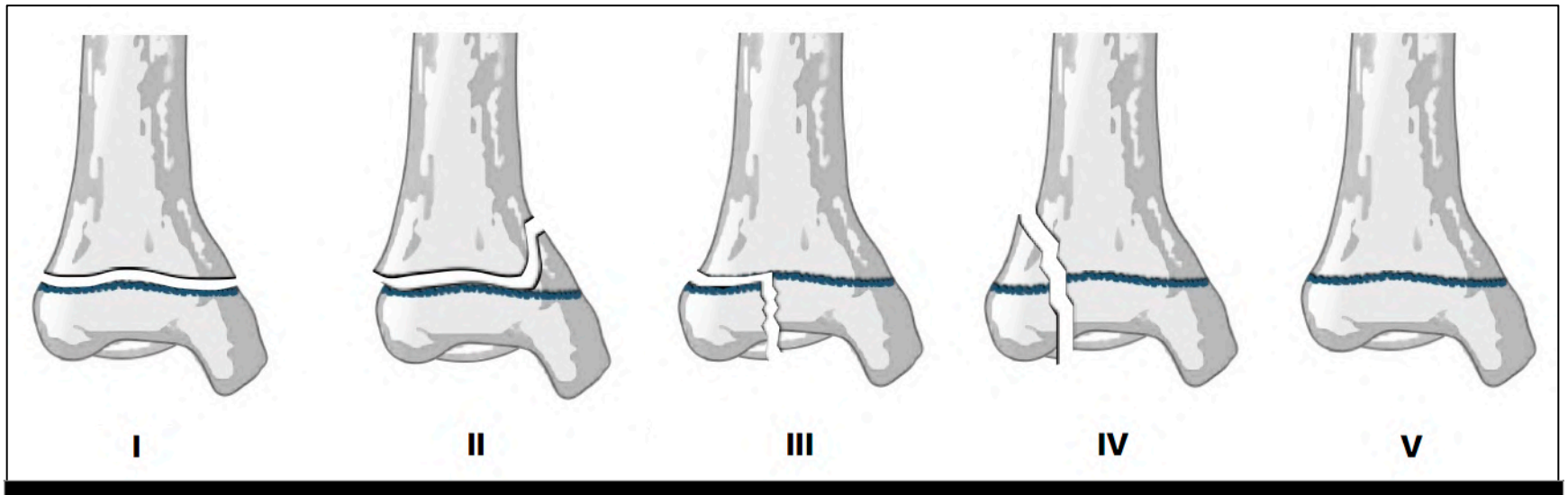
DIAGNOSIS: FRACTURES

Because the epiphyseal growth plates are weaker than ligaments in preadolescents, acute ankle injuries in children are more likely to result in fractures through the physis than a ligamentous sprain.

Isolated fractures of the malleolus are stable if non-displaced. Inversion ankle injuries are associated with a Salter Harris type I fracture of the distal fibula, and typically present with swelling and tenderness of the lateral malleolus. More severe inversion injuries may also include a Salter Harris III of the medial distal tibia. Routine Lateral and AP views are usually diagnostic.

In skeletally immature patients with open ankle physes, any tenderness over the distal fibula physis accompanied by an XRAY without an apparent fracture has classically been considered to be a non-displaced Salter Harris type I fracture of the distal fibula. These ankle injuries were splinted, made non-weight bearing and had a follow up with an orthopedist for re-evaluation in a week. If callous formation was found on a subsequent XRAY then they continue to be managed as a fracture. If pain and tenderness have resolved and no callous formation is identified, then they are managed as a non-fracture.

A recent study challenges this approach. (Boutis JAMA Ped 2016, PubMed ID: 26747077). Patients 5-12 years of age at 2 Children's Hospitals who presented with an acute, isolated lateral ankle injury and with a clinical presumed Salter-Harris type 1 fracture of the distal fibula physis (SH1DF) and with negative 3 view XRAYS were discharged with a removable ankle stirrup splint to be used as needed and recommendation to return to activities as tolerated. They underwent MRI scanning of the bilateral ankles within 1 week of injury. 3% (4/135) 95% CI (0.1-5.9%) had MRI evidence of SH1DF. 89% (108/135) had evidence of ligamentous injury. There was no difference in functional outcomes at 1 and 3 months between those with a SH1DF and either low grade of intermediate-high grade sprains. The authors recommend a less conservative approach which includes a removable splint, a return to activities based on the patients symptoms and follow up of patients only if they are not recovering as expected.

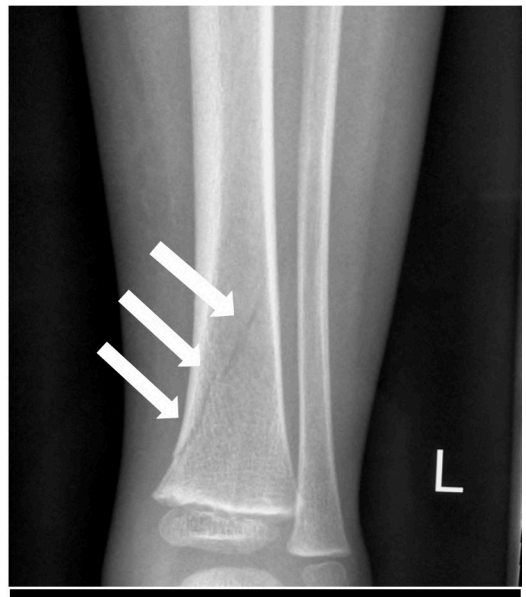


SALTER-HARRIS PHYSIS FRACTURE CLASSIFICATION

Eversion ankle injuries are less common and involve Salter Harris type II fractures through the lateral tibia along with transverse fractures thru the fibula. An eversion ankle injury may also be associated with a proximal fibula fracture (Maisonneuve fracture) and a proximal fibula examination is warranted with this mechanism.

Transitional fracture patterns may result from similar inversion injuries as the child advances into adolescence and the physes begin to close. The juvenile Tillaux fracture occurs when a fragment of the distal anterolateral tibia is torn off by the ATFL during external rotational injuries. Triplanar fractures result from a combination of a juvenile Tillaux and a Salter Harris type II fracture of the distal tibia. Both Lateral and AP views are necessary for diagnosis, though a CT scan may be needed for complete visualization.

TIBIAL SHAFT FRACTURES: Compared to fractures of both the tibia and fibula, isolated fractures of the tibia are usually caused by relatively mild forces. Falls and twisting injuries of the foot are common mechanisms of injury.



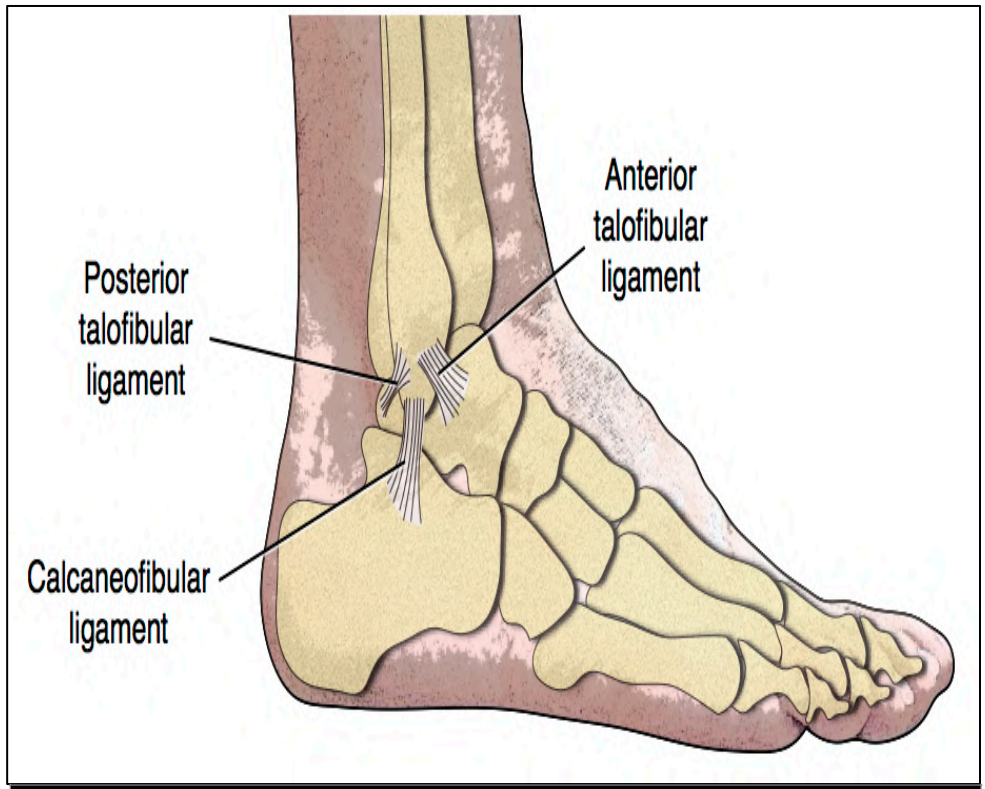
OBLIQUE TIBIA FRACTURE

Toddler's fractures occur most commonly in children younger than 2 years old who are learning to walk. Frequently, there is no definite history of a traumatic event, and the child is brought to the ED because of reluctance to bear weight on the leg. Examine the hip, thigh, and knee first to rule out other causes of limping. A thorough physical examination may be limited by the child's cooperation, but maximal tenderness can usually be elicited over the fracture site. Typical findings are a non-displaced spiral fracture of the tibia and no fibular fracture.

Toddler's fracture often presents in a pattern suspicious for child abuse because there is often no witnessed trauma and the spiral fracture suggests a twisting force. However, presence of an isolated tibia fracture in a toddler, and absence of other signs of inflicted injury (bruises, marks, old fractures) are reassuring and don't necessary warrant further investigations

DIAGNOSIS: SOFT TISSUE INJURIES

Ligamentous injuries are less common in children, though they may occur in combination with avulsion fractures. As skeletal maturity is attained (physes are closed) in adolescence ligamentous sprains constitute the most common sports related ankle injuries.



LATERAL ANKLE LIGAMENTS

The most common mechanism of ligamentous injury is inversion during plantar-flexion. This results in disruption of the lateral ligament complex, including the ATFL, the calcaneofibular ligament, and the posterior talofibular ligament.

The most frequently injured is the ATFL, though stronger forces may lead to combined injuries involving all 3 ligaments. In addition, the peroneus brevis tendon passes posterior and lateral to the lateral malleolus to insert on the base of the proximal 5th metatarsal. Inversion injuries may also result in an avulsion fracture at this location. Forced eversion injuries are less common, and typically involve the medial deltoid ligament. Eversion with or without dorsi-flexion however, may cause injury to the tibiofibular syndesmotic ligaments, which can lead to chronic ankle instability.

GRADING OF ANKLE SPRAINS				
GRADE	LIGAMENT	SWELLING	TENDERNESS	JOINT INSTABILITY
I	Minor stretching	Minimal	Minimal	None
II	Severe tearing	Moderate	Moderate	Mild-Moderate
III	Complete tear	Severe	Severe	Severe

DIAGNOSIS: SUBACUTE INJURIES

An osteochondral fracture may accompany fractures of the talus and can occur in ankle inversion injuries. Osteochondritis dissecans occurs when an articular cartilage segment separates from the subchondral bone and commonly follows ankle inversion injuries. Tenderness over the anterior lateral talus in plantar-flexion is suggestive of either condition, while anterior-posterior or mortise views may reveal a talus dome fracture.

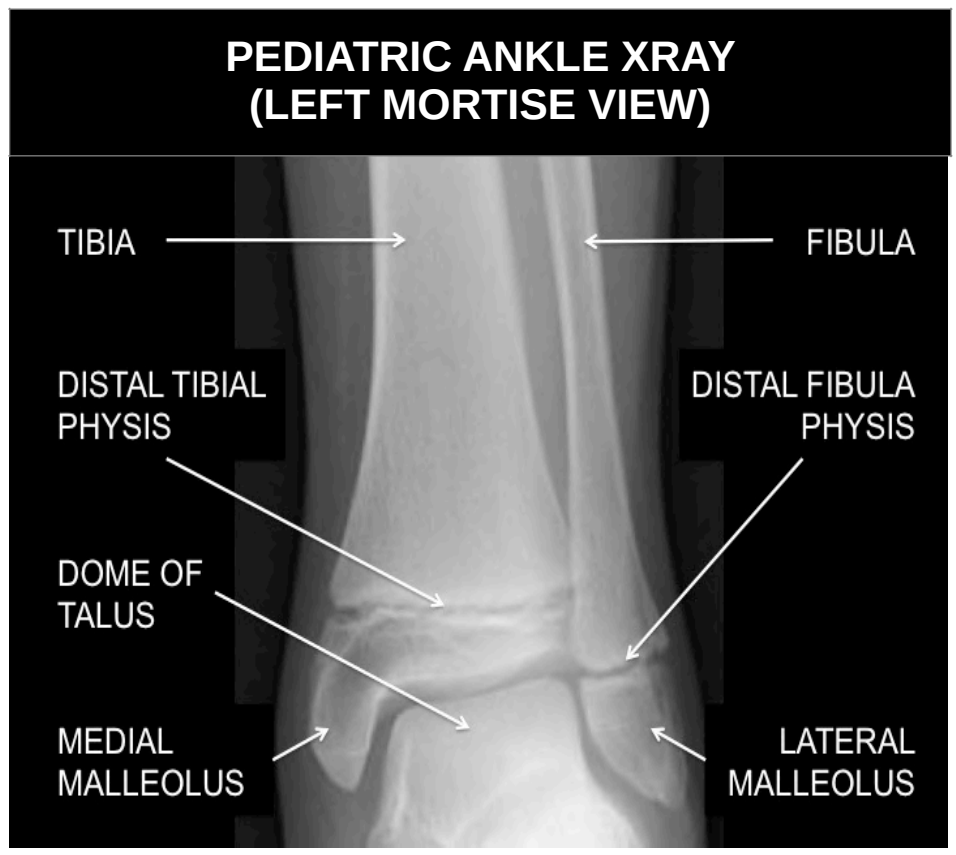
Sinus tarsi syndrome involves a synovitis of the anterior subtalar joint as a complication of recurrent lateral ankle sprains. After the acute swelling and pain recedes, adolescent athletes with this injury often continue to complain of lateral foot pain when running on uneven surfaces. Stress radiographs can be diagnostic.

Peroneal brevis tendonitis is associated with insufficient rehabilitation following inversion ankle injuries. Avulsion of the peroneal brevis tendon may occur acutely or sub-acutely following forced dorsi-flexion in basketball or skiing. An MRI is diagnostic.

Repetitive trauma, improper athletic training, or ill-fitting footwear usually causes Achilles tendonitis. Calcaneal apophysitis (Sever's Disease) can be differentiated by pain localized to the Achilles tendon insertion site. An MRI is diagnostic. Treatment for tendonitis, peritendinitis, tendinosis, retrocalcaneobursitis and calcaneal apophysitis is ice, rest, and nonsteroidal anti-inflammatory drugs. Physical therapy, orthotics, and surgery may be necessary in recalcitrant cases. In patients with tendon rupture, casting or surgery is required.

RADIOGRAPHY

When a fracture is suspected, imaging should begin with plain radiographs (Lateral, AP, and mortise views). Because the overuse of XRAYS exposes children to unnecessary radiation, application of the Ottawa Ankle Clinical Decision Rule can help reduce the use of radiography. When used appropriately, this rule is nearly 100% sensitive in the detection of clinically significant ankle or foot fractures in adults. The presence of an open physis can complicate decision-making. CT scans are often necessary to fully evaluate juvenile Tillaux or triplanar fractures.



OTTOWA ANKLE RULES: XRAY INDICATIONS	
ANKLE	Ankle XRAYS are Indicated if any of Following Criteria are met
	Tenderness over the tip of either malleolus
	Tenderness over the posterior distal 6 cm of the fibula or tibia
	The inability to bear weight both immediately and in the ED for four steps (regardless of limp)
FOOT	Foot XRAYS are Indicated if any of Following Criteria are Met
	Tenderness at the base of the 5th metatarsal
	Tenderness at the navicular bone

A 2009 study validated three pediatric ankle decision rules and compared their accuracy in identifying clinically important ankle fractures (Gravel, Annals EM 2009 PubMed ID: 19647341). The Ottawa Ankle Rule (OAR) was the most sensitive at identifying clinically important ankle fractures with a sensitivity of 100%, 95% CI (93, 100%). The OAR had the potential to decrease XRAY utilization by 7%. The Low Risk Exam Rule (LRER) (Sensitivity: 87%, 95% CI (74, 94%)). and the Malleolar Zone Algorithm (MZA) (Sensitivity: 94%, 95% CI (83, 98%)) had lower sensitivities than the OAR. The MZA would not have reduced XRAY utilization in this study population. The LRER has the potential to decreased XRAY utilization by 46% but at the expense of missing 13% of the clinically important ankle fractures.

MANAGEMENT

Any open fracture, obvious deformity, or neurovascular compromise necessitates immediate orthopedic evaluation and treatment. If vascular compromise is observed and a posterior dislocation is suspected, immediate reduction should be attempted by longitudinal traction to bring the foot and ankle into physiologic position. Immobilize the ankle and proceed with radiographic evaluation.

VIDEO LINK: REDUCTION POSTERIOR ANKLE DISLOCATION

All ankle fractures should be initially splinted in neutral position at 90 degrees to provide appropriate support. If the ankle joint is unstable, operative fixation is indicated. If an emergent condition is excluded and the ankle joint is stable, a short-leg posterior splint or cast will provide adequate support. Orthopedic follow-up should be ensured.

If the history and evaluation suggest a ligamentous injury, the child should be advised of supportive measures (RICE). All grade III sprains and syndesmotic ligamentous injuries require orthopedic referral.

ANKLE SPRAIN MANAGEMENT	
REST	Limit weight bearing by using crutches
ICE	Apply for 20 minutes every 2 hours during the first 48 hours
COMPRESSION	Use elastic bandages to help control swelling
ELEVATION	Elevate the ankle should to reduce swelling
MEDICATIONS	NSAID’s may be prescribed for pain
MOTION	Early mobilization to limit atrophy and inappropriate compensation

ARTHROCENTESIS

INTRODUCTION (REBECCA BURTON, M.D., 5/2021)
In children and adolescents, joint pain and swelling are common manifestations of a wide variety of different disease processes. The broad differential diagnosis includes both benign and serious conditions, some of which can have devastating consequences without prompt identification and medical intervention (i.e. septic arthritis). Arthrocentesis can be a valuable procedural skill used in the evaluation and management of these patients.

INDICATIONS
The primary indication of arthrocentesis is to establish the cause of an acute monoarthritis or polyarthritis, particularly to distinguish bacterial (septic) arthritis from other inflammatory conditions. A timely diagnosis is critical in septic arthritis. Delay in treatment can lead to significant joint destruction, osteonecrosis, growth disturbance, dislocation, and advanced osteoarthritis. Therapeutic use of arthrocentesis is rare in children

DIAGNOSTIC INDICATIONS
Concern for bacterial arthritis (“septic joint”)
Other infections: Lyme disease, gonococcal, tuberculosis, fungal
Crystal arthropathies: Gout, pseudogout

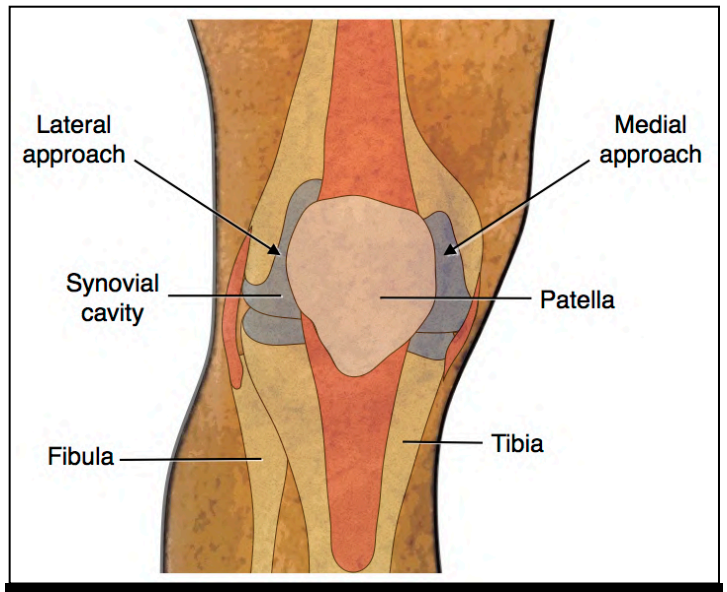
THERAPEUTIC INDICATIONS
Drainage of large effusions or hemarthroses
Rheumatic disorders
Osteoarthritis
Trauma
Bleeding diatheses
Instillation of medications (corticosteroids, local anesthetics)
Rheumatic disorders
Osteoarthritis
Trauma
Determine integrity of joint capsule with overlying soft tissue injury

CONTRAINDICATIONS
ABSOLUTE CONTRAINDICATIONS
Cellulitis or soft tissue infection overlying planned site of needle entry
Allergy to medications being injected
RELATIVE CONTRAINDICATIONS
Suspected bacteremia: Still perform procedure if septic joint is suspected
Patient with a coagulopathy or on anticoagulant medications Consider reversal agents and/or products (FFP, platelets)

ANATOMIC LANDMARKS

KNEE
Largest synovial cavity in body. Easy target for aspiration in presence of clinically significant effusion
Can approach from medial or lateral side
Needle enters skin ~1 cm medial (or lateral) to the superior 1/3 of the patella, directed slightly inferiorly and posteriorly towards the supracondylar notch
Do NOT “walk” the needle along the inferior surface of the patella, as this can damage the delicate articular cartilage

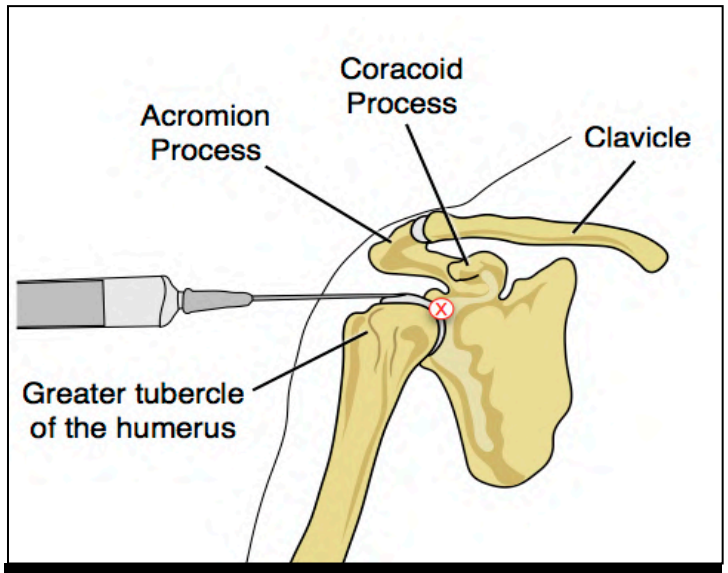
VIDEO LINK: KNEE INJECTION/ASPIRATION



KNEE LANDMARKS

SHOULDER
ANTERIOR APPROACH
Sit patient upright facing you
Insert needle just lateral to coracoid process (between coracoid and humeral head)
Direct needle posteriorly
POSTERIOR APPROACH
Sit patient upright with back facing you
Palpate scapular spine to its lateral limit (the acromion)
Identify the posterolateral corner of the acromion
Insert 1.5-in needle 1 cm inferior and 1 cm medial to this corner
Direct needle anterior and medial toward presumed position of coracoid process
Glenohumeral joint is located at a depth of approximately 1-1.5in

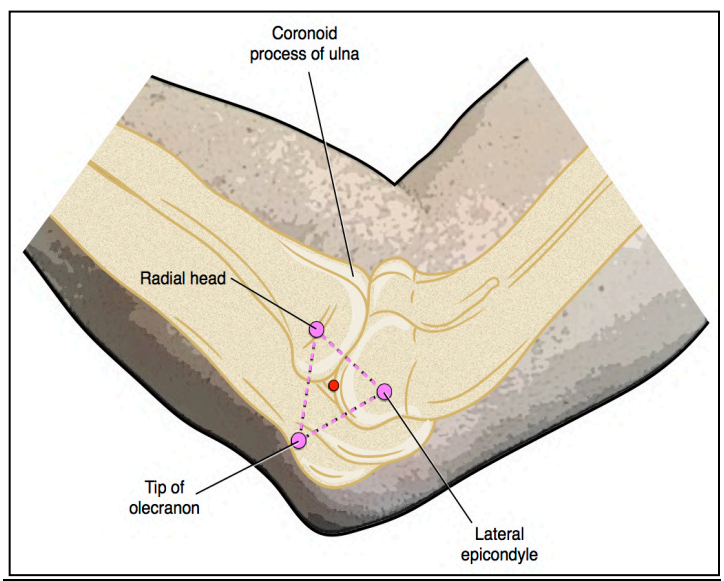
VIDEO LINK: SHOULDER INJECTION/ASPIRATION



SHOULDER LANDMARKS

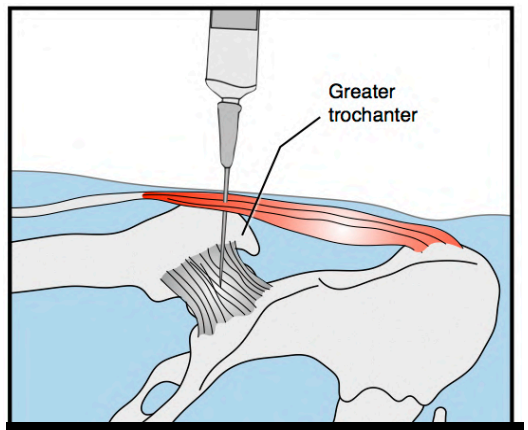
ELBOW
The site of needle insertion is represented
by a red dot
A. Lateral approach
B. Posterior approach
C. Posterolateral approach

VIDEO LINK: ELBOW INJECTION/ASPIRATION

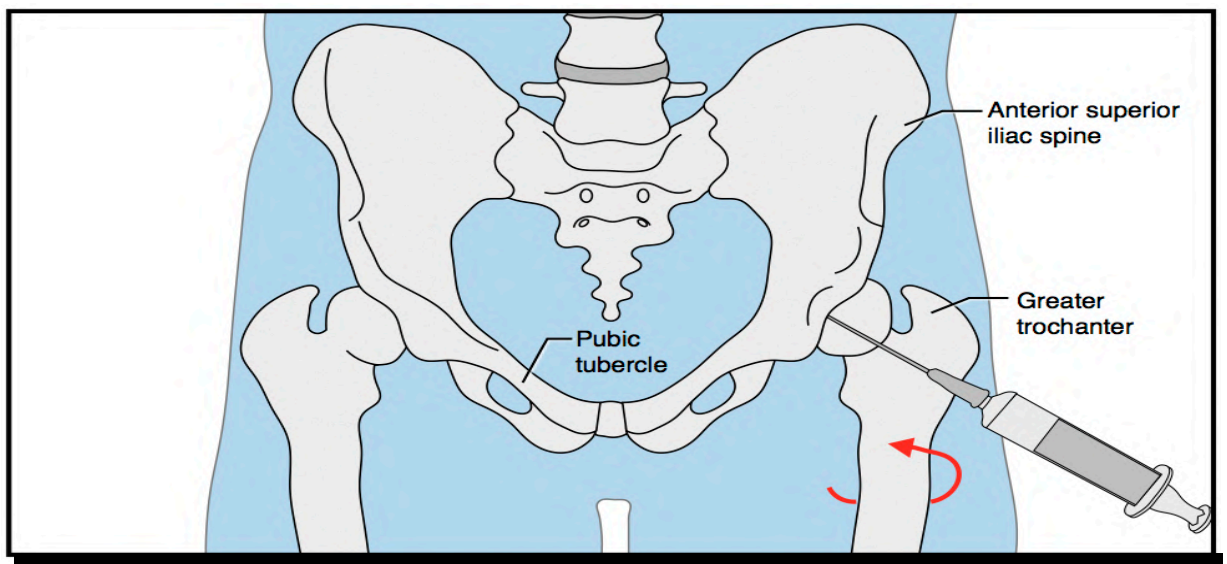


ELBOW LANDMARKS

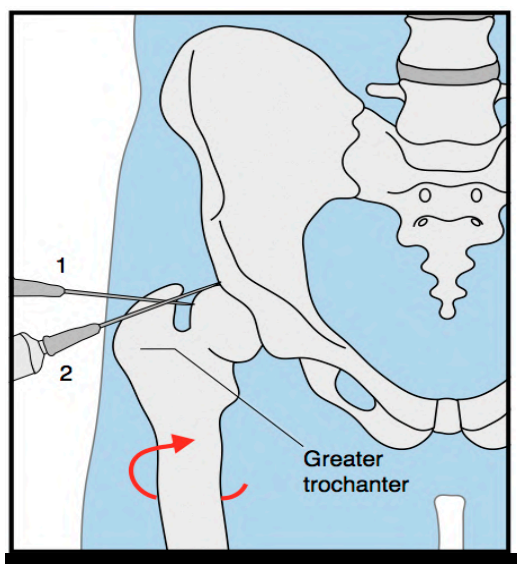
HIP
Curved arrow represents internal rotation of hip
A. Anterior approach
B. Lateral approach
1. Needle is inserted above the greater trochanter and advanced until the femoral neck is encountered
2. The needle has been withdrawn slightly, redirected cephalad, then re-advanced into the joint cavity (*2*).
C. Alternative approach



HIP LANDMARKS (ALTERNATIVE)



HIP LANDMARKS (ANTERIOR)

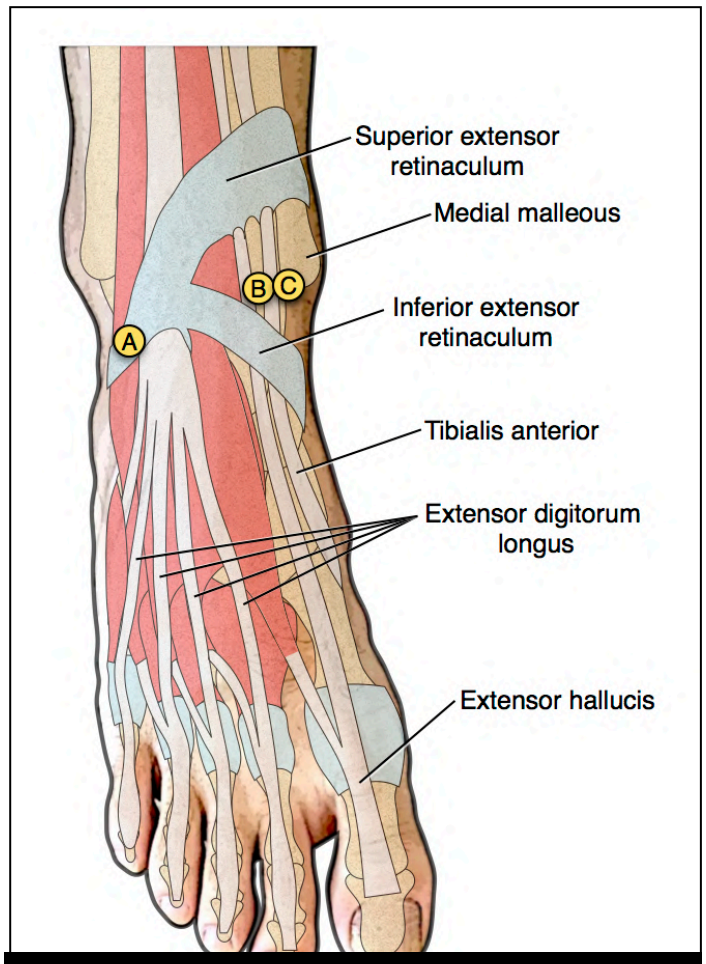


HIP LANDMARKS (LATERAL)

VIDEO LINK:
HIP ASPIRATION/INJECTION (US GUIDED)

ANKLE
The site of needle insertion is represented by A,B,C
A. Anterolateral approach
B. Anteromedial approach
C. Alternative technique for anteromedial approach

VIDEO LINK: ANKLE ASPIRATION/INJECTION



ANKLE LANDMARKS

EQUIPMENT
Observe Universal precautions: Sterile gloves, drape, antiseptic solution
Anesthesia: 1% lidocaine with epinephrine, consider EMLA, ethyl chloride spray
Consider procedural sedation and analgesia
Needle: 18-22 gauge for large joints (knee, hip, shoulder, ankle, elbow) 25 gauge for smaller joints (i.e. interphalangeal joints)
Syringe size appropriate to suspected aspirate amount or medication instillation (Should be heparinized if planning on sending fluid for analysis)
Tubes for synovial fluid analysis
Consider adjunctive imaging modalities such as ultrasound, fluoroscopy

PROCEDURE	
1	Obtain consent: Explain procedure, benefits, and risks to patient and family
2	Position patient as applicable Knee” Supine with knee fully extended OR flexed to 15-20° Hip (anterior or lateral approach): Supine with hip internally rotated
3	Identify landmarks. Mark needle entry site with a sterile pen/marker
4	Prep site with antiseptic solution: Povidone-Iodine or Chlorhexadine
5	Use sterile gloves and use a sterile drape over the region
6	Consider procedural sedation and/or child life consultation
7	Anesthetize the region: 1% lidocaine +/- Epinephrine Anesthetize dermis at entry site using a small-gauge needle Anesthetize deeper along the planned needle trajectory
8	Consider ultrasound/fluoroscopic guidance for difficult joints to a: Ankle, hip
9	Using an appropriately sized needle connected to a syringe, enter the skin and then direct the needle along the proper trajectory (see “Anatomic Landmarks” above).
10	Advance the needle slowly, drawing back continuously on the plunger. Aspiration of fluid indicates entry into the synovial cavity.
11	Aspirate as much fluid as possible (or inject medication) - “Milking” the effusion (eg by compressing on the suprapatellar region) can facilitate aspiration
12	After aspirated, remove the needle, cleanse the skin, and apply a bandage or dressing Consider using a woven elastic bandage or immobilizer to help reduce post procedural discomfort and swelling Some advise 24 hours of bed rest. Others recommend avoidance of excessive activity for 24 hours, along with passive range of motion exercises
13	Distribute aspirate into appropriate containers (Ideally ≥ 2 ml per tube). Send for analysis

ASPIRATE ANALYSIS	
Gram stain and culture (aerobic and anaerobic)	Provides most definitive evidence for septic arthritis. Sensitivity for non-gonoccocal bacterial arthritis is much higher than for disseminated gonococcal infection.
Cell count and differential	Primarily used to differentiate inflammatory (i.e. septic joint, crystal arthropathies) from non-inflammatory (trauma, osteoarthritis) effusions. Cutoff value of > 2000 WBCs/mL and/or > 75% PMNs is often used to diagnose inflammatory effusions. Cannot reliably distinguish between inflammatory etiologies
Crystal analysis	Use of polarizing-light microscope to visualize monosodium urate (gout) or calcium pyrophosphate dihydrate (pseudogout) crystals. Presence of crystals does NOT exclude septic arthritis, as the conditions can coexist.
Glucose, protein, and LDH	Minimal discriminatory value, should NOT be routinely sent.
Other studies	Specific tests for atypical infections Cytologic evaluation for suspected malignant effusion

COMPLICATIONS
Are infrequent and rarely serious
Post-injection inflammatory reaction (s/p corticosteroid injection)
Subcutaneous atrophy and depigmentation (s/p corticosteroid injection)
Intraarticular calcifications (s/p corticosteroid injection); asymptomatic
Infection; decrease risk using aseptic technique, avoidance of procedure if evidence of overlying skin or soft tissue infection or bacteremia
Hemorrhage; increased risk in patients with thrombocytopenia
Effects on growing cartilage: Limited data, but existing studies suggest no long-term negative effects on articular cartilage or skeletal growth

PROCEDURE PEARLS
Arthrocentesis is of limited value in children If joint inflammation is not thought to be infectious in origin.
Failure to aspirate synovial fluid (“dry tap”) may be due to obesity, misdiagnosis of effusion, hypertrophy of synovium due to chronic inflammation, or obstruction of the needle lumen by a synovial fold (pica) or particulate matter
If performing arthrocentesis as a therapeutic procedure, fluid may rapidly re-accumulate, particularly if additional medications are not given
Aspiration of purulent material is an indication for surgical drainage
In septic arthritis, intraarticular antibiotics are not indicated, as intravenous antibiotics reach excellent concentrations in synovial fluid; In addition, intraarticular antibiotics may exacerbate the inflammatory response
Children with early osteomyelitis may develop a sterile sympathetic effusion in the proximate joint; always do a thorough evaluation for bony tenderness to rule-out osteomyelitis.
Sympathetic effusions may also occur in leukemia and other neoplastic conditions.
Gouty arthritis is extremely rare in children before puberty, even among children with Lesch-Nyan

CLAVICLE FRACTURES

INTRODUCTION: (STEPHANIE KRAMER, D.O. 2/2020)
The shoulder is a “ball and socket” joint. The anatomy that allows for the extensive range of motion of the shoulder also makes it an inherently unstable joint. It is this instability that makes it susceptible to injury. In the pediatric population, shoulder pain is more likely to occur acutely because of trauma such as falls, although repetitive motions such as those in overhead sports can cause subacute or chronic complaints. The clavicle is the most common fracture in children (10-15% of all fractures).

ANATOMY

The shoulder consists of three bones: the proximal humerus, the clavicle and the scapula (coracoid and acromion processes). These bones articulate at 4 joints: the humeral head with the relatively shallow glenoid fossa, the sternoclavicular joint, the acromioclavicular joint and the scapulothoracic joint. The shoulder is stabilized by a combination of static and dynamic soft tissue structures that include: the glenoid labrum, the glenohumeral ligament complex that make up the joint capsule and the rotator cuff tendons (supraspinatus, infraspinatus, subscapularis, and teres minor muscles).

The clavicle is a vaguely S-shaped bone which articulates with the sternum medially (sternoclavicular joint) and the acromion process of the scapula laterally (acromioclavicular joint). It is divided into medial, middle and lateral segments. Lateral soft tissue structures consist of the coracoclavicular ligament (trapezoid and conoid ligaments) and the acromioclavicular ligament.

CLAVICLE FRACTURE CLASSIFICATION	
Group 1	Fractures of the middle third (midshaft) of the clavicle (90% of pediatric)
Group 2	Fractures on the lateral (distal) third
Group 3	Fractures on the medial (proximal) third.

HISTORY

In an acute traumatic injury, the mechanism of injury often increases the likelihood of specific diagnoses. It is important to determine the exact site of pain, the position of the shoulder at the time of injury and preceding activities. In a patient presenting with chronic shoulder pain, the positions or activities that exacerbate the pain should be explored, as well as training schedules and activities in the athletic population. Clavicle fractures typically occur because of a fall onto the lateral shoulder, fall onto an arm outstretched to the side or from a direct blow to the clavicle.

PHYSICAL EXAMINATION

Have the patient remove clothing to visualize deformities or asymmetries and the skin for bruising or subtle tenting of the skin, such as that seen with a clavicle fracture. Evaluate neurovascular integrity by palpating distal pulses and assessing strength and sensation distally. Starting at the sternoclavicular joint, palpate along the clavicle to evaluate tenderness, step offs or crepitus. Continue to the acromioclavicular joint and along the spine of the scapula. Palpate the long head of the biceps, and assess symmetry of muscular atrophy. Also assess the cervical spine for referred pain.
Assess the range of motion of the shoulder both actively (by the patient) and passively (by the examiner). The range of motion is typically described in 3 planes: flexion (forward), extension (backward), abduction (away from the body) and adduction (toward the body) and internal rotation (medial) and external (lateral) rotation. Compare the range of motion of the affected side to the contralateral shoulder.

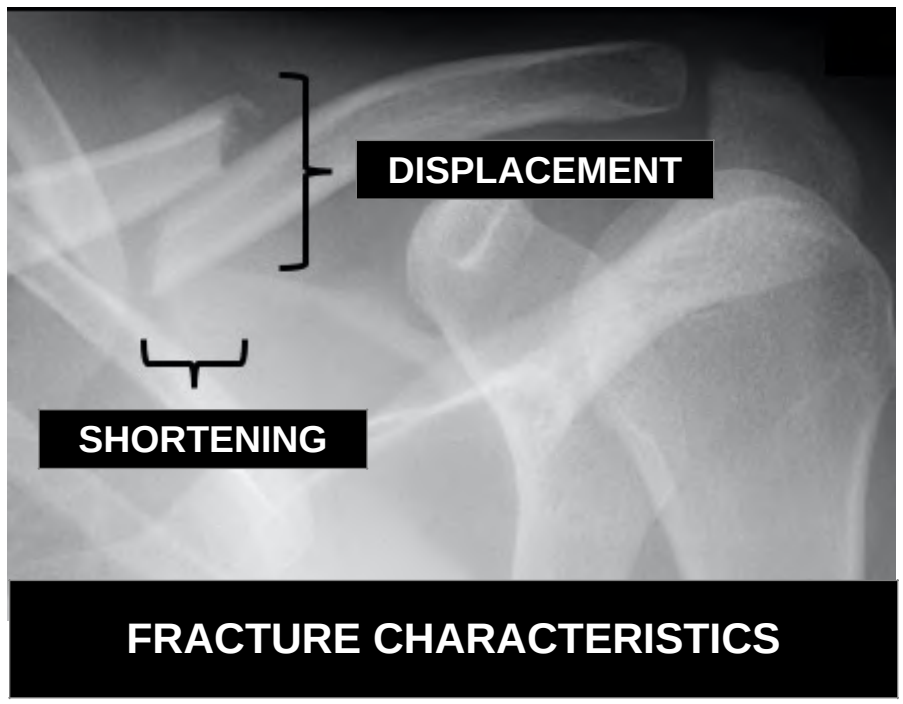
VIDEO LINK: GENERAL APPROACH TO THE SHOULDER EXAMINATION

Also assess for symmetry of scapular motion. The scapula should rotate laterally and superiorly with flexion and abduction. Test the biceps with resisted flexion and supination with the elbow at 90° (VIDEO LINK: YERGASON'S TEST), or with the arm flexed to 90° and fully supinated with a straight elbow resisting a downward force (VIDEO LINK: SPEED'S TEST)

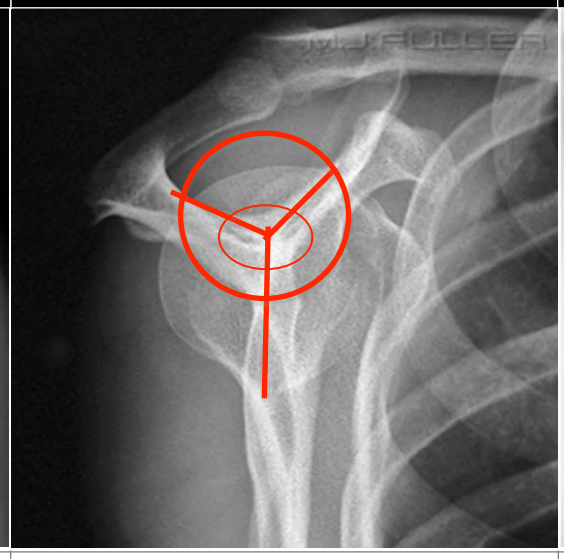
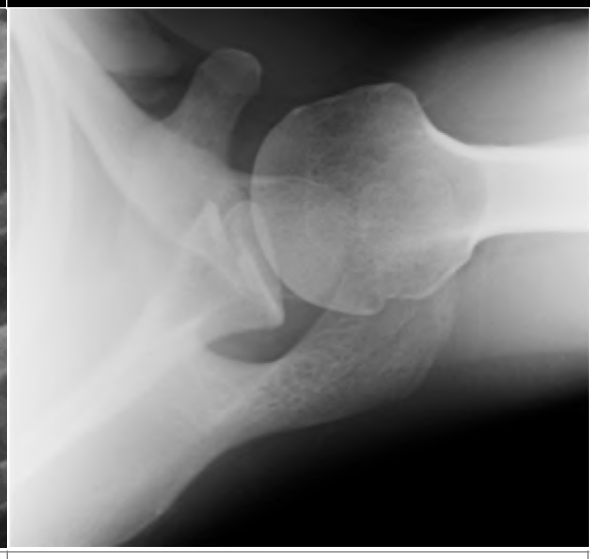
IMAGING

Radiographic evaluation of the shoulder includes upright Anterior-Posterior (AP) X-RAYS, as well as specialized views depending on clinical suspicion of diagnosis. CT is indicated assess the possibility of intra-articular involvement. If there is concern for neurovascular damage an MRI with contrast should be obtained.

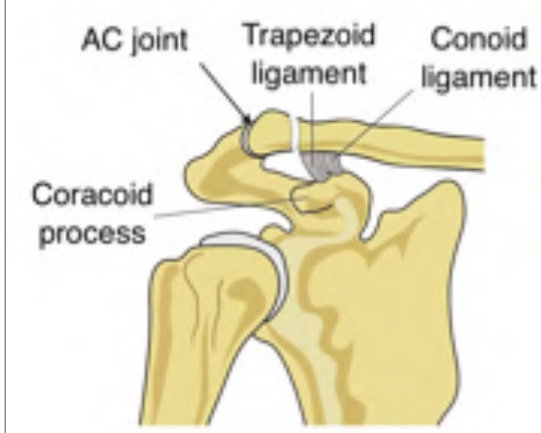
Standard AP view of bilateral shoulders should be obtained to measure clavicular shortening. A 45° cephalic tilt (Serenity view) minimizes the overlap of the ribs and scapula and provides better assessment of superior/inferior displacement. A 45° caudal tilt view can be used to assess determines anterior-posterior displacement. A CT may be useful for sternoclavicular injuries.



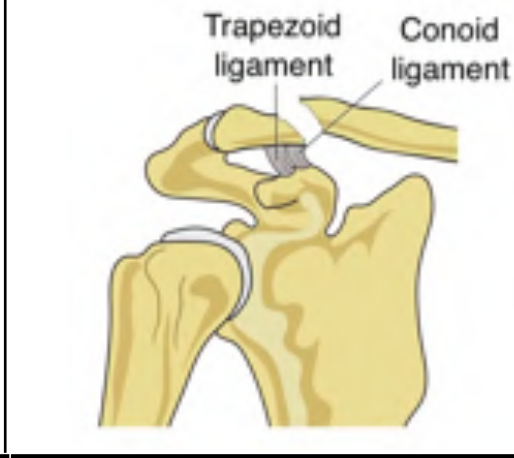
FRACTURE CHARACTERISTICS

AP VIEW	SCAPULA Y VIEW	AXILLARY VIEW
		
1. Clavicle 2. Acromion 3. Coracoid process 4. Glenoid fossa 5. Humeral head	Blade of the Scapula: Anterior and inferior Y Scapula Spine: Posterior Y Glenoid Fossa: Sits at the juncture of the Y (small circle) Head of Humerus: sits in glenoid fossa (large circle)	Coracoid process: Projects anteriorly (upward in this image)

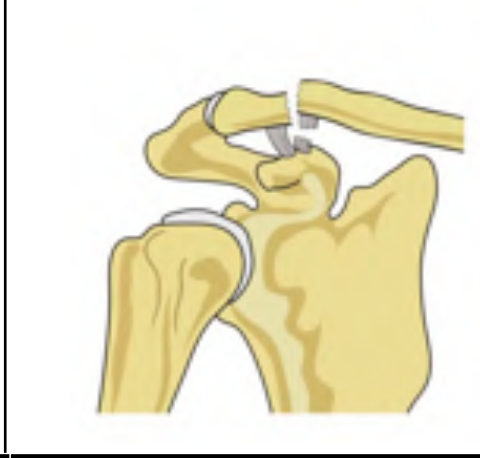
LATERAL CLAVICLE FRACTURES: TOSSY/ROCKWOOD CLASSIFICATION				
		CC* Ligament		
	Fracture Location/Type	Trapezoid	Conoid	
1	Lateral to CC ligament	Intact	Intact	Stable, minimal displaced
2a	Medial to CC ligament	Intact	Intact	Potentially unstable
2b	Between trapezoid and conoid	Intact	Torn	Potentially unstable
	Lateral to CC ligament	Torn	Torn	Potentially unstable
3	Intraarticular (AC joint)	Intact	Intact	
4	Physeal (skeletally immature)	Intact	Intact	
5	Comminuted	Intact	Intact	
*Coracoclavicular ligament: Consists of Trapezoid laterally, Conoid medially				



TYPE I



TYPE IIA



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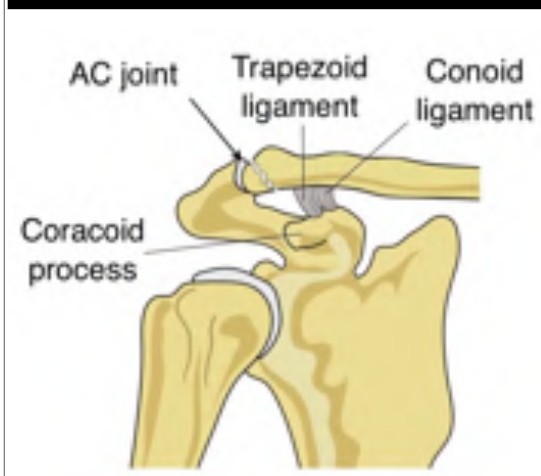

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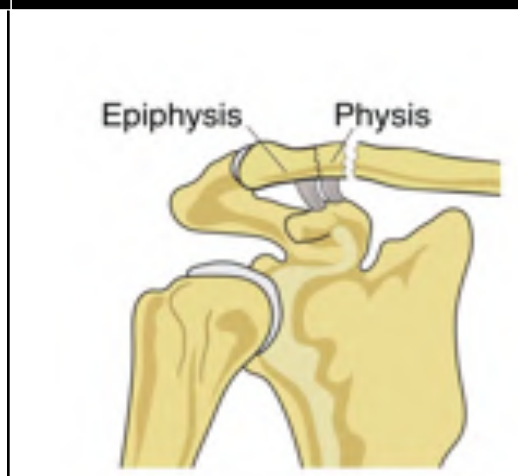
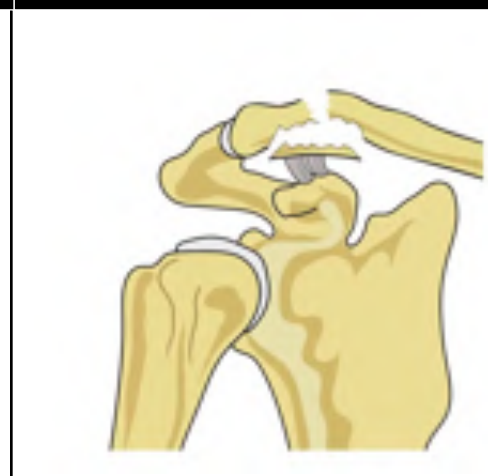


TYPE IV



TYPE V

MANAGEMENT

Pain control is usually sufficient with non-steroidal anti-inflammatory drugs (NSAIDS). For acute injuries, the patient may apply ice for 20 minutes every 2 hours for the first 48 hours after the incident. Most injuries are immobilized with a sling initially. For injuries that are managed non-operatively, range of motion and shoulder strengthening exercises are indicated when feasible.

Most clavicle fractures can be managed non-operatively and should heal in 4-6 weeks. Clavicle fractures that may require operative repair are listed in the table below. Overlapping and shortening need to be monitored during the first 3-4 weeks of non-operative management to avoid deformity.

URGENT ORTHOPEDIC CONSULTATION
Open clavicle fracture. Any laceration/puncture wound over the clavicle
Tenting of the skin: Can lead to pressure necrosis and an open fracture
Neurovascular compromise
Respiratory of hemodynamic compromise: Associated with posterior displacement
“Floating shoulder”: Ipsilateral lateral clavicle fracture and glenoid neck fracture

OUTPATIENT ORTHOPEDIC REFERRAL (MAY REQUIRE SURGERY)
Comminuted clavicle fractures
Displaced fracture: > 1 bone width
Shortening: > 2 cm
Lateral third clavicle fractures: Types 2A, 2B and 5
Medial third fractures: Posterior displacement

The goal should be to minimize pain by providing support for the weight of the patient’s arm. Studies have not shown a difference in outcomes between the use of a sling or figure-of-eight splints. However, the sling may be easier to use. Children often develop a significant callus formation, and it is important to educate parents about this normal progression of healing. Healing usually occurs within four to six weeks. Gentle range of motion exercised may began at 2-4 weeks and strengthening exercises at 6-10 weeks.

STERNOCLAVICULAR DISLOCATIONS

INTRODUCTION

Sternoclavicular joint dislocations are rare. They typically occur due to high-impact trauma and in patients with hypermobility connective tissue disorders.

ANTERIOR DISLOCATIONS: Anterior sternoclavicular dislocations are more common. They are typically the result of lateral blow to the shoulder that pushes the clavicle medially and anteriorly. This ruptures the anterior joint capsule and can tear the costoclavicular ligament. Patients present with a painful lump lateral to the sternum. XRAY can distinguish between anterior dislocation and a fracture.

POSTERIOR DISLOCATIONS: Posterior sternoclavicular dislocations are rarer then anterior dislocation but are more often associated with life-threatening injury to underlying mediastinal structures. They are typically the result of a direct blow to the anteromedial chest or an indirect blow to the posterolateral shoulder. Patients present with signs and symptoms of compression of mediastinal structures including dyspnea, dysphagia, or neurovascular compromise. Pain is localized to the medial clavicle without significant swelling (in contrast to anterior dislocations).

The diagnosis can be made with chest CT with 3-D reconstruction. CT tomographic angiography may be required to assess subclavian artery integrity. Chest XRAYs should be obtained to assess for pneumothorax, hemothorax, and pneumomediastinum.

MANAGEMENT

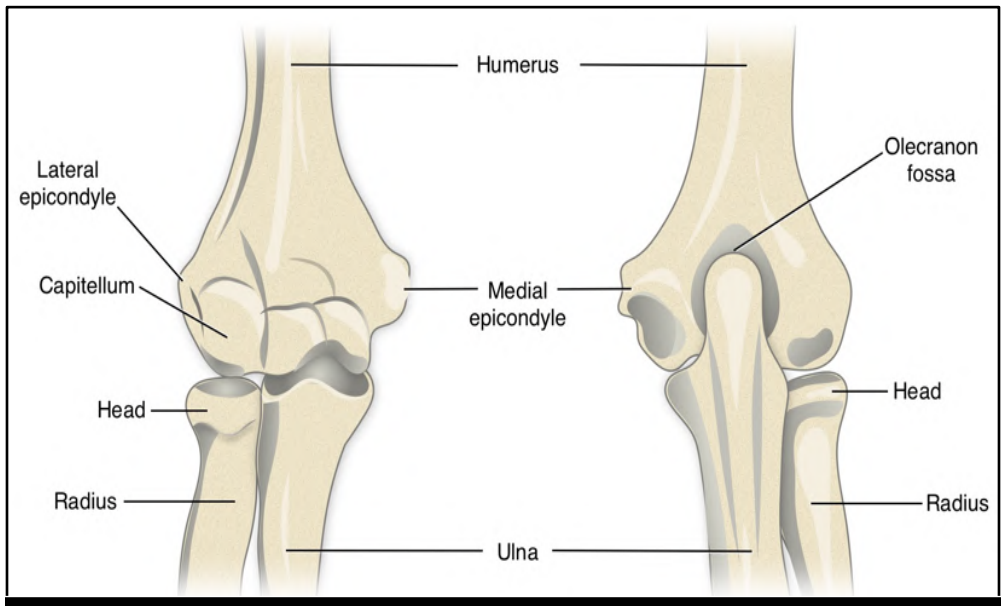
Management depends on the direction of the dislocation, the severity of symptoms, and the presence of complications. Dislocations can be reduced by an experienced orthopedist under procedural sedation though operative closed or open reduction may be required.

ELBOW DISLOCATIONS

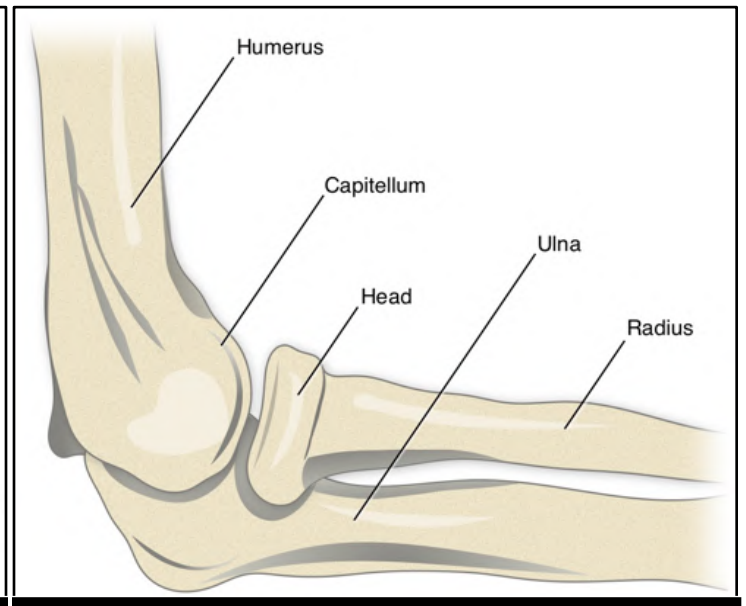
INTRODUCTION (SVETLANA DANI, M.D., 04/2018)
The elbow is one of the most stable joints in the body and requires significant force to dislocate. Yet, it is the most commonly dislocated joint in children and second most dislocated joint in adults, after the shoulder. It is commonly due to a fall onto the outstretched arm and about 40% are as a result of a sporting injury. This PEM Guide will review elbow dislocation and associated fractures. (See: PEM Guide: Orthopedics: Elbow Fractures)

ELBOW ANATOMY

BONES: The elbow is a synovial hinge joint made up of three bones: humerus, ulna and radius. There are two separate bony articulations which allow for stability and function. The first articulation is between the trochlear notch of the ulna and the trochlea of the humerus. The second articulation is the head of the radius and the capitulum of the humerus. The elbow has two main arcs of motion: flexion-extension and pronation-supination. The ulna-humeral articulation is responsible for the flexion and extension while the radio-ulnar joint and the radio-humeral articulation facilitate pronation and supination in concert with the distal radio-ulnar joint at the wrist and the forearm muscles. The contour of the elbow bony surfaces of the elbow allow for a high congruency, making the joint very stable.

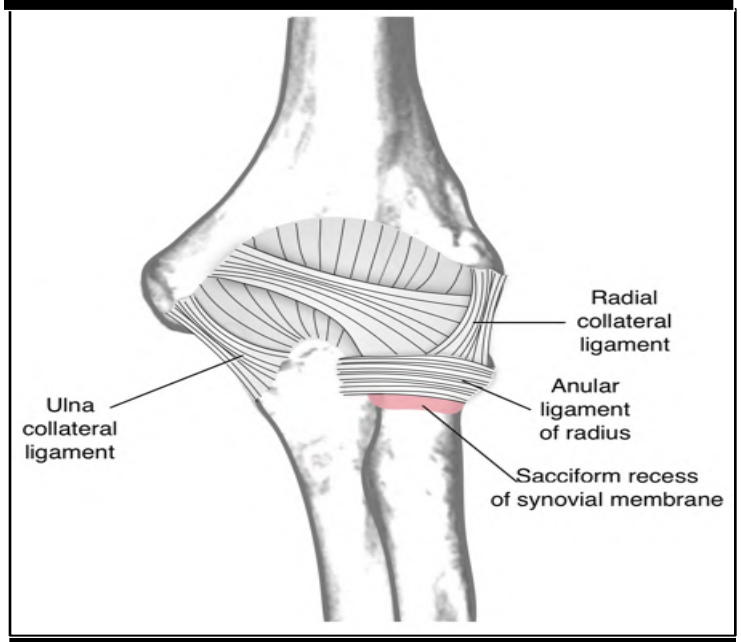


ELBOW BONES: ANTERIOR/POSTERIOR



ELBOW BONES: LATERAL

JOINT CAPSULE: The synovial joint of the elbow is enclosed in a capsule composed of strong fibrous material. The capsule is reinforced by the lateral (radial) collateral ligament complex and the medial (ulnar) collateral ligament complex, stabilizing the joint further. The MCL provides valgus stability while the LCL provides rotational and varus stability. The annular ligament wraps around the head of the radius and retains the radioulnar articulation. In nursemaid's elbow, frequently treated in the pediatric population, we see the radial head slip away from the grasp of the annular ligament. (See also PEM Guide: Trauma: Radial Head Subluxation).

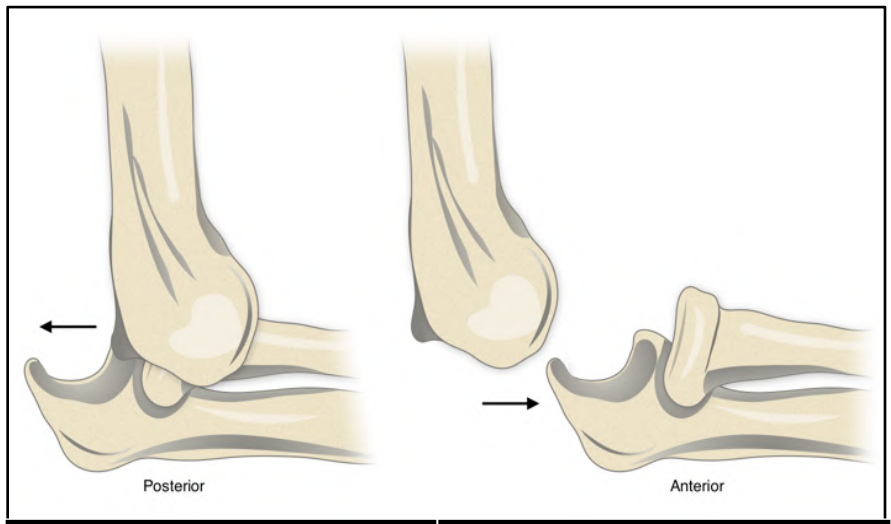


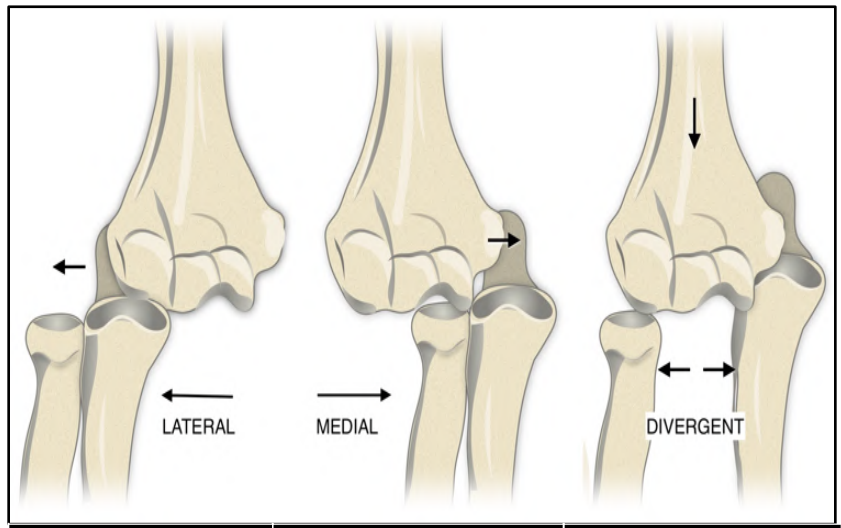
ELBOW: JOINT CAPSULE

NEUROVASCULATURE: The blood supply to the elbow joint comes from the recurrent and collateral branches from the brachial and deep brachial arteries. The median, musculocutaneous and radial nerves run anteriorly to the joint and the ulnar nerve runs posteriorly. The brachial artery is the most commonly injured vessel, especially with anterior and open dislocations. All vessels and nerves run the risk of entrapment either during the dislocation or after the reduction.

MECHANISM

Elbow dislocations are described by the direction of displacement of the radius and ulna relative to the humerus. Dislocation results from an axial loading force across the elbow joint together with a supination force through the forearm and a valgus stress as often seen during a fall on an outstretched arm. Posterior dislocations are the most common, with 80% of all dislocation being posterolateral. The remainder are posteromedial, medial, anterior, lateral or divergent. Elbow dislocations can be simple, with no associated fracture, and complex or associated with one or more fractures.





POSTERIOR	ANTERIOR	LATERAL	MEDIAL	DIVERGENT

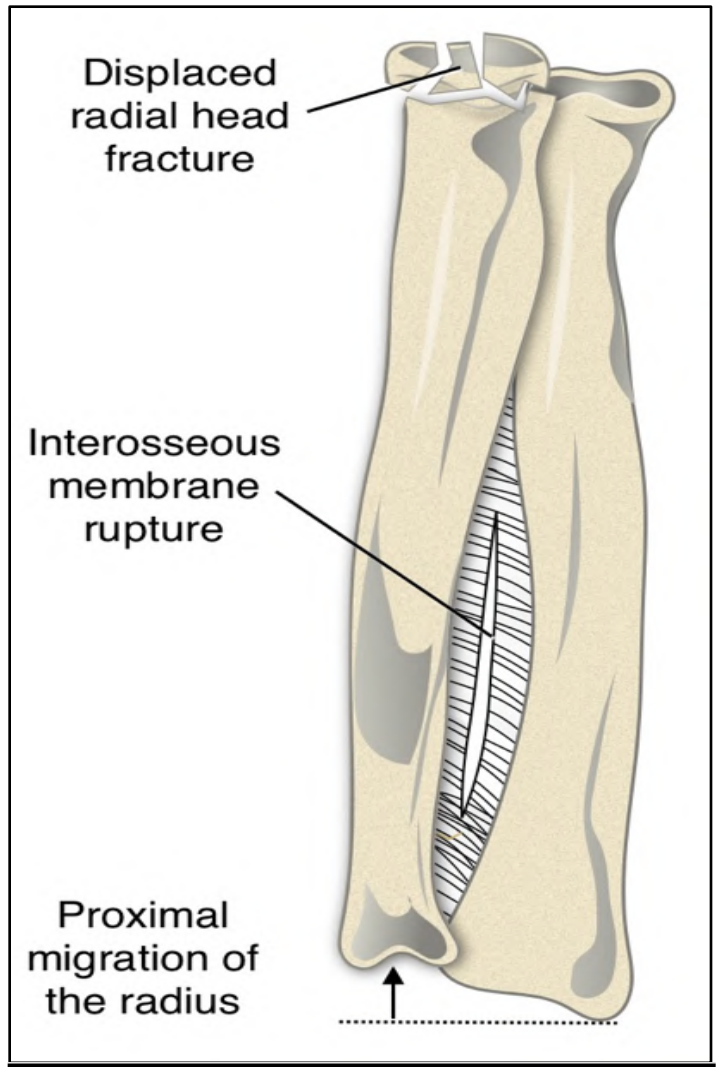
SIMPLE DISLOCATIONS: Simple dislocations account for 50-60% of all elbow dislocations. They are very painful and are usually easily identifiable on physical exam with an obvious posterior deformity of the elbow. Note that the examination may be normal with some partial dislocations. The theory is the elbow dislocates in 3 stages. During the three stages, the capsuloligamentous stabilizers are disrupted in a lateral-to-medial progression.

STAGE	DISPLACEMENT
I	Partial or complete disruption of the LCL with resultant posterolateral rotatory subluxation of the elbow
II	Capsule is disrupted both anteriorly and posteriorly with an incomplete posterolateral dislocation
III	a. Partial disruption of the MCL b. Complete disruption of MCL leading to posterior dislocation of the elbow.

CLINICAL ASSESSMENT

Dislocations usually result from high-impact trauma and are frequently associated with other injuries, including shoulder, forearm, wrist, hand or the viscera. Examine the patient to make sure there are no other injuries present. Examine the arm for any obvious deformity, swelling, tenderness, bone exposure or puncture wounds. Particular attention should be paid to the distal radio-ulnar joint often concurrently affected along with an interosseous membrane injury, as seen in Essex-Lopresti injury (Image to the right)

Next perform a neurovascular exam. Determine the degree of perfusion by palpating the radial and brachial pulses and assessing capillary refill, warmth and color in comparison to the unaffected limb. If a pulse is not palpable a Doppler ultrasound can be used to determine the presence of distal perfusion. Evaluate both the sensory and motor function of the ulnar, median and radial nerves while limiting movement of the elbow as this may precipitate or further exacerbate neurologic injury. The neurovascular exam can change and should be repeated, particularly after manipulation of the arm. All patients with serious elbow injuries must be evaluated for compartment syndrome of the forearm. Pain out of proportion to the injury, severe forearm pain with passive extension of the fingers, pallor, paresthesia, pulselessness, and/or paralysis may indicate a developing compartment syndrome.



FOREARM ANATOMY

NEUROLOGIC ASSESSMENT OF THE DISTAL UPPER EXTREMITY	
MOTOR FUNCTION	
OK sign (against resistance)	Median (Anterior interosseous nerve)
Finger spread (against resistance)	Ulnar nerve
Thumbs up sign	Radial nerve
SENSORY FUNCTION: 2-Point Discrimination at 5 mm	
Second digit (volar)	Median nerve
Fifth digit (volar or dorsal)	Ulnar nerve
Dorsal web space (between 1st, 2nd digit)	Radial nerve

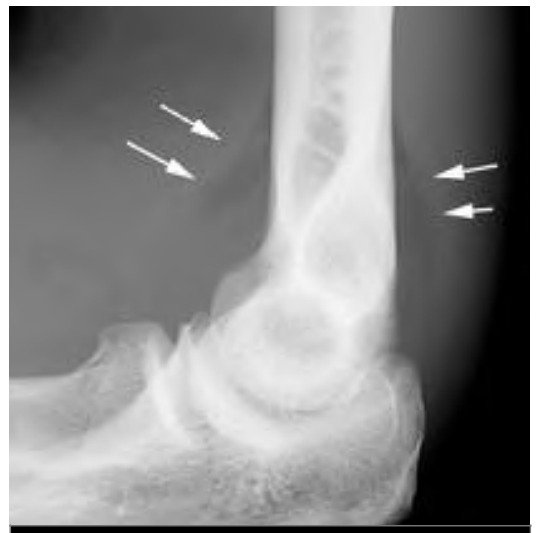
Assess pain and provide analgesia as necessary shortly after arrival to the ED. Patients should be made NPO in case of the need for immediate surgical repair. For patients with an obvious dislocation, immobilize the joint before sending them to radiology, if not already done so by EMS. The limb should be splinted in the deformed position in which it lies. Orthopedic consultation and follow up is indicated for most pediatric elbow injuries, especially those in whom neurologic or vascular compromise is suspected.

RADIOGRAPH INTERPRETATION

AP and lateral radiographs should be used to confirm the extent of the injury. These will suffice in evaluation of simple dislocations. Oblique views may help in evaluation of periarticular fractures. A CT might be helpful in case of more complex fracture patterns and can help with preoperative planning. There is little to no value in obtaining an MRI.

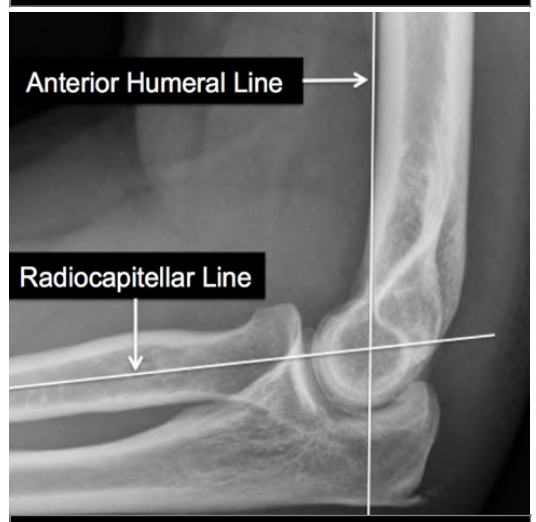
CORTICAL IRREGULARITIES: Inspect the cortical surfaces of each bone for breaks, flecks of bone or buckling. Examine the elbow joint space for any bone fragments or entrapment of the medial epicondyle. Note the direction of angulation or displacement.

FAT PADS: Evaluate the XRAY for the presence of the anterior and posterior fat pad signs. Fat is normally present within the elbow joint. The anterior fat pad is located within the radial and coronoid fossae and normally appears as a slight lucency just anterior to the distal humerus. The posterior fat pad, which rests in the olecranon fossa, is not present on a normal XRAY. Effusion or hemorrhage within the joint capsule displaces the fat, which will then be seen as a triangle-shaped lucency on either side of the distal humerus on the lateral view. A prominent anterior fat pad is called a "sail sign". The presence of a visible posterior fat pad is always pathologic. In the setting of elbow trauma, either fat pad sign may indicate occult fracture.



FAT PADS

ANATOMIC ALIGNMENT: The anterior humeral line is drawn along the anterior surface of the humerus on the lateral view. This line should intersect the middle third of the capitellum. The radiocapitellar line, is drawn through the midshaft of the proximal radius and bisects the capitellum in all radiographic views. Disruption of either of these lines may be the only indication of a displaced elbow fracture (supracondylar fracture, Monteggia fracture with proximal radial head dislocation)



ALIGNMENT

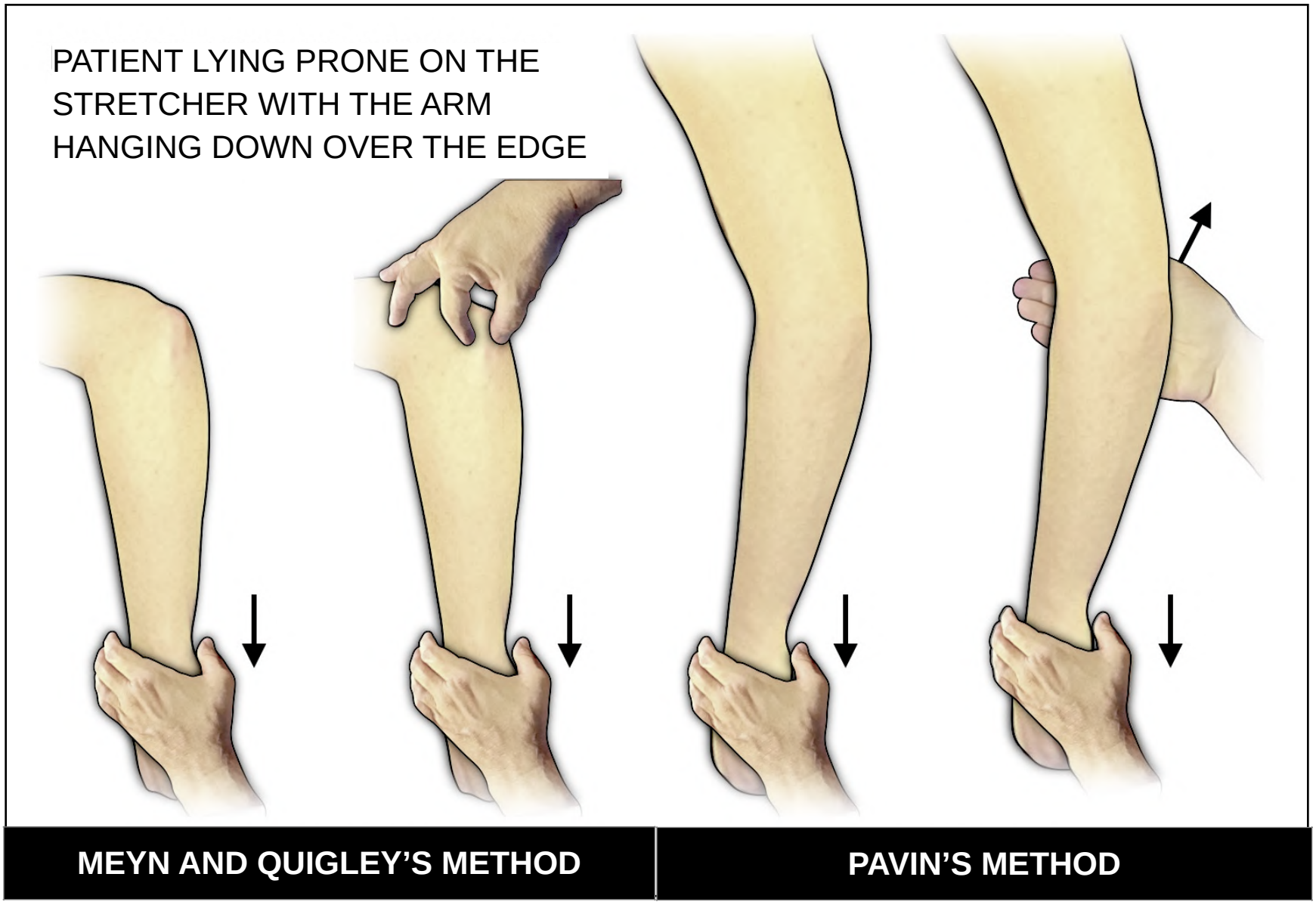
MANAGEMENT: SIMPLE DISLOCATION REDUCTION

Reduction of posterior dislocations is usually performed in the emergency department with analgesia and procedural sedation. There are two main methods of doing this. The first is Parvin's method: with the patient in prone position, gentle downward traction is applied until the olecranon begins to slip back into place. The arm is then lifted up gently. A modification of this maneuver called the Meyn and Quigley's puts the patient in prone position with the arm hanging off the bed. Traction is applied to the forearm and guiding the olecranon back into place, sometimes with the use of weights. Hyperextension of the elbow should be avoided. After the reduction, the arm should be flexed at 90 degrees and rested in a splint and a sling for about 7 days. Patient should follow up with an orthopedic surgeon in 1-2 weeks.

The less common anterior and divergent dislocations, which are usually a result of a higher energy trauma such as a motor vehicle accident, are usually less stable and require operative reduction.

The prognosis after simple dislocations is good with 95% of patients regaining complete function. Although neurologic injury has been reported in 20% of simple dislocation, it is usually paraesthesias due to transient ulnar nerve damage and resolves on its own. Brachial artery has been found to be entrapped either during the dislocation or following reduction.

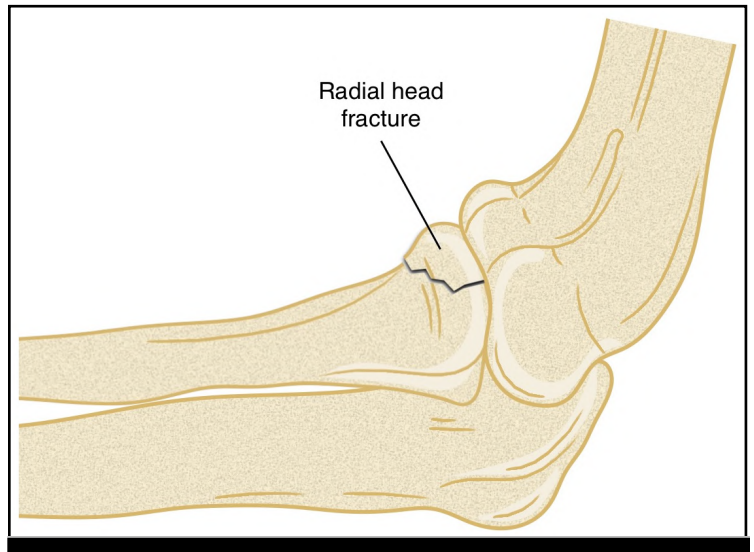
VIDEO LINK: ELBOW DISLOCATION REDUCTION



MANAGEMENT: COMPLEX ELBOW DISLOCATIONS

Complex elbow dislocations are associated with fractures and are inherently less stable. The three most common types are radial head fractures, coronoid fractures, and the "terrible triad" of dislocation with both a coronoid and radial head fractures. Most will require surgical management followed by rehabilitation.

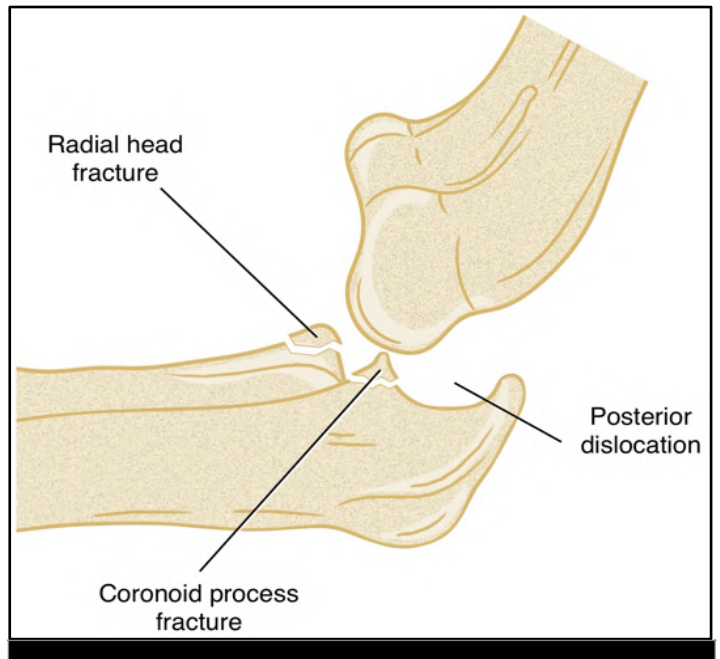
RADIAL HEAD FRACTURE: The most common fracture associated with elbow dislocations is the radial head fracture. During impact, the force from the wrist is transmitted to the head of the radius. The head of the radius is important in stabilizing the elbow and protecting it from valgus stress, especially if the MCL is damaged. It also restrains the proximal migration of the radius. Radial head fractures are classified into 3 different categories, ranging from the most benign nondisplaced fractures to much more involved comminuted and displaced fractures. Nondisplaced fractures are managed nonoperatively and similarly to simple dislocations. All other more involved fractures are managed operatively with some of the most severe radial head fractures requiring a radial head replacement.



RADIAL HEAD FRACTURE

CORONOID FRACTURE: This fracture usually takes place as the humerus is driven against the coronoid during an episode of posterior dislocation. The coronoid process acts as support of the olecranon and contributes to the stability of the ulnohumeral joint. Additionally, the anterior portion of the MCL inserts into the coronoid process and the anterior capsule attaches to it. A sizable fracture may completely detach the MCL and the anterior capsule from the ulna and seriously destabilize the joint. Fractures are classified into 3 categories ranging from involvement of only the tip of the coronoid, to most of the coronoid. Nonoperative treatment is used for those only involving the tip and nondisplaced fractures involving less than 50% of the coronoid. All other fractures are treated operatively.

TERRIBLE TRIAD: This is an injury involving an elbow dislocation with both a radial head fracture and a coronoid process fracture. This type of injury will often lead to chronic instability and debilitating pain and is almost always fixed surgically. The goal of the surgery is to achieve a stable joint that has a pain free range of motion.



TERRIBLE TRIAD

1. POSTERIOR DISLOCATION
2. RADIAL HEAD FRACTURE
3. CORONOID FRACTURE

ELBOW FRACTURES

INTRODUCTION (JANIENNE KONDRICH, M.D., 2/2020)
Elbow fractures account for approximately 5-10% of all fractures in children, compared to less than 2% in adults. The complexities of interpretation of elbow radiographs and the potential for significant neurovascular compromise make elbow trauma challenging to diagnose and manage. See: PEM Guide: Orthopedics: Elbow Dislocations.

CLINICAL EVALUATION

NEUROVASCULAR ASSESSMENT: Perform an assessment to determine if the elbow injury is the most significant injury present. Next perform a neurovascular exam. Determine the degree of perfusion by palpating the radial and brachial pulses and assessing capillary refill, warmth and color in comparison to the unaffected limb. If a pulse is not palpable a Doppler ultrasound can be used to determine the presence of distal perfusion. Evaluate both the sensory and motor function of the ulnar, median and radial nerves while limiting movement of the elbow as this may exacerbate neurologic or vascular injury. The neurovascular exam can change and should be repeated, particularly after manipulation of the arm.

All patients with serious elbow injuries must be evaluated for compartment syndrome of the forearm. Pain out of proportion to the injury, severe forearm pain with passive extension of the fingers, pallor, paresthesia, pulselessness, and/or paralysis may indicate a developing compartment syndrome.

NEUROLOGIC ASSESSMENT OF THE DISTAL UPPER EXTREMITY	
MOTOR FUNCTION	
OK sign (against resistance)	Median (Anterior interosseous nerve)
Finger spread (against resistance)	Ulnar nerve
Thumbs up sign	Radial nerve
SENSORY FUNCTION: 2-Point Discrimination at 5 mm	
Second digit (volar)	Median nerve
Fifth digit (volar or dorsal)	Ulnar nerve
Dorsal web space (between 1st, 2nd digit)	Radial nerve

MUSCULOSKELETAL EXAM: Examine the arm and note any swelling, tenderness or gross deformity of the arm, such as the S-shape seen in severely displaced supracondylar fractures. Search for evidence of an open fracture, which may be as subtle as a small puncture wound where the fractured bone poked through the skin and then receded.

ANALGESIA: Assess pain and provide analgesia as necessary shortly after arrival to the ED. Patients should be made NPO in case of the need for immediate surgical repair. For patients with an obviously displaced fracture, immobilize the joint if not already done so by EMS before sending them to radiology. The limb should be splinted in the deformed position in which it lies.

ORTHOPEDIC CONSULTATION IN THE ED
Fracture with neurovascular compromise including compartment syndrome
Open fracture
Significant deformity
Intraarticular fractures

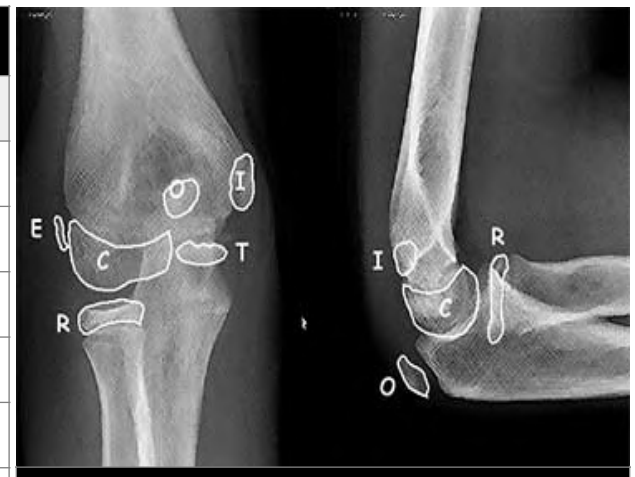
XRAY INTERPRETATION

The elbow is a complex joint that involves the articulation of three bones: the humerus, radius, and ulna, which have numerous ossification centers. Therefore, elbow radiograph interpretation requires a systematic approach.

CORTICAL IRREGULARITIES: Inspect the cortical surfaces of each bone for breaks, flecks of bone or buckling. Examine the elbow joint space for any bone fragments or entrapment of the medial epicondyle. Note the direction of angulation or displacement.

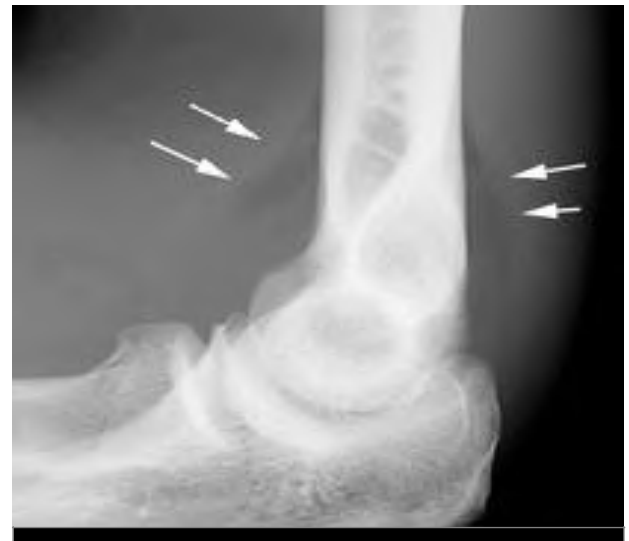
OSSIFICATION CENTERS: It is important to be familiar with these to avoid confusion with fracture when interpreting elbow radiographs. Obtaining x-rays of the unaffected elbow is often helpful for comparison. There is variation in the age at which each ossification center appears, but the order of ossification is always the same. The mnemonic CRITOE is helpful to remember this order.

CRITOE: ELBOW OSSIFICATION CENTERS		
OSSIFICATION CENTER		AGE (YRS)
C	Capitellum	1
R	Radial Head	3
I	Internal (Medial) Epicondyle	5
T	Trochlea	7
O	Olecranon	9
E	External (Lateral) Epicondyle	11



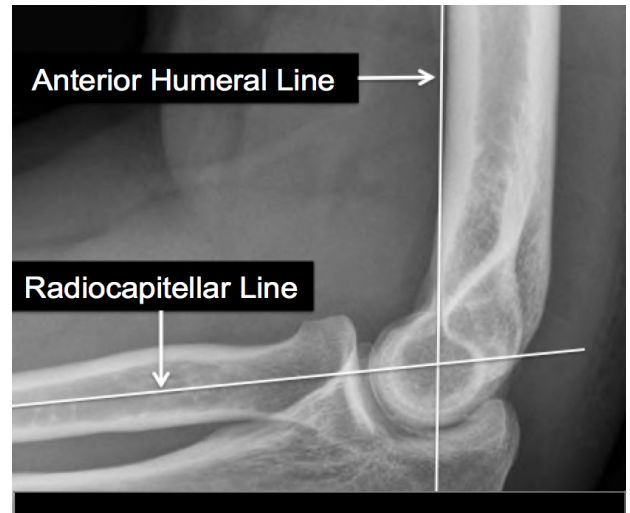
OSSIFICATION CENTERS

FAT PADS: Evaluate the XRAY for the presence of the anterior and posterior fat pad signs. Fat is normally present within the elbow joint. The anterior fat pad is located within the radial and coronoid fossae and normally appears as a slight lucency just anterior to the distal humerus. The posterior fat pad, which rests in the olecranon fossa, is not present on a normal XRAY. Effusion or hemorrhage within the joint capsule displaces the fat, which will then be seen as a triangle-shaped lucency on either side of the distal humerus on the lateral view. A prominent anterior fat pad is called a "sail sign." The presence of a visible posterior fat pad is always pathologic. In the setting of elbow trauma, either fat pad sign may indicate an occult fracture.



FAT PADS

ANATOMIC ALIGNMENT: The anterior humeral line is drawn along the anterior surface of the humerus on the lateral view. This line should intersect the middle third of the capitellum. The radiocapitellar line, is drawn through the midshaft of the radius and bisects the capitellum and should intersect the middle third of the capitellum. Disruption of either of these lines may be the only indication of a displaced elbow fracture (Supracondylar fracture, Monteggia ulna fracture with radial head dislocation).



ALIGNMENT

SUPRACONDYLAR FRACTURES (DISTAL HUMERAL METAPHYSIS)

Supracondylar fractures account for over half of pediatric elbow fractures and occur most frequently from 5-10 years old. Prompt recognition and management of supracondylar fractures is essential due to the potential for uncommon, but significant complications. These include nerve injury and vascular compromise in the immediate setting, and elbow deformity or functional impairment as later sequelae.

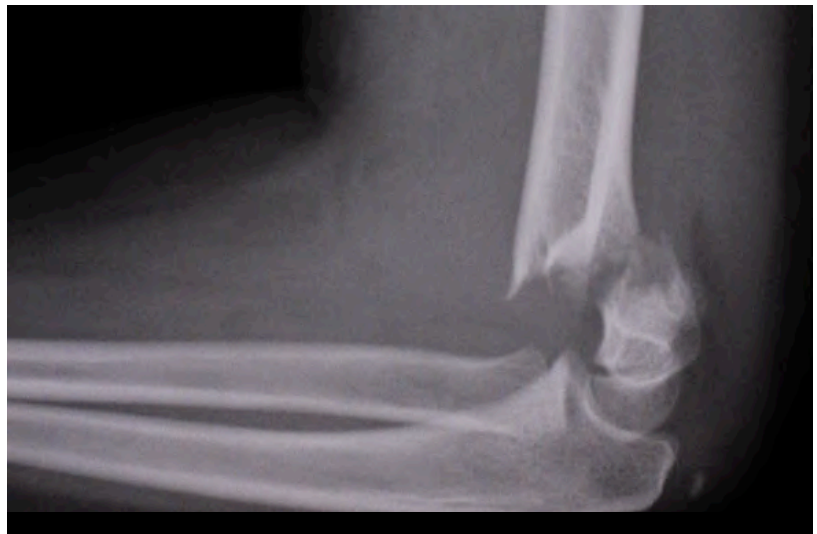
The vast majority of supracondylar fractures are the result of a fall on an outstretched hand (FOOSH) with the elbow in full extension. Direct trauma posteriorly to a flexed elbow can also result in a supracondylar fracture, but is much less common. In children younger than 3 years, the fracture often occurs from a fall of less than three feet, such as from a bed or couch. In older children, these fractures occur with falls from a greater height, classically from monkey bars, swings, or another playground equipment.

The child with a supracondylar fracture will present clinically with elbow pain, swelling, and very limited to absent range of motion at the elbow. There will be pain on palpation of the posterior aspect of the distal humerus. Nondisplaced fractures may have minimal swelling; severely displaced fractures may have an S-shaped configuration or a puckering of the skin immediately above the antecubital fossa. An open supracondylar fracture may present with only a small puncture wound or laceration immediately above the antecubital fossa.

NEUROVASCULAR ASSESSMENT: Because of the extensive collateral circulation it is rare for ischemia of the arm to occur from complete brachial artery occlusion. Extension type supracondylar fractures are the most common and result is posterior displacement and either medial or lateral displacement of the distal humerus. Posterior lateral displacement can damage the anterior interosseous nerve (AIN), a branch of the median nerve. Damage to the AIN results in loss of motor function to the flexor digitorum profundus and the flexor pollicis longus. This will result in weakness or loss of index finger flexion identified as the inability to make an “OK” sign. The AIN is purely motor so that sensation remains intact in the median nerve distribution.
Posterior-medial displacement can damage the radial nerve. Damage to the radial nerve results in both a motor and sensory deficit. Decreased sensation in the dorsal first web space and loss of thumb extension (inability to make the “thumbs up” sign) will be present.

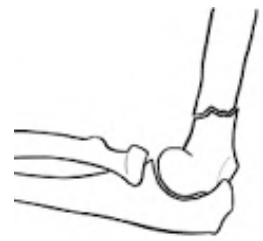
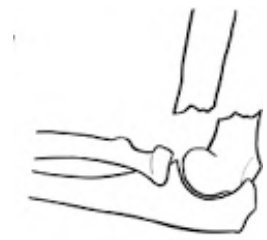
Flexion-type supracondylar fractures are less common and are a result of a fall directly onto the olecranon of a flexed elbow. The distal humerus fragment is displaced anteriorly. The ulnar nerve is most likely to be injured and both a motor and sensory deficit may be present. The ulnar nerve innervates the interosseous muscles in the hand and the patient will be unable to spread the fingers or hold a piece of paper between the middle and index fingers. Sensation the 5th digit is decreased.

All patients with neurovascular compromise require orthopedic consultation. Neurologic deficits are often a result of neuropraxia (a transient conduction block with nerve degeneration) and typically resolve within 3 months.



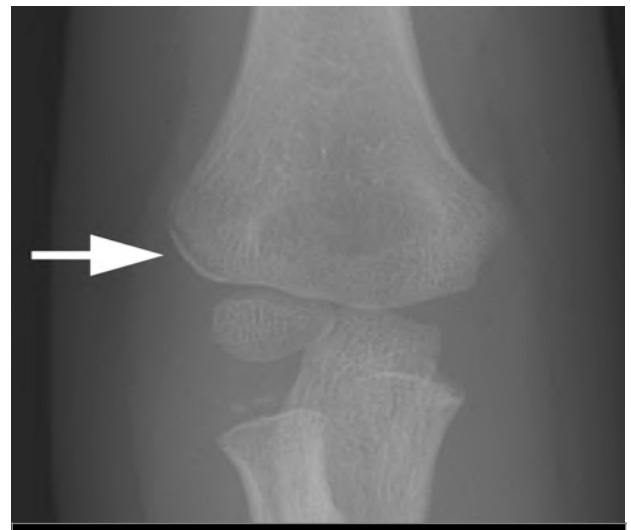
SUPRACONDYLAR FRACTURE (III)

XRAY: The fracture line crosses the distal humerus transversely through the olecranon fossa, right above the medial and lateral epicondyles. When displaced, the distal fracture fragment is most often displaced posteriorly. The Gartland classification system is used to distinguish degree of fracture severity for extension type supracondylar fractures. A Gartland IV fracture was not included in the original classification scheme and is defined intra-operatively as displaced, with periosteal disruption, and is unstable in flexion and extension.

GARTLAND CLASSIFICATION OF SUPRACONDYLAR FRACTURES				
TYPE	HUMERAL PERIOSTEUM		OTHER XRAY FINDINGS	ILLUSTRATION
	ANTERIOR	POSTERIOR		
I	Intact	Intact	(+) Fat pads	
II	Disrupted	Intact	(+) Fat pads Proximal fragment displaced anteriorly	
III	Disrupted	Disrupted	(+) Fat pads Proximal fragment displaced anteriorly No continuity between proximal and distal fragments	

LATERAL EPICONDYLAR FRACTURE

Fractures of the lateral humeral condyle are the second most common type of elbow fracture in children, accounting for 10-20% of pediatric elbow fractures. Lateral condylar fractures usually occur in young children, with a peak incidence at 6 years of age, and most often result from a fall onto an extended and abducted arm. These fractures are Salter-Harris type IV fractures because they extend from the metaphysis through the physis and into the epiphysis and, although rare, can result in growth disturbance if not managed properly. Unlike supracondylar fractures these are much less likely to cause neurovascular compromise.

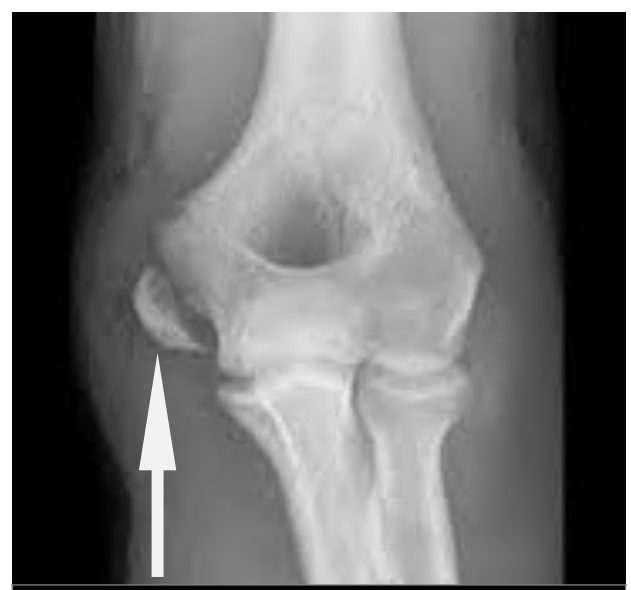


LATERAL EPICONDYLE FX

Lateral condylar fractures, unless significantly displaced, are often best seen on oblique radiographic views. A posterior fat pad may be the only clue on routine AP and lateral elbow films. Clinically the patient will have elbow swelling, decreased to no range of motion, and will be tender to palpation at the lateral aspect of the elbow.

MEDIAL EPICONDYLAR FRACTURE

Medial epicondylar fractures are the third most common elbow fracture seen in children, after supracondylar and lateral condylar fractures. These fractures occur most frequently in older children and adolescents. The mechanism of injury is either direct trauma to the medial aspect of the elbow, a fall on an outstretched hand while the elbow is subjected to a valgus stress, or forceful contraction of the flexor-pronator muscle group, such as a with a violent pitch or throw in baseball or other sport.
Medial epicondyle fractures include: avulsion, avulsion with entrapment of the epicondyle in the elbow joint, and a Salter-



MEDIAL EPICONDYLE FX

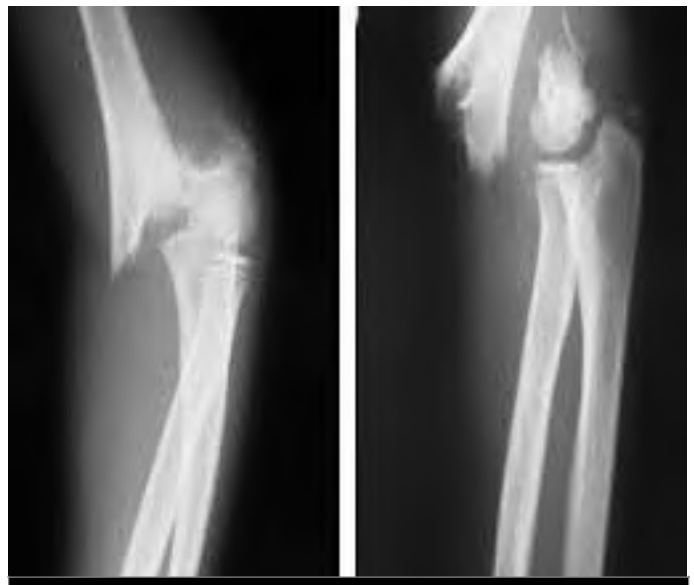
Harris type IV fracture involving the entire medial epicondyle. Medial epicondyle fractures occur often with elbow dislocations. These fractures carry a low risk of vascular compromise. The ulnar nerve runs in the groove at the posterior aspect of the epicondyle, and thus paresis and paresthesias of this nerve can occur.

DISTAL HUMERUS PHYSEAL FRACTURES

Separation of the entire distal humeral epiphysis is a rare injury. Most distal humeral physeal fractures occur in children younger than 2 ½ years old. Recognition is crucially important in infants and young children in whom this injury is often the result of child abuse. The likely mechanism of injury is forceful twisting that shears off the distal epiphysis.

Distal humeral physeal fractures can also occur by lifting an infant by the forearm, or in rare cases from birth trauma. In older children, a fall on an outstretched hand usually results in a supracondylar injury but occasionally leads to this type of fracture instead.

Clinically, this injury most commonly presents with elbow swelling. Posteromedial displacement of the ulna and radius in relation to the humerus is the most important radiographic finding but will not be apparent on physical exam. On XRAY the fracture is more distal than the metaphyseal fracture that is seen with a supracondylar fracture.

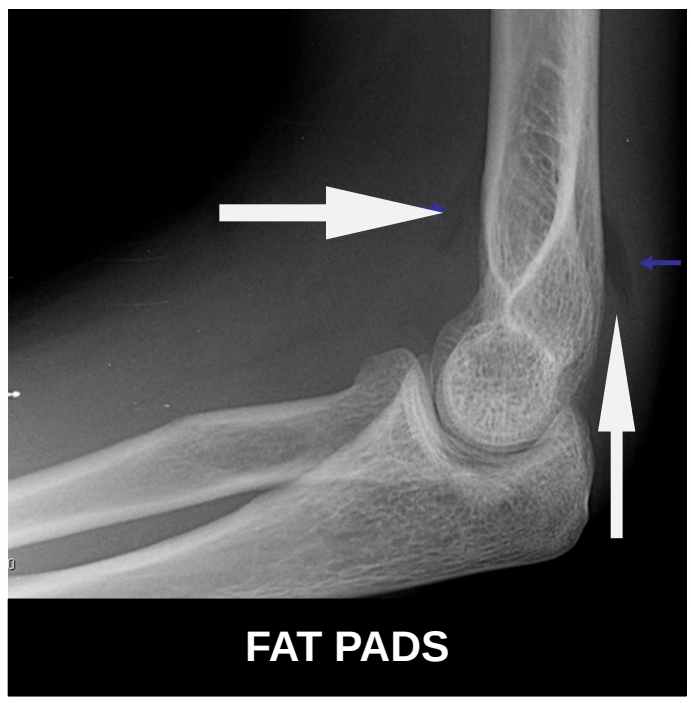


DISTAL HUMERAL PHYSEAL FRACTURE

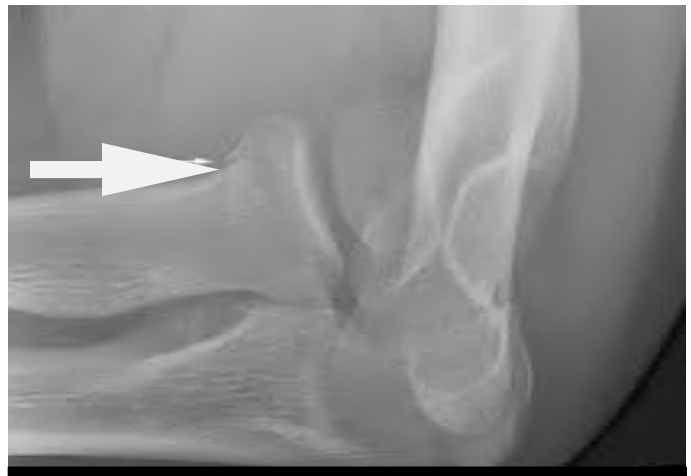
RADIAL HEAD AND NECK FRACTURES

These fractures typically occur in the skeletally mature patient where the physes have closed. The mechanism is a fall onto an outstretched arm with impaction of the radial head into the capitellum. Patients will present with a decreased range of motion at the elbow joint and pain and swelling over the lateral elbow. In addition to the AP and lateral XRAYS a Greenspan view (radio-capitellar view) that isolates the radial head should be ordered.

Patients with simple fractures are managed with early mobilization and are given a sling for comfort. More complex fractures with a higher degree of angulation are managed operatively.



FAT PADS



GREENSPAN VIEW

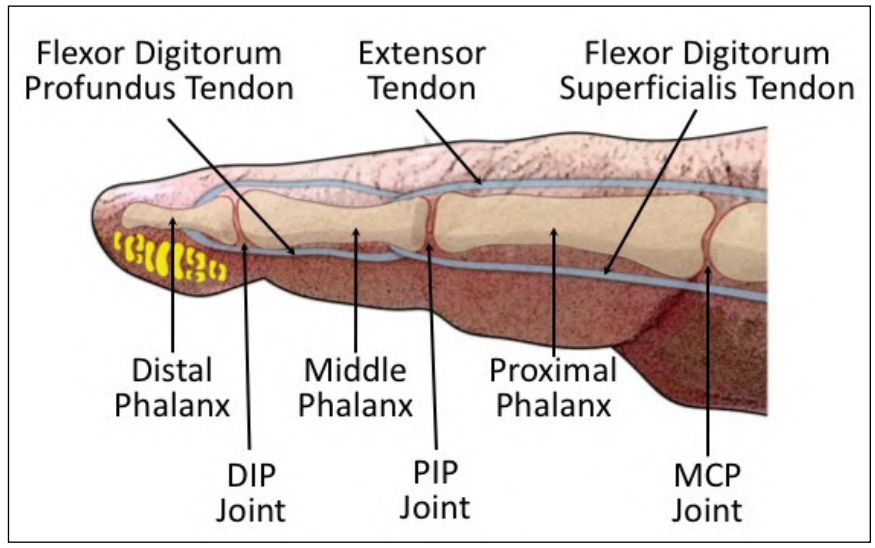
FINGER INJURIES

INTRODUCTION (KELSEY FAWCETT, M.D., 9/2016)
Injuries involving the phalanges are extremely common in the pediatric population. The most common mechanisms of injury are crush, hyperextension and axial load ("jamming"). Injury to the underlying tendons, which are essential for hand grip and function, are easily missed in the setting of normal radiographs particularly in the anxious or uncooperative child. For this reason, an understanding of anatomy and a focused physical exam is essential to proper diagnosis and management of finger injuries. A threatened digit is a true emergency. Careful evaluation and proper management can significantly reduce long-term damage and functional disability.

TYPES OF FINGER INJURIES
Dislocations
Fractures (both open and closed)
Lacerations/Amputations
Tendon and ligamentous injuries
Nail and nailbed injuries

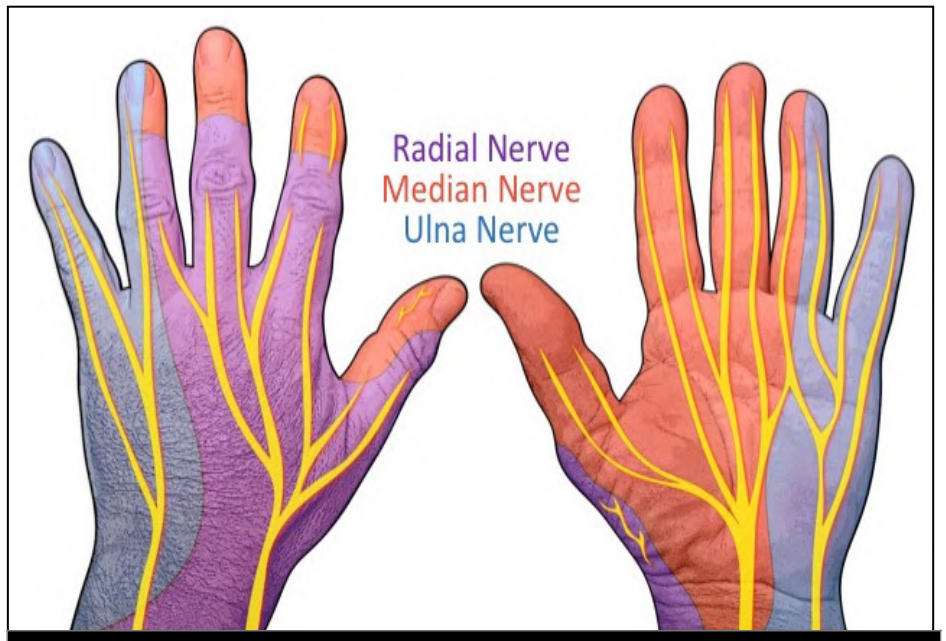
FINGER ANATOMY: THE BASICS

BONES: There are 14 phalanges which make up the fingers and thumb. The fingers are numbered from 1 (thumb) to 5 (little or pinky finger). Each finger, with the exception of the thumb, has 3 phalanx bones: proximal, middle, and distal. There are three finger joints. From proximal to distal they are the metacarpal-phalangeal joint (MCP), the proximal interphalangeal joint (PIP) and the distal interphalangeal joint (DIP). The thumb has only 2 phalanx bones: the proximal and distal phalanx and thus only has two finger joints; an MCP joint and an interphalangeal joint.



TENDONS: Function of the fingers relates most closely to the function of the opposing flexor and extensor tendons that insert onto the distal phalanx. The flexor digitorum superficialis inserts onto the volar (palmar) surface of the middle phalanx and acts to flex the proximal interphalangeal joint. The flexor digitorum profundus inserts on the volar aspect of the distal phalanx and acts to flex the distal interphalangeal joint. The extensor digitorum is the primary extensor of the digit and inserts on the dorsal side of the phalanx. The flexor tendon has a greater resting force then the extensor tendon resulting in slight flexion of the finger at rest. The volar plate is a thickened, fibrous sheath on the volar surface of the interphalangeal joints and MCP joints. It acts to stabilize the joint and prevent hyperextension.

NERVES: Motor innervation to the fingers is supplied by the radial, ulnar, and median nerves. The radial nerve innervates the finger extensors and the thumb abductor. The median nerve innervates the 1st and 2nd lumbricals, the abductors and opponens of the thumb, and the flexors of the wrist and fingers. The ulnar nerve supplies the remaining intrinsic muscles of the hand.



HAND INNERVATION

The radial nerve supplies sensory innervation to the dorsal side of the thumb (1st), the dorsal aspect of the index (2nd) and middle (3rd) fingers, and the dorsal radial half of the ring finger (4th). The median nerve provides sensation to the palmar side of the thumb, index (2nd), middle (3rd), and ventral half of the ring finger (4th). The ulnar nerve supplies sensory innervation, both the palmar and dorsal ulna sides of the hand, in addition to the little finger (5th) and the ulna half of the ring (4th) finger. The 4th digit is unique in that it's sensory innervation is provided by the ulna, radial and median nerves

NEUROMUSCULAR ASSESSMENT OF THE HAND	
MOTOR FUNCTION	
OK sign (1st & 2nd) against resistance)	Median (anterior interosseous nerve)
Finger spread (against resistance)	Ulnar nerve
Thumbs up sign	Radial nerve
SENSORY FUNCTION: 2 point discrimination @ 5 mm	
Second digit (volar)	Median nerve
Fifth digit (volar or dorsal)	Ulnar nerve
Dorsal web space (between 1st, 2nd digit)	Radial nerve

PHYSICAL EXAMINATION	
Inspection	Deformity, laceration/amputation, bone exposure, nail/nail bed involvement
Palpation	Tenderness, capillary refill, sensation (radial, medial, ulnar nerves)
Range of Motion	Open and close hand, flexion/extension at MCP, PIP, DIP passively and against resistance

DIAGNOSIS

The initial assessment of a finger injury should focus on the neurovascular status (see table below). XRAYS can be used to diagnose fractures, dislocation and foreign bodies. XRAYS may not identify rotational deformities and tendon injuries in the absence of an avulsion fracture.

VIDEO LINK: COMPREHENSIVE REVIEW OF THE HAND EXAMINATION

VIDEO LINK: RAPID NEUROLOGIC ASSESSMENT

MANAGEMENT

The management of each injury is discussed separately. Tetanus status should be assessed for open wounds. See also Appendix: Digital Nerve Blocks.

TETANUS PROPHYLAXIS				
	CLEAN. MINOR WOUNDS		ALL OTHER WOUNDS[1]	
History	Td[2]	TIG[3]	Td[2]	TIG[3]
< 3 doses	YES	NO	YES	YES
> = 3	NO[4]	NO	NO[5]	NO
1. Wounds contaminated by dirt, feces, soil, saliva, Puncture wounds, avulsions. Wounds from missiles, crushing, burns, frostbite				
2. For children < 7yrs – DTaP or DT recommended, > 7 years Td recommended				
3. Tetanus Immune Globulin (TIG) 250 Units IM				
4. Yes if > 10 years since last dose				
5. Yes if > 5 years since last dose				

FRACTURES

Open finger fractures do not require emergency washout in the operating room unless grossly contaminated. Washout in emergency department should take place as soon as possible. Irrigation volume and pressure are the most important factors in reducing the rate of subsequent infections. In general, intra-articular phalanx fractures require surgical management if there is greater than 2 mm displacement.

FINGER FRACTURE MANAGEMENT			
	INJURY	IMMOBILIZATION	REFERRAL
Condyle	Can involve 1 or both condyles. Risk of poor bone remodeling Intra-articular	Hand/forearm splint for up to 3 weeks	Early referral for all
Proximal Phalanx	5th digit most common Salter Harris Type II Thumb (see below)	Hand/forearm splint for up to 3 weeks	Intra-articular surface Involvement >30% Unstable fractures Multiple fingers
Middle Phalanx	Primary force is that of flexor digitorum superficialis Fractures distal to insertion: dorsal angulation Fractures proximal to insertion: volar angulation	Hand/forearm splint up to 3 weeks Often require reduction	Intra-articular surface Involvement >30% Unstable fractures Multiple fingers
Distal Phalanx	Most common phalanx fracture Crush injuries Associated with nail/nail bed injuries Tuft fracture, transverse fracture, longitudinal fracture Tendon injuries: Mallet finger, Jersey Finger (see below)	Soft finger splint for 2-3 weeks	Large soft tissue loss Intra-articular surface involvement >30%

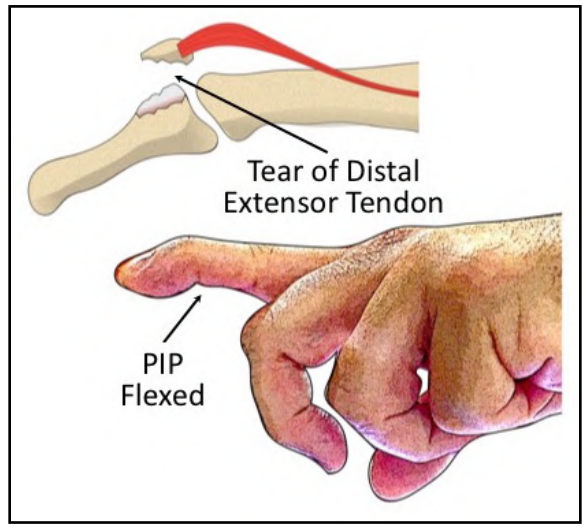
DISLOCATIONS: MCP AND INTERPHALANGEAL JOINTS

Dislocations are most commonly seen in adolescents and adults, and are frequently a result of contact sport injuries. The distal bone is typically displaced dorsally to the proximal bone most commonly as a result of hyperextension. Dislocations place the volar plate at MCP and PIP joints at risk for injury. A lateral XRAY is needed to diagnose a dislocation. Poor film quality and soft tissue swelling can make dislocations easy to miss. Management of dislocations typically involves analgesics (systemic analgesia or digital block) and relocation. Relocation can typically be achieved with axial traction with slight hyperextension while guiding the proximal portion of the dislocated phalanx into appropriate alignment with gentle downward pressure. Dislocations complicated by fractures or by volar plate entrapment in the joint can make relocation difficult and may require surgical intervention.

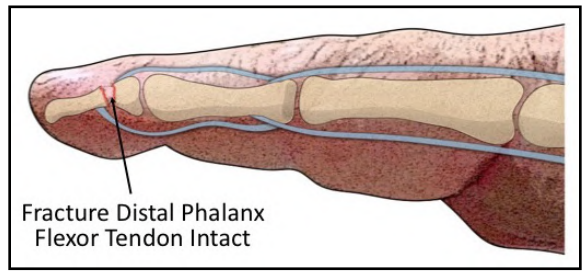
VIDEO LINK: FINGER REDUCTION

LIGAMENTOUS INJURIES

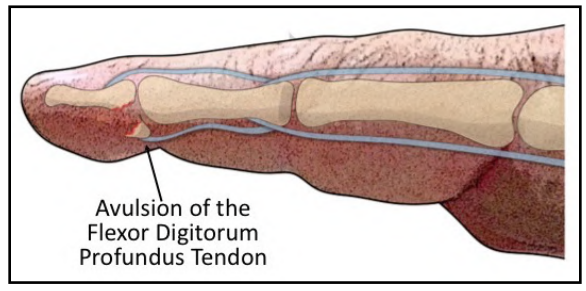
MALLET FINGER: Fracture of dorsal lip of the distal phalanx can avulse the extensor digitorum. This leaves the stronger opposing force from the flexor digitorum profundus unopposed. The result is that the distal phalanx is flexed at the DIP joint and cannot be extended. This can occur with or without a fracture. The typical mechanism is jamming (an axial load with forced flexion at the DIP joint). The finger should be splinted in extension for a minimum of 6-8 weeks. The splint should not be removed for any reason. Surgical repair may be required if splint in insufficient or associated with a large fracture.



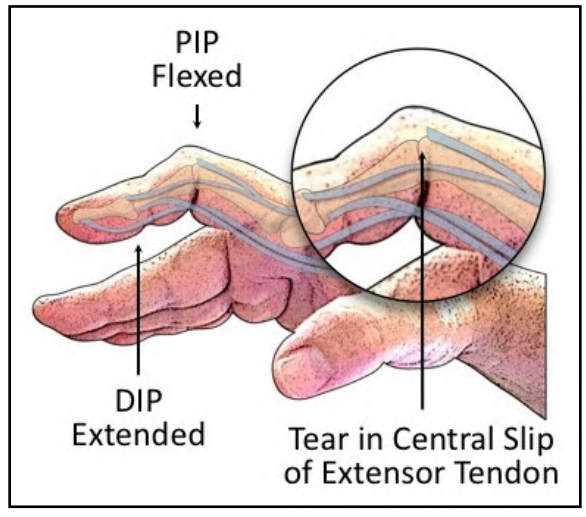
SEYMOUR FRACTURES: (This is not a ligamentous injury but is included here for comparison to a Mallet deformity). Seymour fractures occur more commonly in young children. These are Salter-Harris Type I or Type II fractures of the proximal portion of the dorsal, distal phalanx at the DIP joint. They are often associated with damage to the nail and or nail bed. The exam is similar to a Mallet Finger though the extensor digitorum is intact. The distal phalanx is flexed at the DIP joint and cannot be extended. Treatment is reduction and splinting in an extended position. Surgical repair is required in some cases.



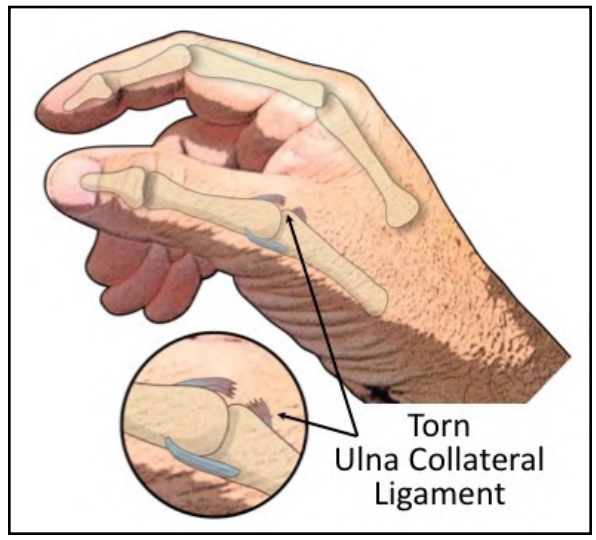
JERSEY FINGER: A fracture of the volar lip of the distal phalanx avulses the insertion of the flexor digitorum profundus which leads to unopposed extension. The finger is extended at the DIP and cannot be flexed (the opposite of a mallet deformity). The mechanism of injury is forced extension at the DIP joint such as occurs when grabbing the jersey of another player with just a finger. Jersey finger may occur with or without a fracture. Surgical repair is required.



BOUTONNIERE DEFORMITY: A Boutonniere deformity occurs when the central slip of the extensor tendon is damaged where it inserts on the middle phalanx. The distal portion of the extensor tendon remain intact at its insertion on the distal phalanx. This results in the inability to extend at the PIP while the ability to extend at the DIP is intact. The finger is held in flexion at the DIP and extension at the PIP. Management consists of either splinting or pinning of the proximal interphalangeal (PIP) joint in full extension for 4-6 weeks. The distal interphalangeal (DIP) joint is not splinted.



GAMEKEEPERS/SKIER'S THUMB: Rupture of the ulnar collateral ligament (UCL) during stress to the thumb away from the hand (hyperextension) is seen most commonly in adolescents and adults. The same mechanism in children, tends to cause a fracture to the base of the proximal phalanx (most commonly Salter-Harris I and II in younger children, Salter Harris III in older children). Stress views with comparison to the unaffected side may be necessary. Treatment is placement of a thumb Spica splint and referral to a hand surgeon.



LACERATIONS/AMPUTATIONS

Lacerations involving the phalanx can range from simple lacerations requiring minimal repair, to complex lacerations and distal amputations which require special attention to avoid significant functional disability. Avulsed finger tips should be wrapped in saline-moistened gauze and placed in a bag in ice-water if re-implantation is to be attempted. A 2 compartment laboratory specimen bag can be used for this purpose. Ice and water are added to the closable department and the saline moistened gauze with the amputated portion of the finger in the second compartment. Even if the avulsed tip does not remain viable, it may still facilitate growth of the tissue below it (i.e. act as a biologic dressing).

When the laceration is extensive or an amputation is present, a digital block may be required for analgesia. (See Appendix: Digital Blocks). However, careful evaluation of neurovascular status prior to a digital block is essential. Oozing wounds may require tourniquet placement. Copious irrigation following analgesia is required. Finger lacerations are often repaired using absorbable sutures. Petroleum laced dressings should be used when the repair is complete. The use of prophylactic antibiotics after a finger laceration/amputation repair is common thought little evidence supports this practice. The most common prophylactic antibiotic prescribed is Cephalexin, a first generation cephalosporin, typically for 5-7 days.

NAIL AND NAIL BED INJURIES

Severe nail bed injuries require removal of the overlying nail. Nail bed lacerations can be repaired with either absorbable sutures (e.g. Chromic Gut) or a tissue adhesive (e.g. Dermabond). Following repair, the eponychial fold should remain patent to allow for the new nail to grow. This can be accomplished using either the salvaged nail or sterile aluminum from suture packaging.

Subungual hematomas occur with crush injuries. Small hematomas require no intervention and typically resolve on their own. Large hematomas involving more than 50% of the nail bed are more likely to be associated with nail bed injuries. The literature has shown that when the nail is intact, there is no difference in outcome with nail removal with nailbed repair or simple trephination. (Becker, Hand Surgery 2012, PubMed ID: 22351556). Trephination should not be used on acrylic nails, as they can be flammable.

APPENDIX: DIGITAL NERVE BLOCKS

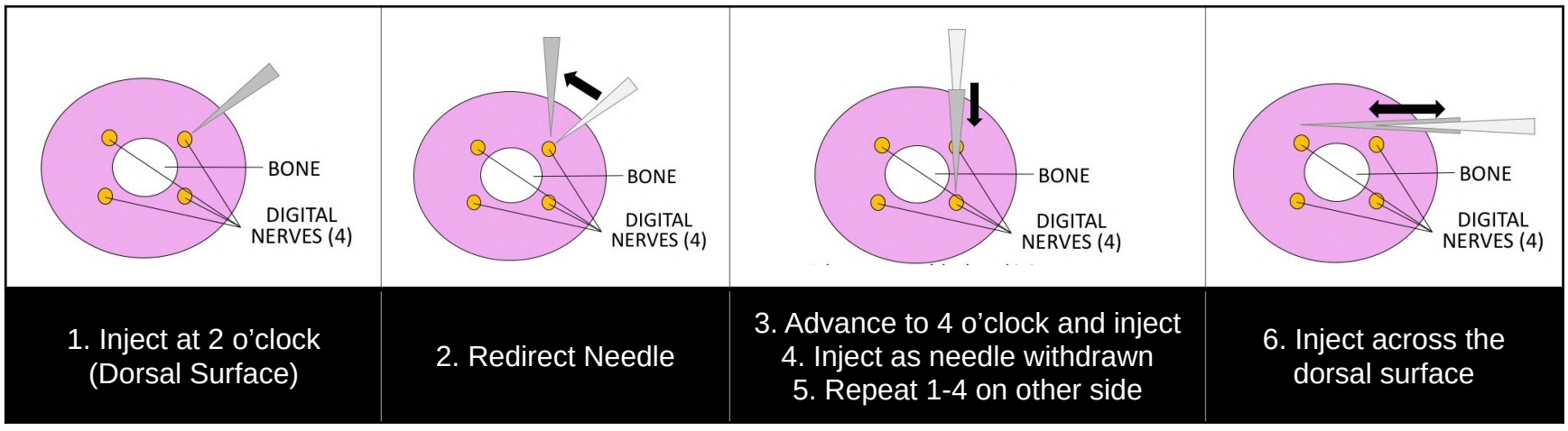
INDICATIONS
Anesthesia of the digit to facilitate repair of a laceration/amputation or a dislocation or fracture reduction.

CONTRAINDICATIONS
Contrary to prior teaching the use of epinephrine with lidocaine for a digital block is not contraindicated. The original evidence on which this recommendation was based has been found to be scant and flawed. Evidence in patients who inadvertently inject themselves in the finger with epinephrine pens have not demonstrated adverse effects.

EQUIPMENT
1. 1% Lidocaine with or without Epinephrine
2. Alcohol prep, betadine or chlorhexadine to prep the insertion site
3. 3 ml syringe with with narrow gauge needle (≤ 25 gauge)
4. Sterile drape

Many approaches to the digital block are available based on the distribution of the digital nerves. This most commonly used are: the web space block, the tendon sheath block (AKA the “single” digital block) and the ring block. The needle insertion site and the number of injections required differ.

RING BLOCK: The traditional rink block anesthetizes the 4 digital nerves. Two injections are required at the base of the finger with the hand held with the palm facing upward. The needle enters the skin at the 2 o’clock position and 0.5-1.0 ml of lidocaine is injected. Without withdrawing the needle, it is redirected and advanced to the 4 o’clock position where an additional 0.5-1.0 ml of lidocaine is injected. An additional 0.5-1.0 ml of lidocaine by can be injected along the needle track as the needle is withdrawn. This procedure is repeated on the other side of the finger (injection at the 10 o’clock position with redirection and advanced of the needle with infection at the 8 o’clock position. A third injection across the horizontal volar surface of the finger may be required for complete anesthesia of the thumb. Do not hold your fingers below the 4 o’clock or 8 o’clock position as you advance the needle downward to avoid a needle stick id the needle is advance through the skin inadvertently. This technique results in the most pain for the patient and may be associated with a higher degree of vascular and nerve injury.



TENDON SHEATH METHOD (AKA SINGLE CUTANEOUS METHOD): A single injection occurs at the midpoint of the finger crease on the volar surface at the junction of the finger and the hand. Others recommend the injection to place over the ventral surface of the MCP joint. 2-3 ml of Lidocaine are injected subcutaneously over the tendon sheath. The technique is equally efficacious to the ring block and may cause less patient discomfort (Cannon, EM Journal 2010, PubMed ID: 20360491). This technique may not be effective for the thumb.

WEBSPACE BLOCK: This technique requires two injections. One in the web space on each side of the finger. A web space block on both sides of a finger can only be accomplished on fingers 3 and 4. The needle is held in the same plane as the hand and advanced into the webspace until just proximal to the MCP joint. 2-3 ml of Lidocaine is injected and the procedure is repeated in the web space on the other side of the finger.

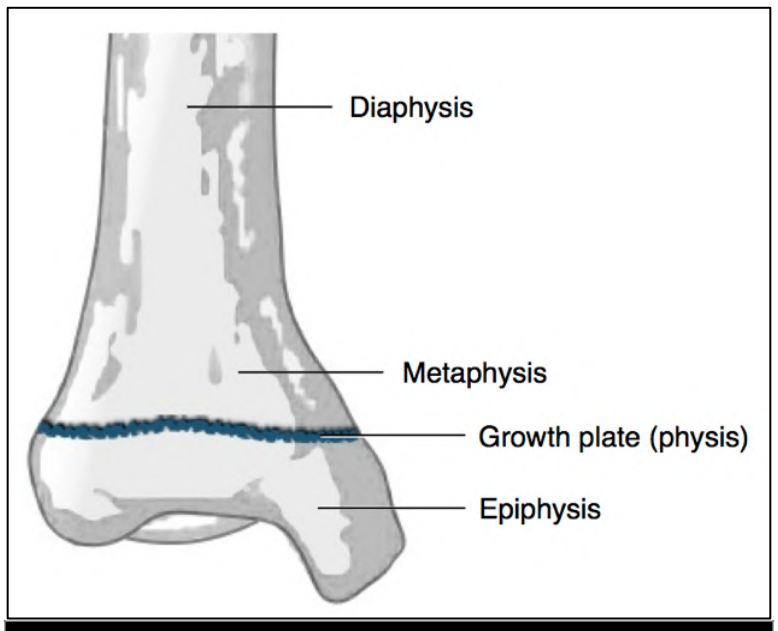
FOREARM FRACTURES

INTRODUCTION (GEORGE KRISTINSSON, M.D., 12/2022)
Forearm fractures account for approximately half of pediatric long bone fractures. Fractures to the distal radius and ulna are most common. The most common mechanism of injury for forearm fractures is a fall onto an outstretched hand (FOOSH) during play. A simple fall may result in a nondisplaced fracture, whereas a fall in conjunction with forward momentum (riding a bicycle) is more likely to produce a displaced fracture. This PEM Guide focuses on fractures of the shaft and distal forearm.
See PEM Guide: Orthopedics: Elbow Fractures for proximal forearm fractures.

Because of differences in bone plasticity, children can sustain unique forearm fractures. These include injuries to the physis, torus (buckle) fractures, plastic deformity and green stick fractures. In addition, due to the relative weakness of the growing distal radius and ulna, children seldom sustain fractures or dislocation of the wrist bones. The potential for intentional injury should be assessed for all pediatric fractures. See PEM Guide: Child Protection: Child Abuse and Neglect

ANATOMY OF GROWING BONE

The major anatomic regions of the bone include the diaphysis, metaphysis, physis, and epiphysis. The epiphysis is located at the end of long bones; it is separated from the rest of the bone by the cartilaginous physis. The age at which ossification centers become visible on a radiograph and the subsequent rates of physis closure vary widely depending on the bone. The relative lack of ossification of many epiphyses in young children and the radiolucency of growth plates can make fracture identification difficult.



BONE SEGMENTS

CLINICAL EVALUATION

The first step in the evaluation of a patient with a forearm injury is to immediately perform an overall assessment to determine if the forearm injury is the only significant injury present. Then examine the arm and note any swelling, tenderness or gross deformity of the arm. Search for evidence of an open fracture, which may be as subtle as a small puncture wound where the bone poked through the skin and retracted.

NEUROVASCULAR ASSESSMENT: Next perform a neurovascular exam. Determine the degree of perfusion by palpating the radial and brachial pulses and assessing capillary refill, warmth and color in comparison to the unaffected limb. If a pulse is not palpable a Doppler ultrasound can be used to determine the presence of distal perfusion. Evaluate both the sensory and motor function of the ulnar, median and radial nerves while limiting movement of the forearm as this may precipitate or further exacerbate neurologic injury. The neurovascular exam can change and should be repeated, particularly after manipulation of the arm.

COMPARTMENT SYNDROME: All patients with serious forearm injuries must be evaluated for compartment syndrome of the forearm. Pain out of proportion to the injury, severe forearm pain with passive extension of the fingers, pallor, paresthesia, pulselessness, and/or paralysis may indicate a developing compartment syndrome. The absence of some of these findings does not exclude compartment syndrome.

NEUROLOGIC ASSESSMENT OF THE DISTAL UPPER EXTREMITY	
MOTOR FUNCTION	
OK sign (against resistance)	Median (Anterior interosseous nerve)
Finger spread (against resistance)	Ulnar nerve
Thumbs up sign	Radial nerve
SENSORY FUNCTION: 2-Point Discrimination at 5 mm	
Second digit (volar)	Median nerve
Fifth digit (volar or dorsal)	Ulnar nerve
Dorsal web space (between 1st, 2nd digit)	Radial nerve

ANALGESIA: Assess pain and provide analgesia as necessary shortly after arrival to the ED (See PEM Guide: Procedures: Analgesia). Patients should be made NPO in case of the need for immediate surgical repair or procedural sedation.

IMAGING: For patients with an obviously displaced fracture, immobilize the joint if not already done so by EMS before sending the patient to radiology. The limb should be splinted in the deformed position in which it lies. Imaging typically includes the joint above to the joint below the suspected injury. For forearm injuries, XRAYs of the forearm and elbow are ordered. Wrist can be included if the patient is skeletally mature.

FRACTURE DESCRIPTIONS
Open or closed
Bone(s) involved and bone segments (diaphysis, metaphysis, physis, epiphysis)
Number of fracture fragments: Comminuted fractures involve fracture in ≥ 2 places
Degree of angulation and plane of angulation (volar/dorsal)
Extent of bone overlap (AKA shortening, apposition or bayonetting)
Presence of any rotational deformity
Associated dislocations: Proximal radius, distal radioulnar joint

CONSULTATION: Orthopedic consultation and follow up is indicated for many pediatric forearm injuries, especially those in whom neurologic or vascular compromise is suspected.

ORTHOPEDIC CONSULTATION: DISTAL FOREARM FRACTURES
Open fractures
Neurovascular compromise
Concern for compartment syndrome
Fracture dislocations: Galeazzi, Monteggia
Physis injury: Displaced/Distracted Salter 1, all higher level physeal injuries

PEDIATRIC SPECIFIC FOREARM INJURIES

In children a strong, thick, and very elastic periosteum acts like a splint around broken bone. Immature bone has the ability to bow rather than break in response to force. This results in a number of fracture types that are unique to immature bone.

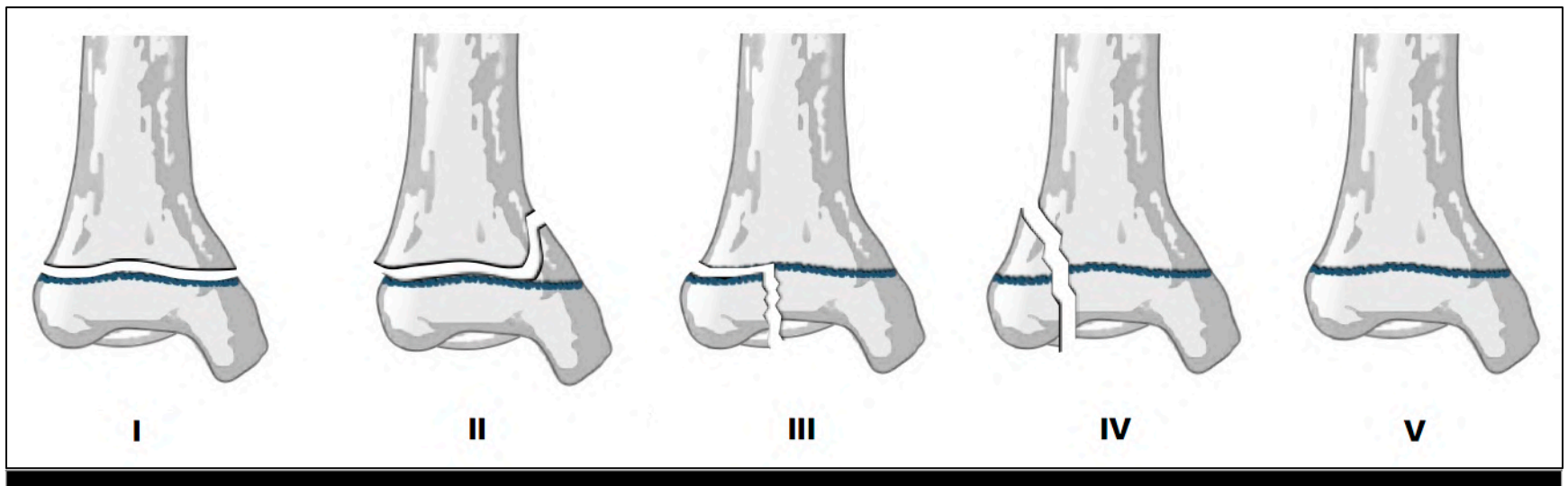
The attachment of the physis to the metaphysis is a point of weakness in the growing bone. Ligaments and tendons are usually stronger than the growing bone in proximity of a growth plate (such as for example in ankle-injuries) and child is more likely to fracture a bone when compared to an adult with a similar mechanism of injury

SALTER-HARRIS FRACTURES: Salter-Harris fractures are fractures through the physis The distal radius is the second most common fracture site in children (after the clavicle) and the distal radial physis is the most commonly injured physis in the body.

The classic Salter-Harris I fracture is the Slipped Capital Femoral Epiphysis (SCFE). SH1 fractures may not be radiographically apparent unless the epiphysis is moved relative to the metaphysis (Distracted: Pulled away or Displaced: Moved laterally). Patients with pain on palpation over the growth plate without radiologic evidence of a fracture are considered potential Salter Harris type 1 fractures and warrant immobilization with splint or cast and follow-up with orthopedics.

Damage to the physis can disrupt future growth. Several factors determine the prognosis for physis injuries. These include severity of injury, degree of displacement, and the location of the physis involved (e.g. weight bearing extremity)

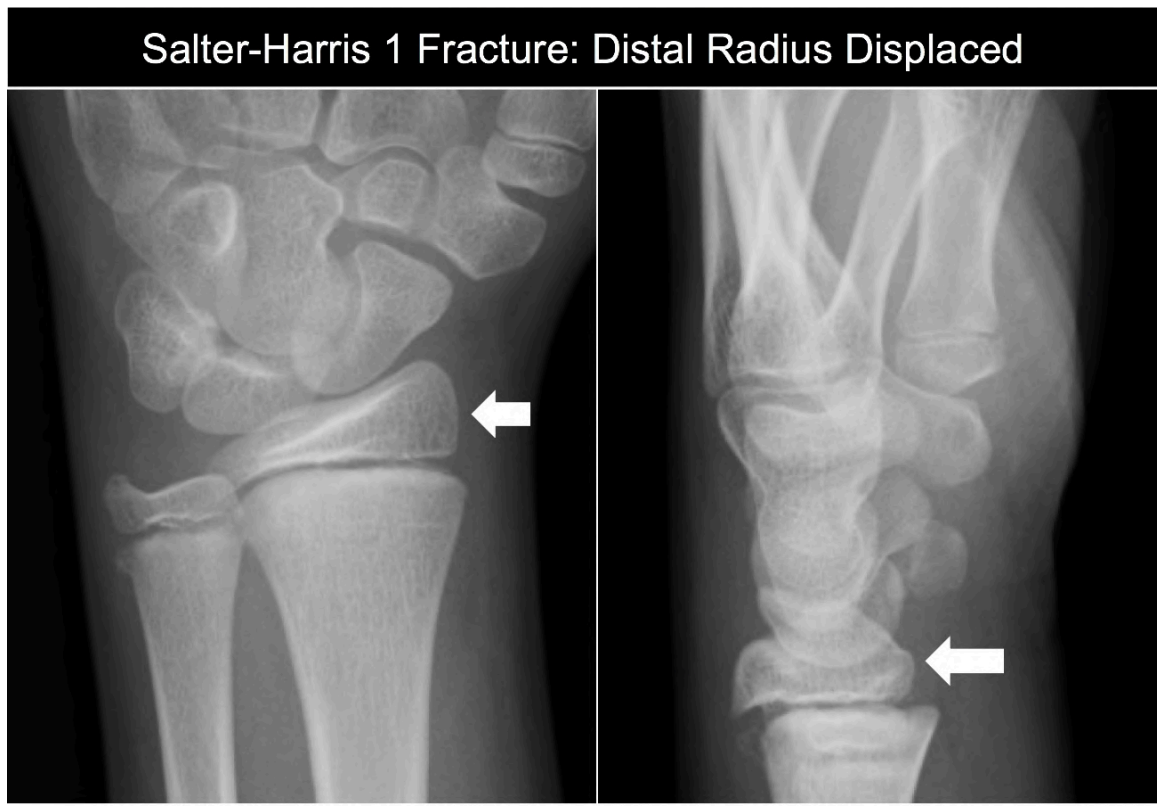
The Salter-Harris classification scheme is designed to stratify injuries according to the physis involvement and implements a relative risk of growth disturbance: Types I and II have a low risk of growth disturbance, and the relative risk increases from type II to V. However, it is important to consider all factors when assessing the risk of growth disturbance and to remember that growth disturbance can occur after any fracture in the region of a physis.



SALTER-HARRIS PHYSIS FRACTURE CLASSIFICATION

Orthopedics should be consulted for Salter Harris Fractures graded higher than a non-displaced Salter-Harris I. Reduction is indicated for all Salter-Harris I or II fractures with unacceptable alignment. Displaced physis fractures should be reduced as soon as possible by an experienced clinician. The longer the delay in reduction, the greater the force that must be applied to obtain an adequate reduction, which puts the physis at greater risk of injury and subsequent growth arrest.

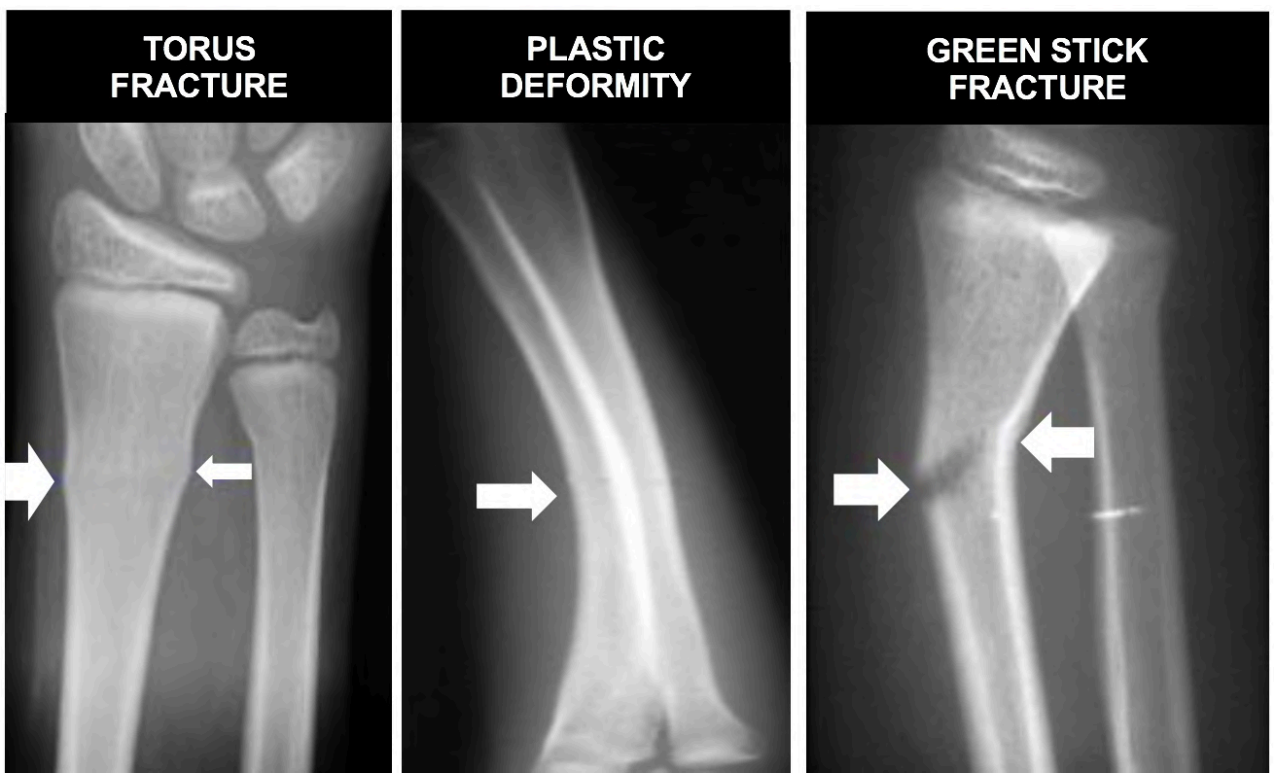
TORUS OR BUCKLE FRACTURE: A compressive force in a child will produce a torus fracture, also called buckle fracture instead of the impacted fractures that occur in adults. Controversy exists regarding the management of buckle fractures of the distal forearm. Classically, these have been casted.



Recent evidence suggests that removable splints may improve function. A randomized clinical trial including 87 pediatric patients with buckle fractures compared the level of functioning at two weeks in patients randomized to either casting for 3 weeks or a removable splint. Patients in the removable splint group had better function at 14 days compared to the cast group (Splint group: 93.77, Cast group: 89.29, Difference: 2.97, 95% CI (0.00 to 6.90). For secondary outcomes, patients reported significantly less difficulty with activities of daily living with the removable splint, less return visits to the ED and a higher preference for the splint regardless of study group (Plint, Pediatrics. 2006, PubMed ID: 16510648). Splints should only be removed for bathing or skin integrity evaluation. Activities that may re-injure the arm should be restricted. The splint should be used for 3 weeks. Should follow up if pain persists after that interval

GREENSTICK FRACTURE: A force applied to the side of a long bone may disrupt one cortex while merely bending the other, producing a greenstick fracture

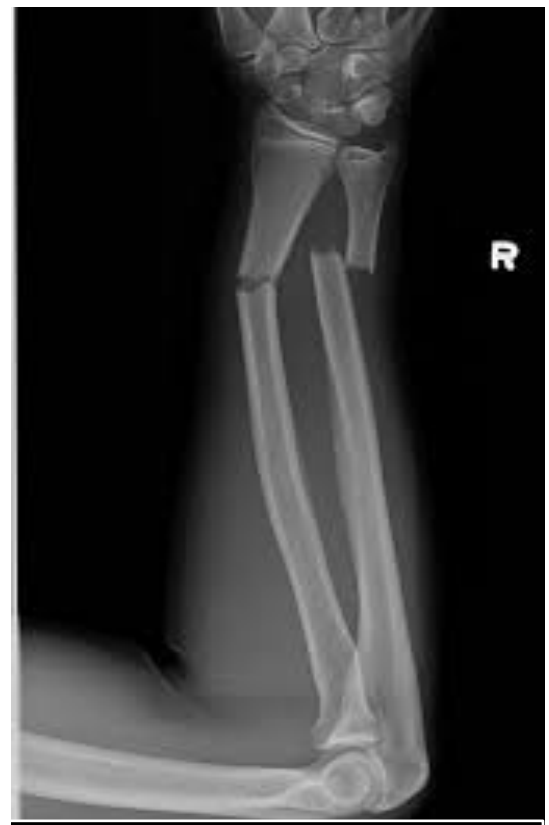
PLASTIC DEFORMITY: In very young children, neither cortex may break, producing a bowing of the bone referred to as plastic deformation. Angulation of less than 20 degrees typically require simple immobilization and analgesia. However, angulation greater that exceed 20 degrees, particularly in the child over 4 years of age, require orthopedic consultation. These fractures may require closed reduction under deep sedation or general anesthesia. The center point of deformity is levered over a roll or block and pressure applied to either end. A 3-point molded cast is then applied.



FOREARM DIAPHYSIS FRACTURES

Fractures of the diaphysis include isolated fractures of the radius, isolated fractures of the ulna and fractures to both bones. The majority of patients require procedural sedation and closed reduction. Operative reduction with pinning or internal fixation may be required for those fractures failing closed reduction.

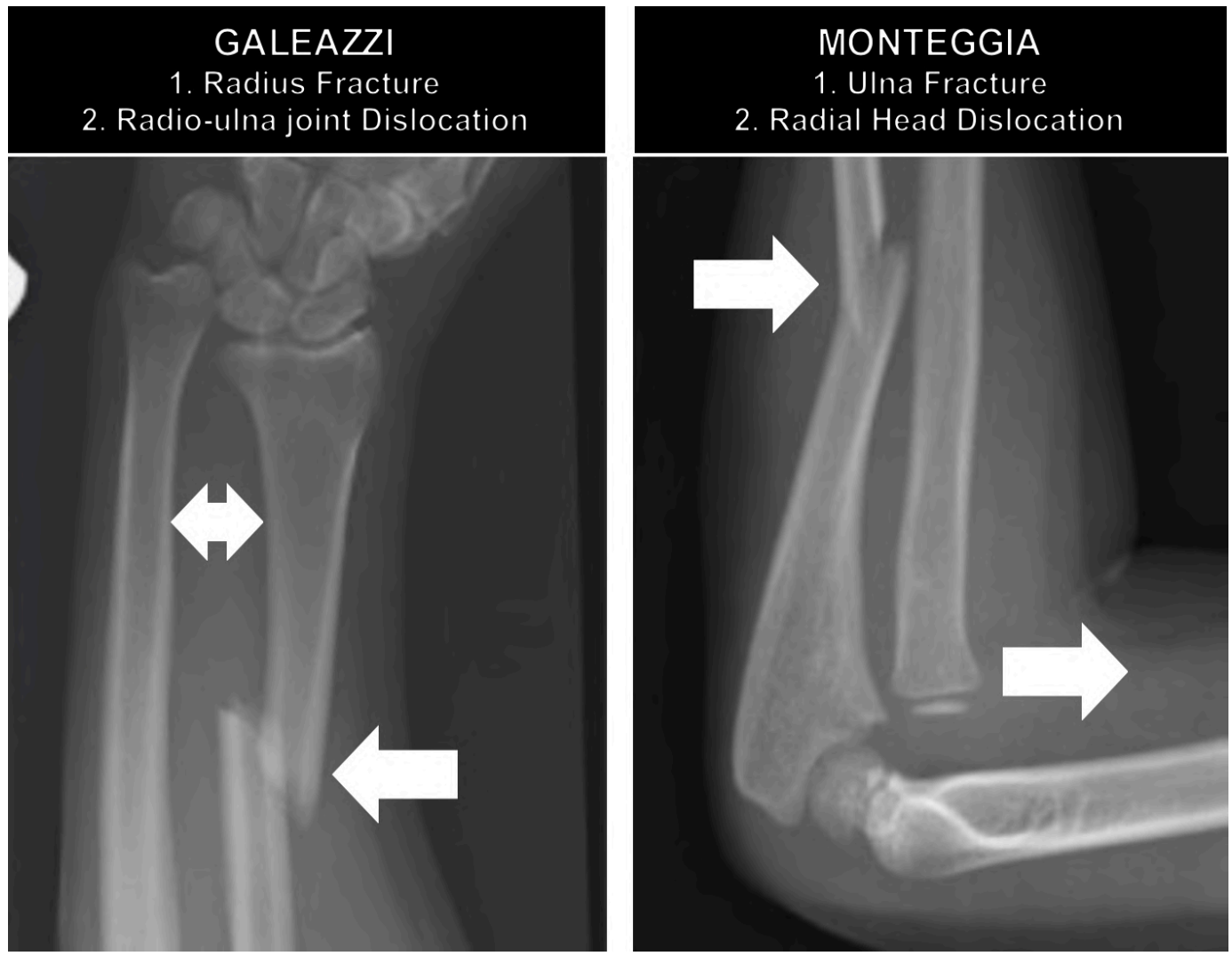
A single center study, retrospective cohort center included 124 patients with an open radial physis (boys < 13 year, girls < 11 year) with minimally angulated distal radius (< 15 degrees of angulation and < 0.5 cm displacement) with or without a distal ulna fracture. Patients did not undergo reduction and a volar or dorsal plaster splint was placed. At 6 week follow-up, there were no deformities or functional limitations (Al-Ansari, CJEM 2007, PubMed ID: 17391594). The same center randomized 5-12 year old patients with minimally angulated or minimally displaced (same criteria as above study) acute greenstick or transverse fracture of the metaphyseal portion of the distal radius to a prefabricated splint (n= 46) or a cast (n=50)(Boutis, CMAJ 2010, PubMed ID: 20823169). There was no clinically or statistically significant difference in function at 6 weeks (Activities Scale for Kids score), angulation at 4 weeks, range of motion, grip strength or complications.



TRANSVERSE FRACTURES
Radius: Angulated
Ulna: Displaced, Overlapping

FOREARM FRACTURE-DISLOCATIONS

The forearm is a “bony ring”, and isolated fractures are rare. The most common missed fracture/injury is the 2nd fracture/injury. Check the radiographs carefully for an associated ulnar styloid. A distal radius fracture may be associated with a dislocation of the radio-ulnar joint (Galeazi injury). Proximal ulnar fractures may associated with dislocation of the radial head (Monteggia injury).



MNEMONIC: MUGR (MU = Monteggia Ulna, GR: Galeazzi Radius)

MANAGEMENT

There is considerable debate regarding the acceptable degree of fracture angulation. Acceptable angulation is determined by the age of the patient, the location of the fracture and the type of deformity (angulation, rotation, bayoneting (overlap)). In general, children less than 9 years of age have a greater ability to remodel and a higher degree of acceptable angulation.

In general, deformities in the plane of motion and distal radial deformities (closer to the physis are more acceptable. Rotational deformities do not remodel. Rotational deformity of the radial shaft of less than 1 cm that do not block rotation is acceptable in those less than 10 years of age. The radius and ulna rotate as a unit. Angulation of 10 degrees can block 20-30 degrees of rotation.

ACCEPTABLE ANGULATION OF PEDIATRIC RADIUS FRACTURES			
	Shaft/Both Bone		Distal Radius/Ulna
Age	Acceptable Overlap	Acceptable Angulation	Dorsal Angulation
< 10 years	< 1 cm	15-20 degrees	30 degrees
> 10 years	None	10 degrees	20 degrees
WEB LINK: ORTHOBULLETS: PEDIATRIC DISTAL RADIUS FRACTURES			

DISTAL RADIAL FRACTURE REDUCTION
Provide adequate analgesia: Hematoma block or procedural sedation
Hang the patients are for 10 minutes using 10lb weight to reduce muscle tone/spasm
Exaggerate the deformity (angulate in the same plane)
Advance to fracture fragment distally and reduce the angulation to normal alignment
Apply a well molder splint
VIDEO LINK: PEDIATRIC FOREARM FRACTURE REDUCTION (2)

HAND FRACTURES

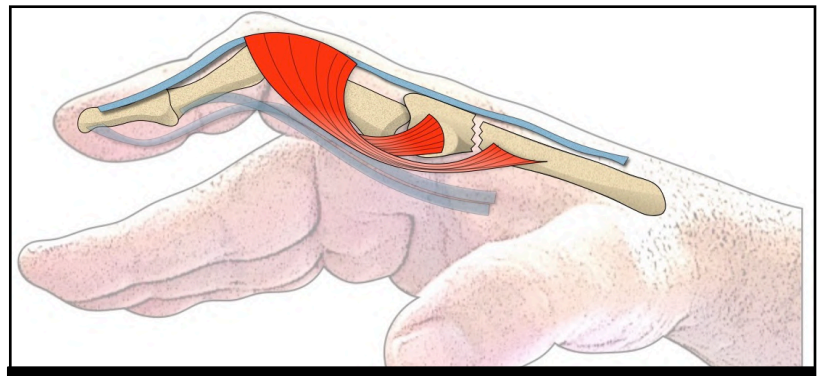
INTRODUCTION (NICOLAS DELACRUZ, MD, 3/2023)
Injuries involving the metacarpal bones are extremely common in the pediatric population. Boys, with median age of 15 years, are three times more likely than girls to sustain a metacarpal fracture. Eighty percent of metacarpal injuries involve the 5th metacarpal bone. These are colloquially referred to as “boxer’s fractures”. This is in reference to the most common mechanism of injury, which is a direct blow with a clenched fist, such as punching a wall. This PEM Guide focuses on metacarpal fractures. Metacarpal 2-5 fractures and 1st metacarpal fractures are discussed separately. See: PEM Guide: Orthopedics: Finger Injuries

METACARPAL 2-5 FRACTURES

ANATOMY
Each hand has 5 metacarpal bones numbered 1 through 5 beginning with the thumb. Proximally, they articulate with the carpal bones of the wrist at the carpometacarpal (CMC) joint as well as with each other via the intercarpal joints. Distally, the metacarpal bones articulate with the proximal phalanges at the metacarpophalangeal (MCP) joint.

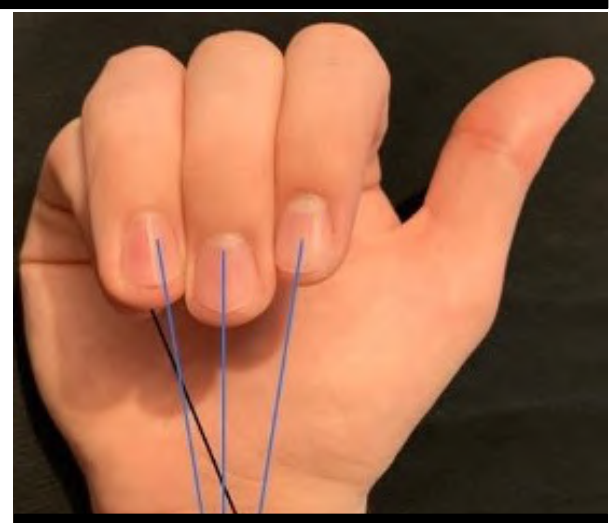
The metacarpal bones are supported proximally by the palmar and dorsal metacarpal ligaments. They are bound together distally via the superficial and deep transverse metacarpal ligament. The interosseous muscles originate on the metacarpal shafts and insert onto the proximal phalanges and act as flexors of the MCP joint. The common palmar digital arteries and nerves run along each metacarpal bone. The superficial and deep palmar arches traverse the metacarpal bones proximally.

PHYSICAL EXAMINATION
The initial physical examination of the hand should focus on four key elements: deformity, finger malrotation, neurovascular status, and soft tissue injuries (including function of the flexor and extensor apparatus).



PSEUDO-CLAWING
Metacarpal Neck Fracture
Extension at MCP/Flexion at PIP

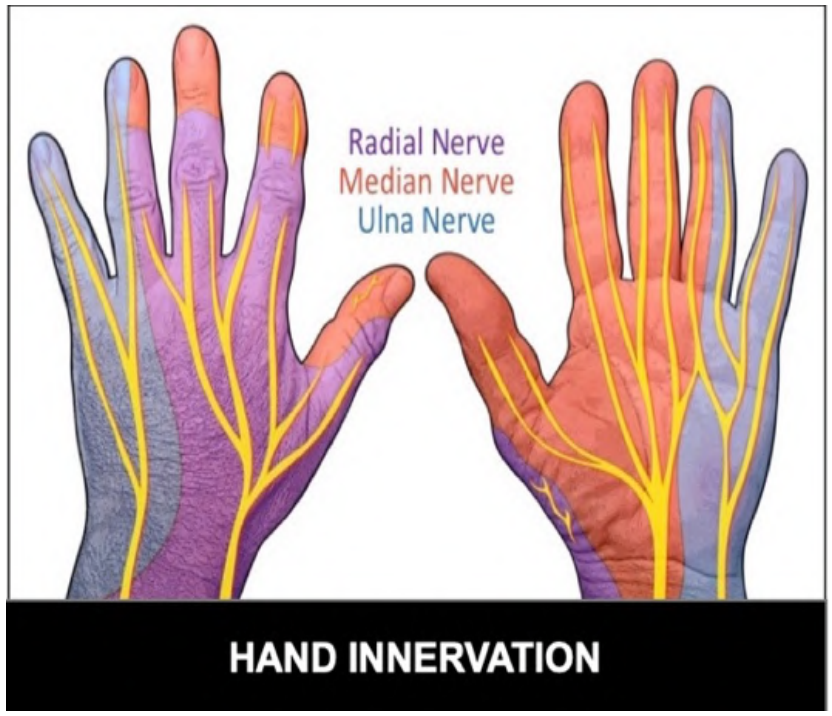
DEFORMITY: When examining for deformity, the injured metacarpal should be examined for displacement and angulation. The interosseous muscles that originate on each metacarpal shaft exert forces on fractured metacarpals that tend to cause apex dorsal angulation. “Pseudo-clawing” may also be seen in metacarpal fractures. This includes hyperextension of the MCP with flexion of the PIP at rest or with attempted extension.



MALROTATION
(5th Digit)

MALROTATION: When examining for malrotation, have the patient attempt to flex the MCP and the PIP joints to about 90 degrees. In a normal hand, the axes of each finger will generally converge at a single point near the wrist. When there is a rotational deformity, the axis of the injured digit will not converge with the other fingers. A careful examination for malrotation is crucial because even a few degrees of rotational deformity can cause significant functional deficits.

SOFT TISSUES: A careful skin exam should also be completed paying special attention to the presence of any associated lacerations, puncture wounds, or protruding bone fragments throughout the full range of motion. The extensor apparatus includes muscles, tendons, fascia and sheaths tendons (retinaculum) that extend the fingers.



HAND INNERVATION

NEUROVASCULAR ASSESSMENT

Vascular integrity should be assessed by testing capillary refill, skin color and temperature distal to the injury. Neurologic testing includes an assessment of motor and sensory function. Assess range of motion, strength and sensation in the ulna, radial and median nerve distributions. Dorsal wounds may affect the dorsal sensory branch of the radial and ulnar nerves. Palmar injuries may injure the digital nerves.

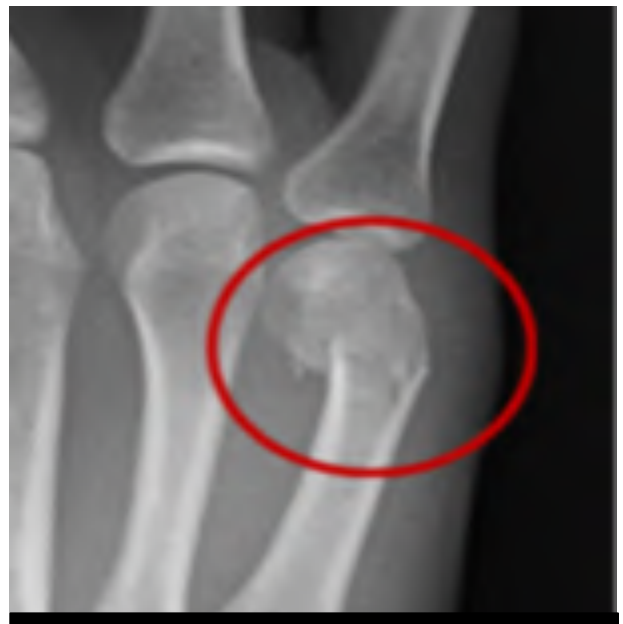
NEUROMUSCULAR ASSESSMENT OF THE HAND	
MOTOR FUNCTION	
Median nerve	OK sign (1st & 2nd) against resistance
Ulnar nerve	Finger spread against resistance
Radial nerve	Thumbs up sign
SENSORY FUNCTION: 2-point discrimination at 5 mm	
Median nerve	Second digit (volar)
Ulnar nerve	Fifth digit (volar or dorsal)
Radial nerve	Dorsal web space (between 1st, 2nd digit)
VIDEO LINK: RAPID NEUROLOGIC ASSESSMENT OF THE HAND (EM IN 5)	

DIAGNOSIS

Diagnosis of metacarpal fractures can be made with PA, lateral, and oblique view radiographs of the hand. Radiographs may not identify rotational deformities.

MANAGEMENT

Metacarpal fractures are divided into fractures of the head, neck, or shaft. Treatment is based on location, associated angulation and deformity of the fracture. The metacarpal neck is the most commonly injured area and the 5th metacarpal is the most commonly injured metacarpal. Most metacarpal neck and shaft fractures can be managed nonoperatively.


5TH METACARPAL NECK FRACTURE

OPERATIVE MANAGEMENT: INDICATIONS
Open fractures
Intra-articular fractures
Metacarpal head fractures
Multiple fractures
Evidence of malrotation on exam
Unacceptable degrees of angulation or shortening (See Table below)

ACCEPTABLE DEGREES OF ANGULATION AND SHORTENING			
	Shaft Angulation	Shaft Shortening	Neck Angulation
Metacarpal 2,3	10-20 degrees	2-5 mm	10-15 degrees
Metacarpal 4	30 degrees	2-5 mm	30-40 degrees
Metacarpal 5	40 degrees	2-5 mm	50-60 degrees
WEBLINK: ORTHO BULLETS			

Patients with fractures that can be managed nonoperatively should be treated with reduction and splinting or casting. Patients with 4th and 5th metacarpal fractures should be splinted in an ulnar gutter splint with the MCP joints flexed to at least 70 degrees. If patients are not casted in the ED, urgent follow up should be arranged with a hand specialist for casting 2-3 days post discharge, once the acute swelling has resolved.

Management of associated puncture wounds or lacerations, colloquially referred to as, “fight bites”, is a key aspect of management. Lacerations and puncture wounds should be copiously irrigated and carefully explored. If the wound involves the joint capsule or tendons, orthopedic consultation is required. Fight bites should be left open to heal by secondary intention and broad-spectrum antibiotics against oral flora (such as Amoxicillin-Clavulanic Acid) should be prescribed. Patients’ tetanus vaccination status should be determined and vaccination should be provided if indicated.

CLOSED REDUCTION: There are several ways to reduce a displaced metacarpal fracture. Adequate pain control can be achieved with a hematoma block into the fracture site or with a nerve block at the wrist (See Appendix). The Jahss technique can be used to reduce displaced metacarpal neck fractures. This technique involves flexing both the MCP and the PIP joints to 90 degrees. The fracture is reduced by pushing dorsally (toward the flexed MCP) on the flexed PIP joint.

An alternative technique involves flexing all joints of the affected finger to 90 degrees. The practitioner then pulls on the affected finger to apply axial traction while simultaneously applying downward (volar) pressure on the affected metacarpal. Radiographs should be repeated after reduction and splinting or casting.

VIDEO LINK: JAHSS TECHNIQUE
VIDEO LINK: REDUCTION AND SPLINTING (ALIEM)

FIRST METACARPAL (THUMB) FRACTURES

INTRODUCTION

The thumb is critically important to hand function and fractures with or without dislocation can limited functionality if not properly managed. First metacarpal fractures are second only to fifth metacarpal fractures in frequency and account for approximately one-quarter of all metacarpal fractures. 80% of first metacarpal fractures involve the base of the thumb. These fractures occur most commonly in young males and are typically a result a fall or direct trauma resulting in an axial load to a partially flexed thumb (jamming), hyperabduction or hyperflexion.

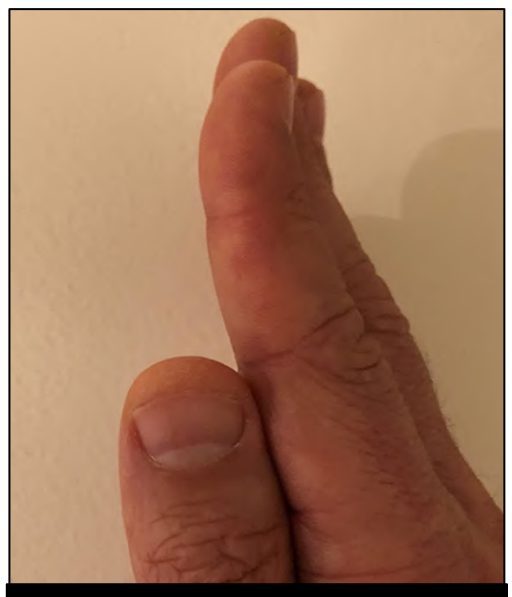
ANATOMY

The thumb is rotated at a 90-degree angle relative to the other digits, and is not directly attached to another metacarpal. The range of motion of the thumb is described as abduction (away) or adduction (toward) in the sagittal plane, flexion and extension in the coronal plane and opposition (positioning the thumb pad in contact to the pad of the 3rd digit) and reposition. Opposition requires abduction as well as medial rotation and flexion at the metacarpophalangeal joint. The range of motion of the thumb, its lack of attachment to adjacent structures and its narrower width increase the risk of fracture and displacement.

CLINICAL ASSESSMENT

Tenderness, swelling and decreased range of motion at the base of the thumb are the primary findings in thumb fractures. This should be carefully distinguished from tenderness of the scaphoid and distal radius. Malrotation of the thumb is less common than the other metacarpals but has a greater importance. In a lateral position the nail of the thumb should be parallel to the nails of the other metacarpals (see image).

The thumb is innervated by the median nerve ventrally and radial nerve dorsally. The motor and sensory exam of the thumb is detailed in the table below. (See Table and Image earlier in this PEM Guide for innervation and assessment of strength and sensation). Perfusion should be assessed by capillary refill, warmth and color of the thumb and supplemented with doppler flow if perfusion is questionable



NORMAL THUMB ALIGNMENT

DIFFERENTIAL DIAGNOSIS	
Wrist	Scaphoid, trapezium fractures
Dislocation/Subluxation	First MCP or carpal-metacarpal joint
Collateral ligament injury	Ulnar or radial at MCP joint*
See PEM Guide: Orthopedics: Finger Injuries*	

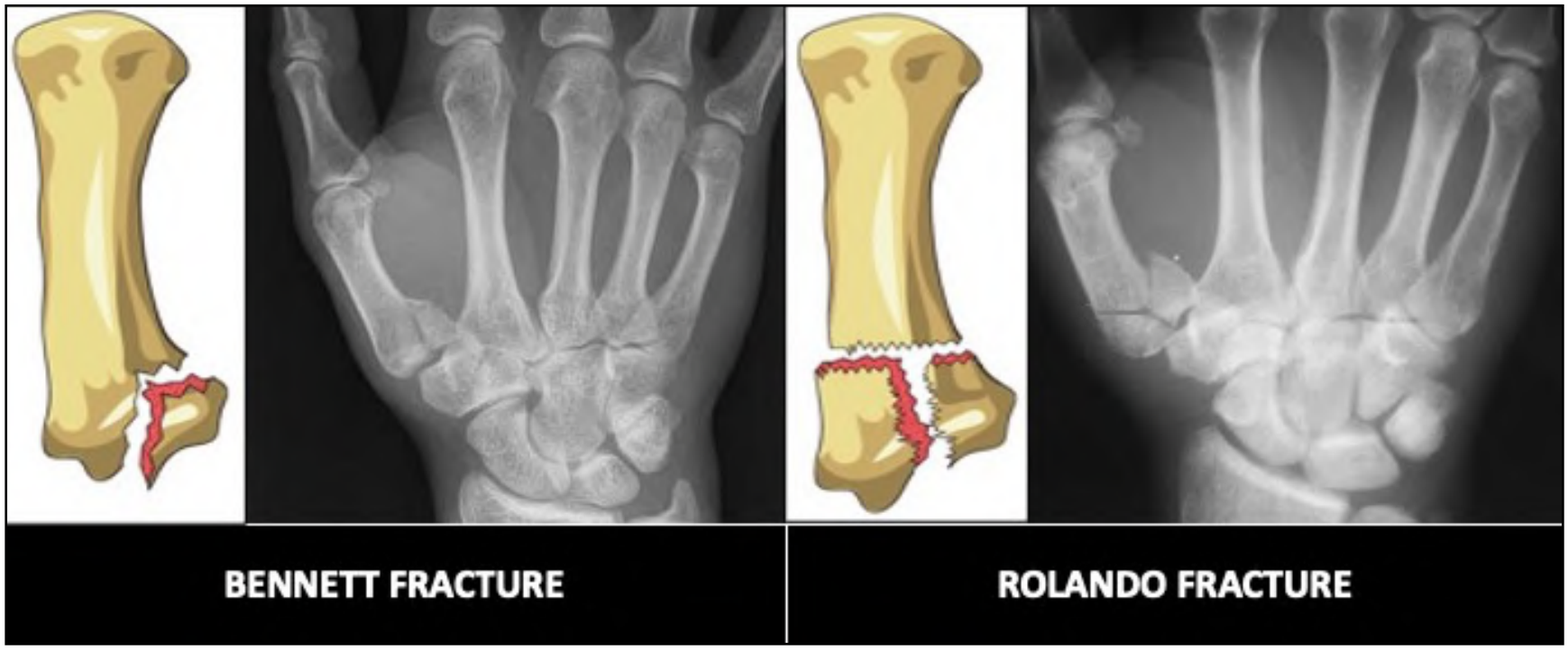
IMAGING

Plain radiography is the most common method of imaging. 3 views are obtained of the thumb. These include a lateral, oblique and true anterior-posterior (Robert view). CT scan may be required to better define possible intra-articular or comminuted fractures.

CLASSIFICATION OF 1ST METACARPAL BASE FRACTURES		
Intraarticular	I	Bennet Fracture
	II	Rolando Fracture
Extraarticular	III	Transverse > Oblique Fractures
	IV	Extraarticular pediatric physis fractures (S-H 2 most common)

BENNETT FRACTURE: The Bennett fracture is a fracture/dislocation. The small fracture fragment located on the ulna side of the metacarpal is held in anatomic alignment by its attachment to the trapezium by the volar or anterior oblique ligaments. The large fragment is displaced dorsally by its attachment to the flexor pollicis longus.

ROLANDO FRACTURE: Rolando fractures are rare and difficult to treat. It is a comminuted version of the Bennet fracture that can take on a Y or T shape or can be severely impacted. Note: T shape in the illustration, Y shape in the XRAY below.



OTHER FRACTURES: First meta-carpal fractures of the head and the mid-to-distal shaft are uncommon. Shaft fractures are classified as transverse or oblique. They are treated the same as other metacarpal fractures though they are more likely to be shortened and displaced. Pediatric fractures involve the physis

CLASSIFICATION OF PEDIATRIC 1ST METACARPAL BASE FRACTURES	
Extra-articular	Shaft fractures
	Salter-Harris 2 fracture: Physis and medial metaphyseal fragment (#1)
	Salter-Harris 2 fracture: Physis and lateral metaphyseal fragment
Intra-articular	Salter-Harris 3 fracture: Physis extending though the epiphysis AKA Pediatric Bennett fracture

MANAGEMENT

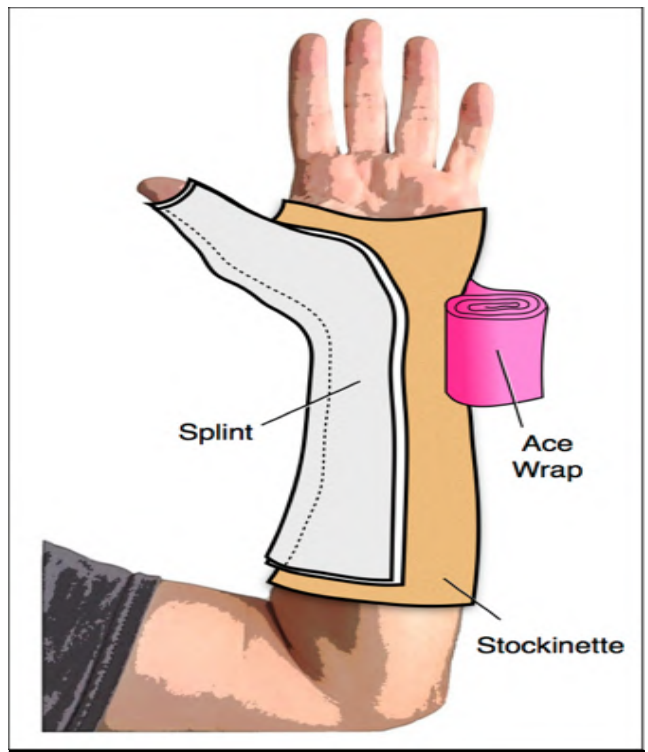
Fracture are initially immobilized in a thumb spica splint. Displaced fractures may require closed reduction. Analgesia and elevation will be required after splinting.

VIDEO LINK: THUMB SPICA SPLINT

INTRA-ARTICULAR FRACTURES: A thumb spica splint is placed with the wrist in 30 degrees of extension and the interphalangeal joint left free. They should follow-up with an orthopedic or hand surgeon in 2-3 days

EXTRA-ARTICULAR FRACTURES: For non-displaced (see criteria in the table below) extra-articular fractures, the thumb spica splint should include the interphalangeal joint and follow-up in a week. Definitive treatment is with a thumb spica cast for 4-6 weeks. Oblique of displaced extra-articular fractures should be referred in 3-5 days.

PEDIATRIC FRACTURES: Displaced or mal-rotated fractures as well as Salter-Harris III fractures require referral to an orthopedic surgeon. Non-displaced Salter-Harris II fracture are managed with a thumb spica splint or cast for 4-6 weeks.



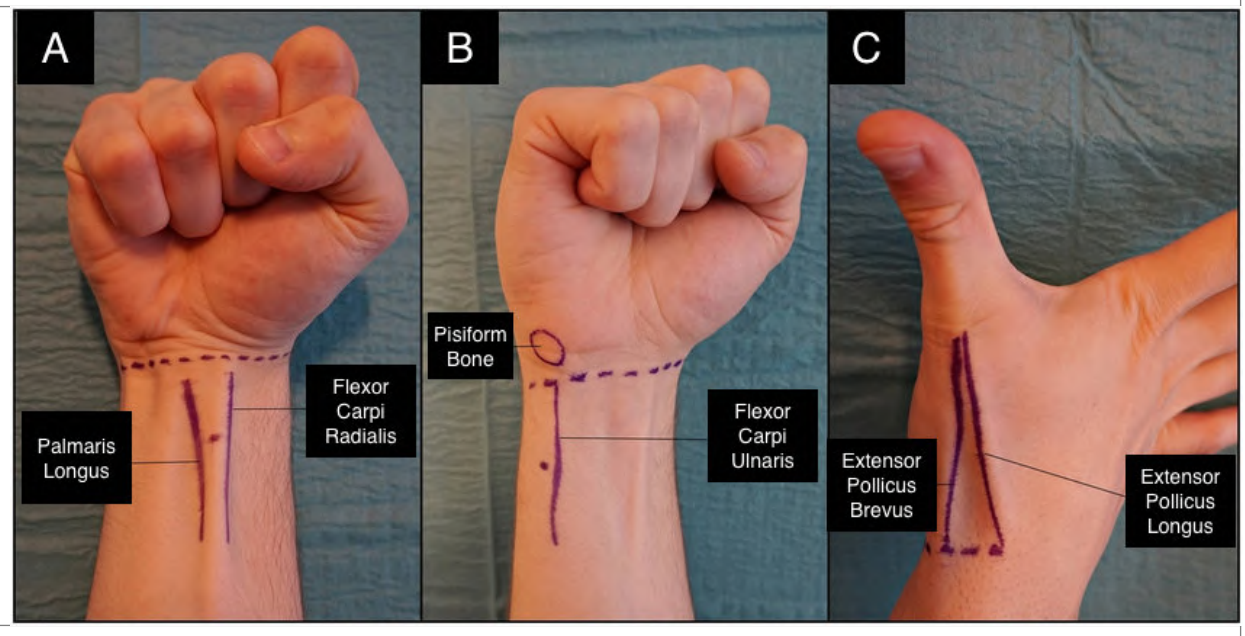
THUMB SPICA SPLINT

CLOSED REDUCTION: Closed reduction, typically by an orthopedist is indicated for angulated extra-articular fractures.

SURGICAL REFERRAL
IMMEDIATE SURGICAL CONSULTATION (RARE)
Open metacarpal neck fractures
Injuries associated with major neurovascular impairment
REFERRAL TO AN ORTHOPEDIC OR HAND SURGEON
Intra-articular fractures (Bennett, Rolando): Within 2-3 days. Most require fixation
Extra-articular fractures: Typically managed non-operatively
Nondisplaced: Within 1 week
Displaced (≥ 1 mm): Within 3-5 days
Shaft/Neck fractures: Typically managed non-operatively.
Refer in 3-5 days if adequate reduction not achieved with closed reduction
Inadequate: >20 angulation OR >2 mm shortening OR any degree of malrotation

APPENDIX: RADIAL, MEDIAN, AND ULNAR NERVE BLOCKS

EQUIPMENT: LANDMARK & ULTRASOUND GUIDED APPROACHES
1% Lidocaine with or without epinephrine
Chlorhexidine swab
Sterile gloves
10 cc syringe with 27-gauge needle
Blunt fill needle for drawing up anesthetic
Linear high frequency ultrasound transducer with sterile probe cover (US guided)

NERVE BLOCKS OF THE HAND: PROCEDURE	
1	Indications: Regional asthenia for fracture reduction, laceration repair, abscess drainage Alternative: Hematoma Block
1	Identify appropriate landmarks or perform ultrasound guided blocks
	Median Block(A): The median nerve runs in the middle of the volar surface of the forearm and courses deep to the carpal tunnel. It is bordered by the palmaris longus and the flexor carpi radialis tendons. It's not located near major vessels
	Ulnar Block(B): Identify the ulnar head and the flexor carpi ulnaris tendon. The ulnar nerve courses in between the flexor carpi ulnaris and the ulnar artery.
	Radial Block(C): Identify the radial artery pulse. The radial nerve lies just lateral to the radial artery. This block is more effective in the mid to upper forearm, before the radial nerve splits into superficial sensory branches at the wrist
	Procedure Video Links: A. Median Nerve Block B. Ulna Nerve Block C. Radial Nerve Block
	
2	Sterilize the entire region around where you will be injecting anesthetic
3	With the high frequency linear probe, identify the target nerve and accompanying structures. Nerves have a "honeycomb" shape on ultrasound.
	A. Median nerve lies between palmaris longus and flexor carpi radialis tendons
	B. Ulnar nerve lies medial to the ulnar artery
	C. Radial nerve lies lateral to the radial artery
4	Under ultrasound guidance, insert a 27-gauge needle into the space under the nerve. Aspirate first to ensure you are not in a vessel, then inject a small amount of lidocaine under the nerve, Proceed to "bathe" the nerve in lidocaine.
5	Wait for 5-10 minutes to allow the anesthetic to appropriately numb the area prior to starting any painful procedures.

KNEE INJURIES

INTRODUCTION (KEVIN CHING, M.D. 9/2017)
Acute injuries of the knee and its accompanying pain or swelling are among the most common pediatric injuries presenting to the ED. A basic familiarity with the anatomy of the knee will help facilitate a better understanding of the common patterns of knee injuries. These can include intra-articular fractures or dislocations, meniscal or ligamentous tears, patellar malalignment, and periarticular tendonitis.

HISTORY

A thorough history should include attention to preceding activities or forces that led to the injury. Any appreciable sensations or noises (i.e. pops, snaps, or tears) should be noted. The onset and progression of swelling, as well as the origin of pain are also important clues to the injury. Consider the possibility of abuse in young children especially if the injury is unexplained or implausible, or if medical care is delayed.

When approaching the child with knee pain, consideration of the location and character of pain may provide clues to the underlying injury.

KNEE INJURY LOCALIZATION	
Medial knee pain	Medial collateral ligament (MCL), medial meniscal tears and tibial plateau fractures.
Lateral knee pain	Lateral collateral ligament (LCL), lateral meniscal tears. iliotibial band syndrome (often accompanied by an audible “snap”).
Anterior knee pain	Injuries to the quadriceps mechanism, patellofemoral pain syndrome, prepatellar bursitis, patellar tendonitis.

PHYSICAL EXAMINATION

INSPECTION: Inspection of the knee should begin with an assessment of neurovascular integrity. Begin by palpating distal pulses. Evaluate peroneal nerve function by checking ankle dorsiflexion, and test the extensor hallucis longus by opposing dorsiflexion of the first toe. Sensation should be evaluated by testing the space between the 1st and 2nd toes.

FUNCTION: Proceed with an overall appraisal of knee function by first assessing the impact of the knee injury on gait and stance. The child’s ability to ambulate and squat depends on intact supporting ligaments and a strong quadriceps mechanism, while the ability to “duck waddle” requires intact collateral and cruciate ligaments. Normal range of motion of the knee is extension to 180 degrees and flexion to between 130-140 degrees.

PALPATION: With the child in a seated position, inspect and palpate the knees for the presence of an effusion, and assess the child’s ability to extend their leg against resistance. Extension requires an intact patellar and quadriceps tendon, and inability to extend may suggest a tendon rupture or fracture of the patella.

Next, examine the child’s knee in a supine position. With the knees extended and quadriceps relaxed, begin by inspecting both knees for symmetry. If an effusion is detected, compress the effusion with both hands and “milk” this fluid into the center of the knee. If an audible “snap” is heard when tapping the patella against the femur, then a moderately sized effusion is likely. If no effusion is detected, but pain or crepitation is elicited, consider patellofemoral pain syndrome. Gently move the patella laterally. Pain or withdrawal is associated with patellar subluxation.

LIGAMENT ASSESSMENT: Palpate along the medial and lateral joint lines; tenderness may suggest a collateral ligament or meniscal injury. To assess the integrity of the medial collateral ligament (MCL) apply valgus stress (VIDEO LINK: VALGUS STRESS). To assess the integrity of lateral collateral ligament (LCL) apply Varus stress (VIDEO LINK: VARUS STRESS) Open of the knee when stressed in comparison to the contralateral side indicates a collateral ligament injury. If pain or a palpable "snap" is heard when palpating along the lateral femoral condyle, suspect an iliotibial band syndrome.

There are several maneuvers that are used to assess the integrity of the anterior and posterior cruciate ligaments (ACL and PCL). A difference of even 1 cm when compared to the contralateral knee suggests a complete tear, while partial tears are associated with pain and loss of elasticity. The posterior draw test is primarily used to determine the integrity of the posterior cruciate ligament. It is done with the knee at 90 degrees and the hip at 45 degrees with the patient' s foot stabilized on the examination table. The tibia is held and pushed firmly posterior (VIDEO LINK: POSTERIOR DRAW). The anterior draw test is done with the knee flexed to 90 degrees and the hip at 45 degrees (VIDEO LINK: ANTERIOR DRAWER). The Lachman maneuver is done with the knee at 30 degrees and may be easier to perform with larger effusions (though it may be falsely negative soon after the injury) and is the sensitive test for ACL injury (VIDEO LINK: LACHMAN MANEUVER). The Pivot shift test is the most specific to assess the ACL. With the patient in the supine position the leg is extended and a valgus stress is placed on the knee (VIDEO LINK: PIVOT SHIFT TEST) The tibia is rotated medially while the knee is flexed. A "clunk" indicates an ACL tear.

MENISCAL ASSESSMENT: The McMurray test helps identify meniscus injuries when evaluating for smooth joint motion (VIDEO LINK: MCMURRAY TEST). The maneuver involves laying the patient in a supine position while varus stress is applied to a flexed knee that is internally rotated as the leg is being extended. A click or snapping sensation may indicate a medial meniscus injury. To identify a lateral meniscus injury, valgus stress is applied while the knee is extended and externally rotated. The Apley test is performed similarly to the McMurray Test but with the patient in a prone position with the lower leg extended upward with the knee at 90 degrees (VIDEO LINK: APLEY TEST) Evaluation of the hip and ankle are also important in all children who present with complaints of knee pain

FRACTURES

Distal femoral epiphysis separation fractures commonly follow significant sports or motor vehicle collisions. Children typically complain of severe pain with significant swelling, and may present with a deformity if displaced. Careful attention to neurovascular integrity is important because of associated popliteal artery and peroneal nerve injuries. Lateral and AP (and often oblique) XRAY views are usually diagnostic.

A proximal tibial epiphysis separation fracture is less common, but more likely to involve an associated injury to the popliteal artery and may present with a hemarthrosis. Lateral and AP views are diagnostic.

An acute traumatic avulsion of the tibial tubercle may follow sudden acceleration (jumping) or deceleration (landing a jump), and presents with tenderness and inability to fully extend the knee. A lateral view is diagnostic. A patellar fracture typically results from direct trauma to the knee. The child usually complains of a tender, swollen knee and resists extension. An AP and sunrise (or patella) view is diagnostic.

Avulsion fractures of the tibial spine follow rotational injuries on a fixed, planted foot. Because the tibial spine is incompletely ossified in children, it may avulse before the ACL ruptures. The Lachman maneuver is positive, while Lateral, AP, and tunnel (or intracondylar views may show the avulsed fragment.

DISLOCATIONS

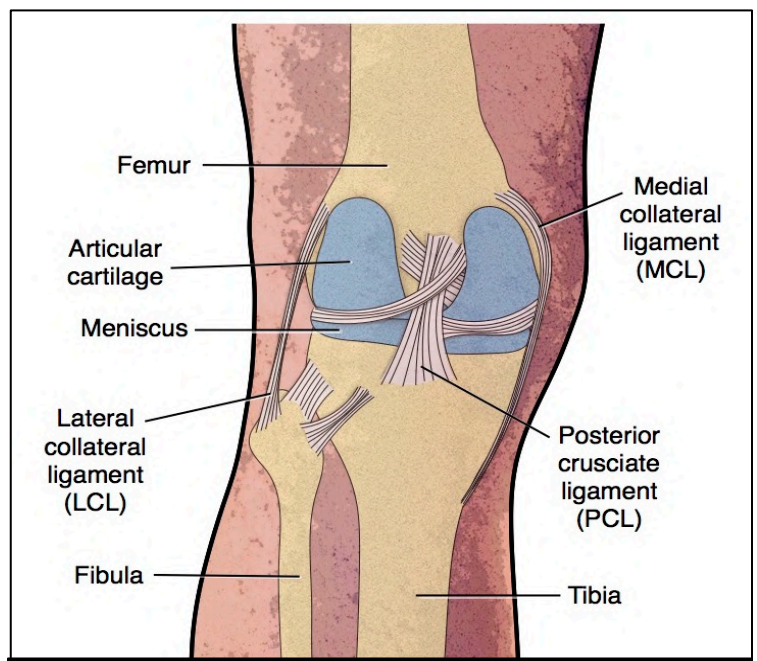
Patellar dislocations commonly occur during gymnastics or dancing, but may follow direct trauma. The patella may be positioned laterally and superiorly while the child's knee is often drawn into a flexed position. If the history is consistent with dislocation but the child is no longer in pain, then any apprehension when moving the patella laterally suggests a subluxated patella (a partial dislocation).

Knee joint dislocations of the distal femoral or proximal tibial epiphysis are rare, but may occur in high-speed MVA's. (e.g. the lower leg hitting the dashboard and moving the lower leg posteriorly relative to the knee). Obvious deformities and limb threatening disruption of the popliteal artery are possible in prominent posterior dislocations. Lateral and AP views are diagnostic. An angiogram may be necessary to demonstrate the integrity of the popliteal artery.

SOFT TISSUE INJURIES

Because the collateral ligaments are stronger than the growth plates, MCL and LCL injuries are rare in younger children with open epiphyseal growth plates. Anterior or posterior tibia spine avulsion fractures may be seen in this age group instead

In older adolescents, the MCL may be damaged by a lateral blow to the knee (valgus force). Laxity is assessed by valgus and varus stress maneuvers. Cruciate ligamentous injuries are also rare before adolescence. A "pop" sensation may indicate an ACL injury following a rotational deceleration on a fixed foot or in a hyperextension of the knee. Rapid swelling, instability, and a positive Lachman's or anterior drawer test may suggest the cause, though an MRI or arthroscopy is required for a definitive diagnosis.



LEFT KNEE (POSTERIOR)

Tears of the menisci typically result when the knee is twisted on a fixed foot during a high velocity activity. As in cruciate ligamentous injuries, a "pop" sensation followed by swelling and instability may accompany joint line tenderness. The McMurray's test is positive and an MRI or arthroscopy is required for diagnosis. An adolescent athletic jumper (basketball, volleyball etc) may rupture their patellar tendon or quadriceps muscle. Lateral and AP views will show an abnormally positioned patella.

SUBACUTE INJURIES

In Osgood Schlatter disease, repetitive contractions of the patellar tendon traumatize the tendinous insertion on the tibial tubercle. Inflammation of a tendon insertion site is termed an apophysitis. Tendonitis refers to inflammation of the tendon itself. This results in localized tenderness and refusal to extend the knee against force. The diagnosis is clinical.

Patellofemoral Pain Syndrome results from repetitive trauma to the patellar cartilage because of mal-alignment from lateral patellar subluxation. Children complain of pain during prolonged knee flexion (for example, when sitting in a movie theater). Tenderness or crepitus are suggestive. XRAYS are normal.

Athletes who run over uneven terrain may complain of pain over the lateral aspect of the knee. Iliotibial band syndrome results when the iliotibial band repeatedly slides across the femoral condyle. XRAYS are typically normal.

Osteochondritis dissecans is defined as a localized lesion in which a segment of subchondral bone and articular cartilage separates from the underlying bone. XRAYS are typically diagnostic though an MRI may be required in some cases

IMAGING

The Ottawa knee rules (Stiell, Annals Emergency Medicine 1995, PubMed ID: 7574120) were derived to determine which adult patients were at low risk of knee fractures. A metanalysis in children (Vijayasankar, Emergency Medicine J 2009, PubMed ID: 19307383) resulted in a sensitivity of 99%, 95% CI (99.4, 99.8%) and had the potential to decrease XRAY utilization by 30-40 percent.
If a fracture is suspected, imaging always begins with plain radiographs (Lateral and AP views).

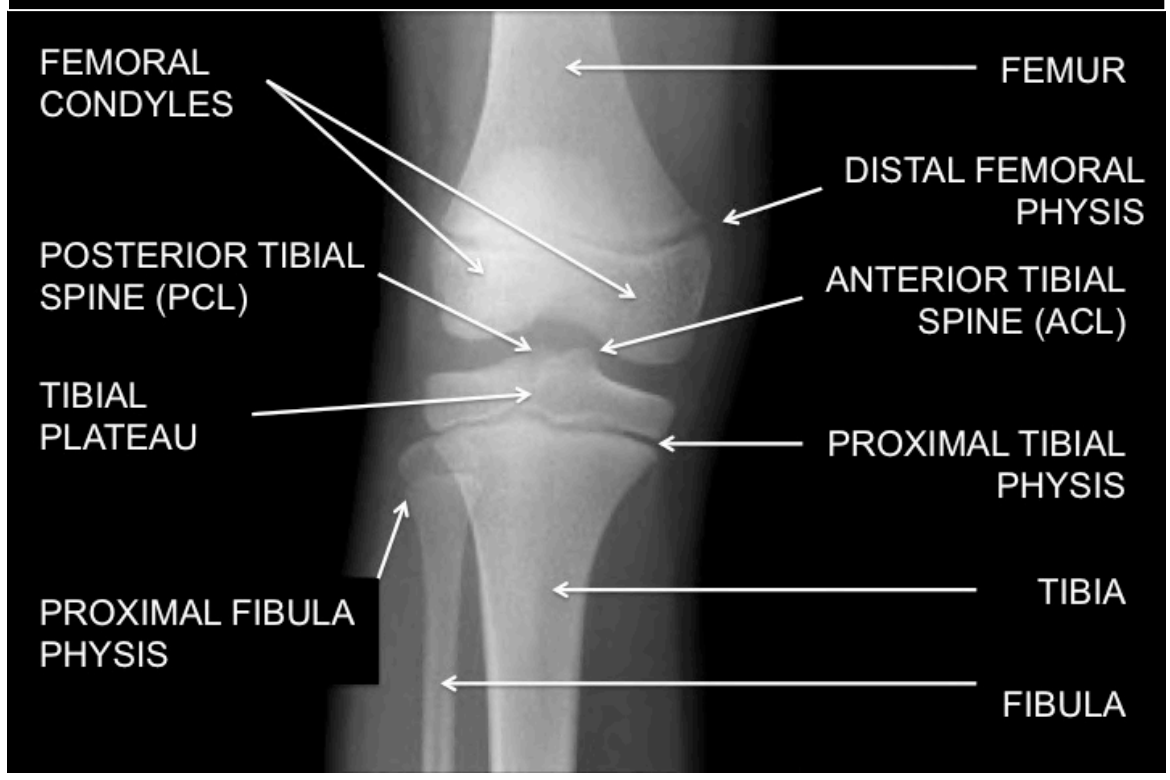
OTTAWA KNEE RULE
X-RAYS OF THE KNEE SHOULD BE OBTAINED IF ONE OF THE FOLLOWING CRITERIA IS MET
Isolated patellar tenderness
Tenderness of the fibular head
Inability to flex 90 degrees
Inability to bear weight immediately and in the ED for four steps

Sunrise views are obtained after patellar dislocations to rule out condylar fractures.

Because the overuse of XRAYS exposes children to unnecessary radiation, application of the Ottawa knee clinical decision rule can help reduce the use of radiography.

Referral for an MRI may be necessary for soft tissue injuries such as ligamentous or meniscal tears.

PEDIATRIC KNEE XRAY (RIGHT: AP VIEW)



MANAGEMENT

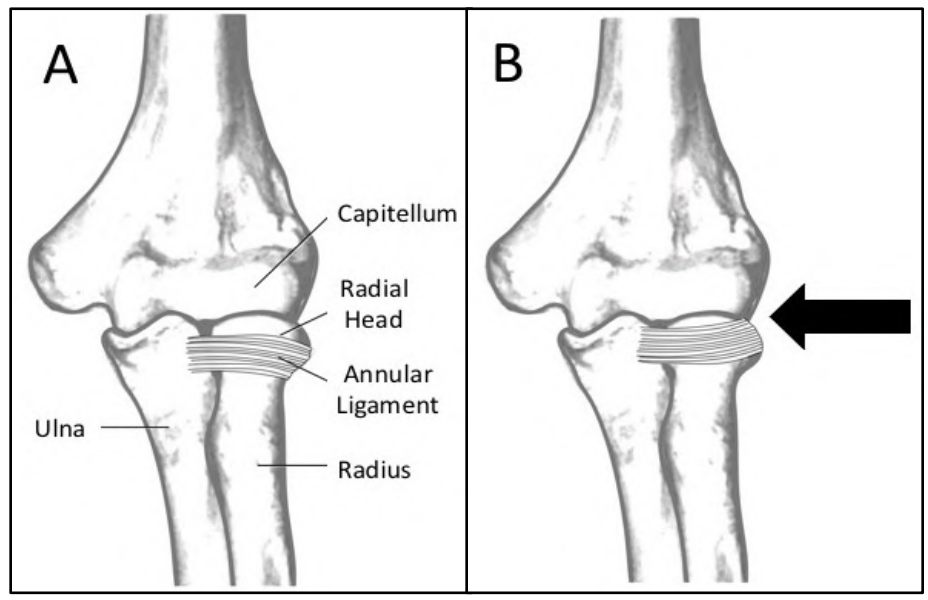
Any fractures, dislocations (other than patellar), or large effusions will necessitate orthopedic consultation. An arthrocentesis may be needed to relieve a tense effusion or hemarthrosis. Any neurovascular compromise or open fracture requires immediate orthopedic evaluation and treatment.

If the history and screening maneuvers suggest a subacute knee injury, the child should be advised of supportive measures and arrangements for close follow-up should be ensured. For mild or moderate pain and stiffness, the leg should be elevated when at rest with application of ice for 20 minutes every 2 hours during the first 48 hours after injury. Walking, standing, and bending should be limited. An elastic compression bandage or knee immobilizer should be used during the day with crutches for 5-7 days. NSAID’s may be prescribed for pain.

RADIAL HEAD SUBLUXATION

INTRODUCTION (JANIENNE KONDRICH, M.D., 9/2011)
Radial head subluxation, also known as Nursemaid's elbow, is the most common elbow injury in children. The term subluxation refers to a joint that is partially out of alignment while dislocation refers to a joint that is completely out of alignment. Radial head subluxation occurs mostly in children one to four years of age. The mechanism of injury involves traction of the arm at the wrist, usually by lifting a child by the wrist or when a caregiver grabs the arm to prevent the child from falling or pulling away. The child will immediately complain of pain, refuse to use the affected arm, and hold the arm close to the body with the elbow slightly flexed and the forearm pronated. The child is often in little distress unless attempts are made to move the elbow.

ANATOMY
The annular ligament secures the radial head to the ulna (Figure A). In young children this ligament is loosely attached to the radius. With traction on the distal radius, a portion of the annular ligament slips over the head of the radius and slides into the radiohumeral joint where it becomes trapped (Figure B). By the time most children are five years old the annular ligament has become thick and strong and is is unlikely to tear or be displaced.



DIAGNOSIS
The diagnosis of radial head subluxation is made clinically. If the history and physical are consistent with the classic mechanism for nursemaid's elbow, X-RAYS are not necessary. However, when the mechanism involves significant trauma to the arm or the physical exam demonstrates any focal tenderness, deformity or swelling, imaging is necessary prior to attempts at reduction.

It is best to have the patient sit on the parent's lap. Start by examining the unaffected arm in order to develop the trust of the patient. Then assess the neurovascular status of the injured arm. Determine the degree of perfusion by palpating the radial and brachial pulses and assessing capillary refill, warmth and color in comparison to the unaffected limb. If a pulse is not palpable a Doppler ultrasound can be used to determine the presence of distal perfusion. Evaluate both the sensory and motor function of the ulnar, median and radial nerves while limiting movement of the elbow as this may precipitate or further exacerbate neurologic injury. The neurovascular exam can change and should be repeated, particularly after manipulation of the arm.

NEUROLOGIC ASSESSMENT OF THE DISTAL UPPER EXTREMITY	
MOTOR FUNCTION	
OK sign (against resistance)	Median (Anterior interosseous nerve)
Finger spread (against resistance)	Ulnar nerve
Thumbs up sign	Radial nerve
SENSORY FUNCTION: 2 point discrimination @ 5 mm	
Second digit (volar)	Median nerve
Fifth digit (volar or dorsal)	Ulnar nerve
Dorsal web space (between 1st, 2nd digit)	Radial nerve

Identify gross deformity of the arm, such as the S-shape seen in severely displaced supracondylar fractures, or for any evidence of an open fracture, which may be as subtle as a small puncture wound at the site that the fractured bone poked through the skin. Patients with radial head subluxation typically hold their arm immobile with slight flexion at the elbow and pronation of the forearm.

If radial head subluxation is suspected, examine the elbow last. Palpate all bones starting from the proximal clavicle and work distally. Take each joint through its range of motion. Patients with radial head subluxation will express pain with slight supination of the forearm.

MANAGEMENT

Two maneuvers are used to reduce a nursemaid's elbow: supination/flexion and hyperpronation. One randomized clinical trial (Macias, Pediatrics 1998, PubMed ID: 9651462) indicated that the hyperpronation technique required fewer attempts than the supination flexion method. A subsequent study (Green, Pediatric Emergency Care 2006, PubMed ID: 16651912) revealed no difference in pain assessed by physicians but less pain in the hyperpronation group when assessed by nurses and parents.

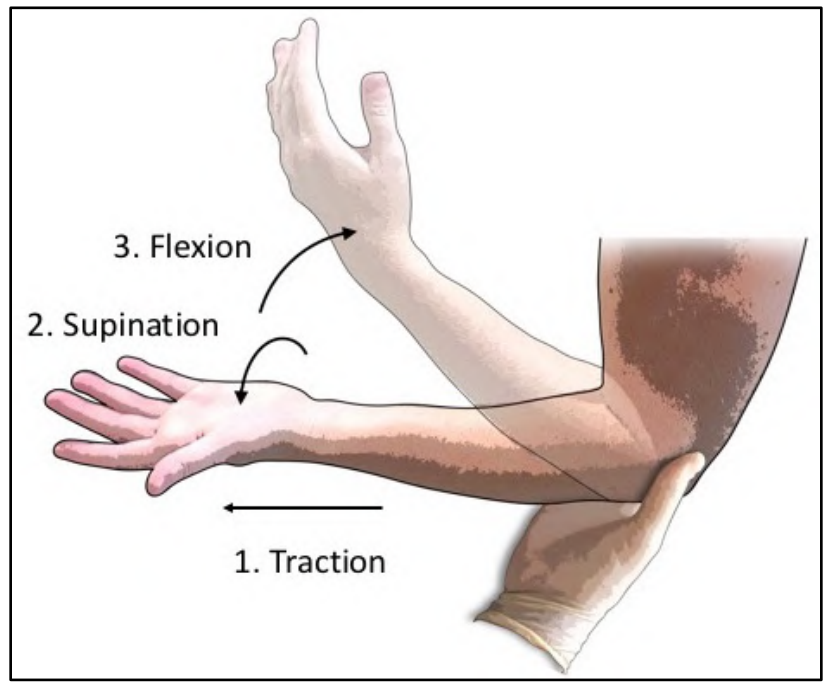
POSITIONING

Have the patient sit in a parent's lap in a chair across from you. The parent's arm can be used to hold the child across the chest and pin the unaffected arm to the side of the chest. Grasp the patients elbow with your arm that is on the same side as the patient's affected arm. Place your thumb at the radiohumeral joint (at the junction of the radial head and the lateral epicondyle). Use your opposite arm to perform the maneuver. You may palpate a "click" or "clunk" at the radiohumeral joint as the radial head relocates.

The images below demonstrate each maneuver with the caregiver using their right hand to hold the patient's left elbow. The caregiver's thumb is at the radiohumeral joint.

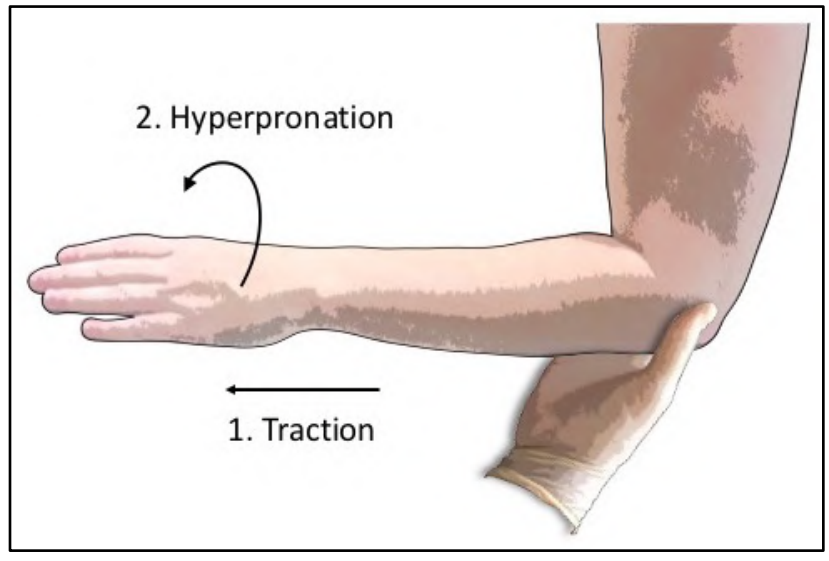
SUPINATION/FLEXION METHOD

The examiner supports the child's arm at the elbow with one hand and with the other holds the child's distal forearm and applies gentle traction. While maintaining slight traction, the examiner supinates the child's forearm and then flexes the elbow in one smooth motion.



HYPERPRONATION METHOD

The examiner supports the child's arm at the elbow and places moderate pressure with a finger on the radial head. The examiner holds the child's distal forearm with the other hand and hyperpronates the forearm while applying slight traction.



POST REDUCTION CARE

After the maneuver it may take some time for the child to realize that there is no longer pain and begin to use the arm. If the attempt at reduction was successful, then the child will begin to use the arm. Generally, if they can reach for an object above their head then the reduction was successful. If the first attempt was unsuccessful at reduction, either make a second attempt with the same maneuver or switch to the alternative maneuver.

Radial head subluxation tends to recur because the annular ligament has stretched in the subluxation process. The parents should be educated to avoid traction on the arm.

ROTATOR CUFF INJURIES

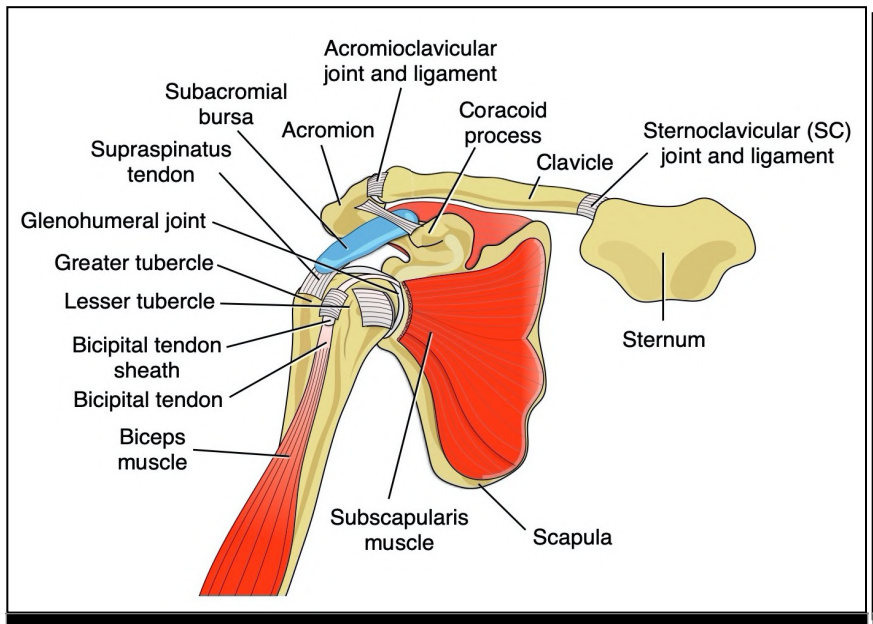
INTRODUCTION: (STEPHANIE KRAMER, D.O. 3/2017)
The shoulder is a “ball and socket” joint. The anatomy that allows for the extensive range of motion of the shoulder also makes it an inherently unstable joint. It is this instability that makes it susceptible to injury. In the pediatric population, shoulder pain is more likely to occur acutely because of trauma such as falls, although repetitive motions such as those in overhead sports can cause subacute or chronic complaints.

In the pediatric population, rotator cuff impingement and overuse injuries are less common than other acute shoulder injuries, but are significantly more common than rotator cuff tears. These typically occur in overhead sports with high volume, such as pitching and other overhead activities that cause fatigue of the rotator cuff tendons and dysfunction of the scapula leading to angulation of the acromion. This can be due to inadequate muscular stabilization of the scapula, either because of strength imbalance or uncoordinated activation forces, resulting in dysrhythmia of the glenohumeral joint and superior movement of the humeral head against the undersurface of the rotator cuff tendons (subacromial impingement). Impingement may begin as sharp, intermittent pain with certain exacerbating movements, however continued impingement may cause increased inflammation and irritation, resulting in a more achy, constant pain. History of prior dislocation or subluxation may suggest rotator cuff injury as well.

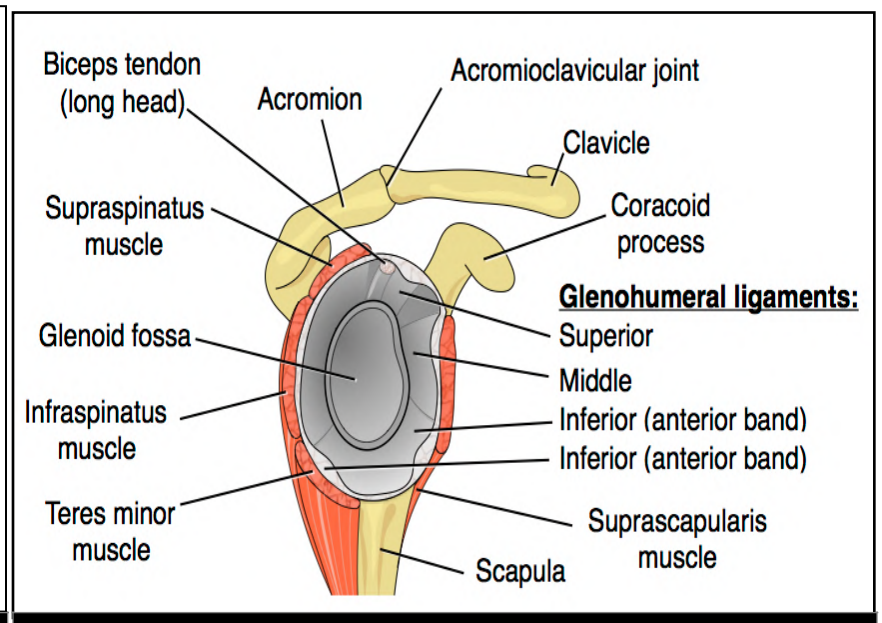
ANATOMY

The shoulder consists of three bones: the proximal humerus, the clavicle and the scapula (coracoid and acromion processes). These bones articulate at 4 joints: the humeral head with the relatively shallow glenoid fossa, the sternoclavicular joint, the acromioclavicular joint and the scapulothoracic joint.

The shoulder is stabilized by a combination of static and dynamic soft tissue structures. Static structures include: the glenoid labrum, and the glenohumeral ligament complex that make up the joint capsule. Dynamic structures consist of the rotator cuff tendons (supraspinatus, infraspinatus, subscapularis, and teres minor muscles).



ANATOMY: ANTERIOR



ANATOMY: LATERAL

HISTORY

In an acute traumatic injury, the mechanism of injury often increases the likelihood of specific diagnoses. It is important to determine the exact site of pain, the position of the shoulder at the time of injury and preceding activities. In a patient presenting with chronic shoulder pain, the positions or activities that exacerbate the pain should be explored, as well as training schedules and activities in the athletic population.

PHYSICAL EXAMINATION

Have the patient remove clothing to visualize visible deformities or asymmetries, the skin for bruising or subtle tenting of the skin, such as that seen with a clavicle fracture. Evaluate neurovascular integrity by palpating distal pulses and assessing strength and sensation distally. Starting at the sternoclavicular joint, palpate along the clavicle to evaluate tenderness, step offs or crepitus. Continue to the acromioclavicular joint and along the spine of the scapula. Palpate the long head of the biceps, and assess symmetry of muscular atrophy. Also assess the cervical spine for referred pain.

VIDEO LINK: GENERAL APPROACH TO THE SHOULDER EXAMINATION

Assess the range of motion of the shoulder both actively (by the patient) and passively (by the examiner). The range of motion is typically described in 3 planes: flexion (forward), extension (backward), abduction (away from the body) and adduction (toward the body) and internal rotation (medial) and external (lateral) rotation. Compare the range of motion of the affected side to the contralateral shoulder. Also assess for symmetry of scapular motion. The scapula should rotate laterally and superiorly with flexion and abduction. Test the biceps with resisted flexion and supination with the elbow at 90° (VIDEO LINK: YERGASON'S TEST**)**, or with the arm flexed to 90° and fully supinated with a straight elbow resisting a downward force (VIDEO LINK: SPEED'S TEST)

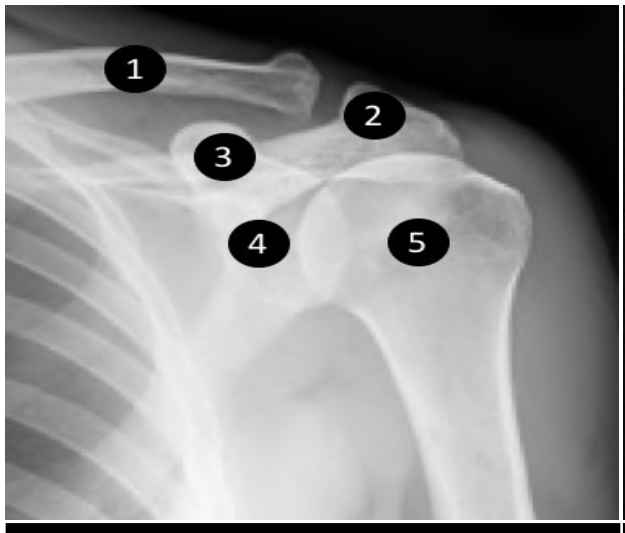
Assess the integrity of the rotator cuff starting with the Jobe's or the Empty Can Test for supraspinatus by resisting superior motion with the arm in 90° of abduction in the plane of the scapula (30-45° anteriorly), with the thumbs rotated down (internally rotated) (VIDEO LINK: EMPTY CAN TEST) Pain may be indicative of tendinitis/tendinopathy, and any weakness should raise suspicion of a tear. The infraspinatus and teres minor are tested by resisted external rotation, with the elbow adducted against the torso and flexed to 90°, thumbs pointing up. The subscapularis internally rotates the arm and should be evaluated in the same position, with the thumbs pointed upward, to eliminate the effect of pectoralis major. Another way to test subscapularis is with the arm internally rotated with the dorsum of the hand on the lumbar spine, resisting the patient as they press their hand away from their back Gerber's Lift off Test is test is positive if the patient has pain or is unable to perform the movement, with degree of weakness/pain indicating degree of injury (VIDEO LINK: GERBER'S LIFT OFF TEST)

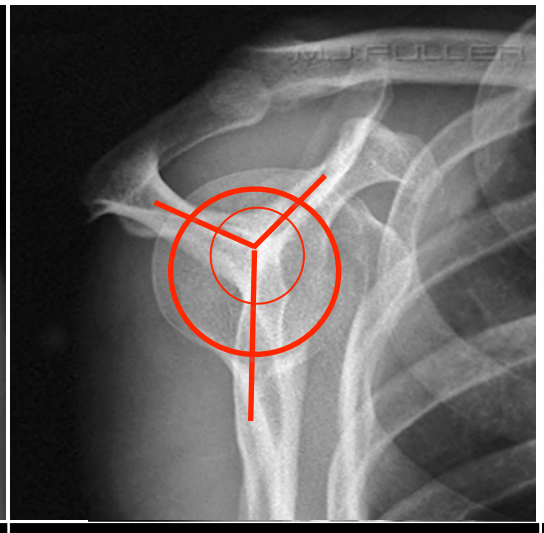
Tests for impingement include Hawkins-Kennedy Test (90° of forward flexion with passive internal rotation, elbow at 90°) a (VIDEO LINK: HAWKINS TEST) nd Neer's test (stabilization of the scapula while moving the arm into forward flexion to bring the greater tuberosity under the acromion). **VIDEO** LINK: NEER'S TEST)

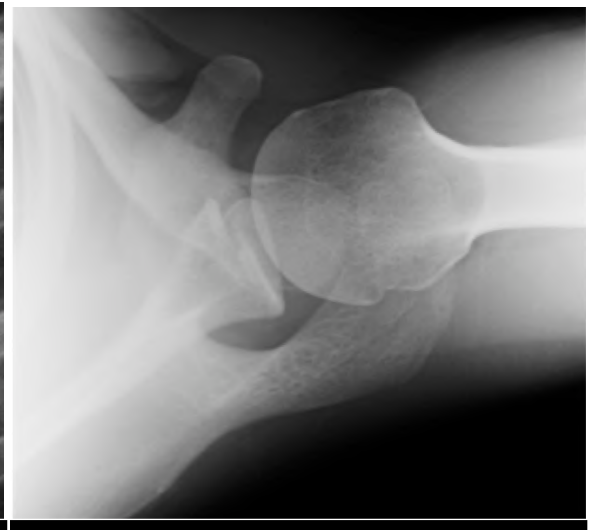
IMAGING

Radiographic evaluation of the shoulder includes upright Anterior-Posterior (AP) X-RAYS, as well as specialized views depending on clinical suspicion of diagnosis. CT is indicated to assess the possibility of intra-articular involvement. If there is concern for neurovascular damage an MRI with contrast should be obtained.

The supraspinatus outlet (scapular Y) view is helpful to evaluate for possible rotator cuff impingement, however an axillary view is the best lateral evaluation of the shoulder. Pediatric patients are unlikely to have pathology on X-RAY in the case of rotator cuff tendinitis or tendinopathy (such as calcium deposits one may see in adults). In experienced hands, bedside ultrasound evaluation of the shoulder may help visualize the soft tissue structures in question. Note any tendon swelling/edema, cortical/tissue irregularity, thickened bursae or abnormal fluid collections. Ultrasound is also helpful as it is a dynamic evaluation; the patient can contract the muscle and there may be retraction of the tendon fibers in case of partial or full thickness tear.







AP VIEW	SCAPULA Y VIEW	AXILLARY VIEW
1. Clavicle 2. Acromion 3. Coracoid process 4. Glenoid fossa 5. Humeral head	Blade of the Scapula: Anterior and inferior Y Scapula Spine: Posterior Y Glenoid Fossa: Sits at the juncture of the Y (small circle) Head of Humerus: sits in glenoid fossa (large circle)	Coracoid process: Projects anteriorly (upward in this image)

MANAGEMENT

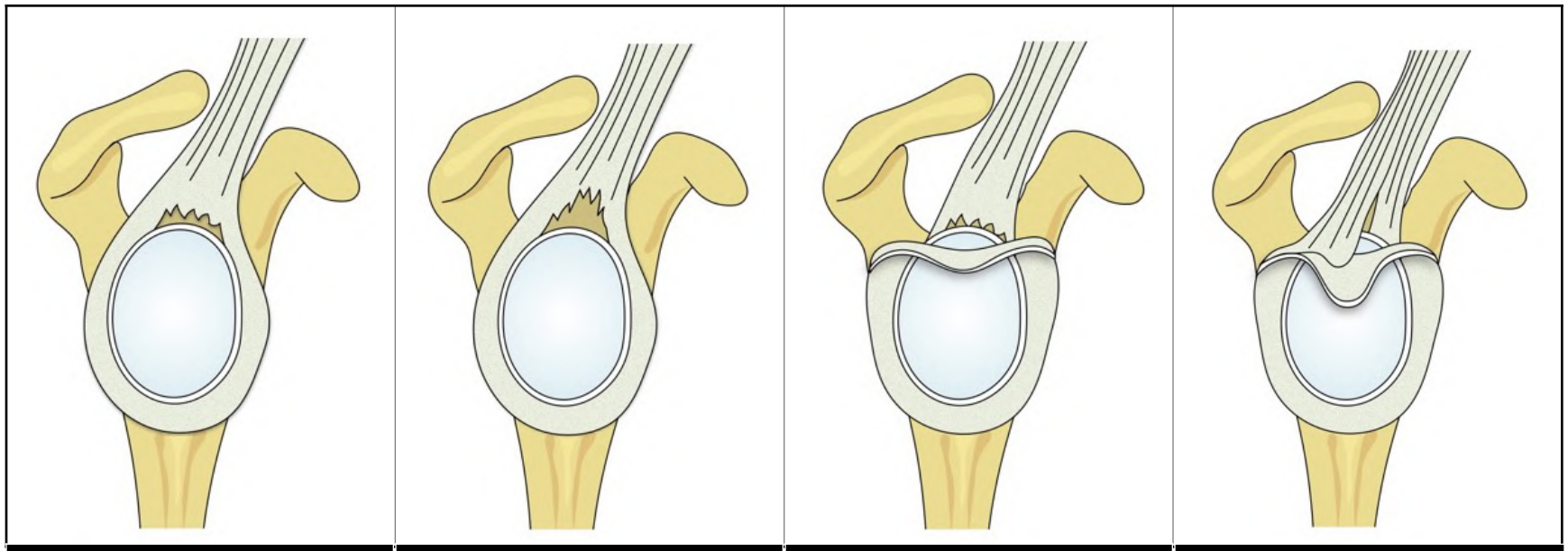
Pain control is usually sufficient with non-steroidal anti-inflammatory drugs (NSAIDS). For acute injuries, the patient may apply ice for 20 minutes every 2 hours for the first 48 hours after the incident. Most injuries are immobilized with a sling initially. For injuries that are managed non-operatively, range of motion and shoulder strengthening exercises are indicated when feasible.

Treatment of rotator cuff injury or impingement should be done in two parts. The first is to allow the inflammation and irritation to recover by avoiding exacerbating movements and managing pain with NSAIDs and/or ice. Once pain has improved, the patient should begin physical therapy to balance the strength of the rotator cuff muscles, as well as the deltoid, trapezius and periscapular musculature.

SUPERIOR LABRUM FROM ANTERIOR TO POSTERIOR TEARS

Tears of the superior labrum from anterior to posterior (SLAP tears), relative to the insertion of the biceps tendon are usually a result of an acute traumatic event (subluxation/dislocation; an episode of rapid and/or forceful pulling on the arm such as catching a heavy object or catching oneself from a fall while climbing), but may be more chronic in etiology if related to repetitive, forceful overhead movements, such as in throwing sports. Patients may complain of feelings of instability, clicking or catching, or a deep, nonspecific and non-palpable pain.

SUPERIOR LABRUM FROM ANTERIOR TO POSTERIOR (SLAP) TEARS		
I	Labral and biceps fraying, anchor intact	11%
II	Labral fraying with detached biceps tendon anchor	41%
II	Bucket handle tear, intact biceps tendon anchor (biceps separates from bucket handle tear)	33%
IV	Bucket handle tear with detached biceps tendon anchor (remains attached to bucket handle tear)	15%



PHYSICAL EXAMINATION

To evaluate the labrum with O'Brien's test have the patient flex their arm to 90° with the elbow straight. Adduct the arm 10-15° medially across the body, and have the patient resist a downward force, first with the arm fully pronated (thumb down) and then with the arm supinated (VIDEO LINK: OBRIEN"S TEST). Pain deep in the glenohumeral joint only when the arm is in pronated is a positive test. Another way to evaluate the labrum is with the arm abducted to 90° with 90° of elbow flexion and maximal external rotation. The patient is asked to press their hand into the examiner's, which should provoke pain in case of a labral tear. Speed's test may also be positive with a labral tear that involves the long head of the biceps tendon (VIDEO LINK: SPEED"S TEST)

IMAGING

While clinical exam may suggest SLAP tears, definitive diagnosis is made by MR arthrogram. Ultrasound evaluation is difficult, however may demonstrate absence or displacement of the labrum with internal rotation.

MANAGEMENT

A steroid injection may be therapeutic and diagnostic if there is relief of symptoms. Treatment of SLAP tears should be done in two parts. The first is to allow the inflammation and irritation to recover by avoiding exacerbating movements and managing pain with NSAIDs and/or ice. Once pain has improved, the patient should begin physical therapy to balance the strength of the rotator cuff muscles, as well as the deltoid, trapezius and periscapular musculature.

SEPTIC ARTHRITIS

INTRODUCTION (VAISHALI SHAH, M.D. 1/2023)
The differential diagnosis of arthritis is extensive including infectious, para-infectious and rheumatologic causes. The term septic arthritis includes joint infections caused by pyogenic bacteria, fungi, and viruses. The evaluation of infants and children with suspected bacterial arthritis should occur promptly as it is a true medical emergency with significant morbidity. This is particularly true of septic arthritis of the hip which has a tenuous blood supple than can be impeded by swelling in the hip capsule resulting in avascular necrosis. The most common entity in the differential diagnosis of septic arthritis is transient synovitis. This PEM Guide will focus on distinguishing septic arthritis from transient synovitis of the hip.

	SEPTIC ARTHRITIS	TRANSIENT SYNOVITIS
DEFINITION	Microbial invasion of joint space	Sudden onset of unilateral hip pain & physical findings in a non-toxic child
EPIDEMIOLOGY	Peak: 3 years	Ages 3-8 years, M>F, # 1 cause of hip pain in children
ETIOLOGY	Neonates: S. aureus, group B strep, gram negative rods	Post-viral synovial inflammation Frequently follows an upper respiratory tract infection. Other risk factors: Obesity
	School age: S. aureus, Kingella Kingae, S. Pyogenes, S. pneumonia, H. influenzae	
	Older Children: S. aureus, S. pyogenes, B. burgdorferi, N. gonorrhea	
	Less common: N. meningitides, Pseudomonas, Candida, Mycobacterium	
PATHOLOGY	1. Hematogenous dissemination 2. Contiguous extension (10-16) 3. Direct inoculation	Unclear.
	<u>Risk factors</u> Joint instrumentation, Skin or soft tissue infection IV drug use, Hemoglobinopathy	

CLINICAL MANIFESTATIONS

Fever and refusal to bear weight or an antalgic gait are the most common presenting symptoms. A recent viral illness increases the likelihood of transient synovitis.

CLINICAL MANIFESTATIONS	
SEPTIC ARTHRITIS	TRANSIENT SYNOVITIS
Fever, malaise, poor appetite, Toxic/Septic appearing	Afebrile or low grade temperature
Knee > Hip > Ankle > Other joints 90% monoarticular	Unilateral hip pain: may manifest as groin, hip, anterior thigh, or knee pain
Refusal to walk, severe joint pain, decreased mobility, joint swelling, erythema, warmth	Limp, occasional refusal to bear weight
Septic hip held flexed and externally rotated	Position of comfort mildly flexed and externally rotated
Symptoms worsen over time	Symptoms improve over time

LABORATORY TESTING

A CBC, ESR, CRP and blood culture should be sent on all patients. In adolescents consider cervical/urethral, throat, rectal or skin lesion testing for Neisseria Gonorrhea and chlamydia. Send serum Kingella PCR in those less than 5 years of age. Consider additional testing for tuberculosis (serum Quantiferon, < 2 years of age also plant PPD) and Lyme disease (EIA with reflex to Western blot) as indicated (See also: PEM Guide: Infections: Lyme Disease).

If more than 1 joint is involved or arthritis is migratory consider testing for acute rheumatic fever (Antistreptolysin O, antiDNAase B) and parvovirus (Parvovirus B19 PCR). (See also: PEM Guide: Rheumatology: Acute Rheumatic Fever. Neisseria and S Aureus may also be polyarticular.

DIAGNOSTIC TESTING	
SEPTIC ARTHRITIS	TRANSIENT SYNOVITIS
CBC: WBC high in 70% CRP: high in 95% ESR: high in 90% Blood Culture: positive in 40%	Diagnosis of exclusion CBC, CRP, ESR: Mildly elevated
Joint Fluid Culture (+) in only 50-60% Yield increased if inoculated directly into blood culture bottle Joint Fluid Aspiration: Cell count	Joint Fluid Aspiration: Cell count (see table below)

SYNOVIAL FLUID FINDINGS: Synovial fluid should be sent for cell count, culture, gram stain and Borrelia (Lyme) PCR as indicated. A PCR joint infection panel identifies 38 bacterial pathogens (including Kingella and antimicrobial resistance genes; See Appendix).

There is significant overlap in synovial fluid parameters. Recently, it has been suggested the synovial fluid lactate may be a significant predictor of septic arthritis. Other causes of arthritis, such as juvenile immune arthritis and serum sickness, may have >50,000 WBC but without a predominance of polymorphonuclear leukocytes. A gram stain of synovial due must be performed due to the low yield of synovial fluid culture, which may be caused by the bacteriostatic effects of synovial fluid.

CHARACTERISTIC SYNOVIAL FLUID FINDINGS			
DIAGNOSIS	Typical WBC/mm3	WBC/mm3 Range	% Neutrophils
Normal	< 150		< 25%
Bacterial	> 50,000	2,000-300,000	> 90%
Tuberculosis	10,000-20,000	40-135,000	> 50%
Lyme	40,000-80,000	180-140,000	> 75%
Candida		7,500-150,000	> 90%
Viral	15,000	3,000-50,000	< 50%
Reiter	15,000	10,000-22,000	> 70%
Rheumatoid Arthritis		2,000-50,000	> 70%

CLINICAL DECISION RULES

In 1999, Kocher published a clinical decision algorithm to distinguish between septic arthritis and transient synovitis of the hip in children. The study population consisted of 168 patients of which 82 had septic arthritis of the hip. (J Bone Joint Surgery 1999, PubMed ID: 10608376). The rule consisted of four predictors: a history of fever, a history of inability to bear weight on the effected limb, an ESR > 40 mm/hour and a serum WBC > 12,000 cells/mm^3. The rule had an area under the receiver operating characteristic curve of 0.96 indicating a very high degree of diagnostic accuracy.

CLINICAL DECISION RULE: PREDICTORS (KOCHER 1999)		
PREDICTOR	ADJUSTED OR 95% CI	LIKELIHOOD RATIO
History of fever	38.6 (10.8 – 137)	29.5
Unable to bear weight	24.3 (5.6 – 85.2)	10.7
ESR > 40 mm/hour	25.9 (6.5 – 112.6)	19
WBC > 12,000 cells/mm^3	14.4 (4.0 – 51.5)	14

CLINICAL DECISION RULE: PERFORMANCE	
NUMBER PREDICTORS	SEPTIC ARTHRITIS (%)
0	0.2%
1	3.0%
2	40%
3	93.1%
4	99.6%

A retrospective validation of the Kocher rule found an area under the receiver operating characteristic curve was 0.79 (compared to 0.96 for the Kocher rule derivation) and that patients with all 4 of the predictors had a 59.1% risk of septic arthritis (compared to 99.6% for the Kocher rule derivation) (Luhman, J Bone Joint Surg AM 2004, PubMed ID: 15118038). A prospective validation of the Kocher rule found that a CRP > 20 mg/liter was a stronger predictor of all but a history of fever (Caird, J Bone Joint Surg AM 2006, PubMed ID: 16757758).

A knee, monoarthritis decision rule underwent multicenter validation in 8 pediatric emergency departments in Lyme endemic areas. No patients with septic arthritis were misidentified by the rule. Rule characteristics were nearly identical to those of the derivation cohort. Both the external validation cohort and derivation cohort had a higher specificity than the Kocher rule. In the validation cohort, 66.3% (303/457) of patients had a negative rule and would be classified as low risk. In low risk patients, use of the rule would decrease the rate of arthrocentesis by 17.2%, operative joint washout by 5.3% and admission by 17.8%.

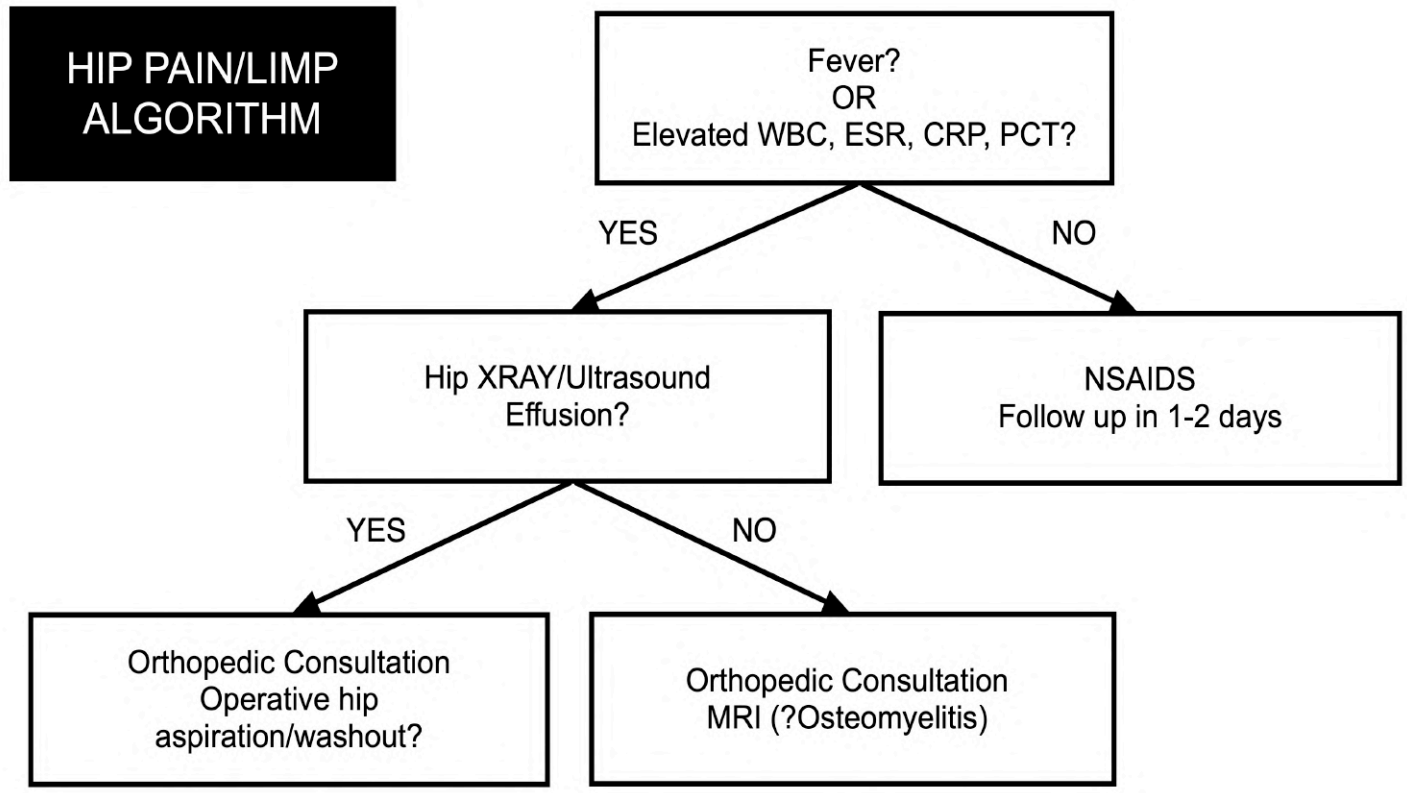
KNEE MONOARTHRITIS DECISION RULE			
	Validation[1]	Derivation[2]	Kocher[2]
Prevalence	2.6% (1.5, 4.4%)	3.1% (1.8, 5.3%)	3.2% (1.9, 5.5)
Sensitivity	100% (75.8, 100%)	100% (77.2, 100%)	100% (77.2, 100%)
Specificity	68.1% (63.6, 72.3%)	62.4% (57.6, 67.0%)	26.5% (22.3, 31.1%)
PV (+) Rule	7.8% (4.5, 13.1%)	7.9% (4.7, 13.1%)	4.3% (2.6, 7.3%)
PV (-) Rule	100% (98.8, 100%)	100% (98.5, 100%)	100% (96.4, 100%)
LR (+) Rule	3.1 (2.7, 3.6)	2.7 (2.3, 3.0)	1.4 (1.3, 1.4)
LR (-) Rule	(0 in calculation)	(0 in calculation)	(0 in calculation)
% (-) Rule	66.3% (61.8, 70.5%)	60.5% (55.7, 65.1%)	25.6% (21.6, 30.1%)
1. Grant, Pediatr Emerg Care. 2021 May 13., PubMed ID: 34160185 2. Deanehan, Pediatrics, 2013., PubMed ID: 23420916			

IMAGING

Hip XRAY for presence of an effusion and bone changes and ultrasound for the presence of an effusion is typically ordered. MRI is the most sensitive imaging modality and can distinguish between septic arthritis and osteomyelitis but will require procedural sedation in young children.

IMAGING	
SEPTIC ARTHRITIS	TRANSIENT SYNOVITIS
XRAY: Hip AP and frog leg lateral films Exclude other causes of joint pain Not diagnostic for septic arthritis May reveal distortion of fat pad, soft tissue swelling, and joint space widening (effusion)	XRAY: Hip AP and frog leg lateral films are normal or demonstrate an effusion
Ultrasound: Preferred initial study to identify excess joint space fluid	Ultrasound: Reveals fluid in contralateral hip in 25% of cases
MRI: Highly sensitive in early detection of joint fluid, detects early involvement of adjacent bone	

MRI INDICATIONS
Age > 4 years
Symptoms > 3 days
CRP > 8.9
Platelet count > 310
Absolute Neutrophil count > 7,200
Strongly consider if ≥ 3 criteria above to identify adjacent bone involvement



MANAGEMENT

MANAGEMENT OVERVIEW	
SEPTIC ARTHRITIS	TRANSIENT SYNOVITIS
Medical Emergency Consult orthopedics Prompt surgical drainage: Joint wash out: Hip, shoulder Needle aspiration: Knee, wrist, ankle Consider joint space irrigation if unable to perform adequate drainage. Antibiotic: (See Table below)	Most cases resolve within 1-2 weeks. Re-occurrence in 10-20%. Avoid weight bearing; encourage bed rest NSAIDS for pain and inflammation Antibiotics and corticosteroids are not indicated Joint aspiration provides dramatic relief but joint effusion rapidly accumulates. Therefore reserve for diagnostic purposes

COMMON ORGANISMS BY AGE			
ORGANISM	< 3 MONTHS	3-36 MONTHS	> 36 MONTHS
Staph Aureus (MSSA, MRSA)	X	X	X
Group B Strep (Strep agalactiae)	X		
Gram negative bacilli	X		
Neisseria gonorrhea	X		X
Kingella kingae		X	
Group A Strep (Strep pyogenes)		X	X
Strep pneumoniae		X	X
H flu type B (unvaccinated)		X	

ANTIBIOTIC SELECTION

Antibiotic selection should be based on the most likely organism for the age of the patient as well as specific patient characteristics. Staph aureus (both MSSA and MRSA) are the most common organism in all age groups.

EMPIRIC ANTIBIOTICS	
Age	Treatment
Birth – 1 month	Vancomycin[1] AND Cefepime
1 month – 4 years	Vancomycin AND Ceftriaxone[2]
≥ 5 years	Vancomycin
	Add Ceftriaxone: Lyme, sexually active, sickle cell, immunocompromise
NYU Pediatric Antibiotic Stewardship (Reissued 12/2022) 1. Vancomycin Allergy: Linezolid (Note: Do not use Clindamycin: NYU 25-30% clindamycin resistant) 2. Ceftriaxone Allergy: Levofloxacin	

ANTIBIOTIC SELECTION: BY ORGANISM		
ORGANISM	POPULATION	ANTIBIOTIC
Staph aureus	All	Vancomycin
Kingella kingae	< 3 years, Gram(-) gram stain	2nd/3rd gen Cephalosporin
H influenza type B	Under-vaccinated with HIB	2nd/3rd gen Cephalosporin
Strep pneumonia	HIV, Sickle cell, Nephrotic	3rd gen Cephalosporin
Neisseria gonorrhea	Sexually active adolescents	3rd gen Cephalosporin
Salmonella sp.	Sickle cell	3rd gen Cephalosporin
Gram negative bacilli	Recent GI surgery	3rd gen Cephalosporin
	Complex GU anatomy	3rd gen Cephalosporin
	Pseudomonas	Ceftazidime
Pseudomonas, Gram(-) bacilli, Staph aureus	Intravenous drug abuser Puncture wound	Vancomycin + Ceftazidime
Lyme*	Early disseminated & late	Doxycycline (< 8 years) Ampicillin or Cefuroxime
	Persistent arthritis	Ceftriaxone
See: PEM Guide: Infections: Lyme Disease		

CORTICOSTEROIDS: A Cochrane systematic review included two studies with a total of 149 children with septic arthritis (Delgade-Noquera, Cochrane DSR 2018, PubMed ID: 30480764). The authors describe the level of evidence as low quality due to concerns about study limitations and imprecision. There was a statistically significant reduction in pain at 12 months (Risk Difference: 24%, 95% CI (5, 43%)), a higher rate of return to normal joint function at 12 months (Risk Difference: 24%, 95% CI (11, 37%)) and a decrease in the number of days of intravenous antibiotics (Risk Mean difference: -2.77, 95% CI (-4.16, -1.39) all favoring corticosteroids steroids.

DOSING: Dexamethasone 0.15 mg/kg/dose (maximum of 10-12 mg/dose) Q6H for 4 days. Can be transition to oral dosing after 24 hours of intravenous therapy

CORTICOSTEROID: CONTRAINDICATIONS
< 2 months of age
Has received antibiotics for > 48 hours
Septic arthritis due to a puncture would
Chronic arthritis, autoimmune, immunodeficiency, Lyme disease
Systemic inflammatory syndrome: Lupus, juvenile immune arthritis

APPENDIX: JOINT PCR TESTING

BIOFIRE JOINT INFECTION PANEL	
GRAM-POSITIVE BACTERIA	GRAM-NEGATIVE BACTERIA
Anaerococcus prevotii/vaginalis	Bacteroides fragilis
Clostridium perfringens	Citrobacter
Cutibacterium avidum/granulosum	Enterobacter cloacae complex
Enterococcus faecalis	Escherichia coli
Enterococcus faecium	Haemophilus influenzae
Finegoldia magna	Kingella kingae
Parvimonas micra	Klebsiella aerogenes
Peptoniphilus	Klebsiella pneumoniae group
Peptostreptococcus anaerobius	Morganella morganii
Staphylococcus aureus	Neisseria gonorrhoeae
Staphylococcus lugdunensis	Proteus spp.
Streptococcal spp.	Pseudomonas aeruginosa
Streptococcus agalactiae	Salmonella spp.
Streptococcus pneumoniae	Serratia marcescens
Streptococcus pyogenes	YEAST
ANTIMICROBIAL RESISTANCE GENES	Candida Spp. Candida Albicans
Carbapenemases:	IMP, KPC, NDM, Oxa-48-like, VIM
Extended Spectrum Beta lactamases:	CTX-M
Methicillin Resistance:	mecA/C, MREJ (MRSA)
Vancomycin Resistance:	vanA/B

SHOULDER DISLOCATION

INTRODUCTION (ERIC WEINBERG M.D., 5/2021)
Dislocation refers to the movement of one bone completely out of joint alignment (disarticulation) relative to another. Subluxation, in contrast, describes movement of one bone relative to another while maintaining some degree of joint alignment. Shoulder dislocation is rarely seen in patients under 12 years old because the weaker physis tends to fracture before dislocation occurs. During adolescence these growth plates fuse, resulting in a greater risk of shoulder dislocation. Over 90% of shoulder dislocations are anterior. Of the anterior dislocations 90% are sub-coracoid, 7% are sub-glenoid and 3% sub-clavicular. The remainder includes posterior dislocations (approximately 5%) and rarely inferior dislocations, also known as luxatio erecta humeri.

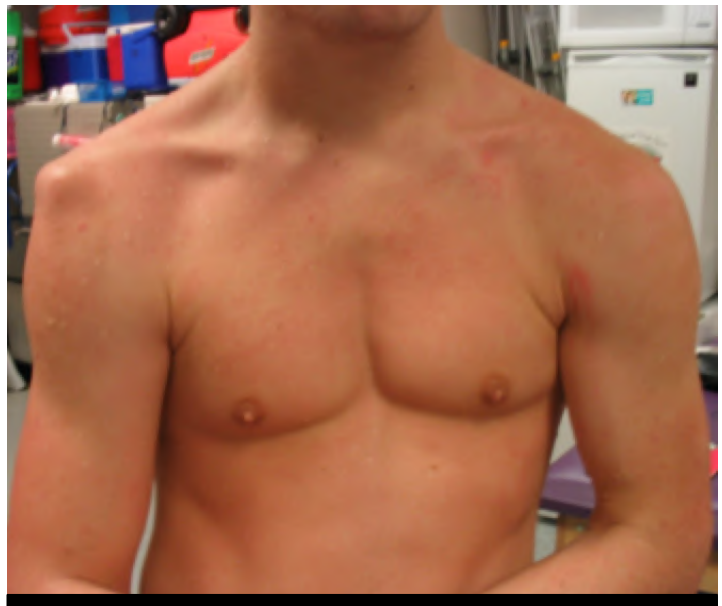
ANATOMY
The humeral head resides in the shallow glenoid fossa of the scapula. The anterior surface of the joint is made up of a thin joint capsule with multiple ligaments and muscle groups (the rotator cuff). These fibrous and muscular structures can be easily stretched or torn with a relatively small amount of force, resulting in anterior dislocation.

The typical mechanism of anterior shoulder dislocation is a forced abduction and external rotation of the shoulder. Shoulder dislocations often reoccur because stretching results in laxity of the anterior capsule . Rates of recurrence range between 80-90% if the original injury occurs before 20 years of age to less than 5-10% if older than 40.

Posterior dislocations, although rare, are caused by a powerful mechanism such as seizures, electrocution, or cardioversion. The movement responsible for posterior dislocation is usually severe internal rotation and adduction. Luxatio erecta humeri occurs secondary to a severe hyper-abduction injury or from a large axial force applied to an arm that is raised overhead.

CLINICAL FINDINGS
Patients typically present with severe shoulder pain and limited range of motion following a history of trauma.

ANTERIOR DISLOCATION: The patient is often leaning forward with the arm in slight abduction and external rotation. The patient is unable to abduct or internally rotate the shoulder. There is a characteristic loss of the normal deltoid contour, creating a boxlike or “squared off” appearance to the shoulder with a prominent acromion. The humeral head can be palpated beneath the clavicle, anterior and inferior to its usual location. (



SHOULDER DISLOCATION (R)

POSTERIOR DISLOCATION: The arm is held in adduction and internal rotation, with the same “squaring off” of the shoulder contour. The posterior shoulder appears “filled out”, and the humeral head can often be palpated beneath the acromion process.

NEUROVASCULAR ASSESSMENT: Axillary nerve sensory function assessed by testing pinprick sensation over the deltoid. Palpating contraction of the deltoid during attempted abduction assesses motor function of the axillary nerve. Peripheral pulses and capillary refill should be evaluated despite the rarity of vascular injuries.

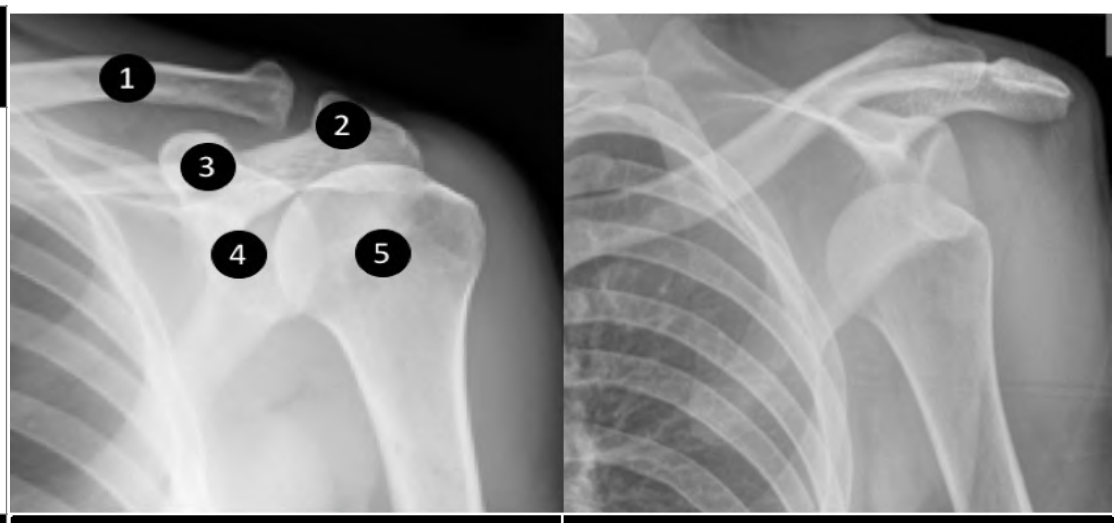
RADIOGRAPHY

Dislocation is often strongly suspected based on history and physical, but is typically confirmed by plain radiographs. Two views are often necessary to confirm the diagnosis: an anterior-posterior view (AP) and either a transscapular Y or axillary view. The axillary view requires movement of the shoulder that will cause the patient pain but provides better visualization of the glenoid fossa to identify associated injuries.

ANTERIOR DISLOCATION: The best view is the scapular Y view, which shows medial/anterior deviation of the humeral head in relation to the Y shaped projection of the scapula. The AP projection shows the humeral head inferior to the coracoid process. In the axillary view the humeral head ("golf ball") is anterior to the glenoid (the "tee").

AP VIEW

1. Clavicle
2. Acromion
3. Coracoid process
4. Glenoid fossa
5. Humeral head



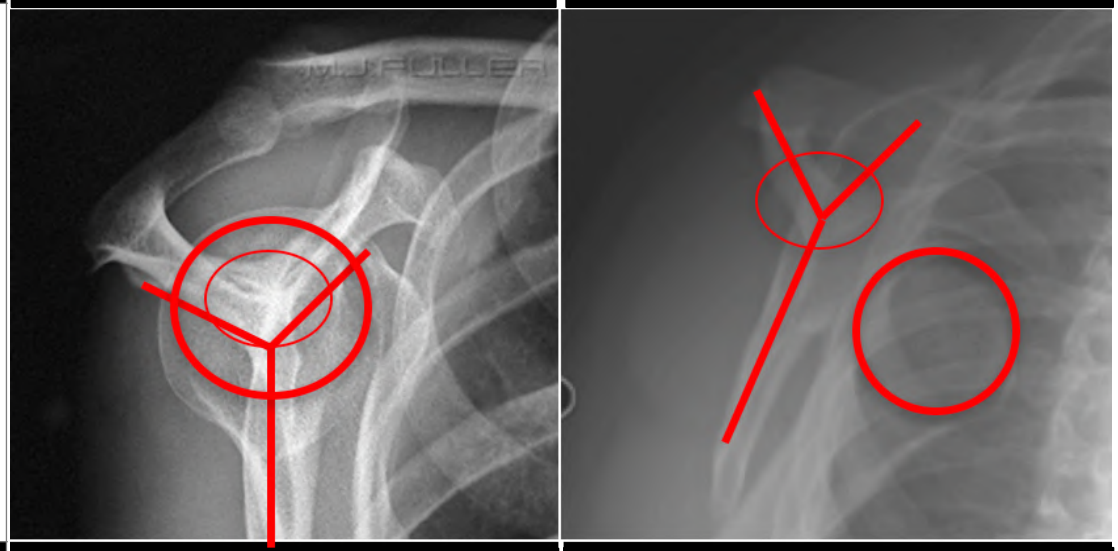
SCAPULA Y VIEW

Blade of the scapula = anterior and inferior Y

Scapula spine = posterior Y

Glenoid fossa sits at the junction of the Y (small circle)

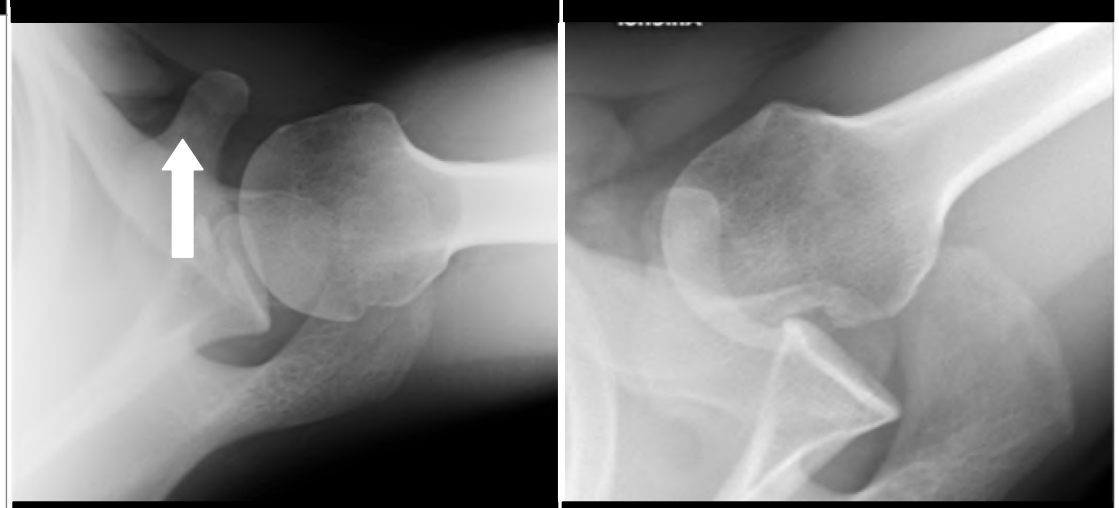
Anterior dislocation: The humeral head (large circle) lies over the ribs and not over the glenoid fossa



NORMAL | ANTERIOR

AXILLARY VIEW

Note that the coracoid process points anteriorly.

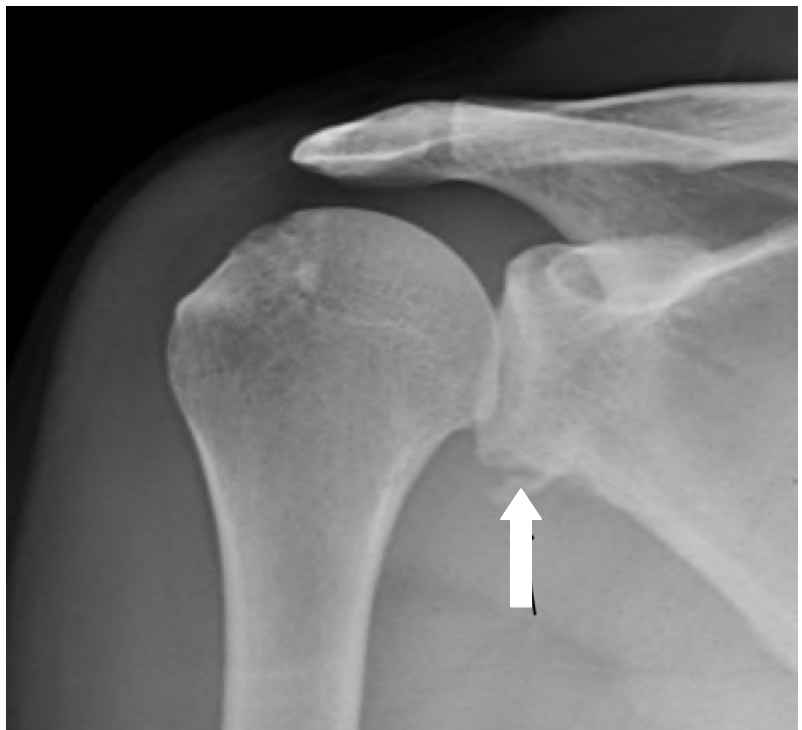


NORMAL | ANTERIOR

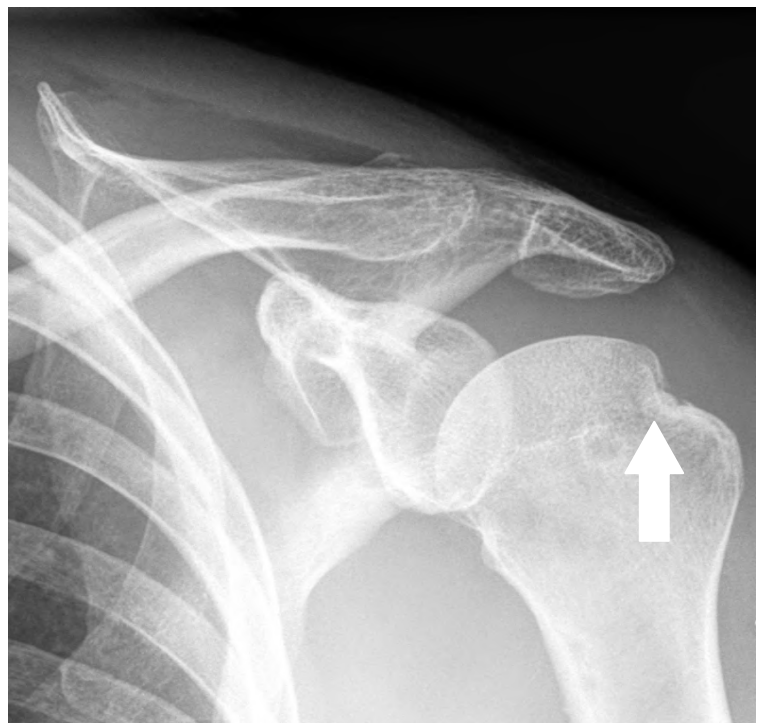
POSTERIOR DISLOCATION: The humeral head lays behind/posterior to the Y formed by the glenoid in the scapular Y view. The AP view may resemble a light bulb or an ice-cream cone, and the axillary view shows the humerus posterior to the glenoid (the “golf ball” falls posterior to the “tee”).

ASSOCIATED INJURIES

Fractures can occur in approximately 25% of anterior shoulder dislocations. Plain radiographs may also reveal fractures that occur when the humeral head impacts the inferior rim of the glenoid. A *Hill-Sachs* lesion is a fracture of the posterior-lateral cortex of the humeral head. Bankart lesions are less commonly occurring fractures of the glenoid rim. Bankart lesions increase the risk of subsequent dislocations. It may involve the cartilaginous labrum only (90%) or bone (5%) as well. A Bankart lesion should be suspected in a patient in whom reduction fails. A CT scan of the shoulder is frequently used to determine the extent of the injury and need for operative repair.



BANKHART FRACTURE



HILL-SACHS FRACTURE

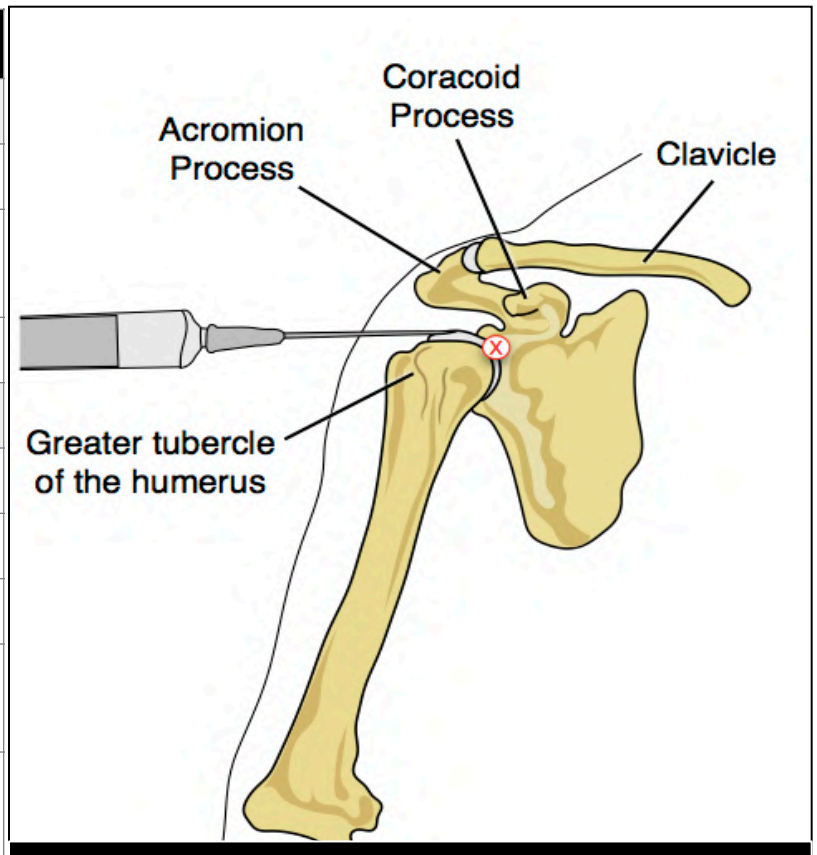
MANAGEMENT

Anterior shoulder dislocations should be reduced in the ED setting. Posterior and inferior dislocations require consultation with an orthopedic specialist. Management includes, appropriate analgesia, reduction maneuvers and post reduction care.

ANALGESIA: Before attempting any reduction maneuvers, the patient should be given analgesic to reduce pain and sedatives to enhance muscle relaxation. Intra-articular lidocaine has been shown in a Cochrane meta-analysis (PubMed ID: 21491392) including 5 studies and 211 patients to result in similar reduction success as procedural sedation with fewer adverse events and a shorter time to discharge. Intra-articular lidocaine may be given with an anterior or posterior approach. Anterior approach - 10-15 ml of 1% Lidocaine is injected at the lateral sulcus directly under the acromion directed posteriorly, medially and inferiorly. Allow 10-15 minutes after injection prior to maneuvers.

VIDEO LINK: SHOULDER JOINT INJECTION

SHOULDER JOINT INJECTION/ASPIRATION
ANTERIOR APPROACH
Sit patient upright facing you
Insert needle just lateral to coracoid process (between coracoid and humeral head)
Direct needle posteriorly
POSTERIOR APPROACH
Sit patient upright with back facing you
Palpate scapular spine to its lateral limit (the acromion)
Identify the posterolateral corner of the acromion
Insert 1.5-in needle 1 cm inferior and 1 cm medial to this corner
Direct needle anterior and medial toward presumed position of coracoid process
Glenohumeral joint is located at a depth of approximately 1-1.5in



SHOULDER LANDMARKS

REDUCTION MANEUVERS: There are several maneuvers that can be used reduce an anterior dislocation, each with advantages and disadvantages. In general maneuvers that avoid traction are considered noninvasive. These include the following maneuvers: Cunningham, scapula manipulation and external rotation. Each of the maneuvers are 70-90% effective with the first attempt. Maneuvers can also be combined. For example, the Stimson maneuver can be used with scapula rotation and external rotation can be preceded by the Cunningham maneuver or followed by the Milch technique. Inability to reduce a shoulder dislocation may be due to an interposed capsule, tendon or bony fragment or an unstable glenoid fracture.

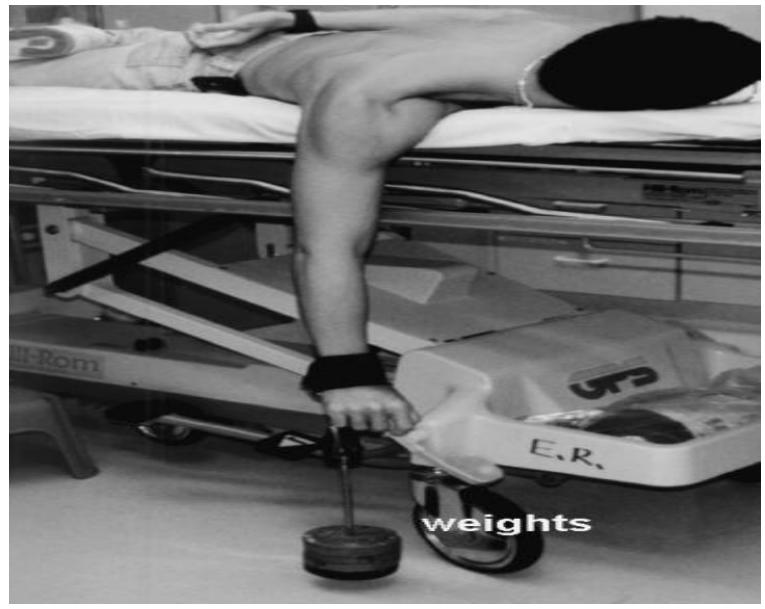
VIDEO LINK: 10 WAYS TO REDUCE A SHOULDER DISLOCATION

CUNNINGHAM
Massage of the deltoid, biceps and trapezius muscles.
May be sufficient muscle relation to allow reduction to occur with manipulation of the shoulder.

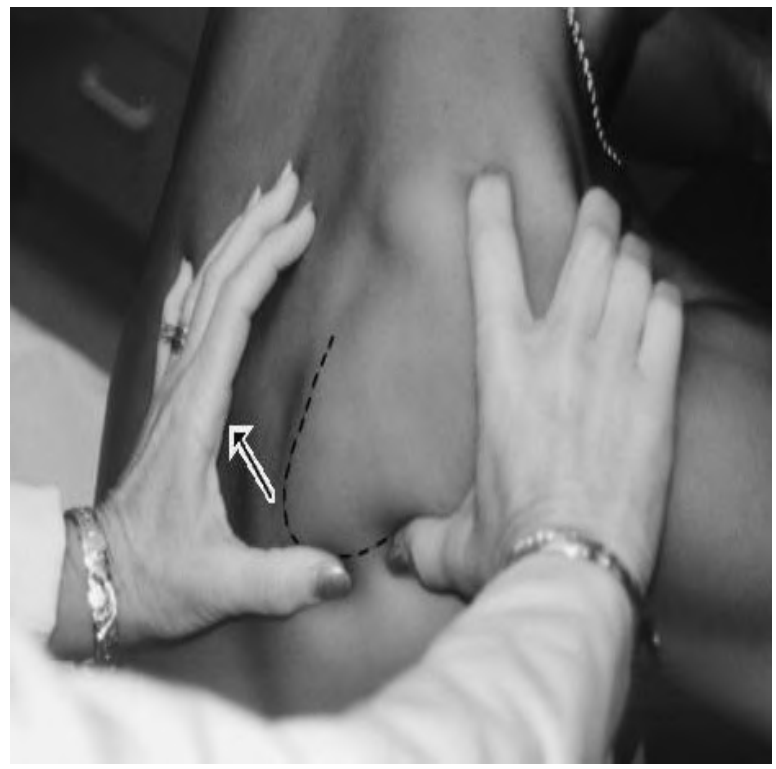
EXTERNAL ROTATION	
1	Have the patient lie supine with the upper arm adducted to the trunk with the elbow at 90 degrees
2	Slowly rotate the arm externally (laterally, pausing whenever the patient experiences pain
3	Reduce the shoulder before reaching the coronal plane.
4	Often reduction is achieved without an audible clunk. Repeat the physical exam to confirm alignment.

MILCH TECHNIQUE	
1	Can be added if external rotation is not successful
2	Abduct the fully externally rotated arm into an overhead position, maintaining external rotation throughout the abduction.
3	Reduction is achieved by applying gentle traction in line with the humerus and direct pressure over the humeral head with the clinician's thumb in the axilla

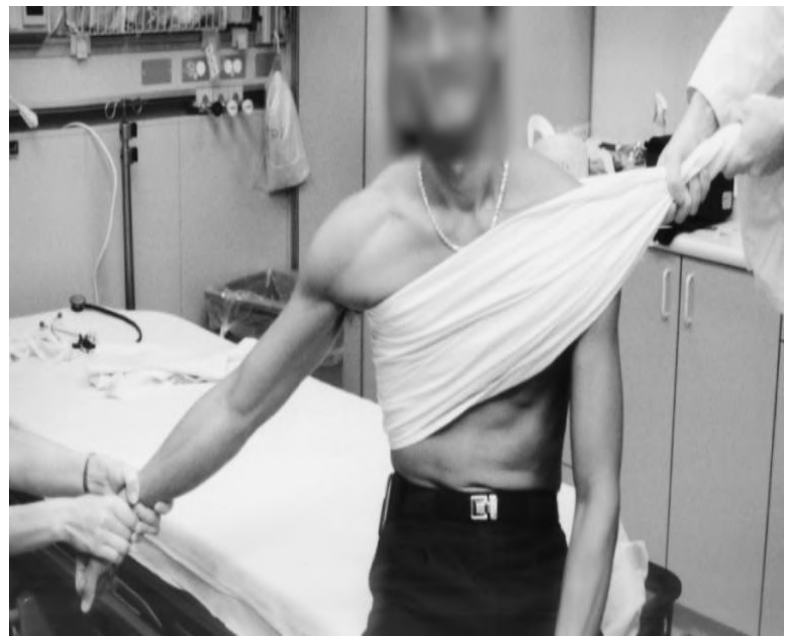
STIMSON (REDUCTION BY GRAVITY)	
1	Have patient lie on stretcher in prone position with affected arm hanging over side.
2	Attach 2-5kg weights to the arm (5 kg for adult).
3	Allow arm to hang 20-40 minutes.
4	Reduction will often be achieved without a noticeable sound. Have the patient swing the arm forward and repeat physical exam to confirm realignment.



SCAPULAR MANIPULATION	
1	Often useful if Stimson fails (because patient is already in prone position with arm hanging off the side).
2	Continue to hang 2-5 kg weight off of the affected arm.
3	Gently rotate scapula by simultaneously pushing its inferior tip medially and its superior aspect laterally. (clockwise for the right shoulder, counterclockwise for the left)
4	Reduction may be appreciated with an audible sound or “clunk”; repeat physical exam to confirm alignment.



TRACTION-COUNTERTRACTION	
1	Patient is in supine position with elbow of affected side in slight abduction and 90 degrees flexion. The patient can hold the physician’s elbow or shoulder.
2	Sheet is looped around flexed forearm distal to elbow, then around clinician.
3	Clinician should be standing next to hip on affected side
4	Have assistant loop second sheet around himself/ herself and then around patient’s chest under axilla on affected side.
5	Exert continuous longitudinal traction on affected arm, gradually increasing force until reduction is achieved. To facilitate a steady continuous amount of force it may be necessary to lean back against sheet during traction.
6	Reduction may be achieved with an audible “clunk”; repeat physical exam to confirm alignment.



POST REDUCTION CARE

After reduction all patients will have a dramatic improvement in their pain. They should be able to touch the unaffected shoulder without pain. The shoulder regains its normal rounded off appearance, and the humerus is no longer palpable inferior to the clavicle.

Repeat radiographs of the shoulder are necessary to confirm relocation. Reassessment of neurovascular status is crucial after reduction because of possible concurrent brachial plexus or vascular injury.

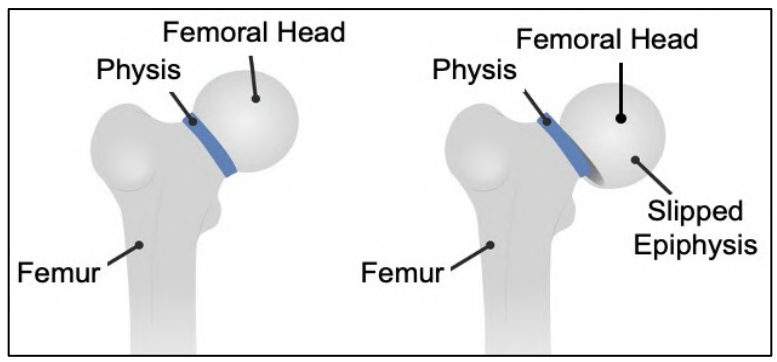
Patients should be placed in a shoulder sling in abduction and internal rotation to limit the risk of re-dislocation. A sling can be used for a few days to a week but mobilization of the shoulder should occur as soon as the patient is comfortable. A gunslinger brace should be used for posterior dislocation in order to avoid re-dislocation.

Orthopedic follow up and physical rehabilitation should be scheduled within 1-2 weeks. In addition, sports activities should be avoided for 3-6 weeks. Patients should be advised to not carry objects greater than 5 pounds or to reach for objects over their head with the affected arm.

SLIPPED CAPITAL FEMORAL EPIPHYSIS

INTRODUCTION (MICHAEL MOJICA, MD, 12/2022)
Slipped capital femoral epiphysis (SCFE) is the most common hip disorder in adolescents. It is more frequent in boys (M:F 1.5:1) between 8-15 years of age. More than 80% occur in obese patients.

PATHOPHYSIOLOGY
SCFE can be categorized as a displaced Salter-Harris 1 fracture through the physis of the femoral head. It is caused by shearing stress that exceeds the structural integrity of the physis. This leads to slippage of the femoral neck relative to the epiphysis. The epiphysis stays in its normal position in the acetabulum.



SCFE can also be seen in patients who have received radiation therapy, have renal failure and in certain genetic disorders. Endocrinologic etiologies should be considered in patients who do not fit the typical high-risk group (< 10 years, > 16 years, weight less than 50th percentile for age and sex). The most common endocrine causes include hypothyroidism and growth hormone deficiency.

SCFE complications include: osteonecrosis (AKA avascular necrosis) of the femoral head, chondrolysis (loss of articular cartilage) and femoro-acetabular impingement (due to narrowing of the joint space). These conditions increase the risk of subsequent osteoarthritis. The risk of complications increases as the severity of SCFE increases.

CLINICAL MANIFESTATIONS
Slipped capital femoral epiphysis typically presents with pain and/or limp. The gait is most commonly antalgic. A Trendelenburg gait may also be seen (downward pelvic tilt during the swing phase due to spasm or weakness of the contralateral gluteus medius muscle). A waddling gait may be seen with bilateral SCFE (WEB LINK: ABNORMAL GAITS).

Depending on the presentation, SCFE can be categorized as: pre-slip, acute, acute on chronic and chronic. The chronic presentation (pain > 3 weeks) is most common. The pain is typically described as dull, or aching and can involve the hip, groin, thigh, or knee. Pain may be constant or intermittent and is frequently exacerbated by physical activity and relieved by rest. Pre-slip presentation occurs with widening of the physis without displacement of the epiphysis. The acute presentation (pain less than 3 weeks) is typically preceded by trauma with acute severe pain, limited range of motion and inability to bear weight. The acute on chronic presentation occurs when a patient with chronic symptoms develops an acute increase in pain.

The diagnosis of SCFE can be missed in those presenting with knee pain unless a hip examination is included. On examination, the affected leg is held in slight flexion and external rotation (Drehmann sign). This position reduces pressure on the hip capsule. Hip range of motion is limited. Full passive flexion or internal rotation can worsen the pain. The same examination findings can be seen with septic arthritis of the hip. The knee examination will be normal.

DIFFERENTIAL DIAGNOSIS: HIP PAIN	
INFECTIOUS	MECHANICAL
Appendicitis	Acetabular labral tear
Lyme Disease	Apophysitis, apophyseal avulsion fracture
Osteomyelitis of femoral head or pelvis	Avascular necrosis: Leg-Calve-Perthes
Psoas Abscess/Pyomyositis	Femeroacetabluar impingement
Septic Arthritis of the hip/sacroiliac joint	Femoral stress dracture
Spinal epidural abscess	Muscle strain
INFLAMMATORY	Slipped Capital Femoral Epiphysis
Familial Mediterranean Fever	Trochanteric bursitis
Idiopathic chondrolysis of the hip	NEOPLASM
Infection related: ARF, glomerulonephritis	Leukemia
Dermatomyositis	Osteoid osteoma
Inflammatory bowel or celiac disease	Pigmented villonodular synovitis
Juvenile Idiopathic Arthritis	Solid tumor, primary or metastatic
Spondyloarthropathy	OTHER
Systemic Lupus Erythematosus	Gaucher disease
Transient Synovitis	Muscular dystrophies
	Sickle cell pain crisis

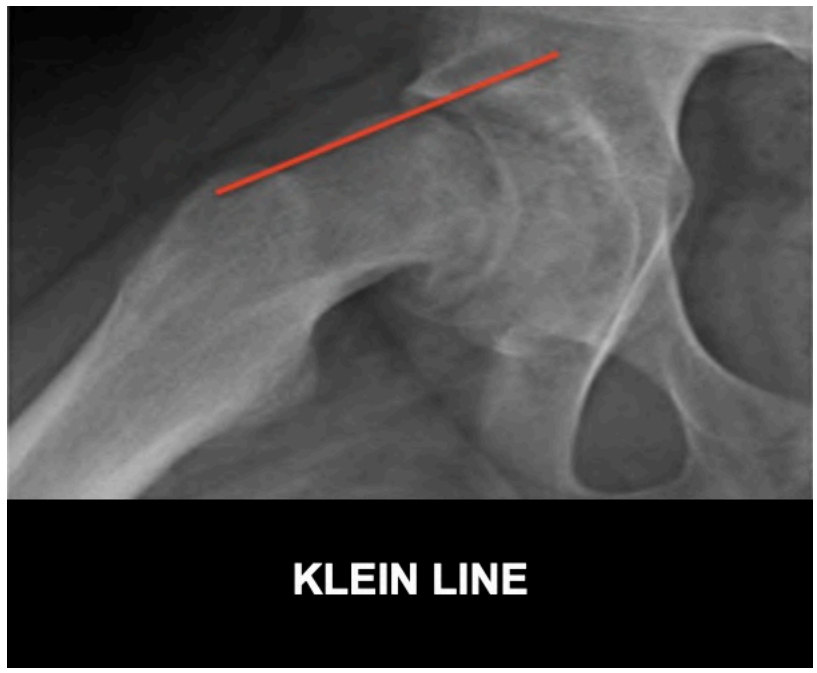
IMAGING

Anteroposterior and lateral view of the affected hip should be obtained. The lateral view can be obtained with “frog leg” view or cross table lateral views. Frog leg views can worsen displacement in patient with acute, unstable SCFE. Bilateral XRAYS are recommended to allow comparison and because 10-25% of SCFE involve both hips. Slippage of the femoral neck anterolaterally and inferiorly gives the appearance of posterior and inferior displacement of the epiphysis.

Early findings include a widening and irregularity of the physis with thinning of the proximal epiphysis. These are best seen on the lateral view. The line of Klein is drawn along the superior aspect of the femoral neck on the AP view. This line should intersect with the epiphysis. However, a normal Klein line does not exclude SCFE. A maximum width of the epiphysis lateral to the line of Klein is more than 2 mm greater than the unaffected side is a more sensitive finding. This approach may be limited in bilateral SCFE. The metaphyseal blanch sign, is when in which the portion of the epiphysis that slipped posteriorly to the femoral neck creates a denser appearance of the metaphysis. As disease progresses, the XRAY ca take on the appearance of the classic “ice cream scoop falling off of the cone”

MRI can be obtained in equivocal cases on plain XRAY. MRI provides a 3-D view in severe SCFE to aid in planning operative management, can identify osteonecrosis and can identify an early or "pre-slip” SCFE. Early findings include a widened physis and bone marrow edema in the metaphysis.

ICE CREAM SCOOP OFF THE CONE (L)



KLEIN LINE

CLASSIFICATION

SCFE can be further classified according to the duration of pain, stability, and degree of displacement. SCFE is classified as acute (pain < 3 weeks) or chronic (pain > 3 weeks). The degree of displacement is determined by the amount of slippage relative to the width of the metaphysis. An unstable SCFE is defined as the inability to bear weight even with crutches (essentially bed ridden). Unstable patients have a higher rate of avascular necrosis. Approximately 90% of patients have a stable SCFE before developing an unstable SCFE.

SCFE SEVERITY CLASSIFICATION		
Duration	Acute	< 3 weeks
	Chronic	> 3 weeks
Stability	Stable	Able to bear weight with crutches
	Unstable	Unable to bear weight with crutches (essentially bedridden)
Displacement	Grade I (pre-slip)	No displacement, widened physis
	Grade II	1/3 of the width of the metaphysis
	Grade III	> 1/3 to 1/2 of the width of the metaphysis
	Grade IV	> 1/2 of the width of the metaphysis

MANAGEMENT

Treatment of SCFE is operative. Pediatric orthopedics should be consulted if SCFE is suspected or confirmed. The goal is to prevent further slippage of the epiphysis and subsequent complications. This includes non-weight bearing and internal fixation with a screw or pin, with or without reduction of the epiphysis. Patients with an unstable SCFE (inability to weight bear even with crutches) and those with bilateral SCFE are typically admitted for imminent operative repair. Patients with stable, unilateral SCFE should be made strictly non-weight bearing (crutches, wheelchair, bed rest) with expedited orthopedics follow-up in conjunction with pediatric orthopedic consultation.

SPLINTING

INTRODUCTION (LOUIS SPINA M.D., 6/2022)
Splints can be applied to most pediatric fractures, dislocations and sprains. Splints may also aid in the immobilization of soft tissue injuries such as fingertip amputations and lacerations over joints where it is important to minimize tension or damage to the healing injury.

Immobilization can decrease pain and bleeding as well as prevent further vascular, nerve and soft tissue damage. Immobilization prevent movement, limiting pain and preventing displacement, angulation and shortening. Unlike casts, which are circumferential, splints allow for swelling in the immediate post injury phase and can reduce the possibility of compartment syndrome. They can be used the primary modality for immobilization during the healing phase of an injury and can be used temporarily until swelling resolved and a cast can be placed definitively.

Many recent studies in the pediatrics have demonstrated that removable splints for minor injuries such as torus fractures provide a faster return to baseline function when compared to traditional casting.

Temporary splints from transport can be used by emergency medical services. Splints can be made from a variety of materials. The most common form is plaster of Paris (powdered for gypsum impregnated in gauze. This has the benefit of being inexpensive and customized to the patient. Plaster typically sets in 2-8 minutes but does not reach maximum strength until 24 hours. Malleable aluminum, air and synthetic splinting materials may also be used (e.g. Fiber glass, Orthoglass). Synthetic splinting materials are more difficult to mold and more expensive. However, they are lighter, set more quickly and are water resistant.

Preformed splints for common uses are more readily available (e.g. thumb spica). There preformed splints come in a variety of sizes but the appropriate size may not be available for smaller children. Preformed splints do not provide the same degree of immobilization as custom splints. Custom splits should be utilized when precise and continuous immobilization is required.

EQUIPMENT
Stockinet (optional)
Plaster or fiberglass splinting/casting material
Webril or cotton wrap (splint padding)
Warm water (room temperature)
Elastic wrap, Tape, Sling

POSITION OF SPLINT IMMOBILIZATION		
Upper Extremity	Elbow	90 flexion
	Wrist	0-30 extension
	Meta-carpal phalangeal	≥ 70 flexion, IP extension
Lower Extremity	Hip	10-30 abduction, 15 external rotation
	Knee	15-30 flexion
	Ankle	Neutral dorsiflexion

PROCEDURE: SPLINTING	
PREPARE	Clean, repair and dress any skin lesions prior to splinting Consider removing clothing that will not be able to be removed after Evaluate neurovascular status
SELECT	Appropriate splint type (See table below)
LENGTH	Use unaffected extremity to measure the materials In general, the plaster is used to immobilize the joint above and joint below the injured area, if this is anatomically possible. The stockinet (if used) should be longer than the splining material so that it can be rolled over the ends of the splints. Cut dry plaster or fiberglass to fit area to be splinted. Plaster of Paris should be slightly longer than needed as it retracts during setting
WIDTH	The size of the plaster used is measured to cover approximately 50% of the circumference of the injured extremity. In an adult, this generally means 2 inch for the fingers, 3-4 inches for the upper extremity and 5-6 inches for the lower extremity
LAYERS	In an average sized adult, upper extremities should be splinted with 8-10 layers of plaster. Lower extremities generally require 12-14 layers.
PADDING	Roll Webril around stockinet. This should be about 2-3 layers thick & each turn should overlap the previous turn's with by 25-50%. Alternatively, layers of Webril (approximately ½ the number of layers as the plaster & the same diameter as the plaster) may be used One additional layer of Webril is placed on the outside of the plaster (non-skin side) to avoid sticking of the elastic wrap to the plaster. Place additional padding (Webril) over boney prominences (such as the ankle malleoli) to avoid pressure injuries. Avoid wrinkles
POSITION	In general, splints are prepared to immobilize the effective limp in a position of function. See individual splints in the following tables. There are exceptions to this rule. 5th metacarpal neck fractures are position with the 5th MCP at 70-90 degrees. Distal finger extensor tendon avulsion leading to Mallet deformity are splinted in extension
WET	Wet plaster/fiberglass material (not the padding) Plaster of Paris and water create an exothermic reaction. The water should be at room temperature (ideally at 24°C) The plaster drying rate is directly related to water temperature. The colder the water, the longer the drying time. As the water temperature approaches 40° C, the potential for serious burns from the splint doubles. Squeeze out excess water. Lie the plaster on a flat surface and smooth out any lumps or wrinkles
APPLY	The Webril-lined splint is then positioned over the area to be immobilized Perform initial splint shaping at large joints. secured with an ACE wrap. Shape splint contours to final form (molding). Maintain splint positioning until it has completely hardened.
FINISH	Re-evaluate and document neurovascular status Provide a sling for comfort (upper extremity), crutches (lower extremity)

VIDEO LINK: SPLINTING BASICS

COMPLICATIONS: RELATED TO IMPROPER SPLINTING	
Pressure sores	Insufficient padding or bone prominences, over-molding
Abrasions/Blisters	Sharp or irregular splint edges
Burns	Use too high water temperature. Exothermic reaction
Compartment syndrome	Too tight application of splint, failure to account for ongoing swelling
Nerve palsy	e.g. peroneal nerve due to ending splint at the fibular neck

SPLINT SELECTION			
	SPLINT	INDICATION	COMMENTS
Upper Extremity Splints	Colle's/Volar	Distal forearm	Alternative to sugar tong (not for young children)
	Long arm Gutter	Wrist, forearm Metacarpal Proximal phalanx	Radial for 2nd/3rd digits Ulnar for 4th/5th digits
	Sugar tong	Elbow Proximal humerus Distal	Useful for most upper extremity fractures *Must use sling*
	Thumb spica	1st metacarpal Proximal phalanx Scaphoid	
Lower Extremity Splints	Long leg	Distal femur Proximal tibia/fibula	Crutches for children over 6 years
	Posterior (short) leg	Distal tibia/fibula Foot Ankle	Crutches for children over 6 years
	Stirrup	Ankle (including soft tissue injuries)	Allows for weight bearing Fits in shoe

SPLINT AFTERCARE

The patient or parent should be advised to avoid wetting the splint and to not to place any objects between the skin and the splint. The lower end of the splint should be elevated to avoid further swelling. For example, a sling on the upper extremity should be position so that the hand is above the level of the elbow. For lower extremity splints the foot should be elevated on a chair if sitting or a pillow if lying. Ice can be applied to the outside of the splint for pain but no longer than 15-20 minutes.

They should return urgently for worsening pain under or distal to the splint. Numbness or paresthesias. Follow up should be arranged within a week with an orthopedist

RADIAL/ ULNAR GUTTER

INDICATIONS

Metacarpal and/or proximal phalangeal fractures.

Ulnar gutter splint immobilizes the plain of 4th and 5th digits.

Radial gutter splint immobilizes plain of 2nd and 3rd digits.

DIMENSIONS

Width to wrap to midline of the hand on dorsal & volar surfaces.

Length to extend from the nail base to the proximal forearm.

POSITIONING

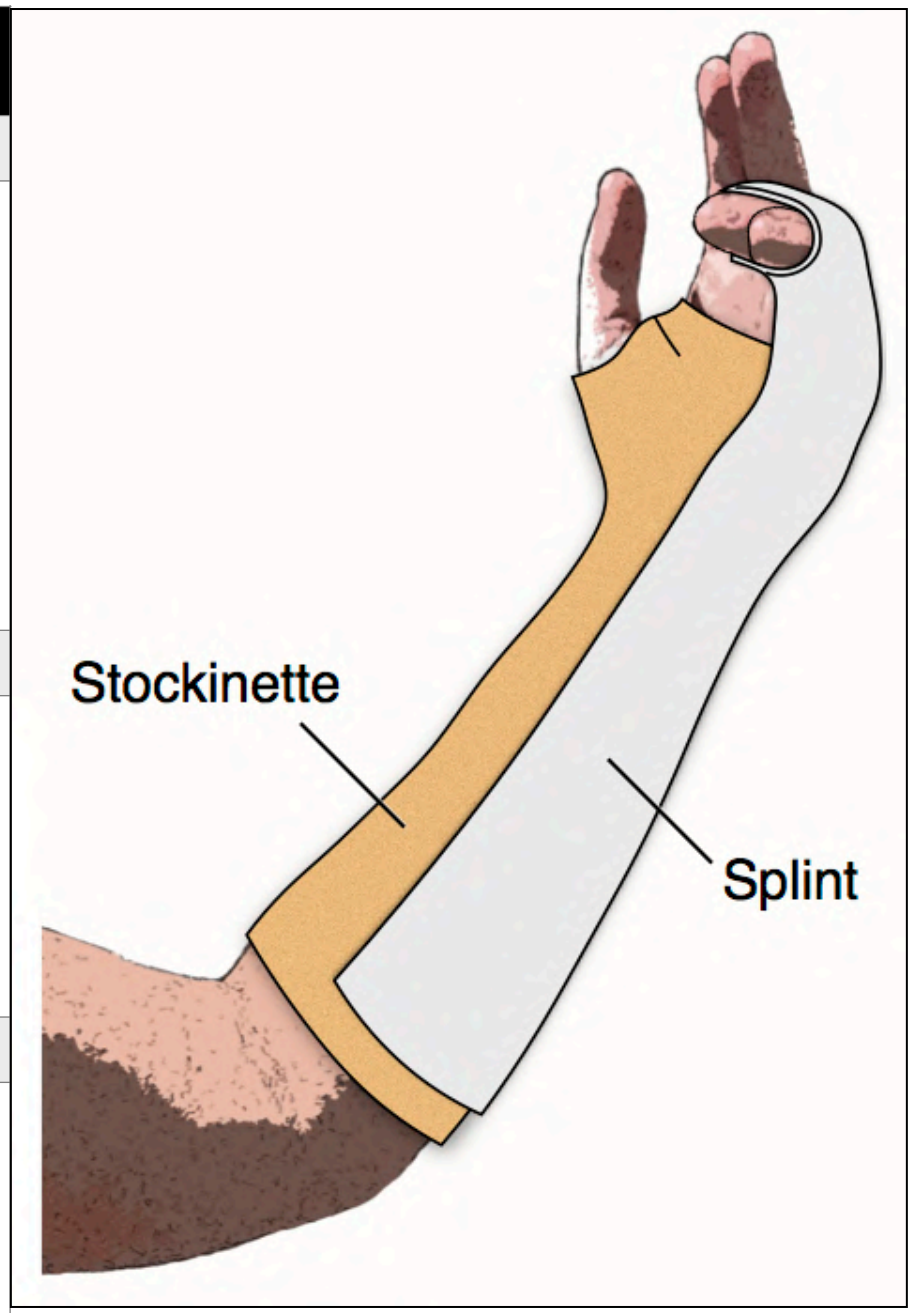
Position patient with forearm vertically erect.

Shape the splint as follows:
Wrist in neutral position
MP joints in ≥ 70° flexion.
PIP joints in 20-30° flexion.

COMMENTS

A thin layer of padding should be placed between the fingers to prevent irritation.

Using a sling is optional to keep arm elevated (not feasible in toddlers & infants



THUMB SPICA

INDICATIONS

A thumb spica splint is essentially a radial gutter splint adapted for immobilization of the thumb.

Indicated for:
Nondisplaced fractures of the first metacarpal bone.
Nondisplaced fractures of the proximal phalanx of the thumb.
Actual or suspected scaphoid fractures.
Sprain of the ulna collateral ligament

DIMENSIONS

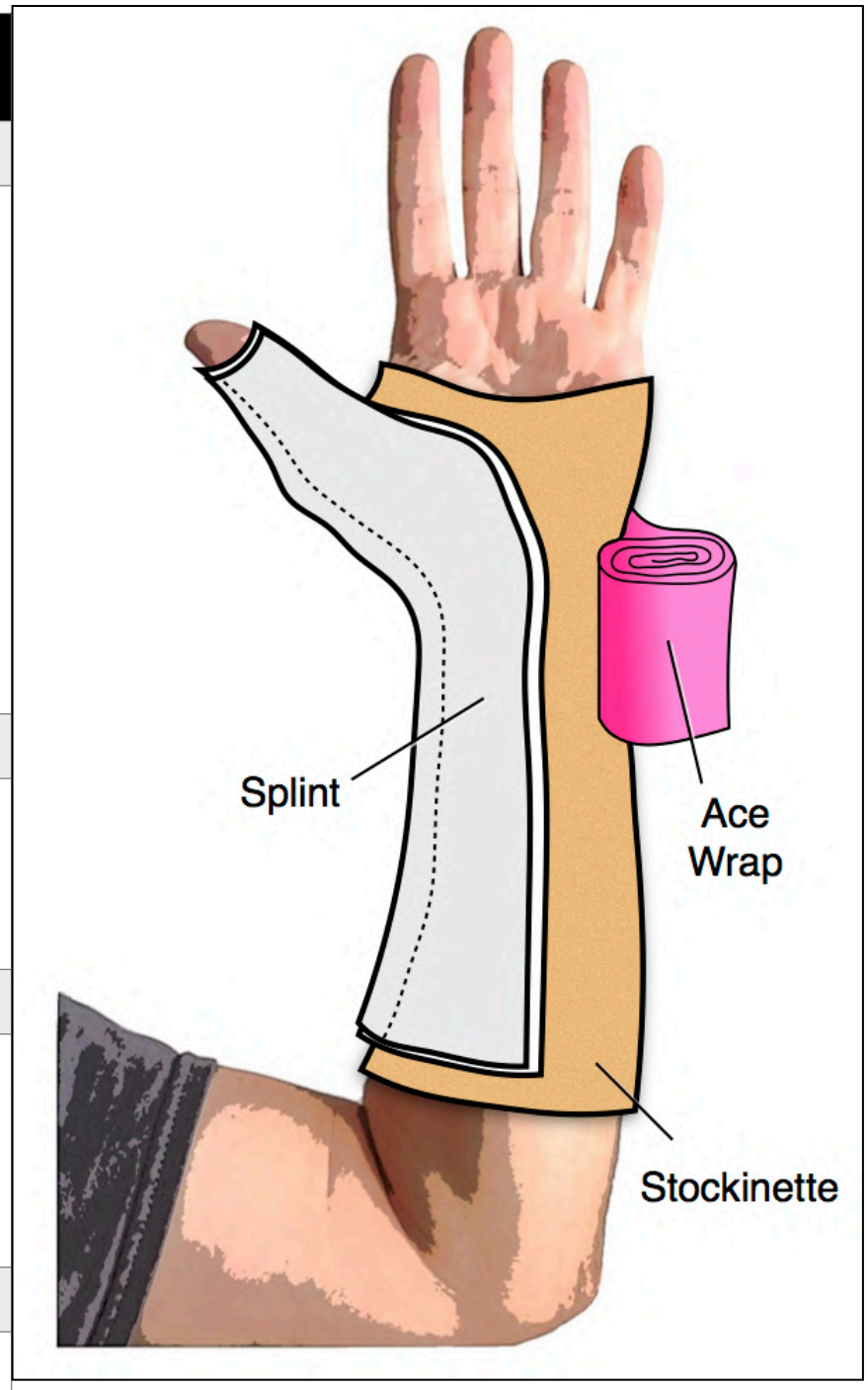
Dimensions are the same as for a radial/ulnar gutter splint.

POSITIONING

Wrist in neutral position.
Thumb abducted & in slight flexion at the MP and IP joints.

COMMENTS

May also make small cuts in plaster/fiberglass on both sides at the base of the thumb to make it easier to wrap around thumb



VOLAR /COLLES

INDICATIONS

Distal forearm and wrist fractures.
Also immobilizes the plane of the 2nd and 3rd digits.

DIMENSIONS

Width to fully cover volar aspect of the forearm.

Length to extend from proximal fingers to proximal forearm along volar side of forearm.

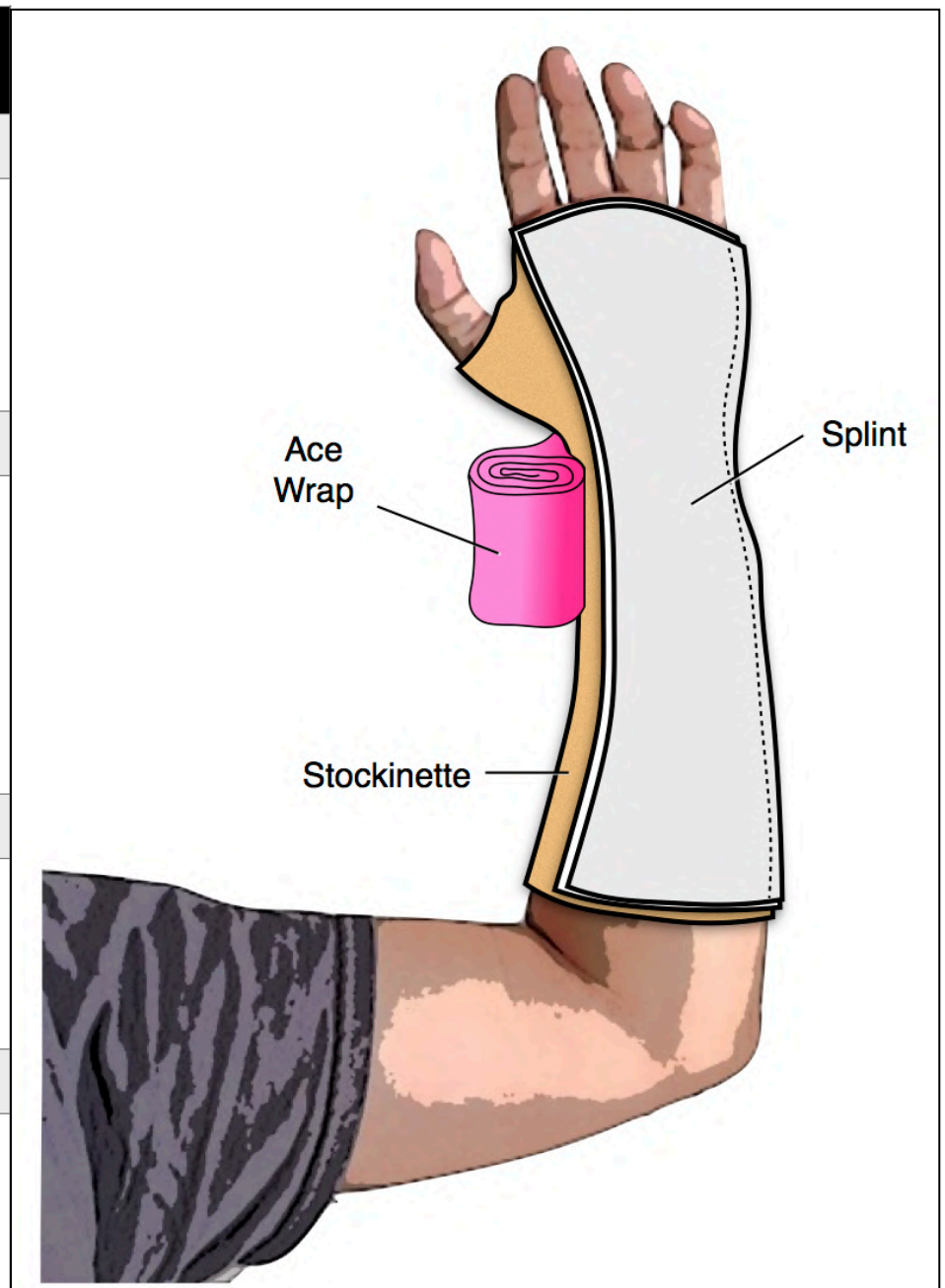
POSITIONING

Position wrist in neutral position and digits slightly flexed at all joints.

COMMENTS

Using a sling is optional to keep arm elevated (not feasible in toddlers & infants)

May be extended to distal fingertips for distal finger fractures or metacarpal fractures of the fingers/metacarpals 2-4.



LONG ARM POSTERIOR

INDICATION

Used for stable injuries in the elbow region. For example, the patient with elbow pain in which no obvious fracture is seen but a joint effusion is present as evidence by an enlarged posterior fat pad. (Orthopedic consults are needed for supracondylar fractures)

DIMENSIONS

Width to cover ½ the arm circumference.
Length to extend from the dorsal aspect of the mid-upper arm, over the olecranon, and down the ulnar aspect of the arm to the distal palmar flexion crease.

POSITIONING

Position the child on his/her stomach with injured arm hanging off stretcher with elbow at 90° angle

After plaster/fiberglass is applied, shape the splint with elbow flexed at 90° and forearm in neutral position.

COMMENTS

To ensure comfort, provide extra padding to any bony prominence.

A sling must be worn to support the arm because many casting materials cannot maintain the 90° angle needed at the elbow.

SUGAR TONG (ARM)

INDICATIONS

Broad range of uses.
Proximally, it can be used for stable humerus fractures.
Distally, frequently used for stable forearm and wrist fractures – provides the most effective immobilization in these areas. Prevents supination and pronation

A double sugar tong (both proximal and distal at a 90 degree angle at the elbow) can be used to immobilize elbow injuries.

DIMENSIONS

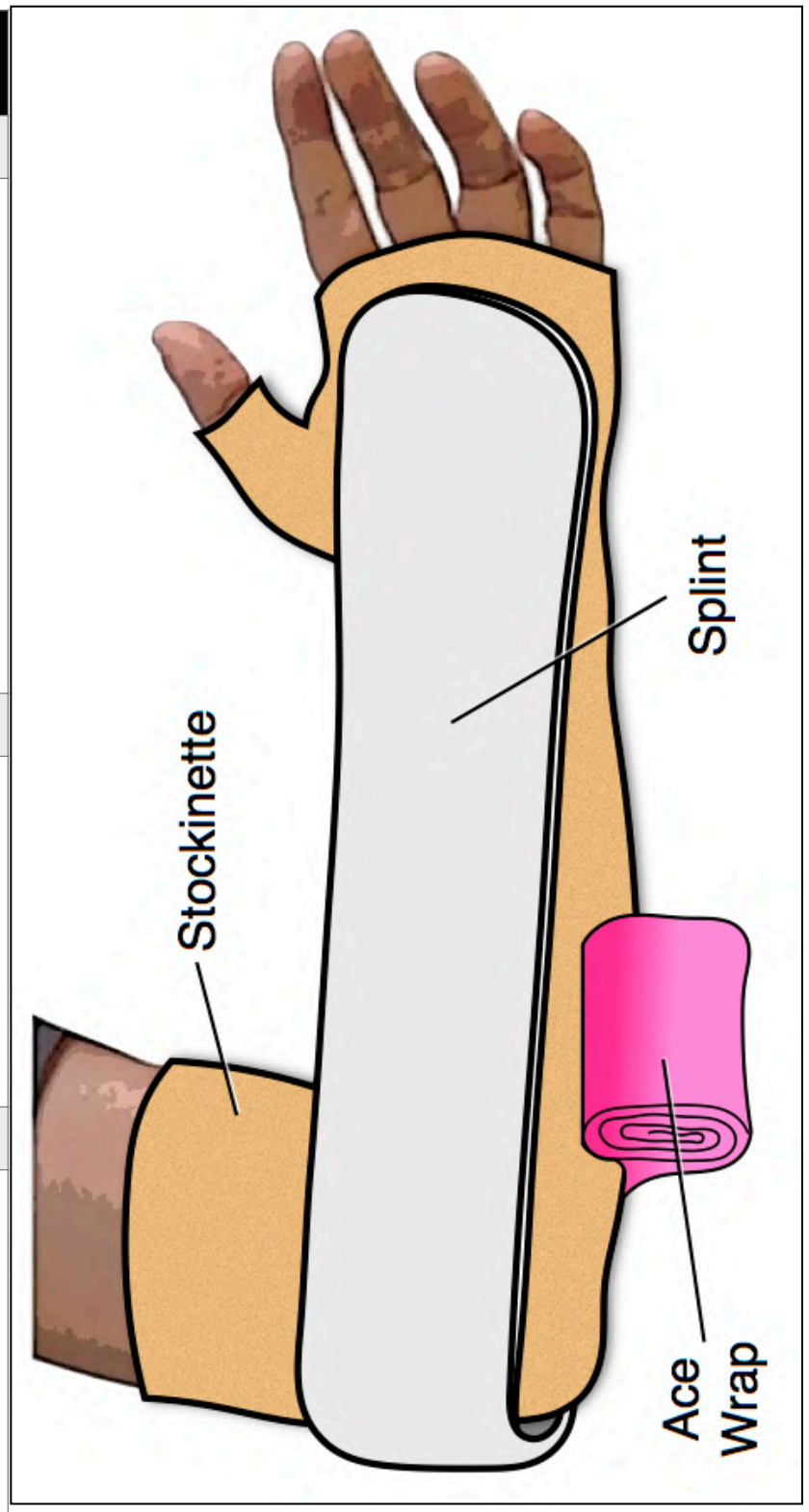
Width of the distal splint should slightly overlap the radial and ulnar edges of the arm.

Length should extend dorsally to the metacarpal head, around the elbow, to the distal palmar flexion crease.

POSITIONING

Position the child on his/her stomach with injured arm hanging off stretcher with elbow at 90° angle

After plaster/fiberglass & overwrap is applied, shape splint and keep elbow flexed at 90° with the wrist in neutral position.



COMMENTS

A sling is necessary to support the sugar tong at the elbow.

Analogous to a ankle stirrup splint

POSTERIOR / SHORT LEG

INDICATIONS

Provides support for injuries in:
Distal tibia/fibula
Ankle
Foot

DIMENSIONS

Width should cover at least ½ the leg circumference.

Length should extend posteriorly from level of the fibular neck over the heel of the foot to the base of the toes.

POSITIONING

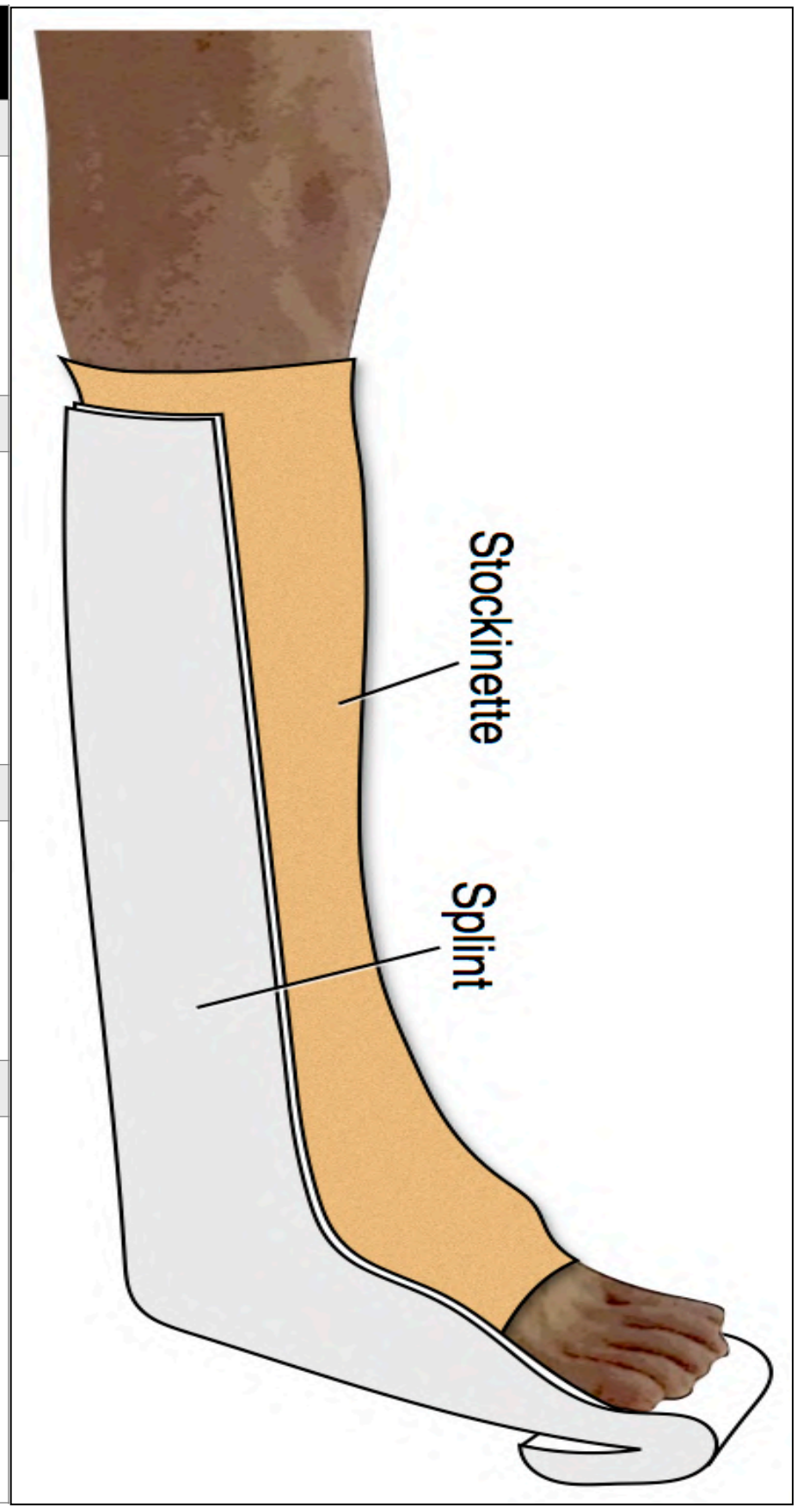
To apply, position child prone on a stretcher with knee flexed at 90 degrees.
The foot should be placed in neutral position at 90° to the leg.

COMMENTS

Provide extra padding at bony prominences before adding plaster/fiberglass layer.

Avoid pressure at fibular neck to prevent compression of peroneal nerve.

Crutches are indicated for ambulation except for children under 6 years of age.



STIRRUP (LEG)

INDICATIONS

Provide lateral support for ankle fractures or soft tissue injuries, preventing inversion and eversion.

Often used in addition to posterior splints to stabilize ankle fractures.

DIMENSIONS

Width to cover at least ½ the leg circumference.

Length to extend medio-laterally from just below the fibular head, around the heel and ending just below the medial aspect of the knee.

POSITIONING

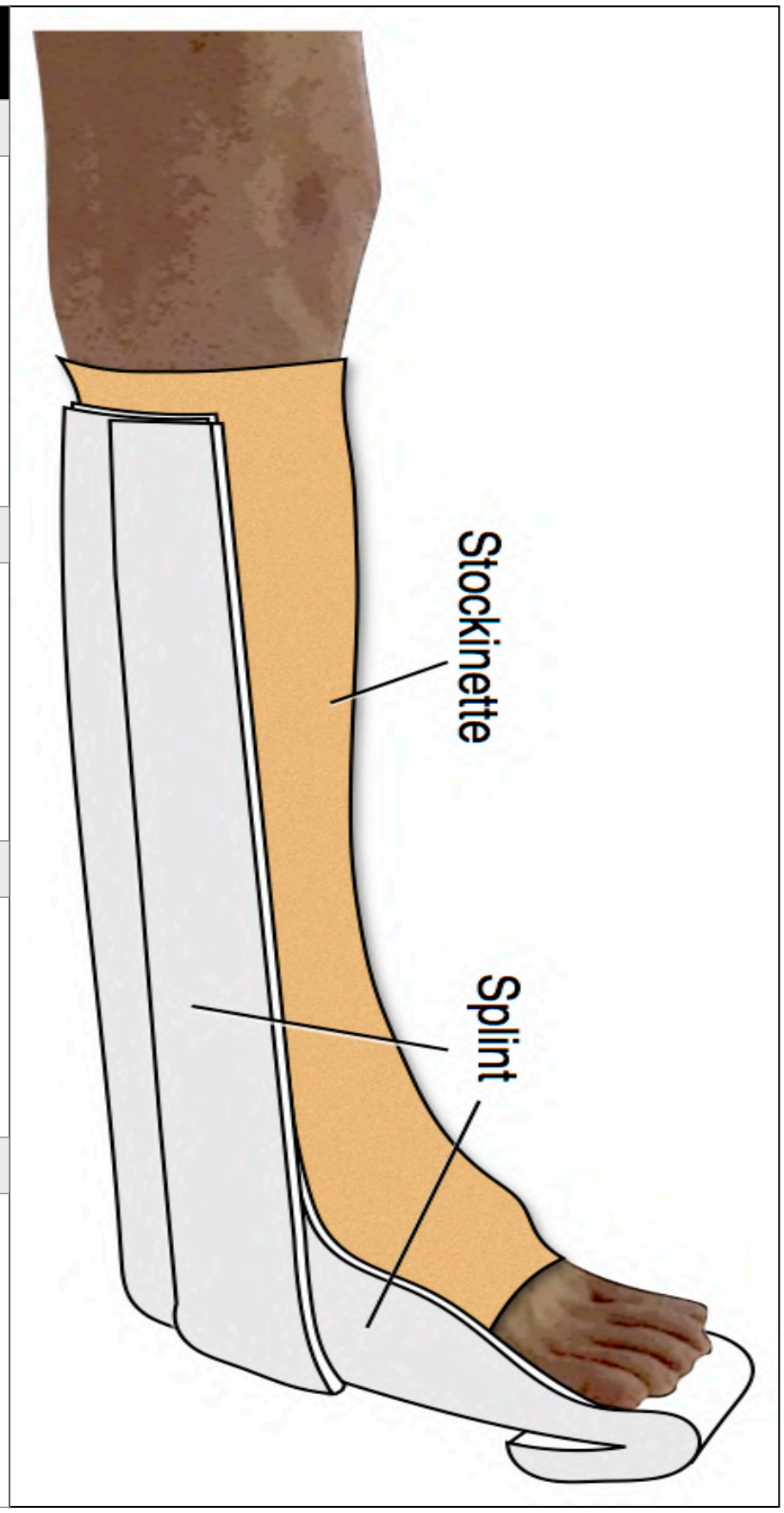
To apply, position child prone on a stretcher with knee flexed at 90 degrees.
The foot should be placed in neutral position at 90° to the leg.

COMMENTS

These splints conveniently fit into a loose shoe.

They allow weight bearing to be initiated.

Crutches should be provided if full weight-bearing is contraindicated.



PAINFUL PROCEDURES

ANALGESIA

INTRODUCTION (LAUREN VRABLIK, MD, KELSEY FAWCETT, MD, 6/2021)
Pain is a frequently encountered problem for children in the emergency department. It may be the primary reason for seeking medical attention or may be the consequence of a necessary procedure. The administration of analgesia and/or sedation should accomplish multiple goals: relieve pain, reduce anxiety, and enhance cooperation of the patient while maintaining the patient's health and safety. In children, physical discomfort may be exacerbated by the emotional distress of unfamiliar faces and places. Additionally, in the pediatric population it can be difficult to accurately quantify the pain of a child who is unable to verbally express his feelings. These factors can make it difficult for providers to select appropriate analgesia.

Pain is categorized as nociceptive or neuropathic. Nociceptive pain occurs as a result of stimulation of pain fibers by tissue injury or inflammation. It is termed somatic when it involves the skin, soft tissue, skeletal muscle or bone and visceral when it originates from internal organs. Neuropathic pain occurs due to damage to sensory nerves and is typically characterized as burning or tingling.

PAIN ASSESSMENT

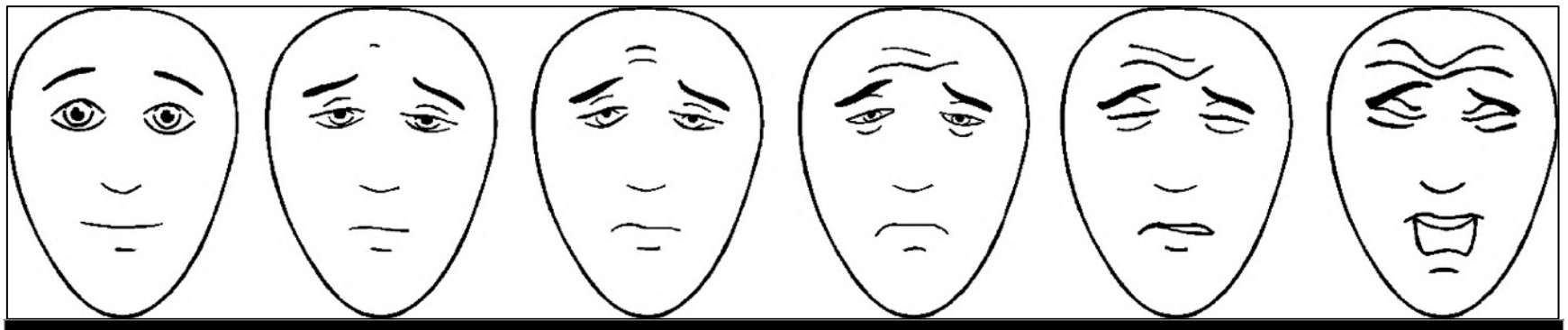
Prior to selecting and administering a pharmacologic agent, the character and severity of pain should be assessed. Many scales have been created to help assess children of varying developmental stages. These tools can be observational, pictorial, numerical, or a combination of these. Each has their own benefits and limitations. Observational scales may lead to significant variation in reporting based on the provider's interpretation of behaviors. The child's developmental stage should be taken into consideration when evaluating patient-given responses. For example, children under 5-6 years of age may have difficulty understanding the progression of a pain scale. Under 12 years of age, children will tend to focus on the extremes of a scale due to dichotomous thinking, and are unlikely to select an intermediate response. In these instances, observational scales may provide useful supplemental information. Conversely, adolescents may intentionally restrict the outward expression of pain, making observational scales less accurate. In instances where a mature child is able to express their pain verbally, this may be more reliable.

PAIN CHARACTERIZATION
Description: Sharp, dull, stabbing burning tingling
Location and radiation
Intensity
Duration
Constant or intermittent
Frequency
Exacerbating and relieving factors.

INFANTS (0-6 MONTHS): The Neonatal Infant Pain Scale (NIPS) is a purely observational tool validated for infants.

NEONATAL INFANT PAIN SCALE (NIPS)			
	0 POINTS	1 POINT	2 POINTS
Facial expression	Relaxed	Contracted	--
Cry	Absent	Mumbling	Vigorous
Breathing	Relaxed	Different than basal	--
Arms	Relaxed	Flexed/Stretched	--
Legs	Relaxed	Flexed/Stretched	--
Alertness	Sleeping/Calm	Uncomfortable	--
1 minute observation period, A score ≥ 4 requires treatment.			

SCHOOL AGE CHILDREN (3-12 YEARS): The most reliable pain tool validated in school aged children is the **Faces Pain Scale Revised (FPS-R).** The commonly seen **Wong-Baker FACES Scale** is also appropriate for this age range.



FACES PAIN SCALE REVISED

WONG-BAKER FACES PAIN RATING SCALE

OLDER CHILDREN (8 YEARS): Children with the ability to read, compare, and understand seriation can use a simple Visual Analog Scale (“no pain” to “worst pain”) or Verbal Numeric Scale and choose where on the spectrum their pain falls.

ALL AGES: The Faces Legs Activity Cry and Consolability (FLACC) is an observational tool validated for all ages. A score of 6 indicates a need for treatment.

FACES LEGS ACTIVITY CRY AND CONSOLABILITY (FLACC)			
	0 POINTS	1 POINT	2 POINTS
Face	Neutral expression	Occasional grimace or frown, withdrawn, disinterested	Frequent/constant quivering chin, clenched jaw
Legs	Normal/relaxed	Uneasy, restless, tense	Kicking/legs drawn up
Activity	Lying quietly, normal, moves easily	Squirming/shifting, tense	Arched, rigid or jerking
Cry	None	Moan, whimper, occasional complaint	Crying steadily, screams/ sobs, frequent complaints
Consolability	Content/relaxed	Reassured by occasional touching, distractible	Difficult to console or comfort
A score of ≥ 6 indicates a need for treatment			

NON-PHARMACOLOGIC MEASURES AND ADJUNCTS

Non-pharmacologic measures for pain reduction should be pursued first. Distraction and redirection by pointing out things of interest such as colorful clothing, shiny objects, or favorite characters may make the encounter less stressful and reduce pain. Additionally, the child should be given time to warm up to an unfamiliar provider. If the child is upset, ignore them and speak directly to the parents for several minutes until the child becomes more used to your presence.

Involving the child in a distracting activity (such as blowing bubbles or watching a movie) and limiting the child’s visual field while a procedure or manipulation of a painful area is occurring can help limit movement. Additionally, the parent or guardian should always remain involved if possible to limit patient anxiety. Examinations should be done in positions of comfort for the child if parents are willing. For example, rather than using a papoose, children should preferentially be restrained in the arms of a caregiver by seating the child with their legs between the legs of the caregiver, and arms and head pressed into the chest of the caregiver in a hugging motion. The caregiver should be directly visible to the child whenever possible.

Adjuncts such as cold or vibration are simple techniques for pain reduction. There are pediatric specific devices such as “Buzzy,” a small plastic bumble bee with ice pack wings which can be strapped to the arm of a child having an intravenous line placed. When turned on, the bee vibrates. This limits pain experienced by the patient by overwhelming the sensory input of other afferent receptors.

Child Life Specialists should be consulted in advance of procedures to help reduce stress in both the child and the parent. They are trained in distraction, positions of comfort, and other techniques. Most importantly, they are also trained in how to explain medical interventions in a developmentally appropriate way to the patient. Unlike in the adult population, this important step is a frequently overlooked. If given sufficient advance notice, they may be able to bring equipment and dolls for the child to play with to better understand and be prepared for what will happen next.

SELECTION OF MEDICATIONS

When non-pharmacologic and anxiety reducing measures are insufficient, the clinician must choose an appropriate analgesic for the patient's pain intensity and clinical status. The least amount of analgesia to improve patient comfort should be selected. Patients undergoing painful procedures for which analgesia is insufficient to both control pain and ability to complete the procedure may require sedation as well as analgesia (See also PEM Guide: Procedures: Procedural Sedation).

LOCAL (TOPICAL) ANALGESIA

LIDOCAINE	
Class	Amide
Routes of administration	Subcutaneous Topical gel, Topical cream (LMX) Oral topical solution (viscous lidocaine 2% or 4%)
Pharmacology	Sodium channel blockade
Dose	Maximum dose: 4.5 mg/kg without Epinephrine Maximum dose: 7 mg/kg with Epinephrine
Onset	Subcutaneously: 1-3 minutes Gel: 20-60 minutes LMX: 30 minutes
Duration	Subcutaneously: 10 min (without epi)/ 2.5 hours (with epi) Gel: 1-2 hours LMX: 1-2 hours
Adverse Effects	Overdose: arrhythmia, perioral paresthesia, seizure Local Anesthetic Systemic Toxicity if administered IV

LET (LIDOCAINE-EPINEPHRINE-TETRACAINE)	
Route of administration	Topical
Pharmacology	Lidocaine: Sodium channel blockade Epinephrine: Local vasoconstriction
Onset	20-30 minutes
Duration	60 minutes
Indications	Good for small, simple lacerations
Adverse Effects	Cannot be used on ears, fingers, toes, genitalia Tetracaine can cause Methemoglobinemia

EUTECTIC MIXTURE OF LOCAL ANESTHETICS (EMLA)	
Routes of admin	Topical
Pharmacology	Na channel blockade (Lidocaine 2.5%, Prilocaine 2.5%)
Onset	60 minutes for peak effect
Duration	45-60 minutes
Indications	Prior to injections of intact skin
Adverse Effects	Cannot be used on ears, fingers, toes, genitalia, or mucosa Prilocaine may cause mild Methemoglobinemia

TOPICAL ANESTHETICS: COMPARISON		
Product	Components/Concentration	Indications
EMLA	Lidocaine(2.5%), Prilocaine(2.5%)	Intact skin Laceration (no vasoconstriction)
LMX	Liposomal Lidocaine (4.0%)	Intact skin Superficial abscess
LET	Lidocaine (4%), Epinephrine, (0.1%), Tetracaine (0.5%)	Cutaneous lacerations Avoid near mucous membranes due to systemic absorption
Lidocaine Gel	Lidocaine Gel (2.8%)	Mucous membrane lacerations

REGIONAL ANALGESIA

For larger but localized areas of involvement or deeper lesions that would not be reasonably numbed by topical agents, regional nerve blocks can be considered. Typically, these are ultrasound guided injections of anesthetics around the nerve sheath. A complete pre- and post-procedural neurological exam of the treated area must be completed.

ANESTHETIC	ONSET	DURATION	MAXIMUM DOSE (MG/KG)	
	MINUTES	HOURS	WITHOUT EPINEPHRINE	WITH EPINEPHRINE
Lidocaine 2%	10-20	0.5-2	4.5	7.0
Bupivicaine 0.5%	15-30	2-4	2.5	3.0

SYSTEMIC ANALGESIA

Systemic pain relievers can be categorized as opioid or non-opioid. When systemic analgesia is required, consider all possible adverse effects. Prior to using medications with risk of respiratory depression, patients should be evaluated by American Society of Anesthesia (ASA) guidelines to stratify their risk. Consider placing the patient on cardiorespiratory monitoring if indicated, have airway supplies handy in the event of unintentional over-sedation, and know your reversal agents.

1. NON-OPIOID ANALGESIA

ACETAMINOPHEN (TYLENOL)	
Routes	IV, PO, PR
Pharmacology	Inhibition of prostaglandin production
Dose	10-15 mg/kg (maximum dose 1 gram)
Onset	PO: < 1 hour, IV: 5-10 minutes
Duration	4-6 hours
Indications	Mild pain, antipyretic

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)	
Examples	Ibuprofen (PO), Naproxen (PO), Toradol (IV/IM)
Pharmacology	COX enzyme inhibition, decreasing downstream production of prostaglandin
Dose	Ibuprofen: 10 mg/kg, maximum dose 600-800 mg Naproxen: 5-6 mg/kg, maximum dose 500 mg Toradol: 0.5 mg/kg/dose (maximum dose 15 mg < 17 years, 30 mg > 17 years
Onset	Ibuprofen: 30-60 minutes Naproxen: 30-60 minutes Toradol: 30 minutes
Duration	Ibuprofen: 6 hours Naproxen: < 12 hours Toradol: 4-6 hours
Adverse Effects	Gastrointestinal irritation, inhibited platelet function

KETAMINE	
Class	Phencyclidine derivative, dissociative agent
Pharmacology	NMDA receptor antagonist
Dose (analgesia only)	0.1-0.15 mg/kg IV 1-2 mg/kg IM
Onset	IV: 1-2 minutes, IM: 5 minutes
Duration	IV: 15-60 minutes, IM: 15-60 minutes
Indications	Painful procedures that may benefit from amnestic effects
Adverse Effects	Respiratory depression < 3 months of age Laryngospasm Increased airway secretions Prolonged emergence/emergence reactions (hallucinations) Debatably causes increased ICP (less evidence recently, less important if patient is mechanically ventilated)

Ketamine is a non-opioid medication that is more popular in ED settings for procedural sedation or induction of anesthesia, though it is less popular for pure analgesia. It is touted for its abilities to provide different effects at different doses. In low doses, it can provide analgesia. Due to attempts to decrease opioid usage, analgesic dose ketamine has become more popular recently. At higher doses it produces dissociative effects, resulting in analgesia and amnesia.

Ketamine is available in PO, IV, IM, and intranasal formulations. However, PO formulations have very low bioavailability and are rarely used. Ketamine can cause hallucinations and other emergence phenomena. Adverse reactions include laryngospasm, increased oral secretions (therefore one may also consider pre-medication with atropine), and increased ICP (though the latter is up for debate and has been shown to be inconsequential in the setting of a mechanically ventilated patient). The following table is for analgesic dosing. See: PEM Guide: Painful Procedures: Procedural Sedation

2. OPIOID ANALGESIA

CODEINE: In 2013 after multiple high profiled mortalities, the FDA issued a black box warning stating that codeine should not be used in children less than16 years of age. Codeine is a prodrug. It has no intrinsic analgesic properties. It is metabolized in the liver by CYP2D6 enzyme, ultimately producing morphine and morphine-6-glucuronide, which have analgesic properties. There is considerable variation among individuals in the efficacy of codeine as a result of the CYP2D6 enzyme, which exhibits genetic polymorphism. This ultimately means that following a normal dose of Codeine, rapid metabolizers may produce very high concentrations of morphine and poor metabolizers may produce no active metabolites at all.

MORPHINE	
Pharmacology	Mu opioid receptor agonist
Dose	IV: 0.05 to 0.1 mg/kg PO: 0.2-0.5 mg/kg
Onset	IV: 5 minutes, PO: 30 minutes
Duration	4 hours
Indications	Severe pain
Adverse Effects	Respiratory depression, pruritus, constipation

OXYCODONE	
Pharmacology	Mu opioid receptor agonist
Dose	PO: 0.1 to 0.2 mg/kg If ≥ 50 kg 5 to 10 mg
Onset	10-15 minutes
Duration	4 hours
Indications	Moderate to severe pain
Adverse Effects	Respiratory depression, constipation

NORCO*	
Pharmacology	Mu opioid receptor agonist
Dose	PO: Hydrocodone 0.1-0.2 mg/kg ≥ 50 kg: Hydrocodone 5-10 mg
Onset	10-20 minutes
Duration	4-8 hours
Indications	Moderate to severe pain
Adverse Effects	Risk of acetaminophen overdose if combining with other acetaminophen containing products for pain control
*Hydrocodone (5, 7.5 or 10 mg) + Acetaminophen (325 mg)	

HYDROMORPHONE	
Pharmacology	Mu opioid receptor agonist
Dose	PO: 0.03 to 0.08 mg/kg IV: 0.015 mg/kg If ≥ 50kg: PO 1-2 mg/kg, IV: 0.2-0.6 mg/kg
Onset	PO 15-30 minutes, IV 5 minutes
Duration	PO 3-4 hours, IV 3-6 hours
Indications	Has longer duration of action compared to other opioid meds, especially if using extended release (XR) formulations which can last 12 hours
Adverse Effects	Respiratory depression, constipation

FENTANYL	
Pharmacology	Mu opioid receptor agonist
Dose	IV 1-2 mcg/kg (If ≥ 50kg give 25-50 mcg) slow push IN 1.5 mcg/kg once
Onset	IV: Immediate IM: 7-8 minutes IN: 5-10 minutes
Duration	IV: 30-60 minutes IM: 1-2 hours IN: variable – can re dose up to 0.5 mcg/kg every 5 minutes, up to 3 mcg/kg
Indications	Short acting but strong pain control
Adverse Effects	Rapid infusion may cause chest wall rigidity Respiratory depression

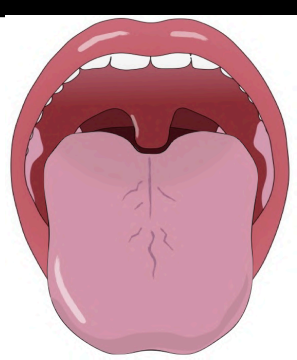
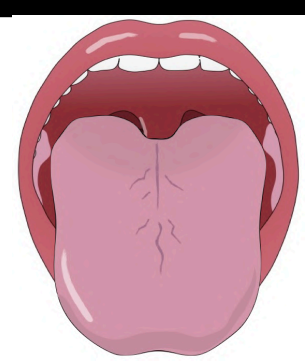
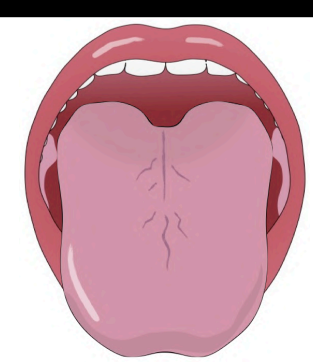
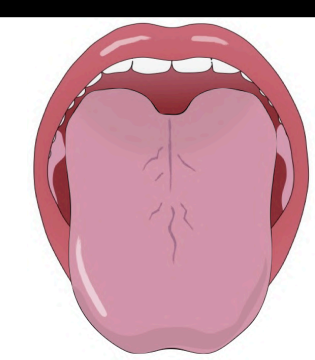
OPIOID COMPARISON		
	ONSET	DURATION
Morphine	5-15 minutes	3-4 hours
Fentanyl	IV: 1-2 minutes IN: 10 minutes IM: 7-15 minutes	IV: 30-60 minutes IN: 60 minutes IM: 1-2 hours
Hydromorphone	IV: Almost immediately PO: 30 minutes	IV: 2-4 hours PO: 4-5 hours

PROCEDURAL SEDATION

INTRODUCTION (DEBORAH LEVINE M.D., 4/2020)
Many medical procedures can be painful or anxiety provoking. Some procedures also require patient cooperation, which may be difficult in the anxious or injured child. Procedural sedation and analgesia describes a technique of administering sedation to allow the patient to tolerate unpleasant stimuli while maintaining airway control. The administration of sedation and/or analgesia should accomplish three goals: relieve pain, reduce anxiety and enhance cooperation while maintaining the patient's safety.

DIRECTED HISTORY: AMPLE	
Allergies	Egg and/or soy allergy may preclude Propofol use
Medications	Medications metabolized by the cytochrome P450 enzyme pathway, (anticonvulsants and psychotropic medications) May interfere with pharmacokinetics of some sedatives
Past medical history	Relevant hospitalizations Prior sedation or anesthesia related adverse events Patient or family history of anesthesia complications
Last meal	Timing, contents (liquids, solids)
Existing medical status	Conditions predisposing to airway obstruction or pulmonary compromise, head trauma, pregnancy status, vital signs

PHYSICAL EXAMINATION
The primary focus of the physical examination is the head and neck exam.This includes the oral cavity (fracture, instability, obstruction) and the neck (mass, swelling, trauma, mobility). The purpose of the exam is to establish if the patient's anatomy increases the risk of a difficult airway. Multiple scoring systems can be used to predict difficult bag-valve-mask ventilation, laryngoscopy, extra-glottic device placement and cricothyrotomy. (See PEM Guide: Airway Procedures: Difficult Airway). If a patient is suspected of having a difficult airway the elective sedation should performed in a controlled environment such as the operating room with all necessary personnel and equipment are available.

MALLAMPATI SCORE			
			
1	2	3	4
Anterior Pillars Posterior Pillars Fauces Uvula Soft Palate	Posterior Pillars Fauces Uvula Soft Palate	Uvula (Base only) Soft Palate	

The Mallampati classification is used to predict the ease of direct laryngoscopy and endotracheal intubation. A high Mallampati score (≥ 3) is associated with more difficult intubation. The score is determined with patient in a sitting position with the jaw thrust forward, the tongue protruded and without phonation. This cannot be performed by young children or in anyone in a supine position or a cervical collar.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS (ASA) CLASSIFICATION	
1	Healthy patient. No medical problems
2	Mild systemic disease
3	Severe systemic disease but not incapacitating
4	Severe systemic disease that is a constant threat to like
5	Moribund. Not suspected to live 24hrs
Scores ≥ 3 suggest an increased risk of adverse events or a difficult airway. Consult anesthesia for sedation in more controlled setting	

FASTING STATUS

ASA: FASTING GUIDELINES	
INGESTED MATERIAL	MINIMUM FAST
Clear liquids	2 hours
Breast milk	4 hours
Infant formula, non-human milk	6 hours
Light meal	6 hours

Anesthesia guidelines were developed for elective operative procedures and may not be applicable to emergency departments. These patients have a higher risk of aspiration because they are undergoing intubation and receiving paralytics.

In a prospective cohort study that included 1,014 pediatric patients who underwent procedural sedation in the emergency department, there was no statistically significant difference in adverse events for those meeting fasting guidelines (8.1%, 95% CI (5.6, 11.2%)) and those not meeting fasting guidelines (6.9%, 95% CI 4.8, 9.4%)), Risk Difference: 1.2%, 95% CI (-2.2, 4.8%), (Agrawal, Ann Emerg Med. 2003, PubMed ID: 14581915). The authors concluded that “Despite the fact that these patients were not fasted for the appropriate duration (as defined by the fasting guidelines), they did not have any additional adverse events, including emesis. Noncompliance with the American Academy of Pediatrics/American Society of Anesthesiologists preprocedural fasting guidelines does not appear to be a contraindication to emergency department procedural sedation and analgesia”

In a retrospective cohort study of 2,085 children sedated by ED physicians at a single emergency department, adverse events were not linked to shorter pre-procedural fasting times. There was no statistically significant difference in the rate of any adverse event for any time intervals when compared to the rate at 0-2 hours (Roback, Ann Emerg Med. 2004, PubMed ID: 15520704).There was also no statistically significant association between fasting time and respiratory adverse events or vomiting when these were analyzed independently. The authors concluded that “Published guidelines for preprocedural fasting exist despite lack of data to support their impact on patient safety. These guidelines are also difficult to implement and impractical in an ED setting. Our data support previously reported conclusions that emergency physicians provided safe procedural sedation and analgesia for pediatric procedures, regardless of preprocedural fasting times.”

The 2014 American College of Emergency Physicians clinical policy on sedation and analgesia in the emergency department recommend to “not delay procedural sedation in adults or pediatrics in the ED based on fasting time. Pre-procedural fasting for any duration has not demonstrated a reduction in the risk of emesis or aspiration when administering procedural sedation and analgesia.” (Level B recommendation) (ACEP, Annals EM 2014, PubMed ID: 24438649).

ADVERSE EVENTS

Adverse events can occur as results of over sedation or due to medication specific properties. Personnel trained in pediatric airway management should be dedicated to monitor the patient and not directly participating in the procedure. Age-appropriate resuscitation equipment including rescue airway equipment and resuscitation drugs and reversal agents should be immediately available. Monitoring should include a pulse oximeter, cardiac monitor and continuous end tidal CO_2 (capnography).

A prospective cohort study included 6,295 children who received sedation for a painful procedure by an ED physician in 6 Children’s Hospital Emergency Departments (Bhatt, JAMA Pediatrics 2017, PubMed ID: 28828486). Sedation-related adverse events occurred in 1 in 10 patients (11.7%, 95% CI (6.4, 16.9%)), and serious adverse events 1 in 100 patients (1.1%, 95% CI (0.5, 1.7%)). Oxygen desaturation (5.6%, 95% CI (2.0, 9.2%)) and vomiting (5.2%, 95% CI (2.4, 8.0%)) were the most common sedation related adverse events. Apnea (0.9%) was the most common serious adverse event. Laryngospasm (0.1%), hypotension and (0.1%), bradycardia (0.1%) occurred less frequently. There was no complete airway obstruction, pulmonary aspiration, permanent neurologic disability or death. Positive pressure ventilation was the only significant intervention required (1.4%, 95% CI (0.7, 2.1%).

Risk factors associated with an increased risk of serious adverse events included the use of Ketamine in combination with other medications or non-Ketamine regimens when compared to Ketamine alone. Risk factors associated with an increased risk for significant interventions included combination Ketamine sedation, laceration repair, and pre-procedural opioids. . In a sub-analysis, earlier administered opioids were associated with a higher rate of oxygen desaturation and vomiting but not with the need for positive pressure ventilation. Preprocedural Fentanyl was associated with approximately half the rate of adverse events compared to pre-procedural Morphine. (Bhatt, Acad EM 2020, PubMed ID: 31894606).

The incidence of adverse events (1 in 10), serious adverse events (1 in 100) and interventions (1 in 70) emphasize the need for close monitoring and the presence of dedicated sedation personnel with pediatric airway skills.

ADVERSE EVENTS REPORTING (NYU)
Apnea > 30 seconds
Desaturation < 90%
Intervention for airway patency
Assisted or controlled ventilation
Hemodynamic instability
Significant arrhythmias
Use of a reversal agent
Unanticipated hospital admission

LARYNGOSPASM: Laryngospasm is a potentially life-threatening reflex closure of the false and true vocal cords with descent of the epiglottis over the laryngeal opening as a result of stimulation of the recurrent laryngeal nerve. Laryngospasm may be precipitated by: airway manipulation in the lightly sedated patient, vocal cord irritation by secretions, vomiting or blood, upper respiratory infection, and medications (e.g. Ketamine).

Laryngospasm results in partial or complete airway obstruction. Laryngospasm should be suspected whenever airway obstruction occurs, particularly in the absence of an obvious supraglottic cause or if there is a sudden loss of carbon dioxide waveform, drop in oxygen saturation or bradycardia.

LARYNGOSPASM MANAGEMENT
Escalate: Consult Anesthesiology. Ensure equipment for a difficult airway is available
Remove noxious stimuli: Use suction to clear the airway of blood and secretions
Positive Pressure: BVM with 100% O_2, tight seal, jaw thrust, closed pop-off valve
Larsen's Maneuver: Inward and anterior pressure at Larson's point (posterior to the mandibular ramus and just anterior to the stylomastoid process bilaterally)
A chest thrust may temporarily open the vocal cords to allow tube passage.
Succinylcholine. 0.1-0.5 mg/kg may be sufficient. If severe, 1-2 mg/kg IV, 3-4 mg/kg IM if intravenous access not available.
VIDEO LINK: LARSON MANEUVER

SEDATION LEVEL				
	MINIMAL	MODERATE	DEEP*	GENERAL ANESTHESIA
Response to Stimuli	Normal To verbal	Purposeful to verbal/tactile	Purposeful to repeated or painful	Unarousable to any stimuli
Airway	Unaffected	No intervention required	May require intervention	Often require intervention
Breathing	Unaffected	Adequate	May be inadequate	Frequently inadequate
Circulation	Unaffected	Usually Maintained	Usually Maintained	May be impaired

SELECTION OF MEDICATIONS

The type of pharmacologic agent used for analgesia and/or sedation is chosen based on a number of factors. The patient's past medical history such as asthma, allergies to medications or eggs and history of present illness such as head trauma should be considered. The type of procedure, in particular whether it will be painful (e.g.) fracture reduction or not painful (e.g. imaging study) and the duration of the procedure will influence the specific medication utilized. Painful procedures require an agent with analgesic properties. Longer procedures will require multiple doses of medications or longer acting agents (See Appendix: Medications for specific medication properties).

Analgesia and/or sedation can be administered by various routes, such as parenteral (intravenous or intramuscular), oral, rectal, transmucosal, intranasal or via inhalation. The ideal agent would have a rapid onset, short duration, minimal adverse effects, a wide safety margin and be reversible. Unfortunately, no agent currently is "ideal." Only the opioids and benzodiazepines are reversible by naloxone and flumazenil, respectively. Intravenous agents are easily titratable and have the most rapid onset. Oral and transmucosal agents tend to have less pain associated with administration.

DOCUMENTATION
Parental consent
Time out: Correct patient, correct location, correct procedure
Vital signs at regular intervals
Medication dosages, time of administration
Level of consciousness of patient
Adverse effects

DISCHARGE CRITERIA
Vitals signs and pulse oximetry back to baseline
Protective airway reflexes intact
Is arousable and at baselines level of verbal ability
Adequate hydration and can tolerate oral fluids
Can follow age appropriate commands and sit unaided

APPENDIX: MEDICATIONS

MEDICATION SELECTION OVERVIEW			
	ANALGESIC	CARDIOVASCULAR DEPRESSION	RESPIRATORY DEPRESSION
Ketamine	YES	NO	NO
Morphine	YES	YES	YES
Fentanyl	YES	NO	YES
Dexmedetomidine	YES	YES	NO
Propofol	NO	YES	YES
Midazolam	NO	NO	YES
Etomidate	NO	NO	YES
With the exception of Ketamine the risk of adverse events is dose dependent			

KETAMINE	
Class	Phencyclidine derivative, dissociative agent
Pharmacology	IV: Onset 1-2 minutes, Duration 15-30 minutes IM: Onset 5 minutes, Duration 15-60 minutes
Benefits	Rapid onset, amnestic, analgesic Sympathomimetic activity, bronchodilation
Adverse Effects	Respiratory depression Laryngospasm (see below for diagnosis and management) Increased airway secretions May increased ICP (thought the significance unclear) Does not increase IOP Emergence phenomena Exacerbates psychosis
Indications	Short duration painful procedures e.g. lacerations, fracture reduction, abscess incision and drainage
Dose	1-2 mg/kg IV 4 mg/kg IM

INTRAMUSCULAR KETAMINE: In a case series of 1,022 pediatric patients receiving 4mg/kg of Ketamine intramuscularly, sedation was deemed adequate in 98% (Green, Annals of EM 1998, PubMed ID: 9624307). Transient airway complications occurred in 1.4%, emesis occurred in 6.7%, mild recovery agitation in 17.6% and moderate to severe agitation in 1.6%. There were no adverse events with sequelae or interventions requiring intravenous access. A clinical trial randomized 218 patients to intramuscular or intravenous ketamine (Roback, Ann Emerg Med., PubMed ID: 17052563). There was no significant difference in desaturations (Risk Difference: IV (8.3%) – IM (4.0%) = 4.2%, 95% CI (-2.8, 11.3%)). Intramuscular administration was statistically associated with a higher rate of vomiting (Risk Difference: IM (26.2%) – IV (11.9%) = 14.3%, 95% CI (3.7, 24.9%) and a longer ED stay (Median IM (129 minutes) vs IV (80 minutes).

ADJUNCTIVE THERAPY: In the past ketamine was given in conjunction with a benzodiazepine to reduce the incidence of emergence phenomena and atropine to decreased hypersalivation. Neither of these interventions were subsequently found to be beneficial and or associated with an increased risk of adverse events.

In a clinical trial including 255 pediatric patients randomized to receive intravenous Ketamine with Ondansetron or Placebo, vomiting in the ED or within 12 hours of discharge was less frequent in the Ondansetron group in patients older than 5 years (Risk Difference = 18.8% - 6.3% = 12.5%, 95% CI (2.8, 22.7%)) (Langston, Ann Emerg Med. 2008, PubMed ID: 18353503).

ETOMIDATE	
Class	Imidazole sedative hypnotic
Pharmacology	Onset: 1 minute Duration: 3-12 minutes
Benefits	Cardiovascular stability, decreases intracranial pressure
Adverse Effects	Transient cortisol depression, myoclonic activity
Indications	Non-painful radiologic procedures (e.g. head CT)
Contraindications	Adrenal insufficiency, chronic steroid use
Dose	0.2-0.4 mg/kg
Comments	Notify parents and CT technicians before administration that myoclonic jerks may occur, that they do not represent seizure activity and that they are typically is very brief in duration

PROPOFOL	
Class	Sedative-hypnotic
Pharmacology	Onset 1-2 minutes, Duration 3-5 minutes
Benefits	Titratable, decreases ICP, Antiemetic, Anticonvulsant
Adverse Effects	Respiratory depression Apnea (usually resolves with jaw thrust) Cardiovascular depression: Hypotension No analgesic properties, painful administration
Indications	Long duration nonpainful, radiologic procedures (e.g. MRI) Post rapid sequence intubation for head trauma
Contraindications	Hypotension: Maximize volume status prior to use < 6 months associated with high rate of complications Egg/Soy allergies are no longer considered a contraindication
Dose	Adults: Initial dose: 0.5-1.0 mg/kg Subsequent dose: 0.25-0.5 mg/kg Q1-3 minutes to effect Infusion: 100-150 µg/kg/minute (0.1-0.15 mg/kg/min) Children: Initial dose: 1.5–2.0 mg/kg Subsequent dose: 0.5-1.0 mg/kg Q1-3 minutes to effect Infusion: 250 µg/kg/minute (0.25 mg/kg/min)
Comments	An IV fluid bolus should be readily available for hypotension

FENTANYL	
Class	Opioid
Pharmacology	Onset 2-3 minutes Duration 20-60 minutes
Benefits	Analgesic Hemodynamic stability (Less histamine release) Reversible with Naloxone
Adverse Effects	Respiratory depression Chest wall rigidity with high doses or rapid administration
Indications	Painful conditions and procedures
Dose	IV: 1 mcg/kg, maximum dose 100 mcg IN: 1-2 mcg/kg, maximum dose 100 mcg
Comment	Chest wall rigidity may require Naloxone or a paralytic

MORPHINE	
Class	Opiate
Pharmacology	Onset 5-10 minutes Duration 2-4 hours
Benefits	Analgesic Hypotension (Histamine release) Reversible with Naloxone
Adverse Effects	Respiratory depression
Indications	Painful conditions and procedures
Dose	0.1 mg/kg

MIDAZOLAM (VERSED)	
Class	Benzodiazepine
Pharmacology	IV: Onset 1-2 min Duration 30-60 min
Benefits	Amnestic, anxiolysis Anticonvulsant Reversible with Flumazenil
Adverse Effects	Respiratory depression Paradoxical agitation in children
Indications	Anxiolysis Use in conjunction with an opioid for painful procedures
Dose	IV: 0.1 mg/kg IN: 0.1-0.5 mg/kg, maximum dose 10 mg

DEXMEDETOMIDINE (PRECEDEX)	
Class	Alpha 2 agonist, increased activity of inhibitory GABA neurons
Pharmacology	Sedative, anxiolytic and analgesic properties Lipid soluble: Readily cross the blood brain barrier
Benefits	Minimal effects on respiratory function
Adverse Effects	Cardiovascular effects: Hypotension, bradycardia Use with caution in patients with liver and renal disease
Indications	Non-invasive imaging
Dose	Loading: 1-3 mcg/kg over 10 minutes, may be repeated Infusion: 0.5-2 mcg/kg/hour Can be given orally and intranasally as well
Comments	Compared to Propofol: Similar cardiovascular adverse events Without respiratory depression Analgesic Longer induction, recovery and discharge times An IV fluid bolus should be readily available for hypotension

PSYCHIATRY

AGITATION

INTRODUCTION (MARC AUERBACH, M.D., 7/2020)
Aggression is defined as a behavior intended to threaten or inflict injury on self, others, or property; and to act in a domineering or forceful manner. Parents present to the ED for help when they feel that their child or others are in danger. Due to the national shortage of pediatric mental health providers, children are sent to the Pediatric ED for evaluation when their behaviors cannot be control. Unfortunately, these behaviors are exacerbated when acutely ill or hospitalized, and by the extended wait times and the chaotic nature of the ED environment. Many children presenting for acute psychiatric evaluation display aggressive behaviors.

RISK FACTORS FOR AGGRESSION
Past psychiatric history
Prior use of pharmacologic treatment for diagnosis
History of inpatient psychiatric admissions,
Current high levels of violence in environment/media
Alcohol or drug intoxication.

SIGNS OF IMMINENT VIOLENCE
Threats of violence
Paranoid ideation
Yelling, pacing
Agitated behavior
Presence of a weapon

ED providers are inexperienced caring for aggressive children and feel uncomfortable and ill prepared when these children present. Staff often do not recognize escalating behaviors early and do not intervene until the child's behaviors are out of control.

AGGRESSION STAGES	
Verbal	Threatening or inappropriate language.
Agitated Motor	Constant motion, pacing, and agitation
Destructive: Property	Act out physically: Property, inanimate objects
Attack: People	Inflicting harm on self or others.

DIAGNOSIS
Aggression/agitation defines one end of the altered mental status spectrum. (coma on the other end). The differential diagnosis of aggression in children is broad, and organic diseases must be considered before making a psychiatric diagnosis of aggression. (See: PEM Guide: Neurology: Altered Mental Status). The pneumonic FINDME can be used to review the differential diagnosis. The pathophysiology of aggression is thought to be related to an increase in Dopamine, Norepinephrine and GABA or to low or high Serotonin. This leads to increased impulsivity and decreased self-control.

DIFFERENTIAL DIAGNOSIS OF AGGRESSION: FINDME	
Functional	Conduct disorder, Bipolar, Oppositional Defiant Disorder, Schizophrenia, Extreme anxiety
Infectious	Meningitis, encephalitis, sepsis, brain abscess
Neurologic	Tumor, trauma, seizures of the temporal or frontal lobes
Drugs	Sympathomimetics (phencyclidine, cocaine, methamphetamines), anticholinergics, antihistamines, carbon monoxide, aspirin, lithium alcohol Withdrawal syndromes: Alcohol, opiates, benzodiazepines
Metabolic	Wilson's disease, PKU, Hypoglycemia, hyponatremia, hypoxemia, hepatic or hypertensive encephalopathy
Endocrine	Thyroid storm, Cushing's disease, hypoglycemia

MANAGEMENT

The goal of management of agitation is to prevent harm to the patient, staff and environment and to facilitate medical evaluation of the patient (e.g. a head CT). The interventions used to manage aggression include verbal de-escalation and chemical, and/or physical restraint. The clinical approach requires early recognition of progression of behavior patterns and early attempts to deescalate these behaviors. Verbal de-escalation techniques should be employed prior to medication or physical restraints.

GOALS
Maximize patient and staff safety
Assist the patient in managing their emotions and behaviors
Apply the least restrictive, age-appropriate restraint methods
Minimize coercive interventions that may exacerbate agitation

GENERAL MANAGEMENT PRINCIPLES
Introduce yourself. "My job is to keep you safe"
Use a soft voice, simple/concise language and relaxed body language
Remain a safe distance from the patient with a clear path to an exit
Explore reasons why the patient is upset. Ask them what they want.
Set clear limits. e.g. I can't help you if you continue to ….
Validate their feelings
Provide for comfort (e.g. food, reading materials)
Separate from the family if they are contributing to the agitation
Explain consequences of their actions to the patient
Reduce environmental stimuli.
Do not block exits or provoke the patient
Engage psychiatry and hospital police early in the process
Prepare medications and physical restraints
Follow hospital and joint commission standards for chemical and physical restraint

VERBAL DE-ESCALATION: Verbal de-escalation requires confidence, empathy (What is the patient currently doing well despite their agitation and curiosity? What triggered the current behavior?). Staff should involve hospital police when escalation is anticipated. Staff and other patient's safety are a priority. The patient should be provided with comfort measures and opportunities for self-control. An attempt should be made to minimize external stimuli. Staff and hospital police should avoid negative body languages such as prolonged eye contact, crossed arms, and sudden movements. These may be interpreted as confrontational and lead to an escalation in behavior.

Verbal de-escalation is effective if done early and well. Inform the patient of their effect on others by talking directly to them in a respectful manner. Question the child regarding their intent to harm self or others and what can be done to help them.

Restriction of the child to a limited space within the ED is the next step in management. Hospital police should be used to enforce 1:1 observation and confinement. This provides safety for child and others in the ED.

CHEMICAL/PHYSICAL RESTRAINT: Involuntary immobilization through chemical and/or physical restraint is the final step in management. Hospital and Joint Commission policy should be strictly adhered to. Prior to taking this action the staff must inform the child and family of the plan for restraint.

CHEMICAL SEDATION/ANXIOLYSIS: Chemical restraint entails the use of medications to control behavior or restrict movement for safety. The goal is a calm but still interactive patient. The three classes of agents typically used for sedation include: benzodiazepines, typical antipsychotics, and atypical antipsychotics. Often one of the antipsychotic classes is used in conjunction with a benzodiazepine. An antipsychotic should be avoided in patients with agitation due to anticholinergic toxicity.

There is some evidence in adults that Haloperidol and Lorazepam in combination have great efficacy the either agent used alone. There is little evidence on the use of these agents for sedation in children. As such, there are no FDA approved medications for chemical restraint in children.

Medication selection is based on the degree of agitation and cooperation and prior history of psychiatric medications. Patients should be offered an oral dose of medication first. This could be an oral dose of their medication. This allows the patient to participate in and control their care as well as engender trust in the care team. See Appendix for dosing.

MEDICATION SELECTION		
Etiology	Mild-Moderate Agitation	Severe Agitation
Medical/Intoxication	Benzodiazepine	Benzo ± Antipsychotic
Psychiatric	Benzo or Antipsychotic	Antipsychotic
Unknown	Benzo or Antipsychotic, Add the other if first is ineffective	

MEDICATIONS: POSSIBLE ADVERSE EFFECTS
Respiratory depression
Hypotension
Paradoxical reaction from benzodiazepines (young and autistic children)
Dystonic reactions
Dysrhythmias: Antipsychotics QTc, exacerbated by other QT medications, dehydration, metabolic abnormalities. liver or kidney disease
Rhabdomyolysis
Cardiorespiratory monitor, obtain EKG

1. BENZODIAZEPINES: Benzodiazepines provide sedation and anxiolysis through an increase in GABA transmission. Complications include: respiratory and central nervous system depression, ataxia and paradoxical reactions. Paradoxical reactions are more common in children with development delay and when given in conjunction with a typical antipsychotic.

Benzodiazepines should be used with extreme caution for those who have ingested other respiratory depressants such as alcohol, barbiturates and opioids. Diazepam is erratically absorbed intramuscularly. Lorazepam and Midazolam are preferred.

2. TYPICAL ANTIPSYCHOTICS: The typical antipsychotics act as dopamine receptor antagonists. They treat the agitation as well as their psychiatric illness. They are less effective in those without underlying psychiatric illness. Haloperidol (Haldol) is the most common agent used. It can be administered orally, intramuscularly or intravenously. The onset is 30-60 minutes and duration up to 24 hours with IM/IV administration. Chlorpromazine (Thorazine) has a greater sedative effect and a higher risk of hypotension than Haloperidol.

TYPICAL ANTIPSYCHOTICS: ADVERSE EVENTS	
Extrapyramidal Symptoms	Dystonia, akathisias (motor restlessness) and Parkinson like effects Treatment: Anticholinergics (e.g. Diphenhydramine, Benztropine)
Dystonic Reactions	Severe muscle contraction resulting in torticollis, tongue protrusion, opisthotonus, oculogyric crisis, laryngospasm. Treatment: Diphenhydramine
Neuroleptic malignant syndrome	Altered mental status, autonomic instability and severe muscle rigidity. Can result in rhabdomyolysis, renal failure, aspiration pneumonia and cardiopulmonary arrest. Treatment: Cooling methods, intravenous fluids, benzodiazepines, Bromocriptine and possibly Dantrolene (off-label use).
Others	Lowers seizure threshold, impairs heat dissipation, prolongs QTc, hypotension, Torsades

3. ATYPICAL ANTIPSYCHOTICS: Atypical antipsychotics target dopamine and serotonin receptors. Agents in this class included: Risperidone (Risperdal), Ziprasidone (Geodon) and Olanzapine (Zyprexa). They are less likely to result in severe adverse events than typical antipsychotics though extrapyramidal symptoms and neuroleptic malignant syndrome can rarely occur. May have a higher risk of dystonia particularly in males and younger patients. Ziprasidone has a greater risk of QTc prolongation than Haloperidol or the other atypical antipsychotics. Olanzapine has been associated with hypotension, bradycardia and respiratory depression. Olanzapine should not be administered with other respiratory depressants such as a benzodiazepine. There is little evidence supporting efficacy and what data does exist is primarily in adults.

PHYSICAL RESTRAINT: The application of physical restraint should be considered as a “Restraint Code” and involve experienced staff with a designated leader. Physical restraint must only be used for safety and never for punishment or due to lack of resources. When applying restraint care must be taken not to restrict circulation, foam should be used to protect points of skin contact, and the patient should never be secured to bed rails.

Physical restraint has been associated with significant morbidity and mortality. Risks include: skin damage, respiratory depression, aspiration, rhabdomyolysis, and death. In national databases, 26% of reported restraint deaths occur in children. Deaths have been associated with prone holds and use by inexperienced providers.

DISPOSITION

Disposition decisions should be made in conjunction with child psychiatry.

ADMISSION INDICATIONS
Suicide attempt or gesture
Depression with suicide plan
Depression with inability to function
Psychotic episode
Conduct deemed to harm self/others
Complications of substance abuse

APPENDIX: MEDICATIONS FOR AGITATION

MEDICATIONS FOR AGITATION			
NAME	DOSE	PEAK	COMMENTS
ANTIHISTAMINES			
Benadryl	1 mg/kg PO/IM/IV 12.5-50 mg PO/IM IV	2 hours	Avoid in delirium Can add to Haldol for EPS
ALPHA AGONIST			
Clonidine	0.05-0.1 mg PO	0.5-1 hours	Monitor BP Avoid: BZD, atypical→↓BP
Guanfacine	0.5-1.0 mg PO	1-3 hours	Monitor BP Sedation < Clonidine
BENZODIAZEPINE			
Lorazepam (Ativan)	Child: 0.05-0.1 mg/kg Adult 2-4 mg PO, IM, IV	IV: 30min IM: 1 hour PO: 2 hours	Onset: 5-10 min IV 15 min IM, 20-30 min PO Avoid: Olanzapine (↓ Resp) Avoid: Other sedative hypnotics
Midazolam (Versed)	0.1 mg/kg PO, IM, IV	IV: 5-15 min IM:15-30 min PO: 60 min	Onset: 5-10 min IV 15 min IM, 20 min PO Avoid: Other sedative hypnotics
1ST GENERATION ANTIPSYCHOTICS			
Thorazine (Chlorpromazine)	12.5-50 mg PO 6.25-25 mg IM	PO: 30 min IM: 15 min	Sedation > Haldol, ↓ BP
Haloperidol (Haldol)	0.025-0.075 mg/kg Child: 0.5-2 mg Adol: 2-5 mg Adult: 5-10 mg PO/IM	IM: 1 hour PO: 3 hours	Onset: 20-30 min IM 45-60 min PO
2ND GENERATION ANTIPSYCHOTICS			
Quetiapine (Seroquel)	25-50 mg PO	0.5 hours	More sedating at lower doses
Risperidone (Risperdal)	Child: 0.25-0.5 mg Adol: 0.5-1.0 mg PO/IM	PO: 1-2 hours	Oral liquid and oral dissolving tables (ODT) as available
Olanzapine (Zyprexa)	Child: 2.5 mg Adol: 5-10 mg Adult: 10 mg PO/IM	PO: 6 hours IM: 15-45 min	Onset: IM: 10-20min PO: 20-30 min Not within 1 hr of BZD due to respiratory depression
Ziprasidone (Geodon)	12-16 years: 10 mg > 16 years: 10-20 mg	IM: < 60min PO: 6-8 hrs	Onset: IM 60 min, PO 4-5 hrs
Combination Regimens: Diphenhydramine + Atypical or Typical Antipsychotic Benzodiazepine + Atypical or Typical Antipsychotic			

DEPRESSION AND SUICIDE

INTRODUCTION (MICHELLE VAZQUEZ, M.D., 12/2018)
At least 15% of children and adolescents suffer from depression. By the age of 14, twice as many females than males will suffer from a depressive disorder. Unfortunately, many of these children will end their own lives. Suicide is the fourth leading cause of death among all children and the third leading cause of death between the ages of 10-19 years. Females have more suicide attempts though males are more successful at completion of suicide. Females are likely to choose the less lethal methods such as medication ingestion and cutting. Males are likely to choose more lethal methods such as firearms, drowning, suffocating and hanging.

DIAGNOSIS
Depression rarely presents as the chief complaint and physicians must be aware of complaints that may represent depression at each development level.

The clinical interview is the most important component of the diagnosis of depression. A detailed history of symptoms and level of functioning should be obtained. Questions about suicidal thoughts and self-injurious behavior should also be asked.

School age children are more likely to present with behavioral problems (such as poor frustration tolerance or temper tantrums) or social withdrawal. In addition, children are more likely to present with an irritable mood (then a depressed mood). Somatic complaints such as fatigue, abdominal pain and headache are common. Weight loss and hypersomnia are less likely. Psychotic features are rare in this age group

In adolescence, depression is twice as common in females. Symptoms mimic those in adults though features seen in early childhood may occur as well. Adolescents should be interviewed alone and collateral information obtained from caregivers. They should be asked about substance abuse, sexual activity, suicidal thoughts, self-harm and high-risk activities.

DEPRESSIVE DISORDER RISK FACTORS
Patient or Family History of depression
Pubertal hormonal changes
Chronic Illnesses
Female sex
Medication induced (Isotretinoin)
Physical, emotional or sexual abuse
Socioeconomic deprivations
Loss of a loved one, parent, or romantic relationship
Anxiety Disorder
Attention deficit hyperactivity disorder
Conduct or learning disorders
Cigarette Smoking, substance abuse

Depression increases the risk of other psychiatric disorders such as disruptive behavioral disorders, personality disorders and substance abuse disorders. The comorbid disorders may interfere with treatment. Episodes of depression can also occur as part of bipolar spectrum disorders.

DEPRESSIVE DISORDERS (DSM V)
Disruptive mood dysregulation disorder
Major depressive disorder (including major depressive episode)
Persistent depressive disorder (dysthymia)
Premenstrual dysphoric disorder
Substance/medication-induced depressive disorder
Depressive disorder due to another medical condition
Other specified depressive disorder
Unspecified depressive disorder
Common: Presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the capacity to function. Differences: Duration, timing, presumed etiology Differences: Duration, timing, presumed etiology

MAJOR DEPRESSIVE DISORDER CRITERIA: DSM V	
FIVE OR MORE SYMPTOMS PRESENT FOR AT LEAST 2 WEEKS	
AND MUST HAVE EITHER:	
1	Depressed mood most of the day, nearly every day.
2	Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.
ADDITIONAL SYMPTOMS	
3	Significant weight loss when not dieting or weight gain, or decrease or increase in appetite nearly every day.
4	A slowing down of thought and a reduction of physical movement (observable by others, not merely subjective feelings of restlessness or being slowed down).
5	Fatigue or loss of energy nearly every day.
6	Diminished ability to think or concentrate, or indecisiveness, nearly every day.
7	Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
8	Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
Must cause the individual clinically significant distress or impairment in social, occupational or other important area of functioning. Must also not be a result of substance abuse or another medical condition.	

A major depressive episode is considered mild when there are a few symptoms and function is not impaired. Severe episodes may be accompanied by psychotic features such as auditory hallucinations and delusions. Dysthymic disorder is usually less severe but may last longer. Depressive disorder not otherwise specified (NOS) occurs when depression symptoms are present but criteria for major depressive disorder or dysthymic disorder are not met.

An adjustment disorder is a response to a stressful event the results in depressive, anxious or behavioral symptoms that do not meet criteria for a major depressive episode.

A number of depression screening instruments exist that have adequate predictive ability. They can provide the basis for obtaining more detailed information. Broadband rating scales assess multiple symptom areas but are less helpful than depression specific scales.

All patients with depressive symptoms should be assessed for suicidal thoughts and behaviors and incidents of self-harm. While it is impossible to confidently predict subsequent suicide a number of factors are associated with an increased risk. If a patient is thought to be of greater than minimal risk in the short term then a mental health care provider should be consulted.

SUICIDE RISK FACTORS
Previous suicide attempt
Mood disorder: Depression, Anxiety
Conduct disorder, Personality disorder, Psychotic disorder
Alcohol and/or substance abuse
Impulsive or violent Behavior
Chronic physical illness
Current plan with active intent and availability of lethal means (meds, firearms)
Isolated, hopelessness
Real or Imagined loss: Relationship, school, or financial loss
Gay, lesbian, bisexual, transgender or questioning youth (particularly males)
Physical or sexual abuse of children in the family
Family History of mental health issues, substance abuse, and suicide behavior
Recent stressful life event (Divorce or Death)

FACTORS PROTECTIVE OF SUICIDE
Problem Solving Skills
Religious Beliefs
Academic Achievement
Family Support and connectedness
Medical and mental health provider support
Lack of access to lethal methods
Community and school support/connectedness

MANAGEMENT

Upon arrival to the ED a thorough history and physical examination must be done to establish origin of depressive symptoms and suicidality. The extent of laboratory and other medical workups should be guided by symptoms and findings. Initial testing generally includes: CBC, electrolytes, beta HCG, serum salicylate and acetaminophen levels, a urine toxicology screen and thyroid functions tests.

ACUTE MANAGEMENT OF A SUICIDE ATTEMPT
Medical stabilization
Place patient on 1:1 observation in a safe environment
Obtain collateral information from guardians/friends/witnesses

MEDICAL CONDITIONS MIMICKING DEPRESSION	
MEDICAL CONDITIONS	DRUGS/MEDICATIONS
Anemia	Alcohol
Autoimmune disorders	Barbiturates
Electrolyte abnormalities	Benzodiazepines
Epilepsy	Cocaine
Hypothyroidism	Contraceptives
Mononucleosis	Corticosteroids
NDMA receptor encephalitis	Isotretinoin
Traumatic brain injury	Marijuana
Vitamin deficiency	Methamphetamines

DISPOSITION

Patients who express a persistent wish to die or have an abnormal mental state should be admitted for their safety. Patients who are assessed as low risk for suicide may be discharged with specific psychiatry follow-up. Concerns about patient safety should be discussed with caregivers. Adequate adult supervision and support should be in place. Any lethal medications or firearms should be removed from access. A plan should be in place indicating what to do and who to contact in the event of a crisis. Patients may agree to suicide prevention contracts.

A 2015 study, attempted to prospectively validate the Columbia Suicide Severity Rating Scale (C-SSRS: See Appendix) in predicting return psychiatric emergency visits for suicide attempts. (Gipson, Pediatr Emerg Care. 2015, PubMed ID: 25285389). The study was conducted at a single center and included 178 adolescents who presented for emergency psychiatric care of which approximately half presented for suicidal ideation or attempt and of which three quarters had a prior psychiatric history. 6.7% re-presented with suicide attempt in the week prior. Three predictors were independently associated with a return emergency psychiatric visit for a suicide attempt. These included: C-SSRS Intensity Scale (aOR 1.09, 95% CI (1.01, 1.17), C-SSRS Intensity Scale: Duration item (aOR 1.80, 95% CI (0.88, 3.65) and a history of non-suicidal self-injury (aOR not presented). The authors concluded that “Psychiatric emergency service providers may use the C-SSRS in conjunction with other suicide risk assessment tools to aid with clinical decision-making”.

SUICIDE PREVENTION CONTRACTS	
No Suicide Assurance	Single question/answer stating no future suicide behavior
No Suicide Agreement	Verbal agreement stating no future suicide behavior for discrete time period, with safety strategies in case of crisis
No Suicide Contract	Written agreement, usually cosigned, stating no future suicide behavior for discrete time period, with safety strategies in case of crisis; usually used in higher risk patients (previous suicide attempts)

APPENDIX: COLUMBIA SUICIDE SEVERITY RATING SCALE

WEB LINK: C-SSRS

Semi-structured Interview measuring the intensity of suicidal ideation and behavior

Severity Sub-scale
0 = no ideation, 1 wish to be dead, 5 suicidal intent with plan
(Score ≤ 3 indicates no intent, 4-5 indicates intent)

Intensity Sub-scale
Applied only to those with severity scale ≥ 1
A severity subscale of 0 results in an intensity subscale score of 0
5 items: Frequency, duration, controllability, deterrents, reasons for ideation
Ordinal scale: Total 2-25

Posner, Am J Psychiatry 2011, PubMed ID: 22193671

EATING DISORDERS

INTRODUCTION (JENNIFER GRAD, MD, 10/2021)
Eating disorders are defined as a persistent disturbance of eating that impairs health or psychosocial functioning. They can be serious and life-threatening disorders. Anorexia has a mortality rate of 5-6%, the highest of any psychiatric illness. The etiology of eating disorders is unknown. There is likely a confluence of etiologies including biologic, environmental, sociocultural influences and psychological traits. Evidence supports heritability. Dieting behaviors are a risk factor for developing an eating disorder.

EATING DISORDER CLASSIFICATION (DSM-5)
Anorexia Nervosa (AN)[1]
Bulimia Nervosa (BN)[1]
Binge Eating Disorder (BED)
Other Specified Feeding and Eating Disorder (OSFED)
Pica
Rumination Disorder
Avoidant/Restrictive Food Intake Disorder (ARFID)
Unspecified Feeding or Eating Disorder (UFED)
Other: Muscle Dysmorphia
Other: Orthorexia Nervosa (ON)
1. See Appendix: DSV-5 Criteria

A systematic review of eating disorder prevalence was conducted on 1994-2015 data and found the prevalence of eating disorders to range from 1.0-22.7% in females and 0.3-0.6% in males (Dahlgren, Int J Eat Disord, PubMed: 27528542). A national cross-sectional survey of adolescents aged 13-18 years found the lifetime prevalence estimates for anorexia nervosa (0.3%), bulimia nervosa (0.9%), and binge-eating disorder (1.6%) with a mean age of onset of 12.5 years (Granillo, J Adolesc Health 2005, PubMed ID: 15737777). There has been an increase in eating disorders in younger children, boys and ethnic and sexual minority groups. This PEM Guide will focus on the medical management of eating disorders in the emergency department.

DEGREE OF MALNUTRITION			
	MILD	MODERATE	SEVERE
% median BMI[1]	80-90%	70-79%	< 70%
BMI Z Score	-1 to -1.9	-2 to -2.9	-3
Weight Loss	>10% body mass	>15% body mass	> 20% (1 year) > 10% (6 months)

1. a. Identify the 50% BMI for patient's age and sex
   b. Convert recent height to meters (m^2)
   c. Use equation kg = BMI x m^2 to determine the weight in kg for 50% BMI
   d. Divide current weight by weight at 50% BMI

WEB LINK: BMI: MALES, BMI: FEMALES

CLINICAL MANIFESTATIONS

HISTORY AND PHYSICAL EXAMINATION	
Weight History	Date of onset of weight loss? Current weight? Intentional vs. Unintentional weight loss? Fear of gaining weight? Weight loss strategies? Body image perception?
Diet	Counting calories? Avoidance of certain food groups?
Exercise	Type? Duration? Frequency?
Menstrual	Age of menarche? Last menstrual cycle? Duration of menses? Cycle length? Contraception?
Review of Systems	Screen for inflammatory bowel diseases, hypothalamic-pituitary tumors, tuberculosis, HIV, oncological processes: Fatigue? Headaches? Weakness? Dizziness? Dental Caries? Nausea? Dysphagia? Abdominal pain? Diarrhea? Constipation? Bloody stool? Hair changes? Dry skin? Cold or Heat intolerance? Purging? Binging? Diet pills? Laxatives?
Past Medical	Fractures? Previous ED evaluations? Psychiatric history? Screen for anxiety, depression, suicidal ideation.
Dermatologic Effects	Lanugo, telogen effluvium, dry scaly skin, yellow discoloration related to carotenemia, brittle nails, angular cheilitis, acrocyanosis, and abrasions/calluses over knuckles.
Dental/Oral Effects	Dental erosions and caries, hypertrophy of the parotid and other salivary glands, and xerostomia from salivary gland dysfunction or psychiatric medication side effects.
Cardiovascular Effects	Bradycardia, orthostasis, chest pain, palpitations, and poor peripheral perfusion.
Gastrointestinal Tract Effects	Nausea, bloating, postprandial fullness due to delayed gastric emptying and slow intestinal transit time, constipation, esophageal mucosal damage from self-induced vomiting, and bleeding secondary to Mallory-Weiss tears.
Renal/Electrolyte Effects	Dehydration and peripheral edema with abrupt cessation of laxatives.
Endocrine Effects	Physical overactivity, stress, amenorrhea, small testicular volumes, growth retardations, short stature, and pubertal delay.
Musculoskeletal	Muscle wasting/atrophy

COMPLICATIONS

Medical complications related to refeeding include night sweats, polyuria, nocturia, electrolyte abnormalities, edema, seizures, and congestive heart failure.

DIFFERENTIAL DIAGNOSIS	
WEIGHT LOSS	
Gastrointestinal	Inflammatory bowel disease; Celiac disease
Endocrine	Hyperthyroidism; Diabetes mellitus; Adrenal insufficiency
Infectious	Chronic infections (Tuberculosis, HIV); Intestinal parasites
Psychiatric	Depression; Psychosis; Anxiety; OCD; Substance use
Other	Neoplasm; Superior mesenteric artery syndrome
VOMITING	
Gastrointestinal	Inflammatory bowel disease; Celiac disease
Endocrine	Hyperthyroidism; Diabetes mellitus; Adrenal insufficiency
Infectious	Chronic infections (Tuberculosis, HIV); Intestinal parasites
Psychiatric	Depression; Psychosis; Anxiety; OCD; Substance use
BINGE EATING OR UNEXPLAINED WEIGHT GAIN	
Endocrine	Hypothyroidism; Hypercortisolism
Psychiatric	Depression
Iatrogenic	Medication side effect
Genetic	Prader Willi syndrome; Kleine-Levin syndrome

COMPLICATIONS	
Constitutional	Cachexia, hypothermia, muscle atrophy, vitamin deficiencies.
Cardiovascular	Congestive heart failure and edema.
	Structural changes: LV mass, LV end diastolic/systolic volume, mitral valve prolapse, pericardial effusion, myocardial fibrosis.
	EKG: Sinus bradycardia, 1st-degree heart block, LV forces, QTc, PR, ST-T wave changes, right axis deviation and repolarization abnormalities that may lead to lethal arrhythmias.
Dermatologic	Dry, yellowing skin, lanugo hair (fine, thin), hair loss.
Endocrine	Euthyroid syndrome, hypoglycemia/hyperglycemia, impaired glucose tolerance, and decreased bone mineral density.
Gastro-intestinal	Superior mesenteric artery syndrome, hepatic transaminitis, pancreatitis, hypercholesterolemia, and elevated coagulation times.
Hematologic	Leukopenia, anemia, thrombocytopenia, elevated ferritin, and depressed erythrocyte sedimentation rate.
Neurologic	Cerebral atrophy, cognitive deficits, peripheral neuropathy, seizures.
Psychiatric	Mood dysregulation, obsessive-compulsive symptoms, anxiety.
Pulmonary	Muscle wasting, decreased pulmonary capacity, respiratory failure, spontaneous pneumothorax and/or pneumomediastinum.
Renal and Electrolyte	Dehydration, disordered osmotic regulation, hypokalemic, hypochloremic metabolic alkalosis (due to vomiting), hypocalcemia, dilutional hyponatremia, hypomagnesemia and renal calculi

LABORATORY STUDIES

Initial laboratory evaluation is important to identify medical complications of eating disorders and to rule out alternative diagnoses. Further laboratory testing may include specific vitamin and mineral deficiencies (vitamin B12, vitamin D, iron, and zinc), a Dual-Energy X-ray Absorptiometry (DEXA) scan to evaluate for bone density if the patient has a history of amenorrhea, and stool studies to evaluate for parasites. However, normal laboratory studies do not exclude an eating disorder or need for hospitalization.

LABORATORY TESTING	
BMP, Mag, Phos	Malnutrition, purging, laxative use, refeeding syndrome
CBC	Anemia and signs of marrow suppression from malnutrition
ESR	Inflammatory bowel disease as cause of weight loss
Albumin/Prealbumin	Malnutrition
Celiac screen	Celiac disease as cause of weight loss
TSH, T4	Thyroid disease as a cause of weight change, but malnutrition also causes thyroid dysfunction
Amylase, Lipase	Abdominal pathology if abdominal pain or purging. Amylase concentrations with normal lipase may be a clue to vomiting due to hypertrophy of salivary glands
Urinalysis	Specific gravity for signs of water loading or dehydration
LH, FSH, Estradiol, Prolactin	Degree of hypothalamic-pituitary-ovarian suppression if history of amenorrhea
Testosterone, Gonadotropin	Central hypogonadism
LFTs	Transaminitis may be present in severe malnutrition
Beta-hCG	Pregnancy

EKG CHANGES: HYPOKALEMIA	
EKG CHANGES	ARRHYTHMIAS
P wave height and width	Premature atrial or ventricular contractions
PR interval (1st degree heart block)	Paroxysmal atrial tachycardias
T waves flattened or inverted	Paroxysmal junctional tachycardia
ST depression	Atrioventricular blocks (2nd/3rd degree)
QTc (due to fusion of T and U waves	Ventricular Tachycardia or Torsades
U waves*	Ventricular Fibrillation
*Most common in precordial leads (V4-6), typically > 50% height of adjacent T wave Normal U waves in patients with slow HR are < 50% height of adjacent T wave WEB LINK: LIFE IN THE FAST LANE: EKG LIBRARY	

MANAGEMENT

Patients should be placed on a cardiac monitor to evaluate for arrhythmic events and bradycardia. Cardiology consultation should be contacted from the ED if a patient has an abnormal EKG. The ED providers should also consider Adolescent Medicine consultation early in order to coordinate admission and care. Other inpatient consults may include the following services: Nutrition, Behavioral Health/Child Psychiatry, Social Work, and Child Life. Consider inpatient admission for medical stabilization and to arrange for comprehensive multidisciplinary services at hospital discharge. See Appendix: Potassium Supplementation, Appendix: Hypomagnesemia

Patients should be monitored for refeeding syndrome, which is defined by clinical complications that can occur with fluid and electrolyte shifts during increasing nutrition in malnourished patients. The main complication of refeeding syndrome is hypophosphatemia. During starvation, phosphate stores are depleted. When nutrition is increased in these patients, glucose leads to the release of insulin and cellular uptake of phosphate to be utilized in ATP. A systematic review found the average incidence rate of refeeding hypophosphatemia to be 14% (O'Conner, Nutr Clin Prac 2013, PubMed ID: 4108292). The greatest risk for refeeding syndrome occurs in the first 1-2 weeks of weight gain.

REFEEDING SYNDROME
Shock: Tissue hypoxia
Myocardial dysfunction
Respiratory failure (inability of diaphragm to contract)
Cell lysis: hemolysis, rhabdomyolysis
Seizures

DISPOSITION

The majority of patients with a new diagnosis of an eating disorder require admission for psychiatric and medical management. In patients with existing eating disorders and without significant medical complications disposition decisions should be made in conjunction with the patient's psychiatrist. Patients with life-threatening complications should be admitted to an intensive care unit.

ADMISSION: PICU
Hemodynamic instability/signs of shock
Hypotension < 80/60
HR < 40
Orthostatic: HR > 20 bpm, systolic or diastolic BP > 20 mm Hg
EKG: Rhythm other than normal sinus rhythm or sinus bradycardia
EKG: Multiple PVCs, QTc 500 msec
BMI < 14 kg/m^2, < 70% Ideal body weight
Marked dehydration
Complications: Severe electrolyte abnormalities, syncope

ADMISSION TO FLOOR WITH TELEMETRY
HR 35 BPM while awake with no ventricular ectopic beats (PVCs)
HR 30 BPM while asleep with no ventricular ectopic beats (PVCs)
HR 40 BPM with simple ventricular ectopy (single PVCs)
Complex ventricular ectopy: Ventricular couplets or triplets, ventricular tachycardia, or atrioventricular block with any type of baseline heart rate
QTc >550 msec on baseline ECG if bradycardic QTc >500 msec if heart rate is normal or elevated, or with known history of purging
Significant electrolyte abnormalities: K <2.5, Phosphorus <2.5, Mag <1.5
Recent unexplained syncope

ADMISSION TO FLOOR WITHOUT TELEMETRY
For all other patients who do not meet criteria as outlined above. The plan would be to transfer to floor after 24 hours of observation if there is no complex ventricular ectopy and patients are stable with asymptomatic bradycardia
Failure to respond to outpatient therapy
Dehydration
Refusal to eat
Potassium < 3.2, hyponatremia, phosphorus < 3.0, chloride < 88
75% median BMI for age and sex
Hypothermia (T < 96°F, 36.6°C)
Syncope, seizures, cardiac failure, pancreatitis, hematemesis (esophageal tear)
Comorbid psychiatric or medical condition that prohibits or limits outpatient treatment (severe depression, suicidal ideation, obsessive-compulsive, type 1 diabetes mellitus
Arrested growth and development
Uncontrollable binging and purging

APPENDIX: POTASSIUM SUPPLEMENTATION

POTASSIUM FORMULATIONS	
Chloride	Most commonly used Preferred for hypochloremia, metabolic alkalosis (vomiting)
Phosphate	Renal loss of K+ and phosphorus
	1. Diabetic ketoacidosis
	2. Proximal tubule dysfunction: Fanconi syndrome, cystinosis
Acetate, Citrate	Metabolized to bicarbonate. Hypokalemia due to acidosis (e.g. RTA 1 and 2, diarrhea)

POTASSIUM SUPPLEMENTATION: DOSING[1]			
		ADULT	PEDIATRIC
Daily requirement		40-80 meq/day	50 kg: 2-4 meq/kg/day > 50 kg: 1-2 meq/kg/day
Prevention (Maintenance IV Fluids)		20-40 meq/day Divided QD-BID	1-2 meq/kg/day Divided QD-BID Max dose: 20 meq
Mild-Moderate Hypokalemia (2.5-3.5 meq/L)	PO	40-100 meq/day PO Divided in 2-5 doses Max dose: 40 meq	2-5 meq/kg/day PO Divided BID Max dose: Lowest of 1-2 meq/kg or 20 meq
	IV	10 meq Max conc: 40 meq/L Max rate: 10 meq/hour	0.2-0.5 meq/kg Max dose: 20 meq Max conc: 20 meq/L Max rate: 0.5 meq/hour
Severe Hypokalemia (< 2.5 meq/L) OR Severe Symptoms (arrhythmia, marked muscle weakness, paralysis)	PO	40 meq PO Q6-8 hours or 20 meq PO Q2-3 hours Max dose: 40 meq	5-10 meq/kg/day PO Divided BID Max dose: Lowest of 2 meq/kg or 40 meq
	IV	40 meq Max conc: 40 meq/L Max rate: 40 meq/hour (Central line or IO)	0.5-1.0 meq/kg Max dose: 20 meq Max conc: 40 meq/L Max rate: 0.5 meq/kg/hr

1. Little evidence on the safety and efficacy of specific dosing regimens. Above dosing adapted from Lexicomp
2. Dosing should be adjusted lower to account for renal or hepatic insufficiency
3. Central line and cardiac monitoring for > 10 meq/hour IV or > 0.5 meq/kg/hour
4. Avoid dextrose contained IV fluids Insulin secretion K+
5. 10 meq IV KCL K+ by 0.1 meq/L
6. Hypokalemia may be refractory to supplementation if hypomagnesemia (diarrhea, diuretics) is not first corrected

APPENDIX: HYPOMAGNESEMIA

PHYSIOLOGY
Intracellular: Bone (primary site)
Extracellular: Ionized (free), bound to anions, bound to protein.
Small GU or renal losses Significant hypomagnesemia (little exchange between serum and bone)
Normal: 1.7-2.1 mg/dL (0.7-0.9 mmol, or 1.4-1.8 mEq/L)

ETIOLOGY
GI Losses: Diarrhea (15 meq/L) > Vomiting (1 meq/L), proton pump inhibitors, pancreatitis, malabsorption, genetic
Renal Losses: Diuretics, aminoglycosides, hypercalcemia, poorly controlled diabetes, tubular dysfunction, genetic, alcoholism
Often associated with
1. Hypokalemia: Mg^{++} Urinary K+ excretion
2. Hypocalcemia: Mg^{++} Parathyroid hormone, end-organ PTH resistance

CLINICAL
Neuromuscular: Tetany, seizures, tremor, weakness, athetoid/choreiform movements, coma
Cardiac: Moderate: QRS, QT, peaked T waves
Severe: PR, small T waves, atrial/ventricular arrhythmias (e.g. Torsades)
Unexplained hypocalcemia
Refractory hypokalemia

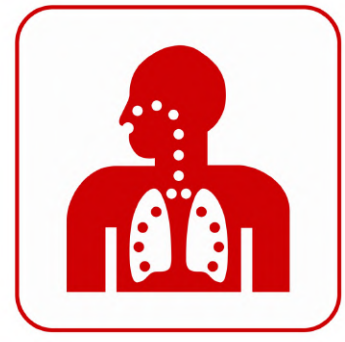
MANAGEMENT
Dose: 50 mg/kg (max 2 grams) over 1-2 minutes (pulseless), 50 mg/kg (max 2 grams) over 15 minutes (with a pulse)
Can be followed by infusion: Adult 3-20 mg/min

APPENDIX: DSM-V EATING DISORDER CRITERIA

ANOREXIA NERVOSA (AN): DSM-V CRITERIA			
Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health.			
Significantly low weight is defined as a weight that is less than minimally normal or, for children and adolescents, less than that minimally expected.			
Intense fear of gaining weight or of becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight.			
Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.			
SUBTYPES			
Restricting type:	During the last 3 months, the individual has not engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas). This subtype describes presentations in which weight loss is accomplished primarily through dieting, fasting, and/or excessive exercise.		
Binge-eating purging type:	During the last 3 months, the individual has engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas).		
SEVERITY			
Mild	BMI > 17 kg/meters^2	Severe	BMI 15.0-15.99 kg/meters^2
Moderate	BMI 16.0-16.99 kg/meters^2	Extreme	BMI < 15 kg/meters^2

BULIMIA NERVOSA (BN): DSM-V CRITERIA			
Recurrent episodes of binge eating			
An episode of binge eating is characterized by both of the following			
Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances.			
A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).			
Recurrent inappropriate compensatory behaviors in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.			
The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 months.			
Self-evaluation is unduly influenced by body shape and weight.			
The disturbance does not occur exclusively during episodes of anorexia nervosa.			
SEVERITY	Average Number of Inappropriate Compulsory Behaviors per Week		
Mild	1-3 episodes	Severe	8-13 episodes
Moderate	4-7 episodes	Extreme	14 episodes

RESPIRATORY



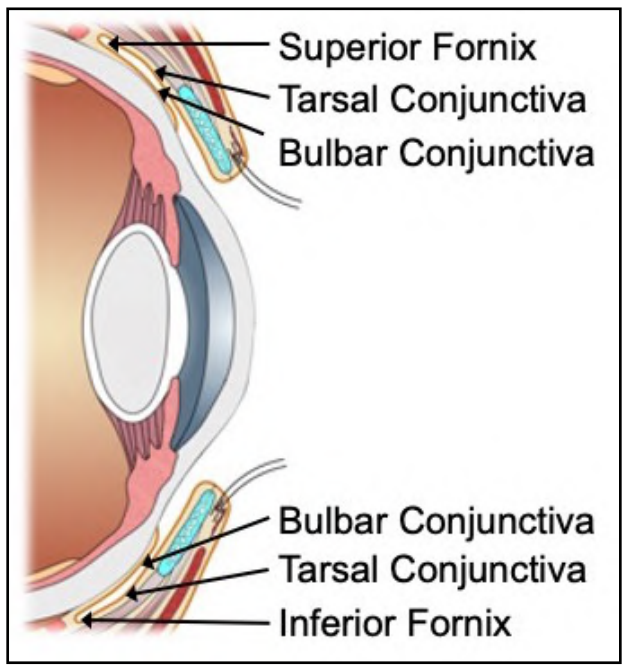
ALLERGIC CONJUNCTIVITIS AND RHINITIS

INTRODUCTION (NICOLE BARNEY, MD, YOSEFA SILBER, MD, 4/2022)
Pediatric allergic disease is very common in the United States and comprises a spectrum of disorders including asthma, rhinitis, conjunctivitis, and urticaria/anaphylaxis. At least twenty-five percent of children will be affected at some point, many of whom will present to the ED for management. The focus of this PEM Guide will be on allergic conjunctivitis and allergic rhinitis. See also: PEM Guide: Respiratory: Anaphylaxis

There are three classifications for allergic rhinitis and conjunctivitis: acute, seasonal and perennial. Acute allergies, such as allergies to pets are due to episodic exposure to an allergen. Seasonal allergies are typically transitory in nature and are triggered by seasonal airborne allergens (most often pollens). Seasonal allergies have a subacute onset and their duration is dependent on peak time of exposure. In contrast, perennial allergies occur in response to indoor allergens such as house animal dander, cockroaches house dust mites, or mold sores. Their presentation is often milder than that of seasonal allergies, with a more persistent, waxing and waning course.

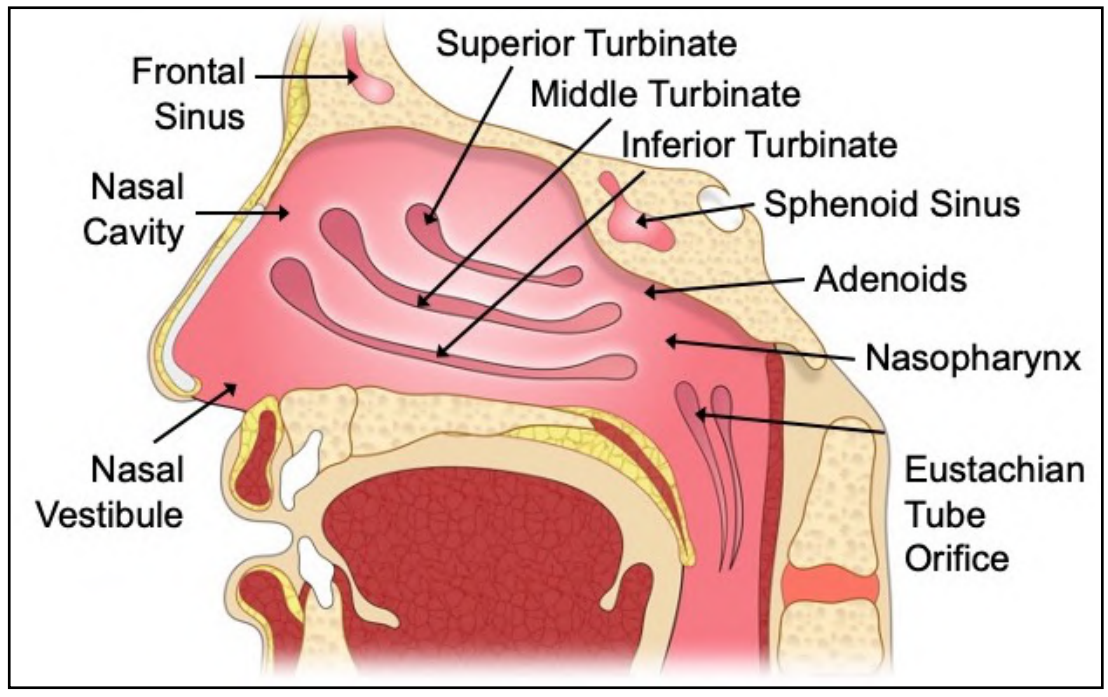
ANATOMY

The conjunctiva is the mucous lining that covers the sclera up to the corneal rim (bulbar conjunctivae) as well the inner surface of the eyelids (palpebral or tarsal conjunctivae). It is typically translucent. Inflammation and vasodilation lead to hyperemia, giving it a pink hue.

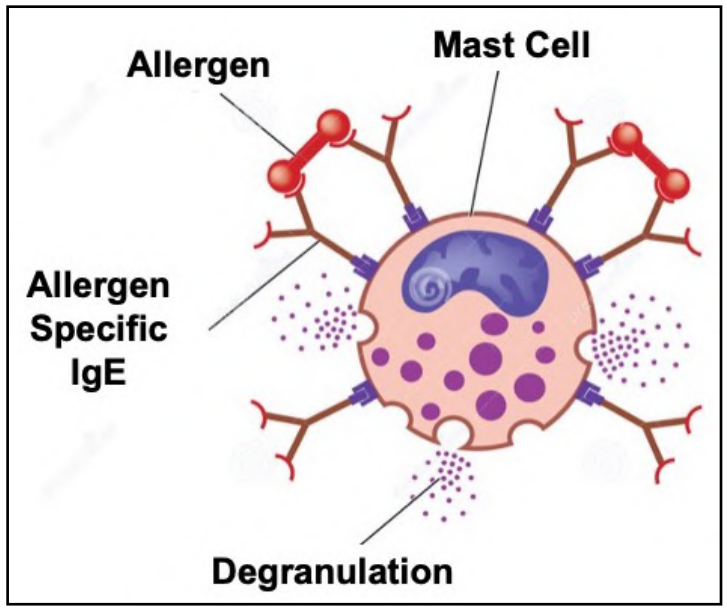


The nasal cavity is the narrowest part of the respiratory tract and is divided by the nasal septum. The turbinates are bony and soft-tissue structures on each side of the septum and serve to warm and moisten the air. The nasal passage is lined by mucous membranes that can become hyperemic and edematous when inflamed.

The nasolacrimal gland creates the tear film covering the ocular surface. The nasolacrimal duct opens lateral to the inferior turbinate. The physical connection via the nasolacrimal apparatus is one reason allergic conjunctivitis and allergic rhinitis are often concomitant processes.



PATHOPHYSIOLOGY



Allergic reactions are exaggerated immune responses to allergens. Both allergic conjunctivitis and rhinitis are a result of type I hypersensitivity reactions. Initial exposure to an airborne allergen triggers an immune cascade ultimately resulting in IgE antibodies specific to that allergen. These IgE antibodies then bind to the surface of mast cells in mucosal tissues. On subsequent exposure, the allergen binds to the IgE antibodies, resulting in mast cell activation and degranulation. This precipitates the release of histamine, cytokines, leukotrienes, prostaglandins, and other immune mediators. Histamine causes increased vasodilation and vaso-permeability, leading to symptoms such as pruritis, watery discharge, erythema and edema of the tissue. The release of cytokines draws in other inflammatory cells resulting in ongoing inflammation and thus persistent symptoms and potential tissue damage.

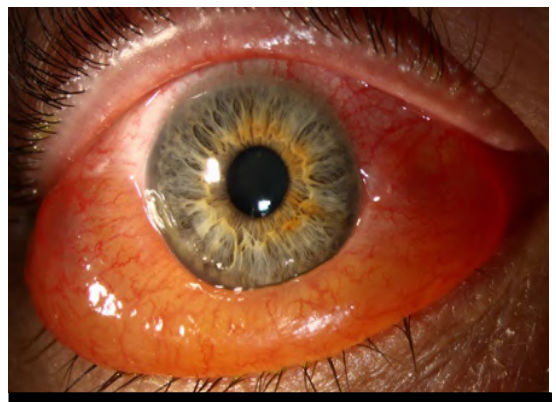
CLINICAL MANIFESTATIONS

Since allergic sensitization make take years to develop, allergic rhinitis and conjunctivitis are uncommon in children under the age of two. Patients presenting with allergic conjunctivitis and rhinitis often have a history of other allergic processes, including atopy, asthma, urticaria, or other specific allergies. A detailed history should be taken to identify potential triggers.

ALLERGIC CONJUNCTIVITIS

Patients with allergic conjunctivitis also describe intense itching of the eyes, which is a cardinal symptom that can differentiate it from viral etiologies. They may also experience mild photophobia. Those with allergic rhinitis describe frequent episodes of sneezing, rhinorrhea, and nasal itching. They can also have a history of cough, mouth breathing, fatigue, and sleep disturbance.

EXAM: CONJUNCTIVITIS: Bilateral bulbar and tarsal conjunctival redness and clear watery discharge are hallmarks of allergic conjunctivitis. Eversion of the eyelids reveals a bumpy or follicular appearance of the palpebral conjunctiva. The eyelids are often soft and edematous as well. The soft swelling is in contrast to the induration seen in periorbital cellulitis. In severe cases, the patient may have bullous chemosis, the edematous conjunctiva bulges forward beyond lid and/or corneal margins.



CHEMOSIS

EXAM: RHINITIS: Inspection of the nasal cavity reveals turbinate edema and a pale, blueish hue to the nasal mucosa. Clear rhinorrhea is often present. In the case of nasal obstruction, there may be rhinorrhea in the posterior pharynx, leading to erythema and hyperplastic lymphoid tissue. This can give a cobblestone appearance.

OTHER EXAM FINDINGS CONSISTENT WITH ALLERGY
Allergic Shiners: Darkening of the lower eyelids (venodilation), infraorbital edema
Dennie-Morgan Lines: Accentuated folds below the lower lids
Allergic Crease: Transverse nasal crease
Allergic Salute: Palm of the hand pushes upward on the nose to open nasal passages

DIAGNOSTIC TESTING

The diagnosis of allergic conjunctivitis and rhinitis is clinical. Routine labs and imaging are often normal and unnecessary. Imaging may be considered if there is a concern for concurrent chronic sinusitis or an anatomical abnormality. Patients who are treatment refractory should be referred to a pediatric allergist for allergy testing.

DIFFERENTIAL DIAGNOSIS	
CONJUNCTIVITIS	RHINITIS
Blepharitis (lid margin)	Adenoidal Hypertrophy
Corneal Abrasion	Acute or Chronic Sinusitis
Foreign Bodies	Chronic Nonallergic Rhinitis
Infectious Conjunctivitis (bacteria, viral)	Congenital Abnormalities (Choanal Atresia)
Keratoconjunctivitis	Foreign Bodies
Nasolacrimal Duct Obstruction	Infectious Rhinitis
Toxic Conjunctivitis (ocular medication)	Nasal Polyps
Other: Uveitis, Kawasaki, MIS-C	Rhinitis Medicamentosa (rebound)

MANAGEMENT

The first steps in managing acute disease is avoiding the allergen and basic eye care. In general, topical therapies are preferred over systemic therapies. Randomized trials have shown that oral antihistamines are less effective and cause more ocular drying than topical antihistamines (Ousler, Clin Ther 2007, PubMed ID: 17617284), (Abelson, Acta Ophthal Scand 2000, PubMed ID: 11057354). However, oral antihistamines may be more practical in a child who is averse to eye drops and/or intranasal sprays.

BASIC EYE CARE
Avoid rubbing eyes: Leads to mast cell degranulation, further exacerbating symptoms
Cold compresses
Artificial tears: Can help dilute and remove the allergen
Discontinue use of contact lenses

Topic antihistamines with mast cell stabilizing properties or a combination topical antihistamine and vasoconstrictor are considered first line therapy for allergic conjunctivitis. Topical glucocorticoids are considered first line therapy for allergic rhinitis. Patients with moderate-severe allergic rhinitis may find the most benefit in a combination therapy of glucocorticoid nasal spray and a topical or oral antihistamine.

In patients with concurrent allergic conjunctivitis and allergic rhinitis, the recommended treatment is a combination of a glucocorticoid nasal spray and ophthalmic antihistamines.

DISPOSITION

Once diagnosed, patients may be discharged home. Initial treatment can be initiated in the Emergency Department, however refractory symptoms warrant referral to an allergist, ophthalmologist, or otolaryngologist.

MEDICATIONS: ALLERGIC CONJUNCTIVITIS			
CLASS	MECHANISM	AGENT	COMMENTS
Antihistamine with mast cell-stabilizing properties (Topical)	Blocks histamine release in conjunctiva and eyelids; inhibits mast cell degranulation	Cetirizine: 1 drop BID	Onset of action is within minutes Takes two weeks to assess full efficacy
		Ketotifen: 1 drop BID	
Vasoconstrictor + Antihistamine combination (Topical)	Blocks histamine release in conjunctiva and eyelids; vasoconstriction Eyelid edema	Naphazoline: 0.012% 1-2 drops QID	Use greater than two weeks leads to rebound hyperemia
		Pheniramine: 1-2 drops BID	
Mast cell stabilizer (Topical)	Inhibits mast cell degranulation	Cromolyn Sodium: 1-2 drops QID	Needs 5-14 days to take effect
Glucocorticoids (Topical)	Suppress late phase reaction from allergic inflammation	Loteprednol: 1-2 drops QID	Reserved for refractory patients Side effects can be vision threatening (cataracts, elevated IOP, glaucoma) Given under supervision of ophthalmologist
Second generation antihistamine (Oral)	Blocks histamine release	Loratadine: 5-10mg daily	Slower acting than topical medications Can cause dry mucous membranes and decreased tear production

MEDICATIONS: ALLERGIC RHINITIS			
CLASS	MECHANISM	AGENT	COMMENTS
Antihistamine nasal spray	Blocks histamine release in nasal mucosa	Azelastine: 0.1% 1 spray BID	Has a bitter taste
		Olopatadine: 1-2 sprays BID	
Glucocorticoid nasal spray	Suppress late phase reaction from allergic inflammation	Beclomethasone: 42 mcg 1-2 sprays BID	Most effective pharmacological therapy
Cromolyn nasal spray	Inhibits release of histamines, leukotrienes from mast cells	Cromolyn Sodium: 1-2 sprays TID	Great safety profile. Not absorbed systemically
Second generation oral antihistamine	Blocks histamine release	Loratadine: 5-10 mg daily	Less sedating Quick onset of action

ANAPHYLAXIS

INTRODUCTION (MICHAEL MOJICA, M.D., 8/2022)

Anaphylaxis is a rapidly developing systemic reaction to an antigen resulting in an increase in bronchial smooth muscle tone (bronchospasm), a decrease in vascular smooth muscle tone (hypotension), increased capillary permeability (cutaneous, mucosal edema, urticaria) and gastrointestinal symptoms (abdominal pain, vomiting, diarrhea).

The most common pediatric triggers are foods and insect stings. The most common adult triggers are medications and insect stings. Common medication triggers include: antibiotics, non-steroidal anti-inflammatory drugs, immunomodulators and biological agents. Risk factors for severe disease include cardiovascular disease, asthma and other comorbidities and older age. Fatalities are rare, occurring in 0.25-0.33% of anaphylaxis admissions and ED visits.

PATHOPHYSIOLOGY

Prior exposure to antigens results in the creation of IgE-mast cells and IgE-basophil complexes. These previously sensitized complexes release vasoactive and chemotactic factors such as: Histamine, Leukotriene C4, Prostaglandin D2, and Tryptase in response to re-exposure to the antigen. In addition, neutrophils, monocytes, macrophages and platelets are thought to also be involved through additional chemical mediators (leukotrienes, complement, platelet activation factors).

PATHOPHYSIOLOGY	
Type 1 Hypersensitivity	Antigen binds with IgE from prior antigen exposure Food: e.g. peanuts, tree nuts, eggs, shellfish, milk Parenteral antibiotics (Penicillins), NSAIDS Hymenoptera stings
Non-immunologic: Anaphylactoid reactions	Mast cell degranulation that is not IgE mediated Contrast media, opiates, physical stresses (cold, heat, vibration), muscle relaxants, tomatoes, strawberries
Complement activation	CI esterase deficiency, Hereditary angioedema

CLINICAL MANIFESTATIONS

The presentation of anaphylaxis is dependent on the pathophysiology and is highly variable. Patients may present with simple cutaneous manifestations such as urticaria, or in severe respiratory distress due to upper or lower airway obstruction and in hypotensive, anaphylactic (distributive) shock. Cardiac arrest can occur within minutes in the untreated patient.

CLINICAL MANIFESTATIONS	
Upper airway	Angioedema: Face, lips, hypopharynx, larynx Dyspnea, stridor, hoarseness, dysphagia
Lower airway	Bronchospasm: wheezing, dyspnea, chest tightness
Cardiovascular	Shock (distributive), dysrhythmias Hypotension, altered mental status, syncope, dizziness, palpitations
Cutaneous	Flushing, urticaria, angioedema (most common)
Gastrointestinal	Nausea, vomiting, diarrhea Abdominal cramps (spasm, bowel edema)

ANAPHYLAXIS DEFINITION*		
Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled		
1	Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (generalized hives, pruritus or flushing, swollen lips-tongue-uvula) AND at least ONE of the following:	
	a	Respiratory compromise: Dyspnea, bronchospasm, stridor, hypoxemia
	b	Reduced blood pressure or associated symptoms of end-organ dysfunction: hypotonia, syncope, incontinence
2	TWO or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours)	
	a	Involvement of the skin-mucosal tissue: generalized hives, itch-flush, swollen lips-tongue-uvula
	b	Respiratory compromise: Dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow rate, hypoxemia
	c	Reduced blood pressure or associated symptoms (hypotonia, syncope, incontinence)
	d	Gastrointestinal symptoms (crampy abdominal pain, vomiting)
3	Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours)	
	a	Infants and Children: low systolic BP (<1 year, < 70 mm hg, 1-11yrs 70 + (2 x age in years or greater than 30% decrease in systolic blood pressure
	b	Adults: Systolic blood pressure of less than 90 mm Hg or greater than 30% decrease from that person's baseline
*National Institute of Allergy and Infectious Disease: 2020 Note: Fulfilling diagnostic criteria is not a required for Epinephrine use		

MANAGEMENT

Basic resuscitation principles take precedence in the management of anaphylaxis. All patients should receive, oxygen, cardiac monitoring and intravenous access. Management decisions include the treatment of anaphylaxis, potential prevention of biphasic reactions, disposition and duration of observation for dischargeable patients. The role of whole body irrigation in those with an ingested allergen and severe respiratory or cardiovascular symptoms is unclear. Laboratory evidence suggest a possible role of activity charcoal in peanut allergy (Kopper, J Agric Food Chem 2011, PubMed ID: 21128612).

AIRWAY: A definitive airway should be provided as soon as possible for those with progressive upper airway obstruction unresponsive to therapy. A delay can change a difficult partly obstructed airway to an impossible completely obstructed airway requiring a cricothyrotomy. The ability to obtain a surgical airway should be readily available. (See also: PEM Guide: Airway Procedures: Difficult Airway, PEM Guide: Airway Procedures: Cricothyrotomy). Indirect laryngoscopy may also be used to evaluate airway edema though its benefit has not been established. Patients with partial upper airway obstruction should remain in a seated position.

BREATHING: Beta$_2$ receptor agonists (Albuterol, Epinephrine) are most commonly used to acutely treat bronchospasm due to anaphylaxis. Epinephrine has the added benefit of inhibiting the release of inflammatory mediators. Albuterol should be used as an adjunct to Epinephrine for bronchospasm and not as a substitute for Epinephrine. Albuterol does not treat upper airway edema or shock. Glucocorticoids to reduce inflammation may be provided as secondary treatment in the patient with a history of asthma.

CIRCULATION (ANAPHYLACTIC SHOCK): Hypotension in anaphylaxis is a result of vasodilation (distributive shock). Patients should be supine with their legs higher than the head to promote central perfusion (unless there is upper airway edema). Aggressive fluid resuscitation is warranted. An Epinephrine infusion (vasoconstriction and increased cardiac output increase blood pressure) is recommended for fluid refractory hypotension. Norepinephrine and Dopamine have been recommended for persistent anaphylactic shock despite maximal Epinephrine dosing. Some suggest Vasopressin based on the theory that anaphylaxis may become refractory to catecholamines. Methylene blue and extra corporeal membrane oxygenation (ECMO) have been suggested as additional therapy for vasoactive medication resistant anaphylaxis.

MEDICATIONS FOR ACUTE ANAPHYLAXIS

Early administration of Epinephrine is one of the few interventions for anaphylaxis that has strong evidence for improving mortality. A delay in Epinephrine administration has been associated with an increased risk of mortality. All patients meeting diagnostic criteria for anaphylaxis should receive Epinephrine though fulfilling diagnostic criteria is not at pre-requisite for Epinephrine. Administration intramuscularly in the anterolateral thigh has been shown to result in the fastest time to maximum concentration (6-10 minutes). See Appendix: Anaphylaxis Medication Dosing.

1. EPINEPHRINE: Epinephrine has potent $beta_1$ and moderate $beta_2$ and $alpha_1$ activity. Epinephrine's response is dose dependent. At low doses, the $beta_1$ activity predominates increasing cardiac output. $Alpha_1$ (vasoconstriction) and $beta_2$ (vasodilation) have offsetting effects on systemic vascular resistance at low doses. At high doses, $alpha_1$ activity (vasoconstriction) predominates increasing systemic vascular resistance. See also; Appendix: Push Dose Pressors: Epinephrine. Antihistamines and corticosteroids should not be administered before, or in place of Epinephrine

EPINEPHRINE: ANAPHYLAXIS EFFECTS	
$Alpha_1$	Vasoconstriction → ↑ Systemic Vascular Resistance → ↑ BP
$Alpha_1$	Vasoconstriction → ↓ Mucosal edema
$Beta_1$	Increase Stroke Volume and Heart Rate → ↑ Cardiac Output → ↑ BP
$Beta_2$	Bronchodilation: Due to $beta_2$ effect and ↓ release of chemical mediators
Cellular	↓ Histamine and leukotriene release from mast cells and basophils

2. ANTIHISTAMINES: Antihistamines stabilize the histamine receptor and prevent histamine release. H1 receptors are the most clinically relevant in anaphylaxis. H2 receptors, located primarily in the gastrointestinal track have a minor role in the pathophysiology of anaphylaxis. H1 antihistamines (e.g. diphenhydramine) have well documented efficacy in treating the cutaneous symptoms of anaphylaxis. Second generation antihistamines (e.g. Loratadine, Cetirizine) have a longer duration of action, are less sedating and have fewer anticholinergic effects. However, there is no evidence of efficacy for non-urticarial symptoms (respiratory, cardiovascular). Antihistamines have a slow onset (Oral: 30 minutes) do not stabilize mast cells or basophils and do not treat cardiovascular or respiratory symptoms of anaphylaxis.

A Cochrane review examined the evidence for the role of H1 antihistamines in the treatment of anaphylaxis, and was unable to find any evidence and concluded that they were "unable to make any recommendations for clinical practice" (Sheikh, Cochrane 2007, PubMed ID: 17620060). The evidence behind H2 blockers is similarly lacking. A systematic review of the use of H2 antihistamines for anaphylaxis failed to find any eligible studies (Nurmatov, Annals Asthma, Allergy, Immunol 2014, PubMed ID: 24468252). Current guidelines recommend that antihistamines can be used as secondary treatment (after Epinephrine) for symptomatic relief of cutaneous symptoms of anaphylaxis.

3. CORTICOSTEROIDS: The potential effectiveness of steroids in anaphylaxis is extrapolated from their use in acute asthma exacerbations. Corticosteroids have a slow onset of action and act by inhibiting the production of new inflammatory mediators. A Cochrane Review of Glucocorticoids for the treatment of anaphylaxis was unable to find any studies that were high enough quality to include in the review. (Chou, Cochrane 2012, PubMed ID 22513951). Current guidelines state that corticosteroids have no proven role in the management of acute anaphylaxis.

BIPHASIC REACTIONS

The length of observation necessary in the emergency department after resolution of initial signs symptoms is an area of considerable debate. This is due to the possibility of a biphasic reaction. There is no standardized definition of biphasic reactions. This makes drawing conclusions from the literature difficult. The most common definition is the recurrence of symptoms after at least 1 hour of being symptom free following the initial presentation of anaphylaxis. Some define it as a recurrence of symptoms requiring additional therapy. Biphasic reactions may occur from 1-72 hours after the initial reaction. A biphasic reaction may be less severe, similar or more severe.

The etiology of biphasic reactions is unknown. Possible etiologies include: an initial massive mediator release finally overcomes the pharmacologic treatment, a second or late phase allergic component that is complement or IgG mediated, or a second immediate IgE type response due to persistence of a trigger (e.g. long acting medication, oral trigger such as food).

RISK FACTORS FOR BIPHASIC REACTIONS

Risk Factor	Adjusted Odds Ratio (95% CI)
Severe initial presentation[1]	2.11 (1.23, 3.61)
≥ 1 dose of Epinephrine received	4.82 (2.70, 8.58)
Wide pulse pressure[2]	2.11 (1.32, 3.37)
Unknown trigger	1.63 (1.14, 2.33)
Cutaneous signs and symptoms	2.54 (1.25, 5.15)
Drug trigger in children	2.35 (1.16, 4.76)

1. Definition of “severe initial presentation” varied among studies in the meta-analysis.
2. Wide Pulse Pressure: Diastolic BP < (Systolic BP x 0.5)

Shaker, J Allergy Clin Immunol 2020, PubMed ID: 32001253

DISPOSITION

Guidelines acknowledge that there is insufficient evidence to recommend a specific duration of observation period to evaluate for biphasic reactions. Patients should be observed until all signs and symptoms have resolved. Those with a prompt response to Epinephrine, resolution of symptoms, non-severe anaphylaxis and reliable access to care and an EpiPen may be discharged after 1 hour of observation. Observation should be extended to 6 hours or longer (including hospital admission) for those with severe anaphylaxis, co-morbid conditions (e.g. asthma) or requiring more than one dose of Epinephrine. (Shaker, J Allergy Clin Immunol 2020, PubMed ID: 32001253). Patient who remain symptomatic and those with severe allergic reaction requiring more than one dose of epinephrine or significant cardiovascular or respiratory support should be admitted.

DISCHARGE MEDICATIONS: 2020 guidelines make a conditional recommendation based on a low evidence rating of no clear evidence for administering glucocorticoids or antihistamines to prevent biphasic reactions. In a retrospective cohort study, children treated with corticosteroids were found to have an increased risk of biphasic reactions though the authors acknowledge that the potential confounding variable of initial presentation severity may not have been accounted for (Michelson, J Pediatr. 2015, PubMed ID: 26095285).

DISCHARGE INSTRUCTIONS
Instructions on antigen avoidance
Signs and symptoms warranting Epinephrine use
Signs and symptoms warranting a return to care
Prescription and instructions for the appropriate sized Epinephrine Pen

ADMISSION
Severe presentation: Hypotension, upper airway obstruction, significant lower airway
Mild-moderate reactions with persistent symptoms despite adequate therapy
Recurrence of symptoms after resolution requiring additional treatment

APPENDIX: ANAPHYLAXIS MEDICATION DOSING

ANAPHYLAXIS MEDICATION DOSING	
Epinephrine:	Intramuscular Epinephrine: Intramuscular injection in the anterolateral thigh is preferred Epinephrine autoinjector use reduces the risk of dosing errors Dose: 0.01 mg/kg of 1 mg/ml (0.01 ml/kg) IM Q15 min, max 0.5 ml < 10 kg: Weight based dosing 10-25 kg: EpiPen Junior (Green cap) = 0.15 mg 20-50 kg: EpiPen Adult (Yellow cap) = 0.30 mg > 50 kg: 0.5 mg (0.5 of 1mg/ml Epinephrine) A longer needle may be required for obese patients. VIDEO: EPIPEN AUTO-INJECTOR USE
	Intravenous Epinephrine: Indicated for fluid refractory shock Start low and titrate up rapidly Low Dose (Inotropy predominates): 0.05-0.3 mcg/kg/min High Dose (Vasoconstriction predominates): > 0.3 mcg/kg/min
Antihistamines	H1 antagonists: e.g. Diphenhydramine 1 mg/kg IV/PO H2 antagonists: e.g. Ranitidine 1 mg/kg IV/PO
Bronchodilators	Albuterol nebulizer (0.5%): 0.15 mg/kg (0.03 ml/kg) with saline to total of 3 ml Alternatively: 2.5 mg < 5 years old, 5.0 mg ≥ 5 years old
Corticosteroids	Solumedrol: 2 mg/kg IV Dexamethasone: 0.6 mg/kg IV/PO Prednisone: 1-2 mg/kg PO
Vasoactive Medications	2nd line agents for Epinephrine refractory anaphylactic shock
	Norepinephrine: 0.1-2.0 mcg/kg/min
	Dopamine (vasoconstrictor dose): 10-20 mcg/kg/min

APPENDIX: PUSH-DOSE PRESSORS: EPINEPHRINE

PUSH DOSE PRESSORS	
Definition	Small bolus doses of vasoactive agents to support blood pressure
History	Used by anesthesiologists in the OR for many years
	Recently, more common in the ED and ICU settings
Indications	Bridge the time until a vasoactive infusion is available
	Expected short lived ↓ BP: e.g. after RSI, during procedural sedation
Adverse Events	Incorrect preparation → ↓ dose (ineffective),↑ dose (adverse events)
	Must label syringes appropriately to avoid dosing errors
Pediatric Dose	Weight base concentration: 1 mcg/kg/ml and dosed in 1 ml aliquots
Adult Dose	Standard Concentration: 10 mcg/ml and dosed in 1 ml aliquots
Other	Norepinephrine and Phenylephrine can also be used in push doses

EPINEPHRINE DOSING: NEW CONCENTRATIONS				
	CONCENTRATION		PEDIATRIC DOSING	
Route	Old	New	mg/kg	mL/kg
Intravenous	1:10,000	0.1 mg/mL	0.01	0.1
Intramuscular	1:1,000	1 mg/mL	0.01	0.01

PUSH-DOSE EPINEPHRINE: STANDARD PREPARATION (ADULT)	
Epinephrine (0.1 mg/ml)	Code Dose: 1 mg = 100 mcg = 10 ml
Normal Saline	9 ml Normal Saline
Preparation	1 ml of Epinephrine (0.1 mg/ml) + 9 ml of NS = 10 ml
Concentration	0.01 mg/ml (10 mcg/ml)
Dosing	0.5-2 ml (5-20 mcg) Q2-4 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION (PEDIATRICS)	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 10 mcg/kg = 0.1 ml/kg
Normal Saline	Normal Saline to total 10 ml
Preparation	0.1 ml/kg + NS to total 10 ml
Concentration	0.01 mg/kg/ml = 1 mcg/kg/ml
Dose	1 ml Q2 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION: 20 KG CHILD	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 0.2 mg, 10 mcg/kg = 200 mcg 0.1 ml/kg = 2 ml
Preparation	2 ml of Epinephrine (0.1 mg/ml) + 8 ml of NS = 10 ml
Preparation (concentration)	200 mcg/10 ml = 20 mcg/ml = 1 mcg/kg/ml
Dosing	1 ml (20 mcg or 1 mcg/kg) Q2 minutes PRN
Infusion Comparison	0.5-1.0 mcg/kg/min (10-20 mcg/min) Push-dose: 1 ml = 20 mcg (1/10th code dose) Equals: 0.5 mcg/kg/min x 2 min, 1.0 mcg/kg/min x 1 min

EPINEPHRINE DOSING: NEW CONCENTRATIONS				
	CONCENTRATION		DOSING	
Route	Old	New	mg/kg	mL/kg
Intravenous	1:10,000	0.1 mg/mL	0.01	0.1
Intramuscular	1:1,000	1 mg/mL	0.01	0.01

ASTHMA

INTRODUCTION (KEVIN CHING, M.D.,6/2022)
An acute asthma exacerbation is characterized by a narrowing of the airways as a result of airway inflammation, mucous plugging and bronchoconstriction. If untreated or under-treated, acute airway narrowing from asthma may deteriorate to complete lower airway obstruction, respiratory failure and death. Early diagnosis and management is key to reversing the pathogenesis of airway hyper-responsiveness and bronchoconstriction.

RISK FACTORS FOR ASTHMA DEATH	
Asthma History	Previous severe exacerbation (intubation or ICU admission for asthma) Two or more hospitalizations for asthma in the past year Three or more ED visits for asthma in the past year Hospitalization or ED visit for asthma in the past month Using > 2 canisters of a short acting beta agonist per month Difficulty perceiving asthma symptoms or severity of exacerbations Lack of a written asthma action plan
Social History	Low socioeconomic status or inner-city residence Illicit drug use Major psychosocial problems
Co-morbid Conditions	Cardiovascular disease Another chronic lung disease Chronic psychiatric disease

CLINICAL MANIFESTATIONS

HISTORY: The history should focus on the duration of symptoms and precipitating factors for the exacerbation (i.e. environmental exposures, upper respiratory tract infection symptoms, or medication non-compliance). Attention should be focused on the child's asthma severity by assessing a history of ED visits, hospitalizations, ICU admissions, and intubations. Determine which medications have been used acutely (e.g. beta agonists) and as maintenance (e.g. inhaled steroids).

PHYSICAL EXAM: Assess the patient's respiratory status. Respiratory rate, bilateral breath sounds, inspiratory to expiratory ratio, and the presence of wheezing should be noted. In more severe exacerbations, older children may assume a "tripod" position (sitting forward and leaning on both arms) to help optimize ventilation. Central cyanosis, inability to speak in complete sentences, altered mental status; diaphoresis, severe accessory muscle use and grunting.

ANCILLARY STUDIES: Pulse oximetry (PaO_2) provides a continuous measure of arterial hemoglobin oxygen saturation (SaO_2). SaO_2 can be used to assess the severity of airway obstruction. Values less than 92% indicates inadequate oxygenation. The peak expiratory flow rate (PEFR) can be useful in older children by providing serial measurements of airway obstruction that can be compared to the child's baseline (if known) or to reference ranges (based on age and height). A PEFR less than 50% of predicted indicates a moderate to severe airway obstruction.

Quantitative end tidal CO_2 can also be trended serially and noninvasively. The child in impeding respiratory failure should have an arterial blood gas (ABG) obtained to provide an objective measure of hypoxemia and hypercarbia. Hypercarbia, or even a normal $PaCO_2$ in a tachypneic patient, may reflect inadequate ventilation and impending respiratory failure.

ASSESSING ASTHMA EXACERBATION SEVERITY

ASTHMA SCORE			
	0	1	2
Room Air Oxygen Saturation[1]	≥ 94%	89-93%	≤ 88%
Breath sounds	Normal	Expiratory wheeze	Inspiratory and expiratory wheeze OR Diminished breath sounds
Accessory Muscle Use[2]	None	Moderate	Maximal
Respiratory Rate[3]	Normal for age	Increased for age	> 60 breaths/min
Cerebral Function	Normal	Depressed or Agitated	Coma
1. Room Air Saturation: After 2 min on RA 2. Accessory Muscle: Mod=2, Severe=3-4 a. Nasal flaring c. Intra-costal b. Supra-sternal d. Sub-sternal 3. RR: Obtain over 30 sec multiply x 2			SCORE MILD 1-3 MODERATE 4-7 SEVERE ≥ 7

ASTHMA SEVERITY (NIH: 2007)		
	DYSPNEA	INITIAL PEF*
Mild	Only with activity	≥ 70%
Moderate	Interferes with or limits usual activity	40-69%
Severe	At rest, interferes with conversation	25-40%
Life Threatening	Too dyspneic to speak	< 25%
*Peak Expiratory Flow: Percent predicted or personal best		

CHEST XRAY: Chest x-rays are typically unnecessary in a known asthmatic and rarely demonstrate anything other than hyperinflation or atelectasis. The 2007 NIH Asthma Guidelines do not recommend CXR on a routine basis. A chest XRAY should be obtained for “for patients suspected of a complicating cardiopulmonary process, such as congestive heart failure, or another pulmonary process such as pneumothorax, pneumomediastinum, pneumonia, or lobar atelectasis” (NIH 2007, PubMed ID: 17983880). The utility of CXR in the febrile asthmatic is unclear. In general, it is best to maximize asthma therapy prior to CXR to avoid mistaking atelectasis for pneumonia.

MANAGEMENT

The initial approach to an acute asthma exacerbation depends on the severity of the exacerbation. Supplemental oxygen, inhaled beta-agonists and corticosteroids form the basis for initial therapy of the majority of patients. Medication dosing in provided in the appendix.

MILD TO MODERATE EXACERBATIONS

OXYGEN: Supplemental oxygen should be provided to achieve a SaO_2 > 90% in a manner that is least disturbing to the patient

ALBUTEROL: Repetitive treatments with nebulized Albuterol (0.5%) at a dose of 0.15 mg/kg (or 2.5 mg for children < 30 kg and 5 mg for children > 30 kg) are effective in rapidly reversing airway obstruction. In general nebulizer treatments are delivered every twenty minutes but may delivered more frequently and at higher concentrations in more severe exacerbations. An equivalent mode of delivery via a metered-dose inhaler (MDI) with a spacer device (90 mcg per inhalation) can be just as effective for older children **(**Ploin Pediatrics. 2000, PubMed ID: 10920157**).**

IPRATROPRIUM: Ipratropium may be given via nebulization every 20-30 minutes with the first 3 Albuterol treatments at a dose of 250 mcg for children and 500 mcg for adolescents (Zorc, Pediatrics 1999, PubMed ID: 10103297). The SaO_2 may initially decline following beta-agonist therapy because of an increase in ventilation/perfusion mismatch.

CORTICOSTEROIDS: Administer systemic corticosteroids to patients who have moderate or severe exacerbations or to patients who fail to respond completely to short acting beta agonists (NIH 2007, PubMed ID: 17983880). All children who receive more than one treatment with inhaled beta-agonists, who have an SaO2 < 95%, a PEFR < 50% predicted, frequent ED visits, or a history of severe acute asthma, will require corticosteroids. Oral prednisone/prednisolone and been found to have similar efficacy to intravenous methylprednisolone. dexamethasone (0.6 mg/kg) has been shown to have similar efficacy to a 5-day course of prednisone. It is unclear if a single dose or 2 doses is required (Keeney, Pediatrics 2014, PubMed ID: 24515516).

In a single center, randomized clinical trial there was no statistically significant difference in unscheduled revisits there was no statistically significant difference in the rate of unscheduled return visits comparing 1 days vs 2 days of Dexamethasone (Odd Ratio: 0.89, 95% CI (0.37, 2.11)). This was true in the subgroups of patients with mild asthma (Odds Ratio: 1.29, 95% CI (0.50, 3.48)) and patients with moderate asthma (Odds Ratio: 0.72, 95% CI (0.10, 4.98)) in comparing a one dose regimen of Dexamethasone to a two dose regimen (Martin, Pediatr Emerg Care. 2022, PubMed: 35507383). In addition, there was no difference in the secondary outcomes of: days to symptom resolution, days of school missed, adverse effects, vomiting since discharge for the group as a whole as well as in the mild asthma and moderate asthma subgroups. The most common adverse effect was vomiting after discharge (6.2%). A number of issues should be considered in applying the results of this study. These include a low rate of follow-up, poor compliance with the 2 dose regimen without a per protocol analysis, lack of comparison of other asthma medications in the Emergency Department and data not presented to justify the conclusion of non-inferiority. If a 2 dose regimen is utilized, it may be prudent to provide the second dose in the ED given compliance issues.

MAGNESIUM: Intravenous magnesium may be considered at a dose of 25 – 75 mg/kg (maximum dose 2 grams) for moderate to severe exacerbations, and requires careful monitoring for hypotension (Cheuk, Arch Dis Child. 2005., PubMed ID: 15613519).

INTRAVENOUS HYDRATION: Patients who have been ill may have decreased oral intake and increased insensible fluid losses through the respiratory system. In addition, beta agonist and magnesium therapy will lead to vasodilation decreasing systemic vascular resistance. Hyperinflation may also lead to impaired venous return and decreased cardiac output. Together, these combine to lower the mean arterial pressure. Intravenous fluids should be administered to maintain perfusion with constant monitoring of lung sounds to avoid fluid overload.

SEVERE EXACERBATIONS: MEDICATIONS

All of the interventions reviewed above for mild-moderate asthma exacerbations should generally be provided to patients with a severe exacerbation. Interventions listed below are specific to those with severe asthma

ALBUTEROL: Continuous Albuterol nebulization may be superior to an MDI in children with severe exacerbations and may be administered at a dose of 0.6-1.0 mg/kg/hour (maximum 20 mg/hour).

INTRAMUSCULAR EPINEPHRINE/TERBUTALINE: In the event of an inadequate or delayed response to inhaled beta-agonists, parenteral injections of either Epinephrine or Terbutaline can be considered in place of or in addition to inhaled Albuterol. Both Epinephrine (1:1,000) and Terbutaline (0.1%) may be given subcutaneously or intramuscularly at a dose of 0.01 ml/kg every 15 minutes for three doses (Epinephrine maximum dose 0.3 ml, Terbutaline maximum dose 0.2 ml). Studies comparing intravenous to inhaled beta-agonists have not demonstrated any advantage to the parenteral route of delivery. However, it makes clinical sense that a patient who is poorly aerating may not receive an adequate dose of an inhaled beta agonist.

INTRAVENOUS BETA-AGONIST THERAPY with Terbutaline may be initiated with a 10 mcg/kg loading dose over 10 minutes. This is followed by a maintenance infusion at 0.4 mcg/kg/min. This infusion may be titrated to effect in increments of 0.2 mcg/kg/min and requires continuous cardiac monitoring for arrhythmias.

KETAMINE: Ketamine is a bronchodilator and may decrease oxygen utilization. It may be used to decrease the anxiety often accompanying non-invasive ventilation and may be considered prior to intubation.

HELIOX: Heliox is a mixture of helium (70%) and oxygen (30%). Helium's low density can enhance flow to obstructed airways, reduce the work of breathing and facilitate deposition of aerosolized medications to distal lung spaces. Heliox is administered via aerosol. The use of heliox is limited to those requiring less than 30% supplemental oxygen.

SEVERE EXACERBATIONS: VENTILATION

If impending respiratory failure is a concern despite optimal therapy with either continuous inhaled or intravenous beta-agonist therapy, adjunctive therapies may be tried to avoid intubation. Mechanical ventilation in an asthmatic requires careful attention to ventilation because of the high pressures generated that may lead to barotrauma and pneumothorax.

NONINVASIVE POSITIVE PRESSURE VENTILATION (NIPPV) with bi-level positive airway pressure (BiPAP) has been used in severe asthmatics that have failed conventional therapy. BiPAP works to decrease the work of the pulmonary musculature and accessory muscle use and reduce distal airway hyperinflation. It can be administered via face mask in an alert and cooperative patient at inspiratory pressures of 8-16cm H_20 and expiratory pressures of 4-8 cm H_20. (See also PEM Guide: Procedures: Non-invasive Ventilation)

MECHANICAL VENTILATION: Endotracheal intubation with mechanical ventilation should be delayed whenever possible to avoid barotrauma. It is indicated in patients where respiratory failure is imminent, if there is refractory hypoxia, altered mental status, or hemodynamic instability despite fluid resuscitation. Rapid sequence induction should proceed with intravenous Ketamine (1-2 mg/kg) because of its bronchodilating properties. Paralysis will facilitate intubation and decrease respiratory muscle use and oxygen utilization. (See also PEM Guide: Procedures: Mechanical Ventilation)

ASTHMA VENTILATIONS GOALS
Reverse hypoxemia (increase O_2 delivery)
Relieve respiratory muscle fatigue (decrease O_2 utilization)
Maintain minute ventilation at acceptable PCO_2 (permissive hypercapnia) and pH
Avoid ventilator-induced barotrauma: pneumothorax, pneumomediastinum

In the intubated patient the goal is to correct oxygen and ventilation deficits while limiting the risk of barotrauma. A combination of low tidal volume, slow respiratory rate and prolonged expiratory time is used to limit peak inspiratory pressure. This controlled hypoventilation is also referred to as permissive hypercapnia. Respiratory rate should be slow enough and the expiratory time should be long enough to allow for complete passive exhalation. Otherwise, air will be trapped in the alveoli at the end of expiration (auto-peep). The next ventilated breath will add to the existing air and result in barotrauma.

ASTHMA VENTILATION SETTINGS	
NIPPV with BiPAP	Inspiratory PAP: Start 8-10 cm H_2O, Typical 8-16 cm H_2O Expiratory PAP: Start 2-4 cm H_2O, Typical 4-8 cm H_2O
Endotracheal Intubation (controlled hypoventilation with permissive hypercapnia)	Mode: SIMV, (CMV if paralyzed) FiO_2: Titrate to O_2 saturation ≥ 94% RR: 8-10 breaths/minute (RR is adjusted to ensure complete exhalation) TV: 5-7 ml/kg (to generate PIP and PP) Peak inspiratory pressure (PIP) < 40 cm H_2O Inspiratory time (IT) 1 – 1.5 sec or I:E ratio > 1:2 PEEP: controversial – 0 in paralyzed patient
Both methods will require fine tuning	

DISPOSITION

Monitoring of the child in the ED for up to 2-4 hours of bronchodilator therapy may be needed to determine a disposition decision.

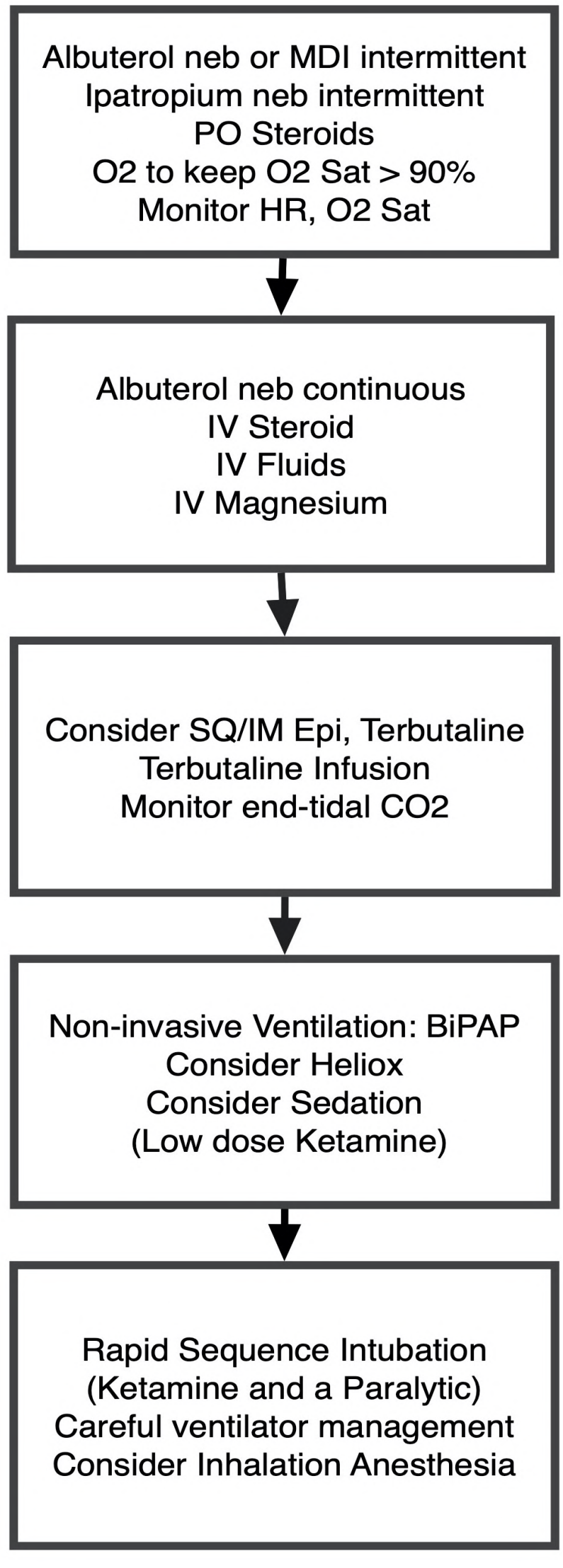
Any child whose condition has improved enough for discharge should continue their maintenance asthma medications and have an asthma action plan completed. Children younger than 5 years should be given an MDI with a spacer or a nebulizer if needed. In this sub-acute phase following discharge, the use of inhaled Albuterol should be continued every 4 to 6 hours as needed until symptoms resolve. Children who require oral corticosteroids should be prescribed an additional 4-day course of Prednisone (2 mg/kg). Oral dexamethasone is an alternative. Follow-up care should be arranged for all asthmatics.

ADMISSION CRITERIA
Any child in persistent respiratory distress
SaO2 < 90% on room air
PEFR < 50% predicted
Underlying cardiopulmonary disease, or a pneumothorax
Medication non-compliance may be an issue
Significant socioeconomic factors that may aggravate their condition

APPENDIX: ASTHMA MANAGEMENT ALGORITHM

ASTHMA ALGORITHM

(See Tables for Medication Dosing and Ventilator Settings)



APPENDIX: ASTHMA MEDICATION/VENTILATOR SETTINGS

ASTHMA MEDICATION DOSING	
Oxygen	Titrate to O_2 sat > 90%
Albuterol	<u>INTERMITTENT NEBULIZER</u> CHILD: 0,15 mg/kg (minimum 2.5 mg) (0.03 ml/kg of 0.5% solution) Q 20 minutes via nebulizer ADULT: 2.5-5.0 mg Q 20 minutes
	<u>INTERMITTENT: MDI</u> CHILD: 4-8 puffs Q20 min x 3 dose then Q1-4 hours PRN ADULT: 4-8 puffs Q20 min for 4 hours then Q1-4 hrs PRN
	<u>CONTINUOUS</u> CHILD: 0.5 mg/kg/hour ADULT: 10-15 mg/hour
Ipratropium	250 mcg/dose (1.25 ml) > 30 kg via neb Q20 minutes x 3 500 mcg/dose (2.5 ml) > 30 kg via neb Q20 minutes x 3
Epinephrine (1:1,000)	CHILD: 0.01 mg/kg IM Q20 min x 3 ADULT: 0.3-0.5 mg IM Q20 min x 3
Terbutaline	CHILD: 0.01 mg/kg IM Q20 minutes x 3 ADULT: 0.3-0.5 mg IM Q20 minutes x 3
	10 mcg/kg IV loading dose over 10 minutes, 0.4 mcg/kg/min IV maintenance Titrated to effect in increments of 0.2 mcg/kg/min Cardiac monitoring for arrhythmias essential
Magnesium	50-75 mg/kg (maximum 2 grams) IV over 20 min
Prednisone	CHILD: 1-2 mg/kg PO daily x 5 days ADULT: 40-80 mg PO daily x 5 days
Dexamethasone	0.6 mg/kg PO x 1-2 days (IM if oral not tolerated)
Methylprednisolone	1-2 mg/kg/day IV/IM divided Q12 (maximum 60 mg/day) (if oral corticosteroids not tolerated)
Ketamine	Sedation: 0.5 mg/kg or 0.05 – 0.5 mg/kg/hour Rapid Sequence intubation: 2 mg/kg

ASTHMA VENTILATION SETTINGS	
NIPPV with BiPAP	Inspiratory PAP: Start 8-10 cm H_2O, Typical 8-16 cm H_2O Expiratory PAP: Start 2-4 cm H_2O, Typical 4-8 cm H_2O
Endotracheal Intubation (controlled hypoventilation with permissive hypercapnia)	Mode: SIMV, (CMV if paralyzed) FiO_2: Titrate to O_2 saturation ≥ 94% RR: 8-10 breaths/minute (RR is adjusted to ensure complete exhalation) TV: 5-7 ml/kg (to generate PIP and PP) Peak inspiratory pressure (PIP) < 40 cm H_2O Inspiratory time (IT) 1 – 1.5 sec or I:E ratio > 1:2 PEEP: controversial – 0 in paralyzed patient
Both methods will require fine tuning	

BACTERIAL TRACHEITIS

INTRODUCTION (MICHAEL MOJICA, M.D., 6/2017)
Bacterial tracheitis is a potentially life-threatening infection of the tracheal soft tissue with a mortality rate of 2-3%. Infection may extend superiorly to the subglottic area and inferiorly to the bronchi and lungs. Infection occurs due to 1. Airway mucosal damage as is seen in laryngeal tracheal bronchitis (viral croup), 2. From extension of an upper respiratory tract infection (e.g. pharyngitis, sinusitis) or a lower respiratory tract infection (e.g. pneumonia) or 3. Because of trauma from airway procedures or due to endotracheal of tracheostomy tubes. Staphylococcal aureus is the most common pathogen though infection may be poly-microbial. (See: PEM Guide: Resuscitation: Airway).

BACTERIOLOGY OF BACTERIAL TRACHEITIS
Staphylococcus aureus (#1)
Streptococcus pneumoniae
Group A streptococcus
Alpha hemolytic streptococcus
Moraxella catarrhalis
Haemophilus influenza non-typeable

CLINICAL MANIFESTATIONS
Bacterial tracheitis is most common in children less than 6 years of age and coincides with viral croup season. Presentation can be a 1. Slow progression of increasing symptoms over 2-3 days or 2. An acute presentation due to sudden complete airway obstruction by a pseudo-membrane.

Signs and symptoms are suggestive of upper airway obstruction and include: stridor, cough, respiratory distress, cyanosis and altered mental status. Diagnosis is made more difficult because symptoms are similar to croup and a benign course of croup can precede bacterial tracheitis. A rash can be seen with staphylococcal toxic shock syndrome (erythroderma) and streptococcal pharyngitis (scarlatiniform rash).

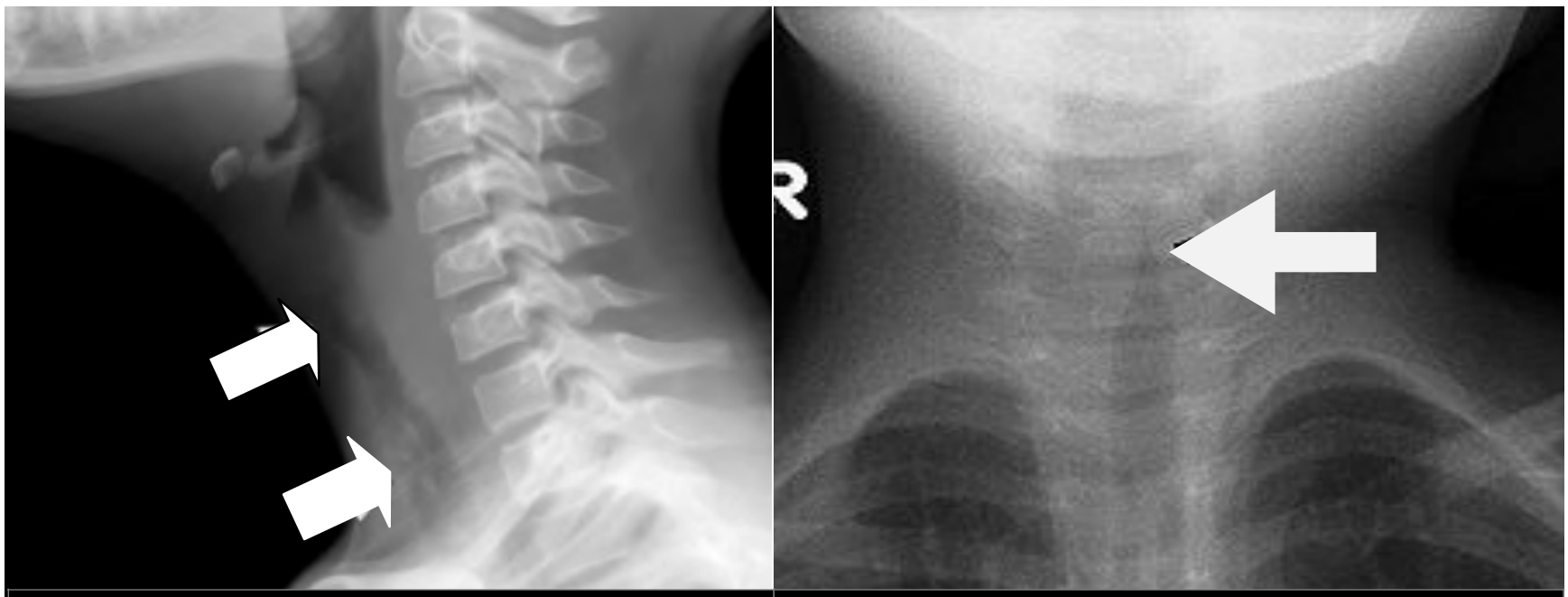
DIFFERENTIAL DIAGNOSIS OF AIRWAY OBSTRUCTION	
Epiglottis	Drooling, tripod position, lateral neck XRAY thumb sign
Croup*	Generally, less fever and less toxic appearing
Peritonsillar abscess*	Decreased neck range of motion, trismus, torticollis
Retropharyngeal abscess*	Decreased neck range of motion
Severe pneumonia*	Focal findings on lung exam
Foreign body aspiration*	Abrupt onset of symptoms, afebrile
Diphtheria	Oro-pharyngeal membrane on examination
Anaphylaxis*	Afebrile, hives, wheezing, angioedema, shock
Smoke inhalation*	Afebrile, history of smoke exposure, burns, co-oximetry
*Reviewed in detail in a separate PEM Guide	

DIAGNOSTIC TESTING

The diagnosis is made clinically based on the severity of upper airway obstruction, the toxic appearance of the child and a lack of response to nebulized epinephrine. The diagnosis can also be confirmed by direct laryngoscopy but only in a setting (e.g. operating room) where definitive airway management can be performed.

A soft tissue lateral neck XRAY could be considered in a clinically stable patient. Findings include a “shaggy” trachea due to irregularity of the tracheal mucosa. A “steeple” sign representing subglottic narrowing can be visualize on the AP view but this does not distinguish between bacterial tracheitis and croup.

Acute phase reactants (WBC, CRP) are typically elevated but are non-specific and do not contribute to clinical management. Blood cultures are rarely positive. If the patient is intubated specimen for culture should be sent from tracheal aspirates.



LATERAL XRAY: “SHAGGY” TRACHEA | AP XRAY: STEEPLE SIGN

MANAGEMENT

Airway management is the priority in patients with bacterial tracheitis. Most patients with bacterial tracheitis require intubation. This should ideally take place in the operating room with all required personal and advanced airway equipment and a clear strategy for progression if early efforts are unsuccessful. Bronchoscopy should be available to clear airway debris. A complete airway occlusion can sometimes be temporarily cleared with bag-valve-mask ventilation.

ANTIBIOTIC SELECTION: Antibiotics should be targeted to the likely pathogens. Vancomycin is administered to cover both methicillin resistant and sensitive staphylococcus aureus as well as streptococcal species. Ceftriaxone is also administered to provide coverage for gram negative organisms such as Moraxella catarrhalis and non-typeable Haemophilus influenza. In the patient with a history of a type 1 hypersensitivity reaction to penicillin, Meropenem or Levofloxacin can be substituted for Ceftriaxone. Clindamycin can be added to decreased toxin production in toxic shock syndrome.

ADDITIONAL THERAPIES: Fluid resuscitation should be provided for those with signs of shock and a maintenance fluids for those with dehydration. There is no evidence to suggest a benefit of corticosteroids.

DISPOSITION

Ultimately the patient requires admission to the PICU after the immediate airway compromise is addressed.

BRONCHIOLITIS

INTRODUCTION (DEBORAH LEVINE, M.D. 5/2023)
The American Academy of Pediatrics defines bronchiolitis as “a constellation of clinical symptoms and signs including a viral upper respiratory prodrome followed by increased respiratory effort and wheezing in children less than 2 years of age” (AAP, Pediatrics 2014, PubMed ID: 25349312).

ETIOLOGY
Respiratory Syncytial Virus (#1)
Rhinovirus (#2)
Human metapneumovirus
Influenza
Adenovirus
Parainfluenza type 3
Enterovirus
Herpes Simplex

Bronchiolitis is an acute, viral-induced inflammation and edema of the airways of the lower respiratory tract resulting in airway obstruction. Smooth muscle constriction appears to play a limited, if any, role. It is the most common lower respiratory tract infection in children under 2 years of age, with a peak between 2 and 6 months of age. Each year approximately 12% of infants develop bronchiolitis and bronchiolitis is a leading cause of infant hospitalization. Respiratory Syncytial virus (RSV) causes the majority of cases of bronchiolitis but many other viruses have been implicated. In temperate climates disease is most common in the late fall and winter seasons. Co-infection with more than one virus may occur in up to 30% of cases and a viral infection with a concomitant bacterial infection can also occur.

CLINICAL FINDINGS
Bronchiolitis is a clinical diagnosis based on signs and symptoms. Bronchiolitis usually presents with symptoms of an upper respiratory infection, such as cough and coryza for 1-2 days. Upper respiratory illness progresses to lower respiratory illness including wheezing, worsening cough and tachypnea on days 5-7 and then gradually resolves. Cough typically resolves at 2 weeks but complete resolution can take up to 4 weeks. Fever may also be present.

Significant accessory muscle use, nasal flaring, grunting and head bobbing in younger infants indicate respiratory distress and the potential for pending respiratory failure. Auscultation findings can include expiratory wheezing, prolonged expiration and both fine and coarse rales. Oxygen saturation and end-tidal CO_2 monitoring in conjunction with respiratory rate, respiratory effort and mental status can be used to determine the presence of respiratory failure and the need for mechanical ventilation.

RESPIRATORY SEVERITY ASSESSMENT*				
		MILD	MODERATE	SEVERE
Respiratory Rate	< 3 months	30-60	61-80	> 80
	3-11 months	25-50	51-70	> 70
	12-24 months	20-40	41-60	> 60
Work of Breathing		Normal, Mild	Intercostal Retractions	Nasal flaring, grunting, head bobbing
Mental Status		Baseline	Fussy, Anxious	Lethargic, inconsolable
Oxygen Requirement		None	< 1.5 liters/min	> 1.5 liters/min
Breath Sounds		Clear	Crackles, wheezing	Diminished breath sounds. significant crackles, wheezing
Cough		Absent/Mild	Moderate	Severe
*The highest rating in any category dictates the patient's severity				

WEB LINK: CHILDREN'S HOSPITAL OF PHILADELPHIA BRONCHIOLITIS PATHWAY

COMPLICATIONS

Complication of bronchiolitis include: respiratory failure, apnea and the development of a secondary bacterial infection (pneumonia, otitis media, conjunctivitis, pharyngitis). In addition, The degree of respiratory symptoms can cause poor feeding and lead to dehydration.

Risk factors for severe disease include: prematurely (< 37 weeks), neonates (< 12 weeks), those with congenital heart disease, or chronic lung disease such as: cystic fibrosis, bronchopulmonary dysplasia, congenital pulmonary anomaly, those who have a primary immunodeficiency or receiving immunosuppressant therapy. Severity of disease is associated with longer hospitalization stays, intensive care admission and need for mechanical ventilation.

APNEA: A study of 892 infants less than 6 months of age with bronchiolitis derived three decisions rules for apnea. Apnea subsequently occurred in 4.6%, 95% CI (3.4, 6.2%) of patients. The simplest of the rules included 3 predictors: Parental report of central apnea, age less than or equal to 6 weeks and birth weight less than or equal to 2.5 kilograms. The rule had a Sensitivity 100%, 95% CI (91, 100%), specificity of 62%, 95% CI (58, 65%) and a negative predictive value of 100% (99, 100%) (Walsh, Pediatrics 2015, PubMed ID: 26482666).

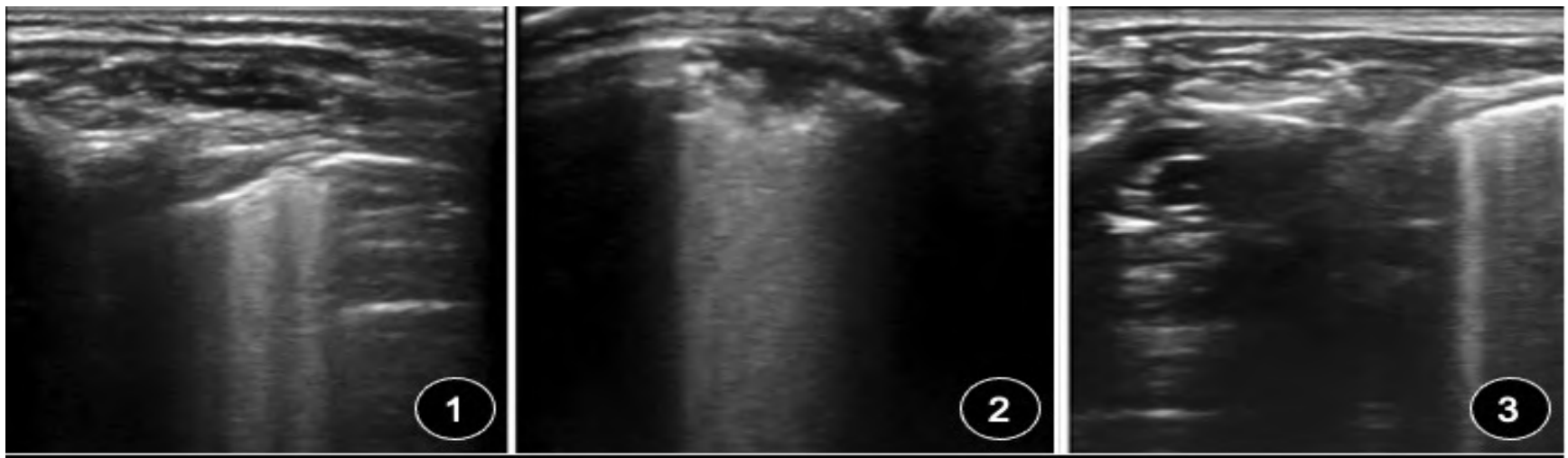
DIAGNOSTIC TESTING

VIRAL: Rapid viral testing is of limited usefulness except for epidemiological surveillance, cohorting on inpatient wards to reduce nosocomial spread and perhaps for designating a febrile patient at lower risk for concurrent serious bacterial infection. Testing for influenza should occur in season. Children less than 2 years of age are considered at high-risk for influenza complications and treatment with oseltamivir is indicated.

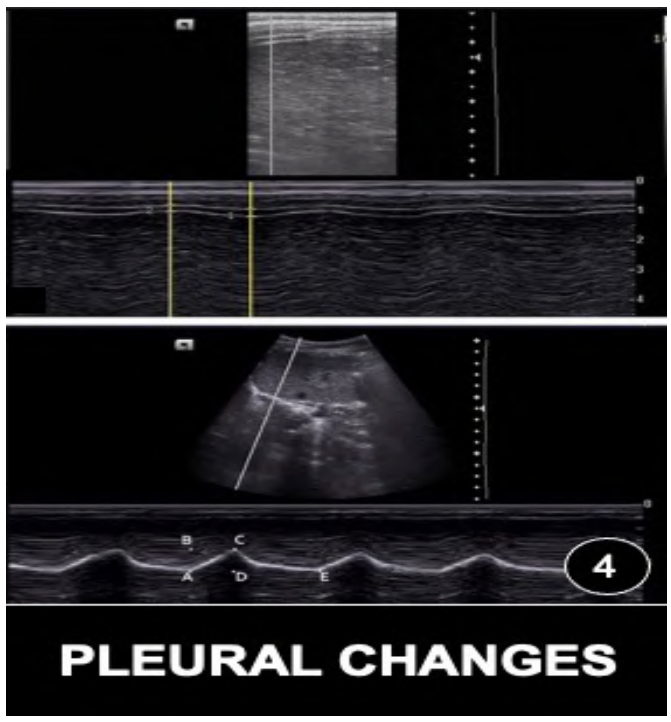
RADIOGRAPHY: Chest radiographs are not routinely recommended to diagnose bronchiolitis but can exclude other disease processes that may present with wheezing such as foreign body aspiration, pneumonia or congestive heart failure. Chest XRAY findings in bronchiolitis may include: hyperventilation with increased interstitial markings, peri bronchial cuffing and patchy infiltrates or atelectasis. Routine utilization of chest XRAYS leads to the over diagnosis of pneumonia (when atelectasis is present) and the unnecessary use of antibiotics.

POINT OF CARE ULTRASOUND: A single-center, prospective study in Italy enrolled 62 infants with bronchiolitis and 29 patients without respiratory disease demonstrated a positive correlation of lung ultrasound with clinical severity (r= 0.62) (La Regina, Ped Pulm 2021, PubMed ID: 33151023).

BRONCHIOLITIS LUNG ULTRASOUND SCORE			
ANTERO-LATERAL	0	1	2
B Lines (+/-)	Limited/Absent	Focal	Confluent
B Lines (# intercostal spaces)	< 1	1-3	>3
Consolidation	Absent	< 1 cm	> 1/Multiple
POSTERIOR	0	1	2
B Lines (+/-)	Limited/Absent	Focal	Confluent
B Lines (# intercostal spaces)	< 1	1-3	>3
Consolidation	Absent	< 1 cm	> 1/Multiple



BRONCHIOLITIS FINDINGS



BRONCHIOLITIS FINDINGS	
1	Focal multiple B lines
2	Confluent B lines
3	Subpleural consolidation: Hypoechoic/hyperechoic area with ill-defined margins at the subpleural region (<1 cm, >1 cm)
4	Thickening (> 0.5 mm) or a course appearance of the pleural line due to subpleural consolidation (M-mode)
Krishna, Indian J Ped 2022, PubMed ID: 35438475	

LABORATORY TESTING: Testing may be helpful in detecting co-infection with bacterial pathogens in febrile infants. Infants less than 60 days with fever should be evaluated for serious bacterial infection such as urinary tract infection. The prevalence of bacteremia (1-2%) and UTI (1-5%) are lower than those without bronchiolitis Levine, Pediatrics 2004, PubMed ID: 15173498).

DIFFERENTIAL DIAGNOSIS

It is important to recognize that the differential diagnosis of tachypnea in the infant includes cardiac disease such as myocarditis, compensation for metabolic acidosis, central nervous system disorders that alter the control of ventilation and toxins such as salicylates.

DIFFERENTIAL DIAGNOSIS: WHEEZING	
Respiratory	Asthma, cystic fibrosis, aspirated foreign body
Cardiac	Viral myocarditis. Congestive heart failure may present with pulmonary edema manifested as wheezing.
Gastrointestinal	Reflux or tracheoesophageal fistula can cause bronchospasm or pneumonia
Infections	Mycoplasma pneumoniae, pertussis or Chlamydia trachomatis can cause paroxysmal cough and mild wheezing in some infants
Allergies	Anaphylaxis
Foreign body	Gastrointestinal or pulmonary
Congenital	Rings, webs or pulmonary sequestrations, laryngotracheomalacia
Toxins	Organophosphates (bronchorrhea) and hydrocarbons (chemical pneumonitis), others (non-cardiogenic pulmonary edema)

MANAGEMENT

Bronchiolitis is a self-limited illness, typically requiring supportive care such as adequate oxygenation and hydration until the disease abates. Patients with severe disease may require assisted ventilation.

AAP BRONCHIOLITIS RECOMMENDATIONS RELATED TO ED CARE: 2014	
1a	Clinical diagnosis
1b	Assess risk factors for severe disease
1c	Radiologic and laboratory testing should not be obtained routinely
2a	Bronchodilators should not be used
3	Epinephrine should not be used
4a	Hypertonic saline should not be used in the ED
4b	Hypertonic saline may be used in admitted patients
5	Systemic corticosteroids should not be used
6a	May choose not to use supplemental oxygen for oxygen saturation > 90%
6b	May choose not to use continuous pulse oximetry
7	Should not use chest physiotherapy
8	Should not administer antibiotics unless concomitant bacterial infection
9	Administer IV/NG hydration in infants who cannot maintain hydration orally

OXYGEN: The American Academy of Pediatrics recommends that practitioners may choose to not use supplemental oxygen for patients with oxygen saturation greater than 90%. Oxygen should be provided in the least invasive method to maintain oxygen saturation greater than 90%. It is common for oxygen saturation for decrease by 1-2% during feeding and sleeping.

A 2014 study demonstrated that artificially elevated oxygen saturations by 3% resulted in lower admission rates without an increase in complications (Shuh, JAMA 2014, PubMed ID: 25138332). A study of infants discharged from the emergency department with home oxygen saturations monitors, with the display and alarms turned off, revealed that a majority of infants (64%) had desaturations to less than 90% for > 1 minute (Principi, JAMA Pediatrics 2016, PubMed ID: 26928704). The presence of desaturations did not result in an increase in unscheduled health care visits or hospitalization. In the regression analysis, only previous medical visits were independently associated with desaturation indicating that those with desaturation could not have been predicted at the time of ED discharge. The authors conclude that: “these findings challenge the concept that infants with desaturations are sicker and suggest that pulse oximetry is not an effective tool to predict morbidity leading to escalated return for care”.

HYDRATION: Hydration is an important component of supportive care and can be administered orally, via a nasogastric tube or intravenously. Bronchiolitis is associated with an increase in antidiuretic hormone resulting in fluid overload and hyponatremia. Hypotonic intravenous solutions may exacerbate this process and should be avoided.

BRONCHODILATORS: Beta-agonists including Albuterol and Epinephrine have been studies extensively with often conflicting results. The literature suggests that the routine use of nebulized bronchodilators does not alter clinical course. The AAP recommendation for a trial of bronchodilators was changed in the 2014 guidelines from “should not routinely be used” to “should not be used”.

HYPERTONIC SALINE: The 2014 AAP Guidelines recommend that nebulized hypertonic saline may be administered in inpatients but should not be administered in the emergency department. This is consistent with a 2011 Cochrane meta-analysis. A 2015 meta-analysis of hypertonic saline for acute bronchiolitis (Zhang, Pediatrics 2015, PubMed ID: 26416925) calls into question the current AAP recommendation. 7 clinical trials including 951 outpatients were included. The pooled relative risk of admission (hypertonic saline/normal saline) was 0.8, 95% CI (0.67-0.96) indicating a decreased risk of admission. The decrease was greatest in those receiving more the two treatments. The authors report a relative reduction of admission of 20%, 95% CI (7, 38%) and an absolute reduction of in 7.9%, 95% CI (2.1, 13.6%). This corresponds to a number needed to treat of 12. 12 patients would need to be treated with nebulized hypertonic saline to prevent 1 additional admission. A multicenter, randomized, blinded clinical trial on the ED efficacy of hypertonic saline in a population of 777 infants 6 weeks to 12 months of age demonstrated a non-significant risk difference for admission to the hospital of –3.2%, 95% CI (-8.7%, 2.2%). In addition, infants in the hypertonic saline group had more mild adverse events (Angoulvant, JAMA Pediatrics 2017, PubMed ID: 28586918).

CORTICOSTEROIDS: A multicenter randomized, clinical trial enrolled 600 infants with bronchiolitis (PECARN, NEJM 2007, PubMed ID: 17652648). Patients received 1 mg/kg of Dexamethasone or Placebo. The absolute risk difference for admission (Dexamethasone (39.7%) – Placebo (41%) was -1.3% 95% CI (-9.2, 6.5%). The authors considered a 12% decrease in admission rate to be clinically significant. The authors concluded that Dexamethasone “did not significantly alter the rate of hospital admission or the respiratory status after 4 hours of observation. Neither did such treatment affect the length of the hospital stay among infants who were initially admitted, subsequent admissions or unscheduled medical visits, or adverse events.”

ADDITIONAL THERAPIES: Treat with Oseltamivir if influenza positive, older than 2 weeks of age and within 48-72 hours of symptom onset (See PEM Guide: Infection: Influenza). There is insufficient evidence to routinely recommend the use of chest physiotherapy or Heliox.

NONINVASIVE VENTILATION

See: PEM Guide: Airway Procedures: Noninvasive Ventilation

CPAP: CONTINUOUS POSITIVE AIRWAY PRESSURE: CPAP delivers a constant level of pressure support (inspiratory and expiratory) without regard to the respiratory cycle. It may be delivered through a variety of interfaces. Short bi-nasal prongs are preferred in neonates and infants due to the difficulty of maintaining an adequate face mask fit and seal.

CPAP SETTINGS
Pressure is usually started at 5 cm H_20
Increased by 1 cm H_20 as needed and tolerated
Typical levels are 5-10 cm H_20 with a maximum of 15 cm H_20

HHFNC: HUMIDIFIED HIGH FLOW NASAL CANNULA: Warm (35-37 C) and humidified nasal oxygen is better tolerated than normal wall oxygen. The pressure from high flow rates can open the soft palate by separating it from the posterior pharyngeal wall. It also provides an oxygen reservoir in the nasopharynx. When HHFNC is used in conjunction with a non-rebreather face mask it can increase the fraction of inspired oxygen (FiO_2) to 100%.

An Australian, randomized clinical trial including 200 children younger than 2 years of age with moderate bronchiolitis admitted to the hospital found no difference in the primary outcome of time to weaning off oxygen between the High-Flow Warm Humidified Oxygen (HFWHO) group (20 hours) and Low Flow (2 liters/minute) group (24 hours) (Kepreotes, Lancet. 2017, PubMed ID: 28161016). The authors considered a 12-hour difference to be clinically significant. However, there was a statistically significant difference in the proportion who remained free from treatment failure within 24 hours of admission (HFWHO: 90%, Standard Therapy: 60%). Hazard Ratio 0.3, 95% CI (0.2, 0.6). In addition, 63% (20/32) of patients who deteriorated on standard therapy and then trialed on HFWHO were successfully rescued and did not require transfer to the ICU or more invasive therapy.

A multicenter (17 regional and tertiary care hospital in New Zealand and Australia), randomized clinical trial included 1,472 infants younger than 1 year of age admitted for bronchiolitis requiring supplemental oxygen. Treatment failure occurred 12% in the HFNC group an 23% in the standard therapy group (Risk difference: 11%, 95% CI (7, 15%). The authors considered a 5% reduction to be clinically significant in their power analysis. 100% of the escalations in care that occurred in the standard therapy group were started on HFNC and 61% responded (Franklin, NEJM 2018, PubMed ID: 29562151).

HHFNC SETTINGS
Infants: Start at 1-2 liters/kg/min
Increase as needed and tolerated to 8 Liters/min
Older children and Adults: Up to 40 liters/min

DISPOSITION

Criteria for discharge, admission and admission to the pediatric ICU are included below. For discharged patients, parents should be educated about signs and symptoms of concern that would warrant seeking care. They should be informed of the risk of passive smoking, proper hand washing techniques and proper bulb suctioning prior to feeding. A follow up appointment with their primary care provider should be made.

DISPOSITION			
	Discharge[1]	Admit Floor	Admit PICU
Severity	Mild	Moderate	Severe
Hydration required	NO	YES	YES
Oxygen required[2]	NO	YES	YES
Ventilation required	NO	NO	YES
Apnea Risk[3]	NO	YES	YES: Witnessed

1. Requires a reliable care giver and ensured access to follow
2. Oxygen Requirement = Oxygen saturation < 90% awake, < 88% sleeping
3. Apnea Risk: Any age: witnessed apnea. <6 mo: Age 6 weeks, birth weight<2.5 kg

CROUP

INTRODUCTION (DENNIS HEON, M.D. 5/2022)
The narrowest part of a child's upper airway is the subglottic region. This is surrounded by a firm ring of cartilage (the cricoid cartilage). Airflow is proportional to the radius of the trachea to the 4th power. A small amount of edema will significantly restrict airflow in the child's smaller airway. Viral laryngotracheobronchitis (Croup) results in inflammation and edema of the tracheal walls. In addition, the vocal cords become impaired because of swelling. Croup may be caused by a number of viruses. In general, bacterial pathogens are not involved unless as a secondary infection.

CROUP PATHOGENS	
COMMON	RARE
Parainfluenza virus types 1-3	Human metapneumovirus
Influenza virus	Measles virus
Adenovirus	Herpes Simplex type1
Respiratory Syncytial virus	Varicella
COVID 19	Human Coronavirus HL-63

CLINICAL PRESENTATION
Narrowing of the airway leads to audible inspiratory stridor. Swelling of the vocal cords results in a hoarse voice. Croup must be differentiated from other causes of upper airway obstruction. Consider factors such as: the presence or absence of fever, age, season and rapidity of onset. (See: PEM Guide: Resuscitation: Airway).

DIFFERENTIAL DIAGNOSIS OF PEDIATRIC AIRWAY OBSTRUCTION	
INFECTIONS (FEBRILE)	MECHANICAL (AFEBRILE)
Peritonsillar abscess*	Tongue, muscle relaxation
Retropharyngeal abscess*	Angioedema (anaphylaxis)*
Croup (Laryngotracheal bronchitis)	Laryngospasm**
Bacterial tracheitis*	Airway foreign body*
Epiglottitis	Trauma: Neck, cervical spine*, oropharynx
Ludwig’s angina (floor of mouth, neck)	Smoke inhalation*
Cervical adenitis	Neck masses: Cystic hygroma, neoplasm
Laryngeal Diphtheria	Laryngomalacia
* Reviewed in greater detail in a separate PEM Guide **Laryngospasm may be caused by: submersion injury, gastroesophageal reflux, hypocalcemia and Ketamine.	

The classic presentation of croup is 1-3 days of nonspecific upper respiratory symptoms with progression to cough, stridor and respiratory distress. Parents often describe the cough as barking or seal-like. Nighttime exacerbations are common. Low-grade fever is often present. Biphasic stridor (inspiratory and expiratory stridor) and increased respiratory rate and work of breathing suggest a high grade of obstruction.

In the child with prolonged symptoms who becomes highly febrile with deteriorating respiratory status the diagnosis of bacterial tracheitis should be considered. (See: PEM Guide: Respiratory: Bacterial Tracheitis). The Westley croup score can be used to determine the severity of illness and guide management decisions (Westley, Am J Dis Child 1978, PubMed ID: 347921).

WESTLEY CROUP SCORE		
CRITERIA	ASSESSMENT	SCORE
Chest Wall Retractions	None	0
	Mild	+1
	Moderate	+2
	Severe	+3
Stridor	None	0
	With Agitation	+1
	At Rest	+2
Level of Consciousness	Normal	0
	Disoriented	+5
Cyanosis	None	0
	With Agitation	+4
	At Rest	+5
Air Entry	Normal	0
	Decreased	+1
	Markedly Decreased	+2
Mild: 0-2, Moderate: 3-5, Severe: 6-11, Impending Respiratory Failure: 12-17		

MANAGEMENT

Management of croup is dependent on the degree of airway obstruction. Supportive maneuvers include humidified air or oxygen (limited evidence), avoidance of agitating the child, suctioning of the nose and mouth and intravenous fluids. Nebulized epinephrine (vasoconstriction) and corticosteroids (anti-inflammatory effects) are used to reduce airway edema.

CROUP MANAGEMENT BASED ON CROUP SCORE		
≤ 4	Mild	Mist therapy, Corticosteroids
5-6	Mild-Mod	Mist therapy, Corticosteroids
7-8	Moderate	Epinephrine, Corticosteroids
≥ 9	Severe	Epinephrine, Corticosteroids, Consider Heliox, intubation

EPINEPHRINE: Nebulized Epinephrine causes alpha adrenergic vasoconstriction. Racemic Epinephrine and L Epinephrine are equally efficacious (Waisman, Pediatrics 1992, PubMed ID: 1734400). Epinephrine can be repeated every 20-30 minutes as needed. Intramuscular Epinephrine can also be administered in those with severe croup. The effect of Epinephrine wears off in 2-4 hours. t is typically recommended that patients should be observed for 2-4 hours for reemergence of symptoms as Epinephrine wears off. The patient may return to pretreatment symptoms but rarely worsen.

An observational study, including 276 patients who received Epinephrine, 93% of which were classified as mild croup, did not demonstrate a difference in return visits within 48 hours comparing those observed for less than 1 hour, from 1-2 hours and longer than 2 hours. This was true in those classified as mild and moderate croup (Udoh, Wisconsin Med J 2022, PubMed ID: 35442575.)

Traditionally, it has been thought that those requiring more than one Epinephrine dose in the emergency department should be hospitalized. A case series of 112 patients who were asymptomatic after a subsequent dose of Epinephrine demonstrated that these patients infrequently require additional interventions. 14% required additional Epinephrine. No patients required intubation or transfer to a higher level of care (Rudinsky, J Emerg Med 2015, PubMed ID: 26242923).

CORTICOSTEROIDS: Corticosteroids reduce the need for hospitalization and intubation. They have been shown to reduce unscheduled return visits in patients with mild croup (Bjornson, NEJM 2004, PubMed ID: 15385657). The intravenous preparation of Dexamethasone can be given intramuscularly and orally. A randomized clinical trial compared Dexamethasone (Low dose: 0.15 mg/kg) or Prednisolone (1 mg/kg) to Dexamethasone (Standard dose: 0.6 mg/kg)) in children older than 6 months with a clinical diagnosis of croup (Parker, Pediatrics 2019, PubMed ID: 31416827). Both interventions were non-inferior to standard dose Dexamethasone in mean Westley croup score at 1, 2 and 3 hours and in the proportion of patients with an unscheduled return visit. However, there was a statistically higher rate of requiring additional corticosteroids in the Prednisolone group (18.9%) compared to standard dose Dexamethasone (11.3%). Whether a 2nd dose of Prednisolone is warranted is unclear,

SUMMARY: PHARMACOLOGIC MANAGEMENT OF CROUP	
Corticosteroids	Dexamethasone: 0.6 mg/kg/dose IV, IM, PO Alternative: Prednisone/Prednisolone 1 mg/kg/day PO x 2 days
Epinephrine	Racemic Epinephrine (2.25 % Solution): 0.05 ml/kg, max 0.5 ml L-Epinephrine (1:1,000, 1.0 mg/ml): 0.5 ml/kg diluted to total of 3 ml with NS 2.5 ml < 4 years, 5 ml ≥ 4 years Can repeat Q20-30 minutes as needed
Heliox	70:30 Helium, Oxygen mixture. Contraindicated in patients requiring > 30% oxygen

HELIOX: Heliox is a combination of 70% helium and 30% oxygen. The lower density of the mixture results in decreased airway turbulence. Heliox cannot be used in in patients requiring more than 30% oxygen. Heliox may be considered in the patient with severe croup to possibly forestall intubation. A 2013 Cochrane systematic review (PubMed ID: 24318607) assessed three trails including 91 children with croup. The trails were found to have a number of methodologic limitations and could not be combined in a meta-analysis. The authors concluded that "There is some evidence to suggest a short-term benefit of Heliox inhalation in children with moderate to severe croup who have been administered oral or intramuscular dexamethasone."

ENDOTRACHEAL INTUBATION: Endotracheal intubation is rarely indicated in croup. In patients with severe or complete upper airway obstruction, endotracheal intubation bypasses the level of obstruction to provide definitive airway protection and oxygenation and ventilation distal to the obstruction. Smaller endotracheal smaller tubes should available due to tracheal narrowing from subglottic edema. Laryngeal mask airways are placed proximal to the level of obstruction and should not be used in patients with upper airway obstruction related to tracheal edema (croup, anaphylaxis, smoke inhalation).

INDICATIONS FOR ADMISSION
Respiratory Distress: Persistent increased work of breathing, stridor at rest, hypoxia
Respiratory Failure: Altered mental status, hypoxia, bradycardia, respiratory fatigue
Dehydration requiring intravenous hydration

PARAPNEUMONIC EFFUSIONS

INTRODUCTION (MICHAEL MOJICA, MD, 11/2022)
A pleural effusion is defined as the accumulation of fluid in the potential pleural space between the parietal and visceral pleura. A parapneumonic effusion is a pleural effusion associated with lung parenchymal infection. This is the most cause of pleural effusion in children and is typically associated with bacterial pneumonia due to Staphylococcus Aureus (MSSA and MRSA), Streptococcus pneumoniae, Streptococcus (pyogenes and viridans) and Actinomyces species. The rates of pneumococcal pneumonia and parapneumonic effusion have decrease since the introduction of 13-valent pneumococcal conjugate vaccine (Prevnar 13) in 2010. See also: PEM Guide: Respiratory: Pneumonia.

Viral, fungal, mycoplasma pneumoniae and mycobacterium tuberculosis are rare causes of parapneumonic effusions in children. Occasionally, infection from the retropharyngeal, retroperitoneal, abdominal and vertebral spaces can result in pleural effusion. Non-infectious, exudative, pleural effusions can be seen in pediatric patients with systemic lupus erythematosus as a result of pleuritis (generalized serositis).

Children with immunodeficiencies, malignancy, cerebral palsy, prior surgery, tuberculosis, congenital heart disease, prematurity and cystic fibrosis are at increased risk of parapneumonic effusions.

PATHOPHYSIOLOGY

Pleural effusions are typically classified as exudative or transudative. This distinction is less relevant in pediatric patients as most effusions are exudative due to infection.

1. EXUDATIVE STAGE: Inflammation from the lung spreads to the pleura. In the first 1-3 days, pleuritis impedes the ability to transport fluids and leads to the leakage of fluids and proteins. This fluid is frequently sterile and free flowing (simple effusion).

2. FIBRINOPURULENT STAGE: In the next 7-10 days, infection spreads to the pleura fluid (empyema). Accumulation of proteinaceous materials and fibrin deposition leads to septation with loculations limiting free flow (complicated or loculated effusion).

3. ORGANIZATIONAL STAGE: Over the following 2-4 weeks, fibroblasts grow on both pleural surfaces, leading to the formation of a “pleural peel”. This inelastic membrane restricts lung expansion and creates a persistent pleural space that increases the likelihood of subsequent fluid re-accumulation.

In contrast, transudates occur as a result of decreased oncotic pressure or increased hydrostatic pressure and are more common in adult patients. Examples of transudates in children are pleural effusions in children with nephrotic syndrome (decreased plasma oncotic pressure) and pleural effusion in children with congestive heart failure (increased hydrostatic pressure).

CLINICAL MANIFESTATIONS

The rapidity of fluid accumulation and the stage at which the child presents (exudative, fibrinopurulent, organizational) govern the clinical presentation. Slowly accumulating pleural effusions are frequently asymptomatic in children. Rapid accumulation may present with symptoms of fever, malaise, pleuritic chest pain, dyspnea and signs of respiratory distress (hypoxia, tachypnea, increased work of breathing). Auscultation on the side of the pleural effusion is characterized by decreased breath sounds and dullness to percussion. Auscultated lung volumes are low due to splinting due to pain. Oxygen saturation, mental status, signs of respiratory distress and poor perfusion (sepsis, dehydration) should be assessed in all children. Sepsis should be considered and managed appropriately. See also: PEM Guide: Infections: Sepsis and Septic Shock

Pleural effusion should also be considered, and a chest XRAY obtained, when pneumonia fails to improve after 48 hours of antibiotic therapy.

DIAGNOSIS: LABORATORY TESTING

BLOOD: Serum analysis typically include leukocytosis and elevation of acute phase reactants (PCT, CRP, ESR, thrombocytosis). However, these findings do not reliably distinguish between pneumonia with or without pleural effusion or non-bacterial causes of infection. Blood cultures are typically recommended but are of low yield.

PLEURAL FLUID: Laboratory analysis of the fluid with culture and sensitivities can be used to guide antibiotic therapy. Polymerase chain reaction (PCR) testing may be helpful in patients already treated with antibiotics. Typically, pleural fluid testing also includes cell count and differential, pH and glucose. However, chemical analysis of pleural fluid infrequently changes management in children because almost all are infectious exudates.

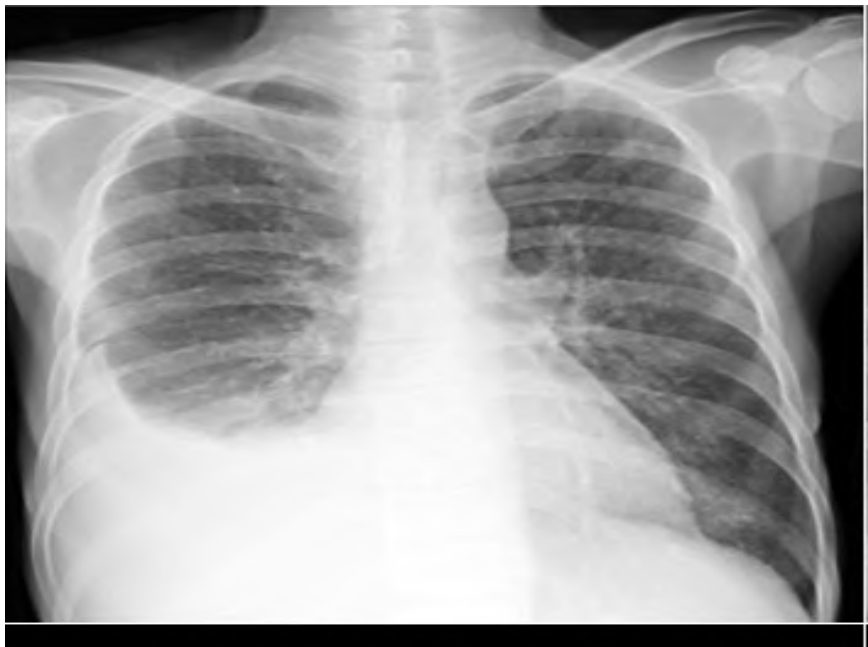
Further pleural fluid analysis may be helpful if tuberculosis or non-infectious causes of pleural effusion are suspected. A pleural fluid to serum protein ratio greater than 0.5, a pleural fluid to serum lactate dehydrogenase ratio greater than 0.6 and a pleural fluid lactate dehydrogenase greater than 200 U/L is usually diagnostic of exudative effusion. Neutrophilic predominance is characteristic of bacterial infections. Lymphocytic predominance is commonly seen in Tuberculosis, autoimmune diseases, malignancy and chylothorax.

DIAGNOSIS: IMAGING: Imaging is required to confirm and characterize pleural effusions.

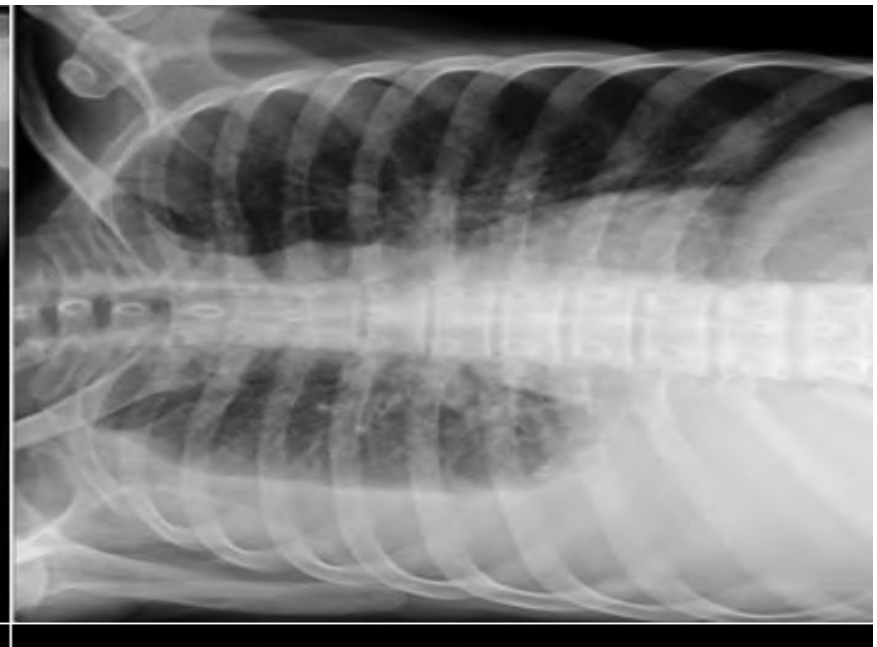
XRAY: Plain XRAY is able to detect pleural effusions greater than 150-200ml. Early signs include blunting of the costophrenic angle and a meniscus shaped area up the lateral chest wall. Lateral decubitus films are used to determine if the effusion is free flowing, and thus more amenable to drainage, or loculated, requiring fibrinolytics and/or surgery.

CHEST XRAY: PLEURAL EFFUSION SIZE		
Effusion	Decubitus View	Upright View[a]
Small	< 1 cm	1/4
Moderate	2 cm[b]	1/4 to 1/2
Large	> 2 cm[b]	> 1/2

a. Vertical Proportion of the hemithorax involved
b. Considered sufficient volume to perform a thoracentesis (See Appendix)

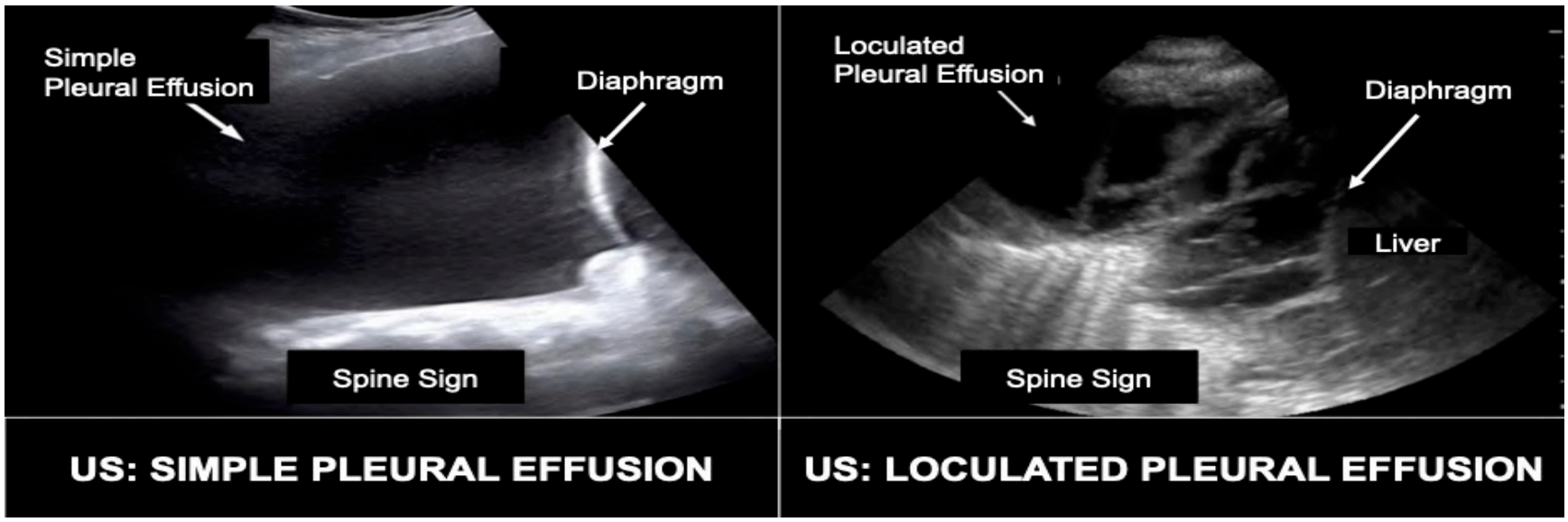


XRAY (AP): PLEURAL EFFUSION



XRAY (DECUBITUS): LAYERING

ULTRASOUND: Ultrasound has been shown to the more sensitive that plain XRAY. It identifies smaller effusions as well as loculations and septations which are not seen on plain XRAY. Unlike CT, ultrasound can be performed at the bedside, does not involve radiation, does not require sedation and can be used to guide the sight for pleural catheter placement. On ultrasound, pleural effusions range from anechoic to hyperechoic. The thoracic spine is typically not seen with an air-filled lung. A fluid collection, such as a pleural effusion or hemothorax make the spine visual (spine sign).



CT SCAN: CT with intravenous contrast is typically reserved to identify underlying lung parenchymal disease such as pulmonary anatomic abnormalities or necrotizing abscesses in patients who do respond to antibiotics and chest tube drainage.

MANAGEMENT

The goals of treatment are the resolution of infection, resolution of the pleural fluid collection and lung re-expansion. Supportive care includes antipyretics, analgesics and intravenous fluid hydration. Fluid balance and serum sodium should be monitored for the development of SIADH. Early ambulation can support pleural fluid mobilization.

There is considerable variability in the management of children with parapneumonic effusions. Algorithms to guide management have been developed by the British Thoracic Society (BTS, Thorax 2005, PubMed ID: 15681514), the Pediatric Infectious Diseases Society of America (IDSA, Clin Infect Dis 2011 PubMed ID: 21880587) and the American Pediatric Surgical Association (APSA, J Ped Surg 2012, PubMed ID: 23164006). Pediatric surgery should be consulted early in the management of these patients.

ANTIBIOTICS: Medical therapy includes appropriate antibiotics. Inpatient antibiotic recommendations includes intravenous Ceftriaxone and Vancomycin. Antibiotic coverage can be narrowed based on culture results. Selected patients with small, simple effusions who are clinically well may be managed as outpatients with appropriate antibiotic therapy if follow-up is assured. Outpatient antibiotic selection should be guided by pediatric community acquired pneumonia guidelines and local sensitivities. Antibiotics should be continued for at least 10 days after fever resolution.

INPATIENT ANTIBIOTIC SELECTION: PARAPNEUMONIC EFFUSION*	
Vancomycin AND	< 12 years: 20 mg/kg/dose Q6H ≥ 12 years: 20 mg/kg/dose Q8H
Ceftriaxone	50 mg/kg/dose IV Q24 hours (max dose: 2 grams)
*NYU Antibiotic Stewardship (2022), Duration of therapy: 2-4 weeks	

DRAINAGE: The need for drainage of pleural effusions is determined by the degree of respiratory compromise, the character of the effusion (simple vs loculated) and the response to initial antibiotic therapy. In general, patients with large effusion and/or respiratory distress and/or without clinical improvement on antibiotics for 24-48 hours should undergo a drainage procedure.

PLEURAL FLUID DRAINAGE TECHNIQUES
Thoracentesis (catheter aspiration): Infrequently performed in pediatrics
Chest Tube: Seldinger technique with a pigtail catheter Fibrinolytics: Preferred
Chest Tube: Surgical Fibrinolytics
Video assisted thorascopic surgery (VATS) Fibrinolytics
Operative thoracotomy

Simple thoracentesis for one-time drainage is infrequent in pediatrics because the etiology is typically known and ongoing drainage is frequently required. Indwelling pigtail catheter placement for continuous drainage is the preferred approach. Compared to standard chest tubes, pigtail catheters are smaller, less invasive (may be placed with the Seldinger technique) and more comfortable. Pigtail catheters may be used without fibrinolytics (simple effusion) or with fibrinolytics (loculated effusion). Pigtail catheters, particularly when used with fibrinolytics, have not been shown to occlude more frequently than standard chest tubes. See Appendix: Pigtail Catheter Placement

INDICATIONS FOR CHEST TUBE PLACEMENT
Respiratory compromise
Large, simple pleural effusions (optional)
Loculated pleural effusions of any size
Lack of clinical improvement with antibiotics alone

A 2017 Cochrane review including 8 randomized clinical trials (6 Pediatric, 2 Adult) and 391 patients concluded that there was “no statistically significant difference in mortality between primary surgical and non-surgical management of pleural empyema for all age groups. Video-assisted thoracoscopic surgery may reduce length of hospital stay compared to thoracostomy drainage alone. There was insufficient evidence to assess the impact of fibrinolytic therapy” (Redden, Cochrane DSR 2017, PubMed ID 28304084).

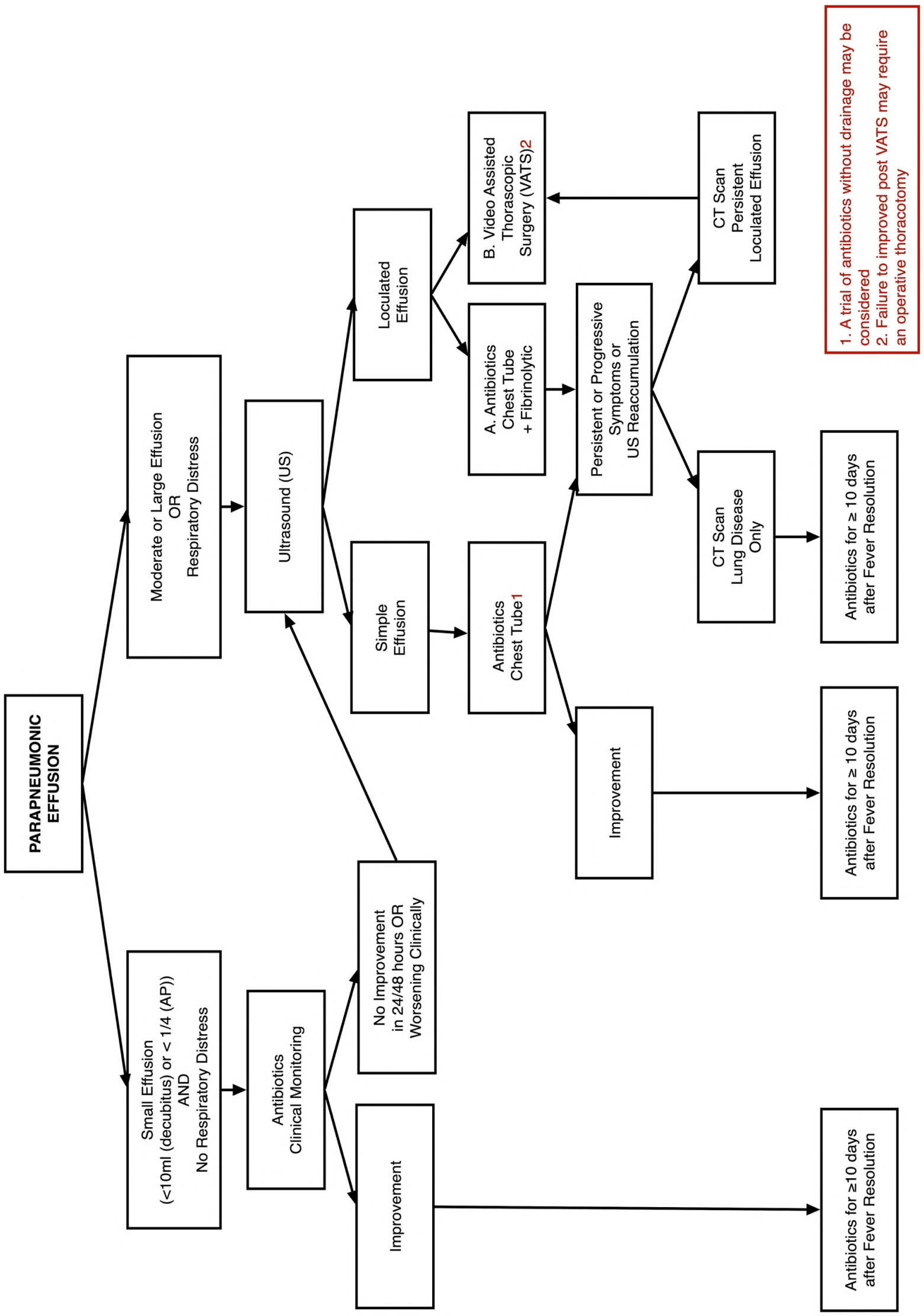
APPROACH: In general, small effusions, in patients without respiratory distress, can be managed initially with antibiotics alone. Chest tube drainage may be reserved for those without clinical improvement or clinical worsening in 24-48 hours and those with enlarging effusions on serial chest XRAY.

Those with moderate to large effusions on XRAY should undergo ultrasound to characterize the effusion as simple or loculated. A trial of antibiotics without drainage can be considered for those with moderate to large, simple effusions who are not in respiratory distress. For those with moderate-large, loculated effusions, a trial of pigtail chest tube drainage with intrapleural fibrinolytics may be considered prior to video assisted thorascopic surgery (VATS). Alteplase, a recombinant tissue plasminogen activator, is the fibrinolytic typically used in the US. Use of fibrinolytics requires clamping of the chest tube, so fibrinolytic use is contraindicated in patients with an ongoing air leak. Ultrasound can be used to guide chest tube placement at the bedside or to mark the site of placement prior to the procedure. Patient who do not improve after chest tube drainage should proceed to VATS. Those who do not improve with VATS and those with a bronchopleural fistula may require an operative thoracotomy. See Appendix: Parapneumonic Effusion Management Algorithm

DISPOSITION

The majority of pediatric patients with a parapneumonic effusion will require admission. Selected patients with small, simple effusions who are clinically well, may be managed as outpatients with appropriate antibiotic therapy if follow-up is assured.

APPENDIX: PARAPNEUMONIC EFFUSION MANAGEMENT



APPENDIX: PIGTAIL CATHETER PLACEMENT

PIGTAIL CATHETER PLACEMENT USING SELDINGER TECHNIQUE	
1	Identify anatomic landmarks, prepare, anesthetize area
2	Make a small incision over desired intercostal space, above the lower rib
3	Insert the needle into the pleural space, aspirate fluid
4	Insert guide wire through the introducer needle and into the pleural space
5	Guide the wire inferior/posterior for pleural effusions
6	Pass the dilator over the wire. Don’t lose the wire in pleura cavity!
7	Remove the dilator and pass chest tube (< 14 French) into pleural space
	a. Ensure that all of the catheter holes are within the pleural cavity
8	Remove guide wire
9	Connect chest tube to a unidirectional pleural drainage system at chest level
10	Drain large effusions gradually to avoid re-expansion pulmonary edema
	a. Clamp drain for 1 hour after 10ml/kg. Only if no air leak
	b. Large children/adolescents: ≤ 1,500 ml at one time or ≤ 500 ml/hour
11	Unclamp immediately for chest pain and/or shortness of breath
	a. Subclinical tension pneumothorax due to air leak
	b. Rapid re-accumulation of fluid
12	Remove chest tube: Analgesia, while patient performs valsalva
	a. Clogged chest tube that cannot be unclogged with a saline flush
	b. Clinical resolution AND minimal drainage (<10-15 ml/day)
	1. Resolution: Fever, WBC, CRP, RR, HR,
13	Chest XRAY post removal to assess for pneumothorax

WEB LINK: PIGTAIL CATHETER PLACEMENT (ESSENTIAL MEDICAL SKILLS)

WEB LINK: ULTRASOUND GUIDED PIGTAIL CATHETER (NEJM)

PERTUSSIS

INTRODUCTION (MICHAEL MOJICA, M.D., 10/2017)
Bordetella pertussis is a gram negative respiratory pathogen that causes destruction of ciliated respiratory cells. The resulting secretions result in the characteristic cough. Pertussis is spread by aerosolized droplets expelled during coughing. The incubation period is from 7-10 days but may be as long as 3 weeks which makes identifying index cases difficult. Pertussis morbidity and mortality is greatest in those less than a year of age.

VACCINATION
Pertussis vaccination began in the 1940's with dead whole-cell pertussis. An acellular pertussis vaccine was introduced in the 1990's with less side effects. The DTaP vaccine (Acellular pertussis with tetanus and diphtheria toxoids) is recommended for those less than seven years of age in a 5-dose schedule (2, 4 and 6 months, 15-18 months and 4-6 years). A single dose of Tdap is given at 11-12 years. Neither vaccination or infection confer life-long immunity. Immunity wanes in adolescence and as a result adolescents and adults serve as a reservoir of Pertussis.

CLINICAL MANIFESTATIONS
Infection with pertussis is called "whooping" cough due to the characteristic inspiratory sound made after a coughing episode. The classic presentation of paroxysms of coughing followed by an inspiratory whoop and post-tussive vomiting occurs most commonly in those less than 10 years of age.
Atypical presentations are common. Infants less than 4 months may have a shortened catarrhal phase with minimal cough and present with gagging, gasping, vomiting bradycardia and cyanosis. Vaccinated and older patients have less severe and nonspecific illness which results in under-recognition and therefore under treatment. More the 50% of adolescents have a cough for more than 10 weeks.

PERTUSSIS STAGES		
STAGE	SYMPTOMS	DURATION
Catarrhal	URI (cough, coryza), cough increases gradually Fever rare (low grade if present) Malaise, Myalgias	1-2 weeks
Paroxysmal	Paroxysms of cough with little inspiratory time leading to forced inspiration (whoop) Whoop most common < 1 year (25-50%) Post-tussive vomiting Precipitated by: yawning, laughing, exercise. Cyanosis, gagging, sweating between episodes	2-8 weeks
Convalescent	Gradual resolution of cough (> 50%, > 1 month)	Weeks to Months

DIAGNOSTIC TESTING
A confirmed case of pertussis is defined by clinical characteristics and laboratory testing (WEB LINK: CDC CASE DEFINITION). The organism is difficult to isolate and is less likely to be identified in the paroxysmal phase or after antibiotics. Appropriate technique and equipment to obtain a specimen from the posterior nasopharynx is essential (VIDEO LINK: SPECIMEN COLLECTION). Culture is the traditional reference standard due to its 100% specificity. Sensitivity decreases after 2 weeks, vaccination or antibiotics Culture also allows for strain and resistance testing. Results take 2-3 days.

Polymerase chain reaction testing is more sensitive and less specific but has a more rapid turn-around than culture. Sensitivity decreases after 3-4 weeks of symptoms, in patients who were previously vaccinated or treated with antibiotics for more than 5 days. Serology testing available from the CDC and state public health labs can be used for later identification (2-12 weeks).

A WBC count > 20,000 with a lymphocytosis > 50% is often seen in infants but not adolescents or adults. The degree of leukocytosis is correlated with disease severity. A chest XRAY should be considered to exclude pneumonia, foreign body aspiration and congestive heart failure.

CDC CRITERIA
CLINICAL
Cough > 2 weeks WITHOUT a more likely diagnosis AND ≥ 1 of the following
1. Paroxysms of cough OR
2. Inspiratory whoop OR
3. Post-tussive vomiting OR
4. Apnea with or without cyanosis (< 1 year only)
LABORATORY
1. Isolation of Bordetella pertussis from a culture of a clinical specimen OR
2. Positive polymerase chain reaction (PCR)
EPIDEMIOLOGICAL
1. Contact with a laboratory confirmed case of pertussis

CDC CASE DEFINITIONS
CONFIRMED CASE
1. Acute cough of any duration AND isolation of Bordetella pertussis (culture) OR
2. Clinical criteria (above) AND positive PCR OR
3. Clinical criteria (above) AND contact with a laboratory confirmed case OR
4. Cough > 2 weeks in the setting of a known outbreak
PROBABLE CASE
1. Clinical criteria (above) without laboratory or epidemiologic criteria OR
2. Infant < 1 year of age with cough of ANY duration of symptoms AND
≥ 1 of the 4 clinical criteria (above) AND
Positive PCR or contact with a laboratory confirmed case

COMPLICATIONS

Complications are due to the infection and mechanical problems due to the severe cough. Complications are most common in preterm and unvaccinated infants including sudden unexplained death. Infectious complications include pneumonia and otitis media. Pneumonia is associated with a necrotizing bronchiolitis and pulmonary hypertension and is a cause of mortality in infants. Apnea is typically associated with coughing episodes but can occur between episodes. It is most common in infants less than 6 months. Seizures and encephalopathy are rare complications. Most deaths occur in those less than 6 months of age. Mechanical complications in adolescents include subconjunctival hemorrhage, rib fractures, lower back strain, urinary incontinence, syncope, pneumothorax, sleep disturbance and rarely stroke and cerebral hemorrhage.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of pertussis includes a variety of bacterial respiratory pathogens (TB, mycoplasma/chlamydia pneumoniae) and viral pathogens (RSV, influenza parainfluenza, adenovirus, human metapneumovirus and rhino viruses). The identification of a respiratory pathogen does not exclude co-infection with pertussis. Pertussis is more likely to be associated with a paroxysmal cough, post-tussive vomiting, a longer duration of symptoms, cyanosis and an elevated WBC and absolute lymphocyte counts. Those with pertussis are less likely to be febrile and have nasal congestion. Foreign body aspiration, asthma, sinusitis, pneumonia, gastro-esophageal reflux and congestive heart failure can present with a prolonged cough.

MANAGEMENT

A high index of suspicion should be maintained in infants (particular those < 4 months) who are at greatest risk of pertussis complications. The majority of patients will clear the infection within 6 weeks without treatment but remain contagious for the first 3 weeks of symptoms. Pertussis should be reported to the department of health.

SUPPORTIVE CARE: Mechanical ventilation may be required for significant apnea. Intravenous hydration may be required. Antihistamines, corticosteroids and antitussives do not appear to be effective. Patients with wheezing may benefit from a trial of a bronchodilator though their effectiveness is questionable.

ANTIBIOTICS: Antibiotics should be initiated in those with a high likelihood of pertussis and those with a high risk of complications and should not be delayed for laboratory confirmation. Antibiotics initiated in the first week of infection may lessen cough severity and duration. Treatment in later stages of illness does not affect symptom duration but may reduce the spread of infection.

Macrolide antibiotics are recommended. Azithromycin should not be used in patients with prolonged QT or other arrhythmia risk factors. Azithromycin and Clarithromycin have been associated with pyloric stenosis in infants less than 1 month of age. Azithromycin should still be utilized due to the high risk of complications in these patients but patients should be monitored for 1 month for the development of pyloric stenosis.
Trimethoprim-Sulfamethoxazole is recommended as a second line agent for those unable to tolerate a macrolide or for those with macrolide resistance though evidence is limited. Penicillins and first generation cephalosporins are not effective.

ANTIBIOTIC INDICATIONS
Laboratory confirmed pertussis: 1. ≥ 1 year of age with symptom duration < 3 weeks 2. < 1 year of age with symptom duration < 6 weeks
Patients with longer symptom duration than above who are in contract with high risk patients (below)
Clinical diagnosis of pertussis with symptom duration < 3 weeks

HIGH RISK PATIENTS
Infants < 1 year
Pregnant women
Immunodeficiency or immunosuppressive medication
Chronic severe lung disease
Contact with infants

PERTUSSIS TREATMENT AND PROPHYLAXIS				
	AZITHROMYCIN	ERYTHROMYCIN	CLARITHROMYCIN	TMP-SMX*
< 1 month	10 mg/kg/day x 5 days	NO	NO	NO
1-5 months	10 mg/kg/day x 5 days	40 mg/kg/day divided QID x 14 days	15 mg/kg/day divided BID x 7 days	(> 2 month only) TMP 8 mg/kg/d divided BID X 14 days
6 months - Adult	10 mg/kg Day 1 (max 500 mg) 5 mg/kg D 2-5 (max 250 mg)	40 mg/kg/day (max 2 gm/day) divided QID x 7-14 days	15 mg/kg/day (max 1 gm/day) divided BID x 7 days	TMP 8 mg/kg/d (max 320 mg/d) divided BID X 14 days
Adult	500 mg Day 1 250 mg Day 2-5	2 grams/day divided QID x 7-14 days	1 gram/day divided BID x 7 days	TMP 320 mg/d divided BID X 14 days
*Alternative: Trimethoprim-Sulfamethoxazole. Dosing in Trimethoprim component				

POST-EXPOSURE ANTIBIOTIC PROPHYLAXIS: PEP is recommended for all household contacts of the index case and other close contacts, including children in child care, regardless of immunization status. Close contact is defined as: face to face exposure within 3 feet, close contact with secretions (respiratory, nasal, oral), living in the same household and sharing a confined space for more than an hour. PEP is also recommended for those at high risk of pertussis complications (see table above). Contacts who are unvaccinated or under-immunized require pertussis vaccine in addition to antibiotic prophylaxis.

DISPOSITION

Patients requiring admission generally require a monitored setting. The progression of illness and complications in young infants cannot be reliably predicted and they will likely require admission. Droplet precautions should be initiated until 5 days of antibiotics. Discharged patients should refrain from attending school until after 5 days of antibiotics or after 3 weeks of symptoms if they have not been treated with antibiotics.

ADMISSION CRITERIA
Respiratory distress
Hemodynamic compromise
Radiographic pneumonia
Inability to feed, dehydration
Seizures
Apnea
< 4 months

PNEUMONIA

INTRODUCTION (MICHAEL MOJICA, M.D. 1/2023)
The most common lower respiratory tract infections in children are bronchiolitis and pneumonia. Pneumonia is defined as inflammation of the pulmonary tissue most often resulting from infection. It is identified by clinical findings and frequently confirmed by chest radiography. This PEM Guide focuses on confirmed or suspected community acquired pneumonia in children over 3 months of age. See also: PEM Guide: Respiratory: Parapneumonic Effusions

MICROBIOLOGY
There are many infectious agents that may cause pneumonia. Both viral and bacterial causes have been implicated and co-infection is common. In a study of 2,222 pediatric inpatients with radiologically confirmed pneumonia, 81% had an identified pathogen. 66% had at least one viral pathogen, 8% had a bacterial pathogen and 7% had both a viral and bacterial pathogen (Jain, NEJM 2015, PubMed ID: 25714161). This has implications for treatment. Importantly, the identification of a viral pathogen decreases but does not exclude the presence of a bacterial pathogen. In fact, a viral infection may predispose to bacterial superinfection.

The predominant pathogens are dependent on the age, vaccination status, season, exposures and underlying conditions. Viral etiologies are more common in infants and young children (see table below). While bacterial pathogens are more common in older children, viral illness still predominates. Unusual organisms should be considered in the immunocompromised host or those patients that do not respond appropriately to initial therapy.

COMMUNITY ACQUIRED PEDIATRIC PNEUMONIA: ETIOLOGY BY AGE GROUP					
	< 2 years	2-4 years	5-9 years	10-17 years	ALL
Resp Syncytial virus	42%	29%	8%	7%	28%
Human Rhino virus	29%	25%	30%	19%	27%
Human Metapneumo	14%	17%	10%	4%	13%
Adeno virus	18%	9%	4%	2%	11%
Para-Influenza virus	7%	8%	6%	4%	7%
Influenza virus	6%	5%	9%	11%	7%
Corona virus	6%	6%	3%	4%	7%
VIRAL TOTAL*	122%	99%	70%	47%	100%
M. Pneumoniae	2%	5%	16%	23%	8%
S. Pneumonia	3%	4%	4%	3%	4%
S. Aureus	1%	1%	1%	1%	1%
S. Pyogenes	1%	1%	< 1%	< 1%	1%
BACTERIAL TOTAL*	7%	11%	22%	28%	14%
*Totals add up to > 100% due to co-infection with more than 1 pathogen					

CLINICAL MANIFESTATIONS

Signs and symptoms of pneumonia will vary with the patient's age, pathogen and the severity of disease. An older child may present with fever, cough, pleuritic chest pain, shortness of breath and tachypnea. Infants may present with nonspecific signs and symptoms such as poor feeding, vomiting, lethargy and irritability. Clinical findings have been found to be inaccurate (Shah, JAMA Pediatr. 2013, PubMed ID: 23229753). Signs and symptoms can overlap with an upper respiratory infection (URI) and a URI typically precedes pneumonia. Pneumonia should be suspected in those with a late developing fever or those whose cough or fever resolves and then recurs.

ACCURACY OF CLINICAL EXAMINATION		
	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)
Clinical Impression	84% (69, 92%)	39% (32, 57%)
Tachypnea	41% (21, 67%)	76% (68, 71%)
Decreased Breath Sounds	24% (13, 40%)	83% (77, 88%)
Rales	24% (13, 40%)	75% (68, 81%)

In general, viral etiologies have a gradual onset of symptoms; typically starting as an upper respiratory tract infection before traveling to the lower respiratory tract. Inspiratory rales may be heard on auscultation or breath sounds may be focally diminished or absent. Wheezing suggests a viral etiology in an infant and mycoplasma and enterovirus D68 in an older child without a prior history of wheezing. Though there is considerable overlap, certain patterns may suggest a specific etiology.

RESPIRATORY DISTRESS		
Tachypnea	0-2 months 2-12 months 1-5 years > 5 years	> 60 breaths/min > 50 breaths/min > 40 breaths/min > 20 breaths/min
Dyspnea		
Increased work of breathing: Retractions, grunting, nasal flaring		
Altered mental status		
Pulse oximetry < 90% on room air		

COMPLICATIONS OF PNEUMONIA	
Pulmonary	Pleural effusion, empyema
	Lung necrosis, abscess
	Bronchopulmonary fistula
	Respiratory failure
Metastatic	Meningitis, central nervous system abscess
	Pericarditis, endocarditis
	Osteomyelitis
	Septic arthritis
Systemic	Sepsis, bacteremia
	Hemolytic uremic syndrome

S. PNEUMONIAE is the most common bacterial etiology of pneumonia presenting with rapid onset of high fever and lobar infiltrates on chest. The pneumococcal protein conjugate vaccines (Prevnar-7) has been shown to significantly reduce the incidence of invasive pneumococcal disease. In 2010, a new version of the vaccine adding coverage for 6 additional serotypes (Prevnar 13) was introduced. Prevnar 15 (Merck) was approved in 2022. Prevnar 20 (Pfizer) is expected to be approved in 2023. The impact on management has yet to been determined but may allow for less antibiotic use in infants and young children with suspected viral disease and targeted macrolide use in older patients likely infected with atypical organisms.

STAPH AUREUS infections typically occur in infants. Pneumatoceles (necrosis/abscess) and subsequent pneumothorax may be seen on XRAY. It should be suspected is severely ill patients and those that do not respond to initial therapy.

CHLAMYDIA TRACHOMATIS is most common in patients 2 weeks to 3-months of age who presents with a staccato cough, who are afebrile and have signs of both upper and lower respiratory tract disease. Conjunctivitis and eosinophilia may also be present.

M. PNEUMONIA AND C. PNEUMONIA are more commonly seen in the school age child and adolescents. The incidence of mycoplasma pneumonia is: 9% (< 5 years), 51% (5-9 years), 74% (9-15 years) and 3-18% (adults). Patients are generally well-appearing (“walking pneumonia”). Clinically, presentation is similar to influenza with a gradual onset of headache, malaise myalgias, sore throat and low-grade fever. Upper respiratory tract findings are more common than seen with Streptococcal pneumoniae.

B. PERTUSSIS may present with upper respiratory symptoms (catarrhal phase) followed by harsh coughing episodes with or without inspiratory stridor (paroxysmal phase). Cough may linger for weeks to months (convalescent phase)(See also: PEM Guide: Respiratory: Pertussis).

LABORATORY TESTING

A CBC may be obtained for inpatients. Acute phase reactants (CRP, ESR, Procalcitonin) do not reliably differentiate between viral and bacterial etiologies but may be used to follow the course of severe disease. In patients less than 5 years of age, a WBC > 20,000 is predictive of occult infection (9%, 95% CI 4, 13%). (Rutman, Pediatr Emerg Care. 2009, PubMed ID: 19116501).

Nasopharyngeal testing for viral pathogens may be helpful for cohorting of inpatients but does not exclude a co-existing bacterial infection and are expensive. Influenza testing may change treatment decisions (Oseltamivir). In addition to viruses, respiratory pathogen panels identify Bordetella pertussis, chlamydia and mycoplasma pneumoniae.

Blood cultures are of low yield in patients with pneumonia. In one study, 2.5% of patients with pneumonia had a positive blood culture and the results did not change management (Neuman, Pediatrics 2017, PubMed ID: 28835382). Contaminants are identified up to four times as frequently as pathogens. Obtain cultures for those requiring admission, who fail to respond to therapy and those with suspected sepsis.

RADIOLOGIC DIAGNOSIS

Chest radiographs are not routinely indicated in children with suspected lower respiratory tract disease but are often used to confirm clinical impression and guide further therapy. Chest radiograph finding are typically divided into diffuse interstitial infiltrates with hyperinflation (most characteristic of virus infection and mycoplasma) and lobar infiltrates (bronchopneumonia with or without an effusion that are typical of bacterial infections) though considerable overlap exists. A chest XRAY should be obtained in patients requiring admission, those with hypoxemia or significant respiratory distress), those that do not respond to initial therapy and suspected complications.

If a chest XRAY identifies a pneumonia complication (e.g. pleural effusion/empyema, pneumatocele) then an ultrasound or chest CT may be indicated.

MANAGEMENT

The majority of children with pneumonia can be managed as outpatients. Those with a likely viral etiology do not require antibiotics. Antibiotic treatment of pneumonia is dependent on: disease severity, clinical course, likely pathogen, results of ancillary testing, radiographic findings and antibiotic susceptibility.

Antiviral therapy may be indicated in influenza (Oseltamivir) and COVID 19 (antivirals or monoclonal antibodies. Therapy for influenza should be initiated early in the course of illness, for those with pneumonia requiring admission and those at increased risk for complications of influenza (See: PEM Guide: Infections: Influenza)

COMPLICATED COMMUNITY ACQUIRED PNEUMONIA
Parapneumonic effusion/empyema
Multi-lobar disease
Necrotizing pneumonia, abscess, cavities
Bronchopleural fistula, pneumothorax
Bacteremia
Pneumonia as a complication of bacterial disease (e.g., retropharyngeal abscess)
Pneumonia associated with mediastinitis, pneumomediastinum

OUTPATIENT THERAPY: Antibiotics are not generally required in the healthy, fully immunized, preschool infant/toddler with mild-moderate pneumonia thought to be of viral etiology. A prospective cohort study assessed the efficacy of outpatient antibiotics in 147 propensity scoring matched pairs of children with a mean age of 3.5 years who did or did not receive antibiotics for community acquired pneumonia after an emergency department visit in which a chest XRAY was obtained for a suspicion of pneumonia. (Lipshaw, Pediatrics 2020, PubMed ID: 32179662). Antibiotics were administered or prescribed to 49.9% of patients. There was no statistically significant difference in the composite outcome of treatment failure (Odds ratio: 0.66, 95% CI (0.19, 2.3) or any of the individual components of the composite outcome (subsequent admission for pneumonia, change or initiation of antibiotics). This is the age when viral pneumonias predominate and thus the group less likely to see a response to antibiotics. Due to sample size, the authors were unable to perform an age stratified analysis so the applicability of the study's results to older children with a higher risk of bacterial pneumonias is unclear.

The majority of bacterial infections are caused by Strep pneumoniae. High dose Amoxicillin (90 mg/kg/day divided BID or TID) is the antibiotic of choice. Alternatively, an oral second or third generation cephalosporin or intramuscular ceftriaxone may be administered. Duration of therapy for uncomplicated, community acquired bacterial pneumonia is typically 5-7 days if clinically improving .

Macrolides (Azithromycin, Clarithromycin) have antibacterial and anti-inflammatory effects. Macrolides can be added for older patients with chest XRAY findings consistent with atypical pneumonia. However, S pneumoniae and M pneumoniae have become increasingly resistant to macrolides. Data on their efficacy is limited.

ANTIBIOTIC SELECTION: PEDIATRIC OUTPATIENTS (DURATION: 5 DAYS)	
PRIMARY	ALTERNATIVE
< 5 years, fully immunized	
Amoxicillin (High dose)	Alternate: 2nd/3rd generation cephalosporin e.g. Cefuroxime, Cefdinir
	Non-severe PCN allergy: Cefdinir
	Severe PCN allergy: Clindamycin, Levofloxacin
> 5 years, fully immunized	
Amoxicillin (High dose)	Consider adding Azithromycin is suspected atypical pathogen or pertussis
	Non-severe PCN allergy: Cefdinir
	Severe PCN allergy: Clindamycin, Levofloxacin
Not fully immunized for H. influenzae type B and S. pneumoniae	
Amoxicillin/ Clavulanate (High dose)	Alternate: 2nd/3rd generation cephalosporin e.g. Cefuroxime, Cefdinir
	Non-severe PCN allergy: Cefdinir
	Severe PCN allergy: Levofloxacin
Aspiration pneumonia	
Augmentin	Severe PCH allergy: Clindamycin
ADDITIONS TO ABOVE COVERAGE: MRSA	
ADD Bactrim	Patient/family history or community at high risk for MRSA
	Alternate: Linezolid
ADDITIONS TO ABOVE COVERAGE: Suspected atypical bacterial or Pertussis	
ADD Azithromycin	May be added if > 5 years and atypical PNA or Pertussis suspected
	Minimal effects on the duration of illness
NYU Pediatric Antibiotic Stewardship Program (Revised 2022) See Appendix: Antibiotic Dosing	

INPATIENT THERAPY: For admitted patients, intravenous Ampicillin (50 mg/kg Q6H) may be used in the setting of low pneumococcal resistance in the fully immunized patient. Alternatively, Ceftriaxone (50 mg/kg Q12-24H) may be used. Clindamycin or Vancomycin should be added if there is a concern of Staph aureus.

A 2017, observational study compared the efficacy of a beta-lactam antibiotic monotherapy to a beta-lactam antibiotic plus a macrolide in pediatric patients admitted to 3 children's hospitals with radiographic pneumonia (Williams, JAMA Peds 2017, PubMed ID: 29084336). The propensity matched cohort (n=560, mean age 27 months), demonstrated no difference in hospital length of stay or any of the study's secondary outcomes (recovery, re-hospitalization. Importantly, the addition of a macrolide did not affect length of stay in those older than 5 year and in those with a documented atypical bacteria.

Seven days of therapy has been most studied (5 days for Azithromycin). A longer duration of therapy may be required for complicated pneumonias (e.g. empyema).

Inpatients can be transitioned to oral therapy when they are able to tolerate oral intake, have a normal respiratory rate per age, baseline mental status, no oxygen requirement and no increased work of breathing.

ANTIBIOTIC SELECTION: PEDIATRIC INPATIENTS (DURATION 5-7 DAYS)	
PRIMARY	ALTERNATIVE
Fully Vaccinated for H influenzae type B and S pneumoniae	
Ampicillin OR Penicillin G	Non-Severe PCN Allergy: Ceftriaxone
	Severe PCN allergy: Clindamycin OR Levofloxacin
Not Fully Vaccinated for H influenzae type B and S pneumoniae	
Ceftriaxone	Severe PCN allergy: Levofloxacin
Patient/family History or Community at High MRSA Risk	
ADD Vancomycin	Alternate: Linezolid
Suspected Atypical Pathogen	
ADD Azithromycin x 5d	Alternate: Levofloxacin
Aspiration Pneumonia	
Ampicillin-Sulbactam	Severe PCN allergy: Clindamycin
Radiographically Complicated Pneumonia x 2-4 weeks	
Ceftriaxone AND Vancomycin	Vancomycin Alternative: Linezolid
	Ceftriaxone Alternative (Severe PCN allergy): Levofloxacin
*NYU Pediatric Antibiotic Stewardship Program (Reissued 2020) See Appendix: Antibiotic Dosing	

PARAPNEUMONIC EFFUSIONS: Parapneumonic effusions include transudates and exudates. Empyema implies the presence of an infectious exudate in the pleural space. Absence of breath sounds, pleural fluid on ultrasound or XRAY, fever, chest pain and a positive blood culture may suggest empyema. Lateral decubitus chest XRAY's, ultrasound or chest CT may be indicated to better characterize a parapneumonic effusion. Pleurocentesis guided by sonography may be used to alleviate symptoms, diagnosis empyema and to identify a pathogen. Surgery may be consulted for complex infections (e.g. loculated empyema) for chest tube with fibrinolytics or video assisted thorascopic surgery (VATS).

See also: PEM Guide: Respiratory: Parapneumonic Effusions

DISPOSITION

Follow up should be arranged in 48-72 hours for patients treated as outpatients. Those who do not improve or who have progressive clinical deterioration should have a chest XRAY, ancillary studies (CBC, Blood culture, acute phase reactants, viral testing) and be admitted.

ISOLATION PRECAUTIONS	
Droplet and contact	Respiratory virus, H. infuenzae
Droplet x 24 hours	H. infuenzae, Strep pyogenes, Bordatella pertussis
Airborne	M tuberculosis

INDICATIONS FOR ADMISSION
Significant Increased work of breathing: Retractions, nasal flaring, grunting
Tachypnea: 0-2 mo > 60/min, 2-12 mo > 50/min, 1-5 yrs > 40/min,, > 5 yrs > 20/min
Oxygen requirement: O_2 Sat < 90% on room air
Age < 3-6 months with suspected bacterial pneumonia
Dehydration, poor oral intact
Suspected MSRA infection (e.g. pneumatocele)
Immunocompromised patient
Significant co-morbidities
Radiographically complicated pneumonia
Inability to comply with treatment or follow up
Persistent or worsening disease after 48 hours of antibiotics

INDICATIONS FOR ADMISSION: PICU
Apnea
Requiring Invasive or noninvasive ventilation
Impending respiratory failure
Sustained tachycardia, hypotension
SaO_2 < 92% on FiO_2 ≥ 50%
Altered mental Status

APPENDIX: ANTIBIOTIC DOSING

ANTIBIOTIC DOSING			
Name	Route	Dose	Maximum Dose
Amoxicillin	PO	45 mg/kg Q12 hours	1 gram/dose
Amoxicillin-Clavulanate	PO	45 mg/kg of Amoxicillin Q12hours	1 gram/dose
Ampicillin	IV	50 mg/kg Q6 hours	2 grams/dose
Ampicillin-Sulbactam	IV	50 mg/kg Ampicillin Q6 hours	2 grams/dose
Azithromycin	PO/IV	Day1 10 mg/kg, D2-5 5 mg/kg	500 mg/dose
Bactrim[1]	PO	4-6 mg Trimethoprim Q 12 hours	160 mg/dose
Cefdinir	PO	7 mg/kg Q12 hours	300 mg/dose
Ceftriaxone	IV	50 mg/kg Q12-24 hours	2 grams/dose
Clindamycin	PO/IV	10-13 mg/kg Q8 hours	600 mg/dose
Levofloxacin	PO/IV	10 mg/kg Q12-24 hours	750 mg/dose
Linezolid	PO/IV	10 mg/kg Q8-12 hours	600 mg/dose
Penicillin G	IV	50,000 units/kg Q6 hours	6 million units/dose
Vancomycin (1mo-11yr)	IV	15 mg/kg Q6 hours	1,250 mg/dose
Vancomycin (12 yrs)	IV	15 mg/kg Q8 hours	1,500 mg/dose
1. Bactrim: Trimethoprim/Sulfamethoxazole NYU Pediatric Antibiotic Stewardship (Reissued 2022)			

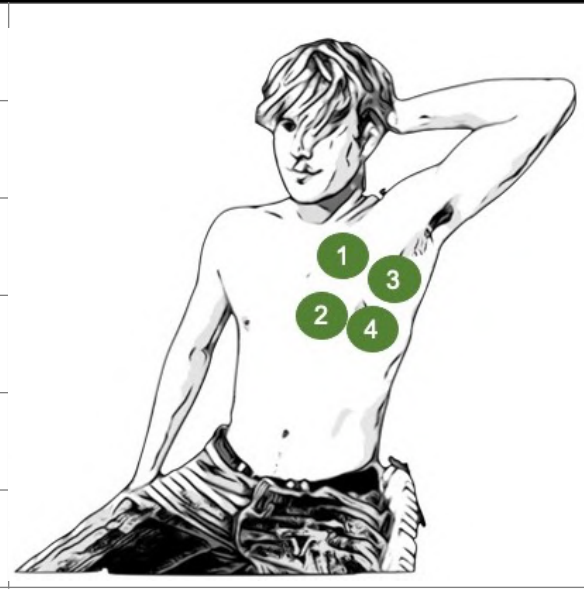
POINT OF CARE LUNG ULTRASOUND

INTRODUCTION (ALEXANDRA VAN OYEN, DO, 5/2023)
In general, air is the enemy of ultrasound imaging. However, the presence of air
In the lungs results in a number of common artifacts. Changes in these artifacts can be used to assess parenchymal and pleural lung disease.

Ultrasound performed at the bedside, provides a more rapid assessment leading to early intervention and can be repeated as needed. It may decrease the need of XRAY imaging. Point of care lung ultrasound Portion is a component of the Rapid Ultrasound Assessment for Shock and Hypotension (RUSH) examination. The RUSH exam provides rapid triage, assessment and expedited management of critically ill patients. The utility of lung ultrasound may be limited in patients with subcutaneous emphysema and severely obese patients. WEB LINK: COMPREHENSIVE LUNG US (POCUS 101)

LUNG ULTRASOUND: INDICATIONS	
Lung parenchyma	Pneumonia, bronchiolitis, pulmonary edema, ARDS
Pleural space	Pleural fluid: Pleural effusion, hemothorax
	Pleural air: Pneumothorax

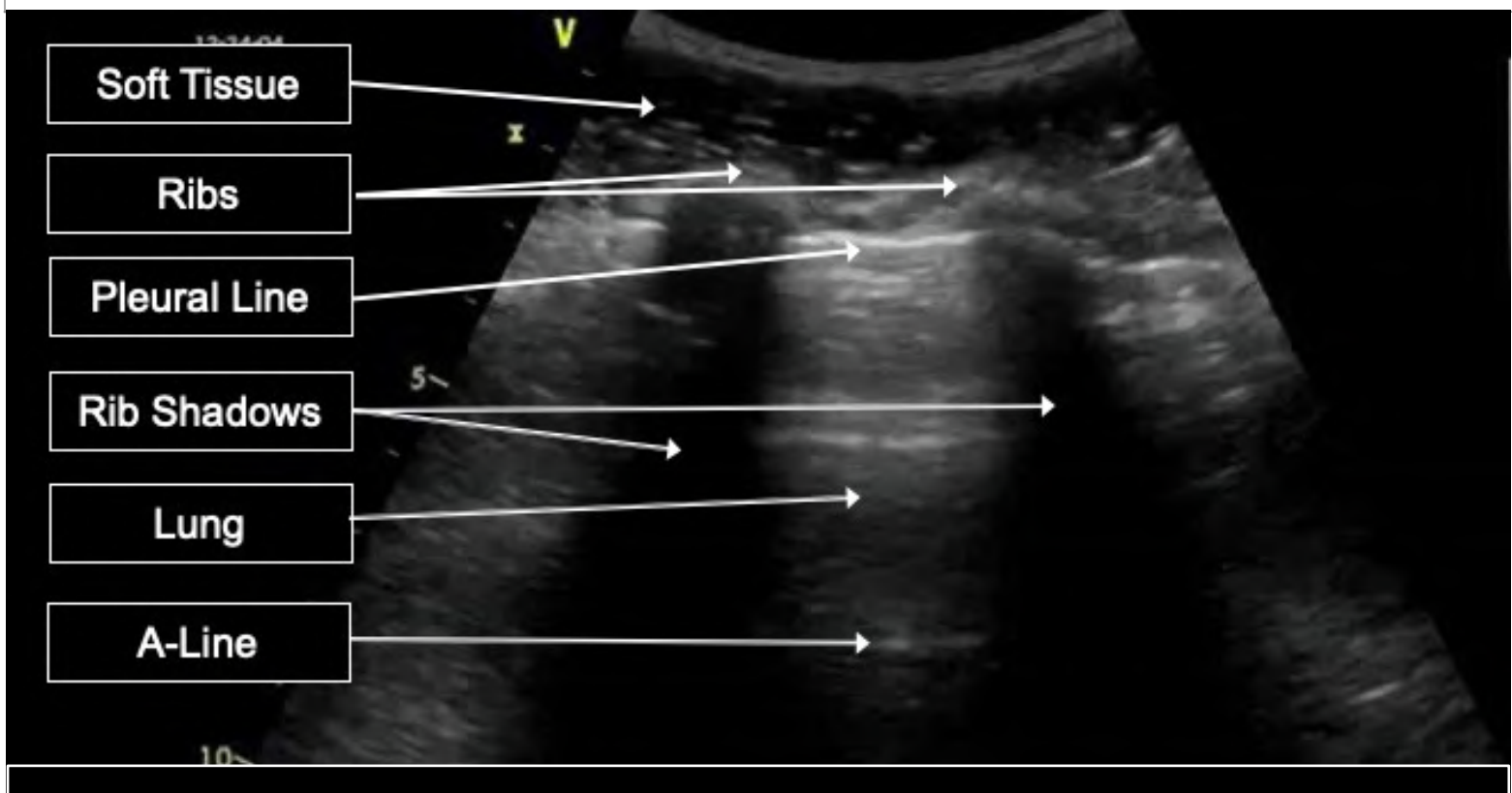
PREPARATION	
Transducer	Linear probe with a lung or small parts preset provides the best resolution though with limited penetration (depth)
	A curvilinear or phase array probe can be considered in adolescents and can provide for greater depth
Transducer positioning	Probe oriented vertically with the marker dot to the patient's head
	The angle of insonation should be perpendicular to the chest wall
Patient position	Patient may lie supine, in lateral decubitus position or sit erect.
Procedure (Pediatric)	6-point lung ultrasound exam; Sagittal/Transverse, Right/Left
	a. Anterior: Mid-clavicular line: Clavicle to the diaphragm
	b. Mid-axially line: Axilla to the diaphragm
	c. Posterior: Paraspinal: Scapula to diaphragm
	Dynamic images as well as M-mode (motion)
Procedure (Adolescent)	12-point lung ultrasound exam (See illustration below)
	a. Anterior: Lateral to sternum: Superior/Inferior (1), Right/Left (2)
	b. Anterior: Axillary Line: Superior/Inferior (3), Right/Left (4)
	c. Posterior: Para-spinal: Superior/Inferior (5), Right/Left (5)
	Dynamic images as well as M-mode (motion)
Layers	Skin, muscle, bone (ribs)
	Visceral and parietal pleural lines
	Lung Parenchyma

ADOLESCENT: LUNG ULTRASOUND (12 POINT: 6 POINTS EACH SIDE)			
1	Anterior-Superior		
2	Anterior-Inferior		
3	Lateral-Superior		
4	Lateral-Inferior		
5	Posterior-Superior		
6	Posterior-Inferior		

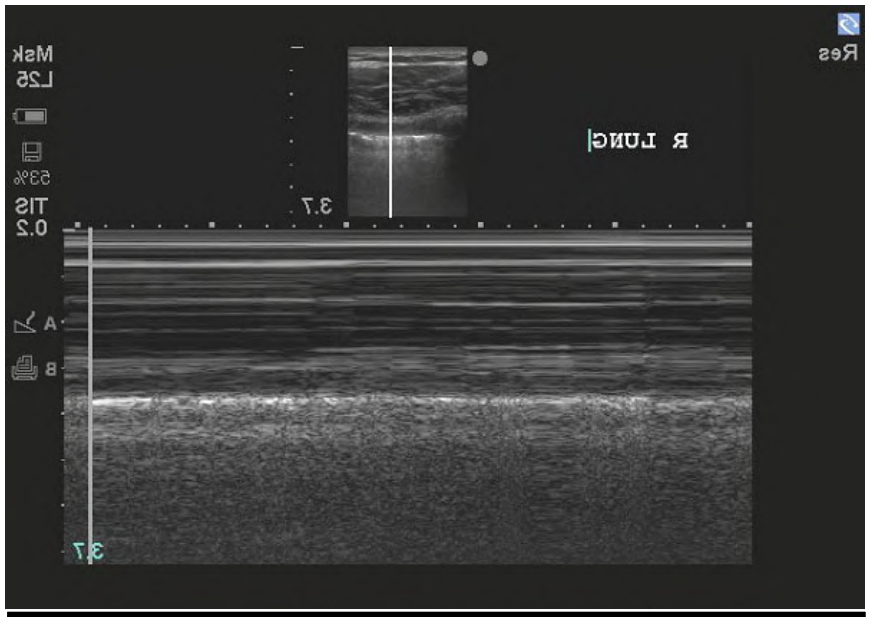
1. ULTRASOUND FINDINGS: NORMAL LUNG

Identifying lung parenchymal and pleural abnormalities requires an understanding of normal lung anatomy and ultrasound findings including knowledge of the artefacts seen due to air in the lungs.

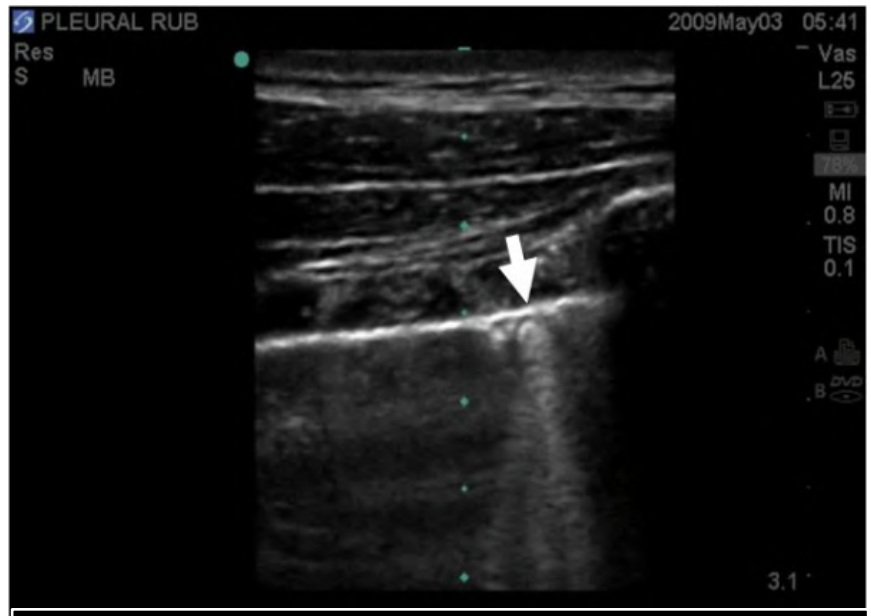
NORMAL FINDINGS
RIB SHADOWS
Posterior acoustic shadowing “anechoic” due to lack of signal penetration
Nearly all ultrasound sound wave reflected back to the transducer from the rib
PLEURAL LINE
Parietal and visceral pleural interface (highly echogenic line)
LUNG SLIDING
Visceral pleura moves relative to the parietal pleura as the patient breathes.
Creates a sliding motion that resembles “ants marching” or “shimmering
If lung sliding is not obvious, if can be further evaluated using M-Mode.
If normal, the patient will have a “seashore shine” or “sandy beach” sign on M-Mode
A-LINES
Linear, parallel to the pleural line (horizontal), equidistant
Due to reverberation artifact from the pleural lining and the air in the lungs
Pathology (consolidation, lung fluid/inflammation) can erase A lines
COMET TAIL ARTIFACTS (AKA Z-LINES)
Originating from the pleural interface (an example of reverberation artifact)
Originating from the pleural line, vertical, short (do not reach the image bottom)
BAT SIGN
A line drawn above the two ribs (wings) down 0.5 cm to the pleural line (body)



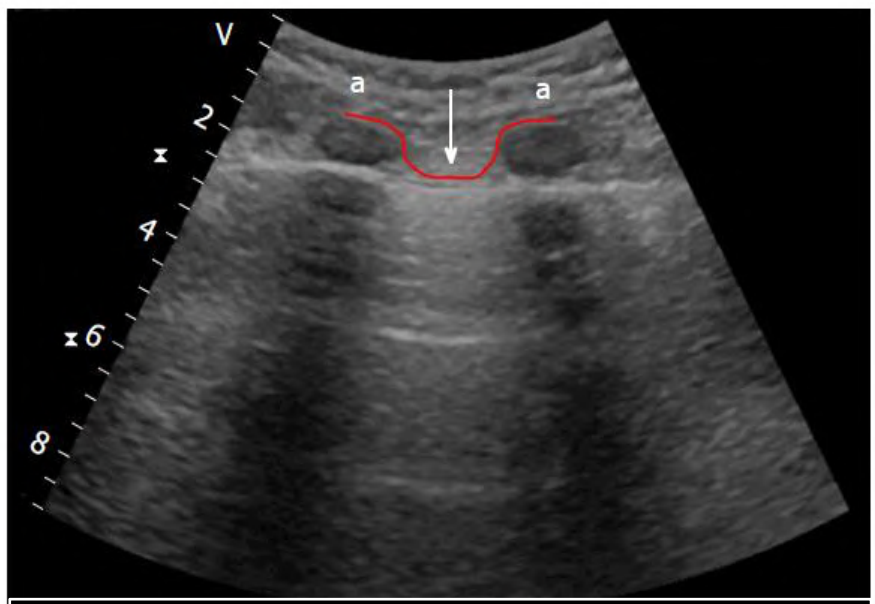
LUNG ULTRASOUND: NORMAL ANATOMY



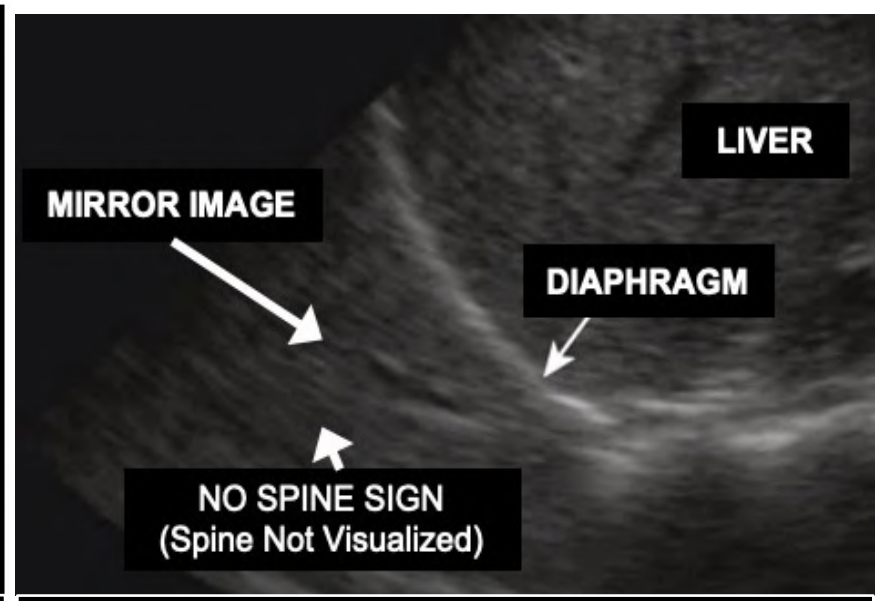
M-MODE: SANDY BEACH



COMET TAIL ARTIFACT



BAT SIGN

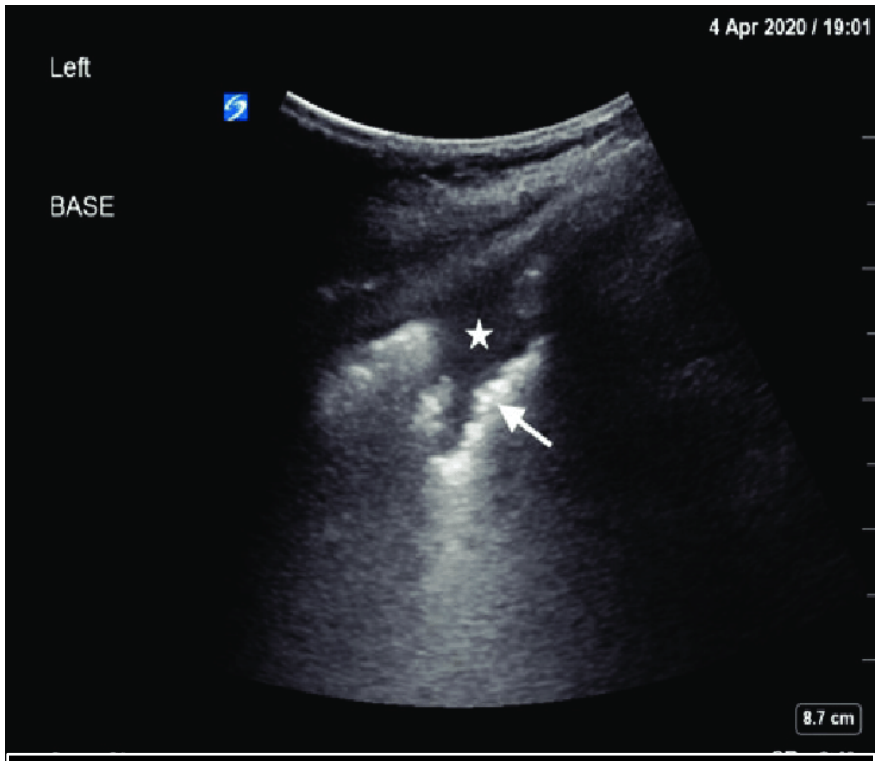


MIRROR IMAGE ARTEFACT

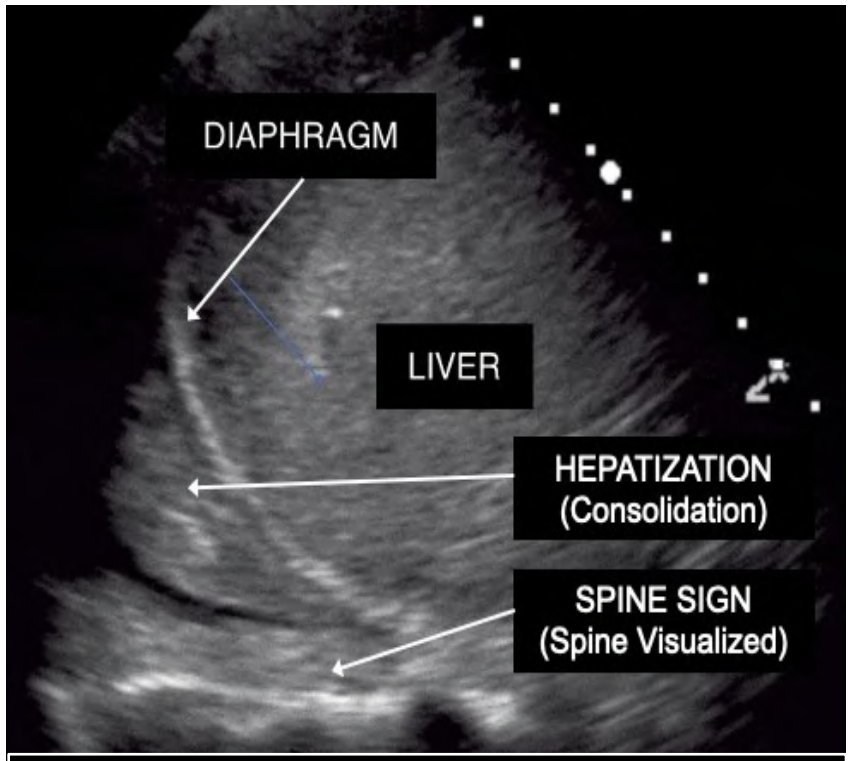
2. ULTRASOUND FINDINGS: LUNG PARENCHYMAL DISEASE

ABNORMAL FINDINGS: LUNG PARENCHYMAL DISEASE
B-LINES
Well defined, hyperechoic, linear, vertical lines, perpendicular to the pleural line
Appear spotlight shaped (rhomboidal, facing downward), move with lung sliding
Extend form the pleural line to the depth of the image (comet tail artifacts do not)
An artifact due to interstitial fluid in the lung
Physiologic fluid < 4 B-lines per intercostal space
Pathologic fluid > 4 or confluent B-lines per intercostal space (obliterates A lines)
Bilateral: Pulmonary edema, ARDS
Unilateral: Pneumonia, pulmonary contusion, bronchiolitis
SHRED SIGN
Jagged, echoic edge visible when fluid interfaces with normal lung parenchyma
HEPATIZATION
Lung parenchyma with the same echogenicity as the liver (lung normally less)
Severe interstitial syndrome: Pulmonary edema, ARDS, pneumonia
AIR BRONCHOGRAMS
Hyperechoic lines and dots within a hypoechoic area
Represent air trapped in small airways within a consolidation
Dynamic air bronchograms (mobile): Pneumonia
Static air bronchograms: Pneumonia or Atelectasis
Still images cannot distinguish static from dynamic air bronchograms (see video link below)
POSITIVE SPINE SIGN (POSTERIOR-INFERIOR VIEW)
Secondary to pleural fluid (effusion, hemothorax) or parenchymal disease
In a normal lung (air present), the spine should not be visible above the diaphragm
With pleural collections (fluid) and parenchymal disease, sound waves can pass through the fluid and the spine is visible superior to the diaphragm

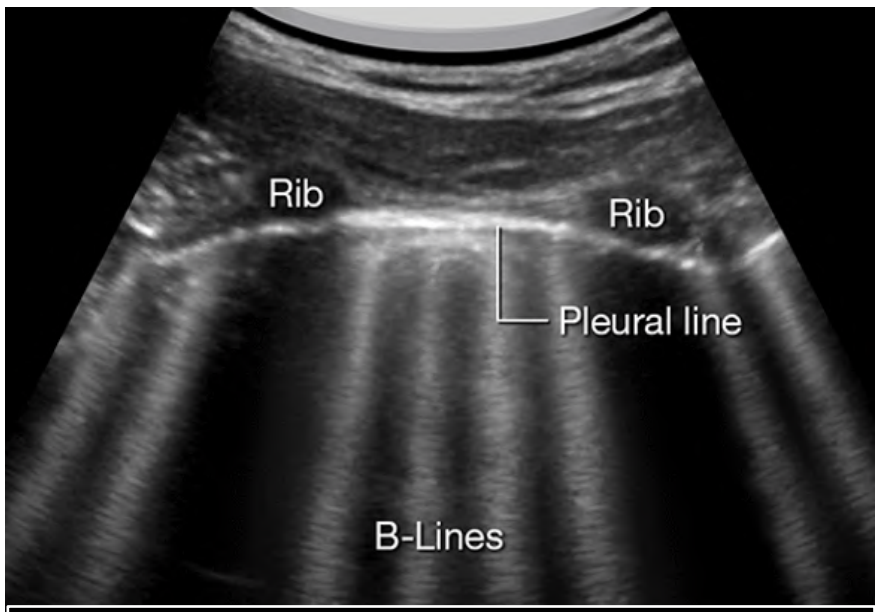
VIDEO LINK: AIR BRONCHOGRAMS



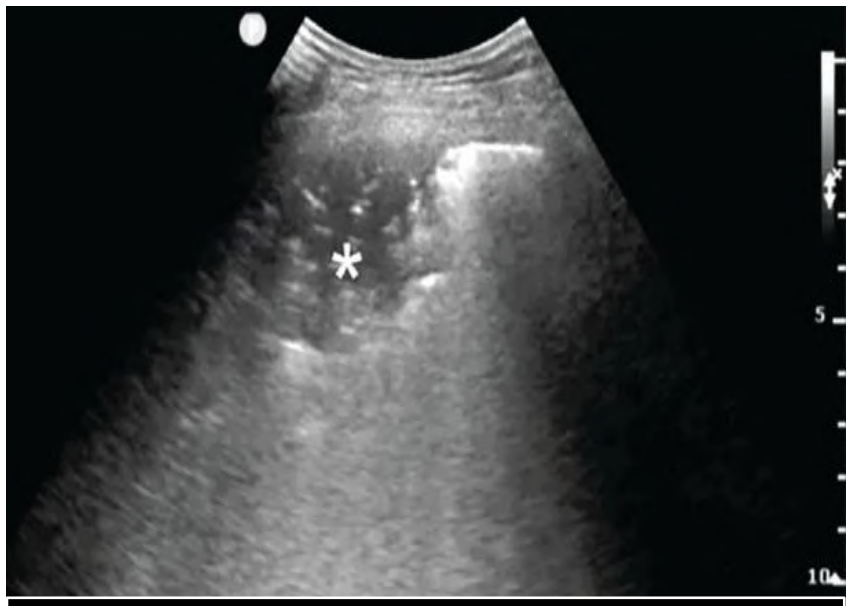
SHRED SIGN



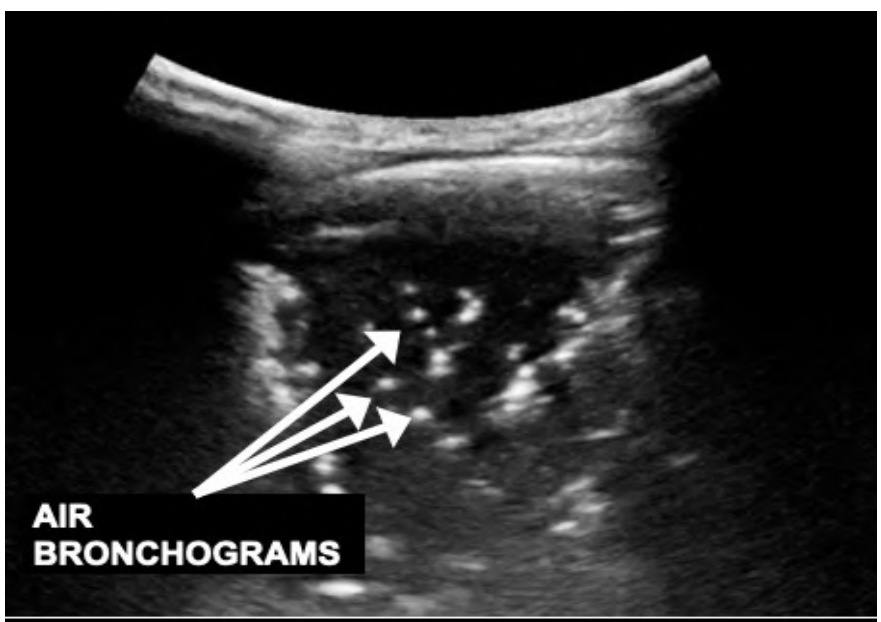
HEPATIZATION + SPINE SIGN



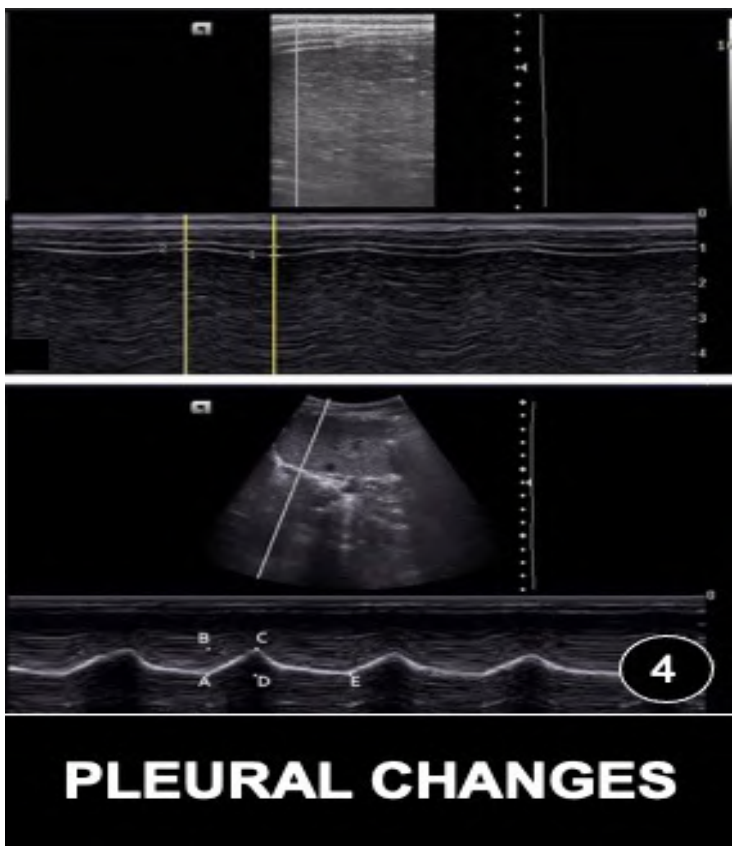
B-LINES



CONFLUENT B-LINES
***SHRED SIGN**



AIR BRONCHOGRAMS



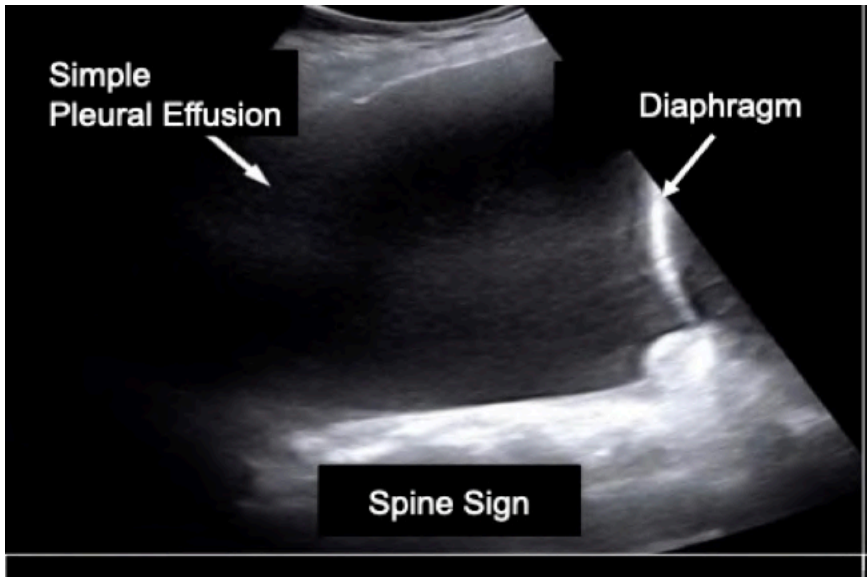
BRONCHIOLITIS FINDINGS	
1	Focal multiple B lines
2	Confluent B lines
3	Subpleural consolidation: Hypoechoic/hyperechoic area with ill-defined margins at the subpleural region (<1 cm, >1 cm)
4	Thickening (> 0.5 mm) or a course appearance of the pleural line due to subpleural consolidation
Krishna, Indian J Ped 2022, PubMed ID: 35438475	

3. ULTRASOUND FINDINGS: PLEURAL SPACE DISEASE

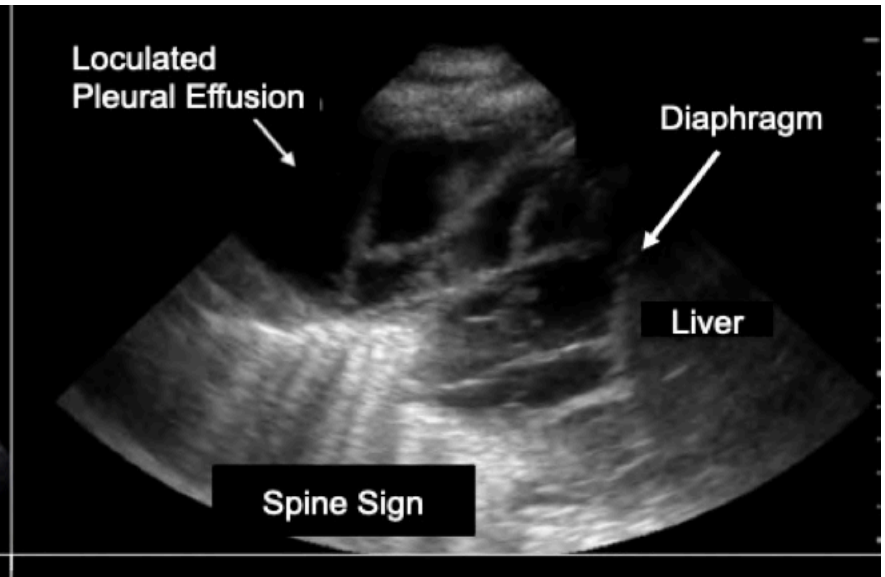
Pleural space accumulations include fluid (exudates and transudates and blood (hemothorax). Ultrasound can be used to identify and characterize pleural fluid collections (size, location, loculations, debris), identify the optimal site for drainage (thoracentesis) and characterize the underlying lung (pneumonia). See: PEM Guide: Respiratory: Parapneumonic Effusions.

ABNORMAL FINDINGS: PLEURAL FLUID (EFFUSION, PNEUMOTHORAX)
SPINE SIGN (POSTERIOR- INFERIOR VIEW)
Secondary to pleural effusion (exudate or transudate) or parenchymal disease
In a normal lung (air present), the spine should not be visible above the diaphragm
With pleural collections (fluid) and parenchymal disease (pneumonia), sound waves can pass through the fluid and the spine (vertebral body acoustic shadowing) is visible above the diaphragm
ABSENT LUNG SLIDING
Due to separation of the pleural layers
DDx: Pneumothorax, pleural fluid, pleural adhesions, atelectasis Non-ventilating lung: Apnea, left lung with right mainstem intubation
M-Mode: “Barcode sign” or “Stratosphere sign”
PLEURAL FLUID
Range from anechoic hyperechoic space between parietal and visceral pleura
Dependent position (if free flowing): Posterior if supine, Inferior if sitting
Transudate: Swirling, hyperechoic debris
Loculated: Fluid divided into pockets

INTERPRETATION: POSTERIOR-INFERIOR VIEW			
	Lung	Pleural Space	Spine
Normal	Mirror Image Artifact: YES	Normal	Not visualized
Pleural Fluid	Mirror Image Artifact: NO	Fluid	Visualized
Pneumonia	Hepatization	Fluid	Visualized



US: SIMPLE PLEURAL EFFUSION



US: LOCULATED PLEURAL EFFUSION

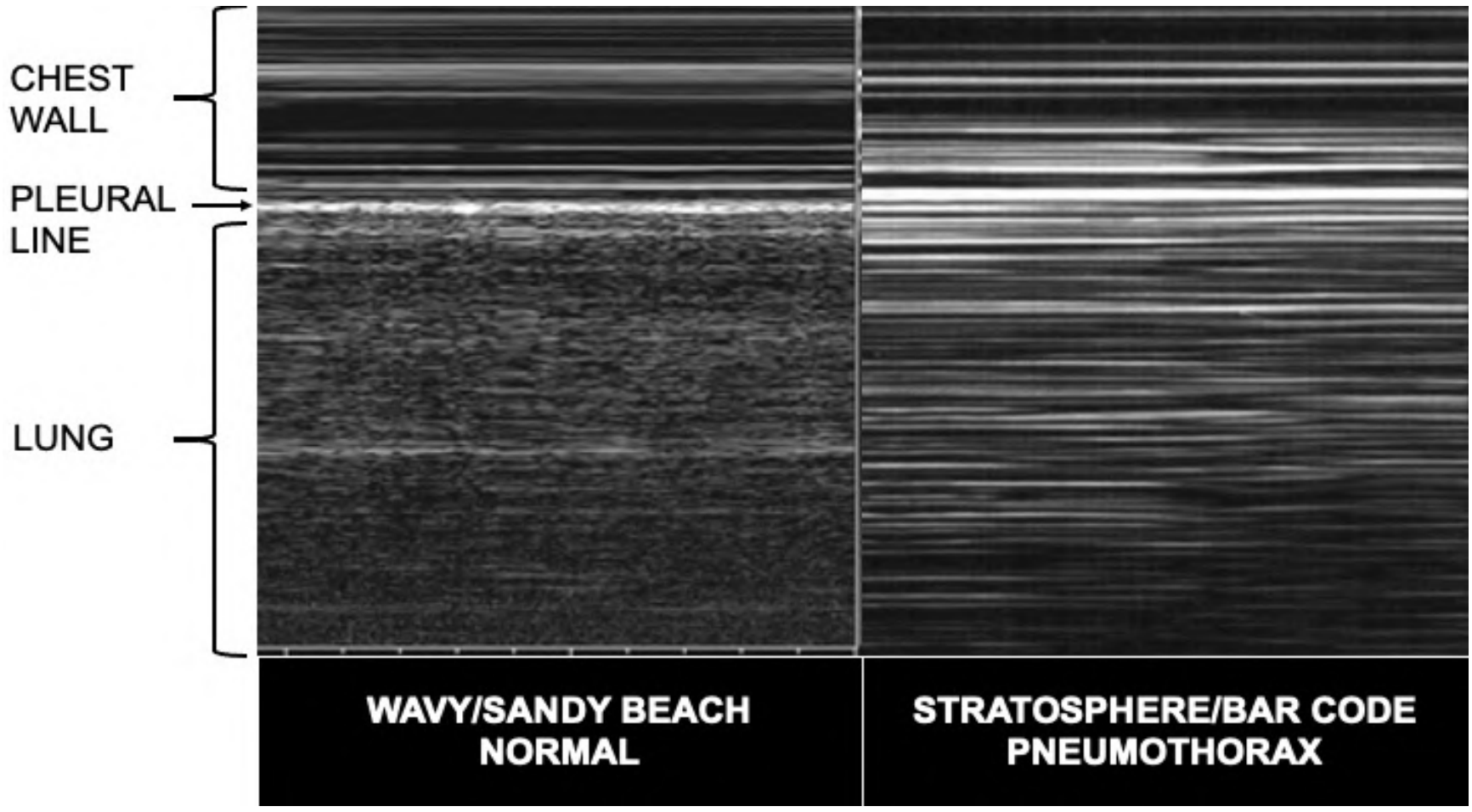
4. PLEURAL SPACE DISEASE: PNEUMOTHORAX

Lung ultrasound has been found to be more sensitive than chest XRAY in identifying pneumothorax and particularly in the supine trauma patient. It can be performed rapidly at the bedside. When the patient is supine, the probe is placed on the anterior chest at the 3rd-4th intercostal space in the midclavicular line oriented in the sagittal position with the marker dot to the patient's head. See also: PEM Guide: Trauma: Extended FAST Exam, PEM Guide: Respiratory: Spontaneous Pneumothorax.

FINDINGS CONSISTENT WITH PNEUMOTHORAX	
1	Absence of lung sliding
2	Absence of B-lines and comet tails
4	Accentuation of horizontal A waves (due to absence of B lines)
3	Presence of "lung point" sign (only in patients with incomplete pneumothorax)
4	M-mode: Absence of the "sandy beach" or "waves on the "beach sign"
5	M-mode: Presence of the "bar code" or "stratosphere"

ABNORMAL FINDINGS: LUNG PARENCHYMAL DISEASE
ABSENT LUNG SLIDING
Separation of the pleural layers
Differential Diagnosis: Pneumothorax, pleural fluid, pleural adhesions, atelectasis Non-ventilating lung: Apnea, left lung with right mainstem intubation
Separation of the pleural layers
LUNG SLIDING: M-MODE
M-Mode: "Barcode sign" or "Stratosphere sign". Lung not moving relative to chest wall
M-Mode: "Seashore" or "Sandy beach): Lung moving relative to the chest wall
LUNG POINT (AKA CONTACT POINT)
Sensitive and specific for pneumothorax
Occurs when an area of lung sliding (no pneumothorax) is adjacent to an area without lung sliding (pneumothorax)
Dynamic and moves with inspiration and expiration.
Seen with a small/moderate pneumothorax.
May not be seen with a large pneumothorax or total lung collapse

ESTIMATING PNEUMOTHORAX SIZE: LOCATION OF LUNG SLIDING*			
	Anteriorly	Mid-axillary Line	Posterior Axillary Line
Small	NO	YES	YES
Medium	NO	NO	YES
Large	NO	NO	NO
*Is their lung sliding? YES or NO?			



WEB LINK: LIFE IN THE FAST LANE

VIDEO LINK: SONOSITE: ULTRASOUND FOR PNEUMOTHORAX

VIDEO LINK: LIFE IN THE FAST LANE: ULTRASOUND FOR PNEUMOTHORAX

PULMONARY EMBOLISM

INTRODUCTION (JOSHUA BEINER, M.D., 8/2022)
Venous Thromboembolism (VTE) is considered a clinical spectrum that includes both Pulmonary Embolism (PE) and Deep Venous Thrombosis (DVT). VTE occurs as a result of either an inherited or acquired disturbance that shifts the normal balance of formation and lysis of venous microthrombi in favor of a pro-thrombotic state. Thrombi often originate in the distal deep venous system before migrating to the lungs where their effects can range from asymptomatic to significant hemodynamic compromise and sudden death depending on the size of the obstructing thrombus and its location within the pulmonary vasculature. PE has a high mortality rate of approximately 10% in both children and adults and risk of sudden death is highest in the hours following the event.

This PEM Guide will focus on the diagnosis of pulmonary embolism. There is very limited evidence on the diagnosis and management of PE in the pediatric population. The evidence discussed in this PEM Guide if primarily from the adult PE literature. Prevalence of PE in children is on the rise likely secondary to improved care of previously lethal conditions such as congenital heart disease, malignancies, extremely low birth weight premature infants, and the increased use of central venous catheters.

CLINICAL MANIFESTATIONS
Diagnosis is often challenging because patients rarely present with classic acute-onset of pleuritic chest pain with associated dyspnea and hypoxia. General appearance may range from clinically stable with subtle respiratory symptoms to obstructive shock due to right heart failure.

Acute respiratory changes include hypoxemia, hyperventilation, and increased alveolar dead space leading to ventilation/perfusion mismatch and intrapulmonary shunting. This augments reflex pulmonary arterial vasoconstriction resulting in increased pulmonary vascular resistance and subsequent right ventricular failure.

DIFFERENTIAL DIAGNOSIS (CHEST PAIN AND/OR DYSPNEA)
Acute chest syndrome (Sickle Cell disease)
Acute coronary syndromes/myocardial infarction
Acute mediastinitis
Acute respiratory distress syndrome
Anxiety disorder and hyperventilation
Asthma
Cardiogenic shock with pulmonary edema
Musculoskeletal chest wall pain (e.g. costochondritis)
Pericarditis
Pleuritis
Pneumonia
Pneumothorax
Salicylate toxicity

Exam findings are typically less apparent in children, presumably due to their greater hemodynamic reserve. In a retrospective case-control study of patients < 21 years of age with PE, limb swelling and/or pain, hemoptysis, cardiac symptoms, and fever were not significantly different between those with and without PE. Compared to adults with PE, cough is more common and hemoptysis and rales less common in children.

PHYSICAL EXAM FINDINGS	
Tachypnea (Respiratory Rate > 16/min)	Diaphoresis
Dyspnea	S3 or S4 Gallop
Pleuritic Chest Pain	Signs/Symptoms of thrombophlebitis
Rales	Lower Extremity Edema
Accentuated S2 heart sound	Cardiac murmur
Tachycardia (> 100 beats/minute)	Cyanosis
Fever (> 37.8 C)	Hemoptysis
Cough	

DIAGNOSTIC TESTING

Chest XRAY and EKG findings are neither sensitive nor specific.

ELECTROCARDIOGRAM (EKG)
Tachycardia & incomplete RBBB
$S_1Q_3T_3$: Neither sensitive nor specific. Not validated after original 1935 publication
ECG changes have not been prospectively validated in diagnosis of PE in children

CHEST XRAY
Often abnormal (atelectasis, infiltrates, effusions) in adults with and without PE
Hampton’s Bump: Wedge-shaped pleural infarct)
Westermarck Sign: Sharp separation of proximal consolidation due to vessel engorgement from distal radiolucency due to local oligemia
Children: Abnormal CXR unable to distinguish PE(+) versus PE(-).

ESTIMATING THE PRE-TEST PROBABILITY OF PULMONARY EMBOLISM

The point of equipoise for initiating a PE work-up is a pre-test probability of greater than 1.8% as the risks from a PE out-weigh the potential adverse effects of imaging and treatment. Multiple scoring systems have been derived and validated. Each score is based on patient history, vital signs, and exam findings. These scores with D-Dimer testing can be used to determine who requires imaging.

Studies on emergency physician’s gestalt impression of the likelihood of pulmonary embolism in adults have been shown to be as accurate as clinical scoring systems (Penaloza, Annals EM 2013, PubMed ID: 23433653). In fact, one of the highest scoring components of the Well’s score (see table below) is “an alternative diagnosis is less likely than PE”. Scoring systems have not been validated in children.

HIGH PROBABILITY: Scoring systems and D-dimer testing should not be applied to patients at high risk for PE (e.g., Lupus, central venous catheters) and signs and symptoms of PE. In these high-risk subsets CT imaging would be indicated regardless of the result of the scoring system or d-dimer as the risk of PE exceed the threshold at which it can be ruled out.

RISK FACTORS
Immobilization
Travel (≥ 4 hours in past 1 month)
Surgery (within past 3 months)
Pregnancy (current or recent)
OCP & Estrogen Replacement
Malignancy (especially lung)
Tobacco Use
Hemolytic Anemias (Sickle cell)
Thrombocytosis
Central Venous Instrumentation < 3mo
Central Venous Catheters
Intravenous Drug Use
Stroke, paresis, paralysis
Heart failure
Varicose Veins & Thrombophlebitis
Trauma: Lower Ext, Pelvis < 3 month

HYPERCOAGULABLE STATES
SLE (Lupus)
Connective tissue disorders
Nephrotic syndrome
Factor V Leiden Mutation
Protein C, S Deficiency
Antithrombin III Deficiency
Inflammatory bowel disease
Hyperlipidemias
Homocystinemia, homocystinuria

MEDICATIONS
Warfarin within days of initiation
Heparin induced thrombocytopenia
Phenothiazines

INTERMEDIATE PROBABILITY: Clinical scoring systems (Well's, Revised Geneva, Years) and D-dimer have been used to assess the risk of PE in patients with low probability of PE and a negative PERC score as well as patients with an intermediate probability of PE. Patients with a low risk classification when combined with a negative D-dimer assay, may forego CT imaging.

WELL'S SCORE	POINTS
Clinical signs and symptoms of deep vein thrombosis*	3.0
An alternative diagnosis is less likely than pulmonary embolism	3.0
Heart Rate > 100 beats/minute	1.5
Immobilization or surgery in the previous 4 weeks	1.5
Previous deep vein thrombosis or pulmonary embolism	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the last 6 months or palliative)	1.0
*Minimum of leg swelling and pain on palpation of deep veins Wells, Annal IM 2001, PubMed ID: 11453709 (Original study) WEB LINK: MD CALC: WELL"S SCORE	

WELLS INTERPRETATION				
Well's Scale	Score	PE (+) Rate Overall	PE (+) Rate with D-Dimer (-)	Interpretation
Well's Dichotomous	≤ 4	5-8%	1.7%	PE Unlikely
	> 4	39-41%	10.3%	PE Likely
Well's Trichotomous	< 2	2-4%	2.7%	Low
	2-6	19-21%	2.9%	Moderate
	> 6	39-41%	20.0%	High

REVISED GENEVA SCORE	Actual	Simple	Probability	Actual	Simple
Previous DVT or PE	3	1	Low	0-3	0-1
Surgery or fracture within 1 month	2	1			
Active malignancy	1	1	Intermediate	4-10	2-4
Age ≥ 64	1	1			
Unilateral lower limb pain	3	1	High	≥ 11	5-7
Hemoptysis	2	1			
Heart rate ≥ 95	5	2			
Heart rate 75-94	3	1			
Calf tenderness & unilateral edema	4	1			
Le Gal, Annals IM 2006, PubMed ID: 23433653 (Original Study) WEB LINK: MDCALC: REVISED GENEVA SCORE					

The benefit of the simple revised Geneva score is that in consists of objective criteria while the Wells score includes one subjective criterion "Is another disorder more likely than PE". (Freund, JAMA 2021, PubMed ID: 34874418).

YEARS CRITERIA
PE is the most likely diagnosis
Clinical sign of deep venous thrombosis
Hemoptysis
van der Hulle, Lancet. 2017., PubMed ID: 28549662 YEARS criteria are considered positive if at least one criteria is present WEB LINK: MD CALC: YEARS CRITERIA

D-DIMER: The primary laboratory test used in the diagnosis of PE is the dimer. D-dimer is a non-specific marker of fibrinolysis. It is often used in conjunction with clinical scoring systems such as the Well's, revised Geneva or PERC scores. False positives include patients with infection (e.g. COVID 19), malignancy, post-surgery, pregnancy and age greater than 70-80 years. False negatives may be encountered with small thrombi and in those with symptoms of longer than 3 days. Test cutoff and test characteristics are assay-specific. Current assays utilize an immunoturbidometric or rapid-ELISA techniques. They are highly sensitive but have poorly specificity. The low specificity can result in a high rate of CT utilization in those with false positive d-dimers. There are no validated cutoffs in the pediatric population

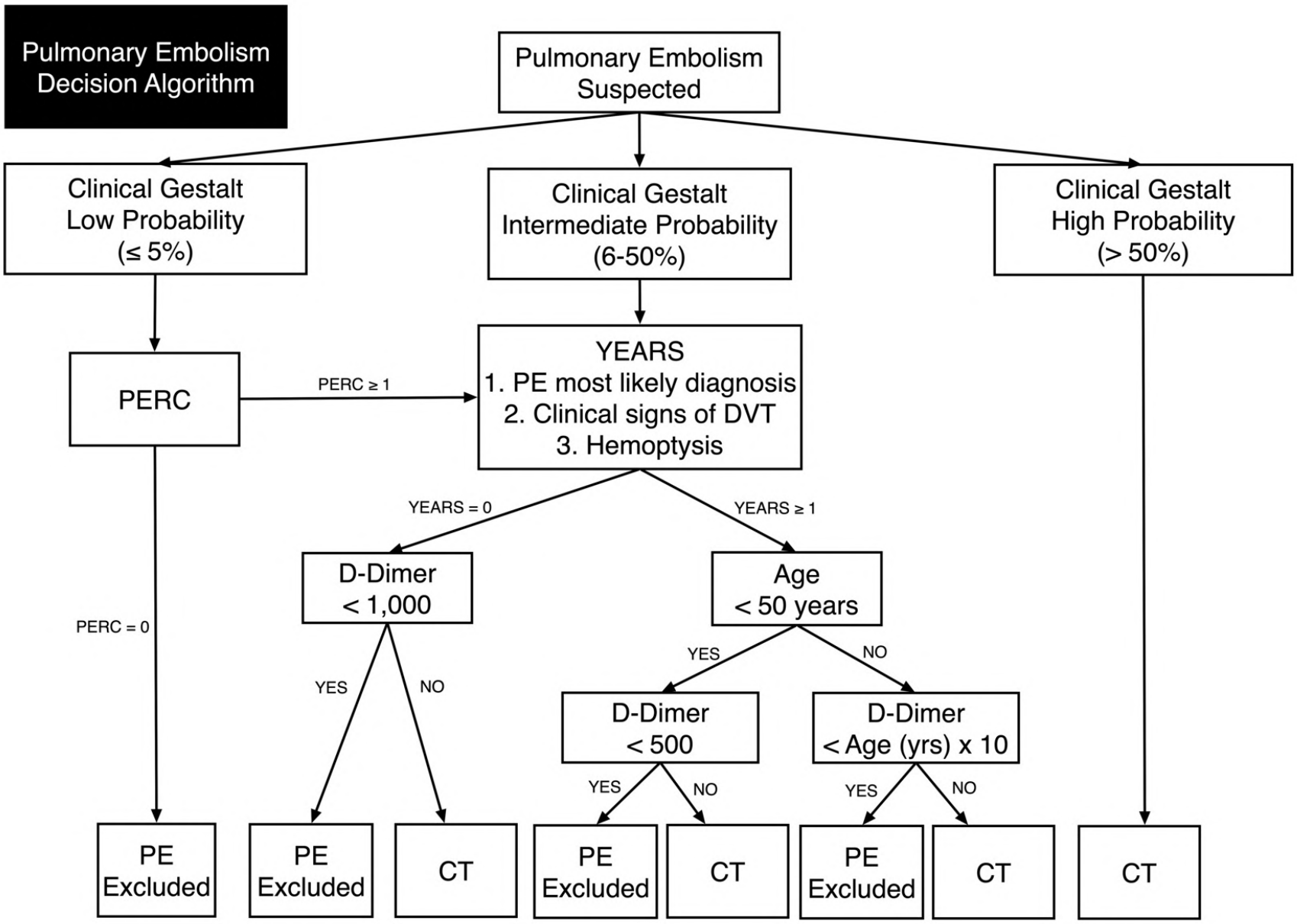
LOW PROBABILITY: The Pulmonary Embolism Rule-Out Criteria (PERC) is an 8-item scale that negates the need for further work-up when every item is absent, as the resultant post-test probability for PE is less than 2%. The patient needs to have sufficiently low (< 5%) pre-test probability in order to apply PERC. In those with a high pretest probability, a negative PERC rule would not result in a post-test probably low enough to warrant foregoing further testing.

A meta-analysis of the PERC score literature, including 13,885 patients, demonstrated a collective predictive value of a positive rule of 12.3%, 95% CI (11.7, 12.9%) and predictive value of a negative rule of 98.6%, 95% CI (98.1, 98.9%)(Post-test probability of PE with a negative PERC of 1.4% (Singh, Ann Emerg Med. 2012., PubMed ID: 22177109).

PULMONARY EMBOLISM RULE-OUT CRITERIA (PERC)*
Age < 50 year
Pulse < 100
Sa02 > 95% on room air
No unilateral leg swelling
No hemoptysis
No surgery or trauma requiring hospitalization within 4 weeks
No previous venous thromboembolism (DVT or PE)
No exogenous estrogen use (e.g. Oral Contraceptive Pills)
*To be applied only to patients with PE probability of < 5% Kline, J Thromb Heamost 2004, PubMed ID: 15304025 (Original Study) WEB LINK: MD CALC: PERC RULE

PULMONARY EMBOLISM DECISION ALGORITHM

The purpose of the decision algorithm is two-fold. The first is to select high-risk patients for CT-PA using a clinical scoring system and d-dimer testing. The second is to identify very low risk patients in order to avoid d-dimer testing which is non-specific and could potentially lead to unnecessary CT scans, particularly in young patients. The algorithm uses clinical data, PE scoring systems and D-dimer testing to determine who is at low enough risk that PE can be excluded or insufficiently low risk so the imaging is required.



DEFINITIVE IMAGING

CT-Pulmonary Angiography with an intraluminal defect is the definitive gold standard for the diagnosis of PE. CT-PA can be used with or without venous compression ultrasound in patients in which PE cannot be excluded based on risk factors, D-Dimer and PE scores. Point of care cardiac ultrasound can be used to directly identify a cardiac thrombus and indirect effects of PE on cardiac function (See Appendix)

CT-PA: PREDICTIVE VALUES COMBINED WITH WELLS SCORE			
	HIGH (Well's > 6)	INTERMEDIATE (Well's 2-6)	LOW (Well's < 2)
PV(+) CTA	96% (78-99)	92% (84-96)	58% (40-73)
PV(+) CTA or CTV	96% (81-99)	90% (82-94)	57% (40-72)
PV(-) CTA	60% (32-83)	89% (82-93)	96% (92-98)
PV(-) CTA and CTV	82% (48-97)	92% (85-96)	97% (92-98)
PIOPED II Study, NEJM 2006, PubMed ID: 16738268			

VENOUS COMPRESSION ULTRASOUND (VCUS)
High specificity for femoral and popliteal vein scans
Sensitivity & NPV can be significantly increased by scanning Iliac veins to malleolus
May be used in cases of discrepant results of pre-test risk stratification & CT-PA

MANAGEMENT

Initial management of PE focuses on respiratory support, hemodynamic support, and anticoagulation. Anticoagulation in children should be guided by a pediatric hematologist. If anticoagulation is contraindicated, alternative treatment strategies include an inferior vena cava filter and embolectomy.

Thrombolysis with TPA may be indicated in those with a large enough PE to cause right heart failure and hemodynamic compromise. A point of care ultrasound can be used to identify right heart strain or failure. Direct evidence of a PE includes a thrombus in right atrium, right ventricle, pulmonary artery or in the left atrium or left ventricle via a patent foramen ovale. Indirect evidence of PE includes right ventricular dysfunction, dilatation, free wall hypokinesia or paradoxical septal wall motion (the ventricular septum typically bows into the right ventricle. With increase pulmonary pressure that bowing may be flattened.

FIBRINOLYSIS	
Indications	Cardiac arrest, hemodynamic instability (SBP < 90 mmHg)
Controversial	Stable patients with RV dysfunction on echocardiography
TPA (Alteplase) Dose	Child: 0.45 mg/kg, Adult: 50 mg. Dosing is controversial: Typically, half the typical stroke dose

INDICATIONS FOR THROMBOLYSIS	
Persistent hypotension or shock	
Considered on a case-by-case basis:	
Right ventricular dysfunction	Severe hypoxemia
Cardiopulmonary arrest caused by PE	Free-floating RA orRV thrombus
Moderate PE	Patent foramen ovale

CONTRAINDICATIONS TO THROMBOLYSIS
ABSOLUTE
Intracranial neoplasm
Intracranial/spinal surgery/trauma within past 2 months
History of hemorrhagic stroke
Active bleeding or bleeding disorders
RELATIVE
Severe uncontrolled hypertension (SBP >200 mmHg or DBP >100 mmHg)
Non-hemorrhagic stroke in past 3 months
Surgery in the past 10 days
Pregnancy
Thrombocytopenia (< 100,000/mm^3)

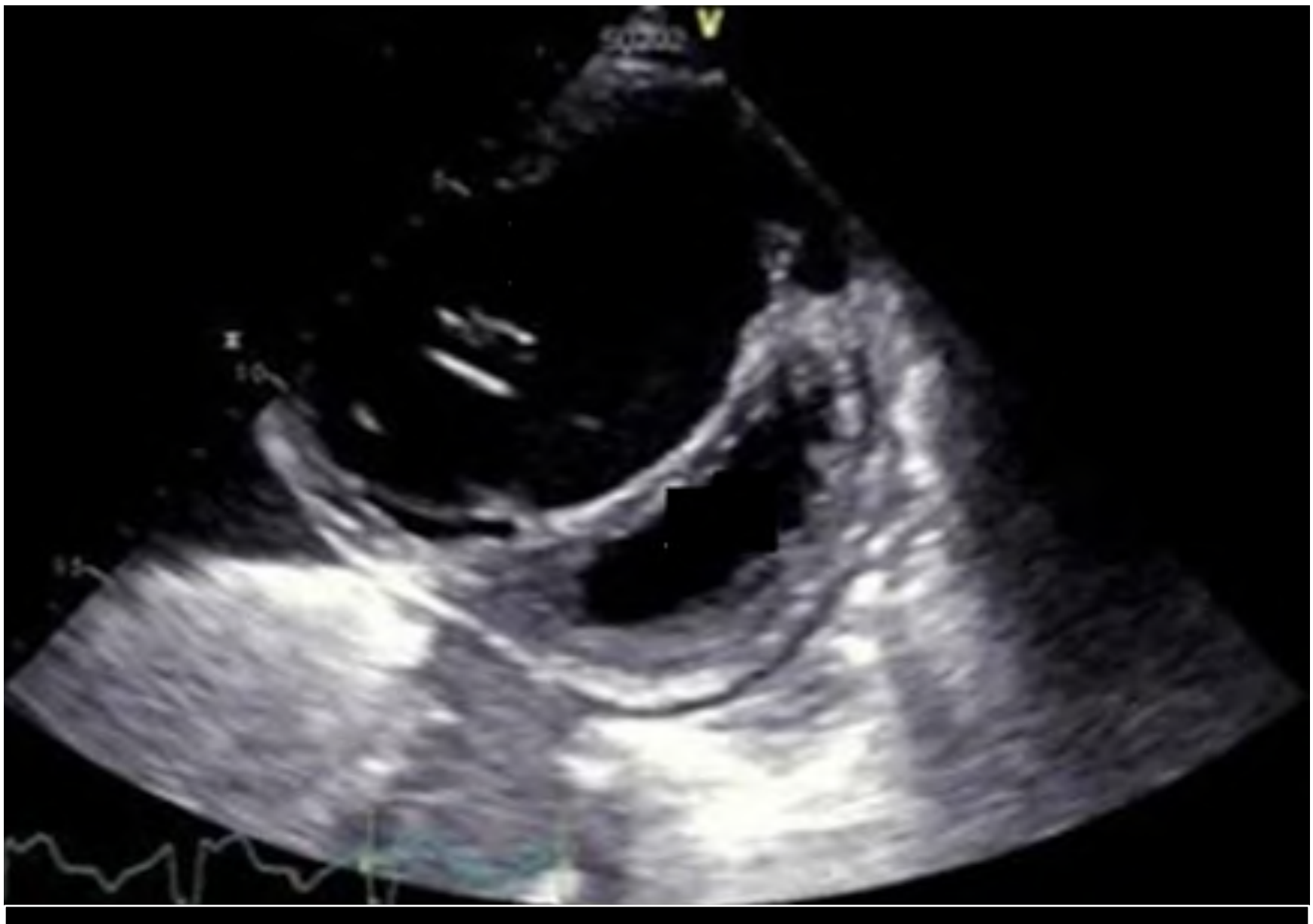
DISPOSITION

Traditionally, pediatric patients with suspected PE are admitted to the hospital for further work-up and management. Treatment and disposition decisions should be made in conjunction with a pediatric hematologist. In adults, outpatient therapy may be safe and effective under certain conditions.

ADULT CRITERIA FOR OUTPATIENT THERAPY
PE Severity Index (PESI) Class I/II[1]
No supplemental oxygen requirement
No narcotic requirement
No respiratory distress
Normal heart rate
Normal blood pressure
No recent bleeding
No significant co-morbidities
Normal mentation
Support at home
Absence of deep vein thrombosis
1. MDCALC LINK: Pulmonary Embolism Severity Index (PESI) Calculator

APPENDIX CARDIAC ULTRASOUND: PULMONARY EMBOLISM

CARDIAC POCUS FINDINGS IN PULMONARY EMBOLISM
Indirect Evidence of PE
Right ventricular wall hypokinesis
Moderate or severe
McConnell's sign: Akinesia of the mid free wall but normal motion at the apex (SN: 77%, SP 94%)
Right ventricular dilatation
End-diastolic diameter > 30 mm in parasternal view (adult)
RV larger than LV in subcostal or apical view with normal LV function
Septum bulging into LV (D sign) rather than into the RV
Paradoxical RV septal systolic motion, Septal flattening consistent with RV pressure overload
Direct evidence of PE: Thrombus in RA, RV, PA, LA/LV via PFO
WEB LINK: LITFL: ECHO IN MASSIVE PULMONARY EMBOLISM



PARASTERNAL SHORT AXIS VIEW:
1. Dilated right ventricle (RV > LV),
2. Ventricular septum bowed into (LV is "D" shaped rather than "O" Shaped)

SPONTANEOUS PNEUMOTHORAX

INTRODUCTION (MICHAEL MOJICA, MD, 11/2020)
A pneumothorax is air in the thoracic cavity in the pleural space (between the parietal and visceral pleura) as a result of a defect in either pleural layer. For example, the parietal pleura can be penetrated by chest wall trauma and the visceral pleural can be damaged due to rupture of a pleural bleb. This PEM Guide will focus on identification and management of spontaneous pneumothorax in the ED setting and does not discuss traumatic pneumothorax or spontaneous pneumothorax in the newborn.

A spontaneous pneumothorax is one that is not due to trauma or procedure complications (thoracentesis, mechanical ventilation, central line placement). A primary spontaneous pneumothorax (PSP) occurs in the absence of underlying lung disease. Secondary spontaneous pneumothoraxes (SSP) occur due to underlying lung disease such as asthma. SSP are associated with higher morbidity and morbidity, likely due to a decreased respiratory reserve associated with underlying lung disease. SPS also have higher rates of tension pneumothorax, persistent air leak requiring surgery and recurrence.

Primary spontaneous pneumothorax peaks in incidence from late adolescence to young adulthood and is more common in males (male to female approximately 4:1). The majority of PSP occur at rest but can rarely occur in association with exertion (e.g. increased pulmonary pressure during weight lifting). Smoking and vaping increase the risk of spontaneous pneumothorax. SSP is more common in older adults.

PATHOPHYSIOLOGY
Spontaneous pneumothoraxes are due to visceral pleura defects, increased pulmonary pressure or a combination of the two. Increased pulmonary pressure can result in alveolar distention and rupture. The rupture of multiple alveoli results in a sub-pleural bleb. The presence of a visceral pleural defect results in equalization of pulmonary and environmental pressures with collapse of the effected lung. Depending on the location of the visceral pleural defect, air can also track into the mediastinum (pneumomediastinum), pericardium (pneumopericardium), abdomen (pneumoperitoneum) and subcutaneous tissue (subcutaneous emphysema). Tension pneumothorax can occur due to a valve like leak. Air can exit the lung during inspiration but is unable to re-enter the lung during expiration. This occurs until unilateral intra-pleural pressure exceeds airway pressure and contralateral pressure.

SPONTANEOUS PNEUMOTHORAX: RISK FACTORS	
Pleural Defects	Increased Pulmonary Pressure
Collagen vascular disease (Marfan)	Airway obstruction with ball-valve effect
Congenital lung abnormalities	Positive pressure ventilation
Foreign body aspiration	Valsalva: Constipation, exercise
Lung: Asthma, cystic fibrosis, pneumonia	
Malignancy	
Systemic inflammatory diseases (SLE)	

CLINICAL MANIFESTATIONS

Symptoms and physical examination findings are dependent on the volume of air, the rapidity of air accumulation, the presence of tension, the extent of lung collapse and the patient's respiratory reserve. Typical symptoms include the sudden onset of shortness of breath, sharp or stabbing pleuritic chest pain with or without radiation to the ipsilateral shoulder and a nonproductive cough. Chest pain can become constant and dull over time. History should be obtained to identify causes of secondary spontaneous pneumothorax (e.g. underlying respiratory disease, connective tissue disorders, inhaled medications/ drugs, foreign body aspiration and the presence of upper and/or lower respiratory tract symptoms).

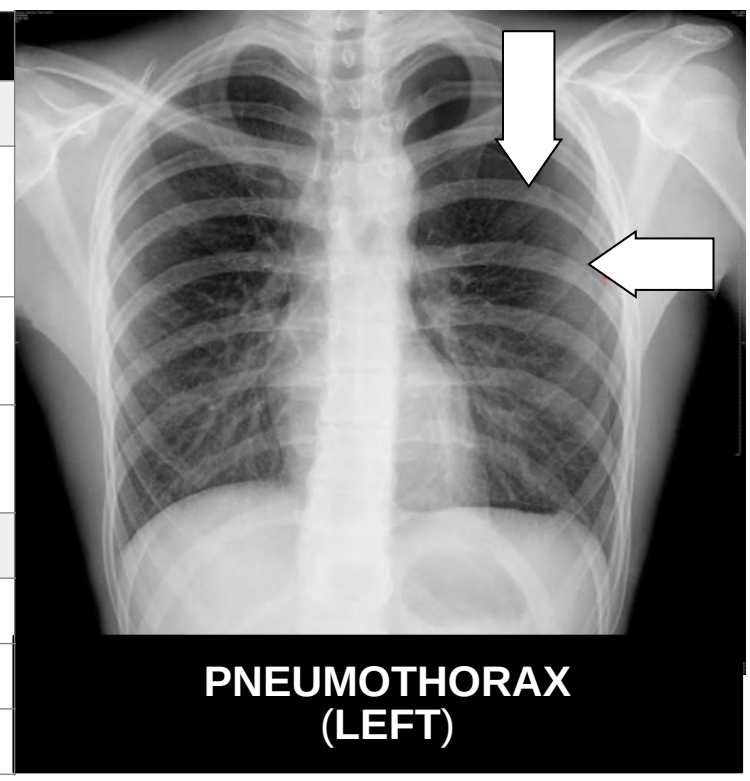
Non-specific respiratory findings may include tachypnea, increased work of breathing and a diminished oxygen saturation. Oxygen saturation may not be accurate in those with poor perfusion due to a tension pneumothorax. More specific physical examination findings may include hyper-resonance and/or diminished breath sounds on the effected side. The presence hypotension, pulseless electrical activity, distended neck veins or a displaced tracheal or displaced heart sounds to the contralateral side indicate tension pneumothorax.

TENSION PNEUMOTHORAX: PHYSICAL EXAM	
Vital Signs	Tachycardia*, hypotension, pulseless electrical activity
Respiratory	Tachypnea*, increased work of breathing*, cyanosis
Breath Sounds	Decreased (Ipsilateral)*
Percussion	Hyper-resonant (Ipsilateral)*
Trachea Position	Shift (Deviation) (Contralateral)
Neck Veins	Distended
Heart Sounds	Normal or displaced (Contralateral)
*May also been seen with moderate-large simple pneumothorax (without tension)	

DIAGNOSTIC IMAGING

The diagnosis of spontaneous pneumothorax can be made based on clinical signs and symptoms but is confirmed by imaging. An upright AP and lateral chest XRAY is most commonly used for radiologic confirmation. Point of care ultrasound can also be used to rapidly identify pneumothorax at the bedside and guide interventions (see Appendix)

CHEST XRAY FINDINGS
SIMPLE PNEUMOTHORAX
A visible visceral pleural line due to an air/visceral pleural interface (typically the visceral and parietal pleura are in close approximation and cannot be distinguished)
Absent lung/vascular markings distal to the air-visceral pleural line (hyperlucency)
Increased lung/vascular markings proximal to the air-visceral pleural line due to lung collapse/atelectasis
TENSION PNEUMOTHORAX: ABOVE PLUS
Contralateral mediastinal or tracheal deviation
Ipsilateral flattened diaphragm, heart border
Widened intercostal spaces



PNEUMOTHORAX (LEFT)

CHEST CT: Chest CT is not routinely warranted. Chest CT is better at assessing the size of the pneumothorax and identify lung abnormalities. Pleural blebs are common but they are not always at the site of the pleural leak. Chest CT may be indicated in those with XRAY findings warranting further investigation (e.g. complex pneumothorax), recurrent pneumothorax, and those with a persistent air leak. Congenital lobar emphysema, and diaphragmatic hernia can mimic air in the pleural cavity. A chest CT or upper GI series may be required to differentiate these from pneumothorax. Decisions regarding chest CT should be made in consultation with pediatric surgery.

PNEUMOTHORAX SIZE: A number of methods (Rhea, Collins, Light index) have been used to the determine the size of pneumothorax on chest XRAY. These methods tend to underestimate pneumothorax size and none have been validated in pediatrics but are likely applicable to adolescents. A large pneumothorax is defined as greater than 20-30%. A distance of greater than or equal to 3 cm from the pleural line at the lung apex to the apical chest wall (American College of Chest Surgeons) or greater than or equal to 2 cm from the lateral lung edge to the chest wall at the level of the hilum (British Thoracic Society) are used in adults to define a large pneumothorax. (See Appendix)

MANAGEMENT

There is limited evidence in the pediatric population on which to base management decisions and most recommendations are based on adult guidelines (British Thoracic Society, Thorax 2010, PubMed ID: 20696690, American College of Chest Physicians, Chest 2001, PubMed ID: 11171742). However, these guidelines differ in their recommendation for type of intervention in specific circumstances. In general, aspiration is more accepted in Europe than in the United States. Point of care ultrasound can be used to improve success and reduce complications of interventions.

MANAGEMENT GOALS
Rapidly identify and decompress tension pneumothorax
Reduce symptoms: Chest pain, dyspnea
Apply the least invasive method that is effective, Identify patients for outpatient care
Identify patients requiring surgical intervention
Prevent recurrence

Treatment options include conservative management (no intervention) and efforts to evacuate air from the pleural space. Methods to remove air from the pleural space include aspiration, chest tube or pleural, pigtail catheter placement. Secondary spontaneous pneumothorax is more commonly managed with an interventional approach and admission due to high morbidity and mortality.

MANAGEMENT RECOMMENDATIONS					
Stability[1]	Tension[2]	Size[3]	PSP/SSP[4]	Recur	Approach
Unstable	Yes	Either	Either	Either	Needle Thoracentesis
Unstable	No	Either	Either	Either	Chest tube, pleural catheter
Stable	No	Small	PSP	No	Conservative, O_2
Stable	No	Small	SSP	No	Conservative, O_2, Rx underlying
Stable	No	Large	PSP	No	Aspiration vs Chest tube
Stable	No	Large	SSP	No	Chest tube or pleural catheter, Rx underlying
Stable	No	Either	Either	Yes	Chest tube or pleural catheter

1. Significant dyspnea, chest pain, hypoxia
2. Unstable above with hypotension, pulseless electrical activity, tracheal deviation
3. Small < 30%
4. PSP (Primary) vs SSP (Secondary) Spontaneous Pneumothorax

The treatment method selected depends on the size of the pneumothorax, the presence of tension, the extent of symptoms, presence of underlying lung disease and if the pneumothorax is recurrent. If a less invasive management technique (observation or aspiration) fail, then a chest tube or pleural, pigtail catheter is indicated.

NEEDLE THORACENTESIS: Patients with a suspected tension pneumothorax should undergo immediate needle decompression without delay for radiologic confirmation. Needle decompression should be followed by chest tube or pleural catheter placement.

PROCEDURE: NEEDLE THORACENTESIS	
Equipment	Performed with an angiocatheter attached to a fluid-filled syringe.
	Unfortunately, standard safety angiocatheters cannot be directly attached to syringe. Alternatively, a syringe can be attached to a catheter from a central line kit.
	In the adult, a 3.5 inch needle is recommended to ensure penetration of the overlying soft tissue. There are no pediatric recommendations for catheter length.
Location	Children: Midclavicular line in the 2nd intercostal space.
	Adults: Just anterior to the midaxillary line in the 5th intercostal space
Procedure	The needle is advanced perpendicular to the chest wall over the superior border of the lower rib to avoid damaging the neurovascular bundle located under the inferior border of the rib.
	The plunger of the syringe should be retracted during needle advancement. Air will bubble into the syringe when the needle penetrates the parietal pleura.
	Angiocath is advanced into intrapleural space and retract the needle.
	Secure the angiocath with tape. Attach the angiocath to an IV tubing extension set and place the distal end of the tubing into a bottle of saline. This prevents air from being drawn into chest when the diaphragm contracts. It also provides an outlet for intra-pleural air so that tension does not recur as air re-accumulates.

VIDEO LINK: LIFE IN THE FAST LANE

VIDEO LINK: THREE KINGS TENSION PNEUMOTHORAX SCENE

CONSERVATIVE MANAGEMENT: Conservative management refers to observation with supplemental oxygen without an intervention to remove air. This relies on resorption of the pneumothorax. Conservative management may be indicated for clinically stable patients with a small, primary spontaneous pneumothorax without a prior pneumothorax. Patients should have a repeat chest XRAY in 6-12 hours and if the pneumothorax is resolving and symptoms are minimal the patient may be discharged (some adult evidence) or admitted for further observation (pediatric recommendation).

The rate of pneumothorax resolution is estimated at 2.2% per day on room air. Supplemental oxygen can intra-increase the rate pleural air resorption 4-fold compared to room air. Because of the potential for oxygen toxicity, supplemental oxygen should be limited to 1-2 days of use. A non-rebreather face-mask is recommended because a nasal cannula at high flow rates can increase airway pressure.

A multicenter, randomized trial included 316 patients 14-50 years of age with a unilateral, moderate to large, primary spontaneous pneumothorax ((Brown, N Engl J Med. 2020, PubMed ID: 31995686). Patients were randomized to conservative management or interventional management. The primary outcome was complete radiographic resolution within 8 weeks. Conservative management was non-inferior to interventional management (Risk Difference: -4.1%, 95% CI (-8.6, 0.05%)(the non-inferiority margin was -9.0%)). In addition, there are fewer invasive procedures, CT scans, hospital revisits, pneumothorax recurrences, adverse events and serious adverse events in the conservative management group.

ASPIRATION: Aspiration may be indicated in the hemodynamically stable patient with a first episode of a large, primary, spontaneous pneumothorax (British Guideline). The American guidelines recommends chest tube placement in this population. Aspiration can be achieved with a catheter over a needle or a pleural pig-tailed catheter.

A meta-analysis, including 5 randomized clinical trials and 385 adult patients with primary spontaneous pneumothorax, demonstrated a shorter length of hospital stay with manual aspiration compared to chest tube drainage (Zhu, Interact Cardiovasc Thorac Surg. 2019, PubMed: 30608581). There was no difference in the immediate and short term success rate, long term recurrence, chest surgery or complication rates.

PROCEDURE: NEEDLE ASPIRATION	
Equipment	16-18 g catheter over a needle, sufficient length for overlying soft tissue depth (can determine with point of care ultrasound)
	Tubing, 3-way stop-cock, 50-60 ml syringes
	Local anesthetic: e.g. Lidocaine, needle and syringe
	PPE, topical antiseptic (e.g. chlorhexadine)
	IV access, cardiac monitor (HR, BP, oxygen saturation)
Time Out	Verify patient, consent obtained, correct side of pneumothorax
Procedure	Position patient supine with head elevated 30-45 (Air → Apex)
	Landmarks: Intercostal space 2 in the midclavicular line
	Anesthetize the skin at the superior border of the 3rd rib
	Anesthetize the deeper intercostal tissue. Penetrate the skin perpendicular to the chest wall at the superior border of the 3rd rib
	Advance the needle into the intra-pleural space while pulling back on the plunger until air bubbles appear in the syringe. Note the depth
	Advance the catheter over the needle to the required depth (until bubbles appear in the syringe) then advance a few millimeters deeper
	Advance the catheter and retract the needle. Cover the catheter opening to avoid air entering the pleural space. Attach the 3-way stopcock and tubing
	Use the 50 or 60 ml syringe to withdraw air. Never open the stop-cock to the chest cavity and outside air at the same time
	Measure the amount withdrawn. Continue until no air remaining.
	a. Aspiration of > 2.5 liters suggests an air leak. Withdraw the catheter. Place a chest tube or pleural pigtail catheter
	b. Withdraw the catheter, place dressing, order upright chest XRAY No re-expansion: Place chest tube or pleural pigtail catheter. Yes re-expansion: Observe for 6 hours, obtain repeat chest XRAY
Complications	SQ emphysema, air embolism, lung laceration, infection, bleeding

VIDEO LINK: NEJM (Requires personal or institutional access)

A multicenter prospective study included 33 pediatric patients with a primary, spontaneous pneumothorax (Leys CM, J Pediatr Surg 2020, PubMed ID: 31706614)**.** All patients underwent aspiration via a pigtail catheter followed by a 6 hour observation and a repeat chest XRAY. Aspiration was successful in 48% (16/33). Management in patients who failed aspiration was based on surgeon discretion. 29% (5/17) underwent immediate video assisted thorascopic surgery (VATS). 71% (12/17) underwent chest tube placement. 42% (5/12) of the patients with chest tube management ultimately required VATS for persistent air leak. Recurrence in the successful aspiration group was 44% (7/16) compared to 83% (10/12) for the failed aspiration group.

CHEST TUBE/PLEURAL CATHETER: A chest tube or pleural (pig-tailed) catheter is indicated in the situations in the table below. In general, large bore chest tubes placed with blunt dissection are discouraged in uncomplicated pneumothorax due the equivalent efficacy and improved comfort of pleural catheters placed placed with a Seldinger technique. A water seal or Heimlich are one-way flow mechanisms that prevent the back flow of air into the thoracic cavity while allowing air to continue to exit the thoracic cavity. If an air leak persists and/or the lung does not expand then suction can be applied (-10 to -20 cm H_2O). However, the early use at high levels of suction can increase the risk of post-expansion pulmonary edema. Suction increases the rate of pleural air extraction in an attempt to bring the visceral and parietal pleura into approximation to allow healing. Relative contraindications may include bleeding diathesis, pleural adhesions and complex or loculated collections. Emergency department chest tube placement is typically at the $4^{th}/5^{th}$ intercostal space in the mid-axillary line though other landmarks may be appropriate.

CHEST TUBE OR PLEURAL PIG-TAIL CATHETER: INDICATIONS
Post needle thoracentesis for tension pneumothorax
Clinically unstable patient
Recurrent pneumothorax
Bilateral pneumothorax
Secondary spontaneous pneumothorax (unclear if required if small, asymptomatic)
Failure of conservative management
Failure of aspiration

CHEST TUBE: EQUIPMENT	CHEST TUBE SIZE*		
Use universal precautions, drape, antiseptic	AGE	WEIGHT	SIZE
1% Lidocaine with Epinephrine if awake	Premature	3 kg	10-14 F
Scalpel	0-6 months	3.5 kg	12-18 F
Large Kelly clamp	6-12 months	7 kg	14-20 F
Small clamp (for clamping the distal end of tube)	1-3 years	10-12 kg	12-24 F
Chest tube	4-7 years	16-18 kg	20-25 F
Silk suture with straight needle, scissors	8-10 years	24-30 kg	28-32 F
Vaseline Gauze, regular gauze, tape	Adult	> 30 kg	28-32 F
Pleural drainage system	*ATLS 2018 Recommendations		

PROCEDURE: CHEST TUBE (BLUNT DISSECTION TECHNIQUE)	
1	Cardiac monitor, consider procedural sedation, analgesia, anxiolysis
2	Use universal precautions, gown, mask, gloves. Use sterile technique
3	Have patient place their arm over their head to expose the lateral chest wall
4	Locate the 4^{th}/5^{th} intercostal space in the mid-clavicular line
5	Inject Lidocaine over the lower rib, then through muscle and into the pleura
6	Make a 2-3 cm incision over the lower rib, down to bone in the intercostal space below and tunneling up to the desired intercostal space to avoid air leaks
7	Blunt dissect superiorly with the Kelly clamp toward the intercostal space
8	With the clamp in closed position, push clamp through pleura over the inferior rib to avoid injury to the neurovascular bundle that parallels the lower rib margin.
9	This may require considerable force. Hold the Kelly clamp close to the distal end to avoid inserting the clamp further than necessary into the pleural space
10	Open the Kelly clamp in the plane parallel to the ribs to further open the intercostal opening wide enough to allow chest tube passage
11	Insert a finger into the pleural space to confirm proper position
12	Clamp the distal end of chest tube with a small clamp
13	Clamp the Kelly clamp over the proximal end of the chest tube
14	With aid of Kelly and finger, guide chest tube: Apically, medially and anteriorly for air, or apically, medially and posteriorly for fluid
15	Advance the tube sufficiently to ensure that the holes are within pleural cavity
16	Connect to pleural drainage system
17	Suture to skin, apply Vaseline gauze, dressing
18	Obtain a chest XRAY and look for condensation to confirm correct placement

VIDEO LINK: NEJM (Requires personal or institutional access)

PROCEDURE: PLEURAL CATHETER (SELDINGER TECHNIQUE)	
1	Identify anatomic landmarks, prepare, anesthetize area
2	Make a small incision over desired intercostal space, above rib
3	Insert the needle into the pleural space, aspirate air
4	Insert guide wire through introducer needle and into the pleural space
5	Guide the wire anterior/apically (air) or inferior/posterior (fluid)
6	Pass the dilator(s) over the wire. Don’t release the wire into the pleura cavity!
7	Remove the dilator and pass the pleural catheter into pleural space
8	Remove the guide wire and connect the pleural catheter to pleural drainage system

CHEST TUBE: COMPLICATIONS	
Hemodynamic instability	Evacuation of a large hemothorax may results in hemodynamic instability if the hemothorax served to tamponade further bleeding into the pleural space. Administer blood components prior to the evacuation of a massive hemothorax.
Mal-positioning of the tube	25% of chest tubes are malpositioned (intra-fissural, intra-parenchymal, or subcutaneous). The majority of these malpositions may not be diagnosed by CXR and may only be identified by CT
Re-expansion pulmonary edema	Patients with a large pneumothorax/pleural effusion and those who have a pneumothorax for a few days are at risk for re-expansion pulmonary edema (RPE). This risk does not appear to be reduced by attempts at limiting re-expansion. The hallmark is cough with frothy sputum. A chest XRAY may reveal near total opacification on the affected side. Treatment is supportive with oxygen and assisted ventilation (non-invasive or mechanical) as required.
Tension pneumothorax	A tension pneumothorax may occur if there is a persistent air leak from the lung and the chest tube is occluded or misplaced. Correction of occlusion, correcting the location of a misplaced tube or needle thoracentesis may be indicated

PLEURODESIS: Pleurodesis may be indicated for those with a persistent air leak or non-expansion of the lung. Pleurodesis is the insertion of sclerosing agents (tetracycline, talc, fibrin glue) into the intrapleural space or the mechanical abrasion of the pleura. The ensuing inflammatory process may occlude the air leak. Pleurodesis is typically administered as part of a surgical procedure but can be administered through a chest tube if a patient is too unstable for surgery or who declines surgery.

SURGERY: Surgery may be indicated for those with a persistent air leak or non-expansion of the lung. Surgical approaches include video assisted thorascopic surgery (VATS), axillary mini thoracotomy or a conventional thoracotomy. The VATS procedure is associated with higher patient satisfaction and early return to activity. Surgery may include over-sowing of ruptured blebs or tears or resection of abnormal lung.

DISPOSITION

There are no consensus recommendation on disposition. This is due to lack of comparative evidence and regional/national differences in care. Recent evidence suggests that a subset of patients who were previously admitted can potentially be managed as outpatients.

In general, those with chest tubes or pleural catheters are likely to be admitted. This is particularly true of those with a persistent air leak or failure of the lung to re-expand. In addition, patients with secondary spontaneous pneumothorax and young children who may not be able to recognize or express worsening symptoms should be admitted. However, discharge with a Heimlich flutter valve may be considered in patients with pleural catheters who are asymptomatic or minimally asymptomatic.

Patients who may be discharged include those with small, primary, spontaneous pneumothorax who are clinically well after observation with conservative management and those who remain well after aspiration. Asymptomatic patients can return to work and normal activity. Patients should avoid extreme exertion and contact sports until complete radiologic resolution. Scuba diving should be avoided unless a there has been a definitive surgical correction. Air travel should be avoided in patients with a undrained pneumothorax and delayed until a definitive procedure or complete radiologic resolution.

RECURRENCE

Patients with SSP (~30%) are more likely to have a recurrence than PPS (~15%). The only modifiable risk factor for PSP is smoking cessation. Initial surgery decreases the rate of SSP recurrence.

APPENDIX: LUNG ULTRASOUND FOR PNEUMOTHORAX

Lung ultrasound has been found to be more sensitive than chest XRAY in identifying pneumothorax and particularly in the supine trauma patient. It can be performed rapidly at the bedside. The probe is place in the midclavicular line oriented in the vertical position with the marker dot to the patient's head.

FINDINGS CONSISTENT WITH PNEUMOTHORAX	
1	Absence of lung sliding
2	Absence of vertical, comet tail artifacts (B waves)
4	Accentuation of horizontal A waves (due to absence of B lines)
3	Presence of "lung point" sign
4	M-mode: Absence of the "sandy beach" or "waves on the "beach sign"
5	M-mode: Presence of the "bar code" or "stratosphere"

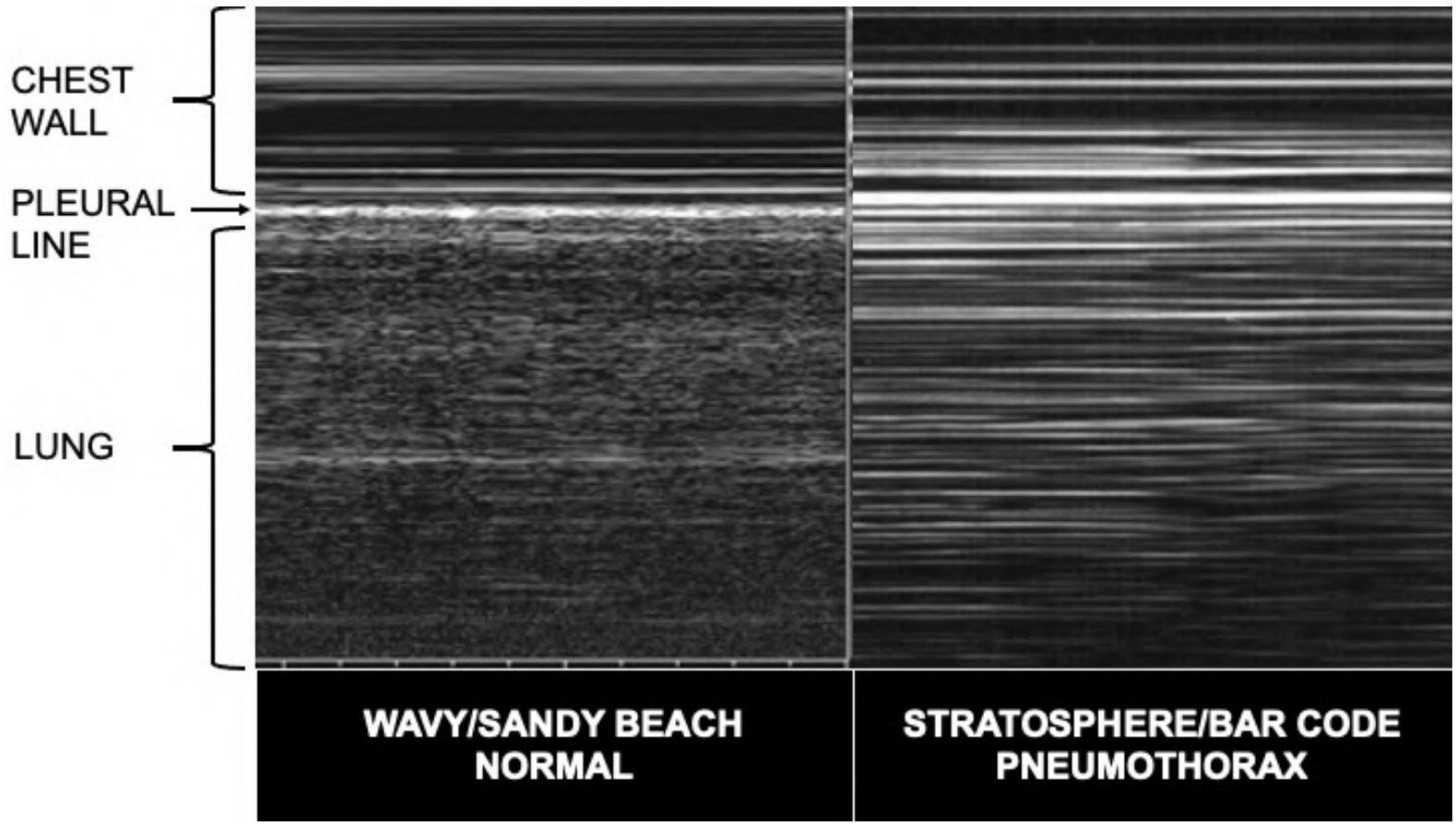
LUNG SLIDING: Lung sliding indicates that the parietal pleura of the chest wall and visceral pleura of the lungs are approximated and moving together as the lungs expand and contract with ventilation. This is seen as a moving shimmering white line. The absence of lung sliding may also be seen with apnea, chronic (e.g. fibrosis) or inflammatory pleural adherence (e.g. ARDS), atelectasis and one-lung intubation (absence of lung sliding on side of non-ventilated lung).

ESTIMATING PNEUMOTHORAX SIZE: LOCATION OF LUNG SLIDING			
	Anteriorly	Mid-axillary Line	Posterior Axillary Line
Small	NO*	YES	YES
Medium	NO	NO	YES
Large	NO	NO	NO
*Is their lung sliding? YES or NO?			

LUNG POINT: A lung point (AKA contact point) is both sensitive and specific for pneumothorax. The lung point sign occurs when an area of lung sliding (no pneumothorax) is adjacent to an area without lung sliding (pneumothorax). This occurs at the junction of normal pleural approximation and a pneumothorax and is typically seen with a small to moderate pneumothorax. The lung point is dynamic and moves with inspiration and expiration. The location of the lung point can also be used to determine the size of the pneumothorax. A lung point may not be seen with a very large pneumothorax and/or a completely collapsed lung.

WEB LINK: LIFE IN THE FAST LANE

M MODE: In a normal patient, the upper half of the image in m-mode is the non-mobile chest wall and the lower half of the image is the mobile lung. Normal lung sliding will result in a grainy image below (the sandy beach sign) while the non-mobile lung results in a stratosphere of bar code sign. .

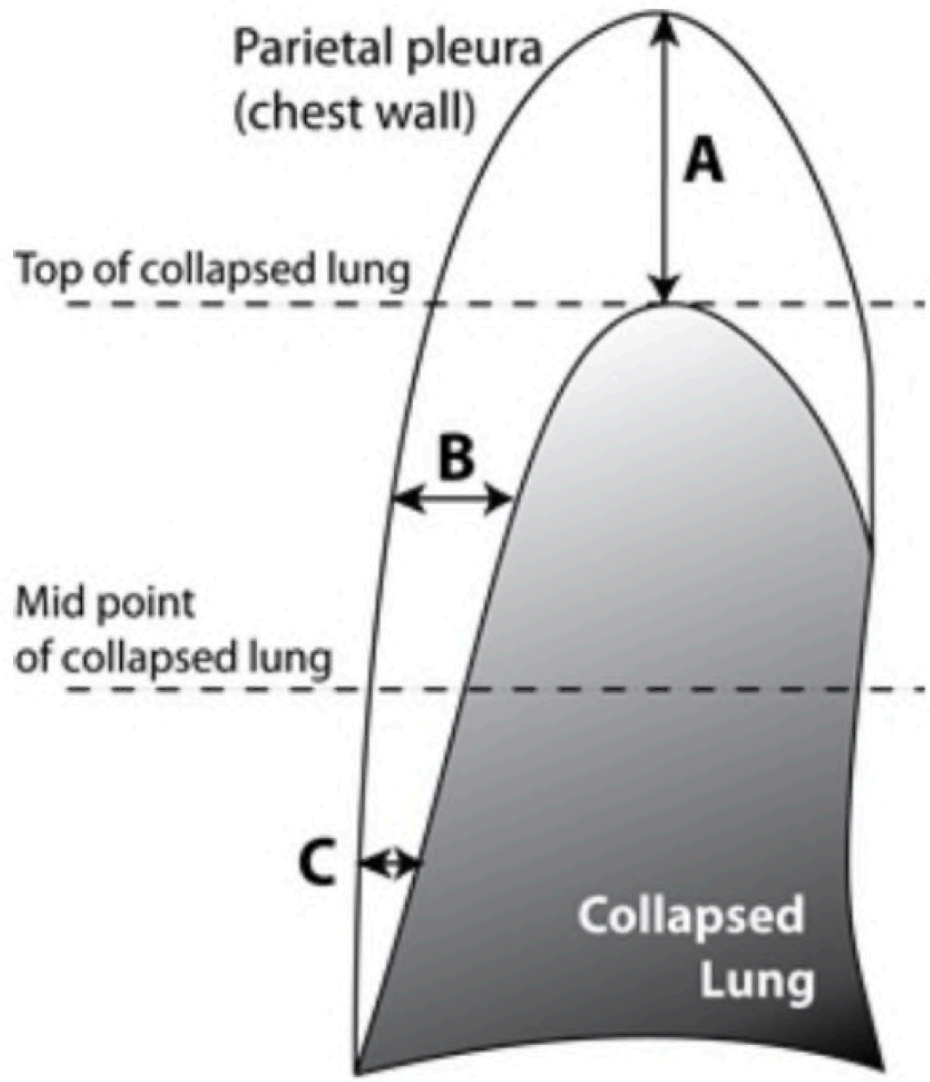


VIDEO LINK: SONOSITE: ULTRASOUND FOR PNEUMOTHORAX

VIDEO LINK: LIFE IN THE FAST LANE: ULTRASOUND FOR PNEUMOTHORAX

APPENDIX: COLLINS ASSESSMENT OF PNEUMOTHORAX SIZE

Collins (%) = 4.2 + 4.7(A + B + C)
(A, B, C in centimeters)



Collins CD, Lopez A, Mathie A, Wood V, Jackson JE, Roddie ME.
Quantification of pneumothorax size on chest radiographs using interpleural distances: regression analysis based on volume measurements from helical CT
AJR Am J Roentgenol. 1995 Nov;165(5):1127-30., PubMed ID: 7572489

RESUSCITATION

AIRWAY

INTRODUCTION (MICHAEL MOJICA, M.D., 2/2020)
The focus of this PEM Guide is on diagnosis and management of problems with the pediatric upper airway defined as the airway that is outside of the thorax and includes the: nasopharynx, oropharynx, larynx and upper trachea. This is intended to be an overview. Many of the PEM Guides address the specific disease entities and airway procedures in greater depth than discussed here.

The anatomy and physiology of the pediatric airway increases the risk of airway obstruction when compared to adults

PEDIATRIC AIRWAY OBSTRUCTION RISK FACTORS
Infants are obligate nasal breathers until at least 2 months of age. Nasal congestion can result in respiratory distress
The tongue is relatively larger than the oropharynx. Loss of muscle tone such as in those with an altered level of consciousness can result to obstruction
A prominent occiput results in flexion of the head and neck when an infant is placed in a supine position resulting in obstruction
A smaller airway diameter increases the risk of airway obstruction with relatively little edema. (Airway resistance = $1/Radius^4$)
Poor coordination of the muscles of mastication, lack of teeth and oral exploratory behaviors result in foreign body aspiration
A higher risk of upper airway infections such as laryngotracheal bronchitis, tonsillitis (relatively larger due to lymphoid hyperplasia until about 7 years of age), bacterial tracheitis, retropharyngeal abscess
Congenital abnormalities of the head and neck e.g. cystic hygroma

CLINICAL PRESENTATION
The differential diagnosis of pediatric airway obstruction is extensive and symptoms vary for each disease entity. General symptoms associated with pediatric airway obstruction include: respiratory distress (tachypnea, retractions, nasal flaring), barking cough, stridor, sudden onset of choking, drooling, a muffled or hoarse voice and swelling of the neck, lips or tongue. Fever may be present with infectious causes.

Physical examination may include an irritable child with signs of respiratory distress. A careful examination of the head, neck and lungs should be conducted. In a patient with a significant sore throat and a normal pharyngeal exam consider a retropharyngeal abscess (child), epiglottitis (an unvaccinated child or an adolescent) or an airway or esophageal foreign body. In a child with complete airway obstruction there may be increased respiratory effort without breath sounds or external airflow.

DIFFERENTIAL DIAGNOSIS OF PEDIATRIC AIRWAY OBSTRUCTION	
INFECTIONS	MECHANICAL
Peritonsillar abscess*	Tongue, muscle relaxation
Retropharyngeal abscess*	Angioedema (anaphylaxis)*
Croup (Laryngotracheal bronchitis)*	Laryngospasm**
Bacterial tracheitis*	Foreign body aspiration*
Epiglottitis	Trauma: Neck, cervical spine*
Ludwig's angina (floor of mouth, neck)	Smoke inhalation*
Cervical adenitis	Neck masses: Cystic hygroma
	Tumors
	Laryngomalacia
* Reviewed in greater detail in a separate PEM Guide ** Laryngospasm may be caused by: submersion injury, gastroesophageal reflux, hypocalcemia and procedural sedation with Ketamine.	

AIRWAY STATUS

Evaluation of the airway should result in the identification of the airway status as: normal, partially obstructed or completed obstruction. Alternatively, this can be classified as clear, maintainable or not maintainable. Oxygen saturation and quantitative end tidal CO2 measurement may suggest respiratory failure.

AIRWAY STATUS	
CLEAR	Open and unobstructed
MAINTAINABLE	Obstructed but maintainable with simple measures such as airway positioning with a head tilt/chin lift
NOT MAINTAINABLE	Obstructed but not maintain able without an advanced airway intervention such as endotracheal intubation

XRAYS may be used to localize the site and cause of obstruction. For example, a soft tissue lateral neck XRAY may reveal a thumbprint sign (epiglottitis) or prevertebral soft tissue swelling (retropharyngeal abscess, cervical spine injury) A chest XRAY may reveal "steeple sign" (croup), a radiopaque foreign body, air trapping with differential hyperinflation (radiolucent airway foreign body). A head and neck CT may be warranted to determine extent of a lesion prior to surgery. Care must be taken when placing the child in a supine position and with the selection of sedative. Ketamine may least likely result in airway problems.

MANAGEMENT

Management should be targeted to the specific etiology though some general principles apply. For example, a supraglottic airway such as the laryngeal mask airway can be used to bypass swelling of the oropharynx but would not be helpful if the airway obstruction is in the trachea.

Options for a poorly visualized airway include: bougie, intubating LMA and techniques to improve visualization such as: video laryngoscopy (glidescope), intubation over a bougie and fiberoptic intubation.

GENERAL MANAGEMENT PRINCIPLES
Minimize agitating the child. Allow to remain in a position of comfort
Airway position. Head tilt/chin lift, avoid hyperextension in the infant. A jaw thrust maneuver should be used if cervical spine injury is suspected
Suction the nasopharynx and oropharynx if copious secretion, blood
Foreign body obstructed airway maneuvers in the patient with complete airway obstruction only and suspected foreign body (see table below)
Airway adjuncts: Oral airway (only if altered mental status with no gag reflex), nasal airway
Non-invasive ventilation techniques: High flow nasal cannula, CPAP, BiPap
Medication to reduce airway edema: Epinephrine, corticosteroids, Heliox
Endotracheal intubation: The use of paralytics is relatively contraindicated in the patient with airway obstruction that cannot be ventilated with a bag-valve-mask. May require as smaller ET then usual Ketamine has bronchodilator activity. Good choice for asthma, anaphylaxis
Supraglottic airway: Laryngeal mask airway
Cricothyrotomy: Needle, surgical, percutaneous, Seldinger technique
Antibiotics for obstruction due to bacterial infection: Retropharyngeal abscess, peritonsillar abscess, epiglottitis, bacterial tracheitis, Ludwig's angina
Surgical drainage of abscess: Peritonsillar, retropharyngeal, parapharyngeal

APPROACH TO FOREIGN BODY AIRWAY OBSTRUCTION
Allow patient without complete airway obstruction to clear foreign body with coughing
Foreign body obstructed airway maneuvers if complete obstruction < 1 year: Sequences of 5 chest thrust and 5 back blows > 1 year: Abdominal thrusts
Begin chest compressions if loss of consciousness
Direct laryngoscopy: Foreign body removal with McGill forceps
Endotracheal intubation with attempt to push foreign body into right mainstem bronchus and ventilate left lung until bronchoscopy
Cricothyrotomy: Needle, surgical, percutaneous, Seldinger technique

APPENDIX: AIRWAY ASSESSMENT AND MANAGEMENT

AIRWAY			
EVALUATE	IDENTIFY	STATUS	INTERVENE
Chest Rise (Look)	☐ Good (normal) ☐ Decreased ☐ None	☐ Normal	☐ Evaluate Breathing
Air Flow (Listen, Feel)	☐ Good (normal) ☐ Decreased ☐ None	☐ Airway Obstruction (Partial)	☐ Minimize agitation ☐ O_2 Delivery ☐ Monitor ☐ Airway Positioning ☐ Suction ☐ Medications ☐ Albuterol ☐ Epinephrine
Stridor	☐ None (normal) ☐ Inspiratory ☐ Expiratory ☐ Both		
		☐ Airway Obstruction (Complete)	Above PLUS ☐ BVM ☐ Foreign Body Obstructed Airway Maneuvers ☐ Back blows, chest thrusts ☐ Heimlich ☐ Remove FB with Magill forceps ☐ Push FB down right mainstem, ventilate the left lung ☐ Oral Airway ☐ ENT, Anesthesia consult ☐ Endotracheal Intubation ☐ Cricothyrotomy

APPARENT LIFE-THREATENING EVENT

INTRODUCTION (DANIEL FENSTER M.D., 9/2015)
An ALTE or apparent life-threatening event is an episode that is frightening to the observer and that is defined by some combination of the following characteristics.

APPARENT LIFE-THREATENING EVENT (ALTE)	
Apnea	Apnea: Central or occasionally obstructive
Color Change	Usually cyanotic or pallid, can be erythematous or plethoric
Change in Muscle tone	Change in muscle tone: Usually marked limpness/hypotonia
Choking	or gagging

In some cases, the observer fears that the infant has died. It is commonplace to stop considering ALTE once children are older than 12 months of age.

ALTE is not a diagnosis but a constellation of symptoms. It should only be considered idiopathic if it is a first incident and there is nothing on history and physical exam to suggest further workup. A large differential diagnosis must be considered which includes both congenital and acquired illness. ALTE appears to be a separate entity than sudden infant death syndrome. ALTE patients tend to be older and the incidence of ALTE has been stable. The incidence of SIDS has decreased with the “Back to Sleep” campaign.

ATLE should be differentiated from periodic breathing, a normal variant that has no associated changes in color, tone, or heart rate and is normal. A study of infants undergoing home monitoring showed that healthy infants can have respiratory pauses of up to 30 seconds and bradycardia up to 10 seconds without adverse effects (Ramanathan, JAMA 2001, PubMed ID: 11325321).

DIFFERENTIAL DIAGNOSIS	
Cardiac	Congenital heart disease, arrhythmia, long QT, myocarditis, cardiomyopathy
Pulmonary	Upper airway obstruction: Anatomical, infectious, foreign body), Respiratory tract infection:* Bronchiolitis, pertussis, pneumonia
Gastrointestinal	Gastroesophageal reflux disease (GERD)*, gastroenteritis, surgical abdomen (e.g. Malrotation with midgut volvulus)
Neurological	Seizure*, intracranial hemorrhage, congenital brain malformation, hydrocephalus, tumor
Infectious	UTI, sepsis, meningitis, pneumonia, bronchiolitis, gastroenteritis
Hematology	Anemia
Metabolic	Inborn error of metabolism, hypoglycemia, electrolyte abnormalities
Trauma	Non-accidental trauma
Environmental	Toxic ingestion, smoke inhalation, hypo/hyperthermia
Idiopathic*	50% of cases
*Most common etiologies. Each account for about 10%	

In May of 2016, the American Academy of Pediatrics (AAP) published a clinical practice guideline (PubMed ID: 27474017) that replaced the term Apparent Life-Threatening Event (ALTE) with a new term, Brief Resolved Unexplained Events (BRUE). The intent of this guideline is to identify a subgroup of infants with these events that are of low risk for significant adverse outcomes and therefore would not require admission or extensive diagnostic evaluation. Where ALTE is a broad term used to describe any event that is frightening to the observer, BRUE is a more specific term characterized by elements of the history and physical examination with specific inclusion and exclusion criteria. (See: PEM Guide: Resuscitation: Brief Resolved Unexplained Events)

CLINICAL FINDINGS

The most important aspects of the care of the patient with ALTE is a thorough history and physical examination as detailed below.

HISTORY
Was baby asleep or awake during event?
If asleep, prone or supine position?
If awake, was baby feeding? What position during feeding?
How long did event last?
Did baby vomit, choke, go limp or turn blue?
Fever, URI symptoms, mental status, recent illness, sick contacts
How did parent/caretaker intervene?
No intervention (resolved spontaneously
Stimulation: Gentle or vigorous
Mouth to mouth
CPR by EMS
Trauma: Accidental or non-accidental
Use of home monitor: If so, did it alarm?
PMHx: Prematurity, GERD, birth trauma, prior ALTE/apnea, co-morbid conditions
Family History: SIDS, ALTE, unexplained death, cardiac, metabolic, genetic
Social History: Caretaker at time of event, smokers, heaters/coolers
Medications: Infants, caregiver’s, herbals

PHYSICAL EXAM	
Appearance	Fever, color, perfusion, mental status, respiratory distress
Airway	Crying, cooing, babbling, stridor
Breathing	Respiratory rate, retractions, nasal flaring, oxygen saturation breath sounds: Crackles, wheezes
Circulation	Color, temperature and pulses of hands and feet Heart rate, blood pressure in upper/lower extremities Cardiac exam: Murmurs, gallops, rhythm, hepatomegaly
Disability	Mental status, tone, bedside glucose Signs of trauma: Bruises, crepitus, range of motion of extremities
Full Examination	With attention to neuro, cardiac, pulmonary

DIAGNOSTIC EVALUATION

No consensus exists on the components or extent of the diagnostic evaluation necessary. The history and physical examination should guide diagnostic testing. A study in pediatrics in 2005 included 243 patients at a single institution that had 3,776 tests performed (15.4 tests/patient). 18% of tests performed were positive and only 6% contributed to the diagnosis. Testing for systemic infections, metabolic diseases and electrolyte abnormalities were not useful (Brand, Pediatrics 2005, PubMed ID: 15805360).

DIAGNOSTIC TESTING OPTIONS
Complete history and physical exam
Vital signs including a bedside glucose determination
12 lead EKG: Attention to QT interval
If patient has home event monitor, contact the service (neonatology, sleep study personnel) in order to arrange for event downloads.
Consider CBC, sepsis evaluation, CXR, RSV/Flu/Pertussis nasal antigen testing as indicated by the history and physical examination

DISPOSITION

There is no clear consensus on the disposition of these infants. The significant intervention rate in may studies has a range of 5-15% suggesting that the vast majority of infants may not require admission if low risk infants can be prospectively identified. It has been suggested that well appearing infants who fulfill low risk characteristics may be safely discharged though this has not been extensively studied**.** Reassurance of the parents is essential. Remember the parents brought the infant to the hospital because they thought he/she was about to die.

A 2012 study derived and internally validated a clinical decision rule to identify infants with ALTE who could be safely discharge from the ED (Mittal, Ped Emerg Care 2012, PubMed ID: 22743742). They enrolled 300 infants of which 76% were admitted to the hospital. 12% overall and 16% of admissions required a significant intervention. The most common significant interventions were: admission to an ICU (n=15), need for supplemental oxygen (n=14), requiring repeated airway suctioning, an abnormal pneumogram leading to discharge with an apnea monitor (n=13), a repeat ALTE requiring intervention (n=11) and cardiology consultation for an echocardiogram (n=10). The authors conclude that those infants in one of the 3 risks group defined in the table below can be safely discharged (Negative predictive value: 96.2%, 95% CI (92.4, 98.1%). Following the rule would decrease their admission rate by 40%.

LOW RISK INFANTS (SIGNIFICANT INTERVENTION RATE)
Full term infants without cyanosis (2.7%)
Full term infants with cyanosis, choking and normal examination (4.8%)
Preterm infants, with upper respiratory symptoms (history of cough or coryza) (6.7%)

Those infants meeting low risk criteria should be monitored in the emergency department for some period of time. All infants should have a follow up appointment with their primary care provider. There is no indication to send patient home on an apnea or event monitor.

DISPOSITION
LOW RISK INFANTS
DISPOSITION: Consider discharge with close outpatient Follow-Up
Normal vital signs and physical examination
1st event, full term
> 2 months of age
No medications or co-morbid conditions
No social (abuse, neglect) concerns
No family history of ALTE, SIDS
No URI/LRI symptoms
Obstructive event (choking, gagging) due to emesis, coughing or crying
NON-LOW RISK INFANTS
DISPOSITION: Admit for cardiac monitoring and further evaluation
Premature infants
< 30 days of age
Multiple ALTEs
History of prior ALTE
EMS provided CPR
Abnormal ED workup
Infant with a questionable social situation

BREATHING

INTRODUCTION (MICHAEL MOJICA M.D., 2/2020)
The goal of respiration is to deliver sufficient oxygen to meet the tissues metabolic demands and regulate acid-base homeostasis by eliminating carbon dioxide. The regulation of respiration is complex. Direct injury to the pulmonary system can occur as a result of trauma, infection or inflammation.

Abnormalities to other systems such as the central nervous system (disordered control of breathing), cardiovascular system (pulmonary edema) and hematologic system (severe anemia) can be manifested by changes in the respiratory system. It is important to remember that tachypnea may be the result of non-pulmonary causes. Irregular breathing may be due to CNS malfunction and hyperpnea (increased rate and volume of respiration) or metabolic acidosis (e.g. diabetic ketoacidosis, inborn errors of metabolism, salicylate ingestion).

CLASSIFICATION OF RESPIRATORY DISTRESS/FAILURE		
TYPE	EXAMPLE	FEATURES
Upper Airway* (↑ Airway resistance)	Croup, Anaphylaxis, Foreign body	Stridor Change in voice
Lower Airway (↑ Airway resistance)	Asthma Bronchiolitis	Wheeze ↑ Expiratory phase (↑ I/E ratio)
Parenchymal (↓ Lung compliance)	Pneumonia Pulmonary edema	Rales, grunting ↓ Breath sounds
Control of Breathing	Toxins, increased ICP Over sedation Post ictal state	Central apnea Variable or irregular respiratory rate
*See: PEM Guide: Resuscitation: Airway		

CLINICAL MANIFESTATIONS
The primary goal of the respiratory system is to maintain minute ventilation
1. Minute ventilation = Tidal Volume x Respiratory Rate (Normal TV = 5-7 ml/kg)
2. Arterial oxygen content (CaO_2) = (Hgb x 1.36 x SaO_2) + (0.0031 x PaO_2)
3. Oxygen delivery (DaO_2) = CaO_2 x Cardiac output

Many pulmonary disease processes can be thought of as a loss of effective tidal volume. The system compensates initially by increasing the respiratory rate (tachypnea). An increase in respiratory rate if often the initial manifestation of a respiratory process. Unfortunately, tachypnea is non-specific and may be seen with fever, pain, anxiety and many non-pulmonary processes as well.

When tachypnea is no longer sufficient to maintain minute ventilation an increase in the work of breathing occurs. This is seen clinically as: retractions, nasal flaring, grunting and see-saw respirations. These require significant effort and increase the metabolic demand for oxygen. Child may tire quickly from these efforts.

The combination of tachypnea and/or increase/inadequate work of breathing defines respiratory distress. Tachypnea without an increased work of breathing is termed “quiet” tachypnea and is more like to originate from a non-pulmonary cause such as metabolic acidosis.

Respiratory failure occurs when the compensatory mechanisms are no longer sufficient to maintain oxygenation and eliminate CO_2. Respiratory failure is the most common cause of cardiopulmonary arrest in children. While we often describe respiratory distress and respiratory failure as distinct entities they represent a continuum from:

Normal Respiration → Respiratory Distress → Respiratory Failure → CP Arrest

Clinical manifestations of respiratory failure may include: altered mental status (initial agitation followed by depressed responsiveness), cyanosis/pallor, bradycardia, bradypnea (low respiratory rate) and eventually apnea and cardiopulmonary arrest.

APNEA	Cessation of breathing ≥ 20 seconds
	Cessation of breathing < 20 seconds if accompanied by pallor, cyanosis or bradycardia

The goal of evaluation is to identify respiratory distress and intervene before it deteriorates to respiratory failure. The diagnosis of respiratory distress and failure should be made clinically and not be delayed by waiting for the results of an arterial blood gas. Oxygen saturation and quantitative end-tidal CO_2 measuring can assist in bedside decision-making.

Arterial oxygen saturation (SaO_2) is the percentage of hemoglobin that is oxygenated. Two wavelengths of light are measured (deoxy Hb and HbO_2) $SaO_2 = HbO_2 / (dHb + HbO_2)$. An SaO_2 less than 94% on room air is considered hypoxemia. Abnormal hemoglobins, severe anemia and severe shock may results in inaccurate readings. For example, carboxyhemoglobin (COHb) will result in falsely high SaO_2. A methemoglobin (MetHb) level greater than 5% will results in an SaO_2 of 85%. A co-oximetry panel should be ordered (may be venous) if COHb or MetHb are suspected.

DIFFERENTIATING RESPIRATORY STATUS		
	RESPIRATORY DISTRESS	RESPIRATORY FAILURE
Respiratory Rate	↑	↑↑RR (early) → ↓RR (late)
Heart Rate	↑	↑HR (early) → ↓HR (late)
Aeration (flow)	↓	↓ → None
Respiratory Effort	↑	↑ (early) → ↓ (late)
Breath Sounds	Abnormal Airway Sounds	Minimal or no Sounds
Skin	Pallor, cool skin	Cyanosis
Mental Status	Irritable. Lethargic	Stupor, Coma

RESPIRATORY RATE	
AGE	BREATHS/MINUTE
< 1 year	30-60
1-3 year	24-40
4-5 year	22-34
6-12 year	18-30
13-18 years	12-16
A respiratory rate < 10 or > 60 breaths/minute are always abnormal Sleeping infants may have irregular respirations (periodic breathing) with pauses up to 10-15 seconds.	

MANAGEMENT

The management of respiratory distress and respiratory failure will be governed by the specific etiology but some basic principles apply. Patients should be kept in a position of comfort. Oxygen should be applied in such a manner that does not increase agitation. Patients in respiratory failure will require ventilation as well as oxygenation. In general, oxygenation takes precedent. Hypercarbia is better tolerated without adverse effects (i.e. permissive hypercarbia).

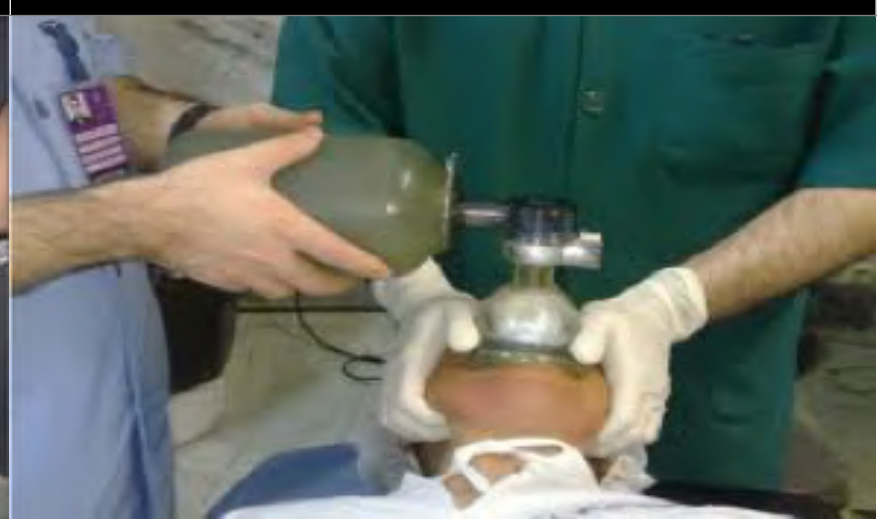
RESPIRATORY DISTRESS	Oxygen delivery Treat underlying cause
RESPIRATORY FAILURE	Oxygen delivery Treat underlying cause Assist ventilation

Positive pressure ventilation can be delivered non-invasively (bag-valve mask ventilation, CPAP, BiPap) or invasively (laryngeal mask airway, endotracheal intubation, cricothyrotomy). Complications of non-invasive ventilation can include gastric distention that can result in bradycardia, regurgitation and limit diaphragmatic excursion. Invasive positive pressure ventilation can result in barotrauma (pneumothorax, tension pneumothorax). This is particularly true in situation like asthma where there are areas of varying airway resistance. Providing adequate ventilation in someone who is compensating for metabolic acidosis (e.g. DKA, salicylate toxicity) can be very difficult. Inadequate ventilation in these patients can result in a worsening of the acidosis.

DISEASE SPECIFIC MANAGEMENT: MEDICATIONS		
Anaphylaxis*	Upper and lower airway	Epinephrine IM, Albuterol neb Antihistamines, corticosteroids
Asthma*	Lower airway obstruction	Albuterol neb, Ipratropium neb Magnesium IV, corticosteroids Terbutaline SQ or infusion
Pneumonia*	Lung tissue disease	Antibiotics
Pulmonary edema	Lung tissue disease	Diuretics IV, Inotrope infusion
Intracranial pressure*	Disordered control of breathing	Controlled hyperventilation Hypertonic saline, Mannitol
*Reviewed in detail is separate PEM Guides		

APPENDIX: BAG-VALVE-MASK VENTILATION

PROCEDURE: BAG-VALVE MASK (BVM) VENTILATION	
FACE MASK	Spans from the bridge of the nose to the cleft of the chin The clear mask should be inflated to obtain a tight seal with the face
BAG TYPE	A self-inflating bag is typically used. (Flow-inflating bag in the OR)
BAG SIZE	Infants, young children: 400-500 ml BVM (The small neonatal BVM's may not deliver sufficient tidal volume)
	Older children, adolescents and adults: 1000 ml BVM
POP-OFF VALVE	Most BVM's will have an automatic pop off valve that limit peak pressures to 35-45 cm H_2O
	These valves may need to be disabled (closed position) if there is high airway resistance or low lung compliance.
OXYGEN	The BVM must be attached to an O_2 supply source at 10-15 liters/minute and have an O_2 reservoir attached or extended
POSITION	The child should be placed in sniffing position with a head tilt/chin lift Jaw thrust maneuver should be used if cervical trauma is suspected
TIDAL VOLUME	The bag should be compressed sufficiently to result in chest rise Excess tidal volume can result in barotrauma and gastric distention In the patient with prolonged expiration the chest should be allowed to recoil passively before starting another ventilation to avoid "stacking of breaths" and barotrauma
RESP RATE	Each breath should occur over 1 second Rescue breathing is 20-30 breaths per minute (1 every 2-3 seconds)
CRICOID PRESSURE	There is insufficient evidence to recommend routine cricoid pressure to prevent aspiration though it may facilitate airway visualization in the child prior to endotracheal intubation
TECHNIQUE	E-C Clamp technique should be used for 1-person ventilation C consists of the thumb and index finger to hold mask firmly to face. The E consists of the 3rd, 4th and 5th which are help on the bottom edge of the mandible and is used to perform the head tilt chin left
	A 2-person technique is required to perform ventilations with the jaw thrust maneuver in the trauma patient
	In both techniques, avoid compression of the soft tissue of the neck

HEAD TILT/CHIN LIFT: E-C CLAMP	JAW THRUST: 2 PERSON
	

APPENDIX: BREATHING ASSESSMENT AND MANAGEMENT

BREATHING			
EVALUATE	IDENTIFY	STATUS	INTERVENE
Color	☐ Normal skin tone ☐ Pallor ☐ Cyanosis ☐ Mottled	☐ Normal	☐ Evaluate Circulation
Respiratory Rate	☐ None (apnea) ☐ Low ☐ Normal ☐ High		
Work of Breathing	☐ None (normal) ☐ Retractions ☐ Nasal flaring ☐ Grunting ☐ Head bobbing	☐ Respiratory Distress	☐ O_2 delivery ☐ Monitor ☐ Airway Positioning ☐ Suction MEDICATIONS ☐ Albuterol ☐ Epinephrine
O_2 Saturation	☐ Normal ☐ Decreased (<95%)		
Breath Sounds	<u>Aeration (Air Flow)</u> ☐ Normal ☐ Decreased <u>Auscultation</u> ☐ Normal ☐ Wheeze ☐ Rhonchi ☐ Rales	☐ Respiratory Failure	Above plus VENTILATION ☐ Non-invasive ☐ BVM ☐ LMA ☐ Endotracheal Intubation
Trachea Position	☐ Midline (normal) ☐ Deviated	☐ Tension Pneumothorax	☐ Needle Thoracentesis

BRIEF RESOLVED UNEXPLAINED EVENTS

INTRODUCTION (NICOLE GERBER, M.D., 5/2023)
In May of 2016, the American Academy of Pediatrics (AAP) published a clinical practice guideline (PubMed ID: 27474017) that replaced the term Apparent Life-Threatening Event (ALTE) with a new term, Brief Resolved Unexplained Event (BRUE). The intent of this guideline is to identify a subgroup of infants with these events that are of low risk for significant adverse outcomes and therefore would not require admission or extensive diagnostic evaluation. Where ALTE is a broad term used to describe any event that is frightening to the observer, BRUE is a more specific term characterized by elements of the history and physical examination with specific inclusion and exclusion criteria. (See: PEM Guide: Resuscitation: Acute Life Threatening Events).

BRUE (BRIEF RESOLVED UNEXPLAINED EVENT): DIAGNOSTIC CRITERIA	
< 1 YEAR OLD, AND THE EVENT MUST HAVE BEEN:	
B (Brief)	Duration < 1 minute
R (Resolved)	Returned to baseline after the event Normal vital signs, normal appearance
U (Unexplained)	Not explained by an identifiable medical condition
E (Event)	Characterized by ≥ 1 of the following
	☐ CENTRAL CYANOSIS OR PALLOR
	Includes cyanosis: Blue or purple coloration of face, gums, trunk
	Excludes: Acrocyanosis or perioral cyanosis
	Includes Pallor: pale coloration of face or trunk
	Excludes: Rubor
	☐ ABSENT, DECREASED OR IRREGULAR BREATHING
	Includes: Central apnea; obstructive or mixed obstructive apnea
	Excludes: Periodic breathing of a newborn, breath holding spell
	☐ MARKED CHANGE IN TONE
	Includes: Hypertonia; Hypotonia
	Excludes: Hypertonia associated with crying, choking or gagging due to gastroesophageal reflux or feeding problems; Tone changes associated with breath holding spell
	☐ ALTERED RESPONSIVENESS
	Includes: Loss of consciousness; mental status change; lethargy; somnolence; post-ictal phase
	Excludes: Loss of consciousness associated with a breath-holding spell

It is important to note that in addition to having inclusion criteria, there are exclusion criteria. The event must be unexplained, meaning that if the event is consistent with another diagnosis such as gastro-esophageal reflux (GER) or child abuse, it cannot be labeled as a BRUE. This is in contrast to ALTEs where a significant portion of those patients were ultimately diagnosed with conditions like GER or respiratory infections that may have been apparent on initial history and exam.

The characteristics of the event also have inclusion and exclusion criteria. Whereas an ALTE was defined as "an episode that is frightening to the observer and is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging." BRUE excludes exam findings like rubor or changes in tone, mental status or breathing that can be attributed to another diagnosis (see below for full inclusion and exclusion criteria). The differential diagnosis for BRUEs is extensive (see Appendix)

Once the event has been identified to meet criteria to be diagnosed as a BRUE, the second step is to determine if the patient meets criteria to be considered low risk. A systematic review from 2013 found that prematurity, multiple ALTEs and suspected child abuse were associated with adverse events and serious underlying diagnoses, putting these children into a separate risk category, and this information contributed to the low risk criteria (Tieder, Pediatrics 2013, PubMed ID: 23415612).

BRUE: LOW RISK CRITERIA
Age > 60 days
Born ≥ 32 weeks gestation and corrected gestational age ≥ 45 weeks
No CPR by trained medical provider
Event duration < 1 minute
First Event
No concerns identified from history (see Appendix for extensive history)
No concerns identified from physical exam (see Appendix for extensive physical)

MANAGEMENT

For patients who fall into the low risk category, studies have not supported routine testing. 4 recommendation categories are advised: should, may, should not and need not. (See Appendix: BRUE diagnosis, risk assessment and management)

For patients who fall into the higher risk category, the AAP guideline does comment on the management of that patients who fall into this higher risk category other than to recommend that these patients should have further evaluation that focuses on the specific area of concern (See Appendix: Differential Diagnosis).

A 2019 study published a framework for the management of higher risk BRUE patients (Lerner, Pediatrics 2019, PubMed ID: 31350360). This study is describes an evidence-informed, consensus framework and not a practice guideline due to the paucity of evidence on the evaluation and management of these patients. A 2-tiered system is recommended. The initial tier is intended to detect conditions that are uncommon but could lead to serious adverse outcomes if not diagnosed or treated promptly or common and unlikely to lead to serious adverse outcomes but in which early diagnosis could prevent recurrent events and preclude unnecessary testing or caregiver concern. These conditions included child maltreatment, feeding problems, cardiac arrhythmias, infections and congenital abnormalities. The second tier is to identify potential causes of recurrent events when clinical concerns regarding less-common characteristics, findings, and evaluations remain after completing the initial tier. The second tier conditions include dysphagia, intermittent partial airway obstruction and epilepsy (See Appendix: Higher Risk BRUE

DISPOSITION
Patients who meet the criteria for low risk BRUE do not need to be admitted to the hospital solely for cardiorespiratory monitoring but close follow up is recommended, with a pediatrician visit within 24 hours after the initial evaluation.

There is little evidence to guide which higher-risk infants with a BRUE are most likely to benefit from hospitalization. The algorithm for higher risk BRUE recommends to admit patients with high risk BRUE for which the initial tier evaluation does not reveal an explanation and to consider admission for which for which the first tier evaluations can not be completed in the Emergency department. It is not expected that all higher risk patients require admission. Disposition decision can be shared with the parents and primary care givers. A parent information sheet is available at the following link (WEBLINK: BRUE What Parents and Caregivers Need to Know

Patient with identified conditions do not meet BRUE criteria and should be managed appropriately.

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BRUE DIAGNOSIS

< 1 year old
Brief, resolved event
Witnessed by caregiver

Patient is Well Appearing →

Sudden, brief, now resolved episode of ≥1 of:
- Cyanosis or Pallor
- Absent, decreased or irregular breathing
- Marked change in tone (hypo or hyper)
- Altered responsiveness

Any Event Criteria Present →

Perform appropriate history and physical exam

No Event Explanation Identified →

DIAGNOSIS OF BRUE MADE

Concerns identified from history and physical examination (e.g. Family Hx of sudden cardiac death or subtle non-diagnostic social, feeding or respiratory problems)

Additional Symptoms or Abnormal Vital Signs (e.g., Cough, Respiratory Difficulties, Fever)

All Event Criteria Absent

NOT A BRUE

Explanation for Event Identified (e.g., GERD, Feeding Difficulties or Airway Obstruction)

MANAGEMENT NOT COVERED BY BRUE GUIDELINE

YES

RISK CLASSIFICATION

NO

RISK STRATIFICATION
- Age > 60 days?
- Born ≥ 32 weeks gestation and corrected gestation age ≥ 45 weeks?
- No CPR by trained medical provider?
- Event Lasted < 1 minute?
- First Event?

NO TO ANY

HIGHER RISK BRUE

YES TO ALL

LOWER RISK BRUE

SEE HIGHER RISK BRUE ALGORITHM (NEXT PAGE)

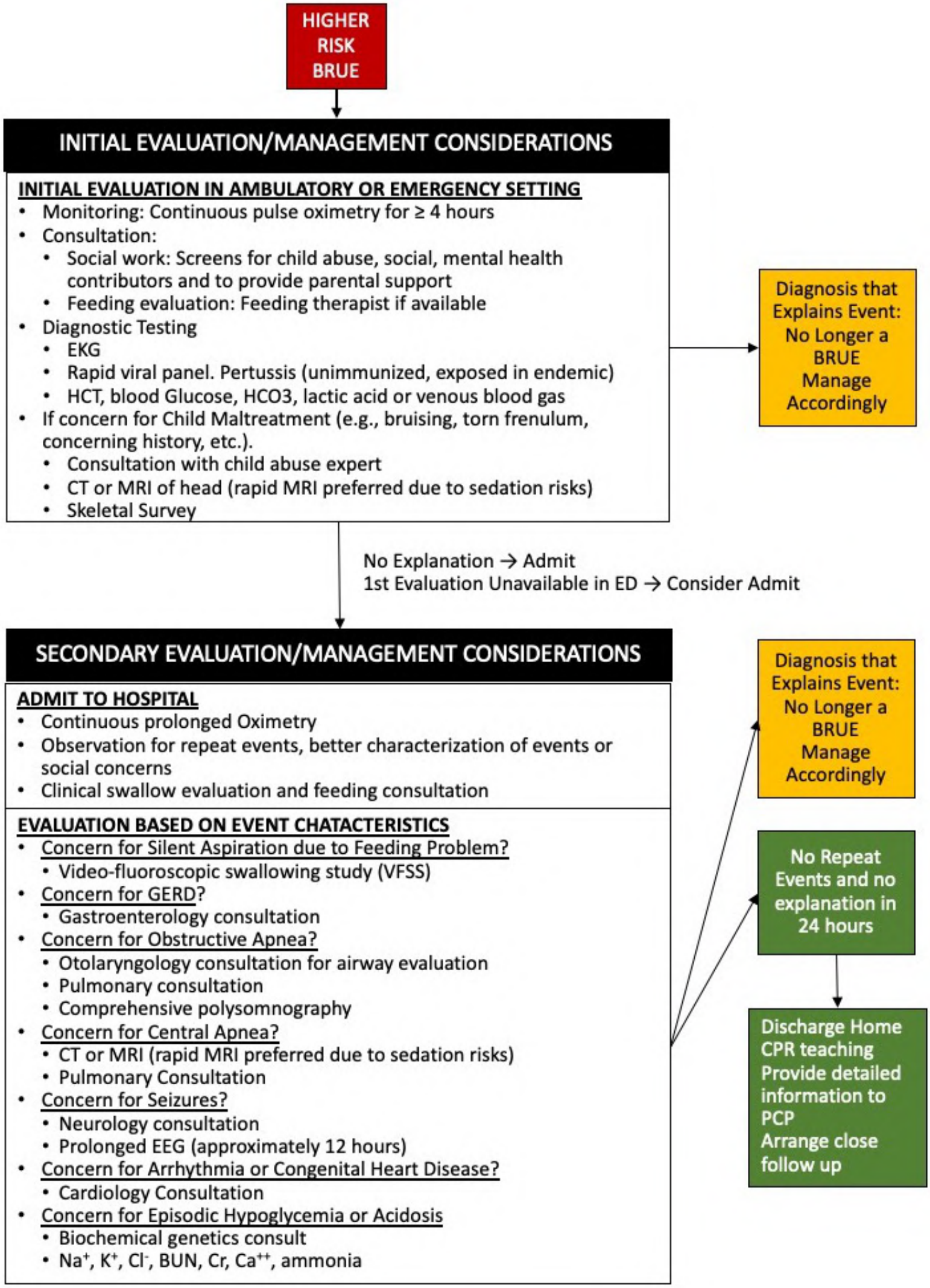
LOW RISK MANAGEMENT

SHOULD
Educate caregivers about BRUE and engage in shared decision making to guide evaluation, disposition and monitoring
Offer resources for CPR training to caregiver

NEED NOT
Obtain viral respiratory testing, blood glucose, serum bicarbonate, serum lactate, urinalysis, neuroimaging.
Admit to hospital solely for cardiorespiratory monitoring

MAY
Obtain pertussis testing and 12 lead EKG
Briefly monitor with continuous pulse oximetry and serial observations

SHOULD NOT
Obtain CBC, Blood culture, CSF, BMP, calcium, ammonia, blood gas, plasma amino acids, urine organic acids or acylcarnitines
Chest XRAY, EEG, Echocardiogram, GERD studies
Initiate home cardio-pulmonary monitor
Prescribe acid suppression or antiepileptic



Lerner S et al
A Framework for Evaluation of the Higher-Risk Infant After a Brief Resolved Unexplained Event
Pediatrics: 144 (2), Aug 2019, PubMed ID: 31350360

APPENDIX: DIFFERENTIAL DIAGNOSIS

DIFFERENTIAL DIAGNOSIS	
OTOLARYNGOLOGIC	GENETIC/METABOLIC
Maxillary hypoplasia	Inborn errors of metabolism
Micrognathia	Mitochondrial disorders
Macroglossia	Electrolyte disturbance
Choanal atresia	Hypocalcemia
Pyriform aperture stenosis	Hypoglycemia
Laryngomalacia/anomalies	CARDIOVASCULAR
Subglottic stenosis	Channelopathies: prolonged or short QT, Brugada
Tracheomalacia/anomalies	Congenital heart disease
Adenotonsillar hypertrophy	Cardiomyopathy/myocarditis
OSA Pneumonia	Vascular ring/sling/compression
Vaso-vagal response	Ventricular pre-excitation: WPW syndrome
Unintentional suffocation	Arrhythmia
PULMONARY	Sepsis
Aspiration	Syncope
Asthma	CHILD MALTREATMENT
Foreign body	Abusive head trauma
Congenital airway anomalies/malacia	Munchausen by proxy or medical child abuse
Infection	Intentional suffocation
Hemorrhage	Poisoning
Upper, lower respiratory tract infection	Medical neglect
INFECTIOUS	NEUROLOGIC
Bronchiolitis	Seizures
Croup	Stroke
Upper respiratory infection	Intracranial mass lesion
Urinary Tract Infection	Brain/intracranial structural, vascular abnormality
Sepsis	Intracranial hemorrhage
Meningitis	Hydrocephalus
Gastroenteritis	Neuromuscular disorder
Viral syndrome	Congenital central hypoventilation
Pertussis, RSV, other resp viruses	Apnea of prematurity
GASTROINTESTINAL	Infant botulism
Gastroesophageal reflux	Demyelination: transverse myelitis, MS, ADEM
Dysphagia/choking	TOXIN EXPOSURE
Esophageal dysmotility	Medication adverse effect
Laryngeal chemo-reflex	Substance exposure via human milk
Bowel obstruction	Environmental exposure
Gastroenteritis	Vaccine reaction
Tracheoesophageal fistulas	MISCELLANEOUS
Esophageal foreign body	Acrocyanosis
Intussusception	Hypothermia
	Breath-holding spell
	Idiopathic

APPENDIX: EVENT CHARACTERISTICS

EVENT CHARACTERISTICS
HISTORY OF THE EVENT
General description
Who reported the event?
Witness of the event? Parent(s), other children, other adults? Reliability of historian(s)?
STATE IMMEDIATELY BEFORE THE EVENT
Where did it occur (home/elsewhere, room, crib/floor)?
Awake or asleep?
Position: supine, prone, upright, sitting, moving?
Feeding? Anything in the mouth? Availability of item to choke on? Vomiting or spitting up?
Objects nearby that could smother or choke?
STATE DURING THE EVENT
Choking or gagging noise?
Active/moving or quiet/flaccid?
Conscious? Able to see you or respond to voice?
Muscle tone increased or decreased?
Repetitive movements?
Appeared distressed or alarmed?
Breathing: yes/no, struggling to breathe?
Skin color: normal, pale, red, or blue?
Bleeding from nose or mouth?
Color of lips: normal, pale, or blue?
END OF EVENT
Approximate duration of the event?
How did it stop: with no intervention, picking up, positioning, rubbing or clapping back, mouth-to-mouth, chest compressions?
End abruptly or gradually?
Treatment provided by parent/caregiver (e.g. glucose-containing drink or food)?
911 called by caregiver?
STATE AFTER EVENT
Back to normal immediately/gradually/still not there?
Before back to normal, was quiet, dazed, fussy, irritable, crying?

APPENDIX: HISTORY AND CHILD ABUSE CONCERNS

HISTORY AND CHILD ABUSE CONCERNS
CONSIDERATIONS FOR POSSIBLE CHILD ABUSE
Multiple or changing versions of the history/circumstances
History/circumstances inconsistent with child's developmental stage
History of unexplained bruising
Incongruence between caregiver expectations and child's developmental stage, including assigning negative attributes to the child
RECENT HISTORY
Illness in preceding day(s)?
If yes, detail signs/symptoms (fussiness, decreased activity, fever, congestion, rhinorrhea, cough, vomiting, diarrhea, decreased intake or sleep
Injuries, falls, previous unexplained bruising?
PAST MEDICAL HISTORY
Prenatal and perinatal history
Gestational age
Newborn screen normal (for IEMs, congenital heart disease)?
Previous episodes/BRUE?
Reflux? If yes, obtain details, including management
Breathing problems? Noisy ever? Snoring?
Growth patterns normal?
Development normal? Assess a few major milestones across categories, any concerns about development or behavior?
Illnesses, injuries, emergencies?
Previous hospitalization, surgery?
Recent immunization?
Use of over-the-counter medications?
FAMILY HISTORY
Sudden unexplained death (including unexplained car accident or drowning) in first- or second-degree family members before age 35, and particularly as an infant?
Apparent life-threatening event in sibling?
Long QT syndrome?
Arrhythmia?
Inborn error of metabolism or genetic disease?
Developmental delay?
ENVIRONMENTAL HISTORY
Housing: general, water damage, or mold problems?
Exposure to tobacco smoke, toxic substances, drugs?
SOCIAL HISTORY
Family structure, individuals living in home?
Housing: general, mold?
Recent changes, stressors, or strife?
Exposure to smoke, toxic substances, drugs?
Recent exposure to infection, particularly upper respiratory illness, paroxysmal cough, pertussis?
Support system(s)/access to needed resources?
Current level of concern/anxiety; how family manages adverse situations?
Potential impact of event/admission on work/family?
Previous child protective services or law enforcement involvement (eg, domestic violence, animal abuse),for this child or others in the family
Exposure of child to adults with history of mental illness or substance abuse?

APPENDIX: PHYSICAL EXAMINATION

PHYSICAL EXAMINATION	
General	Appearance, Craniofacial abnormalities (mandible, maxilla, nasal)
	Age-appropriate responsiveness to environment
Growth	Length, weight, occipital-frontal circumference
	Vital signs
	Temperature, pulse, respiratory rate, blood pressure, oxygen saturation
Skin	Color, perfusion, evidence of injury (e.g., bruising or erythema)
Head	Shape, fontanelles, bruising or other injury
Eyes	General, extraocular movement, pupillary response
	Conjunctival hemorrhage
	Retinal examination, if indicated by other findings
Ears	Tympanic membranes
Nose and mouth	Congestion/coryza
	Blood in nares or oropharynx
	Evidence of trauma or obstruction
	Torn frenulum
Neck	Mobility
Chest	Auscultation, palpation for rib tenderness, crepitus, irregularities
Heart	Rhythm, rate, auscultation
Abdomen	Organomegaly, masses, distention
	Tenderness
Genitalia	Any abnormalities
Extremities	Muscle tone, injuries, limb deformities consistent with fracture
Neurologic	Alertness, responsiveness
	Response to sound and visual stimuli
	General tone
	Pupillary constriction in response to light
	Presence of symmetrical reflexes
	Symmetry of movement/tone/strength

CIRCULATION:
SHOCK OVERVIEW

INTRODUCTION (MICHAEL MOJICA M.D., 2/2020)
Shock is defined as inadequate blood flow and oxygen delivery to meet tissue metabolic demands. Shock should be recognized in tits early get as it becomes more refractory to treatment and may lead to cardiopulmonary arrest as it progresses.

Shock is classified as compensated or hypotensive. Normal physiologic compensatory mechanisms such as tachycardia, increased stroke volume and vasoconstriction act to maintain blood pressure. Children have an ability to increase their heart rate and increase systemic vascular resistance to maintain blood pressure and cardiac output, though less of an ability to increase stroke volume as compared to adults. Children can maintain blood pressure in the face of 25-45% loss of blood volume. The goal is to identify and manage compensated shock before hypotension ensues
Blood is also shifted from the periphery to essential central organs such as the heart and brain. This results in signs of inadequate distal perfusion (weak distal pulses, cold, mottled extremities and prolonged capillary refill). Signs of poor distal perfusion with a normal blood pressure is called compensated shock.

TYPES OF SHOCK: Shock can also be classified by etiology as: cardiogenic, hypovolemic, distributive and obstructive. Many disease states may combine elements of more than one class of shock. For example, in septic shock there is vasodilation (distributive shock) which results in a relative hypovolemia (hypovolemic shock).

CLINICAL FINDINGS
Signs and symptoms of shock include defects in central perfusion and in peripheral perfusion. Tachycardia may be the only early sign of shock and is the most sensitive indicator of volume status in the pediatric patient. Other parameters such as decreased urine output and metabolic acidosis may also be present. Certain findings may be helpful in differentiating one type of shock from another. Capillary refill can be affected by ambient temperature and should not be relied on as a sole indicator of shock.

ASSESSMENT OF CIRCULATORY STATUS	
Central Circulation	Mental Status
	Blood Pressure
	Central Pulses: Rate and Quality
	Signs of congestive heart failure: Rales, Hepatomegaly, JVD
Peripheral Circulation	Peripheral Pulses: Rate and Quality
	Skin Temperature
	Skin Color
	Capillary Refill

HEART RATE			
AGE	AWAKE	MEAN	SLEEPING
< 3 months	85-205	140	80-160
3 months – 2 years	100-190	130	75-160
2 -10 years	60-140	80	60-90
> 10 years	60-100	75	50-90

HYPOTENSION (< 5TH PERCENTILE FOR SYSTOLIC BLOOD PRESSURE		
CATEGORY	AGE	SYSTOLIC BP
Term neonates	< 1 month	< 60
Infants	1-12 months	< 70
Children	1-10 years	< 70 + (2 x age in years)
Adolescent	> 10 years	< 90

CLINICAL FINDINGS IN SHOCK		
	COMPENSATED SHOCK	HYPOTENSIVE SHOCK
Blood Pressure	Normal	Decreased
Distal perfusion	Cool, pale	Mottled
Peripheral pulses	Weak	Weak
Central pulses	Normal	Weak
Metabolic Acidosis	None or Mild	Moderate to Severe
Capillary Refill	> 2 Seconds	> 2 Seconds
Urine output	Normal	Decreased

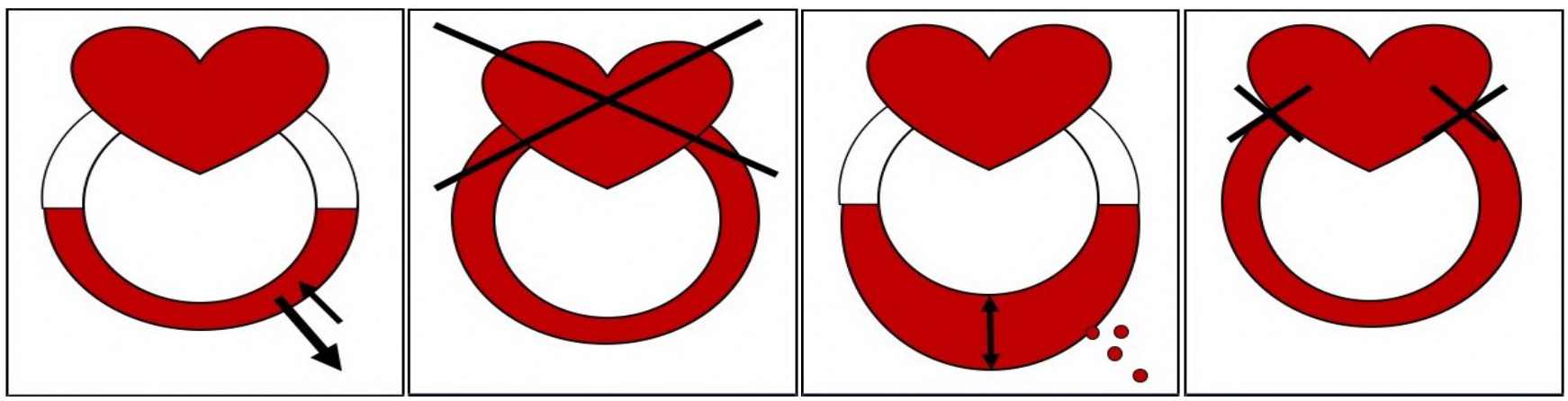
CLINICAL FINDINGS BY ETIOLOGY OF SHOCK	
Hypovolemic	Dry mucous membrane, poor skin turgor Poor distal perfusion (cold shock)
Cardiogenic	Signs of congestive heart failure: Rales, hepatomegaly, ascites
Distributive	Peripheral vasodilation (warm shock early, cold shock late) Early: Widened pulse pressure, Bounding pulses, flash capillary refill Late: Cool/Cold, pale/mottled extremities, weak pulse, prolonged cap refill
Obstructive	Tension Pneumothorax: Tracheal Deviation Cardiac Tamponade: Muffled heart sounds

MANAGEMENT

Management of shock will be governed by both the etiology and degree of impairment. In general, intravenous access is required. Intravenous fluids, infusion of vasoactive medications and treatment of underlying causes (e.g. antibiotics for septic shock) form the basis for the treatment of shock.

GENERAL MANAGEMENT OF SHOCK	
Oxygen	Monitoring, Frequent Reassessment
Support Ventilation	Ancillary Studies
Vascular Access	Pharmacologic Support
Fluid Resuscitation	Subspecialty Consultation

HYPOVOLEMIC	CARDIOGENIC	DISTRIBUTIVE	OBSTRUCTIVE
↑ Fluid out (GI, Renal, Skin, Resp) ↓ Fluid in, 3rd spacing	↓ Cardiac Output	Vasodilation 3rd Spacing of Fluid Relative Hypovolemia	Obstruction to Flow
Vomiting, Diarrhea (GI) Diabetes (DI, DM)(GU) Hemorrhage	Pump Failure (SV) HR Problem (Arrhythmias)	Sepsis (S) Anaphylaxis (A) Neurogenic (N)	Tension Pneumo (T) Cardiac tamponade (C) Ductal dependent (D)
Fill the Pipes Stop the Leak	Fix the Pump Fix the Rate	Fill the Pipes Squeeze the Pipes	Relieve the Obstruction
Fluid Resuscitation PRBC Transfusion	Fluid Resuscitation (Slow and Careful)	Fluid Resuscitation	
None	Inotrope Afterload Reduction	Vasoconstrictor	None
Massive Transfusion TXA Surgery	Antiarrhythmic Cardioversion Defibrillation	S: Antibiotics A: Epinephrine, N: Atropine, Pacing (for bradycardia)	T: Needle Thoracentesis C: Pericardiocentesis D: Prostaglandin E1



HYPOVOLEMIC SHOCK

Hypovolemic shock occurs when the circulating intravascular volume is reduced. Common causes include: hemorrhagic shock in the setting of trauma or clotting disorders, gastrointestinal fluid losses (vomiting and diarrhea), renal losses (diabetes mellitus, diabetes insipidus) and assorted disease states in which fluid shifts from the intravascular space to the extravascular space (“third spacing”). Fluid resuscitation is the mainstay of treatment. The extent of resuscitation is guided by the degree of shock. Initial management should include isotonic fluids such as normal saline or lactated Ringers (20 ml/kg). Multiple boluses may be administered paying careful attention to heart rate, blood pressure, urine output, and signs of peripheral perfusion and signs of congestive heart failure after each intervention. Vasoactive infusions should be avoided in hypovolemic shock since peripheral vasoconstriction may lead to end- organ ischemia. See: PEM Guide: Resuscitation: Hypovolemic Shock.

Hemorrhage results in a consumptive coagulopathy. High volumes or crystalloid or packed red blood cells can result in an additional dilutional coagulopathy. Massive transfusion protocols deliver 1:1:1 PRBC: Fresh Frozen Plasma: Platelets with or without Cryoprecipitate. Definitive treatment typically includes operative or interventional radiological intervention to control hemorrhage. See: PEM Guide: Trauma: Hemorrhagic Shock.

CARDIOGENIC SHOCK

Cardiogenic shock represents a state in which cardiac output fails secondary to poor myocardial contractility ("pump failure") or impaired rhythm generation (dysrhythmia). This may occur in the setting of congenital heart disease with congestive heart failure. It may also occur with acquired diseases of the heart that include cardiomyopathy, myocarditis, rheumatic fever and rarely ischemic heart disease in a child. See: PEM Guide: Cardiology: Cardiogenic Shock

In patients in cardiogenic shock due to poor contractility, agents with inotropic (increase stroke volume) and vasodilator (reduce afterload) properties are preferred. The "inodilators" include: Dobutamine and Milrinone. Fluid resuscitation can increase preload and increase contractility due to the Starling effect. A recommended fluid bolus in cardiogenic shock is 5-10 ml/kg over 10-20 minutes. Care should be taken to avoid over hydration. The patient's lung sounds (rales from pulmonary edema) and hepatomegaly should be monitored continuously. A point of care or cardiologist echocardiogram or central venous line may help to guide further management.

Arrhythmias may also lead to cardiogenic shock. Bradycardia results in a decreased cardiac output. Children have less contractile reserve than adults. In the face of bradycardia they cannot compensate adequately by increasing stroke volume. Tachyarrhythmias result in insufficient time for ventricular filling and a decrease in stroke volume as a result. See: PEM Guide: Cardiology: Arrhythmias: An Overview

DISTRIBUTIVE SHOCK

Distributive shock occurs when the peripheral vasculature is vasodilated leading to decreased systemic vascular resistance. Often there is pooling of the patient's blood volume in the venous system leading to both decreased after-load and pre-load. In addition, there is capillary leakage and redistribution of fluid from the intravascular to extravascular space. Distributive shock is often classified by etiology as: septic shock, anaphylactic shock and neurogenic shock.

1. SEPTIC SHOCK Septic shock is typically described as being distributive although the prodrome of septic shock often includes decreased food and fluid intake and therefore also has a hypovolemic component. Septic shock often starts with a "warm" phase in which the patient appears well perfused due to vasodilation (increased pulse pressure, bounding pulses, flash capillary refill). Subsequently, a "cold" phase develops in which peripheral perfusion is impaired. The presence of fever, meningismus, and/or petechiae or purpura may indicate the possibility of septic shock particularly in the patient with a compromised immune system. See: PEM Guide: Infections: Septic Shock

CLINICAL FINDINGS: DISTRIBUTIVE SHOCK		
	WARM SHOCK	COLD SHOCK
Capillary Refill	Flash refill	> 2 sec
Peripheral Pulses	Bounding	Diminished
Pulse Pressure	Increased	Normal
Skin	Pink, warm	Mottled, cool

The initial treatment of septic shock includes fluid resuscitation. If shock is unresponsive to fluid resuscitation then a vasoconstrictor should be considered. Broad-spectrum antibiotics should be administered.

2. ANAPHYLACTIC SHOCK: Anaphylactic shock is also distributive and is often caused by antigens such as foods or insect bites. Patients present with angioedema, stridor, wheezing, and may have cardiovascular collapse secondary to vasodilation or arrhythmias. The primary treatment includes the administration of intramuscular epinephrine and fluid resuscitation. Antihistamines (both H1 and H2 blockers), steroids, and inhaled beta-agonists are often given as well though evidence on their efficacy is lacking. An Epinephrine infusion is indicated in fluid refractory anaphylactic shock.
See: PEM Guide: Respiratory: Anaphylaxis.

3. NEUROGENIC SHOCK: A less common cause of distributive shock is neurogenic shock, where the sympathetic chain is injured during trauma resulting in a loss of sympathetic tone and unopposed parasympathetic output. Treatment includes fluid resuscitation and peripheral vasoconstrictors.
See: PEM Guide: Trauma: Neurogenic Shock.

OBSTRUCTIVE SHOCK
Obstructive shock may occur because of obstruction to systemic venous return in tension pneumothorax and pericardial tamponade or as result of ductal dependent cardiac lesions associated with obstruction to blood flow (severe aortic stenosis, coarctation of the aorta and interrupted aortic arch). A careful examination should be done to determine the etiology of obstruction. In the first few days of life, neonates may have a congenital heart lesion dependent on a patent ductus arteriosus.

Management is geared to supportive measures such as oxygenation, ventilatory support and fluid resuscitation. Specific therapy should be aimed at the underlying cause such as urgent needle decompression for tension pneumothorax, pericardiocentesis for cardiac tamponade and Prostaglandin E1 for ductal dependent cardiac lesions.

See:
PEM Guide: Cardiology: Ductal Dependent Cardiac Lesions
PEM Guide: Cardiology: Pericardiocentesis
PEM Guide: Trauma: Chest Trauma Primary Survey

VASOACTIVE INFUSIONS
A variety of vasoactive infusions may be indicated for patients in cardiogenic or distributive shock that is unresponsive to fluid therapy. Vasoactive infusions should not be used in isolated hypovolemic shock. As a group, these agents are often referred to a “pressors” or “vasopressors” due to their ability to increase blood pressure. The term catecholamines refers to those agents that act at adrenergic receptors. In general, vasoactive infusions should be targeted to the underlying pathophysiology. For example, in cardiogenic shock due to poor contractility, an agent with inotropic and/or afterload reducing properties (inodilators) may be considered. In distributive shock, an agent with vasoconstrictive properties should be considered. Ongoing therapy should be guided by monitoring of the patient’s fluid and cardiovascular parameters. Monitoring of central venous pressure and other parameters may be indicated in the patient that does not respond to therapy as expected. See PEM Guide: Resuscitation: Vasoactive Medication for Shock

APPENDIX: RAPID ULTRASOUND FOR SHOCK AND HYPOTENSION

Point of care ultrasound can be used to rapidly determine the etiology of shock or hypotension. The evaluation assesses the pump (heart), the tank (peritoneum, pleural space) and pipes (inferior vena cava, aorta, femoral/popliteal veins).

RUSH EXAM QUESTIONS			
	ASSESSMENT	QUESTION	ANSWER
Pump	Pericardium	Pericardial fluid?	Yes = Blood, effusion
	If fluid = Yes	RV Diastolic collapse?	Yes = Cardiac tamponade
	LV contractility	Normal, ↑, ↓?	↓ = Cardiogenic shock
	LV contractility	Normal, ↑, ↓?	↑ = Hypovolemic shock
	RV strain	Septum displaced R→L?	Yes = PE, tension PTX
Tank	IVC volume	Large,↓inspiratory collapse?	Yes = Cardiogenic (↑CVP)
	IVC volume	Small,↑inspiratory collapse?	Yes= Hypovolemia(↓CVP)
	Abdominal FAST	Peritoneal fluid?	Yes = Blood, ascites
	Pleural space	Pleural fluid?	Yes = Blood, effusion
	Lung parenchyma	Multiple B lines?	Yes = Pulmonary edema
	Pleura	Absent Lung Sliding?	Yes = Pneumothorax
Pipes	Abdominal aorta	Diameter > 3 cm?	Yes = AAA, dissection
	Thoracic aorta	Root diameter > 3.8 cm?	Yes = Dissection
	Thoracic aorta	> 5 cm?	Yes = Dissection
	Femoral vein	Non-compressible? clot?	Yes = DVT
	Popliteal vein	Non-compressible? clot?	Yes = DVT

RAPID ULTRASOUND FOR SHOCK AND HYPOTENSION (RUSH)				
	HYPOVOLEMIC	CARDIOGENIC	OBSTRUCTIVE	DISTRIBUTIVE
CARDIAC: Parasternal Long Axis and Apical 4 Chamber				
Pericardium	Normal	Normal	Fluid (effusion)	Normal
Left ventricle Contractility	Increased (Walls touching)	Decreased (< 30%)	Increased (Walls touching)	Increase (early) Decrease (late)
Chambers	Small/Normal	Increased	Dilated RV	
ABDOMEN				
Peritoneal fluid	Yes (blood) Yes (nephrotic)	Yes (ascites)		Yes (peritonitis)
IVC	Flat	Distended	Distended	Small/Normal
Aorta	> 3 cm (dissection)	Normal	Normal	Normal
Veins	No Clot	No Clot	Clot	No Clot
LUNGS				
Lung sliding	Yes	Yes	No (pneumothorax)	Yes
Parenchyma	Normal	Diffuse B lines	Normal	Normal
Pleura fluid	Yes (effusion)	Yes (effusion)	No	Yes (effusion)

APPENDIX: CIRCULATION ASSESSMENT AND MANAGEMENT

CIRCULATION			
EVALUATE	IDENTIFY	STATUS	INTERVENE
Blood Pressure	☐ Normotensive ☐ Hypotensive	☐ Normal	☐ Re-evaluate Airway Breathing, Circulation
Central Pulse Rate	☐ High ☐ Low ☐ Normal		
Central Pulse Quality	☐ Bounding ☐ Strong (normal) ☐ Weak ☐ Absent		
Mental Status (Responsive to:)	☐ A: Alert (normal) ☐ V: Verbal stimuli ☐ P: Painful stimuli ☐ U: Unresponsive	☐Compensated Shock	☐ IV/IO access ☐ Crystalloid bolus ☐ See next page. Shock management by type
Signs of Congestive Heart Failure	☐ None (normal) ☐ Auscultate rales ☐ Heart murmur ☐ Hepatomegaly ☐ JVD, edema		
Peripheral Pulse Rate	☐ High ☐ Normal ☐ Low		
Peripheral Pulse Quality	☐ Bounding ☐ Strong (normal) ☐ Weak ☐ Absent	☐Hypotensive Shock	☐ IV/IO access ☐ Crystalloid bolus ☐ See next page. Shock management by type
Skin Color	☐ Cyanotic ☐ Pallor ☐ Normal skin tone ☐ Mottled		
Skin Temperature	☐ Cold ☐ Cool ☐ Warm (normal)		
Capillary Refill	☐ Flash (immediate) ☐ 2 seconds (normal) ☐ > 2 seconds		

APPENDIX: SHOCK MANAGEMENT BY TYPE

SUMMARY: SHOCK MANAGEMENT		
TYPE	FLUID	PHARMACOLOGIC SUPPORT
Hypovolemic	20 ml/kg bolus 10 ml/kg of PRBC Repeat PRN	None
Distributive	20 ml/kg 10 ml/kg of PRBC (septic shock with hemoglobin < 7 mg/dl)	<u>Septic Shock</u> Hypotensive (warm): Norepinephrine Hypotensive (cold): Epinephrine Consider Hydrocortisone: 2mg/kg, maximum dose 100mg Antibiotics within 1 hour
		<u>Anaphylactic</u> Epinephrine IM (primary) Albuterol Antihistamines (H1, H2) Corticosteroids Epinephrine infusion
		<u>Neurogenic</u> Norepinephrine, Epinephrine
Cardiogenic	10 ml/kg bolus (over 30 min) Repeat PRN	Careful fluid resuscitation Reassess frequently for signs of pulmonary edema, hepatomegaly Inotrope, consider inodilator Treat Arrhythmias: Antiarrhythmics, cardio-version or defibrillation
Obstructive	20 ml/kg bolus (over 5-10 min) Repeat PRN	Pericardiocentesis Needle thoracentesis, thoracostomy Prostaglandin E1 (Ductal dependent cardiac lesion) Thrombolytic agents (Pulmonary embolus)

CRITICALLY ILL INFANT

INTRODUCTION (MICHAEL MOJICA, 12/2019)
The critically ill infant (< 1 year of age) is thankfully a rare event particularly outside of Children's Hospital Emergency Departments. However, the limited clinical exposure to these patients heightens anxiety and limits the development of a structured approach to their care. The goal of this PEM Guide is to develop a mental checklist for both supportive care and specific interventions than can make a difference in the first hour of care. This PEM Guide will focus on the disease processes that are readily identifiable in the ED and are associated with successful interventions.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis is extensive including both congenital and acquired diseases.
The younger the infant the higher the likelihood of congenital disease. The general categories of illness that can occur can be remembered with the mnemonic: THE-MISFITS.

DIFFERENTIAL DIAGNOSIS: THE CRITICALLY ILL INFANT			
T	Trauma	M	Metabolic
H	Heart Disease	I	Inborn Errors of Metabolism
E	Endocrine	S	Sepsis
		F	Formula
		I	Intestinal
		T	Toxins
		S	Seizures

TRAUMA: The approach to trauma in the infant must consider their unique anatomic and physiologic differences. These differences result in injury patterns not typical of adults. For example, the large heads of infants in combination with lax cervical spine ligaments increase their risk of high (C1, C2) cervical spine injury. The greater compliance of the pediatric chest wall and mediastinum decreases the risk of rib fractures but increase the risk of pulmonary contusions and tension pneumothorax. In the abdomen, the spleen and liver are in a more anterior and caudal position and are less protected by poorly developed abdominal musculature. As a consequence, these organs are more prone to injury. Trauma management includes fluid resuscitation with crystalloid or packed red blood cells, targeted imaging and potentially operative repair. Needle thoracentesis followed by chest tube placement is indicated for a tension pneumothorax. Pericardiocentesis is indicated for pericardial tamponade. (See: PEM Guide: Trauma: Trauma Primary Survey, PEM Guide: Cardiology: Pericardiocentesis).

Intentional trauma should be considered in every critically ill infant as a clear history of trauma may not be present. A focused assessment of external signs of trauma (bruising, frenulum tear, retinal hemorrhage) and signs of structural neurologic disease (fixed dilated pupil, seizures, bulging fontanel, posturing) may be the only clue to a traumatic brain injury. (See: PEM Guide: Child Protection: Child Abuse and Neglect, PEM Guide: Trauma: Head Trauma)

HEART DISEASE: Heart disease in the infant may include structural congenital heart disease (e.g. Tetralogy of Fallow) and acquired heart disease (arrhythmias, myocarditis). Signs and symptoms are often nonspecific such as poor feeding, vomiting or decreased activity level. Infant cardiac output is primarily driven by heart rate and not by stroke volume. They have little contractile reserve. As a consequence, bradycardia significantly decreases blood pressure. In contrast, the pediatric vascular system can maintain blood pressure through vasoconstriction then deteriorate precipitously. Compensated shock in the infant may rapidly deteriorate to hypotensive shock if the etiology of shock is not recognized and managed quickly.

Patients with ductal dependent cardiac lesions may present with an acute onset of deterioration when the ductus closes. The right-sided ductal dependent lesions typically present with cyanosis. The left sided ductal dependent lesions typically present with signs of congestive heart failure such as trouble feeding, breathing, sweating, irritability, rales, hepatomegaly, weak or absent pulses and signs of poor distal perfusion. If there is clinical suspicion for a ductal-dependent cardiac lesion, prostaglandin E1 (PGE1) should be used immediately to reopen a patent ductus arteriosus. The primary adverse events after prostaglandin are apnea and hypotension. The clinician should be prepared to intubate and support blood pressure after prostaglandin administration. (See: PEM Guide: Cardiology: Cyanotic Congenital Heart disease).

Arrhythmias are relative rare in the child. The most common pre-arrest rhythms are supraventricular tachycardia and sinus bradycardia. The most common arrest rhythm is asystole. Less than 10% of arrest rhythms are ventricular (tachycardia without a pulse or fibrillation). Arrhythmias are managed with support of airway and breathing, anti-arrhythmic medication and cardioversion or defibrillation.

ENDOCRINE: The primary endocrine problem in the neonate is adrenal insufficiency due to congenital adrenal hyperplasia (CAH). Acute salt loosing crises of CAH typically presents between 3-5 weeks of age with nonspecific symptoms of altered mental status and shock. Physical examination findings may include skin hyperpigmentation due to increased ACTH secretion and ambiguous genitalia (clitoromegaly in females) due to the increased production of androgens by alternative pathways. Characteristic electrolyte abnormalities include hyponatremia and hyperkalemia due to mineralocorticoid deficiency and metabolic acidosis and hypoglycemia due to glucocorticoid deficiency. The primary treatment of CAH is circulatory support and the administration of hydrocortisone. Patients on chronic steroids (e.g. nephrotic syndrome) should be administered stress steroids due to their adrenal glands inability to response to crises. (See: PEM Guide: Endocrine-Metabolic: Inborn Errors of Metabolism).

METABOLIC: The primary metabolic disease not included in the other categories of the mnemonic is hypoglycemia. Hypoglycemia is defined as a glucose less than 60 grams/dl in the infant (neonate < 40). The presentation of hypoglycemia is nonspecific including central nervous symptoms signs such as seizures and altered mental status and signs of adrenergic excess such as tachycardia and diaphoresis. The differential diagnosis of hypoglycemia in the infant is extensive including: sepsis, inborn errors of metabolism and multiple toxins (e.g. ethanol, beta blockers, salicylates and sulfonylureas). A bedside glucose should be obtained in all critically ill infants. Dextrose is administered as in a concentration of D10 in the neonate and young infant and D25 in the older infant and child. The rule of 50's can be used to deliver 0.5 gram/kg of dextrose (# ml/kg x dextrose concentration = 50, 5 ml/kg x D10, 2 ml/kg x D25).

INBORN ERRORS OF METABOLISM: Inborn errors of metabolism are a diverse set of conditions. Two major classes of inborn errors are the result of enzymatic deficiencies in catabolism and include the organic acidurias (carbohydrate catabolism) and the urea cycle defects (protein catabolism). The presentation of an inborn error is nonspecific and overlaps considerably with other childhood disease so a high index of suspicion is warranted. The family history of unexplained infant deaths or consanguinity can contribute to the diagnosis. The most common findings are neurologic ranging from irritability to coma, and gastrointestinal complaints. Management is primarily supportive followed by efforts to remove toxic metabolites and decrease production of toxic intermediaries by preventing catabolism and promoting anabolism. (See: PEM Guide: Endocrine-Metabolic: Inborn Errors of Metabolism)

The organic acidurias are primarily identified by a profound anion gap metabolic acidosis. Hypoglycemia, neutropenia, thrombocytopenia and a mild hyperammonemia may be seen. Management of organic acidurias include: fluid resuscitation**,** correction of acidosis with $NaHC0_3$, and dextrose to correct hypoglycemia and promote anabolism.

The urea cycle defects are identified by a marked hyperammonemia and elevated liver transaminases in the absence of a metabolic acidosis,. Management includes efforts to decrease ammonia production such as dextrose to correct hypoglycemia and promote anabolism and oral neomycin to prevent bacterial ammonia production. Efforts to increase ammonia excretion include: fluid resuscitation, dialysis or exchange transfusion and nitrogen scavengers (sodium benzoate, sodium phenylacetate).

SEPSIS: Infection is the leading cause of critical illness in this population. Infant sepsis risk factors include: Immunocompromised patients such as neonates, diseases such as HIV, Sickle Cell Disease, Nephrotic syndrome and those receiving immunosuppressants or steroids for diseases such as cancer, lupus and juvenile immune arthritis. Those with indwelling devices such as indwelling central catheters, ventriculoperitoneal shunts, and cochlear Implants represent another high-risk group.

Fever or hypothermia, altered mental status, respiratory distress and signs of inadequate perfusion are hallmarks of sepsis but are non-specific. Unless an iron clad alternative diagnosis is identified all critically infants should receive appropriate antimicrobials (antibiotics and antivirals). Typically, this includes a 3rd generation cephalosporin such as Ceftriaxone for gram negative coverage, Vancomycin for gram-positive coverage and Acyclovir for HSV coverage with. Other antibiotics may be warranted based on the suspected site of infection. For example, an antipseudomonal penicillin or cephalosporin should be given to a patient with neutropenia or an indwelling central catheter. For patients with suspected oral, dental, sinus, genitourinary or gastrointestinal tract infection, anaerobic coverage with Metronidazole should be added. (See: PEM Guide: Infections: Sepsis and Septic Shock)

FORMULA: Formula is included in the mnemonic for the possibility of incorrectly mixed infant formula. The addition of too much water results in hyponatremia and the addition of too little water results in hypernatremia. Sodium and water regulation is complex and there are many etiologies of both hyponatremia and hypernatremia. The reported sodium is as a concentration relative to water (meg/liter). Abnormalities of sodium can occur with hypovolemia, euvolemia and hypervolemia.

Hyponatremia is defined as a serum sodium of less than 130 meg/liter. At sodium levels <120 mEq/L or with rapid declines in sodium, central nervous system signs and symptoms predominate. These include: seizures, altered mental status, hyporeflexia, pseudobulbar palsy, hypothermia and have Cheyne-Stokes respiration. Management of hypovolemic hyponatremia states consists of careful fluid resuscitation to avoid rapid shifts in serum osmolality and osmotic demyelination. In patients with altered mental status or seizures, hyponatremia should be corrected quickly corrected with 3-5 ml/kg of hypertonic saline (3NS). (See: PEM Guide: Endocrine-Metabolic: Hyponatremia)

Hypernatremia is defined as a serum sodium of greater than 150 meg/liter. It is rare in pediatrics but can be associated with significant neurologic deficits if severe or occurs rapidly. Severe symptoms occur above 160 mEq/L. These include lethargy, coma, and seizures. In the most severe cases, brain shrinkage, results in vascular rupture with hemorrhage. Management consists of careful fluid resuscitation to avoid rapid shifts in serum osmolality and osmotic demyelination and replacement of the free water deficit.

INTESTINAL: The surgical abdomen in the neonate is a rare event, but is associated with a very high morbidity and mortality. Intestinal obstruction, ischemia or perforation can quickly lead to severe dehydration, electrolyte abnormalities, sepsis and irreversible intestinal damage. Intestinal catastrophes include: malrotation with midgut volvulus, necrotizing enterocolitis with perforation and Hirschsprung's enterocolitis (toxic megacolon). Findings include bilious or bloody vomiting, abdominal distention and bloody stools. Early involvement of pediatric surgery and radiology is essential. Appropriate imaging (abdominal XRAY, upper GI series, abdominal ultrasound) can confirm the diagnosis and need for operative intervention. (See: PEM Guide: Surgery: Malrotation).

TOXINS: A myriad of toxins should be considered in the critically ill infants. The risk of toxin ingestion increases as the infant gains the ability to explore their environment. Intentional exposure should also be considered. Toxidromes may aid in the diagnosis of the class of agent involved. Small doses can be fatal in infants. Medications typically associated with high mortality include: sulfonylureas, opioids, amphetamines and sodium channel blockers (chloroquine, tricyclic antidepressants, propranolol). Household agents typically included on this list include: ethanol (hypoglycemia), toxic alcohols, organophosphate and carbamate insecticides, hydrocarbons and camphor.

Infants are at high risk for methemoglobinemia. NADH methemoglobin reductase is not fully active until 4 months of age and fetal hemoglobin is more readily oxidized. Infants may develop methemoglobinemia from diarrhea, dehydration or sepsis. Premature infants, low birth weight infants and those with underlying hematologic or pulmonary disease are at increased risk. Methylene blue is indicated for patients with symptoms suggestive of oxygen deprivation which occur at methemoglobin levels > 20%. See: PEM Guide: Toxicology: Methemoglobinemia)

Management of most toxins is supportive. However, some toxins may benefits form efforts to eliminate it (activate charcoal, dialysis, alkalization) or from specific antidotes.
Early involvement of a toxicology consultant is essential (American Association of Poison Control Centers: 1-800-222-1222, NYC Poison Control Center: 1-212-POISONS (1-212-764-7667)). See: PEM Guide: Toxicology: Approach to the Poisoned Patient.

SEIZURES: Status epilepticus is defined as 5 minutes of continuous clinical or electrographic seizure activity or recurrent seizure activity without an interim return to baseline mental status. Neonates are at high risk of developing seizures related to CNS abnormalities (hydrocephalus) and metabolic disease (electrolytes, glucose, inborn errors of metabolism). A lumbar puncture and neuroimaging may be considered in the febrile child with signs of meningitis or localizing neurologic findings but should be deferred in the critically ill infant.

Benzodiazepines are first line agents in the critically ill infant in status epilepticus. The can be administered by the intravenous, intraosseous, intramuscular, intranasal and buccal mucosa routes. Second line agents include: Phenytoin, Fosphenytoin, Phenobarbital, Valproate and Levetiracetam. Agents recommended for refractory status epilepticus include infusions of Midazolam, Propofol and Pentobarbital. The underlying causes of seizures should be identified and treated appropriately. A bedside dextrose, oxygen saturation and blood pressure will help to identify some of the rapidly treatable causes of status epilepticus. (See: PEM Guide: Neurology: Status Epilepticus)

TREATABLE CAUSE OF SEIZURES	
CAUSE	TREATMENT
Alcohols: methanol, ethylene glycol	Fomepizole
Hypoxia	Oxygen, ventilation
Hypoglycemia	Dextrose 0.5-1.0 gm/kg
Hyponatremia	3% Normal Saline 10-12 ml/kg
Hypocalcemia	Calcium Chloride (10%): 20 mg/kg (0.2 ml/kg)
Hypertensive crisis	Labetalol, nitroprusside
Increased intracranial pressure	Mannitol, hypertonic saline
Iron	Deferoxamine
Isoniazid, Pyridoxine deficiency	Pyridoxine
Propranolol (beta blocker)	Glucagon
Pesticides (cholinergic)	Atropine, Pralidoxime
Salicylates	Sodium Bicarbonate, dialysis
Sulfonylurea hypoglycemics	Octreotide, dextrose
Tricyclic antidepressants, Cocaine	Sodium Bicarbonate

CLINICAL ASSESSMENT

The younger the infant, the more limited their repertoire of daily activities. An infant eats and drinks, pees and poops, is awake and happy, awake and not happy or sleeping. A rapid history should focus on the disease impact of these activities as well as atypical symptoms. Assessment of the infant is also hampered by anatomic and physiologic differences as well as developmental considerations.

Common complaints typically associated with minor illness may mask a serious underlying disease. For example, the tachypneic infant during bronchiolitis season may have a severe metabolic acidosis from an inborn error of metabolism or have myocarditis. It is important to remember that focal signs and symptoms may represent systemic disease as well as disease in another system. A good example of this is vomiting that may be a sign of gastrointestinal obstruction or increased intracranial pressure from hydrocephalus or intentional head trauma.

COMMON SYMPTOMS ASSOCIATED WITH LIFE THREATENING ILLNESS	
Tachypnea	Metabolic Acidosis, salicylate ingestion
Tachycardia	Myocarditis, internal hemorrhage
Wheezing	Pulmonary edema, airway foreign body
Vomiting	Midgut volvulus, hydrocephalus
Constipation	Hirschsprung’s with toxic megacolon
Crying	Myocardial infarction from anomalous left coronary artery
Coughing	Tracheo-esophageal fistula, diaphragmatic hernia
Sleeping too much	Congestive heart failure, inborn error, hydrocephalus

The pediatric assessment triangle can be used to quickly answer the question: Is this infant sick or not sick? It can identify the primary pathology in order to target effective interventions. It includes a rapid assessment of appearance, breathing and circulation. An abnormality in any phase warrants a more complete evaluation.

PEDIATRIC ASSESSMENT TRIANGLE	
Appearance	General indicator of level of consciousness including the degree of interactivity, muscle tone and verbal response or cry.
Breathing	Includes an evaluation of the patients positioning (e.g. tripod or sniffing), work of breathing and adventitial breath sounds
Circulation	Overall circulatory status: General color (pale, cyanotic, mottled)

MANAGEMENT

Advanced preparation includes having the appropriate equipment and personnel available and trained in pediatric resuscitation and procedures in place to escalate the level of care including transfer of the patient. Interventions include those intended as supportive care and disease specific interventions. It is important to establish a weight for medication dosing and an age for equipment selection. This can be facilitated with the use of a weight based resuscitation tape such as the Broselow tape. See PEM Guides: Resuscitation: Airway, Breathing and Circulation: Shock Overview and the appendices below.

APPENDIX: SUPPORTIVE CARE OVERVIEW

SUPPORTIVE CARE OVERVIEW: ASSESSMENT AND INTERVENTION	
AIRWAY STATUS	
Evaluate	Air flow (Listen and Feel): Normal flow, stridor, No flow Chest rise (Look): Yes, No
Identify	Clear, Maintainable (with position) Not maintainable (requires definitive airway)
Intervene	Positioning: Head tilt/chin lift, Jaw thrust (suspected cervical trauma) Foreign body obstructed airway maneuvers: Chest thrust and Back blows < 1 year of age Attempt Bag-Valve Mask ventilation: Rescue ventilation if chest rise Laryngeal mask airway placement Endotracheal intubation Needle cricothyrotomy Medications: e.g. Racemic epinephrine
BREATHING STATUS	
Evaluate	Respiratory Rate: Normal, high, low Oxygen Saturation: Normal, low Skin Color: Normal, pale, cyanotic, mottled Work of Breathing: Normal, retractions, grunting, nasal flaring, abdominal breathing Breath Sounds (Aeration): Normal flow, decreased flow, no flow Breath Sounds (Adventitial): Wheezing, rales, rhonchi, none Trachea Position: Midline, deviated to side contralateral to tension pneumothorax
Identify	Normal Respiratory Distress Respiratory Failure
Etiology	Upper airway obstruction: Croup, bacterial tracheitis, anaphylaxis, smoke inhalation Lower airway obstruction: Bronchiolitis, asthma Parenchymal disease: Pneumonia, pulmonary edema Disordered control of breathing: Increased ICP, over sedation, opiates
Intervene	Distress: Oxygenation, treat underlying cause e.g. Albuterol Failure: Oxygenation and Ventilation: BVM, LMA, Endotracheal Intubation
CIRCULATORY STATUS	
Evaluate	Central Perfusion: Mental status, blood pressure/pulse pressure, central pulses (rate and quality), signs of congestive heart failure (rales, hepatomegaly, peripheral edema) Distal Perfusion: Peripheral pulses (rate and quality), skin color, skin temperature, capillary refill
Identify	Normal Compensated shock Hypotensive shock (< 60 mmHg < 1month, < 70 mmHg if 1 month-1year) Cardiopulmonary arrest (pulseless): Asystole, PEA, V fibrillation, V tachycardia w/o pulse
Etiology	Hypovolemic: GI or Renal losses, third spacing, hemorrhage (internal, external) Cardiogenic: Structural heart lesion, heart failure, arrhythmia Distributive: Septic, anaphylactic, neurogenic Obstructive: Tension pneumothorax, pericardial tamponade, ductal dependent lesion
Intervene	All: Intravenous/Intraosseous access, fluid resuscitation, continuous monitoring
	Hypovolemic: Fluid resuscitation, blood transfusion
	Distributive: Septic: Antibiotics, antivirals, vasoactive infusions
	Distributive: Anaphylaxis: Epinephrine, antihistamines, steroids
	Distributive: Neurogenic: Vasoconstrictor, cardiac pacing for bradycardia
	Cardiogenic: Arrhythmia: Anti-arrhythmic medications, cardioversion/defibrillation, pacing
	Cardiogenic: Ductal dependent lesion: Prostaglandin E1
	Cardiogenic: CHF: Inotrope, Afterload reducer, diuretic
	Obstructive: Tension pneumothorax: Needle thoracentesis, chest tube
	Obstructive: Pericardial tamponade: Pericardiocentesis

APPENDIX: CRITICALLY ILL INFANT INTERVENTION CHECKLIST

CRITICALLY ILL INFANT: INTERVENTION CHECKLIST		
A	Airway	Positioning: Head tilt/Chin list, Jaw thrust (suspected cervical trauma) Foreign body obstructed airway maneuvers Intubation: LMA, Endotracheal intubation, LMA Medications: e.g. Nebulized Epinephrine
B	Breathing	Oxygenation Ventilation: Invasive, non-invasive Medications to treat the underlying cause: e.g. Albuterol
C	Circulation	IV/IO access Fluid resuscitation Targeted vasoactive infusions
T	Trauma	Fluids resuscitation with crystalloid or PRBC (preferred) Targeted imaging e.g. Head CT Selective operative management Needle thoracentesis for tension pneumothorax Pericardiocentesis for pericardial tamponade ↑ ICP: Controlled hyperventilation, mannitol, hypertonic saline Trauma surgery consultation
H	Heart Disease	Antiarrhythmics: Adenosine, Amiodarone, Atropine, Epinephrine, Lidocaine, Procainamide Cardioversion/Defibrillation Targeted vasoactive infusions Prostaglandin E1 (ductal dependent cardiac lesions) Cardiology consultation
E	Endocrine	Hydrocortisone: Congenital adrenal hyperplasia, chronic steroids Endocrinology consultation
M	Metabolic	Dextrose 0.5-1.0 gram/kg
I	Inborn Errors of Metabolism	Fluid resuscitation Dextrose (treat hypoglycemia, promote anabolism/prevent catabolism) Organic acidurias: $NaHCO_3$ Urea Cycle Defects: Nitrogen scavengers e.g. Na Benzoate
S	Sepsis	Fluid resuscitation Antimicrobials (Antibiotics and antivirals) Targeted vasoactive infusions Infectious disease and Critical Care consultation
F	Formula	Severe hyponatremia: Hypertonic Saline Hypernatremia: Normal saline, replace free water deficit
I	Intestinal	Targeted imaging: AXR, ultrasound, upper GI series Surgery consultation Operative intervention: Midgut volvulus, Hirschsprung's with toxic megacolon, Necrotizing enterocolitis with perforation
T	Toxins	Supportive care: Airway, Breathing, Circulation Elimination methods: e.g. dialysis Antidotes: Methylene Blue (Methemoglobinemia) Toxicology consultation
S	Seizures	Rx underlying cause 1st line AED: Benzodiazepines 2nd line AED: Phenytoin/Fosphenytoin, Keppra, Valproate 3rd line AED: Propofol or Midazolam infusion Hydrocephalus: Operative intervention (VP shunt) Neurology and/or Neurosurgery consultation

HEALTHY NEWBORN

INTRODUCTION (JOHN PARK, M.D., MAY 2019)
Many parents will present to the emergency department for routine newborn care issues. Children under one year of age and in particular those in the first few months of life constitute a disproportionate share of treat and release pediatric ED visits with common discharge diagnoses of: “feeding issues,” “irritability” and “normal physiology.” Emergency practitioners should be well-versed in the care of the normal newborn in order to differentiate these issues from life-threatening congenital and acquired illness. See: PEM Guide: Resuscitation: Critically Ill Infant, PEM Guide: Dermatology: Benign Newborn Rashes

FEEDING

In the immediate neonatal period, infants will require frequent feedings to prevent excessive weight loss and begin to gain weight. This is especially true in breast fed infants who will need to feed about every 2 hours. They may “cluster feed,” spending an extended time of up to several hours with near continual feeding followed by a slightly longer break before beginning again. This feeding pattern is particularly common in the first few weeks and in the early portion of the night when maternal hormones required for milk production are highest. This feeding behavior may cause concern for parents but is normal and over time will stretch to larger volume, less frequent feedings. Bottle fed infants generally tend to take larger volumes initially allowing for 3-4 hours between feeds.

The caloric content of standard infant formulas is 19 kilo-calories/ounce. This is intended to mirror the caloric content of breast milk although breast milk varies widely. Infants require approximately 100 kilocalories/kilogram/day to sustain weight gain. This is roughly 150 milliliters/kilogram/day or 5 ounces/ kilogram/day. Exact intake is harder to assess in breast fed babies than in those that are bottle fed.

ASSESSMENT OF FEEDING ADEQUACY	
Intake	150 ml (5 ounces/) kg/day, difficult to assess if breast feeding
Weight gain	After initial weight loss, gain 30 grams (1 ounce)/kg/day
Pre/Post weight	1 millimeter consumed → 1 gram of weight gain
Infant	Sleeps after feeding
Mother	Notices swallowing during feeding, sensation of breast emptying
Urine output	1 wet diaper/day in first few days then 6-8 wet diapers/day

WEIGHT GAIN

In the first days after birth neonates are expected to lose weight. Traditionally, weight loss of less than 10% is not considered worrisome. This proportion is slightly higher in breast fed infants. If greater than expected weight loss is noted, steps should be taken to ensure the infant returns to appropriate weight gain. This may include increased feeding frequency or volume or introducing bottle supplementation as a last resort in breast fed infants. A calculator and tracker are available to analyze infant weight loss

WEB LINK: WWW.NEWBORNWEIGHT.ORG

After initial weight loss, infants should gain approximately 30 grams (1 ounce) per day for the first several months making infancy the period of most rapid growth in childhood. Most infants should return to birth weight by approximately 2 weeks of life.

SPITTING UP/VOMITING

Many infants will present with spitting up. This will typically occur shortly after a feed and consists primarily of undigested formula. The two most common causes are over-feeding (particularly in bottle fed infants) and gastroesophageal reflux. Neither of these are typically dangerous but may result in a great deal of parental concern. A careful history with attention to feeding volumes and frequencies can be used to distinguishing between the two. Both may improve with smaller more frequent feedings. Reflux may be helped by keeping the infant upright after feeds and attentive burping. Acid suppressing medications are not routinely recommended reflux and should be reserved for those showing poor weight gain or extreme discomfort associated with spitting up.

Poor weight gain or weight loss in an infant presenting with vomiting should always be investigated for more serious medical concerns. Any blood, bile or large volumes of emesis should raise concerns. See: PEM Guide: Surgery: Pyloric Stenosis, PEM Guide: Surgery: Malrotation, PEM Guide Surgery: Hirschsprung's Disease. Jaundice and hyperbilirubinemia are frequently associated with excessive initial weight loss and poor feeding. See: PEM Guide: Hematology-Oncology: Hyperbilirubinemia

STOOLING

Stooling variations and problems are common causes for presentation to the emergency department. Infants may show a wide variety of stooling patterns. Many infants will stool with every feeding while others may go several days without stooling. Infant stools should be soft but not fully liquid. Infant stools may be a rainbow of colors caused by dietary and individual physiologic differences. The stool colors that should raise concern are: acholic or pale stools, black melanotic stools (after the first few day) and bloody stools.

Constipation in infants presents as hard ball-like stools that require a great deal of effort to produce. Less frequent stooling is considered normal as long as stools are soft and do not require excessive straining. A careful feeding and stooling history should be taken to ensure that a normal stooling pattern was previously established and there are no evident causes such as excessive or early introduction of powdered infant cereals or improper mixing of formula. If constipation is deemed to be idiopathic then remedies such as glycerin suppositories or feeding small quantities of fruit or prune juice may be attempted. Lactulose and polyethylene glycol may also be safely in infants although should be used with caution in the first few months of life. Other laxatives should be avoided unless under the direction of a specialist. Severe constipation may be associated with Hirschsprung's disease and other causes of intestinal obstruction.

BLOOD IN THE DIAPER: Infants are often brought to care with concerns of blood noted in the diaper. The first step in evaluating these patients is to determine if there is truly blood or just red coloration. If it is blood, the next step is to determine if bleeding is localized or systemic. Several common benign causes for red coloration in the diaper are detailed in the table below. Any concern for a non-benign cause of gastrointestinal or genitourinary bleeding should be evaluated accordingly.

DIFFERENTIAL DIAGNOSIS: BLOOD IN THE DIAPER	
Anal Fissure	May present with scant amounts of blood in the stool.
	Should be easily identified on exam as a crack in the ring of the rectum and is often noted after passage of a hard stool.
Antibiotics	Some cephalosporins, in particular Cefdinir, are known to cause red to maroon discoloration of the stool. The stools are guaiac negative
Urate Crystals	When dehydrated, before feeding is well established or due to acute illness, infants may precipitate urate crystals in their urine
	Cause a red-orange-brown discoloration in the diaper that may be confused with blood. Urinalysis is negative for heme and RBC's
Urethral Prolapse	A common cause of actual blood in the diaper. Occurs most commonly in African Americans females
	Can raise concern for sexual abuse with blood found in the diaper or redness or mass around the genitals.
	Appear as a beefy red "donut" at the site of the urethra and can be treated with topical estrogen cream and urology referral if interferes with voiding
Vaginal Bleeding	In the first few days after birth, a small amount of vaginal bleeding may occur. This is in response to withdrawal from maternal hormones similar to a withdrawal bleeding during a menstrual cycle.
	It should last a short time. Parents reassured about its benign nature

CARE OF THE UMBILICAL STUMP

Most newborns require very little care of the umbilical stump. The stump should fall off in the first few weeks of life without any intervention. Many parents will ask about putting alcohol or other astringents on the stump. This does not provide any benefit and can cause local irritation. Prior to separating, the umbilical stump may develop a wet appearance or have some scant serous discharge. If it is pulled off prematurely or traumatically some bleeding may result and if necessary can be treated with silver nitrate cautery. See PEM Guide: Gastrointestinal: Umbilical Disorders

Umbilical granulomas can result during initial separation of the stump and will appear as shiny or wet areas of mild erythema. These may also develop light oozing or bleeding if irritated and can be treated with silver nitrate cautery. Omphalitis is a life-threatening infection of the umbilical stump that typically presents with purulent drainage and surrounding erythema/cellulitis of the abdominal wall. Parents should be counseled that until the stump has fallen off and is well healed, they should not submerge the area in a bath as this can increase the risk for omphalitis. Umbilical hernias (see below) and urachal cysts may also be present.

CARE OF THE CIRCUMCISION SITE

Following circumcision there will be a small wound where the foreskin was removed and the glans penis that will be beefy red until a more keratinized squamous epithelium has time to develop. Typically, an ointment or cream is applied to the site at each diaper change to act as a barrier to urine and stool and to keep the raw tissue from sticking to the dry diaper and causing irritation. A small amount of eschar may be present, however any purulent discharge or spreading erythema would indicate infection although this is very rare. The site should heal and keratinize within a few weeks after the procedure.

HERNIAS

Hernias are a common cause of concern for parents of newborns. They are often noted during diaper changes or baths. A hernia is a defect in the muscular wall of the abdominal cavity that, if large enough, allows for bulging of viscera through the defect. The most common sites for hernias in newborns are inguinal and umbilical. Hernias are generally not a cause for emergent concern unless incarcerated (viscera have bulged through the defect and cannot be gently pushed back through) or strangulated (incarcerated and ischemic).

UMBILICAL: Umbilical hernias will be evident as a bulge around the umbilicus. Umbilical hernias may be followed expectantly with intervention if they become problematic or fail to close with time. Urachal cysts can be confused with umbilical hernias.

INGUINAL: Inguinal hernias will be evidence as a swelling or bulge in the groin or scrotum. Inguinal hernias without evidence of incarceration or strangulation warrant surgical referral on a non-emergent basis with plan for repair. Parents should be instructed on the signs and symptoms of incarceration. This included the inability to reduce hernia, inconsolable crying, vomiting, blood in the stool or abdominal distention. Hydroceles are similar in appearance to inguinal hernias and will present as a bulge in the scrotum although with less substance as it is fluid filled as opposed to containing viscera. Hydroceles may be differentiated from hernias based on exam, transillumination or ultrasound.

COLIC

Colic can be one of the most challenging things new parents have to overcome when caring for their child. Colic occurs in 10-26% of infants and is defined as an excess of crying or fussing with crying for more than 3 hours/day, for more than 3 days/week and for more than 3 weeks. It begins between 2-4 weeks of age and resolves by 3-4 months. Colic occurs equally across all socioeconomic groups and in both breast-fed and bottle-fed infants. It is typically worse in the late afternoon to early evening. Although many possible etiologies for colic have been proposed, there is no one definitive mechanism and the etiology is likely multifactorial. After determining that there is no specific cause for the child's discomfort, reassurance is the mainstay of treatment. Parents should be cautioned against shaking or harming infants and given permission to allow them to cry and step away from the child if frustrated. A Cochrane meta-analysis found no evidence for the use of simethicone, herbal agents, sugar, dicyclomine and cimetropium bromide for infants with colic. (Biagioli, Cochrane DSR 2016, PubMed ID: 27631535).

DIFFERENTIAL DIAGNOSIS: PERSISTENT CRYING/IRRITABILITY	
Cardiac	Anomalous Left Coronary Artery, CHF, SVT*
Environmental	Hair tourniquets: Digits, penis
GI/GU	Intussusception*, incarcerated hernia, testicular torsion*, anal fissure
Infectious	Meningitis/encephalitis*, Otitis media*, UTI*
logic	Increased ICP* (obstructive hydrocephalus)
Metabolic	↓ Na*, ↓ Ca, ↓ Glucose
Ophthalmologic	Corneal abrasions*: From infant's nails, fingers, eye foreign body
Trauma	Non-accidental trauma: Intracranial hemorrhage*, fractures*
*Discussed in detail in a separate PEM Guide	

HYPOVOLEMIC SHOCK

INTRODUCTION (MICHAEL MOJICA, M.D. 9/2017)
Hypovolemic shock occurs when the circulating intravascular volume has been reduced. Common causes of hypovolemic shock include loss of fluids externally, inadequate intake of fluids and redistribution of fluids from the intravascular to the extravascular space. Other forms of shock such as distributive shock and cardiogenic shock often have a hypovolemic shock component. Dehydration is used most commonly to refer to intravascular volume depletion. Infants tend to be at greater risk for volume depletion due to their higher metabolic rates, body surface area and body water content and from their inability to self-regulate fluid intake. (See: PEM Guide: Trauma: Hemorrhagic Shock)

ETIOLOGIES OF HYPOVOLEMIC SHOCK	
External losses	Gastrointestinal losses: Vomiting and diarrhea Renal losses: Diabetes insipidus, diabetic ketoacidosis, diuretics Insensible fluid losses: Fever, tachypnea, sweating External hemorrhage: Trauma, bleeding disorder
Inadequate intake	Inability to tolerate or take appropriate fluids by mouth
Redistribution (Third spacing)	Shift of fluid from the intravascular space to the interstitial space: Ileus, burns, nephrotic syndrome, congestive heart failure, renal failure, hepatic failure Internal hemorrhage: Trauma, bleeding disorder

CLINICAL MANIFESTATIONS

The diagnosis of dehydration is made on clinical grounds. A documented recent weight loss is the most reliable sign of dehydration. A clinical decision rule was derived in 186 infants between 1 month and 5 years of age with an assessment of fluid deficit based on weight gain following resolution of illness. 10 predictor variables were evaluated and no single variable was both highly sensitive and specific. Regression analysis generated 4-independent predictors of dehydration (Table below) with an area under the receiver operating characteristic curve of 0.9. There was no statistically significant difference in diagnostic accuracy comparing the 4-predictor model to a 10-predictor model (AUC 0.91). The presence of greater than or equal to two of the four predictors had a sensitivity of 79% and specificity of 87% for 5% dehydration. The presence of greater than or equal to three of the four predictors had a sensitivity of 82% and specificity of 85% for 10% dehydration (Gorelick, Pediatrics 1997, PubMed ID: 9113963).

PREDICTOR	ADJUSTED ODDS RATIO (95% CI)
Capillary Refill > 2 seconds	13.3 (3.4, 5.1)
Dry Mucous Membranes	4.3 (1.5, 12.6)
Absent Tears	4.3 (1.5, 12.4)
Abnormal General Appearance	3.0 (1.0, 8.8)

Some laboratory testing parameters have been suggested to aid in the diagnosis. These include urinary ketones, an elevated urine specific gravity, a decreased serum bicarbonate, and an elevated blood urea nitrogen though recent studies have suggestive that these may not be helpful.

In addition to diagnosing dehydration, the history and physical examination should focus on identifying the underlying cause. Dehydration can be classified according to the degree of dehydration or by the relative loss of water and sodium.

MANAGEMENT

Hypovolemic shock, if left untreated it may lead to cardiopulmonary failure and end organ damage due to hypoperfusion. The goal of therapy is the restoration of normal perfusion through replacement of fluid losses and the identification and treatment of contributing factors.

Aggressive fluid management is the mainstay of treatment of hypovolemic shock. Initial management should include isotonic fluids such as normal saline or lactated Ringers (20 ml/kg). Multiple boluses may be administered paying careful attention to heart rate, blood pressure, urine output, and signs of peripheral perfusion after each intervention.

In the setting of trauma, isotonic crystalloid is typically administered initially. In the patient with a hemorrhagic shock (> 25% blood loss) 10 ml/kg of PRBC's may be administered as well. Definitive treatment typically includes operative or interventional radiological intervention to control hemorrhage. Vasoactive infusions should be avoided in hypovolemic shock since peripheral vasoconstriction may lead to end organ ischemia (See PEM Guide: Trauma: Hemorrhagic Shock)

Oral Ondansetron has been demonstrated to reduce vomiting, improve oral dehydration and decrease IV rehydration rates (Freedman, NEJM 2006 PubMed ID: 16625009). This study used the following dosage scheme of 8-15kg: 2mg, 15-30 kg: 4mg and >30kg: 8mg. Alternatively, a dose of 0.15 mg/kg may be provided. The oral dissolving tablets are better tolerated. The primary concern with its use is the possibility of masking significant underlying illness such as intussusception and appendicitis.

Calculation of fluid requirements can be divided to those related to fluid losses (deficit), ongoing requirements (maintenance) and to ongoing losses.

MAINTENANCE FLUIDS		
	ml/kg/day	ml/kg/hour
First 10 kg	100	4
Second 10 kg	50	2
Each additional kg > 20 kg	20	1
A 25-kg child would require 1600 ml/day or 65 cc/hour as maintenance fluids (10kg x 100ml/kg/day) + (10kg x 50ml/kg/day) + (5kg x 20ml/kg/day) = 1600 ml/day)		

ORAL REHYDRATION THERAPY		
	Over 4 hours	Every 5 minutes
Mild dehydration	50 ml/kg	1 ml/kg
Moderate dehydration	100 ml/kg	2 ml/kg
Frequency and volume administered per feed would be dictated by tolerance. Vomiting losses are replaced ml for ml Diarrheal losses are replaced as 10 ml/kg per unformed stool.		

CLASSIFICATION BY DEGREE OF HYPOVOLEMIA

MILD HYPOVOLEMIA: Both the CDC and AAP recommend oral rehydration therapy (ORT) in dehydration due to acute gastroenteritis. Vomiting is not a contraindication to ORT but it should be avoided in patients with ileus or suspected bowel obstruction. A variety of commercially available glucose/electrolyte solutions are available. These typically contain a low concentration of glucose (e.g. D2.5) to facilitate GI water transport, as well as sodium, potassium, chloride and a base (e.g. $HC0_3$).

An ORT regimen consists of a rehydration phase in which the fluid deficit is replaced over a 4-hour period and a maintenance phase in which maintenance calories and fluids are delivered. A rehydration regimen for a mildly dehydrated child would consist of 50 ml/kg over 4 hours or 1 ml/kg Q5min. If ORT fails or is contraindicated then nasogastric or intravenous rehydration should be initiated.

MODERATE HYPOVOLEMIA: Moderate dehydration may also be treated with ORT (rehydration regimen 100 ml/kg over 4 hours) but may sometimes require intravenous fluids. An oral rehydration regimen for a moderately dehydrated child would consist of 100 ml/kg over 4 hours or 2 ml/kg Q5min. If ORT fails or is contraindicated then nasogastric or intravenous rehydration should be initiated. Typically, one half of the fluid deficit is replaced over the first 8 hours and the second half over the next 16 hours. Maintenance fluids and replacement of ongoing losses also occur at this time. Rapid intravenous rehydration therapy using boluses of 20 ml/kg has also been shown to be safe and effective in preventing hospital admission.

SEVERE HYPOVOLEMIA: Severe dehydration implies hypotension (decompensated shock) and requires immediate and aggressive fluid resuscitation. If intravenous access cannot be obtained then central or intraosseous access should be considered. Initial fluid boluses of 20cc/kg are given until restoration of normal perfusion.

CLASSIFICATION BY CHANGE IN TONICITY

ISOTONIC HYPOVOLEMIA (Na 130-150 meq/liter): Isotonic dehydration occurs when water and sodium are lost in equal amounts and is the most common type of dehydration encountered. Therapy for isotonic dehydration follows the recommendations for mild, moderate and severe dehydration listed above.

HYPOTONIC HYPOVOLEMIA (Na < 130 meq/liter**):** Hypotonic (hyponatremic) dehydration occurs when more sodium is lost then water. This may occur in patients whose deficits are replaced with free water, with adrenal insufficiency, and with gastrointestinal or renal losses. More fluid is lost from the intravascular space compared to isotonic dehydration. Clinical dehydration may be overestimated. (See PEM Guide: Endocrine-Metabolic: Hyponatremia).

The management of hypotonic dehydration consists of administration of intravenous isotonic saline. Water maintenance and deficit are calculated and replaced as for isotonic dehydration. Because sodium is lost in greater proportion than water an extra sodium deficit must be calculated:

Extra Na^+ (in mEq) = (135 - current Na^+) x 0.6 x prior weight (kg)

In patients with severe neurological symptoms, rapid elevation of sodium may be accomplished by the administration of hypertonic saline (e.g. 3% Normal Saline at 5-10 ml/kg).

HYPERTONIC HYPOVOLEMIA (Na > 150 meq/liter): Hypertonic (hyper-natremic) dehydration occurs when more water is lost then sodium. This may occur in patients who are taking improperly mixed infant formulas (not adding enough water). Fluid volume in the intravascular space is maintained compared to isotonic dehydration, therefore clinical dehydration may be underestimated.

The management of severe hypertonic dehydration consists of administration of intravenous isotonic saline. Care should be taken to slowly lower serum sodium (<10 – 15 mEq/l/24 hours) to protect against cerebral edema. Water maintenance is calculated as for isotonic dehydration, and fluid replacement should occur over a 48-hour period. Because water is lost in greater proportion than sodium the extra water deficit must be calculated:

Free water deficit = (Current Na+ - 145 mEq/ml) x 4ml/kg x prior weight (kg)

NEONATAL RESUSCITATION

INTRODUCTION (DANA SUOZZO, M.D., 11/2020)
Every 5 years the American Heart Association reviews the resuscitation literature and updates their recommendations. This PEM Guide reviews the updated guidelines for neonatal resuscitation. The term “newborn” and “newly born infants” are defined as from birth to the end of resuscitation in the delivery area. However, recommendation can be applied throughout the neonatal period (birth to 28 days). The phrase “preterm”, refers to newborns of less than 37 weeks gestational age. The phrase “late preterm” refers to newborns with a gestational age of 34-37 weeks.

This PEM Guide includes recommendations from 2015 that have not changed as well as those from the 2020 update (American Heart Association, Neonatal Resuscitation, Circulation 2020, PubMed ID: 26473001). The guidelines authors acknowledge the low quality of the evidence on which the recommendations are based due to the difficulty of performing randomized clinical trial in the delivery room.

The transition from a water-filled to an air-filled environment can be difficult. Approximately 10% of newborns require some assistance to begin breathing at birth. 2% require intubation and 0.2% require chest compression and/or Epinephrine.

PRIMARY RESUSCITATION GOALS
Establish adequate lung inflation and ventilation (priority)
Establish and maintain cardiovascular stability
Establish and maintain temperature stability
Promote mother-infant bonding and breast feeding

WEB LINK: NEONATAL RESUSCITATION ALGORITHM (AHA 2020)

INTERVENTION SEQUENCE AND TIMING		
1	Warm, dry, stimulate. Clear and position airway if necessary	0-30 seconds
2	Oxygenation and ventilation	30-60 seconds
3	Chest compressions	60-90 seconds
4	Administration of Epinephrine and/or volume expansion	> 90 seconds
5	Post-resuscitation care	> 90 seconds
Neonatal resuscitation retains the Airway-Breathing-Circulation (ABC) sequence compared to the Circulation, Airway, Breathing Sequence (CAB) in children and adults. Advanced Resuscitation is defined as: intubation, chest compressions or Epinephrine		

PRE-DELIVERY PLANNING
In is essential to plan appropriate for delivery so that a sufficient number of caregivers with the appropriate resuscitation skills and equipment is available immediately. A multicenter, case-control study identified 10 perinatal factors associated with the need advanced neonatal resuscitation (Berazategui, Archive Dis Child Fetal Neonatal Ed 2017, PubMed ID: 27269195). Advanced neonatal resuscitation was defined as the need for endotracheal intubation, chest compressions or medications. 0.37% (220/58,429) met this criteria. The area under the receiver operating characteristic curve (AROC) was 0.88, 95% CI 0.62 to 0.91.

PLANNING
At least one person who can perform the initial skills of resuscitation and positive pressure ventilation and who is solely responsible for the care of the newborn (or each newborn) should be present at each delivery.
A standardized risk assessment tool should be used to assess perinatal risk and assemble a qualified team (see below)
A standardized equipment checklist should be used (see below)
At an anticipated high-risk delivery, assemble a team and perform a pre-briefing to assign roles, interventions and responsibilities

RISK FACTOR CHECK LIST*	
ANTEPARTUM	INTRAPARTUM
Gestational age 34–37 weeks	Meconium stained amniotic fluid
Intrauterine growth restriction	Forceps or vacuum delivery
Gestational diabetes	Clinical chorioamnionitis
	Fetal bradycardia
	Abruption placentae
	General anesthesia
	Emergency caesarean section
*Excluded: < 34 weeks' gestation, major congenital malformations	

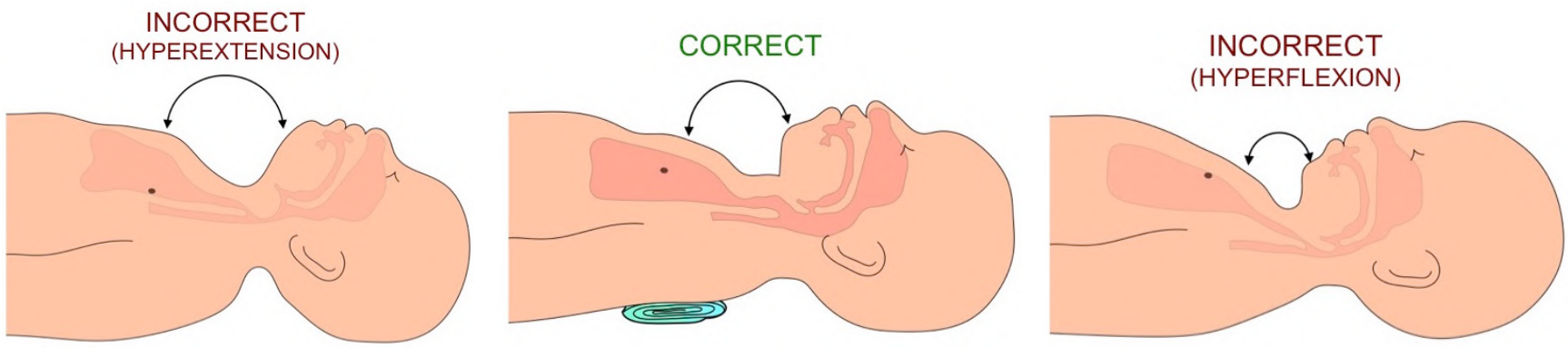
EQUIPMENT
Infant warmer, towels
Suction equipment: bulb syringe, mechanical suction catheters
Bag-valve-mask, O_2 source with flow meter (up to 10L/min)
Intubation equipment: Laryngoscope with Miller blades, ETT, capnograph, LMA
Umbilical vein catheter, intraosseous

ROUTINE CARE (2020)
Remain with mother
Warm, dry and maintain normal temperature
Position the airway in the sniffing position
Stimulate the infant to breath
Clear secretions if needed
Ongoing evaluation

1. INITIAL STEPS: 0–30 SECONDS

Approximately 60 seconds (“the Golden Minute”) are allotted for completing the initial steps, reevaluating, and beginning ventilation if required. This includes warming, drying, stimulating and clearing the airway if necessary. The decision to begin resuscitation is based on the assessment of both respirations (apnea, gasping, or labored/unlabored breathing) and heart rate (greater than or less than 100 bpm). In general, positive pressure ventilation is the most commonly required intervention and an improvement in heart rate is the best guide to a successful resuscitation.

CLEARING THE AIRWAY



RECOMMENDATIONS: CLEARING THE AIRWAY (2020)	
Clear amniotic fluid	Routine oral, nasal, or endotracheal suctioning is not recommended Can decrease respiratory resistance but also cause bradycardia
	Suction may be considered for neonates with airway obstruction or requiring positive pressure ventilation
	If inadequate respirations, tactile stimulation is reasonable
Meconium stained amniotic fluid	In non-vigorous infants with apnea of ineffective breathing effort, routine laryngoscopy with or without tracheal suctioning is not recommended
	In non-vigorous infants with airway obstruction during positive pressure ventilation intubation and tracheal suctioning may be beneficial

ASSESSMENT OF HEART RATE: Assessment of the newborn’s heart rate is used to evaluate the effectiveness of spontaneous respiratory effort and determine the need for subsequent interventions. An increase in the newborn’s heart rate is the most sensitive indicator of a successful response to resuscitation. Heart rate is initially assessed by auscultation of palpation. Clinical assessment of heart rate has been found to be both unreliable and inaccurate. Pulse oximetry tends to underestimate the heart rate in the first few minutes and is slow than EKG. EKG is both rapid and accurate.

RECOMMENDATIONS; ASSESSMENT OF HEART RATE (2020):
Auscultation is the preferred method for the initial assessment of heart rate
During resuscitation of term and preterm neonates, the use of 3-lead ECG for the rapid and accurate measurement of the newborn’s heart rate may be reasonable
An EKG should be used during chest compressions

MAINTAINING NORMAL TEMPERATURE: It is recommended that the temperature of newly born, non-asphyxiated neonates be maintained between 36.5°C and 37.5°C after birth through admission and stabilization. Hypothermia (< 36 C) should be avoided as it has been associated with increased morbidity and mortality in both term and preterm newborns. Temperature must be monitored to avoid hyperthermia (> 38 C) as well.

RECOMMENDATIONS: TEMPERATURE MANAGEMENT (2020)
Place newborns who do not require resuscitation in skin to skin contact with the mother to improve bonding, breast feeding, glucose and temperature control
Perform all resuscitation with temperature controlling interventions
Use radiant warmers, plastic bags, wraps with a cap, increased room temperature, warm humidified inhaled gases, alone or in combination, to prevent hypothermia in preterm newborns
In resource poor settings in may be reasonable to place newborn in food grade plastic bags up to the neck and then swaddle them

UMBILICAL CORD MANAGEMENT: In the past, it was common practice to clamp the umbilical cord immediately after birth to facilitate rapid transfer of the neonate to the pediatric provider for stabilization. There is evidence, primarily in neonates who do not require resuscitation, that delayed cord clamping is associated with less intraventricular hemorrhage, higher blood pressure and blood volume, less need for transfusion after birth, and less necrotizing enterocolitis. Delayed cord clamping conferred no benefit on mortality or severe intraventricular hemorrhage. The only negative consequence seems to be a slightly increased level of bilirubin, associated with more need for phototherapy.

RECOMMENDATIONS: UMBILICAL CORD MANAGEMENT (2020)
For preterm and term newborns who do not require resuscitation, may delay cord clamping > 30 seconds until after the newborn is placed with the mother, dried and assessed for breathing, tone and activity, both term and late preterm neonates
For preterm and term newborns requiring resuscitation, there is insufficient evidence to recommend early or delayed cord clamping
For preterm infants born less than 28 weeks, cord “milking” is not recommended due to a higher rate of intraventricular hemorrhage

2. OXYGENATION AND VENTILATION: 30–60 SECONDS

VENTILATION: The majority of newborns breath spontaneously within 30-60 seconds, sometimes after drying and tactile stimulation. For premature newborns without spontaneous respirations at birth, sustained positive-pressure inflation may reduce the need for intubation at 72 hours. Positive end expiratory pressure (PEEP) should be used for premature neonates as it helps to establish functional residual capacity.

Initial peak inflating pressures are unpredictable and should be individualized to achieve an increase in heart rate and chest expansion with each ventilation. Over-ventilation can result in gastric distention. Gastric distention is a vagal stimulus, can limit diaphragm expansion and increase the risk of aspiration.

RECOMMENDATIONS: POSITIVE PRESSURE VENTILATION: AHA 2020
Positive pressure ventilation is the primary intervention in neonatal resuscitation
Indicated in the newborn who remains apneic, with inadequate respiratory effort or bradycardic (HR < 100 beats/minute) after initial steps (drying, stimulation)
Ventilate at a rate of 40-60 breaths/minute (1 breath every 1 to 1.5 seconds) with an inspiratory time of 1 second
Sustained inflation is potentially harmful in preterm newborns
Use a peak inflation pressure of 20-25 cm H_20 (preterm) and 30 (term). Higher peaks may be required. Avoid pressures greater than required to improve heart rate
It is reasonable to apply positive end expiratory pressure (5 cm H_20)
Effective positive pressure ventilation results in initiation of crying, adequate respiratory effort and improvement in heart rate (HR > 100 beats/minute)
If a newborn has persistent labored breathing or persistent cyanosis, but HR >100, provide supplemental oxygen and consider continuous positive airway pressure (CPAP) as it can reduce the need for intubation with mechanical ventilation. Initiate continuous heart rate and pulse oximetry monitoring.

MR SOPA APPROACH TO DIFFICULT BAG-VALVE-MASK VENTILATION		
CORRECTIVE STEPS		ACTIONS
M	Mask adjustment	Reapply the mask. Consider a 2-handed technique
R	Reposition airway	Place head in neutral position or slightly extended
Re-attempt PPV, reassess for chest rise		
S	Suction mouth and nose	Use a bulb syringe of suction catheter
O	Open mouth	Open the mouth and lift the jaw forward (jaw thrust)
Re-attempt PPV, reassess for chest rise		
P	Pressure increase	pressure in 5-10 cm H_20 steps (max 40 cm H_20)
Re-attempt PPV, reassess for chest rise		
A	Alternative Airway	Endotracheal tube or laryngeal mask airway
Re-attempt PPV, reassess for chest rise and breath sounds		

ENDOTRACHEAL INTUBATION: Endotracheal intubation may be performed at various points during resuscitation. Intubation is required for extreme prematurity, surfactant administration, and suspected diaphragmatic hernia with respiratory distress.

RECOMMENDATIONS: ENDOTRACHEAL INTUBATION (2015)
When bag-valve mask ventilation is ineffective or prolonged
If chest compression are necessary, intubation may facilitate coordination of chest compression and ventilation and maximize the efficacy of ventilation
If Epinephrine is required, administration of Epinephrine directly into the endotracheal tube while venous access is established.
Bag-valve-mask ventilation can result in gastric distention further limiting lung expansion in a neonate with a diaphragmatic hernia. If an infant with diaphragmatic hernia requires positive pressure ventilation they should be intubated.
A laryngeal mask airway can be considered if bag-valve-mask ventilation or endotracheal intubation is not successful for neonates > 34 weeks

ENDOTRACHEAL TUBE & SUCTION CATHETER SIZES			
GESTATIONAL AGE (WKS)	WEIGHT (GM)	ETT SIZE	CATHETER SIZE
< 28	< 1,000	2.5	5F or 6F
28-34	1,000-2,000	3.0	6F or 8F
34-38	2,000-3,000	3.5	8F
> 38	> 3,000	3.5–4.0	8F or 10F

OXYGENATION: A meta-analysis of randomized trials that compared initiating resuscitation of preterm neonates (less than 35 weeks of gestation) with high oxygen (65% or greater) versus low oxygen (21-30%) showed no improvement in morbidity or survival to hospital discharge with the use of high oxygen. Initiating resuscitation of preterm neonates with > 65% FiO_2 is not recommended.

RECOMMENDATIONS: SUPPLEMENTAL OXYGEN: AHA 2020
Supplemental oxygen should be used judiciously and guided by pulse oximetry
In newborns requiring resuscitation, supplemental oxygen can be supplied to maintain oxygen saturation in the interquartile range of pre-ductal saturation (right arm)
Term and late preterm: Initiate with 21% FiO_2 (room air)
Preterm: Initiate with up to 30% FiO_2

PULSE OXIMETRY: The pulse oximeter should be attached to a pre-ductal location (right upper extremity), usually the wrist or the medial surface of the palm. Blood oxygen levels in uncompromised neonates do not reach extrauterine values until approximately 10 minutes following birth. Oxyhemoglobin saturation may remain 70–80% for several minutes after birth, resulting in an acrocyanotic appearance.

TARGETED PREDUCTAL SpO_2	
1 min	60-65%
2 min	65-70%
3 min	70-75%
4 min	75-80%
5 min	80-85%
10 min	85-95%

3. CHEST COMPRESSIONS: 60–90 SECONDS

If the heart rate remains < 100 but > 60 BPM, take ventilation corrective steps. Reposition airway into the “sniffing” position, clear the airway with suction, and visualize adequate chest rise. Continue positive pressure ventilation for 30 seconds, then check the heart rate. If the HR is < 60 BPM, support circulation with chest compressions while continuing positive pressure ventilation. Chest compressions are required in 0.1% of newborns.

OXYGEN DURING CARDIAC COMPRESSIONS: The available animal evidence demonstrated no obvious advantage of 100% oxygen over room air. However, by the time resuscitation of a newborn includes cardiac compressions, the steps of trying to improve the heart rate via effective ventilation with low concentrations of oxygen should have already been tried. It is reasonable to increase the oxygen concentration during compressions and then wean the oxygen as the heart rate recovers.

RECOMMENDATIONS: CHEST COMPRESSIONS: AHA 2020
Indicated if the heart rate < 60 BPM despite adequate ventilation with supplemental oxygen for 30 seconds
The two thumb encircling technique is preferred: Higher pressure, less fatigue
Chest compressions should be delivered on the lower 3rd of the sternum, with a depth of 1/3 the anterior-posterior diameter of the chest
The chest should be permitted to re-expand fully during relaxation. The rescuers thumbs should not leave the chest wall.
A ratio of compression (90/min) to ventilation (30/min) of 3:1 (120 events/minute) should be coordinated to avoid simultaneous delivery.
A higher compression to ventilation ratio of 15:2 if the arrest is cardiac in origin

4. EPINEPHRINE AND VOLUME EXPANSION: > 90 SECONDS

Medications are rarely indicated in neonatal resuscitation. Bradycardia is typically respiratory in origin and resolves with adequate oxygenation and/or ventilation.
Newborns who fail to respond to oxygen, ventilation and chest compression require vascular access to infuse Epinephrine and or volume expansion.

RECOMMENDATIONS: VASCULAR ACCESS (2020)
If peripheral intravenous access is not available, umbilical venous access is preferred
Intraosseous access should be considered when intravenous access is not feasible.
See PEM Guide: Vascular Access: Intraosseous Access and PEM Guide: Vascular Access: Umbilical Venous Catheterization.

RECOMMENDATIONS: EPINEPHRINE: AHA 2020
If despite previous 60 seconds of adequate chest compressions and positive pressure ventilation, the heart rate remains < 60 BPM, administer Epinephrine intravenously (preferred route based on limited data of increase time to ROSC and rate of ROSC).
If the heart rate remains < 60/min may repeat Epinephrine Q3-5 minutes
If Epinephrine is given endotracheally and the response is inadequate, May repeat Epinephrine when intravascular access if achieved regardless of the time interval

EPINEPHRINE 1:10,000 (0.1 MG/ML)		
ROUTE	DOSE	SAFETY CONSIDERATIONS
Intravenous (preferred route)	0.01-0.03 mg/kg	Higher IV doses (0.1 mg/kg) cause high BP, myocardial and neurologic dysfunction
Endotracheal (while access being obtained)	0.05-0.1 mg/kg	Safety & efficacy of endotracheal dosing has not been established

VOLUME EXPANSION: Volume expansion should be considered when blood loss is known or suspected (poor perfusion, weak pulse, pale skin). In premature neonates, rapid infusions of large volumes have been associated with intra-ventricular hemorrhage.

RECOMMENDATIONS: VOLUME EXPANSION: AHA 2020
Consider when hypovolemia due to blood loss is suspected based on history (blood loss from the placenta, umbilical cord or infant) or physical exam (pale skin, weak pulse, persistent bradycardia) despite adequate ventilation, chest compressions and Epinephrine
Isotonic crystalloid solution or blood, at 10-20 ml/kg over 5-10 minutes. May repeat if inadequate response. Un-crossmatched O negative PRBC preferred. Intravenous route recommended. Intraosseous route as an alternative

5. POST RESUSCITATION CARE

POST RESUSCITATION CARE (2020)	
Transfer	Newborn receiving prolonged positive pressure ventilation or advanced resuscitation (intubation, Epinephrine, chest compressions) should be transferred after resuscitation to an environment where close monitoring and expertise in the management of neonates is available.
Unintentional Hypothermia	Newborns < 36°C after resuscitation, may be rewarmed rapidly (0.5°C/hour) or slowly (<0.5°C/hour)
Therapeutic Hypothermia	Newborns > 36 weeks with moderate-severe hypoxic ischemic encephalopathy and should be offered therapeutic hypothermia using clearly defined protocols (impact < 36 weeks is unclear)
Hypoglycemia	Glucose should be monitored and hypoglycemia treated as soon as feasible after advanced resuscitation.

HYPOGLYCEMIA: Hypoglycemia is common after advanced resuscitation and is associated with poor outcomes. Blood glucose concentrations as low as 30 mg/dl are common in healthy neonates within 1-2 hours of birth and typically increase over a few hours. Almost all neonates with symptomatic hypoglycemia have levels lower than 20-25 mg/dl. An American Academy of Pediatrics practice guideline (AAP, 2011, PubMed ID: 21357346) recommends treatment for symptomatic neonates with a glucose level of ≤ 40 mg/dl. However, they acknowledge that it is not possible to recommend a specific protective target glucose range. Dextrose is administered as D10W at 0.2 grams/kg (2 ml/kg).

PROGNOSTICATION: For delivery room assessment at less the 25 weeks, there is insufficient evidence to support any prognostic score over estimated gestational age alone. Care may be individualized based on: the perceived accuracy of gestational age, presence of chorioamnionitis and the level of care available at the delivery facility. The decision to continue or initiate resuscitation for those less than 25 weeks will be influenced by regional guidelines.

An APGAR score of 0 after 10 minutes of resuscitation is a strong predictor of mortality and morbidity in both late preterm and term neonates. In a cohort of neonates greater than 35 weeks, an APGAR score of 0 at 10 minutes was associated with 50% death and 24% survival without moderate or major disability at 18-24 months. If the APGAR score is 0 after 10 minutes of resuscitation and the heart rate remains undetectable it may be reasonable to stop resuscitation. However, the decision to continue should be individualized. Variables to consider include: if the resuscitation is optimal, availability of NICU treatments (e.g. cooling), circumstances pre-delivery (e.g. if timing of insult is known) and family wishes. National guidelines recommend individualization of parent-informed decisions based on social, maternal, and fetal/neonatal factors.

RECOMMENDATIONS: NON-INITIATION/DISCONTINUATION OF RESUSCITATION
Non-initiation and discontinuation of life-sustaining treatment during or after resuscitation should be considered ethically equivalent.
In newly born babies receiving resuscitation, if there is no heart rate and all the steps of resuscitation have been performed, cessation of resuscitation efforts should be discussed with the team and the family. A reasonable time frame for this change in goals of care is around 20 minutes after birth.
If a birth is at the lower limit of viability or involves a condition likely to result in early death or severe morbidity, non-initiation or limitation of neonatal resuscitation is reasonable after expert consultation and parental involvement in decision-making.

APGAR SCORE				
		0 points	1 point	2 points
A	Appearance (skin color)	Cyanotic Pale all over	Peripheral Cyanosis Only	Pink
P	Pulse (heart rate)	0	< 100	100-140
G	Grimace (reflex irritability)	No Response To Stimulus	Grimace, Weak Cry when Stimulated	Cry when Stimulated
A	Activity (muscle tone)	Floppy	Some Flexion	Well Flexed Resists Extension
R	Respiration	Apnea	Slow, Irregular Breathing	Strong Cry
1 and 5 minutes (sometimes at 10 minutes as well)				

PALS UPDATE 2020: ADVANCED LIFE SUPPORT

INTRODUCTION (MICHAEL MOJICA M.D., 11/2020)
Approximately 20,000 pediatric cardiac arrests occur annually. Out-of-hospital cardiac arrests account for 1/3 of pediatric cardiac arrest deaths with a survival rate of 11.4%. The survival rate increases with increasing age (Infants: 4.9%, Children: 13.2%, Adolescents: 17.1%). In-hospital arrest occurs in the remaining 2/3 of pediatric cardiac arrests with a survival rate of 41.1%. The rate of neurologic intact survival is difficult to determine due to the variety of neurologic outcomes assessed. As the rate of survival of pediatric cardiac arrest has plateaued, new emphasis is placed on prevention (e.g. bicycle helmets, bystander CPR), post-arrest care and post hospital discharge and support.

Pediatric cardiac arrest is usually due to progressive respiratory failure or shock. Early identification and intervention of these states is essential for preventing cardiopulmonary arrest. Pediatric cardiac arrest is not usually of a primary cardiac cause. Even when pediatric cardiac arrest is due to a cardiac cause, it is due to a variety of etiologies (congenital heart disease, myocarditis/cardiomyopathy) and not typically ischemic heart disease as in adults.

Every 5 years the American Heart Association reviews the resuscitation literature and updates their recommendations (AHA: Circulation 2020, PubMed ID: 33081526). This PEM Guide reviews the updated guidelines for advanced life support for infant and child resuscitation. This PEM Guide includes the recommendations for 2015 that are unchanged as well as those that are new in the 2020 update. (See also PEM Guide: Resuscitation: PALS Update 2020: Basic Life Support, PEM Guide: Resuscitation: PALS Update 2020: Post-resuscitation Care.

AGE DEFINITIONS		
Infant	< 1 year	1. Female: Breast development Males: Axillary hair 2. Apply adult BLS guidelines
Child	1 year – Puberty[1]	
Adolescent[2]	> Puberty[1]- 18 years	

MAJOR CHANGES: PEDIATRIC ADVANCED LIFE SUPPORT (2020)
Endotracheal Intubation: Cuffed tubes preferred: Attend to size, position, inflation
Cricoid Pressure: Not routinely recommended
Epinephrine: Within 5 minutes of chest compressions for non-shockable rhythms
Septic Shock: Fluid bolus of 10-20 ml/kg with frequent reassessment
Septic Shock: Epinephrine or Norepinephrine (Dopamine if neither available)
Septic Shock: Consider stress steroids for shock requiring vasoactive infusions
Hypoglycemia: Oral glucose slurry under tongue if awake unable/unwilling to swallow

AIRWAY AND BREATHING

Respiratory failure occurs when respiratory effort is insufficient to support oxygenation and/or acid/base status (CO_2 exchange). Respiratory distress and failure can be categorized as due to: upper airway obstruction, lower airway obstruction, lung parenchymal disease and disordered control of breathing. For infants and children with a pulse and inadequate respiratory effort provide rescue breathing at a rate of 20-30 breaths/minute (1 breath every 2-3 seconds).

Advanced airway interventions, such as supraglottic airway (SGA) placement or endotracheal intubation (ETI), may improve ventilation, reduce the risk of aspiration, and enable uninterrupted compression delivery. However, airway placement may interrupt the delivery of compressions or result in a malpositioned device. Advanced airway placement requires specialized equipment and skilled providers, and it may be difficult for professionals who do not routinely intubate children.

ENDOTRACHEAL TUBE SELECTION (2020): Cuffed tubes are preferred for patients with high airway resistance, poor lung compliance or a large glottic air leak. They are not associated with subglottic stenosis and less likely need to be changed. Care should be taken to attend to size, placement location and cuff inflation pressure.

CONTINUOUS END TIDAL CO_2 MONITORING (2020)
In patients with perfusing rhythm: Use for confirmation of ETT placement
In patients with perfusing rhythm: Use for out-of-hospital, intra or interhospital transfer
False positive: Right mainstem bronchus intubation False negative: Non-perfusing rhythms
Correlates with increased cardiac output
< 10-15 mm may indicate ineffective compressions (adults). Pediatric values unavailable
An abrupt rise is often seen prior to return of spontaneous circulation (ROSC)
Epinephrine CO_2 for 1-2 minutes due to pulmonary blood flow (vasoconstriction)

CRICOID PRESSURE (2020): No evidence that it prevents regurgitation or improves intubation success in pediatrics. The esophagus typically slips to the side with tracheal pressure. If used, discontinue if interfere with ventilation of speed or ease of intubation.

ATROPINE (2020)
BRADYCARDIA DURING INTUBATION MAY BE DUE TO:
Hypoxia and metabolic acidosis
Vagal response to laryngoscopy
Reflex response to positive pressure ventilation
Response to medications (e.g. Succinylcholine, Fentanyl)
PRE-INTUBATION ATROPINE
No evidence it prevents arrest or improves survival. Do not use routinely
Atropine 0.02 mg/kg (minimum dose of 0.1 mg of Atropine no longer recommended)
Atropine may be given if there is a high risk of bradycardia (e.g. Succinylcholine use)

OPIOID RELATED RESPIRATORY OR CARDIAC ARREST
Respiratory Arrest with a Pulse: Rescue breathing, Naloxone IM or IN
Cardiac Arrest: Standard resuscitation. No evidence for Naloxone benefit

WEB LINK: OPIOID RESUSCITATION ALGORITHM (AHA 2020)

CIRCULATION: SHOCK

FLUID RESUSCITATION (2015/2020): Both isotonic crystalloids (balanced and unbalanced) or colloids can be effective as the initial fluid choice for resuscitation. Emphasis should be place on iterative assessment of the patient's fluid responsiveness and signs of fluid overload. Patients who develop fluid overload as a result of large volumes of fluid or rapid fluid resuscitation are more likely to have worsening oxygenation and require mechanical ventilation (Sankar, Ped Crit Care Med 2017, PubMed ID: 28777139, Inwald (PERUKI), Arch Dis Child 2019, PubMed ID: 30087153).

SEPTIC SHOCK: The FEAST Trial (Maitland, NEJM 2011, PubMed ID: 21615299) demonstrated that intravenous fluid may be harmful in pediatric septic shock in resource poor settings. Restricting fluids resulted in improved survival at 2 days and 4 weeks. It is unclear which aspects of the setting or population accounted for the results (e.g. malaria, malnutrition). The 2015 recommendation as result of this trial is: when caring for children with severe febrile illness in setting with limited critical care resources (e.g. mechanical ventilation) administration of bolus intravenous fluids should be undertaken with extreme caution because it may be harmful. The 2020 recommendation is to administer a fluid bolus of 10-20 ml/kg with frequent reassessment for effectiveness and signs of fluid overload.

SEPTIC SHOCK (2020)
Administer 10-20 ml/kg bolus of fluid with frequent reassessment for fluid overload
Fluid Refractory: Either Epinephrine or Norepinephrine (Dopamine if neither available)
Fluid Refractory: Consider stress-dose corticosteroids

CARDIOGENIC SHOCK: Expert consultation is recommended. It is reasonable to consider an inotropic infusion of Epinephrine, Dopamine, Dobutamine, or Milrinone.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) (2015): ECMO may be indicated in post pediatric arrest due to a reversible underlying process that is refractory to conventional interventions. There is no overall benefit of ECMO and CPR when compared to CPR alone. ECMO may be considered for pediatric patients with cardiac diagnoses (e.g. myocarditis) and in-hospital pre-cardiac arrest or arrest in settings with existing extracorporeal membrane oxygenation (ECMO) protocols. Specifically, venoatrial ECMO is recommended to provide both pulmonary and cardiac support.

CIRCULATION: ARRHYMIAS

Arrhythmias should be considered in a child with a sudden collapse or known disease that increases the risk of dysrhythmias (cardiac disease, electrolyte disturbances, toxic ingestions). Shockable arrest rhythms (ventricular fibrillation (VF), pulseless ventricular tachycardia (pVT) have a higher rate of survival compared to non-shockable arrest rhythms (asystole, pulseless electrical activity). For shockable, arrest rhythms, a shorter time to defibrillation is associated with improved outcomes. For non-shockable arrest rhythms, a shorter time to Epinephrine is associated with improved outcomes.

A CPR cycle should begin with chest compressions. Chest compressions are given before and after a shock. Shocks should be coordinated to minimize interruptions in chest compression. Rhythm assessment and shock delivery should be initiated as soon as possible after chest compression and chest compression initiated as soon as possible after a shock

MEDICATIONS DURING CARDIAC ARREST

Vasoactive agents (e.g. Epinephrine) during cardiac arrest can improve return of spontaneous circulation by improving coronary and cerebral perfusion. Antiarrhythmics (Lidocaine, Amiodarone) reduce the risk of ventricular fibrillation and ventricular tachycardia after defibrillation and may improve defibrillation success.

CIRCULATION: ARRHYMIAS: CARDIAC ARREST

Pediatric arrest rhythms are divided into shockable rhythms (ventricular fibrillation and pulseless ventricular tachycardia) and non-shockable rhythms (asystole and pulseless electrical activity). In a pulseless patient, attach to the monitor immediately to identify the rhythm. The H's and T's can be used to identify potentially reversible causes of cardiac arrest.

DEFIBRILLATION
DEVICE
AED use is now recommended for all infants and children (previously only > 1 year)
A manual defibrillator is preferred for infants
If that is not available, then an AED with a pediatric attenuator should be used
If neither is available, then an AED without a pediatric attenuator should be used
INTERFACE
Paddles and self-adhering pads are equally effective
Use largest paddles or self-adhering pads that fit and maintain good separation
Self-adhering pads: Either anterior-lateral or anterior-posterior position
ENERGY LEVEL
Biphasic shock is at least as effective as monophasic and is less harmful
Initial 2 Joules/Kg then 4 J/Kg may ↑ to max 10 J/kg or adult dose Use an initial dose of 2-4 J/kg, consider 2 J/kg for ease of teaching (2015) Adult: biphasic (manufacturers suggested) or 120-200J, monophasic at 360J
SEQUENCE
No stacked shocks. Cycles of: Shock → CPR x 2 min → Shock → CPR x 2 min →
Give medications: Epinephrine, Amiodarone, Lidocaine during CPR phase of cycle

SYNCHRONIZED CARDIOVERSION	DEFIBRILLATION
Ventricular Tachycardia WITH a pulse	Ventricular Tachycardia WITHOUT a pulse
Supraventricular Tachycardia	Ventricular Fibrillation
Atrial Fibrillation	
Atrial Flutter	

MEDICATIONS DURING CARDIAC ARREST (SEE APPENDIX)
Intravenous/Intraosseous Epinephrine preferred over endotracheal route
Administer Epinephrine early: Within 5 minutes of chest compressions
Administer Epinephrine every 3-5 minutes until ROSC
Use either Lidocaine or Amiodarone for defibrillation refractory VF or pVT
Sodium bicarbonate is not recommended except for hyperkalemia and sodium channel blockade (e.g. cyclic antidepressant, cocaine)
Calcium is not recommended except for hypocalcemia, calcium channel blocker overdose, hyperkalemia and hypermagnesemia
Use body weight to calculate dosing, not exceeding adult doses
Epinephrine 1:10,000 is now referred to as 0.1 mg/ml Epinephrine 1:1,000 is now referred to as 1.0 mg/ml

PEDIATRIC CARDIAC ARREST ALGORITHM: ASYSTOLE, PEA
Basic Life Support: High quality CPR, O_2, attach monitor
Epinephrine within 5 minutes of CPR and then every 3-5 minutes until ROSC Intravenous/Intraosseous: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/ml Epi, Adult 1 mg Endotracheal: 0.1 mg/kg = 0.1 ml/kg of 1.0 mg/kg Epi, Adult 2.5 mg
Vasopressin is no longer recommended in adults (2015)
Consider and treat underlying causes (H's and T's)

PEDIATRIC CARDIAC ARREST ALGORITHM: VF, pVT	
Basic Life Support: High quality CPR, O_2, attach monitor and defibrillator	
Defibrillation: 2 Joules/kg → 4 J/kg → 4 J/kg (To maximum of 10 J/kg or adult dose) Use an initial dose of 2-4 J/kg, consider 2 J/kg for ease of teaching Adult: Biphasic (manufacturers suggested) or 120-200J, Monophasic at 360J)	
No stacked shocks: Single shock followed by compressions (start with compressions)	
Continue CPR: 2-minute cycles with ventilations, then pulse and rhythm assessment	
Medications: Give during chest compressions	
Epinephrine	Within 5 min of chest compressions, repeat Q3-5 minutes until ROSC IV/IO: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/kg Epinephrine, Adult 1.0mg ETT: 0.1 mg/kg = 0/1 ml/kg of 1.0 mg/ml Epinephrine, Adult 2.5 mg
Amiodarone OR Lidocaine is an acceptable antiarrhythmic agent for shock-refractory pediatric ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT)	
Lidocaine	1 mg/kg IV, repeat Q5-10min, If successful → 20-50 mcg/kg/min
Amiodarone	5 mg/kg IV/IO push. Repeat x 2 to total of 15 mg/kg Maximum single dose: Adult 1st dose = 300 mg, 2nd dose = 150 mg
Magnesium Sulfate	Indicated for Torsade de points (a type of polymorphic VT) 25-50 mg/kg, Maximum dose: 2 grams
See: PEM Guide: Cardiology: Ventricular Arrhythmias	

REVERSIBLE CAUSES (H'S AND T'S)	
Hypovolemia	Tension pneumothorax
Hypoxia	Tamponade, cardiac
Hydrogen ion (acidosis)	Toxins
Hypoglycemia	Thrombosis, pulmonary
Hypo/hyperkalemia	Thrombosis, cardiac
Hypothermia	Trauma

WEB LINK: PEDIATRIC CARDIAC ARREST ALGORITHM (AHA 2020)

WEB LINK: ADULT CARDIAC ARREST ALGORITHM (AHA 2020)

CIRCULATION: ARRHYTHMIAS: TACHYCARDIA WITH A PULSE

Evaluate the QRS duration. Narrow: ≤ 0.09 sec, Wide: > 0.09 sec. Narrow-complex tachycardias primarily include sinus tachycardia and supraventricular tachycardia. If sinus tachycardia is present, identify and intervene based on the underlying cause (shock, fever, pain etc.). Wide complex tachycardias with a pulse include ventricular tachycardia and supraventricular tachycardia with aberrant conduction.

NARROW COMPLEX TACHYCARDIA WITH A PULSE (QRS ≤ 0.09 SECONDS)		
	Sinus Tachycardia	Supraventricular Tachycardia
History	Non-specific onset	Abrupt rate change/onset
P Waves	Present/Normal	Absent/Abnormal
R-R (HR)	Variable	Not variable
Infant	< 220 beats/min	220 beats/min
Child	< 180 beats/min	180 beats/min

NARROW COMPLEX (QRS ≤ 0.9 SEC): SUPRAVENTRICULAR TACHYCARDIA	
ALL PATIENTS	
Maintain airway, ventilation PRN, IV/IO access, 12 lead ECG, monitor/defibrillator Assess for cardiopulmonary Compromise: Altered mental status, shock, hypotension?	
CARDIOPULMONARY COMPROMISE: NO	
Vagal Maneuvers	Infants: ice to face without occluding airway Child: Unilateral carotid massage or Valsalva
IV Access Adenosine	Deliver centrally via a 3-way stopcock followed by rapid flush 0.1 mg/kg (max 6 mg), repeat as needed 0.2 mg/kg (max 12 mg)
Expert consultation	Cardiology consult prior to additional medications (see below) if vagal maneuvers and Adenosine unsuccessful and remains stable
CARDIOPULMONARY COMPROMISE: YES	
IV Access Adenosine	Do not delay cardioversion if IV access not readily available Deliver centrally via a 3-way stopcock followed by rapid flush 0.1 mg/kg (max 6 mg), repeat as needed 0.2 mg/kg (max 12 mg)
Synchronized Cardioversion	0.5 Joules/Kg ® 1.0 J/Kg ® 2 J/Kg (Adult: 50-100 Joules) Sedate if needed as does not delay cardioversion
Expert consultation	Cardiology consult prior to additional medications (see below) if vagal maneuver, Adenosine and cardioversion are unsuccessful
ADDITIONAL MEDICATIONS: Expert consultation advised prior to use	
Consider Amiodarone OR Procainamide (not both, both prolong QRS, QTc)	
Amiodarone	Child: 5 mg/kg IV/IO over 30-60 min. Repeat x 2 to a total of 15 mg/kg Adult: 1st dose = 300 mg, 2nd dose = 150 mg)
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes, monitor QRS duration Adult: 20 mg/min infusion to max dose of 17 mg/kg
Verapamil	Child: 0.1-0.3 mg/kg > 2 years (Not in < 2 years. May cause myocardial depression, BP and arrest) Adult: 1st dose 5 mg, 2nd dose 10 mg)
See: PEM Guide: Cardiology: Supraventricular Tachycardia	

WIDE COMPLEX TACHYCARDIA (QRS > 0.09 SECONDS) WITH A PULSE	
ALL PATIENTS	
Maintain airway, ventilation PRN, IV/IO access, 12 lead ECG, monitor/defibrillator Assess for cardiovascular compromise: Altered mental status, shock, hypotension? a. Ventricular Tachycardia with a pulse (VT) b. Wide-complex Supraventricular Tachycardia (SVT with aberrant conduction)	
CARDIOVASCULAR COMPROMISE: YES	
Synchronized Cardioversion: 0.5-1.0 Joules/Kg ® 2 Joules /Kg (Adult 100 Joules)	
CARDIOVASCULAR COMPROMISE: NO	
Expert consultation prior to antiarrhythmic No pediatric evidence for specific antiarrhythmic in wide complex tachycardia Antiarrhythmics complications may occur in cardiomyopathy, WPW, prolonged QT Do not give both Amiodarone and Procainamide. Both increase QRS, QTc	
Adenosine	Consider adenosine if rhythm is regular and monomorphic. Adenosine: 0.1 mg/kg (max 6 mg) then 0.2 mg/kg (max 12 mg) Distinguish between wide complex SVT and Ventricular Tachycardia
Amiodarone	Child: 5 mg/kg IV/IO over 30-60 minutes. Repeat x 2 to total 15 mg/kg Adult: 1st dose = 300 mg, 2nd dose = 150 mg
Procainamide	Child: 15 mg/kg IV/IO over 20-60 minutes, monitor QRS width Adult: 20 mg/min infusion to max dose of 17 mg/kg
See: PEM Guide: Cardiology: Ventricular Arrhythmias	

WEB LINK: PEDIATRIC TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT TACHYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

CIRCULATION: ARRHYTHMIAS: PEDIATRIC BRADYCARDIA

Bradycardia is defined as a heart rate lower than the lower limit for age. It results from intrinsic dysfunction or injury or external effects to the conduction system. Infants and young children are particularly at risk from bradycardia as their cardiac output is driven to a greater degree by heart rate than contractility. As a result, they have little contractile reserve when compared to older children and adults. They present with nonspecific symptoms such a poor feeding or lethargy. In contrast, older children and adolescents may present with fatigue, syncope, dizziness or exercise intolerance.

BRADYCARDIA: DIFFERENTIAL DIAGNOSIS	
Inflammation: Viral, autoimmune	Medications
Myocarditis*, Pericarditis*	HTN: Clonidine*, Beta blockers*
Lyme*, acute rheumatic fever*	Ca^{++} channel blockers*
Bacterial endocarditis, syphilis	Rhythm: Amiodarone, Digital, Adenosine
Myocardial infarct/ischemia	Other: Cholinergic agents*
Collagen vascular disease	Increased vagal tone
SLE*, neonatal SLE*, dermatomyositis	Breath holding*, cough
Congenital heart disease	Esophageal/Oral stimulation: intubation*
ASD, AV Canal*, VSD, TGV*, PS*	Increased intracranial pressure*
Congenital conduction abnormality	Cardiac surgery: Atrial
Prolonged QT, WPW	Electrolytes: Hyperkalemia*
Respiratory failure*: Hypoxia, acidosis	Hypothermia*
*Discussed in detail in a separate PEM Guide	

BRADYCARDIA: RHYTHM CLASSIFICATION	
Sinus	Normal PR interval, heart rate below normal for age (P=QRS)
Sinus arrest	Irregular or no P waves, junctional or ventricular escape rhythm
First degree	Prolonger PR interval follow by QRS complex (P=QRS)
Second degree	All p waves do not conduct to ventricles (P>QRS)
	Mobitz I (Wenckeback): Progressive increase in the PR interval, last p wave not conducted (may be physiologic if asymptomatic) Typically associated with AV node dysfunction
	Mobitz II: Non-conducting P wave without PR interval prolongation or progressive lengthening of PR interval. Pathologic until proven otherwise. Risk of progressing to third degree block. Typically associated with dysfunction distal to the His bundle
Third degree	Atrial and ventricular rate are independent (AV dissociation). Junction/ventricular escape rhythm slower intrinsic rate (P>QRS)

PEDIATRIC BRADYCARDIA WITH A PULSE AND POOR PERFUSION
ALL PATIENTS
Assess for cardiopulmonary Compromise: Hypotension, altered mental status, shock?
CARDIOPULMONARY COMPROMISE: NO
Support ABC's, O_2, observe, 12-lead EKG, Identify and treat underlying causes
CARDIOPULMONARY COMPROMISE: YES
Maintain airway, O_2, ventilate PRN, cardiac monitor: rhythm, BP, O_2 saturation Identify and treat underlying causes
CHEST COMPRESSIONS: HR < 60, poor perfusion despite adequate O_2, ventilation Pulse check every 2 minutes. Move to cardiac arrest algorithm if becomes pulseless
EPINEPHRINE: Asphyxial, repeat Q3-5 minutes IV/IO: 0.01 mg/kg = 0.1 ml/kg of 0.1 mg/ml Epi, Adult 1.0 mg Endotracheal: 0.1 mg/kg = 0.1 ml/kg of 1.0 mg/kg Epi, Adult 2.5 mg
ATROPINE: Increased vagal tone or primary AV block. Repeat once. IV/IO: 0.02 mg/kg, ET: 0.04-0.6 mg/kg, Max dose 0.5 mg, Min dose 0.1 mg Minimum Atropine dose of 0.1 mg is still recommended for bradycardia
TRANS-THORACIC PACING: Indicated for complete heart block or sinus node dysfunction that is unresponsive to ventilation, oxygenation, chest compressions and medications. Not indicated for post arrest hypoxic/ischemic myocardial insult or respiratory failure.
See: PEM Guide: Cardiology: Cardiac Pacing for Bradycardia

WEB LINK: PEDIATRIC BRADYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

WEB LINK: ADULT BRADYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

TRAUMATIC CARDIAC ARREST
Evaluate and treat underlying causes such a hemorrhage, tension pneumothorax and cardiac tamponade
Consider resuscitative thoracotomy in arrest due to penetrating trauma with a short transport time (not indicated in traumatic arrest due to blunt trauma)

ASSESSMENT OF RESUSCITATION QUALITY (2015)
Use diastolic blood pressure, if invasive arterial blood pressure monitoring is in place
Use $ETCO_2$ monitoring to assess the quality of chest compressions. Specific values to guide therapy have not been established in children
Use a CPR feedback devices to optimize adequate chest compression rate and depth
Echocardiography may identify potentially treatable causes of the arrest. Should be weighed against the harm of interrupting chest compressions.

CIRCULATION: OTHER SITUATIONS

See guidelines for additional recommendations on the management of pediatric patients with:
1. Myocarditis and cardiomyopathy,
2. Single ventricle physiology,
3. Pulmonary hypertension

APPENDIX: PALS MEDICATIONS (2020)

PALS MEDICATIONS (2020)			
	DOSE	INDICATIONS	COMMENT
Adenosine	0.1 mg/kg IV/IO (max 6mg) Repeat PRN 0.2mg/kg IV/IO(max 12mg)	SVT, Wide complex tachycardia with pulse monomorphic	Monitor EKG Rapid IV Push with 3-way stopcock
Amiodarone	5 mg/kg IV/IO Repeat x 2 to total of 15 mg/kg Max 1st dose: 300 mg Max 2nd dose: 150 mg	VF, pVT IV/IO: Push	Monitor QRS Don't give with Procainamide
		VT, SVT IV/IO: Over 20-60 minutes	
Atropine	0.02 mg/kg IV/IO 0.04-0.06 mg/kg ET Repeat PRN x 1 Max 0.5 mg, Min 0.1 mg	Bradycardia related to heart block or increased vagal tone	May need higher doses with organophosphate poisoning
Calcium (10%) Chloride OR Calcium (10%) Gluconate	20 mg/kg IV/IO Ca^{++} Chloride: 0.2 ml/kg Ca^{++} Gluconate: 0.6 ml/kg Slow infusion	Hypocalcemia Hyperkalemia Hypermagnesemia Ca^{++} channel blocker overdose	Ca Chloride: Arrest +/- Central line:
			Ca Gluconate: Non-arrest +/ Peripheral
Epinephrine	0.01 mg/kg IV/IO 0.1 ml/kg of 0.1 mg/ml Max: 1 mg IV/IO	Asystole Bradycardia PEA V fibrillation Vtach without pulse	IV/IO preferred May repeat every 3-5 minutes Do not give with HCO_3 in same line
	0.1 mg/kg ET 0.1 ml/kg of 1 mg/ml Max: 2.5 mg ET		
Glucose	0.5-1.0 grams/kg IV/IO Newborn: D10 5-10 ml/kg Child: D25 2-4 ml/kg Adult: D50 1-2 ml/lg	Hypoglycemia	
Lidocaine	1 mg/kg IV 20-50 mcg/kg/min IV	VF, pVT	Repeat bolus Q5-10min
Magnesium Sulfate	20-50 mg/kg over 12-20 min IV/ IO. Max: 2 grams	Torsade de point Polymorphic VT	
Naloxone	< 20 kg: 0.1 mg/kg IV/IO > 20 kg: 2 mg IV/IO	Opiate overdose Clonidine toxicity	Incremental dosing if chronic user
Procainamide	Child: 15 mg/kg IV/IO Infuse over 20-60 minutes Adult: 20 mg/min infusion to max dose of 17 mg/kg	VT with pulse	Monitor QRS Don't give with Amiodarone
NaBicarbonate	1 meq/kg IV/IO slowly	Tricyclic overdose	
Verapamil	0.1-0.3 mg/kg Max 1st 5 mg, 2nd 10 mg	SVT	Not < 2yrs without Expert consultation

APPENDIX: CARDIOVERSION AND DEFIBRILATION

INTRODUCTION
Use of a defibrillator can be lifesaving. However, several steps are required to use it both effectively and safely.
It is important to be familiar with whichever brand of defibrillator is available at sites that you will be working.
Think of the use of the defibrillator as hitting the electrical reset switch (as opposed to the pharmacologic reset switch). Essentially it stops whatever abnormal rhythm is currently happening with the intent that a normal rhythm will restart
No stacked shocks. Shock ® CPR x 2 minutes ® Shock ® CPR x 2 minutes
Give medications during CPR (no pause): Epinephrine, Amiodarone, Lidocaine

PROCEDURE: DEFIBRILLATION/CARDIOVERSION	
Sedation	Consider sedation and analgesia in an awake, cardiovascularly stable patient
Modes	SYNCHRONIZED CARDIOVERSION: SVT, VT with pulse, atrial fibrillation, atrial flutter
	DEFIBRILLATION: VF, pVT
	MONITOR: Including use of the paddles for a “quick look”
	PACEMAKER
	AED: Some defibrillators may be used as an AED as well
Energy level: Defibrillation	Child: 2 → 4 → 8 Joules/kg Adult: Biphasic: manufacturer recommendation or 120-200 Joules, Monophasic 360 Joules Biphasic at least as effective as monophasic and less harmful
Energy level: Synchronized Cardioversion	Child: 0.5 → 1.0 → 2.0 Joules/kg Adult: SVT: 50-100 Joules, [?] PRN, VT with a pulse monomorphic: 100 Joules
Paddle/Pad Size	Pediatric paddles < 10 kg (must remove adults paddles first)
Interface material	“Electrode” gel, paste, pads. No ultrasound gel or alcohol pads
Paddle/Pad Location	The heart goes between the paddles/pads 1. Sternum and apex OR 2. Anterior and posterior
Safety	“I’m clear, you are clear, we are all clear” The airway person is usually last to leave.
Charge	If using paddles, it is safer to charge while paddles are on the patient’s chest to avoid discharging them by accident on the way to the patient. Use of pads avoids this concern.
Discharge	Discharge can be initiated from the defibrillator or the paddles. Discharge is immediate for defibrillation but may require a second to attain synchronization with cardioversion
Re-evaluate	Both the patient and the monitor

PALS UPDATE 2020: BASIC LIFE SUPPORT

INTRODUCTION (MICHAEL MOJICA M.D., 11/2020)

Approximately 20,000 pediatric cardiac arrests occur annually. Out-of-hospital cardiac arrests account for 1/3 of pediatric cardiac arrest deaths with a survival rate of 11.4%. The survival rate increases with increasing age (Infants: 4.9%, Children: 13.2%, Adolescents: 17.1%). In-hospital arrest occurs in the remaining 2/3 of pediatric cardiac arrests with a survival rate of 41.1%. The rate of neurologic intact survival is difficult to determine due to the variety of neurologic outcomes assessed. As the rate of survival of pediatric cardiac arrest has plateaued, new emphasis is placed on prevention (e.g. bicycle helmets, bystander CPR), post-arrest care and post hospital discharge and support.

Pediatric cardiac arrest is usually due to progressive respiratory failure or shock. Early identification and intervention of these states is essential for preventing cardiopulmonary arrest. Pediatric cardiac arrest is not usually of a primary cardiac cause. Even when pediatric cardiac arrest is due to a cardiac cause, it is due to a variety of etiologies (congenital heart disease, myocarditis/cardiomyopathy) and not typically ischemic heart disease as in adults.

Every 5 years the American Heart Association reviews the resuscitation literature and updates their recommendations (AHA: Circulation 2020, PubMed ID: 33081526). This PEM Guide reviews the updated guidelines for basic life support for infant and child resuscitation with an emphasis on those changes that apply to health care providers. This PEM Guide includes the recommendations for 2015 that are unchanged as well as those that are new in the 2020 update. (See also PEM Guide: Resuscitation: PALS Update 2020: Advanced Life Support, PEM Guide: Resuscitation: PALS Update 2020: Post-resuscitation Care.

AGE DEFINITIONS		
Infant	< 1 year	1. Female: Breast development Males: Axillary hair 2. Apply adult BLS guidelines
Child	1 year – Puberty[1]	
Adolescent[2]	> Puberty[1]- 18 years	

CPR SEQUENCE (CAB VERSUS ABC)	
The 2010/2015 sequence of CPR is reaffirmed in 2020. A CAB sequence (Circulation, Airway Breathing) supplants the traditional ABC sequence (Airway, Breathing, Circulation). The rational for this change includes:	
1	Evidence in adult patients with cardiac arrest due to ventricular fibrillation (most common cause) indicates that compressions are more important than ventilation.
2	Evidence in children with cardiac arrest indicates that compression only CPR is equivalent to standard CPR with both compressions and ventilation.
3	Evidence in children with an asphyxial (airway/respiratory) arrest (most common cause) indicates that outcomes are better with standard CPR than with compression only CPR. However, the optimal sequence of CPR has not been determined. Starting with compressions would only minimally delay the onset of ventilations by approximately 20 seconds.

HIGH QUALITY CPR: COMPONENTS (2015/2020)	
1	Ensure chest compressions of adequate rate
2	Ensure chest compressions of adequate depth
3	Allow full chest recoil between compressions
4	Minimize interruptions in chest compressions
5	Avoid excessive ventilation

HEALTHCARE PROVIDER CARDIOPULMONARY RESUSCITATION

Healthcare providers are more likely to work in teams performing tasks simultaneously. There is less significance of whether compressions or ventilations are initiated first. The CPR sequence may be tailored to the specific etiology of arrest. For example, a sudden, witnessed arrest can be considered cardiac. EMS is activated and AED obtained first. A drowning victim would be considered an asphyxial arrest and ventilations initiated simultaneously with compressions.

Two algorithms are provided for health care provider pediatric BLS. The single rescuer CPR algorithm acknowledges the prevalence of cell phone access eliminating the need to leave the patient to initiate emergency medical system access.

HEALTHCARE PROVIDER CPR SEQUENCE (2015/2020)
1. OBTAIN AED FOR SUDDEN, WITNESSED ARREST (CARDIAC LIKELY)
2. ASSESS NEED FOR CPR
Assess responsiveness: Are you OK?
Assess for chest rise, airflow: Airway?: Patient, partial or complete obstruction
Allow patients in respiratory distress to remain in a position of comfort
If breathing and no neck trauma turn onto side (recovery position)
If unresponsive AND not breathing (or only gasping) initiate CPR
3. PULSE CHECK < 10 SECONDS
Infant: brachial, Child: femoral or carotid, Adult: carotid
a. Pulse present and heart rate ≥ 60 beats/minute with adequate perfusion
Open airway with head tilt-chin lift (non-trauma), jaw thrust (trauma)
Begin rescue ventilations: 20-30 breaths/minute (1 every 2-3 seconds) (2020)
Reassess pulse every 2 minutes
b. Pulse present and heart rate < 60 beats/minute with inadequate perfusion (pallor, mottling, cyanosis despite oxygenation and ventilation)
Begin chest compression (see below), followed by ventilations (see below)
c. Pulse absent or unsure of pulse:
Begin chest compressions (see below), followed by ventilations (see below)

CHEST COMPRESSIONS (2015/2020)
ADEQUATE RATE: “PUSH FAST”
100-120 compressions/minute on a firm surface
Just below the intermammary line
Infants: 2 thumb encircling (preferred for 2 rescuers) or 2 finger technique (2020)
Infants: Heal of 1 hand if other techniques of inadequate compression depth (2020)
Child/Adult: Heal of 1 or 2 hands
ADEQUATE DEPTH: “PUSH HARD”
Infant: 1.5 inches (4 cm) or 1/3 AP diameter of chest
Child: 2 inches (5 cm) or 1/3 AP diameter of chest
Adult: 2 inches (5-6 cm) (Maximum depth of 6 cm after puberty)
ALLOW COMPLETE CHEST RECOIL
Improves cardiac venous return
MINIMIZE INTERRUPTIONS IN COMPRESSIONS
Monitor rescuer fatigue
Rotate rescuers every 2 minutes (5 cycles): Switch should be < 5 seconds

VENTILATION (2015/2020)
OPEN AIRWAY
No trauma: Head tilt chin lift
Trauma: Jaw thrust (if unsuccessful use 2 person jaw thrust or head tilt-chin lift)
INITIATE OXYGEN AT 100%
Titrate oxygen down to oxygen saturation ≥ 94%
BVM: SELF-INFLATING BAG WITH O_2 RESERVOIR
BVM not recommended for single rescuer CPR
Infant/Child: Volume > 450-500 ml, O_2 at 10-15 liters/min
Adolescent/Adult: Volume 1,000 ml, O_2 at 15 liters/min
RESCUE BREATHING
Infant/Child: 20-30 breaths/minute (1 breath every 2-3 seconds)
Adult: 10 breaths/minute (1 breath every 6 seconds)
AVOID EXCESSIVE VENTILATIONS
Initial 2 Breaths: Each breath over 1 second (slow duration limits peak pressure)
Deliver sufficient tidal volume to result in chest rise
↑ intrathoracic pressure → Impedes venous return to the heart
Gastric distention → ↓ diaphragm excursion, vagal stimulus, ↑ regurgitation/aspiration

VENTILATION (2015/2020): CONTINUED
CONSIDER TWO-PERSON BVM VENTILATION
if airway obstruction or poor lung compliance
CRICOID PRESSURE: NOT ROUTINELY RECOMMENDED
Consider only in unresponsive patients when an additional rescuer is present
Esophagus typically slides out from under the trachea
Avoid excessive pressure that may occlude the trachea
Discontinue if interferes with speed/ease of intubation or ventilation

COMPRESSIONS TO VENTILATION RATIO (2015/2020)
One Rescuer: 30:2
Two Rescuer: 15:2 (Infant/Child), 30:2 (Adult)
Advanced airway in place: No coordination of compressions with ventilations
Infant/Child: Ventilation: 20-30 breaths/min (1 breath every 2-3 seconds)
Adolescent/Adult: Ventilation: 10 breaths/min (1 breath every 6 seconds)
Repeat pulse check: Q2 minutes (definitive airway) or 5 cycles (no definitive airway)
Assess rhythm: Q2 minutes for < 10 sec

WEB LINK: PEDIATRIC BASIC LIFE SUPPORT ALGORITHM (AHA 2020)

WEB LINK: ADULT BASIC LIFE SUPPORT ALGORITHM (AHA 2020)

TRAUMA

TRAUMA PRINCIPLES: BASIC LIFE SUPPORT
Anticipate airway obstruction
Provide direct pressure to external bleeding
Minimize motion to cervical spine
Infants may require padding under shoulders for proper airway alignment
Cervical collar or rescuer manually restricts motion (immobilization, not traction)
Open airway with jaw thrust (If not possible use head tilt chin lift)
Transfer serious injuries to trauma center with pediatric expertise

FOREIGN BODY AIRWAY OBSTRUCTION

FOREIGN BODY OBSTRUCTED AIRWAY MANEUVERS (2020)
Sudden onset of respiratory distress with cough, gagging, stridor or wheezing
MILD AIRWAY OBSTRUCTION
Evaluate: Patient can cough and make airway sounds
Intervene: Allow victim to clear obstruction and monitor status
Evaluate: Observe for signs of severe airway obstruction
SEVERE AIRWAY OBSTRUCTION (CONSCIOUS)
Evaluate: Patient can’t cough or make airway sounds
Intervene: Infant: Repeated cycles of 5 back blows and 5 chest compressions
Intervene: Child/Adults: Subdiaphragmatic abdominal thrust (Heimlich maneuver)
Intervene: Continue until foreign body expelled or victim loses consciousness
SEVERE AIRWAY OBSTRUCTION (UNCONSCIOUS)
Evaluate: Unresponsive patient
Intervene: Begin chest compressions (no pulse check)
Intervene: After 30 compression: Finger sweep only if foreign body visualized
Intervene: Attempt ventilation with bag-valve-mask
Intervene: Activate EMS system after 2 minutes (5 cycles)
Intervene: Consider advanced airway techniques
Direct laryngoscopy. Remove foreign body with McGill forceps
Endotracheal intubation
Through a soft foreign body
Push foreign body into right main stem bronchus, ventilate left lung
Needle, percutaneous or surgical cricothyrotomy

PALS UPDATE 2020: POST-RESUSCITATION CARE

INTRODUCTION (MICHAEL MOJICA M.D., 11/2020)
Approximately 20,000 pediatric cardiac arrests occur annually. Out-of-hospital cardiac arrests account for 1/3 of pediatric cardiac arrest deaths with a survival rate of 11.4%. The survival rate increases with increasing age (Infants: 4.9%, Children: 13.2%, Adolescents: 17.1%). In-hospital arrest occurs in the remaining 2/3 of pediatric cardiac arrests with a survival rate of 41.1%. The rate of neurologic intact survival is difficult to determine due to the variety of neurologic outcomes assessed.

Pediatric cardiac arrest is usually due to progressive respiratory failure or shock. Early identification and intervention of these states is essential for preventing cardiopulmonary arrest. Pediatric cardiac arrest is not usually of a primary cardiac cause. Even when pediatric cardiac arrest is due to a cardiac cause, it is due to a variety of etiologies (congenital heart disease, myocarditis/cardiomyopathy) and not typically ischemic heart disease as in adults.

Every 5 years the American Heart Association reviews the resuscitation literature and updates their recommendations (AHA: Circulation 2020, PubMed ID: 33081526). This PEM Guide reviews the updated guidelines for post resuscitation care. As the rate of survival of pediatric cardiac arrest has plateaued, new emphasis is placed on prevention (e.g. bicycle helmets, bystander CPR), post-arrest care and post-hospital discharge and support. This PEM Guide includes the recommendations for 2015 that are unchanged as well as those that are new in the 2020 update. (See also PEM Guide: Resuscitation: PALS Update 2020: Basic Life Support, PEM Guide: Resuscitation: PALS Update 2020: Advanced Life Support).

AGE DEFINITIONS		
Infant	< 1 year	1. Female: Breast development Males: Axillary hair 2. Apply adult BLS guidelines
Child	1 year – Puberty[1]	
Adolescent[2]	> Puberty[1]- 18 years	

POST-RESUSCITATION PHYSIOLOGIC DEFECTS	
Brain	Impaired cerebrovascular autoregulation, cerebral edema, neurodegeneration due to ischemia/inflammation Most common cause of post arrest morbidity and mortality due to limited tolerance for ischemia, hyperemia or edema
Heart	Myocardial hypokinesis → ↓ Cardiac output → Hypotension, arrhythmias, cardiac arrest
Systemic	Ischemia/reperfusion → Systemic inflammation → Coagulopathy, impaired vasoregulation, adrenal suppression, ↑ Susceptibility to infection → Multiorgan failure
	Persistence of precipitation pathophysiology

POST-RESUSCITATION PHYSIOLOGIC GOALS
Diagnose and treat the cause of illness
Preserve neurologic status: Optimize cerebral perfusion
Present secondary organ injury due to hypoperfusion: Optimize cardiac output, maintain normal blood pressure
Avoid hyperthermia
Avoid hypoxia/hyperoxia
Avoid hypocarbia/hypercarbia
Maintain normoglycemia

POST RESUSCITATION: RECOMMENDATION SUMMARY (2020)	
Intra-arrest Prognosis	No single factor has adequate accuracy to recommend continuing or discontinuing CPR.
Post-arrest Prognosis	No single post–cardiac arrest clinical variable was identified to be sufficiently reliable to predict outcomes. Consider multiple factors in to predict outcomes in the post-ROSC setting.
Normothermia	Targeted temperature management: Fever should be avoided when caring for comatose children with ROSC after cardiac arrest. Therapeutic hypothermia should be considered.
Normal Blood Pressure	Fluids and vasoactive agents should be used to maintain systolic blood pressure > 5th percentile for age. Continuous blood pressure monitoring is recommended when available.
Normoxemia	Oxygen administration should be weaned to target an oxyhemoglobin saturation of 94-99% or to specific patient's underlying condition. Avoid hyperoxia and hypoxemia
Normocarbia	After ROSC, $PaCO_2$ should be targeted to a level appropriate to each patient's condition. Avoid severe hypercapnia or hypocapnia
See Appendix: Post Cardiac Arrest Care Checklist	

RESPIRATORY SYSTEM

POST-ARREST OXYGENATION (2020): Hyperoxia can contribute to oxidative stress. Animal data demonstrates a potential association with post resuscitation syndrome. Some adult studies data suggests an increase in mortality with hyperoxia. In a large observational study (Ferguson, Circulation 2012, PubMed ID: 22723307) of over 1,400 pediatric patients with OHCA and IHCA who survived to PICU admission, normoxemia (PaO_2 > 60 mm Hg and > 300 mg/kg) when compared to hyperoxia (PaO_2 > 300 mm Hg) was associated with improved survival to PICU discharge. Hypoxemia and should be avoided. Since an arterial oxygen saturation of 100% may correspond to a PaO_2 between 80-500 mmHg it may be reasonable to target an oxygen saturation of 94-99% or targeted to the patients underlying condition.

POST-ARREST VENTILATION (2020): Cerebrovascular autoregulation may be abnormal after return of spontaneous circulation (ROSC). Hypocapnia ($PaCO_2$ < 30 mm hg) may be associated with worse outcomes. After ROSC, $PaCO_2$ should be targeted to a level appropriate to each patient's condition. Exposure to severe hypercapnia or hypocapnia should be avoided.

AIRWAY/BREATHING
Adjust FiO_2 to oxygen saturation of 94-99% or to patients underlying condition
Maintain adequate oxygen delivery Reduces the risk of oxidative injury (hyperoxemia post ischemic reperfusion)
Positive pressure ventilation for significant respiratory compromise
Tachypnea
Respiratory distress with agitation or decreased responsiveness
Poor air exchange
Cyanosis or hypoxemia
If intubated verify tube location, patency, security and cuff inflation pressure
Correlate ABG's with capnographic end-tidal CO_2 measurements
Monitor for metabolic acidosis, lactate
Control pain with analgesics and anxiety with anxiolytics/sedatives
Consider neuromuscular blockade: Decreases O_2 consumption, shivering
May mask seizures, limit neurologic exam, consider continuous EEG monitoring

CARDIOVASCULAR SYSTEM

INTRAVENOUS FLUIDS AND VASOACTIVE INFUSIONS: Myocardial dysfunction and vascular instability are common post resuscitation. A systolic blood pressure of less than 5th percentile for age and longer periods of hypotension are associated with a poor prognosis. Continuous blood pressure monitoring is recommended when available.

There are no studies evaluating the safety and efficacy of specific vasoactive agents after ROSC. Traditionally Dopamine is considered as the first agent used though clinical studies are lacking and it is falling out of favor. Epinephrine or Norepinephrine may be preferable in patients with marked circulatory instability and decompensated shock. The agent should be selected based on physiologic need. For example, a patient with septic shock (vasodilation, relative hypovolemia) may need an agent that is a vasoconstrictor (vasopressor). Patients with myocardial depression may require an inotrope (contractility) and/or afterload reducer (vasodilation).

CIRCULATION
Monitor heart rate, blood pressure (continuously if possible), urine output
Monitor EKG, electrolytes, glucose, ABG/VBG with lactate
Administer fluids and vasoactive medications to improve myocardial function and organ perfusion
Tailor dosing to individual patient
Monitor for adverse events: ischemia, dysrhythmias

VASOACTIVE MEDICATION: CLASSIFICATION			
Class	Medication	Action	Shock Indication
Inodilators	Dobutamine	$Beta_1 > Beta_2$	Cardiogenic
	Milrinone	↑ cAMP	Cardiogenic
Inopressors	Epinephrine	Low: $Beta_1 > Alpha_1$ High: $Alpha_1 > Beta_1$	Cardiogenic (Low BP), Anaphylactic, Septic
	Norepinephrine	$Alpha_1 > Beta_1$	Septic, Neurogenic
	Dopamine	Dop → $Beta_1$ → $Alpha_1$	Post Resuscitation?
Vasopressors	Phenylephrine	$Alpha_1$	Neurogenic (HR)
	Vasopressin	V_I, V_2	Septic

VASOACTIVE MEDICATION: DOSING		
	Pediatric[1] (mcg/kg/min)	Adult[2] (mcg/kg/min)
Dobutamine	2-10	2-20[4]
Dopamine (Low: “Renal”)	2-5	2-5
Dopamine (Mod: ↑CO > ↑ SVR)	5-10	5-10
Dopamine (High: ↑ SVR > ↑CO)	10-20	10-20
Epinephrine (Low: ↑CO > ↑ SVR)	0.1-0.3	0.1-0.3
Epinephrine (High: ↑ SVR > ↑CO)	> 0.3	0.3-0.5
Milrinone	0.25-0.75[3]	0.125-0.75[3,4]
Norepinephrine	0.1-2.0	0.1-0.5
Phenylephrine	0.1-0.5[4]	0.5-6.0[4]

1. AHA: Pediatric Advanced Life Support Manual 2015 (unless otherwise specified)
2. AHA: Advanced Cardiac Life Support Manual 2015 (unless otherwise specified)
3. Consider a loading dose: 50 mcg/kg over 10-60 minutes
4. Lexicomp 2020

NEUROLOGIC SYSTEM

Seizures are common post arrest. Non-consultive seizures cannot be detected without ongoing EEG monitoring. Both convulsive and non-convulsive status epilepticus are associated with poor outcomes. However, there is insufficient evidence that prophylaxis or treatment of seizures improve outcomes.

CENTRAL NERVOUS SYSTEM (2020)
Continuous EEG monitoring in patients with persistent encephalopathy after arrest
Treat post-arrest clinical seizures aggressively. Identify potential electrolyte causes
Treat post-arrest non-convulsive status epilepticus in consultation with experts
Targeted Temperature Management; Therapeutic hypothermia (see table below)
Avoid routine hyperventilation. Brief hyperventilation may be used as a temporizing measure for impending cerebral herniation

TARGET TEMPERATURE MANAGEMENT (2020): Fever is associated with poor prognosis. Prior recommendations for therapeutic hypothermia were based primarily on adult and neonatal data. A large, randomized, multicenter trial (Moler, NEJM 2015, PubMed ID: 25913022) of therapeutic hypothermia for pediatric out-of-hospital cardiac arrest did not demonstrate a benefit in terms or survival or complications.

THERAPEUTIC HYPOTHERMIA RECOMMENDATIONS (2020)
Consider in children who remain comatose after out-of-hospital or in-hospital arrest
5 days of normothermia (36-37.5 C) OR 2 days of hypothermia (32-34 C) followed by 3 days of normothermia (36-37.5 C)
Ideal method and duration of cooling and rewarming are not known
Prevent shivering by sedation or neuromuscular blockade if needed
Avoid rewarming from 32-34°C faster than 0.5°C per two hours
Continuous temperature monitoring
Treat fever (> 38 C) aggressively with antipyretics and cooling devices

THERAPEUTIC HYPOTHERMIA COMPLICATIONS	
Infection	Thrombocytopenia
Decreased cardiac output	Hypophosphatemia
Arrhythmia	Hypovolemia from cold diuresis
Pancreatitis	Hypokalemia
Coagulopathy	Hypomagnesemia

PROGNOSTIC FACTORS

Early, ongoing and reliable assessment of neurologic outcomes after cardiac arrest is essential to guide therapeutic decisions and provide family support. However, no single factor or decision rule adequately predicts outcomes within 24-48 hours of ROSC. EEG in the first week of post care in conjunction with other factors may be useful.

PROGNOSTIC FACTORS
Patient characteristics
Cardiac arrest characteristics
Post-arrest neurological examination
Laboratory results: e.g. evidence of organ failure
Neurological imaging: CT/MRI
EEG

RECOVERY

Cardiac arrest survivors are at risk for both short-term and long-term adverse outcomes. These include physical, neurological, cognitive, emotional, and social morbidity. Those with favorable neurologic outcomes can have subtle neuropsychologic impairment that may not be apparent until later childhood. A 6th “recovery” link has been added to the chain of survival for both out-of-hospital and in-hospital pediatric cardiac arrest. Pediatric cardiac arrest survivors should be evaluated by rehabilitation services and follow up with pediatric neurology for at least the first year after arrest.

APPENDIX: POST-CARDIAC ARREST CARE CHECKLIST

COMPONENTS OF POST-CARDIAC CARE	
OXYGENATION AND VENTILATION	
Measure oxygenation and target normoxemia 94-99% or appropriate oxygen saturation specific the patient. Limit exposure to hypoxia and hyperoxia	☐
Measure and target $PaCO_2$ appropriate to the patient's underlying condition and limit exposure to severe hypercapnia and hypocapnia	☐
HEMODYNAMIC MONITORING	
Set specific hemodynamic goals during post cardiac arrest care. Review daily	☐
Monitor with cardiac telemetry	☐
Monitor arterial blood pressure	☐
Monitor serum lactate, urine output and central venous oxygen saturation to guide therapies. Monitor laboratory findings suggestive or organ failure	☐
Use parenteral fluid bolus with or without inotropes or vasopressors to maintain a systolic blood pressure greater than the 5th percentile for age and sex.	☐
TARGETED TEMPERATURE MANAGEMENT	
Measure and continuously monitor core temperature	☐
Prevent and treat fever immediately after arrest and during rewarming	☐
If patient is comatose maintain temperature 32-34C followed by 36-37.5C or only 36-37.5C	☐
Prevent shivering with sedative or neuromuscular blockade	☐
Monitor blood pressure and treat hypotension during rewarming	☐
NEUROMONITORING	
If patient has encephalopathy, monitor with continuous EEG if available	☐
Treat seizures	☐
Consider early brain imaging to diagnose treatable causes of cardiac arrest	☐
ELECTROLYTES AND GLUCOSE	
Maintain blood glucose and avoid hypoglycemia	☐
Maintain electrolytes within normal ranges to avoid possible life-threatening arrhythmias	☐
SEDATION	
Treat with sedatives and anxiolytics	☐
PROGNOSIS	
Always consider multiple modalities (clinical, laboratory, imaging) over any single predictive factor	☐
Remember that assessments may be modified by targeted temperature management or induced hypothermia	☐
Consider EEG in conjunction with other factors in the first 7 days after arrest	☐
Consider neuroimaging such as MRI during the first 7 days	☐

VASOACTIVE MEDICATIONS FOR SHOCK

INTRODUCTION (MICHAEL MOJICA, MD, 12/2022)
Vasoactive medications can be used increase blood pressure by increasing systemic vascular resistance (“pressors” or “vasopressors”) and/or by increasing cardiac output (inotropes, chronotropes). Vasoactive medications are indicated for patients in cardiogenic or distributive shock (septic, anaphylactic, neurogenic) that is unresponsive to fluid resuscitation. Vasoactive infusions are not indicated in isolated hypovolemic shock. However, hypovolemia may contribute to other causes of shock and patients may require fluid resuscitation in addition to vasoactive medications.

PHARMACOLOGY
The terminology used to describe vasoactive medications can be confusing. There is a distinction between endogenous and synthetic, selective and non-selective, direct and indirect acting (or both), adrenergic and non-adrenergic and catecholamine and non-catecholamine.

Endogenous, adrenergic medications are released from post synaptic, sympathetic neurons (Norepinephrine) and from the adrenal gland (Norepinephrine, Epinephrine). In contrast, Dobutamine is an example of a synthetic, adrenergic agent. Adrenergic agonists can also be classified as direct, indirect or both. Direct acting medications work at adrenergic receptors. Indirect acting medications cause increased activity of Epinephrine or Norepinephrine by increasing their release, decreasing degradation or decreasing reuptake.

It is most helpful to characterize vasoactive medications by the receptors that they act on in the heart and vasculature. Actions at receptors in other body systems may also be present (See Table below). The term adrenergic refers to receptors that respond to Epinephrine (Adrenaline), Norepinephrine (Noradrenalin) and Dopamine. Adrenergic receptor agonists are sympathomimetics. The primary adrenergic receptors in the vasculature are $alpha_1$ (vasoconstriction) and $beta_2$ (vasodilation). The primary adrenergic receptors in the heart are $beta_1$ (inotropy, chronotropy). Adrenergic medications can be further classified as selective (action at one receptor type) or non-selective (action at more than one receptor type). For example, phenylephrine is selective for the $alpha_1$ receptors in the vasculature while Epinephrine is non-selective with activity at both the $beta_1$ receptors in the heart and $alpha_1$ receptors in the vasculature.

The term catecholamine refers to medications with a catechol side chain. Examples of catecholamines include: Epinephrine, Norepinephrine and Dopamine. The side chain is rapidly degraded by enzymes leading to poor oral efficacy and a short director of action. In addition, the side chain’s hydroxyl groups make it polar, reducing CNS penetration. Non-catecholamines lack the catechol side chain. Examples of non-catecholamine, adrenergic agonists include: Ephedrine, Pseudoephedrine and Phenylpropanolamine. In contrast, they are tolerated orally, have a longer duration of action and better CNS penetration.

RECEPTOR ACTIVITY: CARDIOVASCULAR EFFECTS (RED)		
RECEPTOR	LOCATION	ACTION
$Alpha_1$	Vasculature	1°: Vasoconstriction
	Heart	↑ Duration of contractility (without ↑ HR)
	Eye	Pupil dilation (mydriasis)
	Liver	Glycogenolysis → ↑ Available energy
	Kidney	↓ Renin → ↓ Angiotensin
	Bladder	Sphincter contraction → Urinary retention
$Alpha_2$	Presynaptic	1°: ↓ cAMP → ↓ Norepinephrine release
	Pancreas	↑ Insulin → ↑ Available intracellular energy
$Beta_1$	Vasculature	Minimal vasoconstriction
	Heart	1°: Inotropy (↑SV), chronotropy (↑HR)→↑ CO
	Kidney	↑ Renin → ↑ Angiotensin
$Beta_2$	Vasculature	Vascular smooth muscle → Vasodilation
	Lungs	Bronchial smooth muscle → Bronchodilation
	GI Tract	GI smooth muscle → ↓ Motility
	Uterus	Uterine smooth muscle → ↓ Contractions
	Pancreas	↑ Insulin → ↑ Available intracellular energy
$Beta_3$	Adipose Tissues	Lipolysis → ↑ Available energy
	Bladder	Relaxation
Dopaminergic	Vasculature	Vasodilation: Splanchnic, renal, coronary
	Vasculature	Vasoconstriction: ↑ Norepinephrine
Vasopressin	V1: Vasculature	Vasoconstriction
	V2: Kidney	Increased free water resorption (ADH)
Angiotensin II	Vasculature	Vasoconstriction
	Kidney	Increased free water resorption
Subdivision of receptors (e.g. $alpha_{1a}$, $alpha_{1b}$) are not included for simplicity		

ADRENERGIC VASOACTIVE MEDICATIONS: CARDIOVASCULAR EFFECTS						
	$Alpha_1$	$Beta_1$	$Beta_2$	DOP	SVR	CO
Epinephrine: Low	1+	3+	1+	0	No▲, ↓	↑
Epinephrine: High	3+	2+	1+	0	↑	↑
Norepinephrine	3+	2+	0	0	↑	No▲,↑
Phenylephrine	3+	0	0	0	↑	No▲,↑
Dopamine: 0.5-2.0 mcg/kg/min	0	1+	0	2+	No▲	↑
Dopamine: 5-10 mcg/kg/min	1+	2+	0	2+	↑	↑
Dopamine: 10-20 mcg/kg/min	2+	2+	0	2+	↑↑	No▲
Dobutamine	1+	3+	2+	0	↓	↑

PHARMACOLOGY: ADRENERGIC MEDICATIONS

1. EPINEPHRINE: Epinephrine has potent $beta_1$ and moderate $beta_2$ and $alpha_1$ activity. Epinephrine's response is dose dependent. At low doses, the $beta_1$ activity predominates increasing cardiac output. $Alpha_1$ (vasoconstriction) and $beta_2$ (vasodilation) have offsetting effects on systemic vascular resistance at low doses. At high doses, $alpha_1$ activity (vasoconstriction) predominates increasing systemic vascular resistance. Splanchnic vasoconstriction is more common with Epinephrine than with Norepinephrine or Dopamine. See Appendix: Push Dose Epinephrine

Epinephrine is the first line agent for anaphylactic shock (it also stabilizes mast cells). In adults, it is a second line agent for septic shock after Norepinephrine. In pediatrics, it is the first line agent for hypotensive, cold septic shock. Low-dose Epinephrine has some alpha activity (↑ SVR) and it will tend to prevent hypotension in cardiogenic shock when compared to Dobutamine and Milrinone which are inodilators (↑ CO, ↓ SVR).

2. NOREPINEPHRINE: Norepinephrine has potent $alpha_1$ activity and modest $beta_1$ activity. Alpha induced vasoconstriction can cause a reflex bradycardia that can offset the tachycardia due to $beta_1$ activity. Norepinephrine does not increase heart rate to the same extent as Epinephrine and Dopamine.

Norepinephrine is indicated in normal/high cardiac output states with low systemic vascular resistance (distributive shock). Norepinephrine is the first line agent for adult septic shock. In pediatrics, it is the first line agent for hypotensive, warm, septic shock. It is recommended as the first line agent for neurogenic shock by some sources.

3. PHENYLEPHRINE: Phenylephrine is selective for $alpha_1$ receptors resulting in potent vasoconstriction. Vasoconstriction increases systemic vascular resistant and increases ventricular afterload with a decrease in cardiac output. It can also lead to reflex bradycardia. Phenylephrine is indicated in neurogenic shock without bradycardia.

4. DOPAMINE: The response to Dopamine is dose dependent. Doses less than 5 mcg/kg/min (AKA renal-dose) act at dopamine receptors to improve splanchnic blood flow. The clinical significance of this effect is unclear. At doses of 5-10 mcg/kg/min $beta_1$ activity predominates and at 10-20 mcg/kg/min $alpha_1$ activity predominates.

Dopamine is not a first line agent for any form of shock and is falling out of favor. For example, the pediatric advanced life support course recommends Dopamine in septic shock only if Epinephrine and Norepinephrine are not available. However, it is recommended for post resuscitation shock.

Dopamine is associated with a higher risk of tachydysrhythmias. In addition, it has both direct and indirect adrenergic effects. It indirectly increases the release of Epinephrine and Norepinephrine. This limits its efficacy in catecholamine depleted patients. Low dose Dopamine causes a diuresis. This can worsen hypovolemia and falsely indicate adequate urine output.

5. DOBUTAMINE: Dobutamine is synthetic catecholamine and an “inodilator”. Predominant activity is at the $beta_1$ receptor increasing stroke volume more than heart rate and increasing cardiac output. It has weak $beta_2$ and $alpha_1$ activity. $Beta_2$ activity results in vasodilation and decreased afterload, further improving stroke volume and cardiac output. The effect on blood pressure is variable. If the heart has already maximally responded by increasing stroke volume and heart, hypotension can occur due to vasodilation. However, If Dobutamine can increase stroke volume and heart rate, as well as reduce afterload, then it can increase blood pressure.

Dobutamine is primarily indicated in cardiogenic shock but should be used with caution, if at all, in hypotensive patients. Effects are similar to Milrinone but with a higher rate of tachycardia and dysrhythmias and a lower rate of hypotension.

PHARMACOLOGY: NON-ADRENERGIC MEDICATIONS

ANGIOTENSIN: Angiotensin is part of the Renin-Angiotensin-Aldosterone system and results in vasoconstriction. Renin is released from the juxtaglomerular cells of the kidney in response to decreased renal blood flow.

PHOSPHODIESTERASE (PDE) INHIBITORS: PDE inhibitors, such as Milrinone, are inodilators. The primary inotropic effect is due to an increase in intracellular cyclic AMP leading to an increase in intracellular calcium and increased contractility. In addition, lusitropy (ventricular relaxation) increases the time for ventricular filling and increases stroke volume. These effects are independent of adrenergic receptors making it an effective option for those on beta blockers. Vasodilation (secondary) is a result of inhibition of vascular phosphodiesterase. The effect on blood pressure is variable. If the heart has already maximally responded by increasing stroke volume and heart rate, hypotension can occur due to vasodilation. However, if it can increase stroke volume and heart rate, as well as reduce afterload, then it can increase blood pressure.

Milrinone is primarily indicated in cardiogenic shock but should be used with caution, if at all, in hypotensive patients. Effects are similar to Dobutamine with a lower rate of tachycardia and dysrhythmias but with a higher rate of hypotension.

VASOPRESSIN: Vasopressin acts at V1 (vasoconstriction) and V2 receptors (renal water retention). Venoconstriction may increase preload. Adverse effects associated with Vasopressin are hyponatremia, diabetes insipidus and ischemia of non-essential organs. It is primarily indicated in adult septic shock as a second line agent.

MANAGEMENT

Reversing hypotension is associated with decreased morbidity and mortality. In an study of over 30,000 adult, non-cardiac, operative patients, a mean arterial pressure of less than 65 mmHg was associated with a steep rise in the risk in acute kidney injury and myocardial injury (Walsh, Anesthesiology 2013, PubMed ID: 23835589).

FLUID RESUSCITATION: Adequate fluid resuscitation can limit the need for vasoactive medications. Hypovolemia may complicate cardiac and distributive shock. For example, in septic shock, vasodilation results in a relative hypovolemia (think bigger pipes, same amount of fluid) and an actual hypovolemia due to third spacing of fluids. In cardiogenic shock third spacing of fluids (e.g. ascites, pulmonary edema) can result in intravascular hypovolemia despite a normal total body water). Fluid resuscitation can increase preload and increase cardiac output. However, patients in cardiogenic shock should be monitored closely for fluid overload.

MEDICATION SELECTION: In general, vasoactive infusions should be targeted to the underlying pathophysiology. For example, in cardiogenic shock due to poor contractility, an agent with inotropic and/or afterload reducing properties (Inodilators) should be considered. As a general rule, vasodilators should be used with caution, if at all, in hypotensive cardiogenic shock patients. In distributive shock, an agent with vasoconstrictive (Vasopressors) properties should be considered. Medications should be titrated to targeted parameters (typically mean arterial pressure. See Appendix: Pediatric MAP) balancing efficacy and safety. This PEM Guide will focus on selection of the initial vasoactive medication.

Direct comparisons of vasoactive medications and evidence for specific dosage regimens is very limited. This is particularly true in the pediatric population. A 2016 Cochrane network meta-analysis of vasoactive medications (adults and pediatrics) in shock found no difference in mortality when Norepinephrine was compared to: Epinephrine, Phenylephrine, Dopamine, Vasopressin and Terlipressin (Gamper, Cochrane DSR 2016, PubMed ID: 26878401).

VASOACTIVE AGENT SELECTION: ESSENTIAL CONCEPTS	
1	Medication effects can occur at more than 1 receptor
The inopressors (e.g. Epinephrine) are non-selective and have effects in the heart ($beta_1$ receptors) and the vasculature ($alpha_1$ receptors	
2	Medication effects can be dose dependent
At lower doses of Epinephrine's $beta_1$ receptor effects (chronotropy, inotropy) predominate while at higher doses of Epinephrine's $alpha_1$ receptor effects (vasoconstriction) predominate.	
3	Medication effects can result in reflex actions
Phenylephrine has effect only at the $alpha_1$ receptor causing vasoconstriction. This can result in a reflex bradycardia. Phenylephrine is not recommended for neurogenic shock with bradycardia for this reason	
4	An ideal medication from a physiologic standpoint may not be the best medication due to its adverse effects.
A $beta_1$ receptor agonist can increase cardiac output but at the risk of ↑ myocardial O_2 consumption with ischemia and dysrhythmias in a patient with cardiogenic shock	
5	Indirect acting medications that depend on the release of Epinephrine or Norepinephrine may not beeffective in the catecholamine depleted patient.
In addition to direct adrenergic effects, Dopamine indirectly causes release of norepinephrine from sympathetic neurons	

MEDICATION: CLASSIFICATION			
Class	Medication	Action	Shock Indication
Inodilators	Dobutamine	$Beta_1 > Beta_2$	Cardiogenic
	Milrinone	↑ cAMP	Cardiogenic
Inopressors	Epinephrine	Low: $Beta_1 > Alpha_1$ High: $Alpha_1 > Beta_1$	Cardiogenic (Low BP), Anaphylactic, Septic
	Norepinephrine	$Alpha_1 > Beta_1$	Septic, Neurogenic
	Dopamine	Dop → $Beta_1$→ $Alpha_1$	Post Resuscitation?
Vasopressors	Phenylephrine	$Alpha_1$	Neurogenic (normal, ↑ HR)
	Vasopressin	V_I, V_2	Septic

Recommendations for first line vasoactive medications by type of shock are included in the table below. Recommendations for anaphylactic shock and septic shock are most consistent. Recommendation for cardiogenic shock and neurogenic shock are highly variable often with variation between pediatric and adult recommendations. This inconsistency is due to the paucity of high-quality evidence. Starting vasoactive medications promptly through a peripheral intravenous line should be prioritized over a delayed administration through a central venous line.

MEDICATION SELECTION: FIRST LINE AGENTS		
Anaphylactic Shock	Epinephrine[1]	
Cardiogenic Shock: Normal BP	Dobutamine, Milrinone[2]	
Cardiogenic Shock: ↓ BP	Epinephrine (low dose)[2]	
Neurogenic Shock: Normal or ↑ HR	Norepinephrine, Epinephrine, Phenylephrine[3]	
Neurogenic Shock: ↓ HR	Norepinephrine, Epinephrine[3]	
Septic Shock: Warm	Peds: Norepinephrine[5,6]	Adult: Norepinephrine[4]
Septic Shock: Cold	Peds: Epinephrine[5,6]	Adult: Norepinephrine[4]

1. Guideline: Anaphylaxis: Amer Assoc Allerg, Asth, Im 2020, PubMed ID: 32001253
2. Guideline: Heart failure ACC/AHA, Circulation 2013, PubMed ID: 28455343
   (Dobutamine, Milrinone, Epinephrine listed: No specific recommendation made)
3. No specific recommendation for neurogenic shock could be found
4. Guideline: Adult Sepsis: Surviving Sepsis3, 2016, PubMed ID: 28101605
5. Guideline: Pediatric Sepsis: Surviving Sepsis3, 2020, PubMed ID: 32032273
   (Insufficient evidence to recommend Epinephrine vs Norepinephrine as 1st line)
6. Pediatric Sepsis Algorithm: Pediatric Advanced Life Support Course: AHA 2015

Further evidence for vasoactive medication selection based on the etiology of hypotension can be found in greater detail in the following PEM Guides: PEM Guide: Cardiology: Cardiogenic Shock, PEM Guide: Infections: Septic Shock, PEM Guide: Respiratory: Anaphylaxis and PEM Guide: Trauma: Neurogenic Shock.

ADVERSE EVENTS
VASOCONSTRICTION
Ischemia to non-essential organ systems such as the gastrointestinal tract
Increases afterload potentially decreasing cardiac output in the heart failure
Reflex bradycardia. This is more important in infants and young children whose cardiac output is driven more by heart rate then by stroke volume.
INOTROPY AND CHRONOTROPY
Dysrhythmias: Consider an alternative medication with less beta activity
Inotropy + Chronotropy → ↑ Myocardial oxygen consumption → Myocardial ischemia
OTHER
Extravasation at a peripheral intravenous site → Skin necrosis Not reported with Epinephrine, Phenylephrine Norepinephrine ischemia can be treated with phentolamine (vasodilator) Vasopressin is not recommended for peripheral use: No treatment

ADMINISTRATION: Ideally, vasoactive infusions are administered via a central line. However, that is not always practical and the delay inherent in obtained a central line translates into a delay in administering the vasoactive infusions. Administering a vasoactive infusion via a peripheral intravenous line is a reasonable alternative in this situation. The primary concerns with peripheral vasoactive infusion in extravasation and soft tissue injury.

In a retrospective cohort study, 231 children initially received vasoactive therapy by a peripheral intravenous line (Levy, Pediatr Crit Care Med. 2022, PubMed ID: 35446810). Extravasation occurred in 1.7% (4/231) of patients without long-term complications. Phentolamine was prescribed in 2 patients with Dopamine extravasations. Terbutaline and topical nitroglycerine were prescribed in 1 patient with epinephrine extravasation. In addition, approximately half of the patients did not ultimately require central venous access. The authors concluded that peripheral venous catheters may be used for vasoactive infusion administration while the need for central access is further evaluated.

MONITORING: Ongoing therapy should be guided by monitoring the patient's fluid and cardiovascular parameters such as mean arterial pressure (Adults: MAP > 65 mmHg, See Appendix: Pediatric MAP). Monitoring of central venous pressure and other parameters may be indicated in the patient that does not respond as expected. A central line also delivers medications directly to the heart for systemic distribution. Monitoring cardiac enzymes may also be indicated. The peripheral intravenous sites of patients receiving vasoactive medication should be monitored closely as extravasation can result in skin necrosis.

APPENDIX: VASOACTIVE MEDICATION DOSING

Dosages are starting points. Dosing may need to be titrated up if the desired effect is not achieved or titrated down or discontinued if adverse events occur. A second vasoactive medication may be required.

VASOACTIVE MEDICATION DOSING		
	Pediatric[1] (mcg/kg/min)	Adult[2] (mcg/kg/min)
Dobutamine	2-10	2-20[4]
Dopamine (Low: “Renal”)	2-5	2-5
Dopamine (Mod: ↑CO > ↑ SVR)	5-10	5-10
Dopamine (High: ↑ SVR > ↑CO)	10-20	10-20
Epinephrine (Low: ↑CO > ↑ SVR)	0.1-0.3	0.1-0.3
Epinephrine (High: ↑ SVR > ↑CO)	> 0.3	0.3-0.5
Milrinone	0.25-0.75[3]	0.125-0.75[3,4]
Norepinephrine	0.1-2.0	0.1-0.5
Phenylephrine	0.1-0.5[4]	0.5-6.0[4]
1. AHA: Pediatric Advanced Life Support Manual 2015 (unless otherwise specified) 2. AHA: Advanced Cardiac Life Support Manual 2015 (unless otherwise specified) 3. Consider a loading dose: 50 mcg/kg over 10-60 minutes 4. Lexicomp 2020		

APPENDIX: PUSH-DOSE PRESSORS: EPINEPHRINE

PUSH DOSE PRESSORS	
Definition	Small bolus doses of vasoactive agents to support blood pressure
History	Used anesthesiologists in the OR for many years
	Recently, more common in the ED and ICU settings
Indications	Bridge the time until a vasoactive infusion is available
	Expected short lived ↓ BP: e.g. after RSI, during procedural sedation
Adverse Events	Incorrect preparation → ↓ dose (ineffective),↑ dose (adverse events)
	Must label syringes appropriately to avoid dosing errors
Pediatric Dose	Weight base concentration: 1 mcg/kg/ml and dosed in 1 ml aliquots
Adult Dose	Standard Concentration: 10 mcg/ml and dosed in 1 ml aliquots
Other	Norepinephrine and Phenylephrine can also be used in push doses

EPINEPHRINE DOSING: NEW CONCENTRATIONS				
	CONCENTRATION		PEDIATRIC DOSING	
Route	Old	New	mg/kg	mL/kg
Intravenous	1:10,000	0.1 mg/mL	0.01	0.1
Intramuscular	1:1,000	1 mg/mL	0.01	0.01

PUSH-DOSE EPINEPHRINE: STANDARD PREPARATION (ADULT)	
Epinephrine (0.1 mg/ml)	Code Dose: 1 mg = 100 mcg = 10 ml
Normal Saline	9 ml Normal Saline
Preparation	1 ml of Epinephrine (0.1 mg/ml) + 9 ml of NS = 10 ml
Concentration	0.01 mg/ml (10 mcg/ml)
Dosing	0.5-2 ml (5-20 mcg) Q2-4 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION (PEDIATRICS)	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 10 mcg/kg = 0.1 ml/kg
Normal Saline	Normal Saline to total 10 ml
Preparation	0.1 ml/kg + NS to total 10 ml
Concentration	0.01 mg/kg/ml = 1 mcg/kg/ml
Dose	1 ml Q2 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION: 20 KG CHILD	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 0.2 mg, 10 mcg/kg = 200 mcg 0.1 ml/kg = 2 ml
Preparation	2 ml of Epinephrine (0.1 mg/ml) + 8 ml of NS = 10 ml
Preparation (concentration)	200 mcg/10 ml = 20 mcg/ml = 1 mcg/kg/ml
Dosing	1 ml (20 mcg or 1 mcg/kg) Q2 minutes PRN
Infusion Comparison	0.5-1.0 mcg/kg/min (10-20 mcg/min) Push-dose: 1 ml = 20 mcg (1/10th code dose) Equals: 0.5 mcg/kg/min x 2 min, 1.0 mcg/kg/min x 1 min

APPENDIX: PEDIATRIC MEAN ARTERIAL PRESSURE (1-10 YEARS)

PEDIATRIC MEAN ARTERIAL PRESSURE (BASED ON PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
1	5th	30	35	33	37	34	37	36	39	37	40
	50th	49	53	52	54	53	55	54	57	56	58
	95th	69	71	70	72	72	73	73	74	74	76
2	5th	35	39	38	41	39	42	40	42	41	44
	50th	54	57	56	58	57	59	59	60	60	62
	95th	73	75	75	76	76	77	77	78	79	80
3	5th	39	42	41	44	42	44	44	46	45	47
	50th	58	60	60	61	61	62	62	64	64	65
	95th	77	78	78	79	80	80	81	81	82	83
4	5th	42	45	43	46	46	47	47	47	48	49
	50th	61	63	63	65	64	65	66	65	67	67
	95th	79	80	82	82	83	83	84	84	86	85
5	5th	45	46	47	48	49	49	49	50	51	52
	50th	63	64	66	66	67	67	68	68	69	69
	95th	82	82	84	83	85	85	87	86	88	87
6	5th	47	49	49	50	50	51	52	52	53	54
	50th	66	66	67	68	69	69	70	67	71	71
	95th	84	84	86	85	87	86	88	87	90	89
7	5th	51	50	50	51	52	52	53	53	54	55
	50th	67	68	69	69	70	70	72	71	73	72
	95th	83	85	88	87	89	88	90	89	92	90
8	5th	50	52	53	52	54	54	55	55	56	56
	50th	69	70	71	70	72	71	73	72	75	74
	95th	87	81	89	88	91	89	92	90	93	91
9	5th	51	53	53	54	55	55	56	56	58	57
	50th	70	71	72	71	73	73	75	74	76	75
	95th	88	89	91	89	92	90	93	91	94	93
10	5th	52	54	55	55	56	56	56	57	59	59
	50th	71	72	73	73	75	74	75	75	77	76
	95th	90	90	92	90	93	92	94	93	96	94

Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40
Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55

Haque IU, Zaritsky AL.
Analysis of the Evidence for The Lower Limit of Systolic and Mean Arterial Pressure in Children
Pediatr Crit Care Med. 2007 Mar;8(2):138-44., PubMed ID: 17273118

CONTINUED ON NEXT PAGE →

APPENDIX: PEDIATRIC MEAN ARTERIAL PRESSURE (11-17 YRS)

PEDIATRIC MEAN ARTERIAL PRESSURE (BASED ON PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
11	5th	54	55	57	56	57	57	58	59	59	60
	50th	72	73	74	74	75	75	76	76	78	78
	95th	91	91	92	92	94	93	95	94	96	95
12	5th	54	57	57	58	58	58	60	60	61	61
	50th	73	75	75	75	77	76	78	78	79	79
	95th	92	92	94	93	95	94	96	95	98	97
13	5th	56	58	57	59	59	60	60	61	61	62
	50th	75	76	76	77	77	78	79	71	80	80
	95th	93	94	95	94	96	95	97	97	99	98
14	5th	59	60	59	60	61	61	62	62	63	64
	50th	75	77	78	78	79	79	80	80	82	81
	95th	91	95	96	96	97	97	99	98	100	99
15	5th	58	61	61	61	62	62	63	63	64	64
	50th	77	78	79	79	80	80	82	81	83	82
	95th	96	91	98	97	99	98	100	99	102	100
16	5th	90	61	62	62	63	63	65	63	66	66
	50th	79	79	81	90	82	81	83	82	85	84
	95th	98	96	99	98	101	99	102	100	104	101
17	5th	63	61	63	62	65	63	67	65	69	66
	50th	81	79	83	80	84	81	85	82	87	84
	95th	100	96	102	98	103	99	104	100	106	101

Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40
Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55

Haque IU, Zaritsky AL.
Analysis of the Evidence for The Lower Limit of Systolic and Mean Arterial Pressure in Children
Pediatr Crit Care Med. 2007 Mar;8(2):138-44., PubMed ID: 17273118

RHEUMATOLOGY

ACUTE RHEUMATIC FEVER

INTRODUCTION (LUV MAKADIA, M.D., 4/2020)
Acute Rheumatic Fever (ARF) is a delayed, non-suppurative sequela of group A streptococcal (GAS) pharyngitis. It is most common in those 5-15 years of age and consists of systemic inflammation manifesting as arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules. Cardiac involvement occurs in about half of the patients. It's primary sequela, rheumatic heart disease, is the leading cause of cardiac deaths in those younger than 50 years of age in the developing world.

The incidence of ARF has decreased significantly in affluent countries over the last four decades. This is thought to be due to access to antibiotics, improvement in a variety of socioeconomic factors and a serotype shift away from rheumatogenic strains of GAS. In the US and Europe it occurs in 2/100,000 school age children per year. In contrast, in the developing world, it occurs in 19/100,000 school age children per year and in some indigenous populations (including those within affluent countries), the incidence can be as high 150-400/100,000 school age children per year.

PATHOPHYSIOLOGY
The pathophysiology of ARF is incompletely understood and different mechanisms may be responsible for different manifestations. There is no evidence of direct GAS infection in effected tissue. During GAS infection, antigen-presenting cells present the GAS antigen to CD4+T cells which then differentiate into T2 helper cells. The T2 helper cells then activate B cells that become GAS antibody producing plasma cells. In ARF these antibodies cross react with tissue of the heart, joints, smooth muscle cells of arteries, and perivascular connective tissue. The resulting cytokine release causes tissue injury. GAS skin infections, which can cause post infection glomerulonephritis, do not cause ARF with the exception of some tropical areas (See: PEM: GU-Renal: Post Infectious Glomerulonephritis).

CLINICAL MANIFESTATIONS
There are two main presentation of ARF presentation, the more common febrile illness with joint involvement and carditis and the less common neurological and behavioral form. The acute febrile illness form occurs 2-4 week after GAS pharyngitis. Primary manifestations occur in the heart (carditis), joints (arthritis), central nervous system (Sydenham chorea) and skin (erythema marginatum, subcutaneous nodules). There may be a history of an antecedent sore throat a few weeks prior to presentation though this history is frequently unreliable.

ARF MANIFESTATION PREVALENCE		
Carditis	Pancarditis (primary valvulitis): Subclinical and clinical	50-70%
Arthritis	Migratory polyarthritis: Large joints	35-66%
CNS	Sydenham chorea	10-30%
Nodes	Subcutaneous nodules: Extensor surfaces	0-10%
Rash	Erythema marginatum	< 5%

ACUTE RHEUMATIC FEVER: FORMS		
	ACUTE FEBRILE ILLNESS	NEUROLOGIC ILLNESS
Prevalence	70-75%	25-30%
Onset	2-4 weeks	2-6 months
Fever	Yes	No
Joint Involvement	Yes	No
Carditis	Clinical and Subclinical	> 30% (Often Subclinical)
Inflammatory Markers	Raised	Normal (Often)
Strep antibodies	↑ ASO, ↑ anti-DNAase B	nl ASO, ↑ anti-DNAase B
Rheumatic Heart	75%	50%
Other	Erythema Marginatum	Sydenham chorea
	Subcutaneous nodules	Behavioral changes
	ASA, NSAID → ↓ Arthritis	
	Duration < 6 weeks	

ARTHRITIS: Arthritis is usually the first symptoms of ARF, presenting within 3 weeks of GAS infection (though subclinical carditis may be present). It is typically reported as a migratory (or additive) arthritis with the knees, ankles, elbows, and wrists as the most commonly affected joints. Joint involvement occurs in rapid succession. The use of NSAIDS after the first joint involvement may prevent progression to other joints and mask the typical multi-joint involvement in ARF. The arthritis is usually transient without any long term joint deformity.

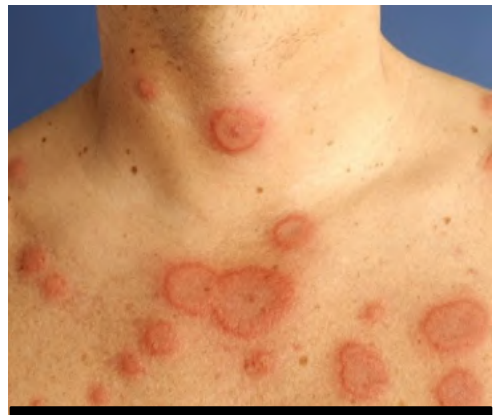
CARDITIS: Carditis is also an early symptoms after GAS infection usually occurring within the first 21 days. Although heart involvement is a pancarditis, the most common manifestation is valvulitis of the aortic and/or mitral valves. Isolated myocarditis or pericarditis without valve involvement is very rare. Auscultation of the heart will usually allow for the detection of a murmur of aortic regurgitation (SOUND FILE: AORTIC REGURGITATION) and/or mitral regurgitation (SOUND FILE: MITRAL REGURGITATION). Carditis is defined as subclinical if there is echocardiogram evidence of valvulitis in the absence of exam evidence of carditis.

Rheumatic heart disease often occurs 10-20 years after the acute illness and can involve the mitral (more common) or aortic valve. The most common clinical finding is mitral regurgitation and may progress to stenosis from fibrosis and/or calcification.

SYDENHAM CHOREA: Sydenham chorea typically presents 1-8 months after GAS infection. It consists of abrupt, non-rhythmic, involuntary movements that may worsen with attempts at intentional movement and that stop during sleep. It usually involve one side more than the other and can also involve the head, face, and tongue. Patients may also have muscular weakness that can be evident on physical exam as the “milk maid’s sign,” where the pressure of the patient’s grip when asked to squeeze the clinician’s hands changes inconsistently. Patient may speak with a halting or jerky speech pattern. Emotional disturbances can include: crying, restlessness, inappropriate behavior and obsess-compulsive behaviors. Psychologic disturbances and psychosis are rarely seen.

VIDEO LINK: SYDENHAM CHOREA

ERYTHEMA MARGINATUM: Erythema marginatum can occur early or late in the course of ARF and almost never occurs as the only symptom of ARF. The non-pruritic rash is mildly erythematous with a pale center and occurs on the trunk and extremities but spares the face. The erythematous border can be rounded or serpiginous. The outer edge of the borders are sharp while the inner edges are diffuse. Outward progression of rash with skin in the center of the lesion resolving as the outer edges become affected. The rash is evanescent with individual lesions appearing and disappearing within hours.



ERYTHEMA MARGINATUM

SUBCUTANEOUS NODULES: Subcutaneous nodules occur within a few weeks of GAS infection and are rarely the sole symptoms of ARF. The presence of subcutaneous nodules is associated with severe carditis. The lesions are firm, painless and less than 2 cm nodules over bony surfaces and tendons. The elbows (over the olecranon) are the most common site. Other sites include the: extensor surfaces of the knees and wrists, occipital and thoracic and lumbar spinous processes. There can be up to a few dozen lesions with a mean of 3-4 lesions. In contrast, the lesions associated with Juvenile Immune Arthritis are typically 3-4 cm in size and occur distally.

OTHER CLINICAL MANIFESTATIONS
Abdominal pain
Precordial chest pain
Malaise
Resting tachycardia or tachycardia out of proportion to fever[1]
CBC: Leukocytosis, normocytic anemia
Complement: Normal (↓ in Post Infectious Glomerulonephritis)
1. HR increases by ↑ 10 beats/minute for each 1 degree Celsius above normal

DIAGNOSTIC TESTING

The Jones criteria for ARF have been modified to account for differences in the clinical manifestation based on ARF risk incidence and the use echocardiography in identifying carditis. Low risk is defined as a population with an ARF incidence of less than 2/100,000/5-14years of age/year and an incidence of rheumatic heart disease of < 1/1,000/all ages/year. ARF is diagnosed if 2 major criteria are present or if 1 major Criteria and 2 minor criteria are present. If the Jones criteria are not met, the diagnosis of ARF can be made if chorea is the sole symptom, there is Isolated indolent carditis months after GAS infection or if 1 major or 2 minor criteria are present in a patient with prior ARF. Confirmation of GAS infection is supportive but not necessary for ARF diagnosis.

LABORATORY: A CBC with differential should be obtained to evaluate for anemia and leukocytosis. CRP and ESR should also be obtained to look for signs of inflammation.

IMAGING: Joint XRAYS may reveal a joint infusion without bone changes. Arthrocentesis may be required if septic arthritis is a consideration (See: PEM Guide: Orthopedics: Arthrocentesis, PEM Guide: Orthopedics: Septic Arthritis).

CARDIAC EVALUATION: EKG is obtained to check for PR prolongation. Additionally, echocardiography to detect valve abnormalities must be obtained in every patient with suspected carditis. The imaging must show both morphologic involvement of the mitral and/or aortic valve and also Doppler signs of mitral and/or aortic valvular regurgitation.

REVISED JONES CRITERIA (AHA 2015): LOW INCIDENCE GROUP[1]	
MAJOR	MINOR
Carditis (Clinical or Subclinical)[2]	↑ PR Interval for age and heart rate[4]
Migratory Polyarthritis[3]	Polyarthralgia
Sydenham Chorea	Fever > 38.5 C (101.3 F)
Erythema Marginatum	ESR > 60 ml/hr, CRP ≥ 3mg/dl (30mg/L)
Subcutaneous Nodules	
Requires 2 Major criteria OR (1 Major criteria AND 2 Minor criteria) 1. Low Risk: ARF < 2/100,000/5-14yo/year, Rheumatic heart < 1/1,000/all ages/year 2. ↑ PR Interval does not count as a minor criteria if carditis is a major criteria 3. Arthralgia does not count as a minor criteria if arthritis is a major criteria 4. PR Interval must be adjusted for age and heart rate (See Appendix) Gewitz, Circulation 2015, PubMed ID: 25908771	

CRITERIA COMPARISON: LOW VS MODERATE-SEVERE INCIDENCE GROUPS		
CRITERIA	LOW-INCIDENCE	MODERATE-HIGH INCIDENCE
Arthritis (Major)	Polyarthritis	Polyarthritis or Monoarthritis
Arthralgia (Minor)	Polyarthralgia	Polyarthralgia[1] or Monoarthralgia
Fever (Minor)	≥ 38.5 C (101.3 F)	≥ 38 C (100.4 F)
ESR (Minor)	≥ 60 ml/hour	≥ 30 ml/hour
1. Polyarthralgia may be considered a major criteria in the moderate-high risk group		

EVIDENCE OF ANTECEDENT GROUP A STREPTOCOCCAL INFECTION
Throat culture (+) for Group A Streptococcus (often negative at ARF presentation)
Rapid streptococcus antigen testing (often negative at ARF presentation)
Streptococcal antibodies: Acute < Convalescent titers (≥ 2 weeks apart) OR > Normal (See Appendix)
Anti-streptolysin O (peak 3-5 weeks after GAS infection)
Anti-deoxyribonuclease B (peak 6-8 weeks after GAS infection)
*Confirmation of GAS infection is supportive but not necessary for ARF diagnosis

DIFFERENTIAL DIAGNOSIS

The differential diagnoses for arthralgias/arthritis, carditis and abnormal movements is extensive. Importantly, Lyme. Lupus and Kawasaki disease all have joint, heart, and skin manifestations and may have CNS signs and symptoms (See: PEM Guide: Rheumatology: Kawasaki Disease, PEM Guide: Rheumatology: Systemic Lupus Erythematosus, PEM Guide: Infections: Lyme Disease). The differential diagnosis for Chorea includes: Huntington's Chorea, Lupus cerebritis, Wilson disease, motor tics, conversion reactions and drug reactions such as dystonic reactions and tardive dyskinesia.

DIFFERENTIAL DIAGNOSIS: ARTHRITIS/ARTHRALGIA	
A	Avascular necrosis (Legg-Calve-Perthes, Sickle cell), epiphyseal injury (SCFE)
R	Reactive and post-infectious arthritis
T	Trauma: Accidental/Non-accidental, hypermobility syndromes
H	Hematologic: Leukemia, hemoglobinopathy (Sickle cell), bleeding diathesis
R	Rickets, metabolic and endocrine disorders
I	Infection: Septic arthritis (e.g. Lyme), osteomyelitis
T	Tumor: Bone (e.g. osteosarcoma), metastasis (e.g. lymphoma), trauma
I	Idiopathic pain: Complex regional pain syndrome, fibromyalgia
S	Systemic: Kawasaki, SLE, JIA, HSP, IBD, IgA vasculitis, sarcoidosis

POST-STREPTOCOCCAL REACTIVE ARTHRITIS (PRSA): PRSA is the development of arthritis after streptococcal infection when other criteria for ARF are not met. It is unclear if this represents a distinct disease process or an atypical presentation of ARF. PRSA should only be diagnosed if the patient does not meet the Jones criteria and after exclusion of other rheumatic diseases.

POST-STREPTOCOCCAL REACTIVE ARTHRITIS VS ACUTE RHEUMATIC FEVER	
Post Streptococcal Reactive Arthritis	Acute Rheumatic Fever
1-2 weeks after GAS infection	2-3 weeks after GAS infection
Poor response to aspirin and NSAIDs	Great response to aspirin and NSAIDs
Tenosynovitis, renal abnormalities	CRP/ESR higher than in PRA
Barash, J Pediatr 2008, PubMed ID: 18657830 Van Bemmel, Arthritis Rheum 2009, PubMed ID: 19333942	

MANAGEMENT

The goals of the treatment for ARF are to provide anti-inflammatory agents for symptomatic relief of joint manifestations, manage heart failure symptoms and administer antibiotics to both eradicate GAS infection and to prophylaxis against future GAS infection and ARF recurrence. Treatment decisions should be made in consultation with pediatric cardiology, pediatric rheumatology and pediatric infectious disease.

MANAGEMENT: OVERVIEW	
GAS Pharyngitis	Treatment for both GAS eradication and secondary prevention
	Penicillin G benzathine intramuscular preferred (See Appendix) Penicillin allergy: Oral cephalosporin or macrolides (See Appendix)
	Household contacts: Test and treat if positive, even if asymptomatic
Arthritis	NSAIDS decrease pain, swelling and progression to other joints. Typically for 1-2 weeks until symptoms resolve and CRP normalizes
	Naproxen (Child): 10-20 mg/kg/day divided Q12H (max 1,000 mg/day) Naproxen (Adult): 250-500 mg BID (max 1,250 mg/day) Aspirin 80-100 mg/kg per day
	Glucocorticoids if cannot tolerate Aspirin and Naproxen
	Proton Pump Inhibitor: Bleeding diathesis, history of GE reflux, GI upset with NSAIDS, develops GI upset during treatment
Carditis	Heart failure: See: PEM Guide: Cardiology: Cardiogenic Shock
	There is no evidence that anti-inflammatories improve carditis
	Surgery: Valve or chordae tendineae rupture
Sydenham chorea	Self-limited. Psychological and social support.
	If interferes with activities of daily living or increased risk of injury consider Carbamazepine or Valproic acid. IVIG or glucocorticoids for resistant cases. Neurology referral

SECONDARY PREVENTION: Patients with ARF are at increased risk of redeveloping the disease after future GAS infections and require long-term antibiotic prophylaxis. This is accomplished with intramuscular penicillin G Benzathine every 21-28 days with consideration of switching to oral prophylaxis in the future. The preferred oral drug is penicillin V and in cases of penicillin allergy, macrolides are preferred.

PROPHYLACTIC ANTIBIOTICS: SELECTION		
	< 27 kg	> 27 kg
Penicillin G Benzathine	600,000 units IM Q28d[1]	1,000,000 units IM Q28d[1]
Penicillin VK	250 mg PO BID	250 mg PO BID
PNC Allergy: Azithromycin	5 mg/kg PO QD[2]	250 mg PO QD
1. Decreased to Q21 days if recurrent ARF 2. Maximum dose 250 mg PO QD		

PROPHYLACTIC ANTIBIOTICS: DURATION	
ARF: No carditis	Longer of: 5 years or until 21 years of age
ARF: Carditis, no residual valve disease	Longer of: 10 years or until 21 years of age
ARF: Carditis, persistent valve disease	Longer of: 10 years or until 40 years of age

DISPOSITION

Unless patients have severe carditis with heart failure, chorea, or severe constitutional symptoms, they can be treated in the outpatient setting.

APPENDIX: ANTIBIOTICS FOR ERADICATION OF GAS INFECTION

GROUP A STREPTOCOCCAL PHARYNGITIS: ANTIBIOTIC SELECTION		
CLASS/NAME	PEDIATRIC DOSE	ADULT DOSE
PENICILLINS		
Penicillin V	250mg BID-TID (< 27 kg) 500mg BID-TID (> 27 kg)	500 mg BID-TID
Amoxicillin	50 mg/kg QD (can also be divided BID or TID)	1 gram PO QD 500 mg BID
PCN G Benzathine (LA Bicillin)	600,000 units IM x 1 (< 27 kg) 1.2 million units IM x 1 (> 27 kg)	1.2 million units IM x 1 dose
CEPHALOSPORINS		
Cephalexin (1st)	20 mg/kg BID	500 mg BID
Cefadroxil (1st)		1 gram PO QD
Cefuroxime (2nd)	10 mg/kg BID	250 mg BID
Cefpodoxime (3rd)	5 mg/kg BID	100 mg BID x 5-10 days
Cefdinir (3rd)	7 mg/kg BID x 5-10 days 14 mg/kg QD	600 mg 300 mg BID x 5-10 days
Cefixime (3rd)		400 mg QD x 10 days
MACROLIDES		
Azithromycin	12 mg/kg D1, 6 mg/kg D2-5	500 mg D1, 250 mg D2-5 500 mg QD x 3 days
Clarithromycin	7.5 mg/kg BID	250 mg BID
LINCOSAMIDES		
Clindamycin	7 mg/kg TID	300 mg TID
All doses are oral except Benzathine PCN (which is IM) All durations are for 10 days unless otherwise specified All pediatric doses are mg/kg/dose (not mg/kg/day to be divided) Pediatric maximum individual doses are the adult individual dose Patients with ARF should be tested by a pediatric allergist if they report PCN allergy		

APPENDIX: PR INTERVAL BY AGE AND HEART RATE

PR INTERVAL BY AGE AND HEART RATE: MEAN (UPPER LIMIT OF NORMAL)								
HR (BPM)	0-1 mo	1-6 mo	6 mo-1 yr	1-3 yr	3-8y r	8-12 yr	12-16 yr	Adult
< 60						0.16 (0.18)	0.16 (0.19)	0.17 (0.21)
60-80					0.15 (0.17)	0.15 (0.17)	0.15 (0.18)	0.16 (0.21)
80-120	0.10 (0.12)				0.14 (0.16)	0.15 (0.16)	0.15 (0.17)	0.15 (0.20)
100-120	0.10 (0.12)			(0.15)	0.13 (0.16)	0.14 (0.15)	0.15 (0.16)	0.15 (0.19)
120-140	0.10 (0.11)	0.11 (0.14)	0.11 (0.14)	0.12 (0.14)	0.13 (0.15)	0.14 (0.15)		0.15 (0.18)
140-160	0.09 (0.11)	0.10 (0.13)	0.11 (0.13)	0.11 (0.14)	0.12 (0.14)			(0.17)
160-180	0.10 (0.11)	0.10 (0.12)	0.10 (0.12)	0.10 (0.12)				
> 180	0.09	0.09 (0.11)	0.10 (0.11)					

APPENDIX: NORMAL VALUES: STREPTOCOCCAL ANTIBODIES

ANTI-STREPTOCOCCAL ANTIBODY TESTING: UPPER LIMIT OF NORMAL (U.S.)		
Age (years)	Anti-streptolysin O	Anti-DNAase B
2	160 IU	240 IU
3	120 IU	60 IU
4		240 IU
5	160 IU	320 IU
6	240 IU	480 IU
7		640 IU
8		
9		
10	320 IU	
11		800 IU
12		480 IU
Kaplan, Pediatrics 1998, PubMed ID: 9417157		

HENOCH SCHONLEIN PURPURA

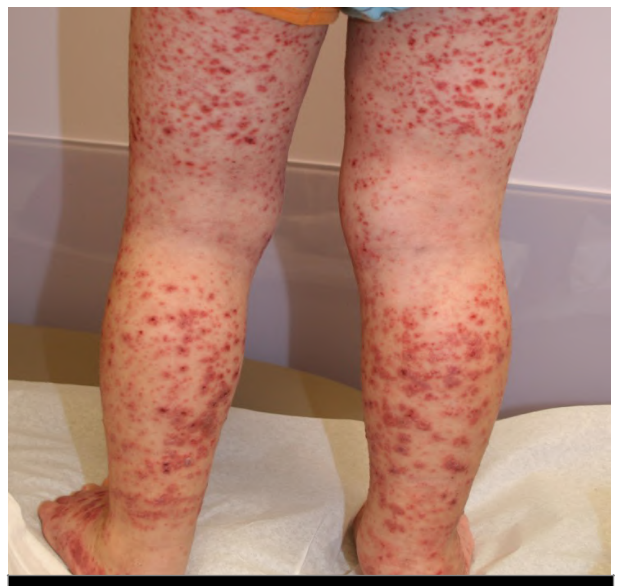
INTRODUCTION (NICOLE PERRY, M.D., 12/2017)
Henoch-Schonlein Purpura (HSP) also known as anaphylactoid purpura and immunoglobulin A vasculitis, is the most common childhood vasculitis. HSP is characterized by leukocytoclastic and IgA deposition in the small vessels of skin, joints, gastrointestinal tract and kidney.

Peak incidence is between 5 and 7 years of age. While the exact cause is unknown, it is more common in the winter months and often is preceded by an upper respiratory infection 1-2 weeks prior. A significant percentage of cases are triggered by hemolytic Streptococcus infections.

CLASSIC TETRAD
Palpable purpura
Oligoarticular arthritis or arthralgias
Abdominal pain
Renal disease

CLINICAL MANIFESTATIONS

RASH: The rash is characterized by palpable purpura and is present in 100% of cases. The rash begins as painless pink macules that mimic the wheel of anaphylactic reactions. The lesions progress to purpura in crops typically lasting 3-10 days before self-resolving. The rash is found typically in the dependent areas of the body and at areas of pressure points; i.e. face, scalp, and back of immobile infants and legs, buttocks and feet of ambulatory children. The rash may be mistaken for non-accidental trauma.



PURPURA

ARTHRITIS: The arthritis that develops is typically oligoarticular (1-4 joints) with a predilection for the lower extremities. The arthritis is present in up to 75% of cases and self resolves by 2 weeks. HSP arthritis has no long-term sequelae.

GASTROINTESTINAL: Gastrointestinal manifestations occur in up to 80% of cases and usually occur within 8 days of onset of the rash and are caused by submucosal hemorrhage and edema in the intestines. The most common manifestations include diffuse abdominal pain, vomiting, ileus, mesenteric ischemia leading to bowel perforation and intussusception. Intussusception is typically ileoileal. Non-HSP intussusception is typically Ileocecal.

RENAL: Renal involvement occurs in about 50% of patients and presents as hematuria, hypertension and edema (in cases with nephrosis). A small percentage of children present with oliguria and acute renal failure.

OTHER SYSTEMS: Other less common, but important, clinical findings include subcutaneous edema of the lips, scrotum and scalp. Neurological manifestations such as headache, seizure and altered mental status can suggest the rare occurrence of intracerebral hemorrhage. Orchitis, testicular torsion, carditis, and keratitis are less frequently seen.

DIAGNOSIS

HSP is a clinical diagnosis but if the classic rash is not present at the time of presentation, early identification may be difficult. Many of the labs obtained in the diagnosis of HSP are collected to other disease states.

CLASSIFICATION CRITERIA
Palpable purpura
Age of onset < 20 years old
Bowel Angina (abdominal pain)
Biopsy demonstrating intramural granulocytes in small arterioles and venules
American College of Rheumatology (1990): PubMed ID: 2202310

DIAGNOSTIC EVALUATION	
CBC	Thrombocytosis, leukocytosis, mild anemia
ESR/CRP	Often elevated
Stool studies	Positive for occult blood
IgA	Often elevated but may be within normal limits early
Urinalysis	Reflects degree of kidney injury; hematuria, casts, and mild-moderate proteinuria can be present
Vital Signs	Hypertension common with moderate-severe kidney involvement, Often afebrile
Ultrasound	Bowel wall edema, ileo-ileal intussusception

Imaging studies are used to determine the degree of involvement of the GI tract and rule out other causes of an acute abdomen. Ultrasound rather than contrast enema should be used in suspected cases of intussusception since contrast enema is neither diagnostic nor curative for ileo-ileo intussusception.

DIFFERENTIAL DIAGNOSIS	
Acute Hemorrhagic Edema	Isolated cutaneous vasculitis (< 2 years). Tender edema, petechiae in dependent areas and mucus membranes
Coagulopathies	Idiopathic thrombocytopenic purpura (ITP), Cryoglobulinemia, Primary antiphospholipid syndrome
Infections	Meningococcemia, Rickettsial diseases
Small Vessel Vasculitides	Wegener granulomatosis, Churg-Strauss Syndrome, Microscopic Polyangiitis, Isolated cutaneous leukocytoclastic vasculitis
Acute Abdomen	Appendicitis, pancreatitis, ovarian torsion
Drug reaction	Drug rash, anaphylaxis

MANAGEMENT

Treatment of HSP is primarily supportive. As HSP is usually a self-limited disease adequate hydration, nutrition and analgesia are often sufficient. Non-steroidal anti-inflammatory agents such as Ibuprofen and Naproxen (5 mg/kg/day divided BID) are typically sufficient analgesia but should be avoided in patients with significant renal dysfunction or gastrointestinal hemorrhage.

For significant renal involvement and gastrointestinal involvement, corticosteroids and other immunomodulating medications are often employed in consultation with a pediatric rheumatologist or nephrologist. A prednisone taper starting at 1 mg/kg/day is recommended for 3 weeks. Potential benefits of corticosteroids have been reported in the literature though the lack of large randomized controlled trails make conclusive recommendations difficult. Benefits may include a shortened duration of abdominal pain and a decreased risk of renal involvement and disease recurrence if administered early. A more recent meta-analysis (Cochrane, 2015, PubMed ID: 26258874) did not demonstrate a benefit or corticosteroids or other interventions on long-term renal function. Severe colitis may limit absorption of oral corticosteroids and parenteral administration may be indicated. Surgical reduction is necessary for ileo-ileal intussusception.

PROGNOSIS

HSP is a self-limited illness. Waves of purpura lasting 5-10 days can recur until complete resolution in 4-6 weeks. HSP recurs in almost one third of children. Recurrence is often milder and more common in those who experienced a more severe initial course. The disease usually recurs within 4-6 months can recur years later. End-stage renal disease develops in 8% of children with nephritis at time of presentation and chronic renal disease occurs in a total of 1-2% of all those diagnosed with HSP. Close nephology follow-up is essential.

KAWASAKI DISEASE

INTRODUCTION (KELLY CLEARY M.D., 5/2020)
Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is an acute, self-limited vasculitis of childhood. Tomisaku Kawasaki first described it in Japan in 1967. KD is an idiopathic vasculitis of small and medium-sized vessels, and is the leading cause of acquired heart disease in children in the developed world.

Although most prevalent in children of Japanese ethnicity (annual incidence is about 150 cases per 100,000 children younger than 5 years old), the disease spans all races. The incidence is higher in boys (3:2) and approximately 76% of cases are in children younger than 5 years old. There is a suggested genetic predisposition with the risk of occurrence in twins at approximately 13%.

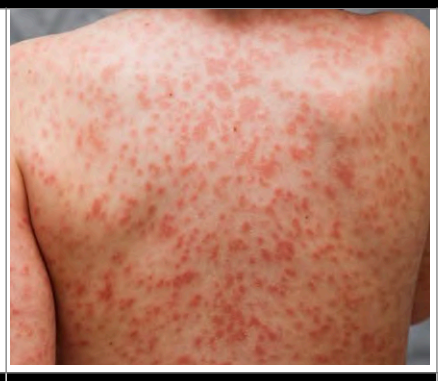
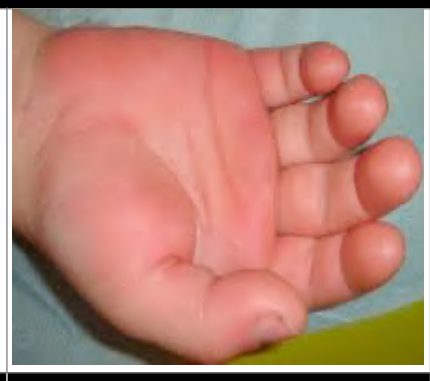
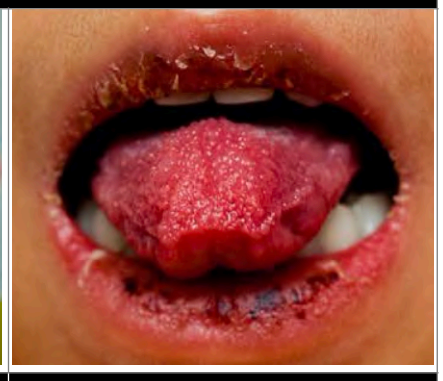
The cause of KD remains unknown. As in other vasculitides, blood vessel damage is secondary to an aberrant immune response. The fact that the disease occurs in epidemics and has been reported in household contacts suggests an infectious, transmissible etiology. Immunoglobulin A plasma cells play a central role and have been found in abundant quantities in the respiratory tract of patients with fatal KD; implicating a possible respiratory pathogen. However, no pathogen has been identified.

Early signs of vasculitis are seen in large muscular arteries with an influx of neutrophils in initial stages. This is quickly transitioned into large mononuclear cells such as lymphocytes and IgA plasma cells. The period of active inflammation is gradually replaced to progressive fibrosis over the course of weeks to months.

CLINICAL MANIFESTATIONS
The generalized vasculitis can manifest itself as signs and symptoms throughout the body. No signs or symptoms are specific to KD. The AAP/AHA diagnostic criteria are based on evidence as well as consensus opinion.

DIFFERENTIAL DIAGNOSIS	
INFECTIONS	RHEUMATOLOGIC
Cervical Adenitis (Bacterial)	Acute Rheumatic Fever*
Leptospirosis	Mercury Hypersensitivity Reaction
Measles*, Adenovirus, Enterovirus, EBV*	Polyarteritis nodosa
Rocky Mountain Spotted Fever*	Sarcoidosis
Staphylococcal Scalded Skin Syndrome*	Serum Sickness
Streptococcal Scarlet Fever	Stevens-Johnson Syndrome*
Toxic Shock Syndrome*	Systemic Onset Juvenile Immune Arthritis
*Reviewed in detail in a separate PEM Guide	

DIAGNOSTIC CRITERIA*	
1. Fever for at least 5 days (usually high and unremitting despite antipyretics) 2. Four of the five following criteria 3. No alternative explanation	
Cervical Lymphadenopathy (25-70%)	Usually unilateral, confined to the anterior cervical triangle over the sternocleidomastoid muscle and greater than 1.5 cm in diameter. Up to half of children with KD do not have lymphadenopathy
Conjunctivitis (> 75%)	Bilateral, bulbar, limbic sparing, non-exudative. Usually painless. Begins shortly after the onset of fever
Polymorphous rash (70-90%)	Most often appears within 5 days of the onset of fever. The most common rash is a scattered, erythematous maculopapular rash. The rash may be pronounced in the perineal area and may involve desquamation. Other rashes may include: urticarial, scarlatiniform, erythema multiforme, or erythroderma. Bullous and vesicular lesions are not commonly seen in KD. If these are present, alternative diagnoses should be considered.
Extremity changes (50-85%)	Acute: Includes erythema and edema of the palms and soles Subacute: Desquamation of the digits of the hands/feet. Desquamation is a late finding that usually occurs 2-3 weeks after the fever onset.
Oral mucous membrane changes	Includes strawberry tongue, fissured lips, injected pharynx
*AAP/AHA 2004, PubMed ID: 28356445	

PHYSICAL EXAMINATION CRITERIA			
			
CONJUNCTIVITIS	RASH	EXTREMITIES	MUCOUS MB

OTHER KAWASAKI FINDINGS	
Cardiac	Congestive heart failure, myocarditis, pericarditis, coronary artery abnormalities, valvular insufficiency, aneurysms of medium size non-coronary arteries, Raynaud's, peripheral gangrene
Musculoskeletal	Arthralgias, arthritis
Gastrointestinal	Vomiting, diarrhea, abdominal pain, hepatic dysfunction, hydropic gall bladder
Central Nervous	Extreme irritability, aseptic meningitis, sensorineural hearing loss,
Genitourinary	Urethritis, meatitis
Hematology	Infants: thrombocytopenia, disseminated intravascular coagulation
Other	Anterior uveitis (mild) Desquamating rash in groin Erythema, induration at BCG site

INCONSISTENT WITH KAWASAKI
Exudative conjunctivitis
Exudative pharyngitis
Discrete intraoral lesions
Bullous or vesicular rash
Generalized adenopathy

LABORATORY EVALUATION

No laboratory studies are included in the diagnostic criteria for typical KD but they can be used to support the diagnosis of both typical and atypical KD.

LABORATORY FINDINGS SUPPORTIVE OF KD	
CBC	WBC: > 15,000 with a left shift
	Thrombocytosis: 500-1,000K (after seven days of illness)
	Anemia: Normocytic, normochromic
APR*	CRP > 3, ESR > 40 (*Acute Phase Reactants)
LFT	Mild-moderate transaminitis: Alanine aminotransferase > 50 U/L
	Hypoalbuminemia: < 3 gm/dl
	Hyperbilirubinemia: Obstructive jaundice due to hydropic gallbladder
UA	Sterile pyuria: > 10 WBC/HPF
CSF	CSF Pleocytosis: Mononuclear cell predominance
BMP	Hyponatremia
OTHER	Hyperlipidemia, synovial fluid leukocytosis

ECHOCARDIOGRAPHY

Echocardiography is used for the assessment of cardiac involvement but should not delay the initiation of treatment. The most common site of aneurysm includes the proximal left anterior descending coronary artery and the proximal right coronary artery. Approximately 1/3 of patients of patients will have evidence of coronary dilation at the time of presentation. Coronary aneurysms are not typically apparent until day 10 of illness. The absence of coronary artery disease on presentation does not exclude the diagnosis of KD or preclude the later development of coronary aneurysms. Some degree of myocarditis is almost universal in patients with KD.

ECHOCARDIOGRAPHY FINDINGS
Coronary Arteritis: Perivascular brightness, ectasia, lack of tapering
Decreased left ventricular contractility
Mild valvular regurgitation: Primarily involving mitral valve
Pericardial effusion

MANAGEMENT

The current standard treatment for KD is a combination of high dose aspirin and intravenous immune globulin (IVIG). A 1984 trial in Japanese children reported that those treated with IVIG had a faster resolving fever and developed fewer coronary abnormalities than controls (Furusho, Lancet 1984, PubMed ID: 6209513) A multicenter randomized trial in the US showed that the combination of IVIG and Aspirin (ASA) had a faster resolution of fever and reduced coronary abnormalities by 85% when compared to treatment with ASA alone (Newberger. NEJM 1986, PubMed ID: 2426590).

TREATMENT INDICATIONS
Fever x 5 days with ≥ 4 principle criteria
Fever x 5 days with < 4 principle criteria and coronary aneurysm on echocardiogram
Fever x 4 days with ≥ 4 principle criteria
Infants ≤ 6 months, fever ≥ 7 days with (+) inflammatory markers should have an echocardiogram even if no other features are present
Atypical KD (See Appendix): Fever x 5 days AND 2 or 3 principle criteria AND other clinical findings consistent with KD AND ≥ 3 supplemental lab criteria
Atypical KD (See Appendix): Fever x 5 days AND 2 or 3 principle criteria AND other clinical findings consistent with KD AND < 3 supplemental lab criteria AND ECHO (+) for coronary aneurysm

ASPIRIN: Aspirin can be administered as high dose ASA (80-100 mg/kg/day divided Q6H in the US) or moderate dose ASA (30-50 mg/kg/day divided Q6H in Japan and Western Europe). There no data that demonstrates the superiority of either aspirin dosing regimen. Aspirin is continued either until after the child has been afebrile for 2-3 days or for 14 days AND the child has been afebrile for 2-3 days. Low dose aspirin (3-5 mg/kg/day divided Q6H) is continued until 6-8 weeks if there are no cardiac abnormalities on repeat echocardiogram. Parents should receive proper instructions on how to recognize the development of rash or fever while on ASA therapy given the risk of Reyes syndrome if infected with varicella or influenza.

INTRAVENOUS IMMUNE GLOBULIN: IVIG appears to have an anti-inflammatory effect. The therapy should be initiated within the first 10 days of illness to provide maximal efficacy (though it should still be given if a child presents after day 10). Even if IVIG is given within the 1st 10 days of fever, 5% of patients will go on to develop some coronary artery dilatation and 1% will develop giant aneurysms.

CORTICOSTEROIDS: Steroids have typically been reserved for patients who remain febrile despite 2 IVIG infusions (refractory KD). A meta-analysis of 16 trials including 2,746 patients (Dong, JAMA Pediatrics 2016, PubMed ID: 27749951) demonstrated significant reduction in the development of coronary artery anomalies in those treated with Corticosteroids and IVIG as initial therapy when compared to those treated with IVIG alone (Odds Ratio: 0.424, 95% CI (0.270, 0.665) and to those treated with IVIG with corticosteroids used as rescue therapy (Odds Ratio: 0.32, 95% CI (0.18, 0.56)).

This effect was most pronounced in patients assessed as high risk of resistance (Odds Ratio: 0.24, 95% CI (0.12, 0.47)). High risk was defined by 3 different Japanese scoring systems that have low sensitivity in US populations. It is unclear if a benefit remained when analyzing the subgroup of patients that were not at high risk of resistance. There was also an inverse relationship between the efficacy of corticosteroids and time to initiation. Methylprednisolone 30 mg/kg for 2 to 3 hours, administered once daily for 3 days.

MEDICATION DOSES	
Aspirin	80-100 mg/kg/day divided Q6H (US) 30-50 mg/kg/day divided Q6H (Japan, Western Europe)
IVIG	2 grams/kg in a single infusion (May be repeated if persistently febrile)
Steroids	Methylprednisolone: 30 mg/kg IV over 2-3 hours, once daily for 3 days.

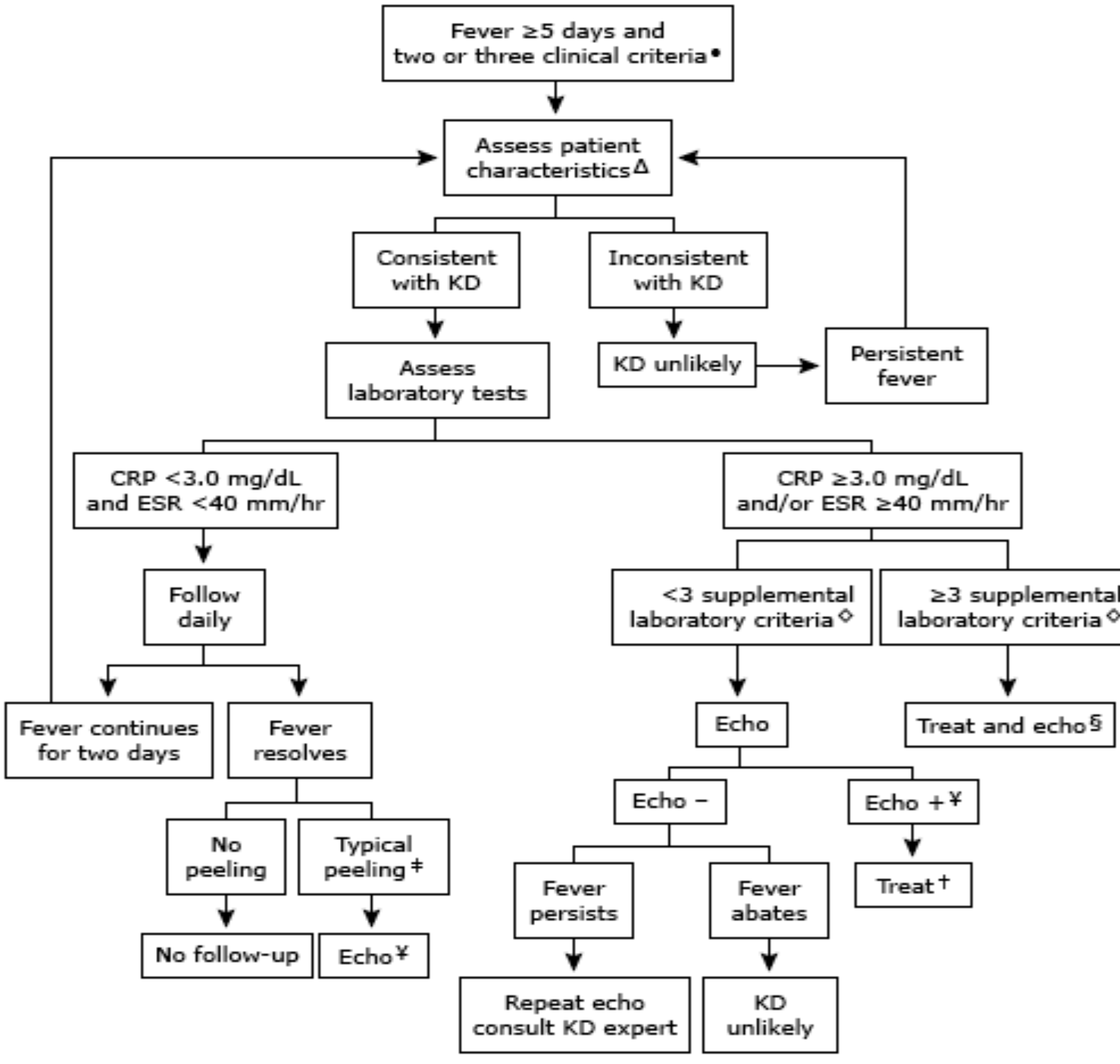
FOLLOW-UP/OUTCOMES

Coronary artery aneurysms occur in 20-25% of untreated patients. Coronary artery dilatation < 8 mm generally regresses over time. Patients with giant aneurysms (diameter > 8 mm) are at greatest risk for myocardial infarction from coronary artery occlusion.

Other cardiovascular complications include myocarditis, pericarditis, valvulitis (most often involving the mitral valve). Echocardiography should be performed at the time of diagnosis, then at 2 weeks and 6 weeks. Treatment is then individualized according to risk levels, recommended by the American Heart Association. Patients with no cardiovascular abnormalities on echo during the acute and subacute phases appear to be clinically asymptomatic 10-21 years later. However, because the long-term risk of cardiovascular sequelae is unknown, patients are still counseled on hypertension, diet, and exercise because of the suspected increased risk for atherosclerotic disease.

APPENDIX: AAP/AHA ALGORITHM: ATYPICAL/INCOMPLETE KAWASAKI

Children suspected of having KD but do not fulfill diagnostic criteria (i.e. have less than 4 signs of mucocutaneous inflammation) may have incomplete or atypical KD. 10% of patients who develop coronary aneurysms never meet criteria for KD. Incomplete KD may be associated with an increased risk of coronary aneurysms.



ΔPATIENT CHARACTERISTICS

1. SEE TABLE OTHER KAWASAKI FINDINGS

SUPPLEMENTAL LABORATORY CRITERIA

1. Albumin ≤ 3.0 gram/dl
2. Anemia for age
3. Elevation of Alanine Aminotransferase (ALT)
4. Platelets > 450,000/mm3 after 7 days
5. WBC ≥ 15,000 /mm3
6. Urine ≥ 10 WBC/HPF Urine ≥ 10 WBC/HPF

MIS-C

(MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN)

INTRODUCTION (MICHAEL MOJICA, MD, 3/2023)
In 2020, there were reports from the Europe of disease in children related to COVID-19 exposure with elements of both Kawasaki disease and toxic shock syndrome. That constellation of signs and symptoms was eventually called multisystem inflammatory syndrome in children (MIS-C). The syndrome is rare, but the true incidence in exposed patients is unknown. The mean age of MIS-C has decreased and it is currently most common in those less than 5 years of age. Older children and adults have also been affected. MISC-C occurs disproportionately in Black and Hispanic children. It is unclear is this is due to genetic or other biologic factors or a higher rate of exposure to COVID-19 in their communities. Patients with MIS-C have predominately cardiac, gastrointestinal and mucocutaneous signs and symptoms.

The diagnosis and management of MIS-C will change as we gain more experience with these patients and the evidence base grows. In unvaccinated Danish children, the risk of MIS-C during the Omicron wave was significantly less than the Delta wave (RR, 0.12; 95% CI (0.06, 0.23)) and wild-type wave (RR, 0.14; 95% CI (0.07, 0.29)). However, the phenotype of MIS-C remained similar (Holm, JAMA Peds 2022, PubMed ID: 35675054).

CLINICAL MANIFESTATIONS
In patients with a known COVID-19-19 exposure or disease, the onset of MIS-C symptoms is typically 2-6 weeks after COVID-19. Many are asymptomatic at the time of exposure. There is a wide spectrum of MISC-C disease severity. These have been categorized as a febrile inflammatory state (fever, elevated inflammatory markers but lacking severe multisystem involvement), a Kawasaki disease like illness (meeting complete or incomplete KD criteria without shock and severe multisystem involvement) and severe MIS-C (markedly elevated inflammatory markers and severe multisystem involvement commonly including cardiogenic shock). Most patients present with 3-5 days of fever. Systemic symptoms such as fatigue and myalgias are common.

CARDIAC: Cardiac manifestations include carditis, pericarditis, arrhythmias and cardiogenic shock. In a systematic review of 39 cases series (n=662 patients), 54% had an abnormal echocardiogram, 52.3% received vasoactive medications and 4.4% were started on ECMO (Ahmed, E Clin Med 2020, PubMed: ID: 32923992).

MUCOCUTANEOUS: Rash is polymorphic, maculopapular or petechial and not vesicular. Mucous membrane finding can include: dry and chapped lips, strawberry tongue and a bulbar, non-exudative conjunctivitis. The hands and feet may be swollen. These signs are very similar to those seen in Kawasaki disease.

GASTROINTESTINAL: Gastrointestinal symptoms are common and include nausea, vomiting, diarrhea and abdominal pain. Abdominal pain may mimic appendicitis and patients with imaging can demonstrate terminal ileitis.

LABORATORY TESTING
Abnormal laboratory findings in MIS-C include abnormalities of blood cell counts, inflammatory markers, cardiac enzymes and hepatic and hematologic function. The degree of elevation of inflammatory markers correlates with disease severity. Patients should be tested for evidence of COVID exposure or disease and more common causes of fever such as infections, rheumatologic and oncologic disease.

COVID TESTING: Over 90% of patients have COVID-19 antibodies at the time of MIS-C presentation and less than half were COVID-19 PCR positive. Approximately 5-10% have negative PCR and antibody testing. As the pandemic continues and exposure grows, many children may have incidental elevation in antibody titers.

LABORATORY FINDINGS	
ABNORMAL BLOOD COUNTS	INFLAMMATORY MARKERS
Lymphopenia (ALC < 1,000/mm^3)	↑ CRP
Mild anemia	↑ D-Dimer
Neutrophilia	↑ ESR
Thrombocytopenia (< 150,000/L)	↑ Ferritin
OTHER	↑ Fibrinogen
Coagulopathy: PT/PTT, INR	↑ Interleukin 6
↑ Lactate Dehydrogenase	↑ Procalcitonin
↑ Liver Transaminases (mild)	ELEVATED CARDIAC MARKERS
Hypertriglyceridemia	BNP (+) or N-terminal pro BNP (+)
Hypoalbuminemia	Troponin (+)
Hyponatremia (< 135 meq/L)	

IMAGING

ECHOCARDIOGRAPHY: Significant cardiac involvement distinguishes MIS-C from primary COVID-19 infection. Abnormalities on echocardiography include decreased left ventricular contractility, coronary abnormalities (dilation or aneurysm), mitral valve regurgitation and pericardial effusion. Ventricular dysfunction is seen in approximately 50% (None: 50%, Mild 25%, Moderate 12.5%, Severe 12.5%).

Less than one-fifth of patients have coronary artery abnormalities (Mild: 90% Moderate: <10%). None had large or giant aneurysms. At 90 day follow up, nearly all with cardiac involvement had returned to normal function and coronary artery size. Compared to Kawasaki disease, MISC-C cardiac abnormalities have a higher rate of ventricular dysfunction and a lower rate or coronary artery abnormalities. Cardiac MRI is an alternative or supplement to echocardiography. EKG findings primarily included ST and T waves changes (consistent with myocarditis) but may also include arrhythmias (first degree heart block is most common).

OTHER IMAGING: Chest XRAYS are typically normal in MIS-C. Pleural effusions are more common in MIS-C than acute, severe COVID. Chest CT findings most commonly include ground glass opacities. Abdominal imaging findings are reflective of the inflammatory state and serositis.

OTHER IMAGING FINDINGS	
CHEST	ABDOMEN
Atelectasis	Ascites
Ground glass appearance (CT)	Bowel or mesenteric inflammation
Patchy or focal consolidation	Mesenteric adenitis/adenopathy
Pleural effusions	Pericholecystic edema

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of MIS-C is broad and includes many infectious, oncologic and rheumatologic diagnoses. The identification of an alternative diagnosis can reduce the likelihood of but not exclude MIS-C. See also: PEM Guide: Dermatology: Toxic Shock Syndrome

WEB LINK: NON-STREPTOCCOCAL TOXIC SHOCK (CDC CRITERIA 2011)

WEB LINK: STREPTOCOCCAL TOXIC SHOCK SYNDROME (CDC CRITERIA 2010)

Approximately half of patients with MIS-C meet criteria for complete or incomplete Kawasaki disease (See PEM Guide: Rheumatology: Kawasaki Disease). It is particularly difficult to distinguish MIS-C from Kawasaki disease shock syndrome. MISC-C also has considerable overlap with severe, acute COVID.

DIFFERENTIAL DIAGNOSIS: INFECTIOUS	
BACTERIAL	VIRAL
Bacterial Sepsis*	Adenovirus
Lymphadenitis	Cytomegalovirus
Pyelonephritis*	Epstein-Barr virus*
Rickettsial: Lyme disease*/RMSF*	Herpangina*
Streptococcal pharyngitis*	Human metapneumovirus
Toxic shock syndrome* (See appendix)	Severe acute COVID-19
*Reviewed in detail in a separate PEM Guide	

DIFFERENTIAL DIAGNOSIS: NON-INFECTIOUS
Appendicitis*, Intussusception*
Hemophagocytic lymphohistiocytosis (HLH) /Macrophage activation syndrome (MAS)
Kawasaki disease*
Systemic lupus erythematosus (SLE): Renal, CNS more common, longer onset *
Vasculitis
*Reviewed in detail in a separate PEM Guide

MIS-C COMPARISONS	
MIS-C vs Kawasaki Disease	MIS-C vs Severe, acute COVID-19
Age: Older	Age: Younger
Ethnicity: Black or Hispanic > Asian	PMHx: Healthy at baseline
Clinical: ↑ GI, cardiogenic shock, neuro	Clinical: ↑ GI, cardiac, mucocutaneous
Lab: ↑ Inflammatory markers	Clinical: ↓ Primary pulmonary disease
Lab: ↓ Cell counts (ALC, platelets)	Lab: ↑ Inflammatory markers, antibodies

DIAGNOSTIC CRITERIA

CDC CASE DEFINITION: The 2020 CDC case definition was intentionally broad but lacked specificity. The definition was revised in 2023 based on new evidence and expert consensus opinion. These criteria were tested against over 8,800 cases meeting 2020 criteria for MIS-C and are intended to reduce complexity and improve specificity.

MIS-C CDC CASE DEFINITION: INCLUSION CRITERIA (2023)	
CLINICAL CRITERIA (ALL REQUIRED)	
Age	< 21 years
Fever	> 38C (100.4 F) of any duration
Illness Severity	Requiring hospitalization or resulting in death
Alternative Diagnosis	A more likely diagnosis is not present (e.g. Kawasaki disease)
Laboratory	Inflammation markers: CRP ≥ 3.0 mg/dL (30 mg/L)
Organ System Involvement	≥ 2 Required
1. Cardiac	Left ventricular ejection fraction < 55%
	Coronary artery dilation, aneurysm or extasia
	Troponin elevated above normal range
2. Shock	Clinical Diagnosis
3. Hematologic	Thrombocytopenia: Platelet count < 150,000 cells/microL
	Absolute Lymphocyte Count < 1,000 cells/microL
4.Gastrointestinal	Abdominal pain
	Vomiting
	Diarrhea
5. Dermatologic/Mucocutaneous	Rash
	Inflammation of the oral mucosa
	Conjunctivitis or conjunctival injection
	Extremity findings
LABORATORY TESTING OR EPIDEMIOLOGIC LINKAGE CRITERIA	
Laboratory Testing	Positive viral test (NNAT, PCR or Antigen) within 60 days
	Detection of SARS-COVID specific antibodies[1]
Epidemiologic Linkage	Close contact with confirmed or probable case within 60 days
WEB LINK: CDC CASE DEFINITION (2023) Confirmed MIS-C: Meets clinical criteria AND the laboratory evidence Probable MIS-C: Meets clinical criteria AND the epidemiological linkage criteria 1. Anti-nucleocapsid antibody: Indicative of SARS-CoV-2 infection Anti-spike protein antibody: Indicative of SARS-CoV-2 infection or COVID vaccination	

MANAGEMENT

The goals of therapy are to stabilize like-threatening manifestations and prevent long term sequela. The optimal treatment of MIS-C is unknown. Evidence is limited primarily to observational studies. Management and disposition decisions should be made in conjunction with a team of pediatric subspecialists including critical care, rheumatology, infectious disease, cardiology, hematology, renal and pulmonary depending on the severity of symptoms and organ systems involved.

SUPPORTIVE CARE: Antibiotics should be initiated for suspected sepsis or toxic shock syndrome and for bacterial co-infections (e.g. bacterial lymphadenitis). Fluid resuscitation is often required with careful and repeated assessment for signs of fluid overload in patients with cardiac, respiratory or renal involvement. Cardiogenic shock should be managed with inotropes such as low dose Epinephrine and Milrinone. ECMO may be required for hemodynamically instability refractory to vasoactive infusions.
See: PEM Guide: Cardiology: Cardiogenic Shock

IMMUNOMODULATORS: The mainstay of therapy for MIS-C is intravenous immune globulin with or without corticosteroids. A step-wise approach to immunomodulatory therapy is recommended. Biologics and high dose corticosteroids may be indicated for refractory disease. Antivirals may be indicated in patients who are COVID PCR positive. Venous thromboembolism prophylaxis should be initiated in those at high risk in consultation with pediatric hematology.

GLUCOCORTICOIDS: A review of 3 observational studies including over 1,200 patients concluded that IVIG with corticosteroids were associated with a reduced need for additional immunomodulatory therapy and in 2 of the 3 studies demonstrated that IVIG with corticosteroids reduced the need for hemodynamic support when compared to IVIG alone (Ouidali, JAMA 2021, PubMed: 33523115).

OTHER: Addition biologics such as inhibitors of Interleukin-1 (e.g. Anakinra), Interleukin-6 and tumor necrosis factor may also be indicated for disease refractory to IVIG and corticosteroids . The majority of patients are COVID PCR negative. Remdesivir may be indicated in those who are COVID PCR positive. Decision on the use of biologics and antivirals should be made in consultation with pediatric infectious disease.

VTE PROPHYLAXIS: Patients with MIS-C have laboratory markers indicating a complement-mediated thrombotic microangiopathy. In a case series of 814 patients with MIS-C, thrombotic complications occurred in 6.5%. Patients at increased risk of thrombotic complications included those with central venous catheters, oncologic disease, Blacks and Hispanics and those with elevated d-dimers. Low dose aspirin (3-5 mg/kg/day. Max 81 mg/day) can be used as thromboembolic prophylaxis.
Patients with severe left ventricular dysfunction, large or giant coronary aneurysms, severe disease requiring PICU admission and patient with current or prior VTE require anticoagulation with low molecular weight heparin. This excludes patients with ongoing bleeding, significant coagulopathy or thrombocytopenia. Pediatric Hematology should be consulted.

INTRAVENOUS IMMUNE GLOBULIN (IVIG)	
Indications	All admitted with moderate-severe MIS-C
	Sufficiently high suspicion of MIS-C to be admitted: Persistent fever, significantly elevated inflammatory markers and elevated d-dimer
	Meeting criteria for complete or incomplete Kawasaki disease
Dose	IVIG: 2 grams/kg (maximum 100 grams) over 8-12 hours
	Duration of therapy may be longer in cardiogenic shock and renal dysfunction with signs of fluid overload (1 gram/kg/day x 2 days)
Testing	COVID and other infection serology should be obtained before IVIG
	IVIG → ↑ ESR, cannot be used to assess disease progression

GLUCOCORTICOIDS	
Indications	All with moderate to severe MISC-C OR
	Mild MIS-C without clinical or laboratory improvement with IVIG alone
Dose	Methyl prednisolone 2 mg/kg/day IV divided Q6H-Q12H. Up to 30 mg/kg/day for refractory disease
	With clinical and laboratory improvement, can we transitioned to oral Prednisone/ Prednisolone to continue for 2-4 weeks and tapered.

DISPOSITION

Disposition decisions should be made on the basis of severity or illness, risk of complications and adequacy of follow up. Those with moderate to high suspicion of MIS-C should be admitted for treatment and to monitor for disease progression. Those under investigation but of low suspicion for MIS-C, clinically well appearing, hemodynamically stable with a clear alternative diagnosis could potentially be discharged with closed follow-up though risk factors for severe disease progression and clinical decompensation have not been established.

Patients with signs of cardiac, respiratory, renal, hepatic, neurologic and hematologic (coagulopathy) dysfunction should be admitted to a pediatric ICU. Telemetry to monitor for arrhythmias is required in patients and cardiac disease including those with left ventricular dysfunction, positive cardiac markers and coronary artery abnormalities.

DISPOSITION	
ADMIT ALL	ADMIT “UNDER INVESTIGATION’
Shock	Abnormal vital signs
Significant respiratory distress	Any respiratory distress
Neurologic: Altered mental status, focal	Neurologic: Deficits or altered mental status
Deficits, encephalopathy, meningitis	Evidence of mild renal or hepatic injury
papilledema	Inflammatory markers e.g. CRP >10 mg/dl
Dehydration	Abnormal EKG, Elevate BNP or Troponin
Features of Kawasaki disease	
American College of Rheumatology (11/2020): PubMed ID: 32705809	

PROGNOSIS

A study of 46 patients found resolution of cardiac disease and systemic inflammation within 6 weeks. At 6 months many patients remained weak with exercise intolerance, anxiety and emotional difficulties (Penner, Lancet Child Adol Health 2021, PubMed ID: 34043958).

NEONATAL LUPUS

INTRODUCTION (MICHAEL MOJICA, MD, 8/2020)
Neonatal lupus (NL) is an autoimmune disease related to passive placental transfer to the fetus of maternal IgG autoantibodies associated with Lupus and Sjogren's disease .
Approximately 40% of women with Lupus and 60-100% with Sjogren's possess these antibodies. However, mothers may not have previously manifested clinical signs or symptoms of Lupus or Sjogren's disease though up to 50% may later develop clinical manifestations. Only 2% of first infants or infants with previously healthy siblings will develop neonatal lupus in mothers with these autoantibodies. In contrast, the risk of developing neonatal lupus is 20% if a previous sibling had neonatal lupus.

The primary clinical manifestation are cutaneous and cardiac though may also involve the hematologic, gastrointestinal and neurologic systems. These manifestation can occur in utero, at delivery or later in the neonatal period. Complete heart block can be life-threatening. Cutaneous, hematologic and gastrointestinal manifestation resolve when maternal antibodies are cleared. In contrast, cardiac manifestation are typically permanent. Less than 5% of those with neonatal lupus develop lupus in later life. This PEM Guide focuses on the diagnosis and management of neonatal lupus in the newborn period.

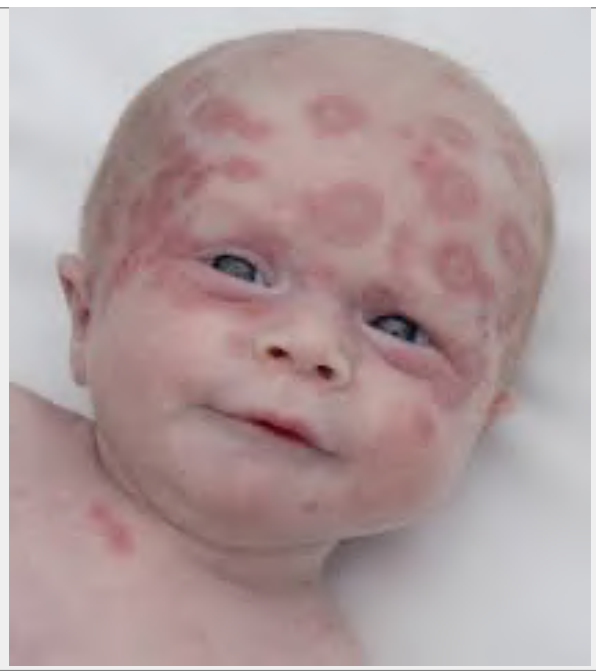
PATHOPHYSIOLOGY
Heart block is thought to be related to the placental transfer of anti-Ro/SSA and or anti-LA/SS (SSB: Sjogren system type A and B antigen). While the exact mechanism of injury is unknown, it is thought that these autoantibodies elicit an inflammatory process leading to fibrosis of the atrioventricular node and/or may effect cardiac calcium channels. Fetal genetic and environmental factors likely play an important role in disease development.

CLINICAL MANIFESTATIONS
Clinical manifestations of neonatal lupus may occur in the skin (40%), heart (25%), hepatic (35%), hematologic (35%) and neurologic (rare) systems. Cardiac manifestation include conduction abnormalities, valvular disease, fibroelastosis and cardiomyopathy. Conduction abnormalities can include any degree of heart block. Complete (3rd degree) heart block is the most common and potentially life-threatening. Neonatal lupus is the most common cause (80-95%) of complete heart block in infants with structurally normal hearts.

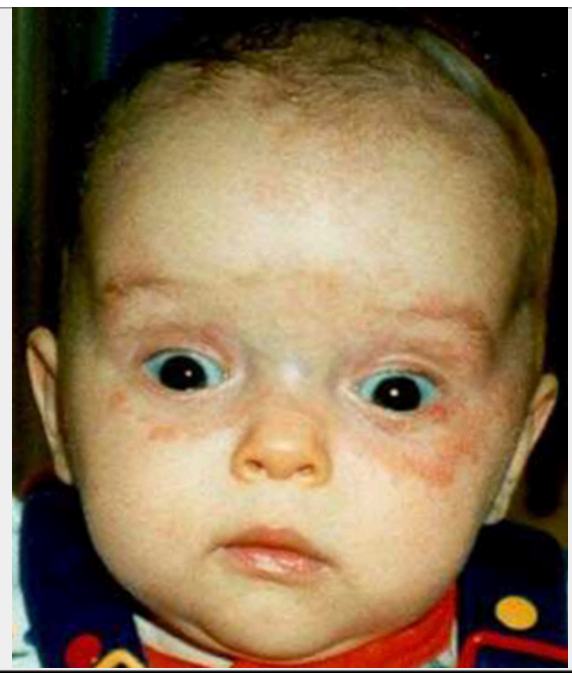
Newborns and neonates with cardiac manifestations can present with bradycardia and signs/symptoms of cardiogenic shock (hypotension, poor perfusion, and fluid overload (hepatomegaly and pulmonary edema)). Cardiogenic shock is most often due to complete heart block. Complete heart block, cardiomegaly, atrioventricular valve regurgitation and hydrops fetalis have been associated with a poor prognosis. (See PEM Guide: Cardiology: Cardiogenic Shock).

CARDIAC MANIFESTATIONS
HEART BLOCKS (Develops at 18-26 weeks in utero)
AV Node Dysfunction: 1st, 2nd or 3rd degree heart blocks
Bradycardia: 2nd/3rd degree heart block
Cardiogenic Shock: 3rd degree (may be life-threatening)
3°: No AV node conduction (dissociation), Atria: Normal rate, Ventricles: 50-80 bpm
SA Node Dysfunction: Rare, present with sinus bradycardia
OTHER CARDIAC (Rare)
Structural/Valvular[1]: ASD, VSD, PDA, PFO, PS, tricuspid chordae tendinea fusion
Endocardial fibroelastosis
Dilated cardiomyopathy
Myocarditis
QT interval prolongation
Aortic dilation
1. Structural heart lesions may be associated with heart block independent of NL. It is difficult to determine if the heart defect or NL is the cause of the heart block

DERMATOLOGIC MANIFESTATIONS
Present in 20% at birth, 80% within the 1st month
Resolves within 6-8 months without sequelae when maternal antibodies cleared
Photosensitive, after exposure to UV light, primarily head and scalp
1. Erythematous, annular/arcuate, raised border, central atrophy, scalp/periorbital
2. Scaly, erythematous, reticular lesions, periocular ± diaper area, palms/soles
3. Telangiectasias, face/genitals, only manifestation or in areas of prior NL rash



1. ANNULAR/ARCUATE LESIONS



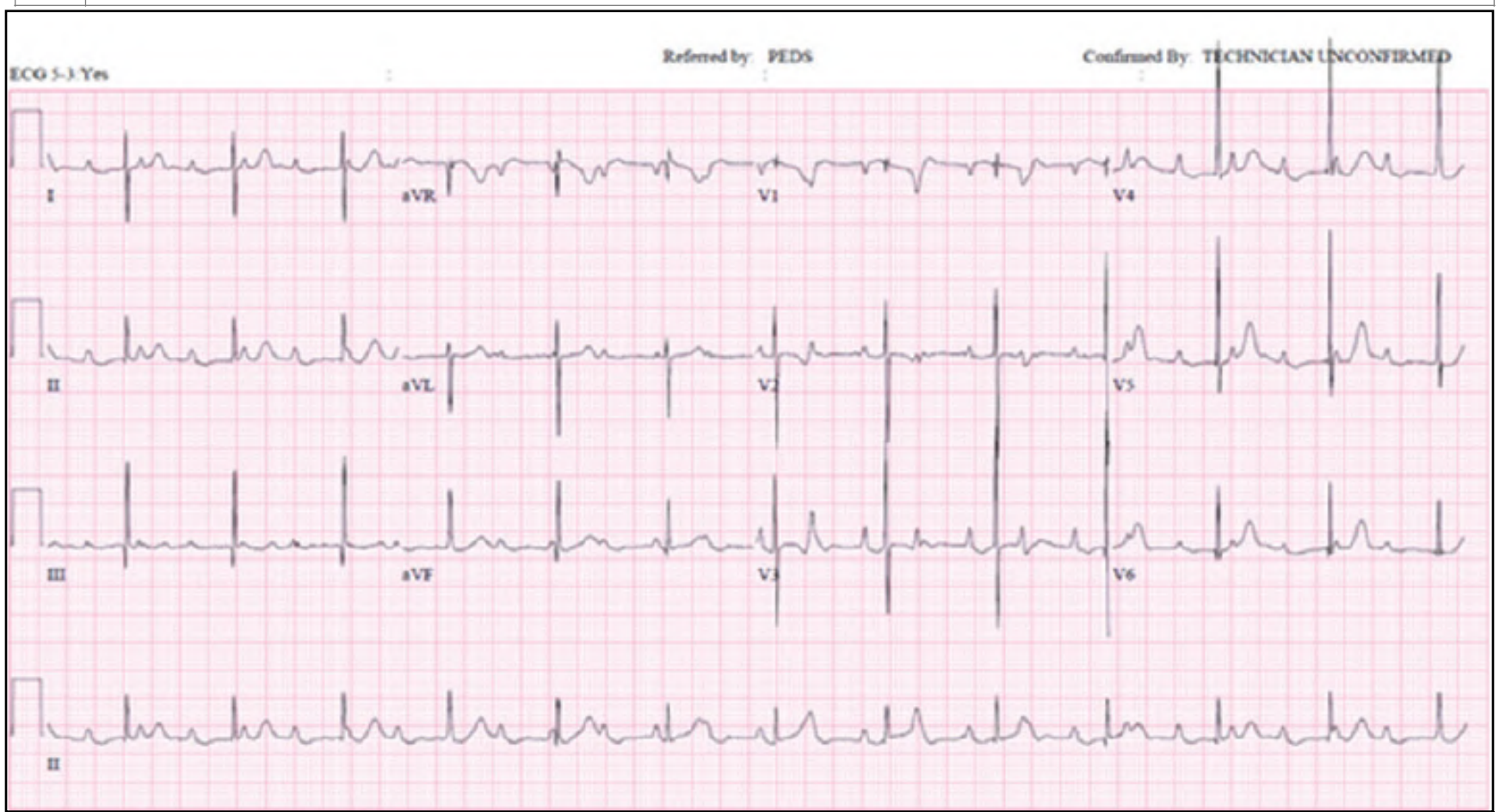
2. SCALY, RETICULAR LESIONS

OTHER CLINICAL/LABORATORY MANIFESTATIONS	
Hydrops fetalis	Accumulation of excess fluids due to complete heart block
Hematologic	Anemia, thrombocytopenia, neutropenia
GI	Hepatitis, cholestasis, mild hepatosplenomegaly
Neurologic	Hydrocephalus, macrocephaly
Skeletal	Chondrodysplasia punctate: XRAY with Epiphyseal stippling
Adrenal	Adrenal insufficiency: Treated in utero with fluorinated steroids

DIAGNOSIS

The diagnosis of neonatal lupus is made on the basis of clinical manifestations, EKG, and laboratory testing (maternal antibodies, CBC, LFTs). An echocardiogram should performed to identify structural

DIAGNOSIS	
1	Heart block or typical rash or hepatic or hematologic manifestations of neonatal lupus in the absence of other explanation
2	Maternal antibodies: anti-Ro/SSA, anti-La/SSA, possibly anti-ribonucleoprotein



EKG FINDINGS: 3rd degree Heart Block (AV Dissociation): Atrial > Ventricular Rate

DIFFERENTIAL DIAGNOSIS

BRADYCARDIA: DIFFERENTIAL DIAGNOSIS	
Inflammation: Viral, autoimmune	Medications
Myocarditis*, Pericarditis*	HTN: Clonidine*, Beta blockers*
Lyme*, acute rheumatic fever*	Ca^{++} channel blockers*,
Bacterial endocarditis, syphilis	Rhythm: Amiodarone, Digitalis, Adenosine
Myocardial infarct/ischemia	Other: Cholinergic agents*
Collagen vascular disease	Increased vagal tone
SLE*, neonatal SLE*, dermatomyositis	Breath holding*, cough
Congenital heart disease	Esophageal/Oral stimulation: intubation*
ASD, AV Canal*, VSD, TGV*, PS*	Increased intracranial pressure*
Congenital conduction abnormality	Cardiac surgery: Atrial
Prolonged QT, WPW	Electrolytes: Hyperkalemia*
Respiratory failure*: Hypoxia, acidosis	Hypothermia*
*Discussed in detail in a separate PEM Guide	

DIFFERENTIAL DIAGNOSIS: SIMILAR NEONATAL RASHES
Annular erythemas: e.g. erythema multiforme, migrating course, peripheral lesions
Autoinflammatory disorders: Fever, multisystem involvement
Cutis Marmorata Telangiectasia Congenita: Later age of onset, unilateral limbs
Langerhans's cell histiocytosis: Multisystem disease, variable rash
Seborrheic dermatitis: Yellow greasy scales, salmon colored plaques
Tinea corporis: Scaly border, (+) KOH prep
Urticaria: Raised center, evanescent

MANAGEMENT

Infants and young children are particularly at risk from bradycardia as their cardiac output is driven to a greater degree by heart rate than by contractility. They have little contractile reserve when compared to older children and adults. They present with nonspecific symptoms such a poor feeding or lethargy. Pediatric cardiology and pediatric rheumatology should be consulted for all patients with clinically suspected neonatal lupus and for all patients with mothers with the causative antibodies.

NEWBORN RESUSCITATION: The sequence of interventions for the newborn are listed in the table below and in the Newborn Resuscitation Program Algorithm (see Appendix). The decision to begin resuscitation is based on the assessment of both respirations (apnea, gasping, or labored breathing) and heart rate. The best guide to a successful resuscitation is an improvement in heart rate.
(See: PEM Guide: Resuscitation: Neonatal Resuscitation)

WEB LINK: NEONATAL RESUSCITATION ALGORITHM (AHA 2020)

NEONATAL INTERVENTIONS: SEQUENCE AND INDICATIONS		
1	Warm, dry, stimulate.	All, Clear/position airway PRN
2	Oxygenation and ventilation	Resp Distress/Failure, HR <100
3	Chest compressions	HR < 60
4	Epinephrine and volume expansion	Persistent HR < 60, hypovolemia

BRADYCARDIA: Management of bradycardia is illustrated by the PALS Bradycardia algorithm (see Appendix). Decisions to intervene are based on the patient's hemodynamic status. Treatment options are based on the etiology of the bradycardia (respiratory vs cardiac) and the presenting rhythm (sinus bradycardia vs sinus arrest vs heart blocks). Patients with complete heart block (3rd degree) are the most likely to present in cardiogenic shock and require intervention.

Primary interventions include efforts to support oxygenation and ventilation, pharmacologic agents and transcutaneous pacing for refractory bradycardia. Epinephrine is recommended for bradycardia of asphyxial origin. Atropine is recommended for bradycardia due to increased vagal tone or atrioventricular blocks. The exception to this recommendation is complete heart block which is unlikely to respond to Atropine as it cannot increase conduction through a non-functional AV node. Medications may serve as a bridge until transcutaneous pacing is available.

PEDIATRIC BRADYCARDIA WITH A PULSE AND POOR PERFUSION	
Maintain patent airway, O_2, monitor, IV/IO access, 12 lead EKG	
CARDIOPULMONARY COMPROMISE? Hypotension, Altered mental status, Shock?	
NO	Support ABC's, O_2, observe, expert consultation: Cardiology
YES	Chest compressions if HR < 60 <u>with</u> poor perfusion despite O_2, ventilation
MEDICATIONS BASED ON LIKELY ETIOLOGY	
<u>Asphyxial</u>: Epinephrine every 3-5 minutes: Intravenous/Intraosseous: 0.01 mg/kg of 1:10,000 (0.1 ml/kg), Adult 1.0 mg Endotracheal: 0.1 mg/kg of 1:1,000 (0.1 ml/kg), Adult 2.5 mg	
<u>Increased Vagal Tone or AV block</u>: Atropine. Repeat once. Intravenous/Intraosseous: 0.02 mg/kg IV/IO, Adult 0.5-1.0 mg Endotracheal: 0.04-0.6 mg/kg ET Minimum dose: 0.1 mg (recommended for bradycardia, not for intubation)	
TRANSTHORACIC PACING	
Indicated for complete heart block or sinus node dysfunction with cardiopulmonary compromise.	

WEB LINK: PEDIATRIC BRADYCARDIA WITH A PULSE ALGORITHM (AHA 2020)

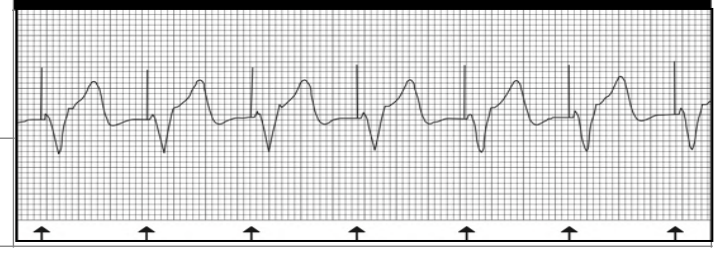
PACING: Transcutaneous cardiac pacing of the ventricles is indicated when bradycardia resulting in poor perfusion or shock and interventions specified in the American Heart Association Pediatric Bradycardia Algorithm are unsuccessful (See appendix). More than 90% of patients ultimately require a permanent pacemaker.

NON-CARDIAC: Non-cardiac manifestation of neonatal lupus typically resolve in 6-8 months with maternal antibody clearance. Neonatal lupus is not a contraindication to breast feeding. Patients with cutaneous manifestations should avoid sun exposure. This includes the use of sunscreen. Patients with hematologic manifestations may require transfusion of red blood cells or platelets. Steroids and intravenous immune globulin have also been utilized in selective cases.

APPENDIX: TRANSCUTANEOUS PACING

(See: PEM Guide: Cardiology: Cardiac Pacing for Bradycardia)

PROCEDURE OVERVIEW		
1	SEDATE	Sedate if indicated and time permits
2	ATTACH	Attach pacing pads
3	SET MODE	Set the pacing mode
4	SET RATE	Set the pacing rate
5	SET OUTPUT	Set the output
6	ADJUST OUTPUT	Adjust output until electrical and mechanical capture occur

PROCEDURE: TRANSTHORACIC PACING				
1	Sedate if indicated: Pretreatment with benzodiazepines in conscious patients			
2	Attach Pacing Pads: Pads placed so that the heart is between the pads			
	a	Anterior/posterior OR Anterior/lateral approach		
		ANTERIOR-POSTERIOR	**ANTERIOR-LATERAL**	
		ANTERIOR	ANTERIOR	
		Left anterior chest between Xiphoid and nipple. Upper edge of pad below nipple line	Left chest Mid-axillary line Intercostal space 4	
		POSTERIOR	LATERAL	
		Posterior chest beneath the scapula and lateral to spine	Right chest Sub-clavicular area	
3	Set the Pacing Mode: Demand versus Fixed. In general, start with demand mode			
	a	Demand mode (synchronous): paces if patient heart rate is below set rate.		
	b	Fixed mode: Continues at set rate regardless of patient's heart rate		
4	Set the Pacing Rate: Generally faster than underlying intrinsic rate			
	a	Adolescents and adults: 80-100 beats/minute		
5	Set the Output			
	a	Average adult requires 60-100 mA for unstable bradycardias		
6	Adjust the Output: Two options: Start high/titrate down or start low/titrate up			
	a	Start high and come down until capture is lost and then increase to the lowest level at which capture is obtained consistently		
	b	Start low and increase every 10 seconds until capture obtained		
	c	Transthoracic pacing involves only the ventricles. Electrical capture of the ventricles is indicated by a pacer spike (indicated by the up arrows) followed by a wide ventricular complex	**ELECTRICAL CAPTURE** 	
	d	Mechanical capture is indicated by a palpable pulse with each QRS complex at the rate set on the pacer.		

APPENDIX: PEDIATRIC HEART RATE, PR INTERVAL, BLOCKS

(See: PEM Guide: Cardiology: EKG Interpretation)

NORMAL PEDIATRIC HEART RATES			
AGE	AWAKE	MEAN	SLEEPING
< 3 months	85-205	140	80-160
3 months – 2 years	100-190	130	75-160
2 -10 years	60-140	80	60-90
> 10 years	60-100	75	50-90

PR INTERVAL BY AGE AND HEART RATE: MEAN (UPPER LIMIT OF NORMAL)								
	0-1mo	1-6mo	6mo-1yr	1-3yr	3-8yr	8-12yr	12-16yr	Adult
> 60						0.16 (0.18)	0.16 (0.19)	0.17 (0.21)
60-80					0.15 (0.17)	0.15 (0.17)	0.15 (0.18)	0.16 (0.21)
80-120	0.10 (0.12)				0.14 (0.16)	0.15 (0.16)	0.15 (0.17)	0.15 (0.20)
100-120	0.10 (0.12)			(0.15)	0.13 (0.16)	0.14 (0.15)	0.15 (0.16)	0.15 (0.19)
120-140	0.10 (0.11)	0.11 (0.14)	0.11 (0.14)	0.12 (0.14)	0.13 (0.15)	0.14 (0.15)		0.15 (0.18)
140-160	0.09 (0.11)	0.10 (0.13)	0.11 (0.13)	0.11 (0.14)	0.12 (0.14)			(0.17)
160-180	0.10 (0.11)	0.10 (0.12)	0.10 (0.12)	0.10 (0.12)				
> 180	0.09	0.09 (0.11)	0.10 (0.11)					

PEDIATRIC BRADYCARDIA: RHYTHM CLASSIFICATION	
Sinus	Normal PR interval*, heart rate below normal for age
Sinus arrest	Irregular or no P waves, junctional or ventricular escape rhythm
First degree	Prolonged PR interval followed by QRS complex (P=QRS)
Second degree	All p waves do not conduct to ventricles (P>QRS)
	Mobitz I (Wenckebach): Progressive increase in the PR interval, last p wave not conducted (may be physiologic if asymptomatic) Typically associated with AV node dysfunction
	Mobitz II: Non-conducting P wave without progressive lengthening of PR interval. Pathologic until proven otherwise, risk of progressing to third degree block.
Third degree	Atrial and ventricular rate are independent (AV dissociation). Junction/ventricular escape rhythm slower intrinsic rate (P>QRS)
*PR interval must be adjusted for age and heart rate (See table above)	

SYSTEMIC LUPUS ERYTHEMATOSUS

INTRODUCTION (ROSHNI PATEL, MD, 1/2018)
Systemic SLE Erythematosus (SLE) is a multisystem, autoimmune disease that is both chronic and episodic. During flares of the disease, there is inflammation of the blood vessels and connective tissue affecting almost every organ system, making its presentation to the emergency department vary greatly. About 20% of patients with SLE are diagnosed in childhood with a female predominance as well as an ethnic predominance to Native Americans, African Americans and Hispanics. Compared to adults, pediatric patients have a higher morbidity and mortality, making their initial diagnosis and management imperative. Delay in appropriate referral may lead to poor outcomes. Given the complexity of this topic, this PEM Guide only reviews issues relevant to the Emergency Department identification and management of SLE and emphasize the importance of including the patient's rheumatologist in the decision-making process.

PATHOPHYSIOLOGY
The etiology of SLE is unclear. Some categorize it as a predominantly genetic disease triggered by environmental conditions. Ten percent of those with SLE have a relative affected by SLE, and family members are more likely to be affected by other autoimmune diseases such as thyroiditis or diabetes. Triggers include infection, medications, hormonal changes (puberty), and ultraviolet light. Drug-induced SLE is classically described in reaction to: Minocycline, Procainamide, Hydralazine, Penillamine, Isoniazid, Quinidine, Phenytoin and Carbamazepine.

DIAGNOSIS
Given the range of clinical manifestations, presentations can vary depending on stage and severity, as well as from patient to patient. The most common presenting symptoms are fever, rash, mucositis and arthritis along with constitutional symptoms like fatigue and weight loss. Children typically develop SLE after 5 years of age with the majority presenting in early adolescence. Neonatal SLE can present as bradycardia in newborns of mothers with SLE, generally resolving within 6 months (See PEM Guide: Procedures: Bradycardia and Cardiac Pacing).

There is no definitive test for SLE. The diagnosis is based on clinical and laboratory evidence. It is crucial to review recent medications as well as family history of autoimmune disease. A thorough review of past medical history is essential given that symptoms can occur over time and may present as several non-concurrent complaints.

The criteria to diagnose SLE was revised in the 2012 (Systemic SLE International Collaborating Clinics Guidelines, PubMed ID: 22553077). These criteria are recommended by rheumatologists caring for adults. An additional criterion of constitutional symptoms has been included based on pediatric systemic review (Tucker, SLE 2007, PubMed: ID 17711886). Children who do not meet these criteria should be followed closely. The differential diagnosis of those with multisystem disease is extensive and includes infection, malignancy and other rheumatologic disorders.

CLINICAL MANIFESTATIONS

SLE can cause multiple, nonspecific symptoms throughout the body. Symptoms suggestive of a SLE diagnosis are included in the table above and are described below. Symptoms related to medication complications may also be present.

ACUTE CUTANEOUS SLE: The classic malar rash (is defined as a butterfly rash of fixed erythema (flat or raised) that crosses the nasal bridge but spares the nasolabial folds. The malar rash may be absent in up to two thirds of patients. The malar rash of SLE should be differentiated from other facial rashes such as that of dermatomyositis and Fifth's disease. Acute cutaneous SLE also includes photosensitivity (rash from sun exposure). Bullous SLE and toxic epidermal necrolysis are rare cutaneous manifestations.

SYSTEMIC LUPUS ERYTHEMATOSUS: SLICC* DIAGNOSTIC CRITERIA (2012)	
To make a diagnosis of SLE based on criteria the patient must meet either of the following (A or B):	
A. 4 of the below listed criteria including at least one clinical and one laboratory criteria laboratory. Criteria are cumulative and need not be present concurrently.	
B. SLE nephritis confirmed by biopsy and ANA or anti-ds DNA antibodies	
CLINICAL CRITERIA	IMMUNOLOGIC CRITERIA
Acute Cutaneous SLE	Anti-nuclear Ab (ANA)
Chronic Cutaneous SLE	Anti-Double Stranded DNA Ab
Oral or nasal ulcers	Anti-Smith Ab
Non-scarring alopecia	Antiphospholipid Ab
Arthritis	Low Complement (C3, C4, CH50)
Serositis	Direct Coombs (+) not due to hemolysis
Renal	
Neurologic	
Hemolytic anemia	
Leukopenia	
Thrombocytopenia (<100,000/mm^3)	
Constitutional: Fatigue, fever, weight loss	
*Systemic SLE International Collaborating Clinics	

CHRONIC CUTANEOUS SLE: An erythematous, discoid (coin shaped) rash that affects the face, ears, scalp and possibly upper chest and back (Figure 1) can be present in those with chronic cutaneous SLE. Lesions have a central hypo-pigmented with a hyper-pigmented border that may scale or crust. Chronic cutaneous SLE may also include chilblains SLE (Figure 2), SLE panniculitis (Figure 3), and verrucous SLE.

ORAL ULCERS: Ulcers of the palate (Figure 4), buccal mucosa, tongue or nares are usually painless.

NON-SCARRING ALOPECIA: Thinning of the hair or broken hairs (Figure 5).

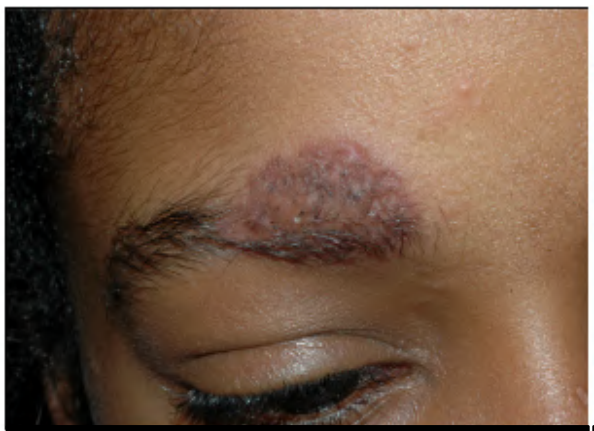


FIGURE 1:
DISCOID LESION

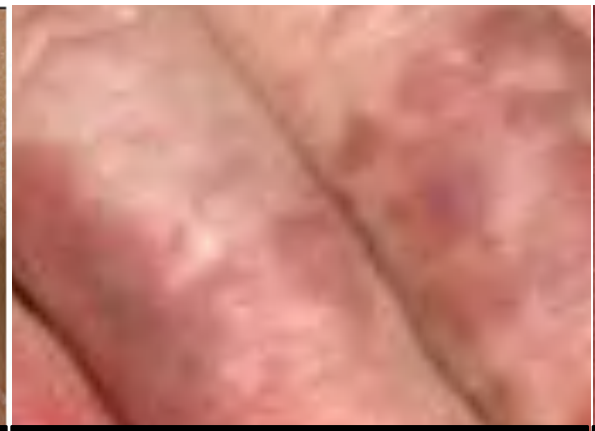


FIGURE 2:
CHILL BAINS

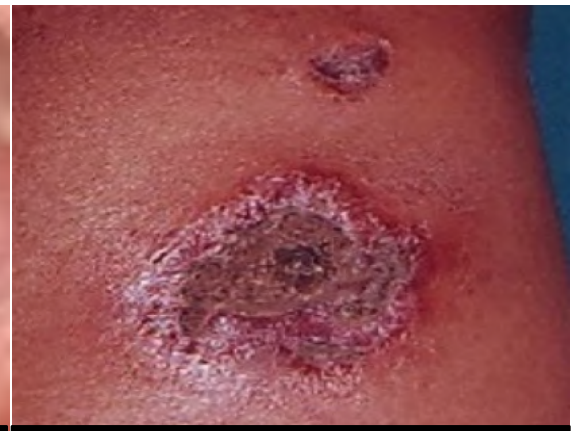
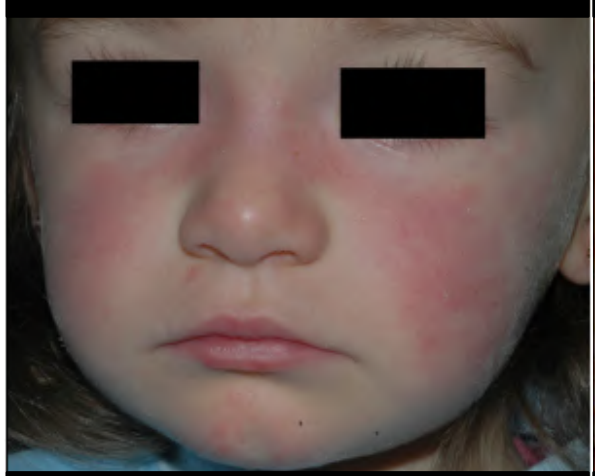


FIGURE 3:
PANNICULITIS



MALAR RASH

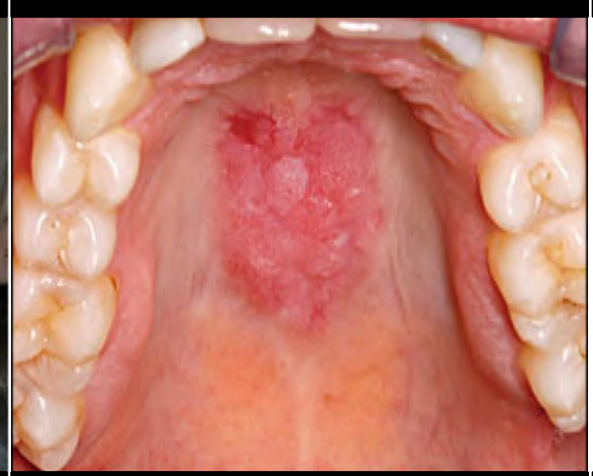


FIGURE 4:
ORAL ULCERS

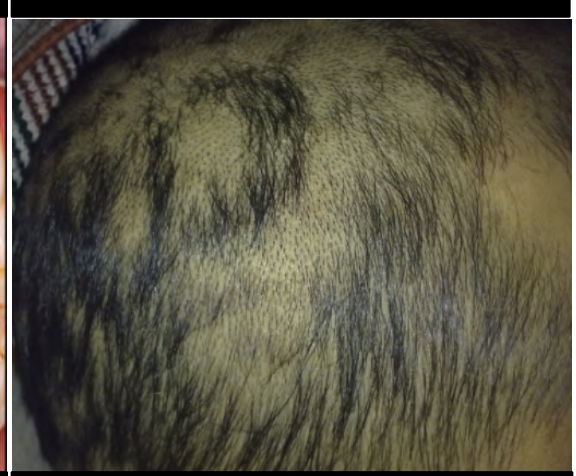


FIGURE 5:
ALOPECIA

SYNOVITIS INVOLVING ≥ 2 JOINTS: Swelling, effusion and tenderness along and morning stiffness that lasts greater than a half hour are suggestive of SLE. Non-erosive arthritis is also common. It typically manifests with symmetric involvement of both large and small joints (knees, wrists, ankles or fingers).

SEROSITIS: Serositis is defined as inflammation of the tissues that line the lungs, heart and abdomen.

Pulmonary: Pleuritic chest pain is most commonly due to a pleural effusion. Patients present with dyspnea and sharp inspiratory chest pain during inspiration. Physical exam may reveal decreased breath sounds. Pleural effusions can be confirmed with chest XRAY or by ultrasound. Other pulmonary manifestations include: pulmonary hemorrhage, pulmonary hypertension, acute pneumonitis.

Cardiac: Any layer of the heart can be affected. Pericarditis is more common than myocarditis and endocarditis. Those with pericarditis often report chest pain that is worse in a supine position or with deep inspiration. A friction rub may be heard on exam. EKG findings can include diffuse decrease in voltages, generalized ST elevations and electrical alternans. Pericardial effusions and contractility can be assessed with echocardiography. Coronary artery disease and heart failure can occur.

Gastrointestinal: Peritonitis is less common and presents with abdominal pain, fever, vomiting and diarrhea. Diffuse tenderness, rigidity and hypoactive bowel sounds occur.

VASCULAR: Anti-phospholipid antibodies are associated with both a coagulopathy and a hypercoagulable state though SLE patients without anti-phospholipid antibodies are also at risk of venous thromboembolism. Pulmonary embolism and coronary artery disease should be considered in the SLE patient with chest pain and shortness of breath. Extremity venous thromboembolism should be considered in those with leg pain and/or swelling.

RENAL: Renal involvement is the greatest cause of morbidity and mortality. Renal involvement is defined as a urine protein-to-creatinine ratio (or 24-hour urine protein) representing 500 mg of protein in 24 hours or red blood cell casts. Proteinuria, microscopic hematuria, hypertension or elevated BUN and creatinine may be present. Associated symptoms can include dehydration, weight gain and decreased urine output. A renal biopsy is required to classify renal disease and can be used to confirm the diagnosis of SLE.

NEUROLOGIC: Manifestation include: stroke, seizures, migraine headaches, meningitis**,** optic neuritis**,** coma and transverse myelitis. Neuropsychiatric effects include: psychosis, cognitive defects, dementia, depression and anxiety. The term “SLE cerebritis” refers to manifestations with an organic rather that a psychiatric basis. Physical exam findings may show cranial nerve palsies or papilledema. Transverse Myelitis with be associated with paraplegia, para paresis, back pain and a sensory level. The headaches can be associated with memory impairment and depression and do
not typically resolve with non-narcotic analgesia.

HEMATOLOGIC: SLE patients may suffer from hemolytic anemia, anemia of chronic disease, iron deficiency anemia, and anemia due to blood loss (GI, renal, pulmonary). Patients may present with fatigue, pallor and edema. Leucopenia (Leukocytes of < 4,000) and/or lymphopenia (Absolute lymphocyte count <1,000) can occur. Thrombocytopenia (<100,000) can occur though correlation with bleeding risk is poor.

Macrophage activation syndrome (MAS), a form of hemophagocytic lymphohistiocytosis (HLH), is a rare but potentially life-threatening manifestation of SLE. Manifestations include hyperpyrexia, pancytopenia, hepatic dysfunction, encephalopathy and coagulopathies.

LABORATORY EVALUATION

Patients with existing SLE should undergo testing to assess renal function (BMP, UA), liver function (LFT’s) and hematologic function (CBC, coagulation profile). Complement levels are often used as a marker of disease severity. Additional testing may be indicated. For example, the patient with chest pain may require cardiac troponins. Of note, patients with SLE are at high risk for venous thromboembolism. A negative D-dimer in this population does not exclude pulmonary embolism.

LABORATORY EVIDENCE OF SLE
A variety of auto-antibodies may be present to varying extent in SLE patients. These are best interpreted by a rheumatologist. These include: Antinuclear Antibodies (ANA), Anti-Double Stranded DNA Ab, Anti-Smith Ab, Anti-Cardiolipin Ab, Anti-phospholipid Ab or Anti Ro, La and ribonuclear protein, Anti-cytoplasmic Ab (ANCA)
Complement levels: Both low C3 and C4. (Low C3 alone is not specific to SLE)
Direct Coombs test (+) in the absence of evidence of hemolytic anemia.
Vitamin D Deficiency
Acute phase reactant: Elevated CRP, ESR
Urinalysis: Hematuria, red cell casts, proteinuria
CBC: Anemia, leukopenia/lymphopenia, thrombocytopenia

IMAGING

Imaging studies should be obtained based on chief complaint and differential diagnosis. Patients with chest pain require a chest XRAY and EKG. A cardiac echocardiogram (pericardial effusion, contractility) or CT angiogram (pulmonary embolism) may be indicated if the Chest XRAY does not reveal the etiology of the chest pain. Neuroimaging may be indicated in the patient with CNS complaints and/or focal neurologic findings. Venous duplex ultrasound is indicated in patients with a high index of suspicion for venous thromboembolism of the extremities.

MANAGEMENT

Ongoing treatment of SLE is geared towards managing disease manifestations and minimizing therapy related toxicity. The effect of therapy on growth is a pediatric specific concern. There are no clear management guidelines and treatment is individualized. In general, low potency medications are utilized initially and for mild disease. Higher potency agents are reserved for moderate to severe disease. Unfortunately, higher potency agents are associated with a higher risk of adverse events. Patients with a SLE flare are managed with either higher doses of their baseline medication or the addition of higher potency medications as directed by their rheumatologist.

COMMON IMMUNO-SUPPRESSIVE MEDICATIONS	
Hydroxychloroquine	Inhibits neutrophils locomotion and chemotaxis of eosinophils. Impairs complement-dependent antigen-antibody reactions
Glucocorticoids	Suppression of migration of neutrophils. Reversal of increased capillary permeability. Reducing activity and volume of the lymphatic system. Suppresses adrenal function at high doses.
Azathioprine	Decrease proliferation of all immune cells
Mycophenolate	(CellCept). Cytotoxic to T and B lymphocytes
Cyclophosphamide	Decrease proliferation of all immune cells
Rituximab	Monoclonal Ab to CD20 antigen on B lymphocytes

EMERGENCY MANAGEMENT

Patients with existing SLE may present to the Emergency Department for disease exacerbations as well as medication complications. Pediatric Rheumatology should be immediately consulted for guidance in management of all SLE patients. A child with known SLE and fever requires prompt attention. These children are at greater risk for infection and sepsis based on their disease manifestations (e.g. pleural effusion → empyema) as well as due to immunosuppressive therapy. Febrile patients require a sepsis evaluation including appropriate cultures and may require empiric antibiotic coverage.

SURGERY

1. Appendicitis	Ramona Warren, MD, MPH
2. Hirschsprung's Disease	Michael Mojica, MD
3. Intussusception	Michael Mojica, MD
4. Malrotation	George Kristinsson, MD
5. Meckel's Diverticulum	Michael Mojica, MD
6. Pyloric Stenosis	George Kristinsson, MD

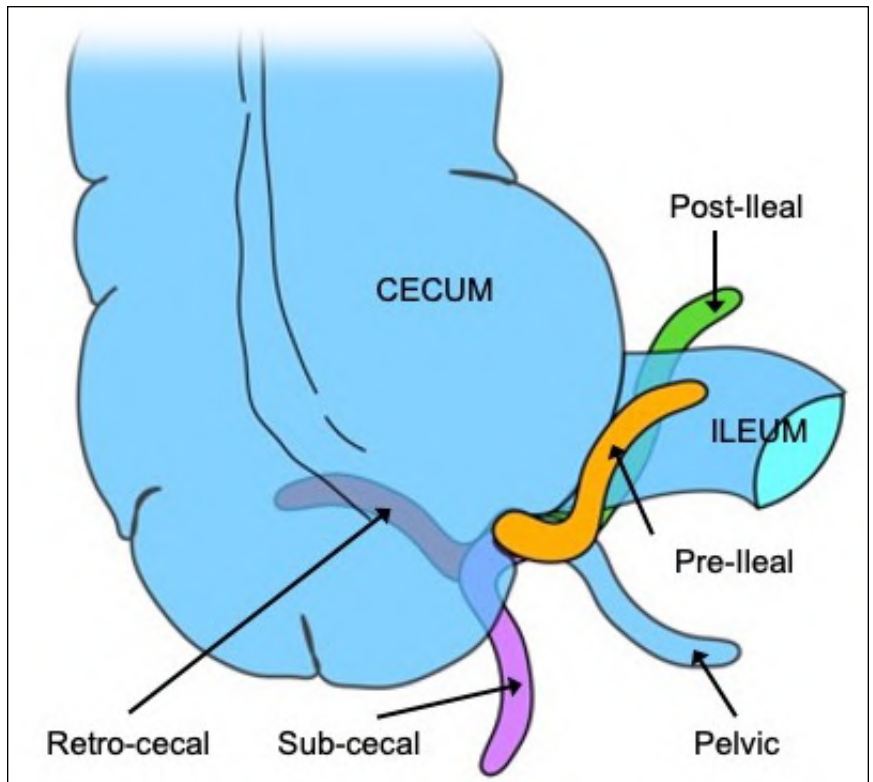
APPENDICITIS

INTRODUCTION (RAMONA WARREN M.D., MPH, 2/2022)
Appendicitis is the most common acute surgical condition of the abdomen in children. It most often occurs in those over 2 years of age, with a peak in adolescents and young adults. The lack of classic clinical signs in younger children makes the diagnosis difficult. The majority of children less than 3 years of age present with a perforated appendicitis after having being seen previously. Young patients may continue to express hunger (often not able to differentiate abdominal pain from hunger) and they are also more likely to have diarrhea (30% of children under age 3). The goal is to rapidly identify appendicitis in order to reduce the morbidity associated with perforation.

DIFFERENTIAL DIAGNOSIS
Renal stones
Testicular or Ovarian torsion
Meckel's diverticulum
Ruptures ovarian cyst
Ectopic pregnancy
Diabetic ketoacidosis
Pharyngitis (mesenteric adenitis)
Inflammatory bowel disease
Pelvic inflammatory disease

COMMON MISDIAGNOSES
Gastroenteritis (# 1)
Upper respiratory infection
Pneumonia
Urinary tract infection
Viral syndrome
Sepsis
Blunt abdominal trauma
Febrile seizure

CLINICAL FINDINGS
The varying location of the appendix may result in pain that is not in the right lower quadrant. For example, an appendix lying in the paracolic gutter can produce more flank pain. A pelvic appendix may produce more generalized pelvic pain, and a retrocecal position can produce RUQ pain. A genital examination should be done in males and sexually active females. A rectal exam is deferred because it is both insensitive and nonspecific. Though constipation is often considered in the differential for lower abdominal pain, an ileus from appendicitis can result in constipation, hard stool in the vault does not exclude the presence of appendicitis and relief of pain with defecation may be due to relief of pressure on the appendix.



APPENDIX LOCATIONS

LABORATORY TESTING

LABORATORY EVALUATION	
CBC	Leukocytosis with left shift
ESR, CRP	Elevated values may be indicative of perforation but do not reliably distinguish uncomplicated appendicitis from no appendicitis
Electrolytes	Abnormalities associated with vomiting (rare) Other diagnosis such as diabetic ketoacidosis
Urinalysis	Pyuria in cases of cystitis or pyelonephritis Specific gravity offers an estimate of dehydration Microscopic hematuria, pyuria sometimes found in appendicitis
Pregnancy Test	In post-pubertal females
Rapid Strep Test	May suggest mesenteric adenitis

RISK SCORES

Two clinical decision rules that combine elements of the history, physical examination and basic laboratory tests as commonly used to determine the likelihood of appendicitis. The MANTRELS score was derived and validated primarily in adult patients. The pediatric appendicitis score was more recently derived. Both scores include essentially the same parameters. The primary difference is that the MANTRELS score uses rebound tenderness in the RLQ and the pediatric appendicitis score used cough or percussion or hopping tenderness in the RLQ.

MANTRELS SCORE		
M	Migration of pain	1
A	Anorexia	1
N	Nausea	1
T	Tenderness in the RLQ	2
R	Rebound Pain	1
E	Elevation of Temperature	1
L	Leukocytosis	2
S	Shift to the left	1

In 2002, Samuel derived the Pediatric Appendicitis Score. (J Peds Surgery 2002, PubMed ID: 12037754). A validation study of the score demonstrated that the PAS could be used to stratify risk of having appendicitis in children 1-17 years of age that presented with acute abdominal pain of less than 7 days duration (Goldman, J Pediatr. 2008, PubMed ID: 18534219).

A PAS of ≤ 2 had a low probability of appendicitis (2.4%), while a PAS ≥ 7 had high probability of appendicitis (96%). A PAS score of 3 to 6 was not accurate in ruling in or ruling out appendicitis (37%). These intermediate risk patients should likely undergo further imaging or observation. Unfortunately, those with intermediate scores make up the majority of patients.

PEDIATRIC APPENDICITIS SCORE	POINTS
Anorexia	1
Nausea or vomiting	1
Migration of pain	1
Fever (>38 C)	1
Tenderness over the right iliac fossa	2
Cough/percussion/hopping tenderness in the RLQ	2
Leukocytosis (>10,000/ml^3)	1
Polymorphonuclear neutrophilia (>7,500/ml^3)	1

An analysis of approximately 300 patients (250 with appendicitis) had an area under the receiver operating characteristic curve (AUC) of 0.74 (0.66 – 0.71) for the MANTRELS score and an AUC of 0.73 (0.65 – 0.71) for the pediatric appendicitis score (Pogerelic, PEC 2015, PubMed ID: 25706925). The analysis demonstrated that a score cutoff of 7 was optimal. The authors concluded that neither score should be used exclusively in the determining the likelihood of appendicitis

The Pediatric Appendicitis Risk Calculator (PARC) was derived and internally validated to determine a continuous risk of appendicitis (Pediatrics Apr 2018, PubMed ID: 29535251) in the children's hospital emergency department setting. It has been subsequently validated in a multicenter community hospital ED based trial (Cotton DM, Ann Emerg Med. 2019 PubMed ID: 31229394). The PARC provides a continuous measure of appendicitis risk divided into 7 pre-defined risk strata.

PEDIATRIC APPENDICITIS RISK CALCULATOR: ED SETTING		
Risk	Risk group	Clinical recommendations
≤5%	Very Low	Outpatient follow up appropriate if PCP evaluation available within 24 hours; no diagnostic imaging required
6-15%	Low	Consider ED observation for 6 hours for serial exams; if improved, ensure outpatient follow-up in 24 hours; no imaging required
16-25%	Low-Moderate	If patients symptoms <24 hours, consider observation for 12 hours; if not improved, obtain ultrasound and repeat CBC If pain ≥24 hours of symptoms, obtain ultrasound to evaluate for appendicitis
26-50%	Moderate	Ultrasound recommended as first line imaging; admit for observation if ultrasound equivocal
51-75%		Ultrasound recommended as first line imaging; CT if ultrasound equivocal
76-90%	Moderate-High	Consult surgery; consider imaging based on surgery recommendations
>90%	High	Consult surgery; imaging not required
WEB LINK: MDCALC: PARC		

In the community validation study, a risk calculation of 5% or greater appendicitis was associated with a sensitivity of 97.5%, 95% CI (95.9, 99.1%) and a specificity of 37.6%, 95% CI (35.3, 39.9%). The rate of appendicitis below this cutoff was 1.4%.

The area under the receiver operating characteristics curve was greater in the PARC (AUC: 0.89, 95% CI (0.87, 0.92) than in the PAS (AUC: 0.80, 95% CI (0.77, 0.82). These AUCs are similar to those obtained in the internal validation cohort of the derivation study. (PARC AUC 0.85, 95% CI (0.83, 0.87), PAS AUS: 0.77, 95% CI (0.75, 0.80). A statistical comparison of the AUC was not presented. Imaging could potentially be avoided in the 32% of patients who were classified a very low risk. An additional 22% could be eliminated if the low risk strata was included (total of 54%). This is similar to the 44% of patients with a risk of less than 15% in the original derivation and internal validation study. In addition, the 4% classified as high risk (85%) could also forgo imaging (6% in the original derivation study). In contrast, the majority of patients are classified as intermediate risk with the PAS.

RADIOLOGIC EVALUATION

Abdominal Ultrasound and CT scan of the abdomen and pelvis have been used to improve diagnostic accuracy and reduce the negative laparotomy rate. These studies have the added benefit of identifying alternative diagnoses. The choice of imaging study should be made in conjunction with surgical and radiology colleagues.

ULTRASOUND: Ultrasound may be useful but its interpretation is operator dependent and the accuracy of ultrasound is reduced in patients with a high body mass index. Ultrasound has the advantage of no radiation exposure. Sonographic findings include a non-compressible distended appendix (> 6mm), periappendiceal fluid (abscess) or inflammation (“fat stranding”) and/or an appendicolith. The limitations of ultrasound is that the appendix is not visualized in a significant number (30-40%) of cases. It is unclear if equivocal ultrasound occur due to non-RLQ appendix locations. An equivocal ultrasound can be followed by cross-sectional imaging (MRI, CT) or observation (inpatient or outpatient).

The table below represents an assessment of appendicitis risk based on a combination of the risk group obtained from the pediatric appendicitis score and the ultrasound result. (Bachur, J Pediatrics, 2015, PubMed ID: 25708690). Those with a low pediatric appendicitis score and an equivocal ultrasound had a 9% risk of appendicitis)

APPENDICITIS RISK: PEDIATRIC APPENDICITIS SCORE AND ULTRASOUND			
PEDIATRIC APPENDICITIS SCORE	ULTRASOUND FINDINGS		
	POSITIVE	NEGATIVE	EQUIVOCAL
Low: 0-3	73% (47-99)	0% (0-3)	9% (0-19)
Medium: 4-6	90% (82-98)	6% (3-9)	13% (5-21)
High: 7-10	97% (95-100)	19% (11-27)	47% (33-61)

CT: CT of the abdomen and pelvis with both oral and intravenous contrast has been the traditional study of choice in those with continued high suspicion of appendicitis with an equivocal ultrasound. Positive CT scan findings include: a distended appendix that does not fill with contrast, signs of inflammation in the periappendiceal fat, a periappendiceal fluid collection (abscess) and an appendicolith.

MRI: MRI is the study of choice after an equivocal ultrasound due to the last a radiation exposure and no need for contrast administration. Non-contrast MRI has shown sensitivity and specificity similar to that of CT in pediatric patients. A meta-analysis of MRI in pediatric patients with suspected appendicitis that included 11 studies found a pooled Sensitivity: 96.5%, 95% CI (94.3, 97.8%), Specificity: 96.1%, 95% CI (93.5, 97.7%), Positive Predictive Value: 92.0%, 95% CI (89.3, 94.0%) and Negative Predictive Value: 98.3% (95% CI: 97.3-99.0%). Alternative diagnoses were identified in approximately 20% of patients (primarily GI and GYN). The use of MRI resulted in an increased time to antibiotics (3.5 hours) and appendectomy (4.8 hours) and a decreased negative laparotomy rate (1.4%). The change in perforation rate was not provided (Moore, Pediatr Radiol 2016, PubMed ID: 27229509).

MANAGEMENT

Patients with appendicitis may be dehydrated due to poor oral intake, gastrointestinal losses from vomiting or third spacing of fluids due to bowel edema. Intravenous rehydration with crystalloid should be considered.

ANALGESIA: Analgesia should not be withheld. This is particularly true in patients in which a decision to obtain imaging has been made. Studies have demonstrated that the used of analgesia does not alter the clinical evaluation significantly. Two small (combined n=198), randomized clinical trials of Morphine compared to Placebo demonstrated significant reduction in pain but no significant change in physical examination findings (Bailey, Ann Emerg Med. 2007, PubMed ID: 17597256, Green, Pediatrics. 2005, PubMed ID: 16199711). However, some pediatric surgeons prefer the opportunity to evaluate the patient prior to opioid analgesia if that does not delay care.

The use of Toradol by pediatric surgeons is variable due to concerns of bleeding from NSAIDS interference with platelet aggregation. A multicenter (n=78,926), retrospective cohort study using a children's hospital database compared perioperative Toradol to no Toradol (Naseem, J Surg Res 2017, PubMed ID: 28985855). Perioperative was defined as administration on the day of or day after operation (day 0 or 1). In the regression analysis, there was no statistically significant difference in post-operative infection within 30 days requiring admission (Adjusted OR: 1.02, 95% CI (0.91, 1.15) or any complication (Adjusted OR: 0.89, 95% CI (0.80, 0.99)). Qualitatively identical results were obtained when the analysis was limited to only those receiving Toradol on day zero. 28% of patients had complicated appendicitis and a subgroup analysis of these patients was not presented. It could not be determined if day zero Toradol was administered pre-operatively or intraoperatively.

ANTIBIOTICS: In general, a pre-operative dose of antibiotics is recommended in all patients with uncomplicated appendicitis with the goal of reducing surgical site infections. Antibiotics with coverage for enteric pathogens is preferred.

Narrow spectrum antibiotic coverage has demonstrated similar efficacy to broad spectrum coverage in reducing surgical site infections. A multicenter study including 1,389 pediatric patients with uncomplicated appendicitis compared Cefoxitin or Ceftriaxone with Metronidazole (narrow spectrum) to Piperacillin/Tazobactam (extended spectrum) after propensity matching (Cameron, Ann Surg 2018, PubMed ID: 28654543). The rates of surgical site infection were similar between the groups (extended spectrum (2.4%) vs narrow spectrum (1.8%)(OR, 1.05, 95% CI, 95% CI (0.34, 3.26)], as was the rate of revisits (extended spectrum (7.9%) vs narrow spectrum (5.1%) (OR: 1.46, 95% CI (0.75, 2.87).

ED ANTIBIOTICS
Initial Operative Management
Ceftriaxone: 50 mg/kg/dose (maximum dose 2 grams), Q24 hours AND
Metronidazole: 30 mg/kg/dose (maximum dose 1.5 grams) Q24 hours
Initial Operative Management: Severe penicillin or cephalosporin allergy[1]
Aztreonam: 30 mg/kg (maximum dose 2 grams) Q8 hours
Metronidazole: 30 mg/kg/dose (maximum dose 1.5 grams) Q24 hours AND
At time of surgery: Vancomycin 15 mg/kg (maximum dose 1-gram) x 1 dose
1. History of anaphylaxis, angioedema, respiratory distress or urticaria/hives NYU Pediatric Antimicrobial Stewardship (9/2021)

The ideal, narrow-spectrum antibiotic regimen is unknown. A multicenter study including 14 hospitals and 846 pediatric patients with uncomplicated appendicitis in a national surgical database compared Ceftriaxone and Metronidazole to Cefoxitin. The combination of Ceftriaxone plus Metronidazole (0.2%) demonstrated a statistically significant lower rate of surgical site infection compared to Cefoxitin (2.7%) (Adjusted OR: 0.10, 95% CI 0.02, 0.60))(Kashtan, Annals Surg 2021, PubMed ID: 32149827).

Antibiotics are continued in appendicitis complicated by perforation and abscess and in patients with uncomplicated appendicitis being managed non-operatively.

DEFINITIVE MANAGEMENT: Traditionally, operative management (open or laparoscopic) has been the treatment of choice in the US. Data from recent studies and Europe have demonstrated to nonoperative management of complicated appendicitis may be a reasonable alternative. A meta-analysis including 10 studies and 763 pediatric patients with uncomplicated appendicitis compared non-operative (n=413) to operative management (n=363)(Georgiou, Pediatrics. 2017, PubMed ID: 28213607). Overall, non-operative treatment of acute uncomplicated appendicitis was successful in 97%, 95% CI (95.5, 98.7%) of children during the initial hospitalization. The adjusted incidence of recurrent appendicitis was 14%, 95% CI (7, 21%). The long-term efficacy (not undergoing an appendectomy), determined at the final reported follow up period, was 82%, 95% CI (77, 87%). The initial hospital stay was shorter by a mean of 0.5 days, 95% CI (0.2, 0.8 days) though hospital stay including the follow up period was similar in the non-operative treatment and appendectomy groups. There was no difference in the rate of complications and no analysis of cost, or patient and family quality of life (e.g. missed days from school or work).

NYU NON-OPERATIVE APPENDICITIS CRITERIA	
Patient	6-17 year
	Pain < 48 hours
	Temperature < 103
Lab	WBC < 18,000
Imaging	No abscess or perforation
	Appendix diameter < 11mm
NYU Pediatric Surgery (2021)	

DISPOSITION

Pediatric surgery should be consulted for patients with imaging results that are not definitive for whom suspicion for appendicitis remain high based on laboratory or examination findings. These patients may be observed as inpatients or discharged with appropriate return precautions and follow up.

All patients with confirmed appendicitis are admitted. Patients with uncomplicated appendicitis may undergo operative appendectomy or non-operative therapy with antibiotics alone. Patients with complicated appendicitis are admitted for antibiotics. Those with a large abscess may require drainage by interventional radiology. A delayed or interval appendectomy is often indicated when the appendix is very inflamed and may have formed a phlegmon (a poorly organized abscess) that is likely to have a problematic intra-operative or post-operative course. Antibiotics help to reduce the inflammation and interval appendectomy has improved outcomes.

HIRSCHSPRUNG'S DISEASE

INTRODUCTION: (MICHAEL MOJICA, MD, 3/2020)
Hirschsprung disease (HD) (Congenital Aganglionic Megacolon) results from the failed migration of hindgut neural crest cells during the first few months of gestation. This results in an aganglionic portion of the colon without motor function. The aganglionic colon fails to relax resulting a pseudo-obstruction. The most important complication of HD is Hirschsprung's associated enterocolitis (HAEC or "toxic megacolon"). HD can also be complicated by mechanical obstruction without enterocolitis and less frequently by volvulus (typically sigmoid).

CLASSIFICATION: COLONIC INVOLVEMENT	
Entire colon	5%
Long segment: Proximal to sigmoid	15-20%
Short segment: All of the rectum and part of the sigmoid	80%
Ultrashort segment: 2-4 cm proximal to the internal anal sphincter	< 5%

The etiology of HD is thought to be multifactorial with both familial and spontaneous cases occurring. It is estimated to occur in 1 in 5,000 live births and most commonly affects males. HD can be associated with other genetic conditions such as trisomy 21. Congenital anomalies are associated with HD in approximately 1 in 5 patients. These include genitourinary, visual/auditory, cardiac and anorectal anomalies.

CLINICAL PRESENTATION

The majority of patients present in the neonatal period. The most common presenting symptoms are those associated with distal bowel obstruction. These include the failure to pass stool, poor feeding, vomiting (may be bilious) and abdominal distention. In the newborn, this may manifest as failure to pass meconium in the 48 hours after birth (which is seen in almost all normal newborns). Bowel movements are often explosive particularly after a suppository or digital stimulation temporarily relieving obstruction (squirt or blast sign). This can be elicited by a digital rectal exam or a rectal temperature.

Those diagnosed later are more likely to have short segment disease. They frequently have recurrent constipation often requiring laxatives of other interventions as well as chronic abdominal pain. Failure to thrive and malnutrition can result.

DIFFERENTIAL DIAGNOSIS: CONSTIPATION
Hirschsprung's and other cause of gastrointestinal obstruction (see Table below)
Congenital hypothyroidism
Infant botulism
Cystic fibrosis with meconium ileus
Cow's milk protein allergy
Functional constipation
Anorectal anomalies, anal fissures

GASTROINTESTINAL OBSTRUCTION IN THE NEONATE	
Proximal	Pyloric stenosis*
	Gastric volvulus
	Malrotation with Ladd's bands*
	Annular pancreas
	Choledochal cyst
	Duodenal atresia
	Duodenal hematoma (due to trauma)
Middle	Malrotation with midgut volvulus*
	Jejunoileal atresia, meconium ileus (cystic fibrosis)
Distal	Intussusception*
	Hirschsprung's disease with enterocolitis (toxic megacolon)
*Covered in detail in a separate PEM Guide	

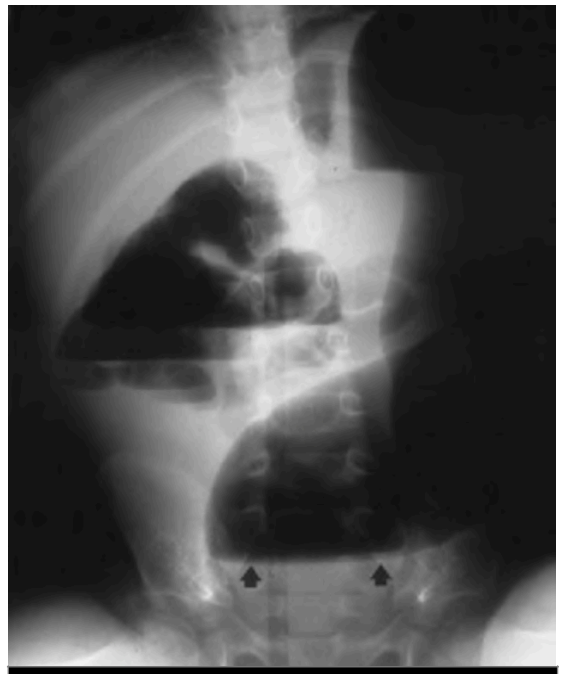
HIRSCHSPRUNG'S ASSOCIATED ENTEROCOLITIS ("Toxic Megacolon"): Hirschsprung-associated enterocolitis (HAEC) is a rapidly progressing, life-threatening condition that can occur prior to definitive surgery, in the immediate post-operative period or many years after surgery. Colonic obstruction leads to significant bowel distention proximal to the transition zone. This results in colonic ischemia and necrosis with ensuing peritonitis and sepsis. Stasis and bacterial overgrowth may also play a role. Symptoms are often nonspecific requiring a high degree of suspicion and mild cases can be misdiagnosed as gastroenteritis. Earlier diagnosis of HD had led to a decrease in frequency of enterocolitis and its associated morbidity and mortality.

Gastrointestinal symptoms include abdominal distention, decreased oral intake, foul-smelling diarrhea, vomiting (may be bilious or feculent) and late rectal bleeding. Systemic symptoms include fever and signs of sepsis (altered mental status, respiratory distress and poor perfusion/hypotension).

HIRSCHSPRUNG'S ASSOCIATED ENTEROCOLITIS: CLASSIFICATION		
Possible (Grade I)	History	Anorexia, diarrhea
	Physical	Abdominal distention
	XRAY	Normal of Mild ileus
Definite (Grade II)	History and Physical ≥ 1 of:	1. Explosive diarrhea 2. Fever, tachycardia or lethargy
		3. Moderate abdominal distention and/or tenderness 4. Explosive gas/stool with rectal exam
	XRAY	Signs if ileus: air fluid levels, distended loops of bowel Distention of the proximal colon with rectosigmoid cutoff
Severe (Grade III) Grade II Criteria Plus	History And Physical	Obstipation (severe or complete constipation)
		Poor perfusion ± hypotension Altered mental status Marked abdominal distention Sign of peritonitis
	XRAY	Pneumatosis intestinalis, pneumoperitoneum

IMAGING

Abdominal radiography may demonstrate signs of obstruction. This includes dilated loops of proximal bowel and air fluid levels. Findings more specific to HD include: a dilated proximal colon with a narrowed distal segment (the cutoff or transition zone) and the absence of air in the rectum (abrupt cutoff of air at the level of the pelvic brim). A normal XRAY does not exclude the presence of HD



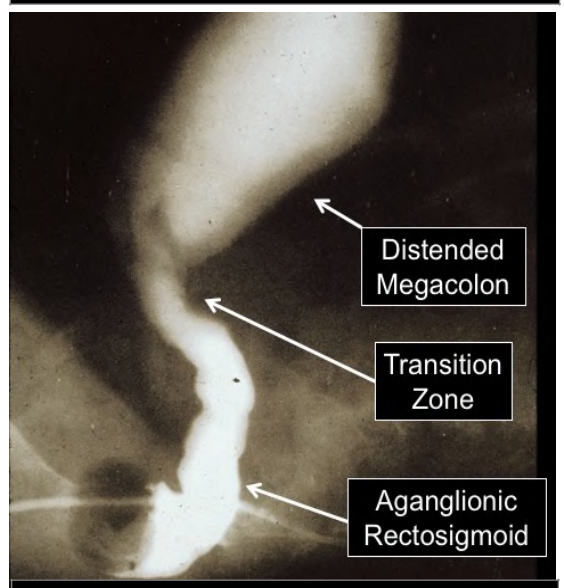
AIR/FLUID LEVELS

A contrast enema with a Hirschsprung's catheter (that avoids distal rectum dilation) may better demonstrate the transition zone. A contrast enema should be avoided in patients with suspected enterocolitis due to the risk of perforation.

A digital rectal exam within a few days of the enema can dilate the rectum resulting in a false negative study. In addition, in infants less than 3 months and those with long segment disease or entire colon involvement, a negative contrast enema can be falsely negative. Therefore, a normal contrast enema does not exclude the diagnosis of HD in a patient with a high pretest probability.

DEFINITIVE DIAGNOSIS

The definitive diagnosis of HD is made by suction biopsy of the rectum. A suction biopsy obtained from the correct location and including a portion of the muscularis mucosa demonstrating the absence of ganglia is diagnostic. Older patients with a thicker rectal mucosa may be missed by suction biopsy. Anorectal manometry can demonstrate the involved colon's failure to relax.



HIRSCHSPRUNG'S

MANAGEMENT

Patients without enterocolitis often undergo non-emergency surgery to resect the involved area of colon. There are multiple approaches to the surgery and it may be approached as a single or multistep process. A One stage definitive pull through is generally preferred. A two stage approach to diverting colostomy followed by pull through is more common in those with HAEC). Surgical complications include: anal sphincter defects with fecal incontinence, enterocolitis and chronic constipation.

ENTEROCOLITIS: Supportive care includes adequate fluid resuscitation and correcting electrolyte disturbances. Patients with definite (grade II) and severe (grade III) Hirschsprung-associated enterocolitis should be admitted. Early surgical consultation is essential. Most patients can be managed non-operatively. Rectal irrigation can be used to lessen the degree of obstruction and distention. Intravenous antibiotics with coverage for gastrointestinal flora including anaerobes (e.g. Ampicillin, Gentamicin plus Metronidazole or Piperacillin/Tazobactam plus Metronidazole) are recommended by the pediatric surgery guideline. Nasogastric or orogastric drainage can reduce proximal distention.

HIRSCHSPRUNG'S ASSOCIATED ENTEROCOLITIS: MANAGEMENT		
	PRIMARY	SECONDARY
Possible (Grade I)	Outpatient Oral hydration Metronidazole PO	Rectal irrigation: Saline, rectal tube
Definite (Grade II)	Most inpatient Clear liquids or Hold feeds, IV hydration Broad-spectrum antibiotics[1] IV plus Metronidazole PO or IV Rectal irrigation: Saline, rectal tube	Nasogastric decompression
Severe (Grade III)	All inpatient NPO, IV hydration Broad-spectrum antibiotics[1] IV plus Metronidazole IV Rectal irrigation	Nasogastric decompression Resection and colostomy: ischemia, bowel perforation, failure of non-operative management
1. Ampicillin and Gentamycin or Piperacillin/Tazobactam American Pediatric Surgical Association 2017: PubMed ID: 28154902		

INTUSSUSCEPTION

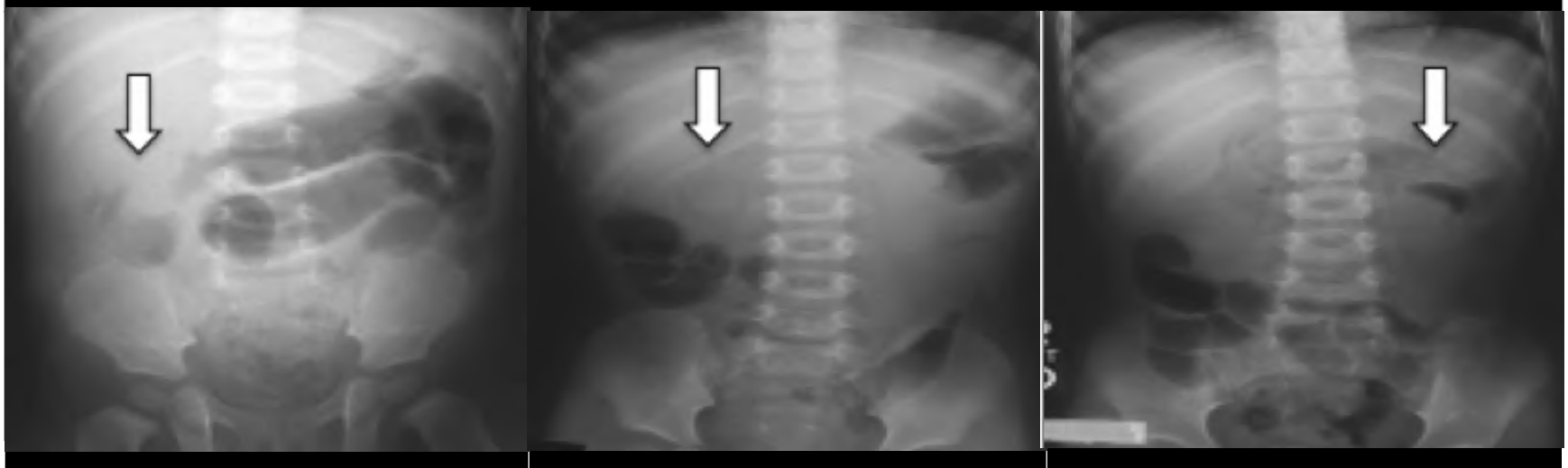
INTRODUCTION (MICHEAL MOJICA, M.D., 1/2019)
Intussusception is the most common cause of intestinal obstruction in children less than 2 years of age. Peak incidence is between 3 months and 1 year with 80% of cases occurring < 2 years of age. Intussusception occurs when a segment of bowel “telescopes” into another segment of bowel. Ileocecal intussusception is the most common. Lymphoid hyperplasia (Peyer’s patches) is the etiology most commonly proposed. In older children and in those with recurrence a pathologic “lead point” may be present. These include, intestinal polyps, Meckel’s diverticulum, tumors (e.g. lymphoma) and intestinal duplications. Henoch Schonlein Purpura colitis is a distinct risk factor for intussusception (commonly ileoileal intussusception)

CLINICAL MANIFESTATIONS
History and physical examination findings are often nonspecific. History should focus on gastrointestinal symptoms. There may be a prodrome of gastroenteritis making it difficult to distinguish the two entities. There typically is a history of paroxysmal, crampy abdominal pain with infants drawing their legs up. Bilious vomiting and lower gastrointestinal bleeding are late findings. The classic “currant jelly” stools occur in less than 50% of cases. It has been reported that intussusception can present with mental status changes. Classically, this takes the form of alternating periods of lethargy and irritability. A sausage shaped mass may be palpated in the right upper quadrant. A stool exam for blood may or may not be positive.

DIAGNOSTIC IMAGING
Abdominal radiographs may be helpful to rule in the diagnosis of intussusception though it should be remembered that the most common finding is “non-specific bowel gas pattern” and the XRAY may not be used to rule out intussusception. An XRAY may reveal signs of obstruction or a soft tissue mass. Specific findings include: absent liver edge sign (soft tissue mass in the RUQ), target sign (intussusceptum seen in a transverse plane) and crescent sign (the head of the intussusception).

Recent evidence suggest that the presence are air in the ascending colon on a three view XRAY series (prone, supine and lateral decubitus) may effectively rule out intussusception (Roskind, Pediatr Emerg Care 2012, PubMed ID: 22929143). In this study, the presence of air in the ascending colon on 2 of the 3 views reduced the likelihood of intussusception, while presence of air on all 3 views ruled out all cases of intussusception. In a population, with 14.8% probability of intussusception, the probability of intussusception with the presence of air on all 3 views resulted in a 0% (1 – predictive value of a negative test) probability of intussusception. It is important to note that only 14.8% (19/128) of patients had air identified on all 3 views.

XRAY FINDINGS OF INTUSSUSCEPTION

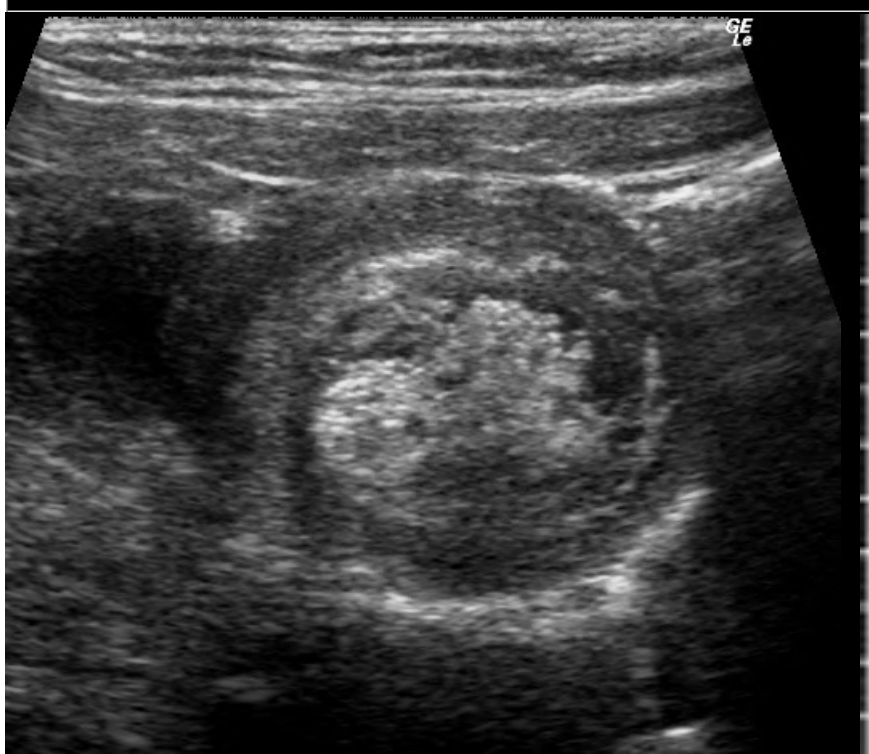


ABSENT LIVER EDGE	TARGET SIGN	CRESCENT SIGN

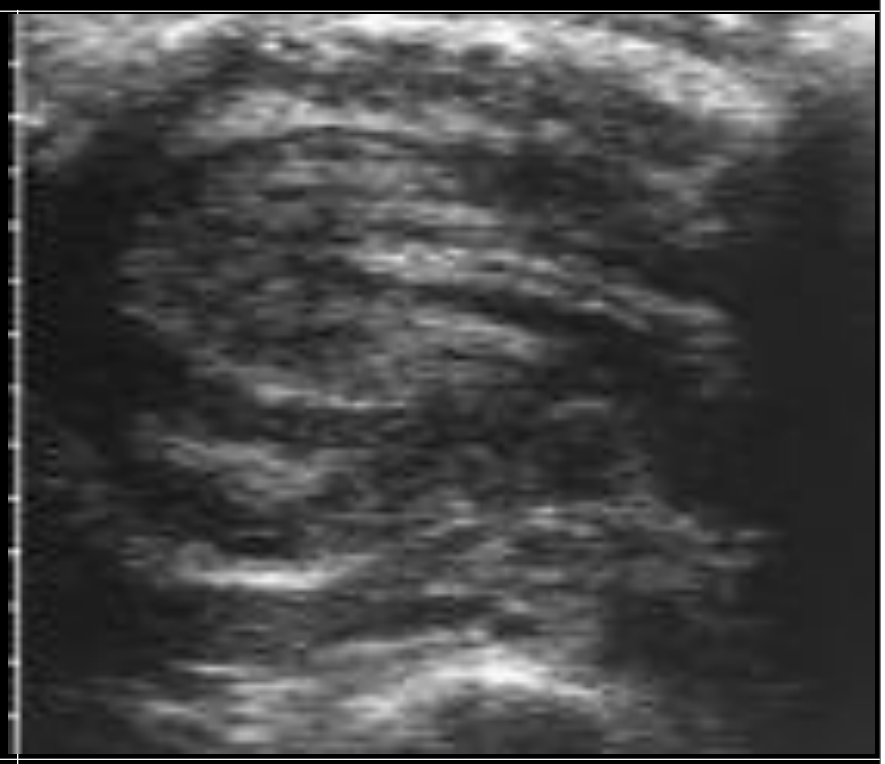
Ultrasound has been found to be accurate in the diagnosis of intussusception. In the transverse cut, one can see a ring of bowel within bowel giving it a donut appearance. The longitudinal appearance on ultrasound has been reported as having a submarine sandwich or pseudokidney appearance with multiple layers. A negative ultrasound by an experienced radiologist may limit the need for an enema.

The accuracy of point of care ultrasound performed by relatively novice pediatric emergency medicine faculty and fellows was assessed in a single center study including 82 patients of which 16% had intussusception (Riera, Ann Emerg Med 2012, PubMed ID: 22424652). The bedside ultrasonography had a specificity (97%, 95% CI (89, 99%)), which would make it an excellent test to rule in intussusception. The lower sensitivity (85%, 95% CI (54, 97%)) makes point of care ultrasonography less useful as a screening test to rule out intussusception

SONOGRAPHIC FINDINGS OF INTUSSUSCEPTION



DONUT SIGN



PSEUDO-KIDNEY SIGN

MANAGEMENT

A contrast enema has the benefit of being both diagnostic and therapeutic. Air enemas decrease the risk of contrast material peritonitis in the case of perforation with similar rates of success. Success rates for hydrostatic reduction of intussusception via enema have been reported as high as 80-90%. Successful reduction is indicated by flow of air into proximal bowel. Patients are typically admitted after successful reduction for observation. Complications of hydrostatic reduction may include perforation, partial reduction, reduction of a necrotic segment of bowel and missing a pathologic lead point. A surgeon should be available immediately in case the bowel becomes perforated during the procedure or the reduction is unsuccessful.

OPERATIVE EXPLORATION/REDUCTION: INDICATIONS
Signs of peritonitis or perforation
Failed hydrostatic reduction
Suspicion of a pathologic lead point* (older patients, multiple recurrences.)
*Meckel’s diverticulum common (Diagnosed by Nuclear scan)

DISPOSITION

Patients who have had their intussusception reduced are typically admitted to the hospital for a period of observation though a recent study has suggested that admission may not be necessary. Rates of both late and early recurrence (approximately 15%) were similar in the group observed in the ED for 4 hours and as an inpatient for 24 hours (Mallicote, Am J Surg 2017, PubMed ID: 28969892). Over a 10 year interval, 245 episodes of intussusception occurred in 210 patients. Six patients (2.45%) had a recurrent ileocolic intussusception within 7-28 after initial successful reduction. Simanovsky, Emerg Radiol. 2018, PubMed ID: 30143943).

MALROTATION

INTRODUCTION (GEORGE KRISTINSSON M.D., 2/2022)
The surgical abdomen in the neonate is a rare event, but is associated with high morbidity and mortality. Intestinal obstruction can quickly lead to severe dehydration, electrolyte abnormalities, sepsis and irreversible intestinal ischemia. Early recognition and intervention are crucial to maintain intestinal perfusion and prevent the serious sequelae of short gut syndrome.

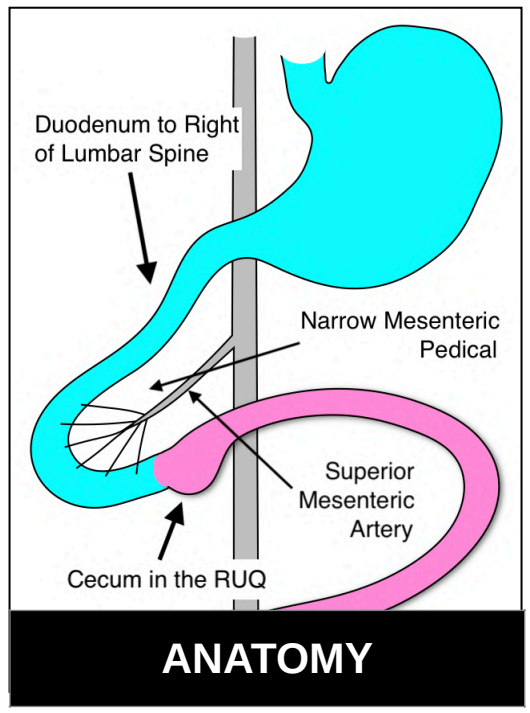
In almost every case of intestinal obstruction the neonate will present with vomiting. Vomiting in the neonatal period is a common complaint and often associated with benign etiologies such as gastroesophageal reflux. Parents may confuse spitting up secondary to food-regurgitation and overfeeding with vomiting.

Vomiting in this period should always raise concern of a serious underlying disease. The differential diagnosis of vomiting is extensive. Though gastrointestinal obstruction should be considered, it is helpful to think about vomiting etiologies in other systems such as metabolic, infection, toxicologic, cardiac and neurologic before focusing entirely on gastrointestinal etiologies.

LIFE-THREATENING NON-GI CAUSES OF VOMITING	
Central nervous system	Hydrocephalus*, tumor, intracranial hemorrhage*
Renal	Obstructive uropathy e.g. posterior urethral valves
Infectious Disease	Sepsis*, meningitis*, pyelonephritis*
Metabolic	Inborn errors of metabolism*, electrolyte abnormalities*
Toxicologic	Methemoglobinemia*
Cardiac	Congenital heart disease*, congestive heart failure*
*Covered in detail in a separate PEM Guide	

GASTROINTESTINAL OBSTRUCTION IN THE NEONATE	
Proximal	Pyloric stenosis*
	Gastric volvulus
	Malrotation with Ladd’s bands
	Annular pancreas
	Choledochal cyst
	Duodenal atresia
	Duodenal hematoma (e.g. intentional trauma)
Middle	Malrotation with midgut volvulus
	Jejunoileal atresia, meconium ileus (cystic fibrosis)
Distal	Intussusception*
	Hischsprung's disease with toxic megacolon (enterocolitis)*
	Meconium ileus
*Covered in detail in a separate PEM Guide	

The age of the patient and presenting symptoms may help in to narrow the differential diagnosis of gastrointestinal causes of vomiting. Neonates are more likely to have a congenital abnormality. Older infants are more likely to have an acquired etiology or a late complication of a congenital abnormality. Bilious vomiting and abdominal distention suggests a level of obstruction below the sphincter of Oddi (e.g. malrotation with midgut volvulus). In contrast, non-bilious vomiting and gastric distention may indicate a more proximal cause of obstruction (e.g. pyloric stenosis).



MALROTATION

During embryonic life, the colon and small bowel grow rapidly, rotating 270 degrees in a counter-clockwise direction, with the cecum passing anterior to the superior mesenteric artery and coming to rest in the right lower quadrant. In malrotation, the rotation ceases after 90 degrees. The duodenum and ascending colon are juxtaposed around the superior mesenteric vessels, with the entire midgut suspended from a narrow mesenteric pedicle. Malrotation is not, in itself, a problem. However, two distinct clinical situations may complicate malrotation. The most severe is midgut volvulus. The other is duodenal obstruction due to Ladd's bands.

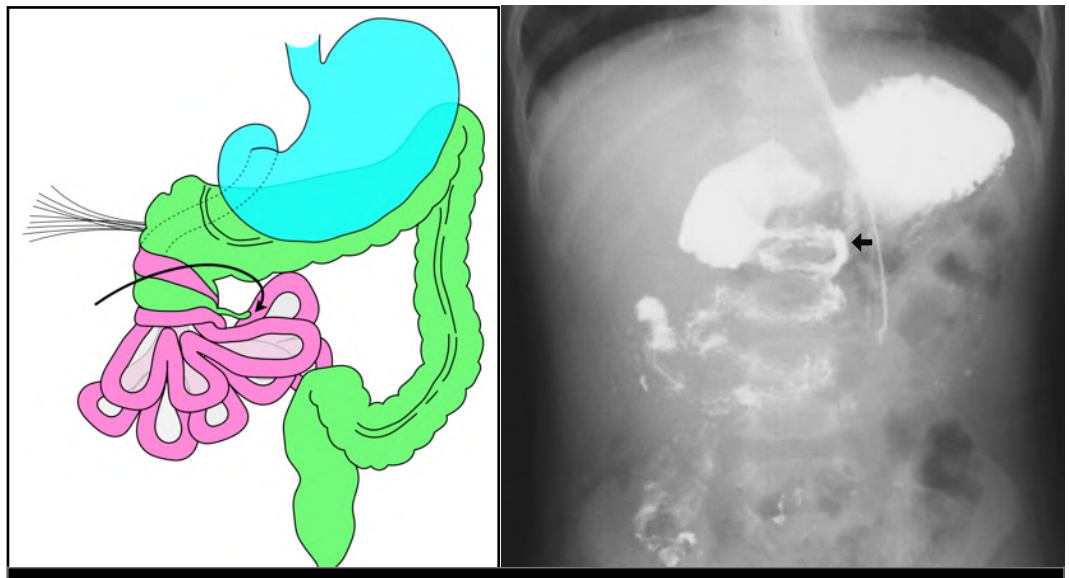
IMAGING: Malrotation is diagnosed with an upper GI series. Ultrasound can be diagnostic by an experienced pediatric radiologist. Ultrasound finding include an inverse relationship of the superior mesenteric artery and view and whirlpool sign (direct visualization of the superior mesenteric vein and proximal small bowel swirling around the superior mesenteric artery). A meta-analysis of 17 studies including 2,257 patients found a pooled sensitivity of 94%, 95% CI (89, 97%) and pooled specificity of 100%, 95% CI (97, 100%) of ultrasound for malrotation with or without midgut volvulus (Nguyen, Arch Dis Child 2021, PubMed ID: 33879472). The pooled sensitivity for an inverse SMA/SMV relationship was 95%, 95% CI (89, 98%) with a pooled specificity of 100%, 95% CI (96, 100%). The pooled sensitivity whirlpool sign as an indicator of midgut volvulus was 92%, 95% CI (82, 97%) with a specificity of 99%, 95% CI (96, 100%).

UPPER GASTROINTESTINAL SERIES FINDINGS: MALROTATION
CONSISTENT WITH MALROTATION
Duodenum that is located to the right of the spine (normally c-shaped loop crossing lumbar spine)
Cecum is located in the right upper quadrant (normally RLQ)
Absence of the ligament of Treitz (normally LUQ)
CONSISTENT WITH MALROTATION COMPLICATIONS
Obstruction at the second portion of the duodenum (Ladd's Bands: Cecal mesentery)
Corkscrew or coiled spring" appearance of small bowel (Midgut volvulus)

DUODENAL OBSTRUCTION DUE TO LADD'S BANDS: With normal rotation the cecum migrates to the right lower quadrant and the cecal mesentery attaches to the abdominal wall in that location. In malrotation, the cecum remains in the right upper quadrant. The cecal mesentery (Ladd's Bands) crosses the duodenum to attach to the liver and can obstruct the mid duodenum.

MIDGUT VOLVULUS: The midgut can twist around its narrow mesenteric pedicle resulting in a midgut volvulus. Progressive bowel strangulation results in an ischemic loss of extensive bowel. Most patients with malrotation develop midgut volvulus within the first weeks of life. Bilious vomiting is often the initial symptom. The abdomen may or may not be distended. The clinical course is rapid progression from midgut ischemia to necrosis with perforation leading to hemodynamic instability, sepsis and metabolic acidosis.

Depending on the progression of the strangulation an abdominal XRAY will show evidence of small bowel obstruction or lack of any gas in the abdomen. Free air may be seen due to ischemic bowel perforation. An upper GI series will demonstrate a “cork screw” appearance of the small bowel. Emergent operative intervention to preserve bowel is essential.



MIDGUT VOLVULUS

INITIAL MANAGEMENT: MIDGUT VOLVULUS
IV access, fluid resuscitation
Bedside glucose determination, CBC, electrolytes, type and screen
Blood culture, catheterized UA/Urine culture
Consider a lumbar puncture if febrile and hemodynamically stable
Antibiotics: broad spectrum coverage e.g. Piperacillin and Tazobactam (Zosyn)
Urgent upper GI series or ultrasound: Clinical suspicion or abnormal abdominal XRAY
Abdominal XRAY: supine AP and upright (or cross table lateral) with AP chest
Surgical consult early in the process
Consider nasogastric tube (French 8-10)

JEJUNOILEAL ATRESIA

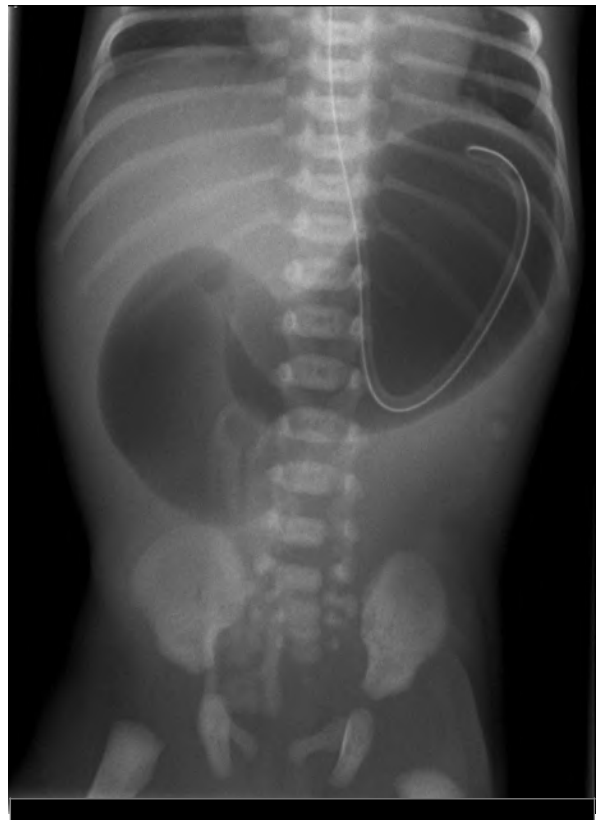
Jejunoileal atresia is caused by a mesenteric vascular accident during fetal life. In jejunoileal atresia abdominal distention with bilious vomiting is observed within the first 24 hours after birth. Abdominal films show air-fluid levels proximal to the lesion, confirming the diagnosis of bowel obstruction. Preoperatively, stomach decompression, with a nasogastric tube, intravenous hydration, and correction of any electrolyte disturbance should be achieved. An interval of 12-24 hours is allowed for preoperative preparation._

DUODENAL ATRESIA

Duodenal atresia is a congenital obstruction of the second portion of the duodenum. Its etiology is believed to be failure of canalization of this bowel segment during the early gestational stage. Duodenal atresia may be seen more commonly in patients with trisomy 21 and those with trachea-esophageal fistulas.

The neonate with duodenal atresia presents with feeding problems from day 1 of life. In 80 percent of these patients, the papilla of Vater opens into the proximal duodenum and the vomiting is bilious. Abdominal plain film shows a characteristic "double-bubble" sign, demonstrating gastric distention (proximal bubble) and the dilated proximal duodenum (distal bubble). The narrowing between the two bubbles is the pylorus and the duodenal obstruction occurs at the end of the distal bubble. Surgery is required but is not urgent. A 24-48-hour delay may be allowed before operation for transport, further evaluation, electrolyte replacement and fluid resuscitation.

DOUBLE BUBBLE SIGN
Duodenal atresia
Duodenal hematoma due to trauma
Malrotation with Ladd’s bands
Annular pancreas
Obstructing choledochal cyst



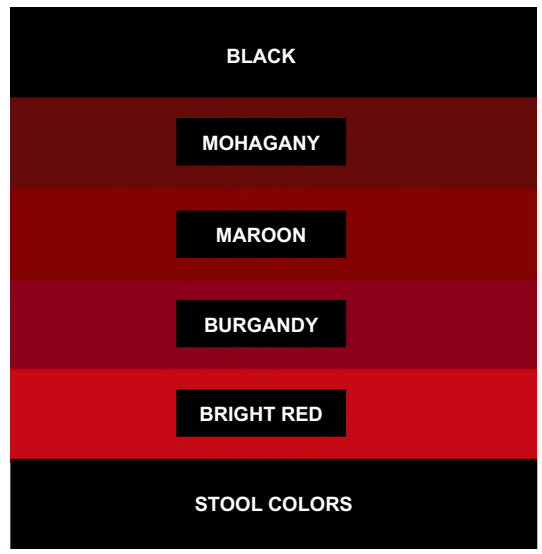
DOUBLE BUBBLE

MECKEL'S DIVERTICULUM

INTRODUCTION (MICHAEL MOJICA, MD, 11/2022)
A Meckel's diverticulum of the middle to distal ileum is a remnant of the omphalomesenteric duct. The diverticulum may or may not contain heterotopic tissue. The "rule of 2s" is often used to describe a Meckel's diverticulum. It is the most common gastrointestinal tract abnormality found in approximately 2% of the population with a 2:1 male to female ratio. It is typically found in the ileum within 2 feet of the ileocecal valve opposite the mesenteric surface and is a proximately 2 centimeters in length. The majority of patients with a Meckel's diverticulum are asymptomatic. Approximately 2% experience complications.

CLINICAL MANIFESTATIONS
Patients may present with lower GI bleeding, abdominal pain or with bowel obstruction. Unfortunately, clinical features do not reliably distinguish a Meckel's diverticulum from the extensive list of other causes of these presentations.

BLEEDING: The most common presentation in pediatric patients is painless rectal bleeding. The source of bleeding is ulceration of adjacent intestine by acid secreted by ectopic gastric within the diverticulum. Bleeding is usually large volume and dark maroon in color. The maroon color is a consequence of oxidation as blood passes through the colon. In contrast, bleeding from juvenile polyps (typically colonic) is characterized as small volume and bright red in color. In intussusception, stool color is described as currant jelly due to ischemia. The absence of abdominal pain, an abdominal mass, vomiting and lethargy help distinguish Meckel's diverticulum bleeding from intussusception. To complicate matters, a Meckel's diverticulum can serve as a lead point for intussusception.



ABDOMINAL PAIN: Abdominal pain may be related to diverticulitis, ulceration of adjacent intestine or obstruction as described above. Peritoneal signs may be present in the those with perforation of the diverticulum or adjacent bowel.

OBSTRUCTION: Obstruction can occur by a number of mechanisms. These include: serving as a lead point for intussusception or volvulus, torsion of the diverticulum, abdominal wall hernia, inversion of the diverticulum or inflammatory obstruction due to diverticulitis. Abdominal pain, vomiting and abdominal distention may be present

A complete physical exam includes an evaluate of the skin (bruising, petechiae, hemangiomas) and mucous membranes (including the nasopharynx and oropharynx) and a complete abdominal examination. Peritoneal signs suggest a perforation.

DIFFERENTIAL DIAGNOSIS
The differential diagnosis of lower GI bleeding is extensive and varies by age. Lower GI bleeding is defined as a source of bleeding distal to the ligament of Treitz (small bowel and colon). In general, bright red blood or clots in the stool is typically a sign of lower GI hemorrhage. An upper GI bleed is typically associated with melena (black or tarry stools). However, stool color does not reliably distinguish between upper and lower GI sources. Melena (hemoglobin oxidized to hematin by gut bacteria) can be seen with a proximal lower GI source and bright red blood (hematochezia) can be seen with an upper GI source due to rapid GI transport in infants and young children.

It is important to first determine is if bleeding is local or systemic. Bleeding can occur from a GI location but from a non-GI etiology (e.g. coagulopathy, thrombocytopenia). Bleeding in conjunction with epistaxis, mucous membrane bleeding, hematuria, bruising or petechiae suggest a systemic cause of bleeding. The common causes of pediatric lower GI bleeding that are localized to the GI tract are listed below.

DIFFERENTIAL DIAGNOSIS: LOWER GASTROINTESTINAL BLEEDING	
Neonate	Swallowed maternal blood
	Anal fissure
	Necrotizing enterocolitis
	Malrotation with midgut volvulus
	Hirschsprung enterocolitis
Infant/Toddler	Anal fissure
	Mild/Soy Protein colitis
	Intussusception
	Meckel diverticulum
Child/Adolescent	Infectious enteritis/colitis
	Henoch Schonlein Purpura
	Juvenile polyps
	Inflammatory bowel disease

DIAGNOSIS

The initial assessment should determine the patient's hemodynamic status based on heart rate, blood pressure and perfusion. Hypotensive, hemorrhagic shock requires urgent therapy and should not be delayed in the search for a specific etiology.

LABORATORY TESTING
CBC: Anemia (no change initially due to loss of whole blood), thrombocytopenia
BMP: Increased BUN in the absence of renal disease associated with UGI > LGI
Lactate: Perfusion/shock
Coagulation studies: PT, PTT, INR, fibrinogen
LFTs: Liver damage, function
Lipase: Pancreatitis associated with gastritis/peptic ulcer, duodenitis
Type and Screen: Significant bleeding with potential need for transfusion

IMAGING

A technetium-99m pertechnetate Meckel's scan is the diagnostic study of choice in the hemodynamically stable patient. Technetium identifies a Meckel's diverticulum with functional gastric mucus cells only. Sensitivity is approximately 90% in children. False positives (inflammatory bowel disease, intussusception) and false negatives can occur. Glucagon, cimetidine and gastrin, prior to the study, may enhance uptake. Contrast mesenteric arteriography can identify an anomalous superior mesenteric artery branch to the diverticulum. However, the procedure requires arterial access. An abdominal computed tomography with angiography is an alternative diagnostic modalities if a Meckel's scan is negative. Upper endoscopy and colonoscopy cannot identify a Meckel's diverticulum of the small bowel.

Abdominal XRAYS may be indicated for concern for intestinal obstruction, foreign body (button battery, magnets, long-sharp objects or iron pill ingestion) or perforation.

IMAGING SELECTION	
Appendicitis	Abdominal ultrasound, cross-sectional imaging
Intussusception	Abdominal ultrasound
Juvenile Polyps	Colonoscopy
Malrotation with Midgut Volvulus	Upper GI series (ultrasound option emerging)
Meckel’s Diverticulum	Technetium-99m pertechnetate (Meckel’s) scan

MANAGEMENT

Management of the Meckel’s diverticulum involves hemodynamic stabilization of the patient, followed by surgical resection. Bleeding with clinical instability is an indication for early surgical intervention. Patients should be stabilized, to the extent possible, prior to endoscopy or surgery. Those with obstruction may require nasogastric drainage. A proton pump inhibitor may be started in those with bleeding. Aluminum hydroxide should be avoided as it decreases the sensitivity of a Meckel’s scan

BLOOD TRANSFUSION: Patients with significant hemodynamic instability should be urgently transfused. The same principles that apply to traumatic hemorrhagic shock can be applied to gastrointestinal hemorrhagic shock (See PEM Guide: Trauma: Hemorrhagic Shock). A consumptive coagulopathy occurs with significant hemorrhage and when large volumes of PRBC’s are transfused. In addition to packed red blood cells (10 ml/kg), platelets and fresh frozen plasma (FFP) may be indicated in a 1:1:1 ratio as part of a massive transfusion protocol. Some protocols add cryoprecipitate. Fully typed and cross matched PRBC’s are preferred but takes the longest time to prepare. If time is not sufficient for fully typed and cross matched PRBC’s then type specific PRBCs or type O PRBCs can be transfused.

Hemodynamically pediatric stable patients are typically transfused PRBC’s for a hemoglobin of < 8 mg/dl. Patients with significant cardiac or pulmonary disease may require transfusion at a higher hemoglobin threshold.

TRANEXAMIC ACID: Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine that inhibits fibrinolysis by blocking the lysine binding sites on plasminogen. The HALT-IT trial randomized 12,009 adult patients who were at risk of bleeding to death from upper or lower GI hemorrhage at 164 hospitals in 15 countries to TXA or placebo. There was no difference in the primary outcome of death due to bleeding in the modified intention to treat analysis (Relative Risk: 0.99, 95% CI (0.82, 1.17)) (Brenner, Lancet. 2020., PubMed ID: 32563378). The authors postulate that gastrointestinal hemorrhage typically presents later in its course so may not be amenable to TXA. There was a slightly higher risk of pulmonary embolism and deep vein thrombosis in the TXA group though the 0.4% risk difference is of questionable clinical significance and there was no statistically significant difference when PE and DVT were analyzed independently.

PYLORIC STENOSIS

INTRODUCTION (GEORGE KRISTINSSON, M.D., 4/2015)
The surgical abdomen in the neonate is a rare event, but is associated with a very high morbidity and mortality. It can quickly lead to severe dehydration, hypoglycemia, electrolyte imbalance, and to irreversible ischemia to the intestine. Early recognition and early intervention are crucial.

INTESTINAL OBSTRUCTION IN THE NEONATE	
Proximal	Pyloric Stenosis
	Gastric Volvulus (more common in patients with gastrostomy tubes)
	Malrotation with Ladd's Bands (Duodenal obstruction)*
	Annular Pancreas
	Choledochal Cyst
	Duodenal Atresia
Middle	Malrotation with Midgut Volvulus*
	Jejunoileal Atresia
	Intussusception*
Distal	Hirschsprung's Disease with Toxic Megacolon
	Necrotizing Enterocolitis
*Reviewed in more detail in a separate PEM Guide	

In almost every case of an intestinal obstruction the neonate will present with vomiting. Vomiting is rare in the neonatal period or early infancy and should always raise concern of a serious underlying disease. Parents may confuse spitting up secondary to food-regurgitation and overfeeding with vomiting. It is helpful to know that a newborn normally feeds approximately 1/6th of its body weight a day or 1 ounce/ kg every 4 hours.

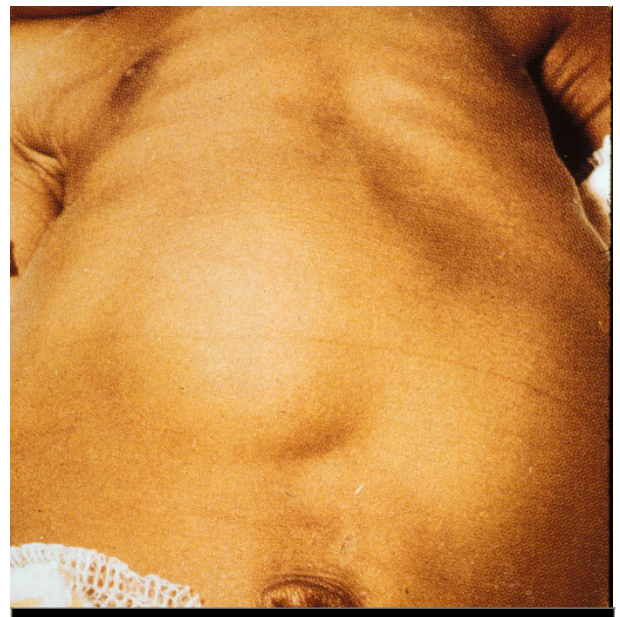
Age and presenting symptoms may help in the differential diagnosis of the surgical abdomen in the newborn and early infancy: Bilious vomiting suggests a level of obstruction below the sphincter of Odi. Abdominal distention (as apposed to gastric distention) occurs due to more distal obstructions. Certain presentations are suggestive of a specific etiology of obstruction

CHARACTERISTIC PRESENTATIONS	
Congenital GI obstruction	A lethargic neonate with bilious vomiting
Pyloric stenosis	A young, male infant with non-bilious, projectile vomiting
Intussusception	Infant beyond neonate period (peak 5-10 months of age) whose vomiting occurs with bouts of pain, a change in mental status, or bloody stools

PYLORIC STENOSIS

INTRODUCTION

Hypertrophy of the pyloric musculature results in progressive narrowing of the pyloric channel and varying degrees of gastric outlet obstruction. Classically a male infant (Male:Female ratio of 4:1) who has been feeding well previously presents at 2 to 5 weeks of age with a history of progressive vomiting after feeding. They look well initially and wish to feed after vomiting. As more complete obstruction develops, the vomiting becomes more forceful and projectile. Clinical findings depend on the extent of obstruction and degree of dehydration.



GASTRIC DISTENTION

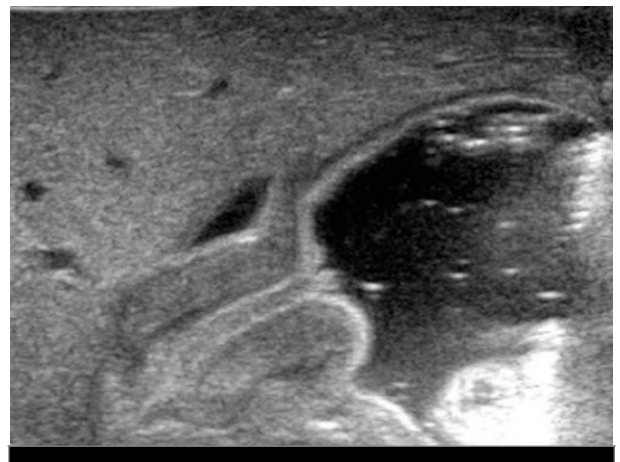
PHYSICAL EXAMINATION

There are two physical examination findings that are somewhat specific to pyloric stenosis. The first is the observation of a gastric peristaltic wave as the stomach peristalsis against the narrow pyloric channel. The patient will exhibit gastric distention (as opposed to generalized abdominal distention).

The second is direct palpation of the hypertrophied pyloric channel. This is described as a small mobile mass or “olive”. Palpation of the “olive: can be facilitated by examining the infant immediately after vomiting (with an empty stomach). The infant’s feet are held in one hand with the hips flexed (relaxing the abdominal musculature). The other hand gently palpates the right upper abdomen in an upward direction. Signs of dehydration should also be noted.

LABORATORY FINDINGS

Serum electrolytes may be abnormal because of gastric losses. The classic electrolyte findings are that of hypokalemic, hypochloremic, metabolic alkalosis. In essence the infants are vomiting hydrochloric acid. Potassium is excreted by the kidney in exchange for resorption of hydrogen ions in response to alkalosis. As dehydration progresses a metabolic acidosis may be seen. A recent case series revealed that the classic electrolyte abnormalities are infrequently present and that normal electrolytes are the most common finding (Tutay, Pediatric Emergency Care 2013, PubMed ID: 23528507). This is very likely due to the earlier diagnosis of pyloric stenosis with ultrasound.



US: PYLORIC STENOSIS

IMAGING

Ultrasound is useful to identify pyloric stenosis. The criteria for the sonographic diagnosis are 1.4 cm or longer length of the pyloric canal with 0.3 cm or greater thickness of the circular muscle. If the ultrasound study does not show a hypertrophic pylorus, an upper GI series can be done to demonstrate a narrowed pyloric channel and identify other causes of gastrointestinal obstruction such as Malrotation with midgut volvulus or Ladd’s bands.

MANAGEMENT

Management of suspected pyloric stenosis depends on the degree of obstruction and the presence of electrolyte disturbances and dehydration. Definitive therapy includes a surgical pyloromyotomy.

In the case of an ill appearing child with protracted vomiting and signs of dehydration or electrolyte abnormalities, intravenous fluid resuscitation should be initiated pending confirmation of the diagnosis with an ultrasound or upper GI series. Intravenous fluids should be 5% dextrose in normal saline. If hypotonic solutions are used, there is significant risk of hyponatremia.

Nasogastric drainage should be avoided as it may worsen electrolyte abnormalities. The patient should be admitted for correction of acid base and electrolyte abnormalities. Surgical repair is performed later. In the well appearing, well-hydrated neonate with normal electrolytes the differential diagnosis is early pyloric stenosis versus benign regurgitation and the child is safe to continue oral feeding pending official ultrasound study. The neonate may be discharged pending ultrasound study if ultrasound confirmation is not available at the time of presentation.

INITIAL MANAGEMENT: SUSPECTED GI OBSTRUCTION
IV access, Fluid resuscitation
CBC, Electrolytes, Bedside glucose determination
Febrile: Blood Culture, Catheterized UA/Urine Culture, Consider a lumbar puncture
XRAY: Abdomen supine AP and upright or cross table lateral with AP Chest
Upper GI Series: Concern for malrotation with midgut volvulus
Consider orogastric or nasogastric tube (French 8-10)
Avoid in pyloric stenosis. It may worsen electrolyte abnormalities
Surgical and Radiology consults
Antibiotics: Coverage of enteric pathogens

TOXICOLOGY

18. NSAIDS	Michael Mojica, MD
19. Opioids	Eric Weinberg, MD
20. Salicylates	Michael Mojica, MD
21. Sedative/Hypnotics	Eric Weinberg, MD
22. Serotonergic Agents	MaryAnn Mansour, MD
23. Stimulants	Eric Weinberg, MD
24. Toxic Alcohols	Seema Awatramani, MD

APPROACH TO THE POISONED PATIENT

INTRODUCTION (MICHAEL MOJICA, M.D., 2/2023)
The combination of crawling, walking, fine pincer grasp, and oral exploration leads children to ingest substances that they find, particularly parents' and grandparents' medications as well as household products. Inhalational and dermal exposures also place children at risk. Millions of young children are "exposed" to potentially toxic substances each year; the peak is at 2-3 years of age. Nonetheless, most children experience no or only mild symptoms. Poisoning morbidity and mortality are higher among suicidal or substance using adolescents.

Consultation with a local or regional poison control center is an essential part of the diagnosis and management of the poisoned patient.

American Association of Poison Control Centers (1-800-222-1222).
NYC Poison Control Center: 1- 212-POISONS (1-212-764-7667).

TOXIC IN A SMALL DOSE	
Antihistamines	Lindane
Benzocaine	Methanol
β-adrenergic antagonists	Methyl salicylates (oil of wintergreen)
Calcium channel antagonists	Opioids (e.g. methadone, codeine)
Camphor	Phenothiazine
Clonidine	Quinine, chloroquine
Diphenoxylate-atropine	Sulfonylurea antidiabetic agents
Ethanol	Theophylline
Ethylene glycol	Tricyclic antidepressants

DIAGNOSIS
A careful history, physical examination and selected testing may help to identify the agent in an unknown exposure and set initial management strategies. The history should focus on the availability of specific agents in the home, potential amount taken, timing of exposure, allergies, medical conditions and any first aid administered.

Changes in vital signs and physical examination findings can be used to identify the possible toxins or class of toxin. A "toxidrome" is a constellation of signs and symptoms the may be useful in identifying a specific agent or class of agents (See also: Appendix A: Toxidromes).

HEART RATE	
TACHYCARDIA	BRADYCARDIA
Anticholinergics	Alpha$_2$ adrenergic agonists
Antipsychotics	Beta adrenergic antagonist
Cyclic Antidepressants	Calcium channel antagonists
Ethanol withdrawal	Cardioactive steroids (e.g. Digoxin)
Phencyclidine	Opioids
Sedative Hypnotic withdrawal	Organophosphates
Sympathomimetics	

RESPIRATORY RATE	
TACHYPNEA	BRADYPNEA
Cyanide	Alpha$_2$ adrenergic agonists
Carbon Monoxide	Ethanol
Methanol, ethylene glycol	Opioids
Methemoglobin producers	Organophosphates
Methylxanthines	Sedative hypnotics
Nicotine	
Pulmonary irritants (e.g. hydrocarbons)	
Salicylates	
Sympathomimetics	

BLOOD PRESSURE	
HYPERTENSION	HYPOTENSION
Amphetamines	ACE Inhibitors
Alpha$_1$ adrenergic agonists	Alpha$_1$ adrenergic antagonists
Alpha$_2$ adrenergic antagonists	Alpha$_2$ adrenergic agonists
Cocaine	Beta adrenergic antagonists
Ergot alkaloids	Calcium channel antagonists
Lead (chronic)	Cyanide
Monoamine Oxidase Inhibitors	Cyclic antidepressants
Nicotine	Ethanol, other alcohols
Phencyclidine	Iron
Sedative/Narcotic withdrawal	Nitrates and nitrites
Sympathomimetic agents	Opioids
	Phenothiazines
	Sedative-hypnotics

TEMPERATURE: HYPERTHERMIA		
CLASS	EXAMPLE	MECHANISM
Alpha adrenergic	Amphetamines, cocaine	Vasoconstriction
Anticholinergics	Antihistamines	Impaired sweating
Cyclic antidepressants	Imipramine, Nortriptyline	Anticholinergic
Neuroleptics	Haloperidol	Hypothalamic dysfunction
MAOI	Phenelzine	↓ Serotonin metabolism
SSRI	Fluoxetine	Blocks serotonin uptake
Salicylates	Aspirin	↓ Oxidative phosphorylation

HYPERPYREXIA SYNDROMES*	TREATMENT
Neuroleptic malignant syndrome	Benzodiazepines
Serotonin syndrome	Benzodiazepines
Malignant Hyperthermia	Dantrolene
*Altered mental status, neuromuscular changes (hypertonia), autonomic dysfunction	

TOXICOLOGY PHYSICAL EXAMINATION	
Pupils (See Table Below)	Size (miosis, normal (4mm), mydriatic), reactivity
Skin (See Table Below)	Dry, normal, diaphoretic, flushed, color (cyanotic)
Mental status	Depressed (down), normal, agitation (up)
GI, bladder	Distension, bowel sounds
Musculoskeletal	Tone (hypotonic, normal, hypertonic), clonus, fasciculation

PUPILS (NORMAL = 4MM)			
MIOSIS		MYDRIASIS	
C	Cholinergics, Clonidine	A	Antihistamines
O	Opiates, Organophosphate	A	Anticholinergics (non-reactive: inhibits constriction)
P	Phenothiazines, Pilocarpine	A	Antidepressants
S	Sedative hypnotics	S	Sympathomimetics (reactive)

SKIN CHANGES	
Diaphoresis	Sympathomimetics
	Organophosphates
	Salicylates
	Phencyclidine (PCP)
Dry Skin	Anticholinergic
Red Skin	Cyanide
Blue Skin	Methemoglobinemia

SEIZURES	
P	Pesticides, Propranolol
L	Lead
A	Alcohols, Amphetamines
S	Sugar (hypoglycemic, beta blockers), Salicylates, Sedative hypnotic withdrawal
T	Tricyclic antidepressants
I	Isoniazid, Iron
C	Cocaine, Camphor, Carbon monoxide

LABORATORY TESTING

Standard laboratory urine toxicology screening is generally not helpful in the initial management of the patient but may be helpful subsequently for counseling and rehabilitation. The limitations of urine toxicology screen should be considered in their interpretation.

URINE TOXICOLOGY SCREEN		
SUBSTANCE	NYU	BELLEVUE
Amphetamines	YES	NO
Phencyclidine	YES	NO
THC (Tetrahydrocannabinol)	YES	YES*
Tricyclic Antidepressants	YES	NO
Barbiturates	YES	YES
Benzodiazepines	YES	YES
Cocaine	YES	YES
Opiates	YES	YES
Methadone	NO	YES
*Requires a separate order		

URINE TOXICOLOGY LIMITATIONS		
	FALSE POSITIVE	FALSE NEGATIVE
Amphetamines	Nasal Decongestants Trazadone, Bupropion	MDMA Methamphetamines
Benzodiazepines		Lorazepam, Alprazolam, Midazolam, Clonazepam
Cocaine		Inactive Metabolite (+) for 3 days after use
Opioids	Poppy Seeds	Fentanyl, Methadone Tramadol, Buprenorphine
Phencyclidine (PCP)	Tramadol, Dextromethorphan Diphenhydramine	
Tetrahydrocannabinol (THC)	Metabolite (+) for 1 month in chronic users	K2, Spice

ANION GAP METABOLIC ACIDOSIS			
C	Carbon monoxide, Cyanide	P	Paraldehyde, Propylene glycol
A	Aminoglycosides, Acetaminophen	I	Iron, Isoniazid, Inborn errors*
T	Theophylline, Toluene	L	Lactic acid
M	Methanol, Metformin	E	Ethylene Glycol, Ethanol (lactate)
U	Uremia	S	Salicylate
D	Ketoacidosis: Diabetic ketoacidosis, alcoholic ketoacidosis, starvation ketosis		
Anion Gap = ((Na^+ - [Cl^- + $HCO3^-$]), normal = 8-12), *e.g. Organic acidurias			

OSMOLAR GAP	
Ethanol	Paraldehyde
Isopropanol	Ethyl ether
Methanol	Mannitol
Ethylene Glycol	Renal Failure
Acetone	Lactic Acidosis
Trichloroethane	Alcoholic ketoacidosis
Osmolar Gap = Measured Osmols – Calculated Osmols Calculated Osmols = {(2*Na) + (Glucose/18) + (BUN/2.8)}	

SERUM DRUG CONCENTRATIONS*	
Acetaminophen	Methanol
Salicylates	Ethylene Glycol
Iron	Carbon Monoxide
Lithium	Methemoglobin
Phenobarbital	Carbamazepine
Theophylline	
*Each of the agents listed have levels that correspond to toxicity and specific antidotes. Acetaminophen and Salicylates should be screened for in most ingestions.	

MANAGEMENT

The management of the poisoned patient should focus on supportive care (“treat the patient not the poison”). In specific situations, enhanced elimination and/or specific antidotes may be indicated. (See Appendix B for a list of agents and their antidotes)

GENERAL APPROACH TO MANAGEMENT OF ACUTE POISONINGS	
1	Resuscitation
	A. Protect the airway. Intubate as needed B. Maintain oxygenation and ventilation, Naloxone for respiratory depression C. Cardiopulmonary monitoring, fluid resuscitation, consider vasopressors D. Disability: Altered mental status, Seizures: Check for hypoglycemia Decontamination: Remove clothing and place in plastic bags for dermal Exposures: Wash skin, identify medication patches E. Environment: Assess for child abuse, suicidal intent, substance abuse
2	Clinical Evaluation (History/Physical Exam) to determine likely agent/agent class
3	Testing (as indicated)
	Screen for acetaminophen, salicylates in all ingestions, pregnancy in women CBC, electrolytes, bedside glucose. Specific drug levels as indicated EKG: Signs of drug toxicity, prolonged QRS, QTc, dysrhythmias CXR: For respiratory depression (aspiration pneumonitis, pulmonary edema) AXR: Iron, enteric coated, heavy metals
4	Administer specific antidotes (see appendix), remember oxygen and dextrose
5	Consider agent specific elimination techniques

ENHANCING TOXIN ELIMINATION

1. PREVENTION OR REDUCTION OF ABSORPTION

Most toxins are not toxic to the gastrointestinal tract itself. Prevention of absorption can be accomplished by removing the toxin from above, from below or via neutralization. Efforts at gastrointestinal decontamination have not been demonstrated to be beneficial and are generally now indicated only in specific circumstances.

SYRUP OF IPECAC	
Mechanism	Plant extract that causes vomiting May be abused by bulimic patients
Indications	NO LONGER RECOMMENDED
Contraindication	Acids, alkalis, hydrocarbons, unprotected airway, depressed level of consciousness, seizure, cardio-pulmonary instability
Complications	Protracted vomiting, aspiration, esophageal rupture

ORO-GASTRIC LAVAGE	
Mechanism	Use of a large bore tube, gastric irrigation, remove pill fragments
Indications	NO LONGER ROUTINELY RECOMMENDED Has limited utility in preventing toxicity Best within 1 hour for life-threatening agents, agents not adsorbed by activated charcoal or agents which do not have an antidote
Contraindication	Acids, alkalis, hydrocarbons, altered mental status, unprotected airway
Complications	Aspiration (airway can be protected with endotracheal intubation) Gastric/ esophageal rupture

ACTIVATED CHARCOAL	
Mechanism	Adsorption by charcoal prevents absorption “GI dialysis”: Adsorption of drug already in the blood stream
Indications	Ingestion of potential dangerous amount of a substance adsorbed by charcoal within 1 hour of ingestion May be considered after 1 hours for substances that delay gastric emptying
Contraindication	Absence of intact or protected airway, bowel obstruction, perforation Not adsorbed by activated charcoal: Acids/alkali, hydrocarbon, metals (Fe, Li), cyanide, pesticides, solvents, alcohols
Complications	Aspiration
Dose	Child: 1 gram/kg PO/NG Adolescent/Adult: 50-100 grams PO/NG OR Binding Ratio of 10 grams of Activated Charcoal per 1 gram of Toxin

MULTIDOSE ACTIVATED CHARCOAL	
Mechanism	Uses gastrointestinal tract as a dialysis membrane
Indications	Agents with entero-hepatic or entero-enteric circulation: Phenobarbital, Carbamazepine, Theophylline, Dilantin, Digoxin, Salicylates

2. ENHANCEMENT OF EXCRETION

CATHARTICS (SORBITOL)	
Mechanism	Hyperosmolar agent that increase stool output
Indications	NO LONGER RECOMMENDED Little evidence to support its use May be given with the first dose of activated charcoal
Contraindication	Children < 6 years
Complications	Electrolyte abnormalities

WHOLE BOWEL IRRIGATION (POLYETHYLENE GLYCOL)	
Mechanism	Large volumes used to flush the GI tract; no fluid/electrolyte abnormalities
Indications	Useful for small molecules or ions such as Fe or Li, and sustained release or enteric-coated preparations.
Contraindication	Ileus, GI tract obstruction and/or perforation, colitis
Dose	Child: 25 ml/kg/hour Adult: 1-1.5 liters/hour

ION TRAPPING (URINARY ALKALINIZATION)	
Mechanism	Alkalinization of the urine may enhance the excretion of acids. Alkalinization leaves the toxin in the ionic form which decreases absorption and promotes excretion
Indications	Significant Salicylate or Phenobarbital ingestions Dose 1-2 meq/kg $NaHCO_3$ Q3-4 hours (Goal urine PH 7.0-8.0)
Complications	Must maintain normokalemia Hypokalemia will decrease K+/Acid exchange in the kidneys

HEMODIALYSIS	
Mechanism	Direct removal of agents from the blood Filters blood across a series of membranes A steep concentration gradient allows for diffusion Corrects metabolic abnormalities
Indications	Worsening metabolic derangements unresponsive to supportive care and antidotes Toxins with the following properties: Small (low molecular weight) Little protein binding Primarily in the blood (have a low volume of distribution) High water solubility Slow endogenous clearance (will not be cleared quickly naturally)
	Toxic Alcohols: Methanol, Ethylene glycol, Ethanol, Isopropyl alchohol Antiepileptics: Phenobarbital, Valproic acid, Carbamazepine Other: Salicylates, Lithium, Methotrexate, Metformin, barbiturates
Contraindications	Patients with hemodynamic instability may not tolerate dialysis Drugs that have a prolonged half life and are excreted by the kidney in patients with renal impairment may benefit from renal replacement therapy.

APPENDIX A: TOXIDROMES

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics[2]	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime

1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome Hyperpyrexia syndromes may mimic the sympathomimetic toxidrome with a addition of muscle rigidity/clonus
2. The anticholinergic toxidrome refers to antimuscarinic agents

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET

*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size

APPENDIX B: ANTIDOTES

ANTIDOTES	
AGENT/CLASS	ANTIDOTE
Acetaminophen	N-Acetyl cysteine
Anticholinergics (e.g. Benadryl)	Physostigmine*
Beta Blockers (e.g. Propranolol)	Glucagon, High dose Insulin/Dextrose, Intralipids
Benzodiazepines	Flumazenil (avoid if TCA, seizure potential)
Bupivacaine	Intralipid emulsion
Calcium Channel Blockers	Calcium, High dose Insulin/Dextrose, Intralipids
Carbon Monoxide	O_2, Hyperbaric oxygen
Crotalid Envenomation	Crotalidae Polyvalent Immune Fab Antivenom
Cyanide	Hydroxocobalamin, Sodium thiosulfate
Digoxin	Digoxin specific Fab
Ethylene Glycol	Ethyl alcohol, 4-methylpyrazole, Pyridoxine*
Heparin	Protamine*
Iron	Deferoxamine
Isoniazid	Pyridoxine* (Vitamin B6)
Lead	BAL, $CaNa_2EDTA$ (encephalopathy) Dimercaptosuccinic acid (DMSA)
Malignant Hyperthermia	Dantrolene
Methanol	Ethyl alcohol, 4 Methylpyrazole
Methemoglobin inducers (Nitrates)	Methylene blue
Neuroleptic Dystonic Reaction	Diphenhydramine
Neuroleptic Malignant Syndrome	Bromocriptine
Opioids	Naloxone
Organophosphates	Atropine, Pralidoxime* (2-PAM)
Sulfonylurea Hypoglycemic Agents	Dextrose, Octreotide
Tricyclic Antidepressants	$NaHCO_3$ (dysrhythmias) Benzodiazepines (seizures), Intralipids
Warfarin	Fresh frozen plasma, Vitamin K_1
*BEWARE The 4 P's with similar sounding names Physostigmine: Anticholinergics Pralidoxime: Organophosphates Pyridoxine: Isoniazid Protamine: Heparin	

AGENTS: OVERVIEW

INTRODUCTION (JEFFREY FINE, M.D., 4/2020)
This PEM Guide provides an overview of multiple toxins. Almost all of the agents reviewed are discussed in greater detail in a specific PEM Guide. Consultation with the regional poison control center is an essential part of the diagnosis and management of the poisoned patient. National 1-800-222-1222. In NYC can also call 212-POISONS (212-764-7667).

ACETAMINOPHEN	
Example	Found in many over the counter preparations. Screen for in most overdoses.
Mechanism	In overdose, excess drug is shunted through the P450 pathway with production of a toxic metabolite (NADQI). There is inadequate glutathione to detoxify the metabolite leading to centrilobular hepatic necrosis.
Presentation	Initial 24 hours: Asymptomatic or mild nausea/vomiting 24-48 hours: Asymptomatic, LFT abnormalities 48-96 hours: Clinical hepatitis, hepatic failure and coagulopathy > 96 hours: Resolution in survivors Acetaminophen level >150 mcg/mL at 4 hours indicates high likelihood of developing hepatoxicity and is an indication for therapy
Treatment	Activated charcoal if less than 4 hours since ingestion
Antidote	N-acetyl cysteine within 8 hours of ingestion prevents hepatotoxicity Guided by potential for toxicity (Rumack-Matthew nomogram) PO 140 mg/kg then 70 mg/kg Q4H for a total of 17 doses IV 150 mg/kg over 1hr, 50 mg/kg over 4hrs, 100 mg/kg over 16 hours
See: PEM Guide: Toxicology: Acetaminophen	

ACIDS	
Example	Hydrochloric, sulfuric acid.
Mechanism	Coagulation necrosis primarily to the stomach Gastric perforation is common
Presentation	Crying (pain), refusal to eat, drooling, oropharyngeal burns, abdominal pain, stridor, vomiting.
Diagnosis	Extent of injury and need for surgery is determined by endoscopy, clinical evaluation and possibly CT. Chest and/or Abdominal XRAY for suspected perforation
Treatment	GI decontamination is contraindicated Steroids bases on injury grade Antibiotics for perforation No indication for dilution, neutralization
See: PEM Guide: Toxicology: Caustics	

ALKALINE AGENTS	
Example	NaOH, Drano, oven cleaners, hair relaxers
Mechanism	Liquefaction necrosis penetrates deep into the airway, esophagus and stomach.
Presentation	Crying (pain), refusal to eat, drooling, oropharyngeal burns, abdominal pain, stridor, vomiting. Esophageal stricture (late) if severe injury.
Diagnosis	Extent of injury and need for surgery is determined by endoscopy, clinical evaluation and possibly CT. Chest and/or Abdominal XRAY for suspected perforation
Treatment	GI decontamination is contraindicated. Steroids bases on injury grade Antibiotics for perforation No indication for dilution, neutralization
See: PEM Guide: Toxicology: Caustics	

ALPHA-2 ADRENERGIC AGONISTS	
Example	Clonidine
Mechanism	↓ Blood pressure by reducing sympathetic outflow from the CNS (in overdose, may cause peripheral vasoconstriction as well)
Presentation	Significant altered mental status, hypotension, bradycardia, Respiratory depression/apnea, miosis (mimic opioids)
Treatment	Activated charcoal Whole bowel irrigation: Clonidine patch ingestion IV fluids, Dopamine or Epinephrine for fluid refractory hypotension Atropine for bradycardia, consider cardiac pacing
Antidote	Naloxone 0.1 mg/kg (max 2 mg), repeat PRN
See: PEM Guide: Toxicology: Antihypertensives	

ANTICHOLINERGIC AGENTS	
Example	Diphenhydramine, jimson weed
Mechanism	Block peripheral and central muscarinic receptors
Presentation	Mydriasis (“blind as a bat”), pupils nonreactive (inhibits constriction) Dry skin (“dry as a bone”) Red skin (“red as a beet”) Fever (“hot as Hades”) Altered mental status (“mad as a hatter”) Tachycardia, urinary retention, and ileus, seizures
Treatment	Generally supportive
Antidote	Physostigmine is used for treatment of significant symptoms, especially severe agitation, hallucinations, profound hyperthermia, uncontrolled seizures. Dose 0.5 mg IV (child), 1-2 mg (adolescent/adult) Give over 2-3 min. Alternate: Benzodiazepines
See: PEM Guide: Toxicology: Anticholinergics	

BENZODIAZEPINES (BZD)	
Example	Valium, Xanax, Klonopin
Mechanism	Enhanced GABA activity leads to increased sedation. Variations in the GABA receptor allow for the variable physiologic effects of these agents (sedation, hypnosis, anxiolysis, amnesia, and muscle relaxation).
Presentation	Sedative-hypnotic toxidrome: Decrease in vitals signs, mental status, no increase or decrease in bodily fluids. Respiratory depression in large doses, ↑ with co-ingestant (e.g. ETOH)
Diagnosis	Altered mental status, Bedside glucose, ethanol level, BMP, EKG
Treatment	Supportive care (airway, breathing) typically sufficient
Antidote	Flumazenil; Nonspecific benzodiazepine competitive antagonist Only indicated in clinical over-dosing Contraindicated in chronic BZD abuse → Life-threatening withdrawal Contraindicated in patients needing BZD for actual/potential seizures
See: PEM Guide: Toxicology: Sedative Hypnotics	

BETA ADRENERGIC ANTAGONISTS (BETA BLOCKERS)	
Example	Propranolol
Mechanism	Block beta-adrenergic receptors
Presentation	Bradycardia, hypotension, hypoglycemia, bronchospasm
Treatment	IV fluids, Dopamine or Epinephrine for fluid refractory hypotension Calcium, phosphodiesterase inhibiters may improve cardiac output Atropine for bradycardia, consider cardiac pacing Dextrose for hypoglycemia
Antidote	Glucagon is a specific antidote. Initial 50 mcg/kg, may repeat in 10 min Refractory: High dose Insulin/Glucose or lipid emulsion therapy
See: PEM Guide: Toxicology: Antihypertensives	

CARBON MONOXIDE (CO)	
Example	House fires, motor vehicle exhaust, methylene chloride metabolism
Mechanism	Carbon monoxide is the leading cause of “poisoning” deaths. Fetus/neonate are more sensitive to CO than adults. High affinity for hemoglobin results in the production of carboxy-hemoglobin, which has decreased O_2 carrying capacity and shifts the O_2 dissociation curve to the left.
Presentation	Headache, confusion, dyspnea, chest pain, coma, shock, myocardial ischemia. May cause delayed neuropsychiatric effects.
Diagnosis	Co-oximetry panel (does not need to be arterial)
Treatment	Room air (CO T½ = 4 hours), 100% O_2 (CO T½ = 60-90 min)
Antidote	Hyperbaric oxygen (CO T½ = 15-30 min)
See: PEM Guide: Toxicology: Carbon Monoxide	

CALCIUM CHANNEL BLOCKERS (CCB)	
Example	Nifedipine (Dihydropyridines), Diltiazem (Non-dihydropyridines)
Mechanism	Block L-type calcium channels (selectivity lost in overdose) 1. Vascular smooth muscle (vasodilation) (Dihydropyridines), 2. Myocardium (↓ conduction, contractility)(Non-dihydropyridines) 3. Pancreas: ↓ insulin release (hyperglycemia)
Presentation	Dihydropyridines: Hypotension, reflex tachycardia Non-dihydropyridines: Bradycardia, conduction abnormalities Less altered mental status than beta blockers, alpha adrenergic agonists
Diagnosis	Hypotension, brady/tachycardia, hyperglycemia
Treatment	Whole bowel irrigation for extended release CCB's IV fluids, Dopamine or Epinephrine for fluid refractory hypotension Calcium, phosphodiesterase inhibiters may improve cardiac output Atropine for bradycardia, consider cardiac pacing
Antidote	Glucagon: 50 mcg/kg, may repeat in 10 min Refractory: High dose Insulin/Glucose or lipid emulsion therapy
See: PEM Guide: Toxicology: Antihypertensives	

CYANIDE (CN)	
Example	House fires (released from burning wood, nylon, silk), laboratory chemicals, silver polish
Mechanism	Cyanide's probable principal toxicity is the result of inactivation of cytochrome oxidase (binds to ferric iron) and the resulting impairment of cellular respiration
Presentation	CNS depression, dyspnea, shock, profound anion gap metabolic acidosis, seizures, cyanosis (late finding), smell of bitter almonds
Treatment	100% 0_2, ventilation, $NaHC0_3$ IV fluids and vasopressors for hypotension
Antidote	Hydroxocobalamin is the preferred antidote. Some toxicologists recommend the addition of Sodium Thiosulfate if: 1. Severe toxicity 2. Insufficient Hydroxocobalamin available 3. Insufficient response to Hydroxocobalamin
	Hydroxocobalamin (Cyanokit): Chelates CN 70 mg/kg (max 5 grams) IV over 30 min (may push quickly for arrest) May repeat to max 15 gm. Subsequent doses given over 6-8 hours
	Sodium Thiosulfate: Facilitates the formation of thiocyanate. Adult: 12.5 grams (50 ml of 25% solution) Child: 0.5 grams/kg (2 ml/kg of 25% solution) maximum 12.5 grams As a bolus or over 10-30 minutes depending on severity Repeated prn at ½ the initial dose if manifestation reappear or at 2 hours as prophylaxis
See: PEM Guide: Toxicology: Cyanide	

CYCLIC ANTIDEPRESSANTS	
Example	Amitriptyline, Nortriptyline
Mechanism	Na+ channel blockade. Direct myocardial depression, inhibition of norepinephrine uptake, anticholinergic properties
Presentation	CNS: Agitation, delirium, coma, seizures Cardiovascular: wide QRS dysrhythmias, hypotension Initially asymptomatic then rapid deterioration within 2 hours
Diagnosis	Right axis deviation of terminal 40 msec (R in AVR, S in AVL)
Treatment	QRS > 100 msec is a risk for dysrhythmia: Rx: $NaHCO_3$ 1-2 meq/kg Hypotension: Crystalloid Seizures: Benzodiazepines Consider intralipid emulsion No Physostigmine: Results in cardiovascular collapse
See: PEM Guide: Toxicology: Cyclic Antidepressants	

DIGOXIN	
Mechanism	Inhibits $Na+/K^+$/ATPase and interferes with Na/Ca exchange into/out of the sarcoplasmic reticulum
Presentation	Nausea, vomiting, dysrhythmias, hyperkalemia (acute toxicity)
Treatment	Hyperkalemia with bicarbonate, insulin, and glucose (NO calcium for hyperkalemia (intracellular Ca++ is already high)
Antidote	Specific antidote is digoxin-specific antibodies (Digibind)

ETHANOL	
Examples	Alcoholic beverages, mouthwash, over-the-counter cough and cold preparations
Mechanism	CNS and respiratory depressant
Presentation	Characteristic odor, altered mental status
Diagnosis	Lab: >100 mg/dl intoxication, > 500 mg/dl can be lethal
Treatment	Supportive care: Assisted ventilation In young children hypoglycemia due to low hepatic glucose stores
See: PEM Guide: Toxicology: Sedative Hypnotics	

HALLUCINOGENS	
Examples	A variety of agents are taken to alter perception, thought process, emotion, arousal, self-image and mood (PCP, LSD, Ketamine etc.)
Mechanism	Altered serotonin (Central 5-HT_{2A} receptors), dopamine, aspartate. Kappa opioid receptors agonism (Salvia divinorum) NMDA receptors (Dextromethorphan)
Presentation	Sympathomimetic effects are common Serotonin syndrome: LSD, MDMA, dextromethorphan, psilocybin. Neuropsychiatric: Desired (euphoria), Undesired (panic)
Treatment	Supportive care, quiet environment. Benzodiazepines if agitated
See: PEM Guide: Toxicology: Hallucinogens	

HYDROCARBONS	
Example	Gasoline, kerosene, mineral oil, furniture polish, glues
Mechanism	Low surface tension: aspiration with chemical pneumonitis, ARDS
Presentation	Many hydrocarbons (e.g. glue, spray paints or gasoline) are abused by sniffing or huffing with inadvertent death due to asphyxia
Treatment	GI decontamination is contraindicated Discharge if asymptomatic for 6 hours and normal chest XRAY Symptomatic: supportive care
See: PEM Guide: Toxicology: Inhalants	

GAMA HYDROXY BUTYRATE (GHB)	
Examples	GHB act at GHB receptors primarily as a CNS depressant Used a date-rape drug Used by body builders due to ↑ growth hormone
Mechanism	CNS and respiratory depressant
Presentation	Sedative-Hypnotic toxidrome: Decreased vital signs, mental status Bradycardia, hypotension, coma, myoclonic jerks and rarely seizures. Stimulant effects (agitation, self-injurious behavior) may be seen early or alternating with sedative effects.
Treatment	Supportive care: Assisted ventilation
See: PEM Guide: Toxicology: Sedative-Hypnotics	

IRON (FE)	
Example	Iron supplements, present in many multivitamins
Mechanism	Excess Fe leads to the formation of superoxide free radicals which interfere with metabolic processes, directly damaging GI mucosa Ferrous Sulfate (20% Elemental Fe), fumarate (32%), gluconate(10%) Toxic dose: 250 mg/kg
Presentation	GI Stage (corrosive effect): Nausea, vomiting, and bloody diarrhea Relative Stability Stage (not symptom free): No more than 6-12 hours Shock Stage (primary cause of mortality): Altered mental status, shock, and anion-gap metabolic acidosis. Hepatotoxic Stage (secondary cause of mortality): within 48 hours
Diagnosis	Serum Fe Level > 500 mcg/dl at 2-6 hours risk of shock, death Abdominal XRAY to identify adult iron pills, concretions Leukocytosis and hyperglycemia do not correlate with toxicity
Treatment	Fluid resuscitation Fe is not absorbed by charcoal Consider whole bowel irrigation
Antidote	Antidote: Deferoxamine (chelation) for Fe > 350 mcg/dl Dose 15 mg/kg/hour to maximum of 6 grams/day
See: PEM Guide: Toxicology: Iron	

ISONIAZID (INH)	
Mechanism	Interferes with pyridoxine metabolism
Presentation	Anion gap metabolic acidosis, seizures, coma
Treatment-Antidote	Antidote: Pyridoxine (vitamin B6) 1 gram B6 for each 1 mg INH If unknown amount give 5 grams and repeat in 15 minutes

LEAD (PB)	
Example	Leaded paint, crystal, contaminated soil
Mechanism	Inhibits enzymes by binding to sulfhydryl groups and by interfering with calcium mediated processes
Presentation	Anemia, abdominal pain, encephalopathy, peripheral neuropathy
Treatment-Antidote	Encephalopathy: BAL, $CaNa_2EDTA$ Asymptomatic or mild symptoms: Dimercaptosuccinic acid (DMSA)

LITHIUM (LI)	
Example	Lithium Carbonate: Manic-depressive disorder, refractory depression
Mechanism	Mechanism of action unclear. 95% eliminated by kidneys, 60% reabsorbed. ↓ GFR, dehydration, → ↑ reabsorbed → ↑ Lithium levels Medications: NSAIDs, ACE inhibitors, thiazide diuretics, calcium channel blocker can ↑ Lithium levels
Presentation	GI (Acute) : Nausea, vomiting, diarrhea → dehydration Neurologic (Chronic): Altered mental status, tremors, fasciculation, clonus, seizures Renal (chronic): Nephrogenic diabetes insipidus, nephritis Cardiac: T wave inversions, ST elevation, sinus bradycardia,
Diagnosis	Serum lithium level (do not send in tube (typically green top) with lithium heparin
Treatment	IV hydration, consider whole bowel irrigation Hemodialysis for severe symptoms. high levels
See: PEM Guide: Toxicology: Lithium	

MARIJUANA	
Example	Dried leaves of *Cannabis septiva,* hashish (dried resin) and hash oil (liquid extract).
Mechanism	delta-9-tetrahydrocannabinol (THC) most psychoactive component. Brain cannabinoid 1 receptors (CB1) inhibits the release of: norepinephrine, dopamine, serotonin, acetylcholine, gamma hydroxyl-butyric acid and glutamate.
Presentation	Euphoria, relaxation, analgesia, impaired motor, speech, short-term memory, perceptual distortion, increased appetite, dry mouth, conjunctival injection, tachycardia Heavy usage: agitation, panic attacks, anxiety, paranoia, delusions/delirium, cannabinoid hyperemesis syndrome
Diagnosis	Based on signs and symptoms, Utox false negative with synthetic marijuanas
Treatment	Supportive care, quiet environment, benzodiazepines for severe agitation
See: PEM Guide: Toxicology: Marijuana	

METHEMOGLOBIN INDUCERS	
Example	Nitrates (in well water), Pyridium, Dapsone, Neonates with diarrhea
Mechanism	Oxidize hemoglobin to methemoglobin, decreased O_2 carrying capacity. Shifts O_2 dissociation curve to the left.
Presentation	Cyanosis, headache, dyspnea, CNS depression, Chocolate brown-colored arterial blood Monitored O_2 Sat approximately 85% despite O_2 therapy
Diagnosis	Co-oximetry panel
Treatment-Antidote	Methylene blue for significant symptoms or MetHb > 20%, 1-2 mg/kg over 5 min (0.1-0.2 ml/kg of 1% solution) repeat 1hr prn
See: PEM Guide: Toxicology: Methemoglobinemia	

NICOTINE	
Example	Patches, gum lozenges, nasal spray, snuff, liquid nicotine to refill e-cigarettes
Mechanism	Nicotine mimics effects of acetylcholine release at nicotinic receptors in the brain, spinal cord, autonomic ganglia, adrenal medulla, neuromuscular junctions, and chemoreceptors of the aortic and carotid bodies. High doses result in effects at both nicotinic and muscarinic receptors
Presentation	Nicotinic: muscle fasciculations, paralysis, coma, seizures Muscarinic: vomiting, diarrhea, lacrimation, salivation, bronchorrhea, bradycardia, miosis
Diagnosis	Cholinergic toxidrome
Treatment	Supportive care, Atropine, fluids, decontamination Pralidoxime is not effective (acts on ACHE, not at the acetylcholinereceptor)
See: PEM Guide: Toxicology: Nicotine	

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)	
Example	Ibuprofen, Naproxen
Mechanism	Cyclo-oxygenase inhibitor, Reduces prostaglandin and thromboxane synthesis
Presentation	< 100 mg/kg (asymptomatic) 100-400 mg/kg (symptomatic within 4 hours) > 400 mg/kg (life threatening) GI: Nausea, vomiting, epigastric pain, GI hemorrhage CNS: Depressed mental status, seizures, hallucinations, tinnitus Hypotension, apnea, anion gap metabolic acidosis (hyperpnea)
Treatment	Care is primarily supportive Ventilatory support: must increase minute ventilation to match patient Consider activated charcoal: large dose, within 1 hour, alert patient Antacids, Antiemetics Sodium bicarbonate for fluid refractory metabolic acidosis Benzodiazepine for seizure
See: PEM Guide: Toxicology: NSAIDS	

OPIATES (NATURAL), OPIOIDS (SYNTHETIC)	
Example	Morphine, fentanyl, heroin, methadone, codeine
Mechanism	Opioid receptor agonists
Presentation	Depressed mental status Respiratory depression Non-cardiogenic pulmonary edema Miosis, bradycardia, seizures with Meperidine
Treatment	Ventilatory support
Antidote	Naloxone (pure antagonist) Full reversal (opiod naive): 0.1 mg/kg or 2 mg (< 5yo) Partial reversal (opioid-dependent adolescent or adult): 0.04 mg. Titrate Up PRN Goal: Reverse respiratory depression, not to normal mental status, Monitor for withdrawal
See: PEM Guide: Toxicology: Opioids	

ORGANOPHOSPHATES	
Example	Malathion insecticide, sarin nerve gas Carbamates (carbaryl flea powder, pyridostigmine) are nearly identical but do not permanently inactivate acetylcholinesterase and therefore have shorter duration of effect.
Mechanism	Inhibits acetyl cholinesterase increasing synaptic acetylcholine
Presentation	Cholinergic Syndrome Muscarinic (SLUDGE): Salivation, Lacrimation, Urination, Defecation, GI motility, Emesis. Also bronchorrhea, bronchospasm, bradycardia (“Killer Bs”), miosis, seizures Nicotinic: muscle fasciculations, muscle weakness
Treatment	Significant dermal absorption. Remove clothing and wash skin. Airway protection with ventilation Anticonvulsant therapy
Antidote	Initial therapy is Atropine (an anti-muscarinic anticholinergic) Titrate dose to reverse bronchorrhea, bronchospasm, and respiratory distress. May require very large doses of atropine.
	Pralidoxime prevents permanent inactivation of acetylcholinesterase Effect at nicotinic receptor: 25 mg/kg IV over 5-30 min then infusion
See: PEM Guide Toxicology: Cholinergics	

SALICYLATES (ASA)	
Example	Found in many OTC preparations. Should be screened for in unknown overdoses Methyl salicylate (icy hot), Oil of Wintergreen (high concentration)
Mechanism	Central hyperventilation resulting in respiratory alkalosis. Uncouples oxidative phosphorylation → fever, metabolic acidosis
Presentation	Anion-gap metabolic acidosis. In adults, mixed acid-base disturbance (resp alkalosis, met acidosis) In children, acidosis predominates. Clinical: nausea/vomiting, tinnitus, altered mental status, fever, tachycardia, hyperpnea, pulmonary edema, shock, seizure
Diagnosis	ABG, salicylate level (Use of the Done nomogram is not recommended) < 150 mg/kg (mild), 150-300 mg/kg (moderate), > 300-500 mg/kg (serious). > 500 mg/kg (severe)
Treatment	Multiple dose activated charcoal
	Urinary alkalization: D5W with 50 mEq/L NaHCO3 at 10-15 ml/kg over 1-2 hours, maintain urine PH > 7 and normal K+
	Hemodialysis: Indicated for salicylate level > 5000 mg/dL, pulmonary edema, renal failure, persistent CNS disturbance, congestive heart failure, refractory acidosis
See: PEM Guide: Toxicology: Salicylates	

SEROTONERGIC AGENTS	
Examples	Many medications/drugs of abuse: Fentanyl, SSRI, SNRI, MAOI, TCA, antiemetics (ondansetron, metoclopramide), antiepileptics (carbamazepine, valproate), triptans, cocaine, MDMA, Methamphetamine, Dextromethorphan
Mechanism	Many: acts as a serotonin precursor or agonist, decrease metabolism or reuptake, increase release
Presentation	Aspects of sympathomimetic toxidrome + neuromuscular signs Hyperpyrexia Altered mental status: Agitation, anxiety, coma, lethargy Autonomic instability: Mydriasis, flushing, diaphoresis Neuromuscular changes: Hypertonia, clonus, hyperreflexia, tremor Citalopram (Celexa), Escitalopram (Lexapro) → prolonged QT, QRS, Torsades (polymorphic ventricular tachycardia)
Treatment	Removal of inciting medication, drug, aggressive cooling Hypotension: IV fluids, epinephrine, phenylephrine
Antidote	Cyproheptadine (serotonin antagonist). Available in oral preparation only Children: 0.25 mg/kg/day divided Q6 hours.
See: PEM Guide: Toxicology: Serotonergic Agents	

SULFONYLUREA HYPOGLYCEMIC AGENTS	
Example	Glyburide, Glipizide, Tolbutamide, Chlorpropamide
Mechanism	Stimulate pancreatic islet beta cells to secrete insulin
Presentation	Hypoglycemia, altered mental status, coma, seizure Symptoms may be delayed or prolonged
Treatment	Glucose for hypoglycemia
Antidote	Octreotide is a synthesized, longer acting analog of Somatostatin Adults: 50 mcg SQ Q6H. Child: 1-1.25 mcg SQ Q6H (max 50 mcg/dose)

SYMPATHOMIMETIC AGENTS	
Example	Cocaine, amphetamine (Theophylline toxicity has similar presentation)
Mechanism	Increased release of catecholamines into synapse
Presentation	Sympathomimetic toxidrome: Agitation, diaphoresis, fever, mydriasis, tachycardia, seizures, neuropsychiatric effects
Treatment	Primary therapy is sedation with benzodiazepines Bicarbonate indicated for cocaine-induced wide complex tachydysrhythmia No beta agonists (will result in unopposed alpha agonism)
See: PEM Guide: Toxicology: Stimulants	

TOXIC ALCOHOLS	
Example	Ethylene Glycol (antifreeze) Methanol (windshield washer fluid)
Mechanism	Ethylene Glycol (EG) forms glycolic acid, oxalic acid Methanol forms formic acid. Ethanol and isopropanol do not cause a metabolic acidosis
Presentation	Delay in presentation due to time to toxic metabolite production Both: CNS depression, anion gap metabolic acidosis, osmolar gap. Ethylene Glycol causes oxalate crystalluria, renal failure Methanol causes ocular symptoms (e.g. blindness) Ethanol and isopropanol can cause an osmolar gap though not typically an elevated anion gap metabolic acidosis
Treatment	Hemodialysis eliminates the parent compound and toxic metabolites.
Antidote	4-methylpyrazole (4MP or Fomepizole) inhibits the metabolism of the parent compound by alcohol dehydrogenase. Loading 15 mg/kg IV (dilute in 100 ml NS or D5W give over 30 min) then Q12 hour PRN 4MP in some cases obviates the need for hemodialysis
See: PEM Guide: Toxicology: Toxic Alcohols	

WARFARINS	
Example	Brodifacoum rat poison, Coumadin
Mechanism	Inhibit Vitamin K reductases, and thus Vitamin K function. “Superwarfarins” may have protracted duration
Presentation	Increased bleeding
Treatment	Life threatening: FFP 15 ml/kg followed by Vitamin K_1 10 mg/kg IV

ACETAMINOPHEN

INTRODUCTION (MICHAEL MOJICA, M.D., 2/2020)
Acetaminophen is also known as APAP (n-Acetyl-P-AminoPhenol) or Paracetamol in Europe. It is the most common drug used for analgesia & antipyresis in children. It is commonly found in combination with many over-the-counter and prescription products. Because of its ubiquity and because patients may not be symptomatic at presentation it (and salicylates) should be screened for in all ingestions.

Acetaminophen is the most common cause of acute liver failure in the United States and is the 2nd leading cause of toxin related death. Oral, immediate release preparations reach peak plasma levels in less than 1 hour. An intravenous preparation is now approved in US. The infant drops concentration (100 mg/ml or 80 mg/0.8 ml) has been discontinued because of the potential of dosing errors resulting in overdose. Acetaminophen elixir (160 mg/ml) is the only currently available concentration. The FDA is recommending the acetaminophen not be paired with opiate drugs (e.g., Percocet) in order to prevent acetaminophen toxicity.

PHARMACOLOGY
Acetaminophen is metabolized in the liver by three pathways: 1. glucuronidation, 2. sulfation and through the 3. cytochrome p450 system. In toxic doses the glucuronidation and sulfation pathways become saturated and the c-p450 system takes on a bigger role in metabolism. The c-p450 system requires glutathione as a co-factor. With toxic doses of acetaminophen, glutathione is depleted resulting in the accumulation of the toxic hepatotoxic metabolite NAPQI. A toxic dose of acetaminophen is typically 150 mg/kg in a child or 7.5 grams in an adult.

PRESENTATION

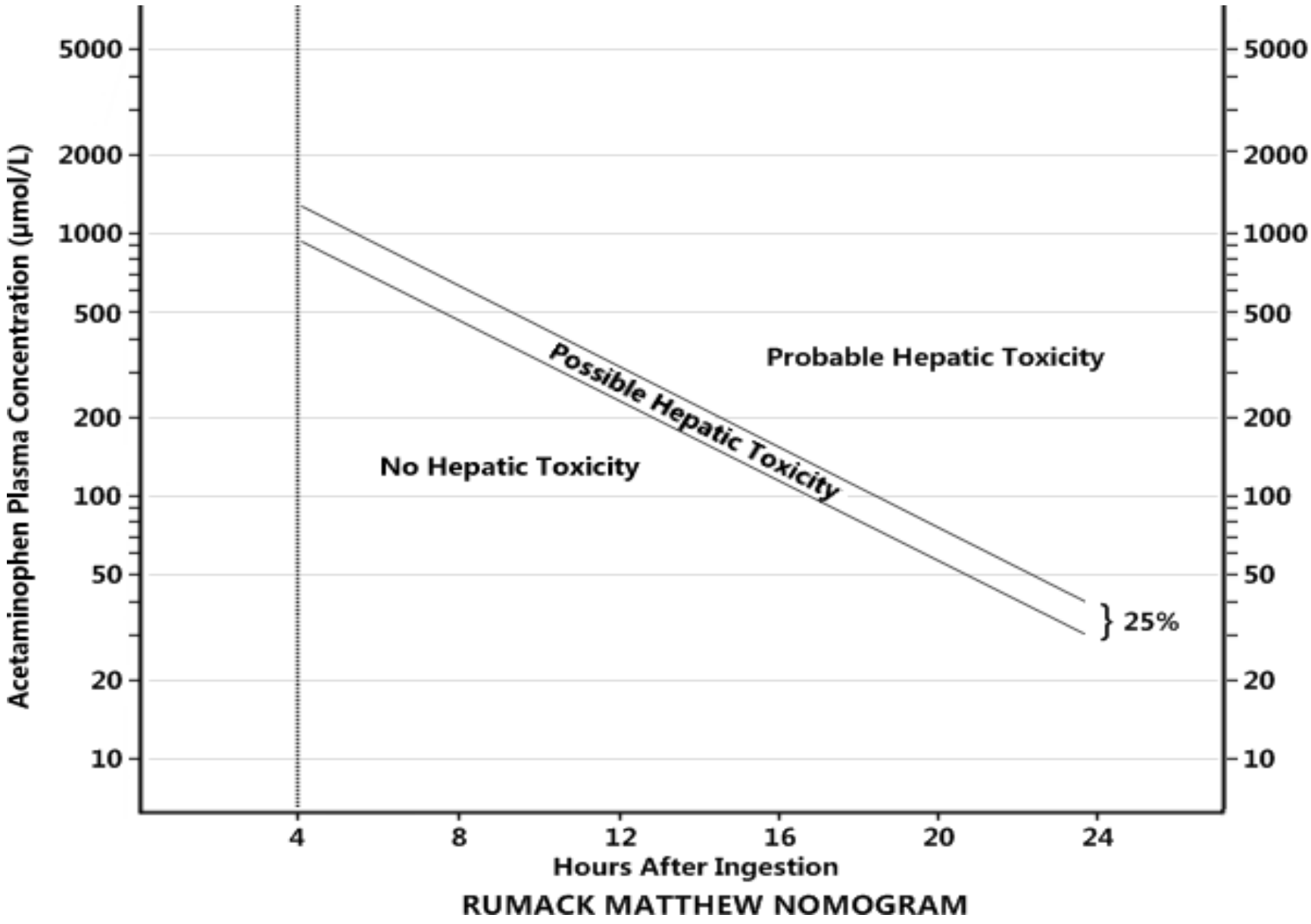
STAGES OF ACETAMINOPHEN TOXICITY		
1	1st 24 hours	No hepatic damage. LFT's normal Asymptomatic OR Nausea, vomiting, malaise, diaphoresis
2	24-72 hours	Onset of hepatotoxicity (small % of overdoses), RUQ abdominal pain AST (injury) elevated prior to elevated PT (function)
3	72-96 hours	Maximal hepatotoxicity → Fulminant hepatic failure Death from hepatic failure or coagulopathy (3-5 days)

MANAGEMENT (SINGLE, ACUTE INGESTION)
The National ((800) 222-1222) or NYC (212-POISONS) center should be consulted. This is particularly important for multiple or chronic ingestions and intravenous or sustained release preparations. If the patient has an altered mental status consider the possibility of a co-ingestant. Send an acetaminophen level 4 hours after ingestion or immediately if it is greater than 4 hours post ingestion or if the time of ingestion is unknown. If the time of ingestion is unknown or more the 24 hours have elapsed obtain an acetaminophen level and aspartate aminotransferase (AST) level. Treatment is indicated if the AST is elevated regardless of acetaminophen level.

Supportive care includes the control nausea and vomiting with antiemetics. Activated charcoal may be administered at a dose 1 gram/kg. Importantly, charcoal does not significantly affect the administration of oral N-Acetyl-Cysteine (NAC).

The Rumack-Matthew nomogram can be used to determine the risk of hepatotoxicity and the need for NAC. The nomogram is intended for use only in a single, acute ingestion of a non-sustained release preparation. The upper line of the nomogram represents the original line below which there is no hepatotoxicity. The lower line was lowered by 25% to allow for a margin of error.

RUMACK-MATTHEW NOMOGRAM: ACUTE, SINGLE ACETAMINOPHEN OVERDOSE



WEB LINK: RUMACK-MATTHEW NOMOGRAM:ACETAMINOPHEN OVERDOSE

N-ACETYL-CYSTEINE: N-Acetyl-Cysteine reduces hepatotoxicity by: 1. serving as a glutathione precursor, 2. enhancing the sulfation pathway and by 3. directly conjugating NAPQI. Studies have demonstrated the absence of hepatotoxicity if it is administered within 8 hours of ingestion. Though it is most effective within 8 hours of ingestion, it may be used after that time as well. (Smilkstein, NEJM 1988, PubMed ID: 3059186).

Intravenous dosing has the benefit of a shorter period of administration (21 hours) than oral dosing (72 hours). It is not dependent on patient compliance and tolerability. In a retrospective cohort study (n=2,086 Intravenous) with an historical cohort (n=1,962 Oral) the relative risk of toxicity was dependent on the time to initiation of therapy (Yarema, Ann Emerg Med. 2009, PubMed ID: 19556028). When N-acetylcysteine was administered within 12 hour of Acetaminophen ingestion there was a decreased risk of hepatotoxicity in the 20-hour regimen compared to the 72-hour regimen. There was no difference in the rate of hepatotoxicity for the two regimens when N-acetylcysteine was administered between 12 and 18 hours after Acetaminophen ingestion. When N-acetylcysteine was administered more than 18 hours after Acetaminophen ingestion there was a decrease risk of hepatotoxicity in the 72-hour regimen compared to the 20-hour regimen. Intravenous dosing is associated with a 7.1%, 95% CI (6.1, 18.3%) risk of anaphylactoid reactions of which 77% were limited to cutaneous reactions. The majority of these reactions are mild and will resolved with a slower rate or discontinuing the infusion. 51% of those with reaction had their infusion stopped either completely of transiently.

N-ACETYL-CYSTEINE: INDICATIONS
An acetaminophen level plotted on the nomogram indicating a risk of hepatotoxicity
A potentially toxic ingestion presenting greater the 8 hours post ingestion

N-ACETYL-CYSTEINE: ORAL DOSING	
PO/NG	140 mg/kg loading dose Followed by 70 mg/kg every 4 hours for 17 additional doses Total treatment time 72 hours

N-ACETYL-CYSTEINE: INTRAVENOUS DOSING			
	LOADING DOSE	2nd DOSE	3rd DOSE
Dose	150 mg/kg	50 mg/kg	100 mg/kg
Duration	Over 1 hour	Over 4 hours	Over 16 hours
Dilution	Dilute in D5W	Dilute in D5W	Dilute in D5W
> 40 kg	200 ml	500 ml	1000 ml
30 kg	100 ml	250 ml	500 ml
25 kg	100 ml	250 ml	500 ml
20 kg	60 ml	140 ml	280 ml
15 kg	45 ml	105 ml	210 ml
10 kg	30 ml	70 ml	140 ml
Concentration = 200 mg/ml Hyperosmolar: Compatible with H_20, D5W and ½ NS Total treatment time 21 hours			

WEB LINK: INTRAVENOUS NAC DOSING CALCULATOR

ANTICHOLINERGICS

INTRODUCTION (SEEMA AWATRAMANI, M.D., 2/2022)
In 2009, the American Association of Poison Control Centers (AAPCC) reported approximately 20,000 anticholinergic exposures, with 46 major outcomes but no recorded deaths. (See also PEM Guide: Toxicology: Cyclic Antidepressants)

Substances with anticholinergic properties include plants and medicines. There are over 600 substances that possess anticholinergic activity, either as a direct therapeutic effect or an adverse effect. Antihistamines (particularly diphenhydramine) are the most common overdose that produces anticholinergic toxicity. Other notable pediatric exposures include hyoscyamine-containing agents to treat colic, and topical diphenhydramine-containing salves. (e.g. Caladryl lotion, a combination of calamine and diphenhydramine)

Anticholinergic toxicity has also been reported in the adolescent age group who abuse Jimson weed for its hallucinogenic effects. Illicit drugs like heroin and cocaine are sometimes “cut” with scopolamine or atropine. Inadvertent poisonings from Chinese herbals teas and medications have also been reported.

Anticholinergic toxicity can also occur if atropine is administered as the antidote to misdiagnosed cholinergic poisoning in a patient with suspected exposure to a nerve agent or organophosphate insecticide.

PHARMACOLOGY
An anticholinergic agent is a substance that selectively blocks the neurotransmitter acetylcholine from blinding to its receptors in the peripheral and central nerve cells.

ACETYLCHOLINE RECEPTORS	
NICOTINIC	Located at the neuromuscular junction, the autonomic ganglia (both sympathetic and parasympathetic), CNS and adrenal medulla.
	The majority of anti-nicotinic agents that work at these receptors are non-depolarizing skeletal muscle relaxants for surgical use.
MUSCARINIC	Located in the parasympathetic ganglia of the autonomic nervous system, affecting smooth muscle (intestinal, bronchial, and cardiac), the secretory glands (salivary and sweat), the ciliary body of the eye, and also in the CNS.
	The majority of substances with anticholinergic properties work at the muscarinic receptor only.

Anticholinergic poisoning can occur after ingestion, inhalation, parenteral, or ocular use. The rate of absorption varies depending on the drug and the route of exposure. After an oral exposure, symptoms usually occur within one to two hours. This might be lengthened by delayed gastric emptying.

ANTICHOLINERGIC AGENTS	
Anticholinergic	Atropine
Antihistamines	Diphenhydramine, meclizine, promethazine, cyproheptadine
Tricyclic antidepressants	Amitriptyline, doxepin, imipramine, nortriptyline
Antispasmodics	Hyoscyamine, oxybutynin
Belladonna alkaloids	Atropine, hyoscyamine
Antipsychotics	Chlorpromazine, clozapine, olanzapine, thioridazine
Plants	Jimson weed (Datura stramonium) Deadly nightshade (Atropa belladonna) Amanita mushroom (Amanita muscaria, Amanita pantherina)

CLINICAL PRESENTATION

Anticholinergic toxicity is characterized by both peripheral and central clinical features. The classic anticholinergic toxidrome is well known. However, anticholinergic toxicity should be suspected even if all features are not present. The toxidrome can be thought of as UP (agitation, increased HR, BP, RR, temperature, mydriasis) and DRY.

ANTICHOLINERGIC TOXIDROME	
RED as a BEET	Cutaneous vasodilation occurs as a means to dissipate heat to compensate for the loss of sweat production by antimuscarinic activity in the sweat glands.
DRY as a BONE	Anhidrosis and dry mouth occur from inhibition of sweating and salivation.
HOT as a HARE	Anhidrotic hyperthermia: Lack of sweating interferes with normal heat dissipation mechanisms.
BLIND as a BAT	Non-reactive mydriasis: Pupillary dilation and ineffective accommodation manifests as blurry vision. Mydriasis is often a late sign.
MAD as a HATTER	CNS effects may include anxiety, agitation, dysarthria, confusion, disorientation, visual hallucinations, bizarre behavior, delirium, psychosis (usually paranoia), coma, and seizures. “Alice in Wonderland-like" or "Lilliputian type," (small people) hallucinations are described, where people appear to become larger and smaller. Patients with altered mental status may appear to grab invisible objects from the air.
FULL as a FLASK or STUFFED as a PIPE	Reduced detrusor contraction and increased tone of the urethral sphincter reduce the desire to urinate and contribute to urinary retention. Bladder distension may be palpable.
OTHER	Tachycardia (the earliest and most reliable sign though nonspecific) Decreased or absent bowel sound (ileus)

The toxic manifestations associated with a particular agent may be only partly explained by muscarinic receptor blockade. For example, the most life-threatening complications of tricyclic antidepressant overdose, wide-complex tachydysrhythmias, are a result of the sodium channel–blocking effects on the heart. The anticholinergic effects of different tricyclic antidepressants vary considerably.

DIFFERENTIAL DIAGNOSIS
Acute psychotic disorder: Diagnosis of exclusion
Alcohol and sedative-hypnotic withdrawal
Head trauma
Neuroleptic malignant syndrome
Postictal state
Reye syndrome
Serotonin syndrome (usually diaphoretic)
Viral encephalitis: e.g. HSV

LABORATORY EVALUATION

The diagnosis of anticholinergic toxicity is based on clinical findings. Serum levels of specific anticholinergics are neither readily available nor helpful.

LABORATORY TESTING	
Bedside glucose	Determine if hypoglycemia is the cause of altered mental status.
Acetaminophen, Salicylate levels	Rule out common co-ingestions. Salicylates can cause agitated, hyperthermic patients with altered mental status.
Electrocardiogram	Many anticholinergics also increase the QRS or QTc intervals due to sodium channel blockade.
Pregnancy test	In women of childbearing age
Creatine kinase	Should be measured in cases of severe psychomotor agitation or seizures to assess for rhabdomyolysis

MANAGEMENT

The poison control center should be consulted (National Poison Center: (800) 222-1222). In most cases observation, monitoring and supportive care are the only treatments needed. Adjunctive therapy may be considered based on the patient's symptom severity. All ingestions should be assessed for suicidality and undergo psychiatric evaluation as indicated.

GASTROINTESTINAL DECONTAMINATION: If the ingestion was oral and recent (within one hour), the patient maintains protective airway reflexes and is cooperative, activated charcoal (1gram/kg, maximum 50 grams) may be considered. Due to the delayed gastric emptying caused by anticholinergics, some experts advocate for its use after the first hour. Data on the efficacy of activated charcoal for tricyclic overdose is limited. The risk of aspiration (after a seizure or dysrhythmias) should be considered in these patients.

AGITATION: Benzodiazepines may be used to control agitation to prevent worsening hyperthermia, rhabdomyolysis, and traumatic injuries. Sedation with benzodiazepines can make it difficult to assess for alternative diagnoses such as encephalitis and other CNS abnormalities.

HYPERTHERMIA: Temperature monitoring and treatment of hyperthermia are crucial. Severe hyperthermia should be treated in typical fashion, including evaporative cooling for moderate to severe cases.

SEIZURES: Benzodiazepines are the first line agent for seizures. phenytoin should be avoided because of their sodium channel blockade effect. Propofol is typically recommended as the 2nd line antiepileptic after benzodiazepines.

ARRHYTHMIAS-PROLONGED QTc/QRS; Intravenous sodium bicarbonate should be used for the treatment of prolonged QRS intervals and for the treatment of wide-complex tachydysrhythmias. Class IA antiarrhythmic agents (procainamide) should be avoided due to their sodium channel blockaid effects.

PHYSOSTIGMINE (ANTIDOTE): Physostigmine is a reversible acetylcholinesterase inhibitor that is useful in reversing the peripheral and central effects of anticholinergic toxicity. Studies have demonstrated improved control of agitation and delirium when compared to benzodiazepines. Its use should be reserved for patients with moderate to severe anticholinergic effects such as agitation and delirium not controlled by benzodiazepines. Historically, its use has been controversial because of its adverse effects. Recent data demonstrates that this is may be over-stated. The major adverse effects from physostigmine are dysrhythmias, profound bradycardia, seizures and the potential to induce cholinergic toxicity. One of the benefits of physostigmine compared to benzodiazepines is that physostigmine results in a relatively normal patient within 15 minutes who is not extremely sedated. This will make excluding some of the alternative diagnoses and limit unnecessary lumbar puncture and CTs.

A clinical trial randomized 19 children, 10-18 years of age, with symptoms consistent with the antimuscarinic toxicity who ingested an antihistamine, antimuscarinic, or jimson weed with agitation (RASS score ≥ 1 and delirium (CAM-ICU Positive) to receive a bolus of Physostigmine (n=9) followed by a 4 hour infusion or to Lorazepam (n=10) bolus followed by a 4 hour infusion (Wang, Clin Toxicol 2021, PubMed ID: 33295809).

In the physostigmine group, there was a statistically significant lower rate of delirium after the first bolus (Risk Difference: 55.6%, 95% CI (15.5, 81.1%) and after the 4 hour infusion (Risk Difference: 77.8%, 95% CI (35.0, 93.7%). The authors considered a 60% difference to be clinically significant in their sample size determination. In the physostigmine group there was a significantly higher rate of the proportion with a decrease in RASS score (less agitation) from pre-bolus to post-bolus (Risk Difference: -58.9%, 95% CI (-80.2. -14.5%) but not in pre-bolus to post-infusion (Risk Difference: -20%, 95% CI (-51.0, 13.2%). The unusual use of a Physostigmine infusion should be considered in interpreting this study's results. In addition, the small same size (n=19) resulted in very wide confidence intervals around the efficacy outcomes and no conclusions could be made on the frequency of rare adverse events.

Physostigmine is a short-acting drug that requires close patient monitoring and frequent dosing. The drug should be given by slow intravenous push over five minutes with cardiac monitoring for prolongation of the QRS and arrhythmias. Rapid infusion may result in cholinergic symptoms or seizures. Repeat doses may be necessary after 20 to 30 minutes. Patients who are going to receive physostigmine should have cardiac monitoring and should be frequently assessed for cholinergic toxicity (DUMBBELLS: Diarrhea, Urination, Miosis, Bronchospasm, Bronchorrhea, Emesis, Lacrimation, Lethargy, Sweating/Salivation). Atropine and resuscitation equipment should be readily available in the event of cholinergic toxicity, seizure or dysrhythmias.

PHYSOSTIGMINE DOSING	
Adult	0.5 to 2 mg over 5 minutes
Children	0.01-0.03 mg/kg (max 0.5 mg)
Contraindications	Cyclic antidepressant ingestion, prolonged QRS

DISPOSITION

Toxicity from most anticholinergic drugs will produce symptoms within a few hours of the time of ingestion. Patients with mild or no symptoms of anticholinergic toxicity can be discharged after 6 hours of observation. Certain anticholinergic agents (e.g., scopolamine) can have effects for 24-48 hours. These patients require a longer period of observation. More symptomatic patients usually require admission for at least 24 hours. Moderate toxicity from Diphenhydramine has been reported around 300 mg in adults and 7.5 mg/kg in children. Patients who have severe anticholinergic toxicity, and patients treated with physostigmine, should be admitted to an intensive care unit for close observation, as dosing will likely need to be repeated.

APPENDIX: TOXIDROMES

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is Up (agitated, ↑vital signs, mydriasis) and Wet (sweating)

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/ Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET
*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size					

ANTIHYPERTENSIVES

INTRODUCTION (JANIENNE KONDRICH, M.D., 4/2020)
Antihypertensive medications work by several different mechanisms, most notably by β adrenergic antagonism, calcium channel blockade, and central α_2 agonism. These drugs are also used in the treatment of a migraine headaches, coronary artery disease, arrhythmias, essential tremor, performance anxiety, ADHD and are thus present in many American households. This availability increase the risk of accidental or intentional overdose. The most common clinical presentation of antihypertensive overdose is hypotension and bradycardia.

DIFFERENTIAL DIAGNOSIS: BRADYCARDIA	
Inflammation: Viral, autoimmune	Medications: Antiarrhythmics: Clonidine
Myocarditis, Pericarditis	Beta blockers, Ca^{++} channel blockers
Lyme, acute rheumatic fever,	Amiodarone, Digitalis, Adenosine
Bacterial endocarditis, syphilis	Other medications: Cholinergic agents
Myocardial infarct or ischemia	Increased vagal tone
Collagen vascular disease	Breath holding, cough
Lupus, dermatomyositis	Esophageal/Oral stimulation: intubation
Congenital heart disease	Increased intracranial pressure
ASD, AV Canal, VSD, TGV, PS	Cardiac surgery: Atrial
Congenital conduction abnormality	Electrolytes: Hyperkalemia
Prolonged QT, WPW	Hypothermia
	Sleep

DIFFERENTIAL DIAGNOSIS: TOXIC BRADYCARDIA
Alpha$_2$ adrenergic agonists: Altered mental status, miosis
Beta adrenergic antagonist
Calcium channel antagonists
Cardioactive steroids (e.g. Digoxin)
Opioids: Altered mental status, miosis
Organophosphates: Cholinergic Toxidrome (“SLUDGE” or “DUMBBELLS”)

BETA-BLOCKERS (BB)

PHARMACOLOGY

There are three subtypes of β receptors that are found in cardiac muscle (β_1), bronchial and peripheral smooth muscle (β_2) and adipose tissue (β_3). The toxicity of a particular agent depends on whether it is cardio-selective, its lipophilicity, its membrane stabilizing activity, and intrinsic sympathomimetic activity.

Beta blockers are available as immediate or sustained-release oral tablets and as ophthalmic drops. They are either cardioselective (selective for primarily the β_1 receptor), or nonselective and have effects at both the β_1 and β_2 receptor.
Selective β_1 blockade results in decreased contractility, automaticity of pacemaker cells, and AV node conduction velocity. Nonselective β blockade will result in more systemic effects including bronchoconstriction and impaired gluconeogenesis.

BETA-BLOCKERS	
β-1 Specific Blockade	Membrane Stabilizing Agents
Acebutolol	Propranolol
Atenolol	Carvedilol
Esmolol	Acebutolol
Metoprolol	High Lipophilicity
	Propranolol
	Carvedilol

CLINICAL PRESENTATION

β-blocker toxicity most commonly manifests as bradycardia and hypotension. Any bradydysrhythmia can occur but ventricular dysrhythmias are seen more frequently with agents with more membrane stabilizing activity. β-blockers in overdose will often cause alterations in mental status including delirium, coma and seizure activity. These symptoms occur most commonly in the setting of severe hypotension but can be present in patients with normal blood pressure. Hypoglycemia often occurs with β-blocker toxicity, perhaps more frequently in children than in adults. Bronchospasm can also occur, but usually only in patients with pre-existing pulmonary disease.

CALCIUM CHANNEL BLOCKERS (CCB)

PHARMACOLOGY

Calcium-channel blockers (CCB) are available as oral immediate or extended-release preparations and are divided into two main categories. Although both work on the cardiovascular system, the dihydropyridines act primarily on the peripheral vasculature and the non-dihydropyridines act almost entirely on the heart.

The dihydropyridines, such as Nifedipine, primarily block the vascular smooth muscle L-type calcium channels and are strong vasodilators with little negative myocardial inotropic or conduction effects. In contrast, non-dihydropyridines, like Verapamil and Diltiazem, preferentially block the L-type calcium channels in the myocardium. They are weak vasodilators but have a strong negative effect on cardiac conduction and contractility. This selectivity is often lost in overdose, and all CCB will cause hypotension and bradycardia to varying degrees at toxic levels. CCB also block L-type calcium channels in the pancreas, preventing the release of insulin. They also lead to systemic insulin resistance, causing hyperglycemia with impaired glucose uptake.

CALCIUM CHANNEL BLOCKERS	
Dihydropyridines (Tachycardia[1])	Non-dihydropyridines (Bradycardia[2])
Amlodipine	Verapamil
Nifedipine	Diltiazem
Nicardipine	
1. Reflex tachycardia due to vasodilation (note, names all end in “pine”) 2. Direct effect on cardiac conduction	

CLINICAL PRESENTATION

Dihydropyridine toxicity results in arterial vasodilation and hypotension with reflex tachycardia, whereas non-dihydropyridine toxicity causes decreased contractility, bradycardia, and conduction abnormalities. Hypoperfusion may lead to altered mental status, seizures, renal failure, liver infarction, respiratory depression, and metabolic acidosis. Patients with CCB overdose, in comparison to β-blocker overdose, are more likely to maintain a surprisingly normal mental status even with other signs indicating significant calcium channel blocker toxicity. When decline in neurologic status does occur, it is often precipitous and in the setting of severely decreased cerebral perfusion.

Hyperglycemia can be seen in overdose as CCB prevent insulin release and cause a degree of insulin resistance. Angioedema and noncardiogenic pulmonary edema related to CCB toxicity have been described in case reports.

CENTRALLY ACTING α_2 ADRENERGIC AGONISTS (α_2)

PHARMACOLOGY

Clonidine is a centrally acting α_2 adrenergic agonist and is available as oral tablets and in transdermal patches. Its chemical structure puts it in the category of the imidazolines. Other imidazolines are sold as over-the-counter topical ocular vasoconstrictors and nasal decongestants. All imidazolines have similar systemic effects when ingested orally.

The imidazolines decrease blood pressure by reducing sympathetic outflow from the central nervous system. At therapeutic levels these medications have little effect on the periphery, but stimulation of peripheral α_2 receptors in overdose can cause vasoconstriction.

CLINICAL PRESENTATION

Toxicity of Clonidine and other imidazolines results in central nervous system depression, bradycardia, hypotension and miosis. The CNS depression may range from drowsiness to coma. Pallor, hypothermia and dry mouth can also sometimes be seen. Respiratory depression and apnea often occur, especially in children. This presentation can easily be confused with opiate overdose. Paradoxically, hypertension can be present with clonidine toxicity, either early in presentation or with massive overdose. Small ingestions of only one clonidine tablet or one swallow of imidazoline-containing eye drops can result in life-threatening toxicity in pediatric patients.

α_2 AGONISTS	
Clonidine	Naphazoline
Guanfacine	Oxymetazoline
Guanabenz	Tetrahydrozoline
Methyldopa	

CLINICAL COMPARISON: ANTIHYPERTENSIVE TOXICITY			
	β-Blockers	Ca^{2++} Channel Blockers	α_2 Adrenergic Agonists
CNS Depression	++	–	+++
Bradycardia	++	+ / –	+
Hypotension	+++	+++	+++
Glucose Metabolism	Hypoglycemia	Hyperglycemia	Normoglycemia
Time From Ingestion to Symptom Onset	2–6 hours (Up to 24 hours for sustained release)	1–5 hours (Up to 24 hours for sustained release)	30-90 minutes
Additional	Bronchospasm	Angioedema	Miosis, Hypothermia

LABORATORY EVALUATION

Antihypertensive medication overdose is largely a clinical diagnosis, as serum or urine toxicological assays are frequently not readily available or results will not be obtained in time to aid with diagnosis and management. There are, however, certain tests that should be conducted on all patients with suspected toxic ingestion, and others that may provide clues as to which type of antihypertensive agent has been ingested.

RECOMMENDED LABORATORY STUDIES
EKG (Bradycardia, otherwise non-specific), continuous monitoring
Bedside glucose determination (BB → ↓ glucose, CCB → ↑ glucose, α_2 → ↑ glucose)
Serum electrolytes including calcium, BUN and creatinine
Acetaminophen and salicylate levels
Pregnancy test (in females of childbearing age)

MANAGEMENT

Management begins with the assessment of airway, breathing and circulation. Consider intubation in patients with a depressed or altered mental status. All patients will need continuous cardiac monitoring, pulse oximetry, and intravenous access.

Even if asymptomatic with normal initial vital signs, all patients must undergo immediate evaluation if ingestion is suspected given the propensity of many antihypertensive agents to cause major morbidity and mortality in overdose. The national poison center (800-222-1222) or the NYC Poison Control Center should be contacted early to help guide patient management (212-POISONS) See Appendix: Management Overview.

Despite the differences in clinical presentation, management of calcium channel blocker, β-blocker, or α_2 agonist intoxication is very similar and is directed at maintenance or improvement of cardiac output and peripheral vascular tone.

Symptomatic bradycardia may be treated with atropine but it is not typically effective. Intravenous intralipid is not indicated. Evidence for its use has been based on intravenous toxicity models. Use with an oral ingestion may increase serum levels.

GI DECONTAMINATION: Gastrointestinal decontamination may be used to decrease systemic absorption. Activated charcoal is administered ideally within one hour of ingestion but can still be of potential benefit if given hours later or if the time of ingestion is unknown. Charcoal should only be given to intubated patients or those with an intact mental status who can protect their airway. Consider whole bowel irrigation for sustained release preparations of calcium channel blockers or ingested clonidine patches.

INTRAVENOUS FLUIDS: If the patient is hypotensive and there is no evidence of congestive heart failure or pulmonary edema, fluid boluses of 20 mL/kg of isotonic crystalloid should be given and repeated as indicated.

VASOACTIVE INFUSIONS: Hypotension unresponsive to fluid resuscitation or complicated by persistent bradycardia may require vasoactive infusions. Inotropes (e.g. Milrinone) are preferred over vasoconstrictors (vasopressors). Epinephrine, Norepinephrine and Vasopressin increased systemic vascular resistance and therefore afterload. Their use is associated with early improvement but later mortality.

CALCIUM: Several other treatments have proven effective for antihypertensive overdose. Administration of calcium ion (chloride or gluconate) may improve cardiac contractility and hypotension. Calcium chloride is preferred in resuscitation due to its more rapid dissociation in the blood compared to calcium gluconate. However, calcium chloride extravasation can cause significant tissue injury so administration by a central line is preferred.

GLUCAGON: Glucagon has inotropic and chronotropic effects and has proven useful in both calcium channel blocker and β-blocker overdose. These effects are believed to be due in part to an increase in cardiac cAMP. Phosphodiesterase inhibitors such as milrinone will also increase intracellular cAMP concentrations by preventing its breakdown, and thus may be helpful in management.

NALOXONE: Naloxone is effective in reversing signs of clonidine overdose, though it’s mechanism of action is unclear.

HIGH DOSE INSULIN AND GLUCOSE: Insulin prevents calcium efflux from cells increasing intracellular calcium and enhancing contractility. Hyperinsulinemia euglycemia therapy has been used for severe poisoning, especially with CCB or β-blockers. Onset approximately 30 minutes. WEB LINK: MDCALC

MECHANICAL CIRCULATORY SUPPORT: The most severe cases of beta blocker or calcium channel blocker poisoning may be refractory to pharmacologic intervention and require advanced hemodynamic support such as cardiac pacing, intra-aortic balloon pump, or extracorporeal membrane oxygenation (ECMO).

DISPOSITION

Given the propensity for significant morbidity and mortality, all patients who manifest any signs or symptoms of toxicity after a confirmed or suspected antihypertensive overdose should be admitted to an intensive care until for monitoring.

Ingestion of extended release preparations requires 24 hours of observation in a monitored setting, even if initially asymptomatic. Pediatric and adolescent patients who remain asymptomatic after ingestion of an immediate release preparations of β-blockers or CCBs can be discharged after 6 hours of observation in the ED. Patients who have ingested clonidine tablets may also be discharged after a 4 – 6 hours observation period. Exposure to clonidine patches either via ingestion or transdermal contact necessitates more careful monitoring. All intentional overdoses due to a desire to cause self-harm require psychiatric evaluation.

APPENDIX: MANAGEMENT OVERVIEW

<table>
<tr><th colspan="3">MANAGEMENT OF ANTIHYPERTENSIVE TOXICITY</th></tr>
<tr><td>β-Blockers</td><td>Ca^{2+} Channel Blockers</td><td>α_2 Agonists</td></tr>
<tr><td colspan="3">INITIAL ASSESSMENT</td></tr>
<tr><td colspan="3">Assess ABCs.
EKG, Cardiac Monitor
Establish IV Access
Laboratory: Bedside Glucose, BMP (Ca++), Aspirin, Tylenol, beta HCG</td></tr>
<tr><td colspan="3">GI DECONTAMINATION</td></tr>
<tr><td colspan="3">Activated charcoal 1 gram/kg PO/NG (max 50 grams)
(Normal mental status and intact airway or Protected Airway (Intubated)</td></tr>
<tr><td></td><td colspan="2"><u>Whole bowel irrigation</u>
Polyethylene Glycol: 0.5-1.0 L/hour until effluent clear
1. Extended-release CCB
2. Clonidine transdermal patch ingestion</td></tr>
<tr><td colspan="3">HYPOTENSION</td></tr>
<tr><td colspan="3">Normal saline of Ringer’s lactate 20 ml/kg</td></tr>
<tr><td colspan="3">Inotropic/Chronotropic agents for fluid-refractory hypotension
Phosphodiesterase inhibitors: Milrinone, Inamrinone
(Avoid Pressers: NE, EPI, Vasopressin)</td></tr>
<tr><td colspan="3">Mechanical Circulatory Support: Intra-aortic balloon pump, ECMO</td></tr>
<tr><td colspan="3">BRADYCARDIA (SYMPTOMATIC)</td></tr>
<tr><td colspan="3">Trial of Atropine 0.02 mg/kg IV (Child: 0.5 mg child, Adult 1.0 mg)
Cardiac Pacing</td></tr>
<tr><td colspan="3">HYPOGLYCEMIA</td></tr>
<tr><td><u>Dextrose</u>
(0.5-1.0 grams/kg)
D50: 1-2 ml/kg IV (adult)
D25: 2-4 ml/kg IV (child)
D10: 5-10 ml/kg IV (infant)</td><td></td><td></td></tr>
<tr><td colspan="3">OTHER</td></tr>
<tr><td colspan="2"><u>Calcium</u>
Chloride (10%) 20 mg/kg (0.2 ml/kg)
Gluconate (10%) 60 mg/kg (0.6 ml/kg)</td><td rowspan="3">Naloxone
0.1 mg/kg
(Maximum dose 2 mg)
May repeat PRN</td></tr>
<tr><td colspan="2">Glucagon: 50 mcg/kg
(Repeat if no effect in 10-15 minutes)</td></tr>
<tr><td colspan="2"><u>High-dose Insulin and Glucose (Onset 30 minutes)</u>
Insulin (regular) Bolus: 1 unit/kg
Insulin Infusion: 1.0 unit/kg/hour
Dextrose Bolus: 0.5 grams/kg
(If initial Glucose < 250 mg/dl)
Dextrose Infusion: 0.5 grams/kg/hour
(D10: Peripheral, D25/D50: Central)</td></tr>
</table>

CARBON MONOXIDE

INTRODUCTION (TAMAR LUBELL, M.D., 5/2011)
Carbon monoxide poisoning is a common cause of poisoning death in the United States. Smoke inhalation is responsible for most cases of unintentional CO poisoning. Unintended poisoning tends to occur most commonly during winter months in cold climates or during blackouts when alternative heating sources are used. Children and family members may also be exposed from sources such as poorly functioning heating systems, improperly vented fuel-burning devices and motor vehicles operating in poorly ventilated areas (e.g., ice rinks, parking garages). Intentional carbon monoxide poisoning is a leading cause of suicide deaths.

PATHOPHYSIOLOGY

Carbon monoxide (CO) is an odorless, tasteless, colorless and nonirritating gas formed by hydrocarbon combustion. CO is rapidly absorbed across the pulmonary endothelium binding to hemoglobin (Hb) with approximately 240 times the affinity of oxygen forming carboxyhemoglobin (COHb). This decreases both the oxygen carrying capacity and the ability of hemoglobin to off-load oxygen in the peripheral tissues.

CO is also causes direct tissue damage independent of its effects on oxygen delivery. It has been found to bind to intracellular myoglobin and impede the functioning of mitochondrial cytochrome oxidase (similar to cyanide).

The central nervous system and cardiovascular system are most sensitive to oxygen deprivation and are especially susceptible to CO exposure. Children have a higher metabolic rate with increased oxygen utilization and minute ventilation. This makes them more sensitive to the effects of CO than older children and adults. Therefore; symptoms can result in children at lower concentrations of CO than in adults. The developing fetus is particularly vulnerable to CO toxicity. The fetal oxyhemoglobin dissociation curve lies further to the left than that of the adult. In addition, the normal oxygen content of fetal blood is relatively low, and the half-life of COHb is prolonged resulting in an exaggerated hypoxic effect in the exposed fetus. Fetal hemoglobin and bilirubin may falsely elevate COHb levels in infants.

CLINICAL PRESENTATION

Clinical signs and symptoms of CO poisoning are highly variable and nonspecific making a high index of suspicion essential. Multiple patients presenting with vague complaints such as headache, dizziness and nausea, should raise the suspicion of CO poisoning. Viral syndromes are the most common misdiagnosis. Signs and symptoms only roughly correlate with the CoHb level at the scene of exposure.

CLINICAL MANIFESTATIONS	
Headache	Vomiting
Nausea	Ataxia
Dizziness	Confusion
Weakness	Syncope
Chest pain	Dysrhythmias
Dyspnea	Myocardial infarction
Blurred vision	Tachypnea

In the absence of associated trauma or burns, physical findings are usually confined to alterations in mental status. A careful neurologic exam and in particular a mental status and cerebellar exam is essential. Vital sign abnormalities are non-specific. In infants the only suggestion of toxicity may be irritability and difficulty feeding. Cardiac toxicity commonly manifests as tachyarrhythmias in children, but in older patients CO may precipitate angina or acute myocardial infarct. The “cherry red” appearance of the lips and skin as often described is an insensitive sign of CO poisoning.

LABORATORY STUDIES
Blood Gas with Co-oximetry panel (a venous sample is adequate)
1. Pulse oximetry misinterprets carboxyhemoglobin as oxyhemoglobin resulting in a falsely elevated O_2 saturation
2. Normal CO levels are less than 5%. Heavy smokers may have CO levels up to 15%. Emergency department levels at presentation may not represent peak level
3. Blood PO_2 measurements tend to be normal because PO_2 reflects O_2 dissolved in blood and thus is not affected by COHb.
4. Consider cyanide poisoning especially in those with smoke inhalation and a severe or persistent metabolic acidosis. Consider empiric treatment (See PEM Guide: Toxicology: Cyanide)
Assess pregnancy status
EKG and cardiac monitor. Consider cardiac enzymes (chest pain, cardiac history)
Head CT: Consider in patients with altered mental status to rule out other etiologies

MANAGEMENT

Treatment of carbon monoxide poisoning consists primarily of supportive care and delivery of supplemental oxygen. Provide high flow oxygen via non-rebreathing face mask (70-90% FiO2) or endotracheal tube to all CO poisoned patients regardless of pulse oximetry or PaO_2. The addition of oxygen via high flow nasal cannula to the non-rebreathing face mask can further increase the FiO_2. Concomitant injuries such as burns, smoke inhalation or trauma should be addressed. (See: PEM Guide: Environmental Injury: Burns, PEM Guide: Environmental Injury: Smoke inhalation)

CARBON MONOXIDE HALF LIFE	
Room air	300 minutes
High flow with non-rebreathing face mask	90 minutes
Hyperbaric oxygen (2.5 atmospheres)	30 minutes

Indications for hyperbaric oxygen (HBO) therapy are controversial. A 2011 Cochrane review of 6 randomized clinical trails found design or analysis flaws in all of the trials. They concluded that existing randomized trials have failed to establish whether the administration of HBO decreased the incidence of neurologic sequelae. Specific indications for HBO also differ among centers. HBO centers can be located by contacting the regional poison center (1-800-222-1222). The closest HBO center to NYU/ Bellevue is at Jacobi Medical Center. (1-718-918-7470). Risks of HBO include increased pressure of the sinus and middle ear and rarely pneumothorax and seizures.

Other criteria often sited include seizures, dysrhythmias, persistent symptoms despite supplemental oxygen (headache, ataxia, abnormal neuropsychiatric testing) and focal neurologic findings (particularly cerebellar findings).

CRITERIA FOR HYPERBARIC OXYGEN THERAPY*
Evidence of End organ toxicity (with CO level > 3-5%)
1. Persistent metabolic acidosis
2. Initial loss of consciousness or syncope
3. Altered Mental Status: Confusion, disorientation, cognitive defects, coma
4. Myocardial ischemia: Abnormal EKG or angina chest pain
CO level > 25%
Pregnancy
1. CO level > 10%
2. Third trimester monitoring suggestive of fetal distress
*Jacobi Hospital Hyperbaric Center (May 2011)

DISPOSITION

Patients who do not fulfill criteria for hyperbaric oxygen and who are asymptomatic with a normal physical exam may be discharged home if the home environment is deemed safe. Efforts should be made to determine the mechanism of exposure in cases of accidental poisoning and alert the local fire department in order to limit risk to others.

Patients and caretakers should be alerted to the possibility of delayed neurocognitive sequelae including headaches, memory disturbance and irritability. It is difficult to predict who will develop delayed neurologic sequelae. Therefore, follow-up for all patients for neurologic reassessment is important.

CAUSTICS

INTRODUCTION (MARIA LAME, M.D., 1/2023)
A caustic (or corrosive) is a chemical capable of causing injury on contact with a tissue surface. Children commonly ingest cosmetics and personal care products and caustic agents transferred from their original containers to household drinking containers (e.g. water or juice bottles). Child tend to ingest small amounts limiting the extent of injury. In contrast, adolescent tend to ingest large amounts in suicide attempts resulting in significant injury. (See also PEM Guide: Environmental Injuries: Gastrointestinal Foreign Bodies for a discussion of button battery ingestion).

COMMON CAUSTIC AGENTS		
Ammonium Hydroxide	Alkali	General cleaner and grease remover
Sodium or Potassium Hydroxide	Alkali	Drain opener, oven clearer, hair relaxer
Sodium Hypochlorite	Alkali	Bleach[1], pool chlorinator
Acetic Acid	Acid	Food pickling, photographic stop bath
Hydrochloric Acid	Acid	Toilet cleaner, mold/mildew remover
Oxalic Acid	Acid	Metal polish
Phosphoric Acid	Acid	Rust remover
Selenous Acid	Acid	Gun bluing agent (protective finish)
Sulfuric Acid	Acid	Drain opener, large lead-acid batteries
Cationic Detergents[2]	Other[3]	Surface cleaner, preservative
Hydrofluoric acid	Other[3]	Rust and graffiti remover
Hydrogen peroxide	Other[3]	Surface and food cleaner
Phenol	Other[3]	Surface disinfectant
Zinc Chloride	Other[3]	Soldering flux

1. House bleaches: 5%, pH 11. Rarely cause injury unless large amounts
2. Example: Benzylalkonium chloride
3. Miscellaneous or unique caustics

PATHOPHYSIOLOGY
The extend of injury is the result of several factors including the duration of contact, volume, concentration, physical state (solid versus liquid) and pH. A strong alkali (pH ≥ 12) and a strong acid (pH ≤ 2) tend to produce significant tissue injury. Powdered products are more likely to result in airway injury. Solid agents are more adherent increasing the extent of injury.

It is not only the pH that result in injury. The tissue attempts to neutralized the pH. This causes an exothermic reaction that contributes thermal injury. Fluoride from hydrofluoric acid causes direct tissue injury. In addition, the fluoride is electronegative and binds to cations causing hypocalcemia and hypomagnesemia.

PATHOPHYSIOLOGY			
pH	Pathology	Necrosis	Penetration
Alkali	Fat Saponification	Liquefaction	Deep
Acid	Protein Denaturing	Coagulation	Superficial

ALKALIS: Alkalis are bases that dissolve in water and include potassium, sodium and ammonium hydroxide. Alkalis cause liquefaction necrosis, with saponification of fats, collagen destruction and dissolution of proteins, allowing for deeper penetration into tissues. Alkalis can also cause blood vessel thrombosis resulting in ischemia and necrosis.

ACIDS: Acids cause coagulation necrosis. Hydrogen ions desiccate the epithelial cells creating an eschar. The eschar limits penetration and decreases the risk of esophageal perforation with acids. The eschar also allows more acid to flow into the stomach. In addition, the esophagus has a better tolerance for acids and pylorospasm and gastric atony prolong gastric exposure.

CLINICAL MANIFESTATIONS

Young children tend to ingest little of the agent likely due to poor taste and pain with ingestion. Significant ingestions are more likely in adolescents and adults intentionally ingesting the agent as part of a suicide attempt. Symptoms are primarily localized to the gastrointestinal tract but may involve the eyes, skin, upper airway and lungs.

CAUSTIC INGESTION: SIGNS AND SYMPTOMS	
GASTROINTESTINAL	AIRWAY/RESPIRATORY
Severe pain of lips, tongue, pharynx	Aphonia, hoarseness, stridor
Drooling, dysphagia, odynophagia	Shortness of breath
Hematemesis, abdominal pain	Chest pain (mediastinitis)

AIRWAY: Swelling of the oropharynx and tongue can results in upper airway obstruction. Erosion into blood vessels can result in significant bleeding. Patients may present with drooling, vomiting or stridor and may require endotracheal intubation.

GASTROINTESTINAL: Esophageal perforation can result in mediastinitis. Gastric perforation can result in peritonitis. Erosion into blood vessels can result in upper GI hemorrhage and hemorrhagic shock and death if it involves the aortic arch, which lies immediately posterior to the mid-esophagus. Late complications include esophageal strictures which may result in esophageal carcinoma over decades.

RESPIRATORY: Aspiration can occur with powdered caustics or as a result of vomiting.
OCULAR: Ocular involvement has both functional and cosmetic implications

DIAGNOSIS	
Airway	Presence/extent of upper airway obstruction. Need for intubation
History	Intent, symptoms, substance ingested (alkali vs acid)
Exam	Face/eyes, oropharynx, respiratory, abdominal
LABS	Alkali: Significant tissue injury → Acidemia, ↑ Lactate Acids: ↑ Absorption → ↑ Anion gap metabolic acidosis Hydrofluoric acid: Non-anion gap metabolic acidosis, ↓ Ca^{++}, ↓ Mg^{++}
XRAY	Chest XRAY: indicated for significant chest pain, respiratory signs and symptoms to evaluate for parenchymal injury, mediastinitis, free air

INDICATIONS FOR ENDOSCOPY

Endoscopy can diagnose and grade the extent of gastrointestinal injury.. In general, it is recommended that endoscopy occur in the first 24-48 hours after exposure. Endoscopy less than 12 hours post ingestion may not reveal the extent of injury and endoscopy after 4 days may increase the risk of perforation. There is general agreement that endoscopy is indicated in patients with intentional ingestions, acid ingestions and in children with unintentional alkali ingestions with vomiting and drooling together or stridor alone (See Appendix: Caustic Ingestions Decision Algorithm

ENDOSCOPIC CLASSIFICATION AND PROGNOSIS		
0	Normal esophagus	Complete Recovery
1	Mucosal hyperemia and edema	Complete Recovery
2A	Friability, hemorrhage, shallow ulcers	Stricture Unlikely
2B	2A + Deep ulcers (circumferential or discrete)	Risk: ↑ Stricture, ↓ Perforation
3A	Small or scattered areas or necrosis	Risk: ↑ Stricture, ↑ Perforation
3B	Extensive necrosis	Risk: ↑ ↑ Stricture, ↑↑ Perforation
4	Perforation	Often Fatal

Several studies have assessed the utility of clinical symptomatology as a predictor of serious esophageal injury with alkali ingestion in children. The results of these studies are not applicable to those with acid ingestions or to adults with large volume, intentional ingestions.

A study including 378 children with caustic ingestion demonstrated that 82% of those who were symptomatic had minimal or no disease on endoscopy while 12% of those who were asymptomatic had severe injury (Gaudrault, Pediatrics 1983, PubMed ID: 6835760). The authors concluded that signs and symptoms should not be used to predict esophageal injury

In a case series of 156 children, 61.6% showed no visible signs of contact with the caustic substance yet 37.5% had burns in one or more visceral site on endoscopy. Of the 38.4% with visible findings only 50% had esophageal injury on endoscopy (Previterra, Ped Emerg Care 1990, PubMed ID: 2216918).

In a retrospective study of 79 children with a history of caustic ingestion the presence of signs and symptoms (vomiting, drooling, stridor and oropharyngeal burns) were compared to endoscopy findings. The presence of oropharyngeal burns did not identify patients with serious esophageal injury (defined as 2nd or 3rd degree esophageal burns). 50% (7/14) with two or more of vomiting, drooling or stridor had serious esophageal injury. In contrast, no patients (0/64) with none or one of vomiting, drooling or stridor had serious esophageal injury (Crain, Am J Dis Child 1984, PubMed ID: 6475876).

IMAGING

Fever, abdominal pain, peritonitis and hypotension are suggestive of perforation. Chest, soft tissue neck and abdominal radiographs should be obtained if symptoms suggest perforation.

CT of the chest and abdomen with intravenous contrast have been studied as an alternative to endoscopy (Asalino, Dis Esoph 2022, PubMed ID: 35649393). This approach avoids the risk of perforation that is associated with endoscopy. A small study (n=34) compared CT with endoscopy (Bahrami-Matlagh, Emerg (Tehran) 2017. PubMed ID: 28894776). Accuracy was moderate. Agreement rate between CT scan and endoscopy had a kappa of 0.38 (moderate agreement) for the grade of esophageal injury and had a a kappa of 0.17 (fair agreement) for gastric injuries. The sensitivity was 96.3%, 95% CI (79.1, 9.8%) and the specificity was 57.1%, 95% CI (20.2, 88.2% for esophageal damage. The area under the ROC curve of CT scan in detection of esophageal injury was 0.76 (95% CI (0.52, 1.00). For gastric damage, the sensitivity was 89.7%, 95% CI (71.5, 97.3%) and the sensitivity was 40.0%, 95% CI (7.3, 83.0%). The area under the ROC curve of CT scan in detection of gastric damages was and 0.64, 95% CI (0.35, 0.94).

MANAGEMENT

The emergency department goals of management are to: identify and manage immediate injury and identify those who would benefit from endoscopy. The primary concern is for airway compromise and/or gastrointestinal perforation. Patients with airway compromise (e.g. stridor, hoarseness, aphonia, unable to tolerate secretions) require urgent intubation or placement of a surgical airway. Approximately 10% of children (Cowan, Int J Ped Otolaryngol 2019, PubMed ID: 23786788) and 50% of adults require intubation (with 20% of adult intubations classified as difficult (Struck, Scand J Trauma Resusc Emerg Med 2016, PubMed ID: 27068119). Pediatric surgery should be consulted for signs of esophageal or gastric perforation.

Provide ongoing cardiac monitoring and consult the local poison control center (1-800-222-1222 anywhere in the US) as well as a pediatric gastroenterologist. Obtain intravenous access and provide hydration and analgesia. Allow the patient nothing by mouth. Clothing should be removed and areas of skin contact copiously irrigated. Determining eye pH (normal 7.0-7.3), irrigate until pH normalizes followed by Ophthalmology consult, eye examination when pH normalizes.

Antibiotics should be administered if perforation is suspected or confirmed.

GASTRIC ELIMINATION: Activated charcoal is contraindicated; it will not absorb the caustic agent, may worsen mediastinitis if a perforation exists and interfere with endoscopic evaluation. Vomiting should not be induced. It may re-expose the esophagus to injury and result in aspiration.

NEUTRALIZATION: Neutralization with acid or alkaline is not recommended as it may cause an exothermic reaction and further thermal injury. There is no need for oral dilution. In animal studies, dilution with milk is only found to be effective if given within minutes of ingestion. There are no human studies to support this and dilution can result in an increase in intraluminal pressure leading to vomiting or perforation. Some sources recommend dilution with water within minutes of ingestion in a patient with mild or no symptoms.

CORTICOSTEROIDS: Steroids have been shown to decrease granulation, inflammation and fibrous formation in animal models. In a single study, children with grade IIb degree injury showed decreased esophageal injury and decreased the need for dilatation of the esophagus (Boukthir, Arch Peds 2004, PubMed ID: 14700754).

However, other animal studies have demonstrated that steroids can significantly increase mortality and morbidity due to overwhelming sepsis. A meta-analysis concluded that steroids do not decrease the incidence of stricture formation and therefore have no beneficial effects (Katibe, J Ped Gastro Nutr 2018, PubMed ID: 29216023). In a 2014 randomized trial of 3 days of methylprednisolone (with Ceftriaxone and Ranitidine) in children with grade 2B alkaline injuries, those receiving methylprednisolone had a shorter duration of parenteral nutrition without an increase in complications (Usta, Pediatrics 2014, PubMed ID: 24864182

ANTACIDS (H-2 BLOCKERS): H-2 blockers are believed to suppress gastric reflux thus potentially decreasing injury to the esophagus. However, one study showed increased gastric injury when H-2 blockers are used (Mamede, Laryngoscope 2006, PubMed ID: 11175619). H-2 blockers immediately after an ingestion may lessen the neutralizing effect of gastric acidity and possibly lead to increased gastric injury.

APPENDIX: LIQUID LAUNDRY DETERGENT PACKS

Liquid laundry detergent packs (e.g. Tide pods) consist of liquid detergent in a water-soluble membrane. This packs are brightly colored, making them attractive to young children. Adolescents have ingested them as a challenge because they are adolescents. The packs may also be ingested in a suicide attempt so identifying the intent is essential.

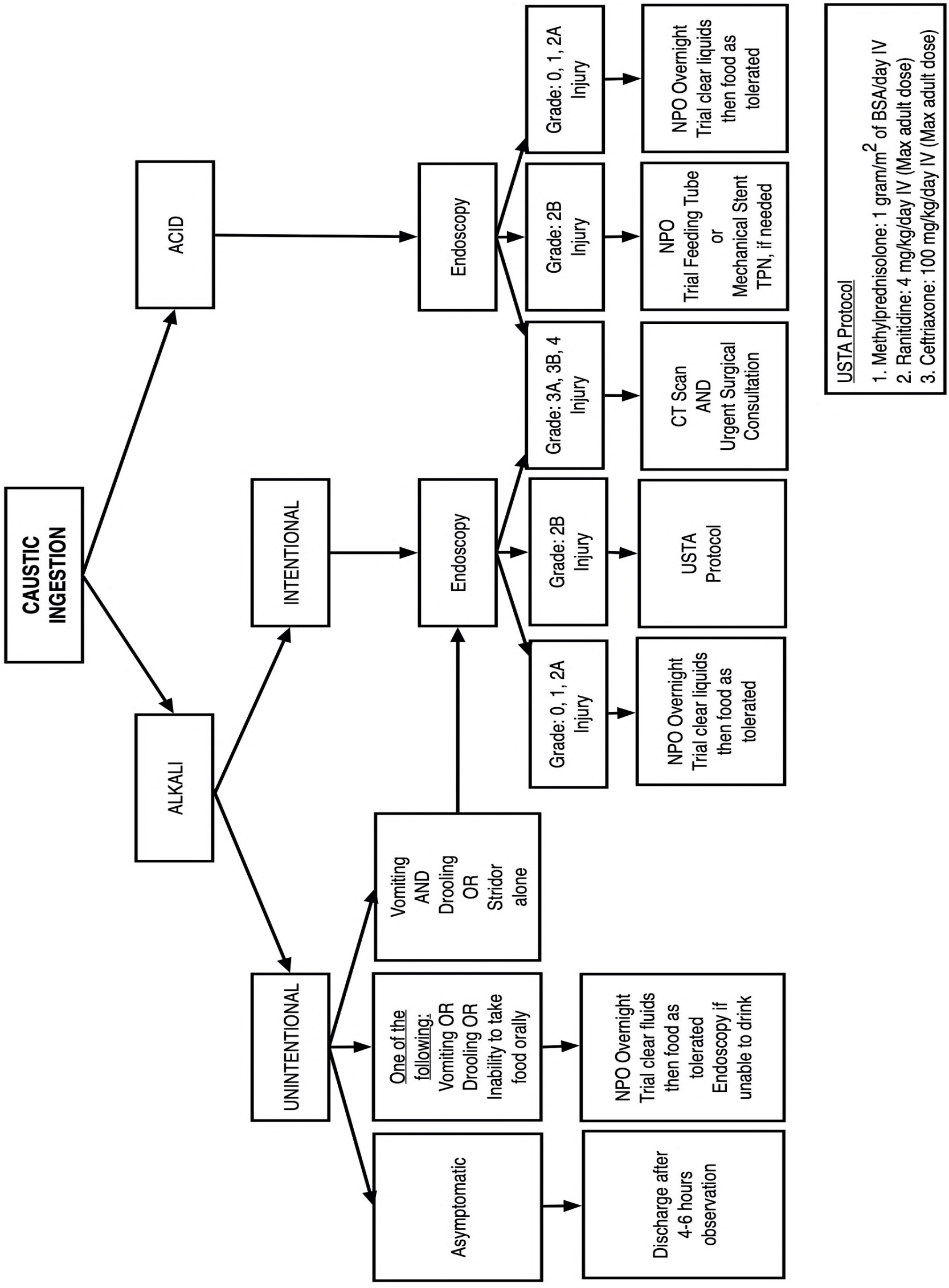
The packs are caustic. The pH varies based on the specific brand but in general, the pH is less than the pH of the non-pack detergent. The packs also contain propylene glycol and alcohol ethoxylate that contribute to their toxicity. Manufacturers have responded by changing the packaging to prevent ingestions and changing the formulation to reduce toxicity.

Signs and symptoms are primarily localized to the gastrointestinal tract (esophagus), but can include airway edema/obstruction, aspiration, eye involvement, altered mental status and seizures. In general, management is similar to other alkaline exposures

CLINICAL MANIFESTATIONS AND MANAGEMENT	
Airway	Airway edema, altered Mental status → Airway obstruction
	Observation, preparation for advanced airway management
Gastro-intestinal	Common: Nausea, vomiting immediately after exposure
	Drooling, refusal to swallow, persistent pain → Observation/Endoscopy
Respiratory	Aspiration (rare < 0.5%)
	Hx: Vomiting, choking, or associated difficulty breathing
	PE: Hypoxia, respiratory distress, or focal lung sounds
Neurologic	Altered mental status, seizures
Ocular	Determining eye pH (normal 7.0-7.3), irrigation until pH normalizes Ophthalmology consult, eye examination when pH normalizes
Psych	Consultation if suicidal intent
	Screen for acetaminophen, aspirin, pregnancy, EKG abnormalities

APPENDIX: CAUSTIC INGESTION DECISION ALGORITHM

Hoffman, NEJM 2020, PubMed ID: 32348645



CHOLINERGICS

INTRODUCTION (ELISE PERLMAN, MD, 2/2018)

In 2016, pesticides were the 9th most common substance reported to poison control centers. They are commonly used as a suicide agent in the developing world due to their ready availability. Pesticides are the 8th most common substance involved in pediatric cases less than 5 years of age and were responsible for 3% of fatalities secondary to substance exposure. Organophosphate and carbamate insecticides have been used since the early 1960s for insect control both in the home and in agriculture. They are the most widely known acute poisoning syndromes that can be diagnosed clinically and have available antidote therapy. Organophosphates, such Sarin gas in the 1995 Tokyo subway attack, can also be used as chemical warfare agents. (i.e. “nerve gas”). Chronic toxicity and delayed toxic syndromes can also occur but are not discussed in this PEM Guide.

PHARMACOLOGY

The autonomic nervous system innervates and regulates smooth muscle, cardiac muscle and glands. In contrast, the somatic nervous system innervates skeletal muscle. The autonomic nervous system is divided into the sympathetic, parasympathetic and enteric nervous systems and are composed of preganglionic and postganglionic neurons that communicate via neurotransmitters. Cholinergic neurons release acetylcholine either within ganglia or at the level of the target organ and then bind to its corresponding post synaptic receptor to create the ultimate effect. Acetylcholine binds to both nicotinic and muscarinic receptors. The enzyme acetylcholinesterase hydrolyzes acetylcholine to acetic acid and choline. Inhibition of acetylcholinesterase results in accumulation of acetylcholine in the synaptic cleft and cholinergic toxicity.

NICOTINIC ACTIVITY: Nicotinic receptors are located in the autonomic ganglia of both the sympathetic and parasympathetic nervous systems, in the adrenal medulla, the CNS and at the neuromuscular junction (skeletal muscle). They are activated by acetylcholine and produce excitation.

MUSCARINIC ACTIVITY: Muscarinic receptors are located in the parasympathetic ganglia of the autonomic nervous system of smooth muscle (intestinal, bronchial and cardiac) and exocrine glands (salivary and sweat). They are activated by acetylcholine to cause an inhibitory effect on the heart (i.e. decreased heart rate) and excitatory effects on smooth muscle and glands (i.e. increase motility and secretions).

CHOLINERGIC AGENTS

Organophosphates and carbamates are potent acetylcholinesterase inhibitors primarily used as pesticides. Though structurally different, they are both capable of occupying the enzymatic binding site on acetylcholinesterase leading to an increase in cholinergic activity. They are well absorbed through the lungs, gastrointestinal tract, skin, conjunctiva and mucous membrane.

ORGANOPHOSPHATES: Organophosphates bind the enzyme acetylcholinesterase. With time, this compound will undergo a conformational change known as “aging” such that the enzyme binding becomes permanent and is irreversible. Cholinergic toxicity can also results for the bites of the black widow spider and the bark scorpion (See: PEM Guide: Environmental Injuries: Snake Bites, PEM Guide: Environmental Injuries: Spider, Scorpion and Bee Bites).

The properties of organophosphates have been coopted for use as nerves agents in chemical warfare. Agents include VX gas, Sarin, Soman and Tabun. Most solids agents are irritants. They are generally not absorbed through the skin and contamination can be blocked by particle mask and gloves. Liquid agents can be absorbed through the skin. Heavy-duty gloves and Impervious splash suits are required. If it is volatile (like Sarin gas) inhalation risk is a possibility and chemical filter masks are required. An aerosolized agent is the mist form of a liquid. If it is absorbable or volatile the same issues apply as to non-aerosolized liquids.

For chemical warfare incidents, risk assessment entails: identification of the agent, the extent, route and duration of exposure and notification of local emergency services and law enforcement agencies. Chemical agent specific management options can be obtained through the Local Poison Center (1-800-222-1222).

CARBAMATES: Carbamate also bind to acetylcholinesterase but differ from organophosphates in two respects. Unlike organophosphates, their binding is reversible with spontaneously hydrolysis occurring within several hours. This results in a shorter duration of symptoms. Compared to organophosphates, CNS effects are less frequent due to poor absorption across the blood brain barrier though CNS symptoms can occur with massive exposures.

CLINICAL MANIFESTATIONS

Accumulation of acetylcholine due to inhibition of acetylcholinesterase results in continuous cholinergic stimulation at both nicotinic and muscarinic receptors. The initial signs and symptoms of cholinergic toxicity are often initially muscarinic and are later followed by nicotinic stimulation.

SLUDGE and DUMBBELLS are convenient mnemonics to remember the signs and symptoms of the cholinergic toxidrome. The toxidrome can be remembered as “down” and “wet”. “Down” refers to depressed mental status, bradycardia and miotic pupils while “wet” refers to increased fluid output from nearly every orifice (sweating, vomiting and diarrhea, lacrimation, salivation and increased bronchial secretion).

Excess nicotinic receptor stimulation at the neuromuscular junction results in: fasciculations and muscle spasms followed by muscle fatigue and paralysis. Excess nicotinic receptor stimulation in the central nervous system can cause agitation, confusion, seizures and respiratory depression.

Fatality from cholinergic toxicity is typically a result of respiratory failure which occurs due to a combination of CNS effects on the respiratory drive, neuromuscular weakness/fatigue and excessive pulmonary secretions.

CHOLINERGIC TOXIDROME			
D	Diarrhea	S	Salivation
U	Urination	L	Lacrimation (tearing)
M	Miosis*, muscle weakness	U	Urination
B	Bronchorrhea**	D	Defecation or Diarrhea
B	Bradycardia	G	GI Distress
E	Emesis	E	Emesis (vomiting)
L	Lacrimation	*Miosis most consistently encountered **Severe. May mimic pulmonary edema	
L	Lethargy		
S	Salivation, sweating		

DIAGNOSIS

The diagnosis of cholinergic toxicity is made clinically, though the diagnosis can be easily missed because the signs and symptoms are nonspecific (See Table below).

A high index of suspicion is required given the constellation of clinical features of cholinergic toxicity. Key features that can help with the diagnosis include: a “garlic-like odor”, a history of playing in the grass or garage, and multiple patients with similar symptoms or fasciculations at the time of presentation. Onset and duration may vary based on the agent. Generally oral and respiratory exposures present within 3 hours, while dermal exposures may take up to 12 hours to present.

DIFFERENTIAL DIAGNOSIS	
MIMIC	CHOLINERGIC SIGNS/SYMPTOMS
Asthma Attack	Tachypnea, wheezing, bronchorrhea, dyspnea
Opiate overdose	Depressed mental status, miosis, respiratory depression
Alcohol intoxication	Depressed mental status
Influenza	Fatigue, rhinorrhea, fever, emesis
Mental Illness	Confusion, agitation, anxiety, depression, emotional lability
Diabetic Ketoacidosis	Confusion, ketosis, tachypnea, coma
Gastroenteritis	Nausea, emesis, diarrhea
Myasthenia crisis	Muscle weakness, fatigue
Nicotine poisoning	Nicotinic signs and symptoms (NMJ/CNS stimulation)
Muscarine	Certain mushrooms
Latrodectism	Black widow spider envenomation. Muscle rigidity, pain

DIAGNOSTIC TESTING	
RBC cholinesterase	Decreased, measures degree of toxicity, typically not available
CBC	May show leukocytosis
ABG	Assess ventilation, oxygenation
BMP/LFT	Electrolyte abnormalities with severe emesis/diarrhea
EKG	QT prolongation, polymorphic ventricular tachycardia
CXR	Severe cases may be associated with pulmonary edema

Determining whether the exposure was to a carbamate or organophosphate is important. The window during which an oxime antidote (Pralidoxime) will be effective is shorter with organophosphates. Recall that organophosphates undergo “aging” after which their inhibition of acetylcholinesterase cannot be reversed.

If the diagnosis is unclear, an Atropine challenge 0.01-0.02 mg/kg can be administered. The absence of the development anticholinergic signs or symptoms (e.g. tachycardia, mydriasis) would suggest a diagnosis cholinergic excess.

MANAGEMENT

Management decisions should be made in consultation with the regional poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494. Hospital incident command, emergency services and law enforcement agencies should be notified if chemical warfare is suspected.

MANAGEMENT OVERVIEW
Assess and manage: Airway, Breathing and Circulation
Deliver 100% 0_2 via face mask, place on monitor, bedside glucose determination
Succinylcholine should not be used for intubation as it is metabolized by plasma cholinesterase and use will result in prolonged paralysis. Use a non-depolarizing agent such a Rocuronium instead
Decontamination to prevent continued exposure and secondary toxicity
Removal of clothes and other items, place in an impervious (e.g. plastic) bag
Irrigation. Avoid scrubbing which can increase uptake
If emesis has not occurred, perform nasogastric lavage after an oral ingestion
Administer activated charcoal 1 gm/kg if not contraindicated
Medical staff: Personal protective equipment to prevent secondary contamination
Provide antidote(s) as indicated: Atropine and Pralidoxime (see Appendix)
Seizing due to central cholinergic toxicity: Diazepam 0.1-0.2 mg/kg
Bronchospasm: Consider nebulized Ipratropium 0.5 mg (500 mcg)

CHOLINERGIC TOXICITY ANTIDOTES		
	ATROPINE	PRALIDOXIME (2 PAM)*
Mechanism	Competitively blocks central and peripheral muscarinic receptors	Reactivates acetylcholinesterase by releasing toxin
Indication	Improve muscarinic symptoms of organophosphate and carbamate toxicity	Improve muscarinic and nicotinic symptoms of organophosphate and carbamate toxicity Neuromuscular weakness or significant Atropine requirement
Dosing	0.05 mg/kg IM or 0.02 mg/kg IV Toddler: 0.5 mg, Child: 1.0 mg, > 40 kg: 1-2 mg (mild-moderate) > 40 kg: 3-5 mg (severe) Double dose Q3-5 minutes PRN Titrate dose to reverse bronchorrhea, bronchospasm, and respiratory distress. There is no maximum dose Very large doses may be required.	Administer immediately with Organophosphates to prevent permanent inactivation (“aging”) Adult: 1-2 grams IV Child: 20-40 mg/kg IV (max 2gms) over 15-30 minutes If severe initiate an infusion of: Adults: 250-500 mg/hour Children: 10-20 mg/kg/hour
Adverse Reactions	Signs of anticholinergic toxicity if too large a dose is given (hot, dry, flushed skin, tachycardia, urinary retention, mydriasis, CNS agitation, tachycardia	Transient dizziness, blurred vision, elevated diastolic BP. Rapid IV admin may result in cardiac/ respiratory arrest due to muscle rigidity and laryngospasm
*Pralidoxime sounds very similar to Physostigmine (antidote for anticholinergic toxicity) and Pyridoxine (Vitamin B6, antidote for Isoniazid toxicity). Be careful ordering		
Auto-injector (IM): Atropine 2 mg + 2-PAM 600 mg. May require up to 1-3 IM injections (AKA: DuoDote or Mark I Nerve Agent Antidote Kit (NAAK))		

APPENDIX: CHOLINERGIC TOXIDROME

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/ Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET

CYANIDE

INTRODUCTION (MICHAEL MOJICA, M.D. 5/2016)
Cyanide is one of the most rapidly fatal toxins. The dose of cyanide necessary to result in toxicity is dependent on the duration of exposure, route (inhalation, parenteral, ingestion or dermal exposure) and form of exposure (gas or salt). Rapid identification and provision of antidotes is essential.

PHYSIOLOGY
Cyanide is an inhibitor of multiple enzymes. It binds the ferric ion (Fe3+) of cytochrome oxidase causing an arrest of oxidative phosphorylation. Anaerobic metabolism ensues generating lactic acid. Hydrogen that typically binds to oxygen in the electron transport chain accumulates and with lactic acid contributes to an anion gap metabolic acidosis. Cyanide toxicity results in a functional hypoxia. Oxygen is present in high concentration in the blood but cannot be utilized by the cells. Cyanide is a potent neurotoxin that is selective for regions of high metabolic activity (e.g. basal ganglia).

Cyanide is principally eliminated by conversion to thiocyanate by the enzyme rhodanese, a process that requires a sulfur donor. Thiocyanate is then excreted in the urine. In addition, hydroxocobalamin combines with cyanide to form cyanocobalamin (vitamin B12) which is excreted in the urine.

CYANIDE EXPOSURES
Smoke inhalation (e.g. burning plastics)
Intentional ingestion (e.g. suicide, homicide)
Iatrogenic: Sodium Nitroprusside
Industrial exposures: jewelers, photography, metallurgy, textiles

PRESENTATION
Initial symptoms are nonspecific and may include: headache, anxiety, confusion and abdominal pain. Similar symptoms (altered mental status, seizure, hypotension and lactic acidosis) can be seen with a variety of toxic exposures (cyclic antidepressants, Isoniazid, salicylates, organophosphates and medications that induce methemoglobinemia). Collapse after a gas exposure can also be seen with: carbon monoxide, hydrogen sulfide, and asphyxiants such as carbon dioxide and methane.

CLINICAL MANIFESTATIONS	
Central Nervous System	Headache, anxiety, confusion, vertigo, coma, seizure
Cardiac	Early: tachycardia, hypertension Late: ↓ HR, hypotension, atrioventricular blocks, ventricular arrhythmias
Respiratory	Early: tachypnea Late: respiratory depression, pulmonary edema
Gastrointestinal	Vomiting, abdominal pain, hepatic necrosis
Renal	Renal failure
Skin	Flushing (cherry red), irritant dermatitis (skin exposure)

LABORATORY FINDINGS

A bedside glucose determination should be obtained for all patients with an altered mental status. In patients with an intentional ingestion, acetaminophen and salicylate levels and a beta HCG (in females) should be sent. A co-oximetry panel (carbon monoxide and methemoglobinemia) should be sent for patients with smoke inhalation or those who have taken medications that can induce methemoglobinemia. Cyanide levels are available but results are not available in time to effect management.

Anaerobic metabolism results in an anion gap metabolic acidosis (primarily lactate). Venous hyperoxia (oxygen accumulates in the blood because it is not being utilized by the tissues) results in red appearing skin, cherry red venous blood and narrow A-a gradient

MANAGEMENT

The primary goals are to resuscitate and to provide early antidotal therapy to the patient. Patients typically require early intubation. Hypotension should be managed with fluid resuscitation and use of vasoactive infusions. Seizures are typically managed with benzodiazepines. A single dose of activate charcoal (1 gm/kg, max of 50 grams) can be considered in a patient with a normal mental status and an intact airway.

In a dermal exposure, patients should be decontaminated. Patient clothing should be removed and skin cleaned of any residue. Healthcare providers should utilize personal protective equipment including an impervious gown, mask and eyewear.

Antidotes work through three mechanisms. They can bind cyanide (Hydroxocobalamin), induce methemoglobinemia (Amyl and Sodium Nitrite) and provide a sulfur donor that enhances excretion (Sodium Thiosulfate). The most common recommendation is to treat with Hydroxocobalamin (if available) and thiosulfate. (See: PEM Guide: Toxicology: Carbon Monoxide and PEM Guide: Environmental Injuries: Smoke Inhalation)

HYDROXOCOBALAMIN	
Mechanism	Chelation: The central cobalt atom binds cyanide Hydroxocobalamin + CN → Cyanocobalamin (Vitamin B12) Rapidly enters the mitochondria Safer, faster, though not always readily available, higher cost
Indications	Suspected cyanide toxicity
Dosing	Adult: 70 mg/kg (max 5 grams) IV over 30 min (may push in an arrest) May repeat to max 15 grams. Subsequent doses given over 6-8 hours
	Pediatric: 70 mg/kg (max 5 grams), subsequent dose 35 mg/kg
	Do not give at same site or time of thiosulfate. Thiosulfate binds to Hydroxocobalamin rendering it inactive
Adverse events	Dark red skin, mucous membranes and urine (hours-day) Allergic reactions, local reaction at the infusion site, lymphopenia Interfere with subsequent laboratory testing, particularly colorimetric testing (AST, bilirubin, creatine, magnesium, iron

SODIUM THIOSULFATE	
Mechanism	A slow acting sulfur donor. With the enzyme rhodanese coverts cyanide to thiocyanate which is excreted in the urine Works synergistically with nitrites and Hydroxocobalamin
Indications	Suspected cyanide toxicity
Dosing	Adult: 12.5 grams (50 ml of 25% solution) bolus or over 10-30 min Child: 0.5 grams/kg (2 ml/kg of 25% solution) maximum is adult dose
	Administer as a bolus or over 10-30 minutes based on severity Onset up to 30 minutes May be repeated at ½ the initial dose if manifestation reappear or at 2 hours as prophylaxis Do not give at same the same site or at the same time of Hydroxocobalamin. Thiosulfate binds to Hydroxocobalamin rendering it inactive
Adverse events	Hypotension, nausea, vomiting

CYCLIC ANTIDEPRESSANTS

INTRODUCTION (MICHAEL MOJICA, M.D., 12/2014)
Depression, in theory, is caused by a deficiency in monoamines (Norepinephrine, Epinephrine, Dopamine and Serotonin). Classes of agents used to increase monoamines and utilized as antidepressants include: cyclic antidepressants (CA), selective serotonin reuptake inhibitors (SSRI), serotonin/norepinephrine reuptake inhibitors (SNRI) and monoamine oxidase inhibitors (MAOI). This PEM Guide will focus on toxicity associated with cyclic antidepressants.

Cyclic antidepressants have been used for more than fifty years. (Initially called tricyclic antidepressants but newer agents have 4 rings). While effective they are associated with significant toxicity in overdose and have a narrow therapeutic window. Their use as antidepressants has largely been replaced by the SSRI's. The CA's have an approximately 5 times risk of mortality in overdose. (CA: 0.73%, SSRI: 0.14%). CA's are also used for a number of other purposes such as: chronic pain syndromes, migraines, nocturnal enuresis, obsessive-compulsive disorder, school phobia and ADHD. In children, ingestion of CA's is one of the most lethal unintentional ingestions. 1-2 adult strength pills can result in serious toxicity and death. An acute ingestion of greater than one gram can be life threatening in an adult.

PHARMACOLOGY
CA's inhibit presynaptic uptake of norepinephrine and or serotonin. CA's also have effects at many other receptors. CA's are weak acids, are highly protein bound and have a large volume of distribution. Acidemia increases the amount of free drug. In overdose, elimination is decreased. Anticholinergic effects such as delayed gastric emptying and ileus may increase the duration of symptoms.

CYCLIC ANTIDEPRESSANT PHARMACOLOGY		
RECEPTOR	MECHANISM	CLINICAL EFFECT
Norepinephrine	Inhibit presynaptic reuptake	Fever, tachycardia
Serotonin	Inhibit presynaptic reuptake	Fever, agitation
Acetylcholine	Anticholinergic (Muscarinic)	Delirium, tachycardia
Peripheral alpha adrenergic	Antagonize receptor	Hypotension
Cardiac Na channels	Block membrane	Dysrhythmias
Histamine	Block receptor	↓mental status
GABA	Antagonize receptor	Seizures

CLINICAL MANIFESTATIONS
The classic syndrome of CA intoxication includes symptoms of the anticholinergic toxidrome as well as a depressed mental status, seizures, wide complex tachycardia and hypotension. Symptoms can progress very rapidly and unpredictably.

CYCLIC ANTIDEPRESSANT TOXIDROME	
S	Shock/Seizure
A	Altered mental status
L	Long QRS
T	Terminal R Wave in AVR

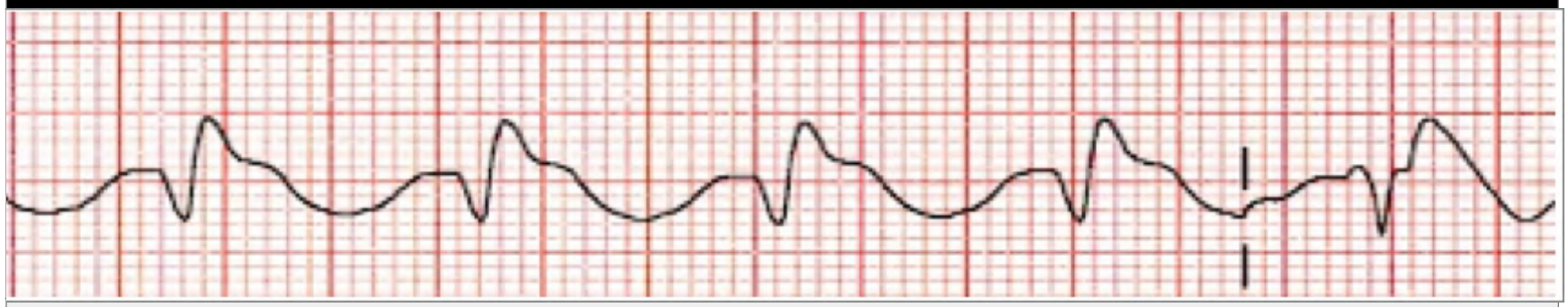
ANTICHOLINERGIC TOXIDROME	
RED AS A BEET	Cutaneous vasodilation (flushing)
DRY AS A BONE	Dry mouth
HOT AS A HARE	Anhidrotic hyperthermia
BLIND AS A BAT	Nonreactive mydriasis
MAD AS HATTER	Altered mental status: Agitation to coma
FULL AS A FLASK	Urinary retention and palpable bladder.
OTHER	Tachycardia, Decreased or absent bowel sounds

CLINICAL MANIFESTATIONS	
CARDIAC	Dysrhythmias: Sinus tachycardia with aberrancy (widened QRS) Ventricular tachycardia, Asystole, Atrioventricular blocks
	Hypotension
CENTRAL NERVOUS SYSTEM	Altered mental status: Delirium, agitation, psychosis, hallucinations Followed by lethargy and rapid progression to coma
	Seizures: Brief, generalized, non-status epilepticus

CARDIAC: Cardiac manifestations are the primary cause of death. Persistent hypotension results from myocardial depression (Na channel blockade) and vasodilation (alpha blockade). Na channel blockade increases the duration of depolarization. EKG changes include a prolonged PR, QRS and QTc. A QRS duration greater than 100 msec is predictive of seizures and greater than160 msec of ventricular tachycardia.

A rightward shift of the terminal 40 milliseconds of the QRS axis is the most sensitive indicator of cardiac involvement (R wave in AVR > 3mm or R/S ratio in AVR > 0.7).
The most common dysrhythmia is sinus tachycardia due to anticholinergic activity (antimuscarinic), reflex tachycardia (vasodilation) and direct sympathomimetic effects.

EKG CHANGES	
INTERVALS AND PATTERNS	ARRHYTHMIAS
↑ PR interval, ↑ QTc	Sinus tachycardia
↑ QRS (terminal 40 msec prolongation)	Sinus tachycardia w/aberrancy (↑QRS)
↑ QRS > 100 msec in Lead II	Atrioventricular Blocks
Brugada Pattern: RBBB, down sloping ST elevation in V_{1-3}	Ventricular ectopy
	Ventricular tachycardia
AVR: R wave > 3mm. R/S > 0.7	Ventricular fibrillation
I, AVL: Deep slurred S wave	Asystole

AVR

Terminal 40 msec prolongation, R > 3mm, R/S ratio > 0.7 QRS prolongation may be seen in therapeutic doses Absence of R in AVR makes cyclic antidepressany toxicity unlikely

NEUROLOGIC: Patients can present on the agitated end (anticholinergic) of the altered mental status spectrum and rapidly progress to lethargy and coma (antihistaminic). Seizures are generalized and limited in duration and are thought to be related to GABA receptor antagonism. They typically occur within the first 2 hours of ingestion. A QRS duration greater than 100 msec is predictive of seizures. A seizure may worsen acidemia and precipitate ventricular dysrhythmias.

DIAGNOSTIC TESTING

Cyclic antidepressant levels do not correlate with toxicity. All patients should have a 12 lead EKG and cardiac monitoring. Intravenous access should be obtained. Bedside glucose determination, ABG and BMP should be sent. A mixed acidosis both metabolic (hypotension) and respiratory (respiratory depression) may be present. Hypokalemia is the most common electrolyte disturbance and may limit the effectiveness of alkalinization. Screen for acetaminophen and salicylates in any intentional ingestion.

MANAGEMENT

Consider early intubation for altered mental status and hemodynamic instability.
GI decontamination can be considered with gastric lavage within 1 hour of presentation and/or activated charcoal within 2 hours of presentation if the airway is protected. Induction of emesis with syrup of ipecac is contraindicated in a patient who can rapidly lose consciousness. Flumazenil can lower the seizure threshold and is contraindicated. Physostigmine may worsen cardiac function and lead to cardiac arrest (asystole).

SHOCK: Supportive care includes fluid resuscitation and vasoactive infusions to maintain blood pressure, anticonvulsants for seizures and antiarrhythmics for dysrhythmias. After fluid resuscitation an alpha agonist such as Norepinephrine or Phenylephrine is preferred. Dopamine may be ineffective due to depletion of endogenous catecholamines.

ARRHYTHMIA: Lidocaine and Magnesium Sulfate preferred for ventricular tachycardia.

ANTIARRHYTHMICS TO AVOID IN VENTRICULAR TACHYCARDIA	
Type 1a	Procainamide: block sodium channels
Type 1c	Flecanide: block sodium channels
Type 3	Amiodarone: prolongs the QT interval
Type 4	Calcium channel blockers (verapamil): decrease cardiac output
Type 5	Beta blockers (propranolol): decrease cardiac output

SEIZURE: Benzodiazepines are the preferred antiepileptic with barbiturates as second line agents. Phenytoin, which blocks sodium channels, is contraindicated.

SERUM ALKALINIZATION AND SODIUM LOADING: Alkalinization decreases the amount of CA's available to tissues. Sodium loading also increases the sodium gradient and overcomes sodium channel blockade. $NaHCO_3$ reduces QRS prolongation, increases blood pressure and reverse or suppresses ventricular dysrhythmias. There is a clear benefit of $NaHCO_3$ over hyperventilation, hypertonic saline (3NS), and other non-sodium buffered solutions. Hypertonic saline will result in hyperchloremic metabolic acidosis and should be used only if alkalinization is not possible. Hyperventilation is more rapid and easily titratable but not as effective as $NaHCO_3$. It could be considered in patients at increased risk for a high sodium load such as CHF and acute lung injury. There is no evidence for prophylactic use or clear evidence supporting repeat boluses versus continuous infusion.

ALKALINIZATION INDICATIONS
Altered Mental Status
Hypotension
QRS > 100 msec
Ventricular arrhythmias
pH < 7.1

OTHER THERAPIES: Extracorporeal membrane oxygenation, cardiac bypass and intravenous lipid infusions are reserved for severe toxicity refractory to other therapies. Hemodialysis is infective due to the large volume of distribution of CA and the fact that they are highly protein bound.

THERAPY OVERVIEW: CYCLIC ANTIDEPRESSANT TOXICITY	
GI Decontamination (intact airway/intubated)	Gastric lavage within 1 hour of ingestion Activated charcoal: 1 gm/kg within 2 hours
ET Intubation	Mild hyperventilation
Sinus tachycardia with QRS > 100 msec	$NaHCO_3$:1-2 meq/kg IV bolus Repeat Q30 min, Consider infusion Target serum pH 7.5-7.55
Ventricular tachycardia	$NaHCO_3$: 1-2 meq/kg IV bolus Lidocaine bolus: 1 mg/kg slow IV Lidocaine infusion: 20-50 mcg/kg/min
Torsades	$MgSO_4$:20-50 mg/kg (max 2 gm) IV bolus over 2 minutes Overdrive pacing
Hypotension	Fluid resuscitation $NaHCO_3$: 1-2 meq/kg IV bolus Norepinephrine or Phenylephrine infusion
Seizures	Benzodiazepines: Lorazepam Barbiturates: Phenobarbital Propofol or Midazolam infusion NO Phenytoin: Worsens sodium channel blockade Paralysis, general anesthesia with EEG monitoring

MEDICATIONS: CYCLIC ANTIDEPRESSANT TOXICITY		
$NaHCO_3$	Adult	2-3 meg/kg then 132 meq in 1L D5W at 250 ml/hour
	Pediatric	2-3 meg/kg then 132 meq in 1L D5W at 2 x maintenance
Norepinephrine	Adult	8-12 mcg/min then 2-4 mcg/min
	Pediatric	0.05-0.1 mcg/kg/min
Phenylephrine	Adult	Bolus: 100-500 mcg/kg IV, Infusion: 100-180 mcg/min
	Pediatric	Bolus: 5-20 mcg/kg, Infusion: 0.1-0.5 mcg/kg/min
Lidocaine	Adult	0.5-1 mg/kg (max 100 mg) then 1-4 mg/min
	Pediatric	0.5-1 mg/kg (max 100 mg) then 20-50 mcg/kg/min

DISPOSITION

Unintentional ingestions that remain asymptomatic and with a normal EKG may be safely discharge after 6 hours with poison control center consultation. Those with significant manifestations requiring alkalinization should be admitted to an intensive care unit and alkalinization continued for 12-24 hours after the QRS with normalizes. All intentional overdoses should be evaluated by psychiatry.

HALLUCINOGENS

INTRODUCTION (ERIC WEINBERG, M.D., 8/2016)
Hallucinogens are substances that are taken to alter perception, thought process, emotion, arousal, self-image and mood. A variety of agents are taken for this purpose. The term hallucination refers to a sensory perception in the absence of external stimuli. In contrast, illusion refers to a distorted perception based on a real stimulus. The effect of the majority of hallucinogens is based on alterations in serotonin, dopamine and aspartate. Central 5-HT_{2A} receptors are thought to be the site of hallucinogenic properties. Exceptions include Salvia divinorum with agonism at kappa opioid receptors and Dextromethorphan at NMDA receptors. (See: PEM Guide: Toxicology: Drugs of Abuse: Stimulants, PEM Guide: Toxicology: Drugs of Abuse: Marijuana)

HALLUCINOGENS
Lysergic acid diethylamide (LSD)*
Dextromethorphan*
Phenylethylamine (e.g. Mescaline)
Psilocybin (Magic mushrooms)*
Salvia divinorum
Marijuana and synthetic cannabinoids
Methylenedioxymethamphetamine (MDMA)*
Ketamine
Phencyclidine (PCP)
* Denotes risk of serotonin syndrome

CLINICAL MANIFESTATIONS
Neuropsychiatric effects are a balance between desired and unwanted effects. Physiologic effects typically precede perceptual changes. Sympathomimetic effects are common though rarely result in severe abnormalities (See Appendix: Sympathomimetic Toxidrome). In addition to typical sympathomimetic manifestations, piloerection, dizziness, hyperactivity, muscle weakness, altered mental status, ataxia and coma may be seen. Nausea and vomiting are more prominent with Mescaline and Psilocybin. The combination of hyperthermia and psychomotor agitation can result in rhabdomyolysis leading the renal failure, disseminated intravascular coagulation (DIC) and hepatic injury. Serotonin syndrome may occur most typically with LSD, MDMA, dextromethorphan and psilocybin. (See Appendix: Serotonin Syndrome). Severe injury and death are most commonly the result of trauma secondary to impaired judgment.

NEUROPSYCHIATRIC EFFECTS	
DESIRED	UNWANTED
Passive observation (out of body)	Panic
Euphoria, sense of well being	Dysphoria
Synesthesia (blending of senses)	Fear, sense of dread, frightening imagery
Distorted sense of time	Disorientation
Heightened sensory perception	Psychosis

LYSERGIC ACID DIETHYLAMIDE (LSD)

LSD was initially used as an adjunct to psychotherapy before its widespread usage as a drug of abuse. LSD is available in several forms, including liquid-impregnated blotter paper, microdots, tiny tablets, “window pane” gelatin squares, liquid, powder, and tablets. LSD is usually ingested and has rapid GI absorption. Onset is within 30-60 minutes and last from 10-12 hours. The use of LSD has largely been replaced by the use of other hallucinogens.

LSD’s “psychedelic” effects include existential experiences, intensified perceptions, hallucinations and paranoia. Synesthesias are classic and involve a blending of senses such as the perception of “seeing sounds”. Clinical signs of LSD intoxication include sympathomimetic effects: tachycardia, palpitations, hypertension, blurred vision (mydriasis), diaphoresis, tremors, incoordination and fever. These effects are most intense in the early part of the intoxication. LSD users may experience “flashbacks” during which an individual re-experiences aspects of the acute intoxication. These episodes are short-lived and self-limited but may provoke anxiety. Serotonin syndrome may occur.

PHENCYCLIDINE (PCP)

PCP was commercially available in the 1950’s as an anesthetic and reemerged as a recreational drug in the 1960s. PCP can be used orally, intravenously, smoked, or inhaled. PCP is a noncompetitive antagonist at the N-methyl-D-Aspartate (NMDA) receptor where it results in dissociative and psychotic effects. PCP also produces sympathomimetic effects by blocking the reuptake of dopamine and norepinephrine. The clinical effects of PCP can last up to 48 hours following a large dose. PCP use has largely been replaced by other hallucinogens.

KETAMINE

Ketamine is a PCP derivative and is used medically as a dissociative anesthetic. It is difficult to synthesize and is most commonly available via diversion of legitimate supplies. In addition to antagonist effects a the NMDA receptor, Ketamine has both peripheral and central opioid and sympathomimetic effects. Ketamine is also a popular recreational agent because of its short duration, low cost, and hallucinatory effects. Recreational Ketamine is available for oral, intramuscular, subcutaneous and intravenous use. Ketamine is pharmacologically similar to PCP but differs with respect to pharmacokinetics. Intoxication will typically last for approximately 8 hours after oral exposure and 90 to120 minutes following intramuscular or intranasal exposure. Ketamine is often used in conjunction with MDMA, GHB and methamphetamines.

CLINICAL MANIFESTATIONS OF PHENCYCLIDINE (PCP) AND KETAMINE: PCP and Ketamine cause a dissociative psychotic reaction manifesting as changes in body image and feelings of spiritual separation from the body. Users may have difficulty seeing themselves as separate from their environment. PCP users may experience bizarre, dangerous or violent behavior and the emotional state created by PCP is frequently unpleasant. A catatonic stupor can also be seen.

Physical signs of PCP and Ketamine intoxication include nystagmus, ataxia, sensory impairment, catatonia, tachycardia, hypertension, and increased secretions. Ketamine intoxication is usually less severe and more short-lived than PCP intoxication. Both Ketamine and PCP also have sympathomimetic effects. A high doses, hypotension and bradycardia may be seen. With massive doses or co-ingestants respiratory depression may occur.

DEXTROMETHORPHAN

Dextromethorphan is similar to the codeine analog levorphanol. It is readily available in many over the counter cough and cold preparations. (“Triple C” for Coricidin Cough and Cold which contains Chlorpheniramine and Dextromethorphan, “Robo-tripping” for Robitussin DM which contains Guaifenesin and Dextromethorphan). Since these are combination products the co-products can also cause toxicity. Anticholinergic toxicity can be seen with antihistamines (see Appendix: Toxidromes). Acetaminophen toxicity should also be considered and screened for. Serotonin syndrome may occur.

PSILOCYBIN

Psilocybin is a tryptamine that is found in a number mushroom species (“magic mushrooms”. Other tryptamines include serotonin and melatonin. Nausea vomiting and diarrhea occur early and are prominent. This is in contrast to other mushrooms with greater toxicity with gastrointestinal symptoms that are delayed. Symptom onset is within 1 hour and includes: ataxia, hyperkinesis and visual hallucinations and illusions. Peak symptoms occur at 4 hours and the duration is approximately 6-12 hours. As a tryptamine, serotonin syndrome may occur.

MUSHROOM TOXICITY		
TOXIN	SYMPTOMS	MANAGEMENT
Alpha amantin	Liver damage	N-acetylcysteine (NAC)
Caprine	Disulfiram reaction with alcohol	Supportive care only
Gyromitrin	Neurotoxicity, GI, hemolysis	Pyridoxine
Ibotenic acid	Neurotoxicity (similar to Glutamate)	Supportive care only
Muscarine	Cholinergic toxidrome (see appendix)	Atropine
Muscimol	CNS depression, hallucinations	Supportive care only
Orellanine	Delayed renal failure	Dialysis
Psilocybin/psilocin	Hallucinations	Supportive care only

PHENYLETHYLAMINES

Mescaline (3,4 trimethoxy-phenyethamine) is the active ingredient of the peyote cactus. Its clinical effects are similar to LSD though not as potent. Phenylethylamines also include: Dopamine, Norepinephrine and Tyrosine. Many designer phenylethylamines are available.

SALVIA DIVINORUM

Salvia divinorum is a perineal herb in the mint family. The active compound is salvinorin A diterpene alkaloid which is a kappa opioid receptor agonist. Mild sympathomimetic effects may be seen. Onset is nearly immediate after exposure and lasts for 1-2 hours.

DIFFERENTIAL DIAGNOSIS

The majority of patients who take a hallucinogen and seek care are sufficiently coherent to tell you what they have taken. Consider other etiologies if there is overt psychosis, severe agitation or markedly abnormal vital signs. Screening for acetaminophen and salicylates should be considered for ingestions of over-the-counter preparations containing dextromethorphan. Consider obtaining a creatine phosphokinase (CPK) for those who are hyperthermic or have psychomotor agitation.

DIFFERENTIAL DIAGNOSIS	
Stimulants	Auditory hallucinations (not visual), higher HR, BP
Withdrawal syndromes	Alcohol, sedative hypnotics
Medical	Hypoglycemia, hypoxia, intracranial hemorrhage
Hyperpyrexia syndromes	Serotonin, Neuroleptic malignant, Malignant hyperthermia
Psychiatric illness	New onset schizophrenia
Anticholinergics	Confusion (“mad as a hatter”), garbled speech

MANAGEMENT

Supportive care in a quiet environment with minimal loud or noxious stimuli is usually all that is needed for hallucinogens. Verbal and physical contact with friends or family members may be helpful.

Benzodiazepines should be administered for those who are agitated or have an elevated heart rate, blood pressure or temperature. Rapid cooling should be initiated for hyperthermia. Intravenous fluids should be considered if there is a concern for rhabdomyolysis. Neuroleptic agents may be considered if psychotic symptoms persist.

Prolonged or severe psychosis will require psychiatric evaluation after evaluation for medical etiologies is complete. This may include a head CT and a lumbar puncture. Cyproheptadine may be considered for those meeting criteria for serotonin syndrome.

APPENDIX: SYMPATHOMIMETIC TOXIDROME

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/ Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET
*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size					

APPENDIX: SEROTONIN TOXICITY CRITERIA AND AGENTS

Toxicity is often a result of administering a second medication with serotonergic properties to a patient already taking a serotonergic medication. In the Libby Zion case, which lead to regulation of resident duty hours in New York State, Meperidine was given to a patient already receiving an MAOI. See: PEM Guide: Serotonergic Agents

HUNTER SEROTONIN TOXICITY CRITERIA	
At least one of the following in the presence of a serotonergic agent	
1	Spontaneous Clonus
2	Inducible Clonus **AND** [Agitation **OR** Diaphoresis]
3	Ocular Clonus **AND** [Agitation **OR** Diaphoresis]
4	Tremor **AND** Hyperreflexia
5	Hypertonic **AND** [Temperature > 38 C **OR** Inducible Clonus]
Dunkley EJ et al., Quarterly Med J 2003 (PubMed ID: 12925718)	

SEROTONERGIC MEDICATIONS	
Analgesics	Meperidine, Tramadol, Methadone, Fentanyl, Cyclobenzaprine
Anti-depressants	Class: SSRI, SNRI, TCA, MAOI, Lithium
Anti-emetics	Metoclopramide, Ondansetron
Anti-epileptics	Valproate, Carbamazepine
Anti-migraines	Class: Triptans
Anti-Parkinson’s	Selegine
Anti-psychotics	Trazadone, Buspirone
Drugs of abuse	Cocaine, MDMA, Methamphetamine, Dextromethorphan, LSD, Psilocybin
Others	Linezolid, Methylene blue

INHALANTS

INTRODUCTION (ERIC WEINBERG, M.D., 7/2016)
Substance use among adolescents and young adults is a significant cause of morbidity and mortality. Adolescents use many drugs in including: marijuana, ethanol, cocaine, methamphetamine, hallucinogens, inhalants, and prescription medications. Inhalant abuse is becoming more prevalent with 12% of students reporting inhalant use at some point in their lifetime in 2005. Inhalants are attractive to adolescents in that they are legally available and inexpensive. This PEM Guide will focus on the acute effects of inhalant abuse.

A wide variety of chemical compounds with may be inhaled with the intent to “get high”. Volatile hydrocarbons are the most common products used for this purpose. Examples include: gasoline, toluene, lighter fluid, spray paint and model glue. Volatile hydrocarbons are lipophilic and readily absorbed across pulmonary membranes into the bloodstream. Subcategories of volatile hydrocarbons such as the volatile alkyl nitrites (e.g. Amyl nitrite – “poppers’) and halogenated hydrocarbons (e.g. carbon tetrachloride) may exhibit class specific toxicities. Other agents, such as nitrous oxide can also be inhaled.

INHALATION METHODS	
Huffing	Most common, poured onto a cloth and inhaled (e.g. spray paint)
Bagging	Sprayed into a bag covering the mouth and nose or the entire head
Sniffing	Inhaled directly from container (e.g. model glue)

The desired effects of euphoria and intoxication are thought to occur due to alterations at GABA receptors and may involved glutamate activity and MDMA receptors as well. The volatile alkyl nitrites do not have direct CNS effects and their effects are thought to be due to smooth muscle relaxation. Symptoms are typically short lived and last approximately 15-30 minutes.

CLINICAL MANIFESTATIONS
Presenting signs and symptoms vary, may be subtle and are often non-specific. These may include: CNS symptoms (depressed mental status, dizziness and headache), gastrointestinal symptoms (nausea, vomiting and abdominal pain), tachypnea and tachycardia. A characteristic odor may by identified on the clothing or from the patient’s skin or breath.

The primary, acute effects of hydrocarbon inhalation are a depressed mental status. At high doses, inhalation may cause significant CNS depression, coma, and respiratory depression. Asphyxiation can occur when there is significant CNS depression in a person with a plastic bag over their head.

“Sudden sniffing death” occurs when a patient who has been inhaling volatile hydrocarbons, exerts themselves (e.g. sexual activity or running away from police) and develops ventricular fibrillation. This is most commonly seen with the halogenated hydrocarbons such as typewriter correction fluid (Trichloroethane). These agents are thought to “sensitize the heart” to catecholamines by prolonging repolarization. Subsequent exertion results in a catecholamine surge that precipitate an arrhythmia.

CLINICAL MANIFESTATIONS	
Central Nervous System	Initial euphoria, hallucination (auditory and visual) Headache, dizziness, tremor, weakness CNS depression, slurred speech, confusion
Respiratory	Hypoxia: decreased FiO_2 and rebreathing of exhaled CO_2 (bagging) Chemical pneumonitis: fever, tachycardia, rales, Chest XRAY findings, leukocytosis. Barotrauma: pneumothorax, pneumomediastinum, Pneumopericardium due to prolonged exhalation against a closed glottis in attempt to prolong drug effect. Upper airway edema/obstruction Respiratory depression
Cardiac	Arrhythmias: halogenated hydrocarbons
Dermatologic	Vesicles resembling frostbite
Hematologic	Methyl chloride metabolized to carbon monoxide Alkly hydrocarbons (e.g. amyl nitrite) result in methemoglobinemia
Renal	Toluene leads to Na, K loss in urine, Severe hypokalemia, weakness
Trauma	Injuries due to disinhibition, intoxication

DIAGNOSTIC TESTING

Diagnostic testing should be targeted to the presenting signs and symptoms. Because these are often non-specific a broad differential diagnosis should be entertained. A specific history of inhalant use may focus the differential but the presence of co-ingestants and trauma should still be considered.

TESTING INDICATIONS
Bedside glucose: all patients with an altered mental status
Urine toxicology screen: inhalants are not detected
Chest XRAY and co-oximetry panel: tachypnea, hypoxia, cyanosis or rales
EKG: tachycardia, hypotension, pulseless, irregular heart beat
Basic metabolic profile (K+), CPK, phosphorus: muscle weakness
XRAY, CT: signs of trauma

MANAGEMENT

Management decisions should be made in consultation with the regional poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.

Treatment of inhalant intoxication is predominantly supportive, as its effects are short-lived and usually benign. In the case of inhalant-induced dysrhythmias, appropriate therapy should be initiated as per PALS/ACLS guidelines (e.g. CPR, defibrillation, and epinephrine for ventricular fibrillation). Electrolyte abnormalities should be corrected. Supplemental oxygen and endotracheal intubation may be required. Albuterol if wheezing is present. Treatment of carbon monoxide toxicity (See: PEM Guide: Toxicology: Carbon Monoxide) or methemoglobinemia should be initiated if indicated by symptoms and co-oximetry testing.

DISPOSITION

Since the clinical manifestations are typically short lived, the majority of patients may be discharged after an observation period. Those with ongoing symptoms or manifestation of severe toxicity (e.g. chemical pneumonitis) should be admitted.

IRON

INTRODUCTION (MICHAEL MOJICA, M.D., 10/2011)
Iron is a common pediatric ingestion. In the 1990's it became leading cause poisoning death in children < 6 years but has become less common due to child proof packaging. Iron is available from a number of preparations including: pills (prenatal vitamins and ferrous sulfate), liquids and chewable tablets. In overdose, it may be potentially lethal secondary to gastrointestinal hemorrhage with shock and metabolic acidosis. In general, poison center refer to a medical facility those with ingestions of > 40 mg/kg of adult preparations, those that are intentional and those with severe symptoms

IRON PREPARATIONS		
TYPE	PREPARATION	ELEMENTAL IRON
Ionic (salts)	Ferrous Chloride	28%
	Ferrous Fumarate	33%
	Ferrous Gluconate	12%
	Ferrous Lactate	19%
	Ferrous Sulfate	20%
Nonionic	Carbonyl Iron	98%*
	Iron polysaccharide	48%*
*Despite a high percentage of elemental iron the non-ionic preparations are associated with a lower risk of toxicity Prenatal vitamins have a higher amount of iron compared to that found in multivitamins and iron only containing prescriptions		

PATHOPHYSIOLOGY
Iron is critical to organ function. It is able to accept and donate electrons and has an essential role in cytochromes, myoglobin and hemoglobin. Iron transfers electrons between the ferric state (Fe^{3+}) and ferrous state (Fe^{2+}). After oral intake iron is stored as ferritin or released to ferrin an iron binding protein. Once absorbed by cells, Iron is oxidized to the Ferric form (Fe^{3+}).

In overdose, iron causes an oxidative stress that results in loss of cellular integrity. Damage to the gastrointestinal tract further enhances iron absorption. Once iron-binding capacity is saturated both free iron and ferric hydroxide are produced.

CLINICAL MANIFESTATIONS	
Gastrointestinal hemorrhage	Mucosal cell necrosis
Metabolic acidosis	Mitochondrial toxicity → Inhibition of Krebs cycle and uncoupling of oxidative phosphorylation
Shock	Direct vasodilation, negative inotropy, hemorrhage
Coagulopathy	Inhibits thrombin (independent of hepatotoxicity)

CLINICAL PRESENTATION

Five phases of iron toxicity are described. Clinical phase should not be assigned solely based on time since ingestion, as the phases are highly variable and may be accelerated with larger ingestions.

STAGES OF IRON TOXICITY		
1	GI Phase	Local toxic effects predominate Nausea, vomiting, abdominal pain and diarrhea Hematemesis, melena due to GI edema, ulceration and rarely infarction, necrosis Asymptomatic 6 hrs post ingestion generally excludes serious toxicity
2	Latent Phase	6-24 hours post GI symptom resolution, before overt systemic toxicity. This phase is not always present and does not represent resolution Ongoing cellular toxicity → lethargy, tachycardia, metabolic acidosis
3	Shock Phase	Massive ingestion (few hours), Moderate Ingestion (12-24 hours) Multifactorial: hypovolemia, vasodilation, ↓ cardiac output, coagulopathy CNS effects: Lethargy, hyperventilation, seizures, coma
4	Hepatic Failure	2-3 days post ingestion. Oxidative damage due to hepatic uptake rare with levels < 700 mcg/dl
5	Post Ingestion	(2-8 weeks): Scarring as a result of mucosal injury. Gastric outlet obstruction, fistulas due to strictures

DIAGNOSTIC TESTING

LABORATORY AND RADIOGRAPHIC TESTING	
Abdominal Radiograph	Absence of pills does not reliably to exclude toxicity as liquid and chewable formulations are not radio-opaque Best utilized to guide ongoing GI decontamination
Laboratory Testing	Serum iron level (at 4 hours): gauge toxicity, success of treatment Peak level at 4-6 hours. A single value may not represent peak Fe > 300 mcg/ml represent the upper range of total iron binding capacity
	Anemia: Due to blood loss, late finding due to initial hemoconcentration
	ABG/VBG, BMP with anion gap metabolic acidosis, primarily lactate
	Elevated Glucose and WBC: Little predictive value. Should not be used to guide management decision

SERUM IRON LEVELS	
CLINICAL MANIFESTATIONS	mcg/dl
Gastrointestinal symptoms	> 300
Significant gastrointestinal symptoms, moderate systemic toxicity	300-500
Pronounced systemic toxicity, shock	500-1000
Significant morbidity and mortality	> 1000

MANAGEMENT

Initial priorities include an evaluation and management of airway, breathing and circulation. Intubation may facilitate decontamination (whole bowel irrigation) in patients with altered mental status or hemodynamic instability. Intravenous access should be obtained and fluid resuscitation initiated as indicated.

GI DECONTAMINATION: Small molecules and metals such as iron are poorly absorbed by activated charcoal and are not dialyzable. If iron is visualized in the stomach on XRAY, lavage may be indicated. The effectiveness of orogastric lavage is limited by size and poor solubility of pills and iron's tendency to form adherent masses (concretions) and it is not routinely recommended. Whole body irrigation should be considered if the iron has moved past the pylorus. For patients with severe toxicity, upper endoscopy or gastrotomy with surgical removal may be necessary.

WHOLE BOWEL IRRIGATION	
Polyethylene glycol electrolyte solution (Osmotically neutral)	
	Young children: 0.5 liters/hour (25 ml/kg/hour)
	Adolescents/Adults: 0.5 – 2 liters/hour (20-30 ml/minute
Indication: Symptomatic patients or who have retained pill fragments on XRAY	
Continued until rectal effluent is clear	
Contraindications: Bowel obstruction, perforation, ileus, significant gastrointestinal bleeding, a comprised airway or hemodynamic status	
An antiemetic such as Metoclopramide or Ondansetron may be required	

ELIMINATION: Deferoxamine binds free iron and iron in transit between transferrin and ferritin. The resulting complex is eliminated by the kidneys.

DEFEROXAMINE INDICATIONS
Metabolic acidosis
Repetitive vomiting
Lethargy or toxic appearance
Hypotension or signs or shock
Serum iron concentration > 500 mcg/ml
Large number of pills on XRAY

DEFEROXAMINE DOSING
Intravenous: Increase to a maximum rate of 15 mg/kg/hours as tolerated
Intramuscular: 50 mg/kg Q6H maximum dose Children: 1 gram, Adults: 2 grams

The optimal duration of therapy is unknown. Due to toxicity and limited effectiveness over time, therapy for greater than 24 hours is not recommended. Adverse effects may include hypotension, renal failure, acute respiratory distress syndrome and sepsis with Yersinia species. Intramuscular injection as part of a deferoxamine challenge and monitoring urine color changes as a guide to treatment are no longer recommended.

DISPOSITION

DISCHARGE WITHOUT TREATMENT
< 20 mg/kg elemental Fe ingested
Ingestion of carbonyl or pediatric formulation
Symptom free for > 6 hours post ingestion
No other coingestants
Non-intentional, single acute ingestion
Reliable caregiver with ability to return

LITHIUM

INTRODUCTION (SASHA GIFFORD, M.D. 4/2020)
Lithium is a naturally occurring element that is used as first-line maintenance treatment for bipolar-affective disorder and as refractory treatment for depression. The drug has a narrow therapeutic window and clinical signs of toxicity may be seen at the upper limit of the therapeutic range.

Toxicity can be a result of an intentional ingestion, dosage error, altered metabolism secondary to co-ingestion of other medications, impaired kidney function and/or dehydration. Lithium is handled similarly to sodium by the kidney. A situation that would lead to sodium reabsorption by the kidney (dehydration, salt restriction) will increase Lithium resorption. Dehydration can occur during an acute illnesses (fluid losses, fluid redistribution, decreased fluid intake) or can be chronic secondary to nephrogenic diabetes insipidus as a side effect of Lithium. There are several medications that cause dehydration or renal impairment that can cause an increase in serum Lithium levels.

MEDICATIONS THAT INCREASE PLASMA LITHIUM	
MECHANISM	MEDICATION
↓ GFR	NSAIDs, ACE inhibitors (Enalapril, Lisinopril)
↑ Renal Tubular Absorption	Thiazide diuretics (Chlorothiazide), Spironolactone
Unknown	Calcium channel blockers (Diltiazem, Nifedipine)

PATHOPHYSIOLOGY/PHARMACOLOGY
The mechanism of action of Lithium is not completely understood. However, clinical efficacy has been well demonstrated. Lithium has been shown to decrease dopamine and noradrenaline release from nerve terminals and to transiently increase serotonin levels, making it useful in mood stabilization.

A 300 mg Lithium carbonate pill contains 8.12 meq of Lithium. Oral Lithium reaches a peak at 1-2 hours, sustained release preparations at 6-12 hours and up to 24 hours for the brain to reach equilibrium. These times are increased in overdose.

The half-life of Lithium is 18-30 hours. Gastrointestinal absorption is typically rapid though it is not absorbed well on an empty stomach. The therapeutic range is 1.0-1.5 mEq/L for acute treatment and 0.6-1.2 mEq/L for chronic treatment. Lithium is freely filtered by kidneys but over 60 percent is then reabsorbed by the proximal tubules. Dehydration increases reabsorption. Lithium is not protein bound and has a small volume of distribution making it amendable to dialysis. Lithium is contraindicated in cardiovascular and kidney disease. It is also not recommended in pregnancy due to a 2-3-fold increased risk in fetal cardiac abnormalities (e.g. Ebstein anomaly).

CLINICAL MANIFESTATIONS
Toxicity is categorized as acute, chronic and acute on chronic. Chronic is the most common presentation and is usually unintentional. Acute toxicity is an acute ingestion of Lithium in someone without a steady state concentration of Lithium at baseline. Acute on chronic toxicity is an acute ingestion of Lithium in someone with a steady state concentration of Lithium at baseline. The clinical manifestations of Lithium toxicity differ in each these category.

Mortality from toxicity is low and most patients fully recover after management. However, persistent neurological complications have been described. Lithium toxicity is rare in the pediatric population.

Acute poisoning presents usually with gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Dehydration from GI losses increases Lithium absorption by the kidneys and exacerbates toxicity. Neurologic manifestations are a late finding due to the slow redistribution of Lithium to the CNS. Chronic poisoning often presents with neurologic findings. Lithium concentrations in acute ingestions often do not correlate with clinical signs of toxicity.

LITHIUM SIDE EFFECTS: Lithium can have several side effects at therapeutic levels when take chronically. Lithium induced nephrogenic diabetes insipidus is the most common adverse effect. Lithium makes the distal tubule less sensitive to vasopressin (ADH). This can lead to dehydration and subsequent toxicity due to increased Lithium resorption by the kidney. Other renal effects include chronic tubulointerstitial nephropathy. Endocrine adverse effects include hypothyroidism and hyperparathyroidism. Other side effects include but are not limited to: leukocytosis (↑ neutrophils), aplastic anemia, acne and weight gain.

CLINICAL MANIFESTATIONS	
Cardiac	Common: Flattened or inverted T waves in the precordial leads (not associated with ↓ LV function, ↑ cardiac markers)
	Other: Sick sinus syndrome, sinus bradycardia, Wandering atrial pacemaker, Brugada syndrome, heart block, ST-segment elevation, ↑ QT
	Rare: Serious arrhythmias, clinical effects
Central Nervous System	Mental Status: Lethargy, ataxia, confusion, agitation
	Neuromuscular Excitability: Irregular coarse tremors, fasciculations, myoclonic jerks, hyperreflexia, choreoathetoid movements, clonus
	Other: Seizures (rare, severe toxicity), dysarthria, nystagmus
	SILENT: Syndrome of Irreversible Lithium Extenuated Neurotoxicity: Permanent: 2 mo after stopping Lithium without another neurologic cause
GI	Nausea, vomiting, diarrhea, ileus
Renal	Tubulo-interstitial nephritis, nephrogenic diabetes insipidus
Acute: Primarily GI, minor EKG changes Chronic: Primarily Neurologic Acute on Chronic: Symptoms of both Acute and Chronic (GI and Neurologic)	

PHYSICAL EXAM

Special attention should be made to assess for clinical dehydration. A thorough neurological exam should be performed. Look for alterations in mental status, ataxia, and signs of neuromuscular excitability (e.g., tremors, myoclonus).

DIAGNOSTIC TESTING

Monitor serum electrolytes and renal function. Consider coingestants. The serum Lithium level does not correlate with acute toxicity due to delayed CNS distribution. The Lithium level is better correlated with toxicity in chronic ingestions. Follow Lithium levels serially until peak and beginning of descent.

DIAGNOSTIC TESTING
Point of care glucose if altered mental status
EKG
Lithium level[1]: Repeat Q2-4 hours until peak levels then less frequently
BMP: Sodium (monitor for hypernatremia), BUN/Cr (renal function)
CBC
UA: ↓ Specific gravity as an indicator of nephrogenic diabetes insipidus
TSH
Acetaminophen and Salicylate levels if intentional ingestion
Pregnancy test if appropriate
1. Do not send in Lithium heparin serum separator tube → Falsely elevated levels

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of Lithium toxicity includes both toxicologic and non-toxicologic causes. Neuroleptic malignant syndrome (NMS) and serotonin syndrome (SS) should be considered in those with preexisting psychiatric illness. Fever is typically prominent in NMS and SS but fever can also precipitate Lithium toxicity.

DIFFERENTIAL DIAGNOSIS
TOXICOLOGIC
Neuroleptic Malignant Syndrome: Fever, muscle rigidity (“lead pipe”)
Serotonin Syndrome: Fever, clonus more prominent in lower extremities
Withdrawal: Alcohol, Benzodiazepine: Less prominent neurologic symptoms
Anticholinergics
Sympathomimetics: Phencyclidine (PCP), Cocaine
NON-TOXICOLOGIC
CNS: Infection, Head trauma, Stroke, Seizures
Endocrine: Hypoglycemia, Hypothyroidism, Thyrotoxicosis

MANAGEMENT

Management of Lithium toxicity is primarily supportive. It is important to determine if the formulation is immediate acting or sustained release and whether the patient is taking Lithium chronically. Hemodialysis may be required for severe toxicity though the exact indications are controversial. Renal should be consulted early if the need for hemodialysis is anticipated. Toxicology consultation is essential (National Poison: 800-222-1222, NYC Poison Control Center: 212-POISONS (212-764-7667)). Psychiatry consultation is required for intentional ingestions with suicidal intent.

FLUID RESUSCITATION: It is essential to restore intravascular volume in those with GI losses due to an acute or acute on chronic ingestion and those with altered renal function due to chronic or acute on chronic ingestion.

SUMMARY: MANAGEMENT OF LITHIUM TOXICITY
Airway, Breathing, Circulation
Intravenous access, cardiac monitoring, EKG
Assess bedside glucose if altered mental status
Send Labs, Lithium level
Discontinue Lithium administration
<u>GI Decontamination</u>: Large, acute ingestion only (no role in chronic ingestion) 1. Lithium is a small molecule that does not readily bind to activated charcoal 2. Consider whole bowel irrigation or gastric lavage if acute ingestion Polyethylene glycol 500-2000 ml/hour PO or NG until rectal effluent is clear
<u>Intravenous Hydration</u>: To facilitate Lithium excretion (↑ GFR, ↓ resorption) Normal saline: 2x maintenance, Adult: 2-3 liters depending on cardiac function May require free water if hypernatremic: Nephrogenic DI + Normal Saline → ↑ Na
If nephrogenic diabetes insipidus, monitor serum Na every 4-6 hours
Seizures: Benzodiazepines are 1st line
Consider renal consult early for significant ingestion, potential need for hemodialysis

HEMODIALYSIS INDICATIONS
Lithium Level: > 5 mEq/L
Lithium Level: > 4 mEq/L with renal impairment (Creatinine > 2 mg/dl)
Lithium Level: > 2.5 mEq/L with: 1. Significant toxicity: Seizures, depressed mental status OR 2. Renal insufficiency or condition that decreases Lithium excretion OR 3. Factors precluding intravenous volume resuscitation (e.g. heart failure)

DISPOSITION

Patients with Lithium toxicity require admission. those with significant toxicity to an ICU setting. Patient are generally discharged when they are asymptomatic with a Lithium level < 1.5 mEq/L and cleared by psychiatry if indicated.

MARIJUANA

INTRODUCTION (ERIC WEINBERG, M.D., 3/2023)
Substance use among adolescents and young adults is a significant cause of morbidity and mortality. Marijuana is the illicit drug most commonly used by children and adolescents in the United States, with 40 percent of students reporting use at some point in their lives (2005). Marijuana intoxication is generally benign in comparison to other drugs of abuse. However, it is considered a gateway drug to other substance use. Legal availability and and an increase in edibles looking and packaged like candy has resulted in an increase in marijuana related emergency department visits. Greater availability in the home has resulted in a higher risk of young pediatric exposures.

Marijuana is made from the dried leaves from the plant *Cannabis septiva*. Extracts of the *cannibis* plant are also available as hashish (dried resin) and hash oil (liquid extract). These various forms can be smoked or eaten. Medical marijuana is available in pill form as Dronabinol.

PHARMACOLOGY
Marijuana consists of more than 60 compounds. The most psychoactive component in marijuana is delta-9-tetrahydrocannabinol (THC). THC's action is at both the cannabinoid 1 (CB1) receptor and the cannabinoid 2 (CB2) receptor.

CB1 receptors are predominantly found in the central nervous system (cortical and subcortical regions of the brain) and in the dorsal root ganglion of the spinal cord. CB1 receptors are responsible for most of the psychoactive effects. Activation of the CB1 receptor inhibits the release of: norepinephrine, dopamine, serotonin, acetylcholine, gamma hydroxyl-butyric acid and glutamate. THC activates the mesolimbic dopaminergic pathway ("reward pathway"). Agonism at the CB1 receptor has been shown induce analgesia, euphoria and relaxation, decrease anxiety, decrease motor function, impair memory and sense of time, and affect auditory and visual cognition.

In contrast, CB2 receptors are found mostly in peripheral tissue such as blood cells, immune tissues, and spleen and may exist in the brainstem, cortex, and cerebellum. Less is known about their function. They are thought to influence anti-inflammatory and immune-modulating effects through they may also have a role in controlling pain and emesis.

THC is lipophilic and easily crosses the blood-brain barrier. When inhaled the onset of psychoactive effects can occur within minutes, the peak effect occurs in 8-10 minutes and lasts for up to 4 hours. Ingestion results in slower onset of action with a peak at 1-3 hours and a duration of up to 12 hours. Because of the delay in onset, inexperienced users may ingest large quantities because they expect a more immediate response and think they may have taken an insufficient amount.

CLINICAL MANIFESTATIONS
The clinical presentation of cannibis intoxication varies by age and the amount ingested. Infants and small children receive a relatively large dose per body weight resulting in a higher degree of neurotoxicity. Neurotoxicity may include altered mental status (coma), abnormal motor movements (hyperkinesis , myoclonic jerks) and seizure. Non-specific neurological manifestations can mimic postictal states, encephalitis, or sepsis.

In rare circumstances, particularly with heavy, regular usage, patients may experience nausea, agitation, panic attacks, anxiety, paranoia, delusions/delirium, psychosis and myoclonic jerks. Postural hypotension can occur due to a decrease in vascular resistance. The incidence of cannabinoid hyperemesis syndrome is increasing (See section below)

CLINICAL MANIFESTATIONS BY AGE	
Children > 6yrs Adolescents, Adults	Cardiovascular: Tachycardia, hypertension, chest pain (pneumothorax)
	Ophthalmologic: Conjunctival injection, nystagmus
	Respiratory: Tachypnea, bradypnea, pneumothorax (breath holding during inhalation)
	Gastrointestinal: Dry mouth, increased appetite
	Neurologic: Sleepiness, ataxia, slurred speech, analgesia, perceptual distortion
	Behavioral: Euphoria, relaxation, impaired short term memory
Children < 6yrs Infants	Neurologic (Primary): Tremor, ataxia. Lethargy, coma. Hypotonia, seizures (rare)
	Cardiovascular: Tachycardia, bradycardia, hypotension
	Respiratory: Bradypnea, hypoventilation, apnea
	Gastrointestinal: Nausea, vomiting

DIAGNOSIS

Cannibis intoxication is a clinical diagnosis. THC can be detected on urine toxicology screens may be positive for 3-5 days for a single use. In those with chronic use or high body fat content, metabolites may accumulate in adipose tissue with regular use and may be detectable in the urine for 1 month. A positive screen for THC in a young child could limit unneccesary testing, imaging and interventions. This could limit unneccesary testing, imaging and interventions. A positive screen for THC in an adolescent could indicate use within the previous month and not necessarily the cause of their current presentation. THC can be detected in the urine for 10-14 days in the causal user and 4-6 weeks in the consistent user.

EVALUATION: ALTERED MENTAL STATUS OR UNKNOWN INGESTION	
Electrolytes: Bedside glucose, VBG, BMP	Urine Tox Screen: Co-ingestants
EKG: Rhythm, QTc, QRS width	Consider non-contrast head CT
Tox Labs: Acetaminophen, salicylates, ETOH	Consider LP: Febrile, progressive/persistent AMS

MANAGEMENT

Compared to other hallucinogens, the effects of marijuana are usually mild and self-limited, requiring minimal medical intervention and supportive care focusing on airway, breathing, and circulation. Children with apnea or risk of aspiration require rapid sequence intubation and mechanical ventilation. Intravenous fluids should be administered to correct hypovolemia.

Benzodiazepines may be required in the agitated or seizing patient. Efforts should be made to identify co-ingestants and they should be managed accordingly. Naloxone will not reverse coma due to cannabis toxicity but response to naloxone may unveil opiate toxicity. Child protection should be consulted.

CANNABINOID HYPEREMESIS SYNDROME

INTRODUCTION

Cannabinoid hyperemesis syndrome (CHS) is characterized by cyclic episodes of nausea and vomiting in those who use cannabis chronically. Rarely, it may occur with acute or acute-on-chronic use. Symptoms are often relieved by hot showers. The mechanism of CHS is unclear. Tetrahydrocannabinol (THC) is stored in fat. This can accumulate in long term uses. Cannabidiol in high doses and Cannabigerol have pro-emetic properties

CLINICAL PRESENTATION

Patients often have multiple ED visits with extensive, non-diagnostic laboratory and imaging studies. Consideration if cannabinoid hyperemesis syndrome can limit the diagnostic evaluation and target effective therapies.

PHASES OF CANNABINOID HYPEREMESIS	
Prodromal	Early AM nausea and abdominal discomfort without vomiting*
Hyperemetic	Debilitating nausea and vomiting
Recovery	Resolution of nausea and vomiting, able to eat normally
*Patients often self-treat with more marijuana thinking this will cure their symptoms	

MANAGEMENT

Discontinuing cannabis use typically results in resolution of symptoms in 1-2 days. Patients may require intravenous rehydration. Antiemetics (Ondansetron, Metoclopramide, Promethazine and Prochlorperazine) are commonly ineffective.

Symptoms may be relieved with topical capsaicin cream applied to the abdomen and typically relieves symptoms in 20-30 minutes. (Sorensen, J Med Toxicology 2017, PubMed ID: 28000146). This effect can aid in the diagnosis or CHS. Opiate medications can exacerbate symptoms of abdominal pain and vomiting.

Case studies/series have demonstrated the efficacy of Haloperidol. In a randomized trial of 34 patients that was stopped early due to a strong benefit, Haloperidol demonstrated a statistically and clinically significant change in both nausea and abdominal pain visual analog scores at 2 hours. 9.1% (3/33) of patients had a prespecified adverse medication event (moderate akathisia (n=1) and dystonic reaction requiring a return visit (n=2) (Ruberto, Ann Emerg Med. 2021, PubMed ID: 33160719). These 3 outcomes occurred in the 0.1 mg/kg dose Haloperidol group. Since there was no difference in efficacy between the 0.05 mg/kg and 0.1 mg/kg of Haloperidol, it may be prudent to utilize the 0.05 mg/kg Haloperidol dose. The administration of an antidopaminergic emetic such as metoclopramide prior to Haldol may increase the rate of Haloperidol adverse events such as dystonic reactions.

SYNTHETIC CANNABINOIDS

INTRODUCTION

Synthetic cannabinoid alternatives are the second most common drug (after Marijuana) used by adolescents. They are marketed as K2 and Spice and by numerous other names. They are readily available via the internet, at gas stations and convenience stores. They are often labeled as “not for human consumption” to avoid the law and are frequently cheaper than other substances. They can be smoked, used in electronic cigarettes or ingested.

Synthetic cannabinoid alternative are similar in effect of tetrahydrocannabinol (THC) at the cannabinoid receptors but also have clinical manifestation different from THC. They do not contain cannibis. There is no consistency in what is contained in the different products. While THC is a partial agonist at the cannabinoid receptors, synthetic cannabinoids are complete agonists with a higher affinity than THC. This results in a greater potential for toxic effects. Synthetic cannabinoids should be distinguished from synthetic THC (e.g. Marinol) which is FDA approved. All 50 states have banned synthetic cannabinoids. The Synthetic Drug Abuse Prevention Act (2012) placed 26 synthetic cannabinoids into schedule one of the Controlled Substances Act.

CLINICAL MANIFESTATIONS

The duration of symptoms may be longer or shorter than THC depending on the contents of the product. There are two clinical presentations. The first is with a sympathomimetic toxidrome similar to that seen with PCP or methamphetamine. Symptoms include: nausea, vomiting, hyperthermia, hallucinations, aggressive behavior, psychosis, extreme agitation and paranoia. Rhabdomyolysis with acute kidney injury, myocardial infarction, seizures and stroke can occur.

CLINICAL MANIFESTATIONS	
Cardiovascular	Tachycardia, hypertension, myocardial infarction, SVT
	Bradycardia, hypotension
Neurologic	Agitation, irritability, anxiety, hallucinations, psychosis, seizures, stroke
Ophthalmologic	Conjunctival injection
Gastrintestinal	Xerostomia (dry mouth), nausea, vomiting
Musculoskelatal	Rhabdomyolysis with acute kidney injury

DIAGNOSIS

The diagnosis of synthetic cannabinoid toxicity is made clinically. Synthetic cannabinoids are not identified on current urine drug screens.

MANAGEMENT

Symptoms are generally short lived and most patients do well with supportive care. Benzodiazepines can be used to treat sympathomimetic symptoms of agitation, anxiety and seizures. Hypotension should be treated with intravenous fluids. Norepinephrine is indicated for fluid refractory hypotension.

Hyperthermia requires aggressive cooling. Patients can generally be observed in the ED until they return to baseline.

METHEMOGLOBINEMIA

INTRODUCTION (CHELSEA KADISH, M.D., 12/2018)
Methemoglobinemia is a disorder of red blood cells that occurs when the iron atom in hemoglobin loses an electron to an oxidant, transforming the normal ferrous (Fe2+) hemoglobin to a ferric (Fe3+) state. The ferric (Fe3+) methemoglobin is unable to bind oxygen. In addition, the remaining hemoglobin that is oxygenated has a greater oxygen affinity making it more difficulty to release oxygen to the tissues (creates a left shift of the hemoglobin-oxygen dissociation curve). These two processes results in a functional anemia. It is normal to have a small amount (up to 3%) of methemoglobin (MetHb).

$$\underset{\text{(ferrous)}}{\text{Hb Fe}^{++}} \xrightarrow[\text{OXIDANT}]{} \underset{\text{(ferric)}}{\text{metHb Fe}^{+++}}$$

PATHOPHYSIOLOGY
The erythrocyte has several pathways to reverse oxidation by donating an electron to the ferric hemoglobin (Fe3+), converting it to the ferrous hemoglobin (Fe2+) which can bond oxygen. The most common pathway utilizes NADH, that is generated from glycolysis, and the enzyme NADH methemoglobin reductase within the RBC to donate an electron to methemoglobin. This enzyme is not fully active until four months of age, making infants more susceptible to methemoglobinemia. Additionally, γ(fetal)-hemoglobin which is predominant in the first 3-6 months after birth is more readily oxidized to methemoglobin than is α-hemoglobin or β-hemoglobin.

$$\text{metHb Fe}^{+++} + \text{NADH} \xrightarrow[\text{Erythrocyte Cytochrome B5 Reductase}]{} \text{Hb Fe}^{++} + \text{NAD+}$$

A second method of reducing MetHb is via the enzyme NADPH methemoglobin reductase. This makes use of NADPH from the hexose monophosphate shunt to reduce methemoglobin. This pathway normally only reduces a small amount of methemoglobin. It becomes the primary pathway of detoxification with Methylene blue serving as an electron donor.

$$\text{metHb Fe}^{+++} + \text{NADPH} \xrightarrow[\text{NADPH Methemoglobin Reductase + Methylene Blue (electron donor)}]{} \text{Hb Fe}^{++} + \text{NADP+}$$

ETIOLOGY
Methemoglobinemia may be hereditary or acquired. Hereditary methemoglobinemia is rare, occurs earlier in life, and patients have mild symptoms or are asymptomatic. Hereditary methemoglobinemia is categorized by two types of gene mutations, methylene blue responsive (mutations in NADH reductase) and methylene blue unresponsive (caused by mutations in the hemoglobin chain). Patients with hereditary methemoglobinemia have levels of 10-50% at baseline. They typically present with cyanosis in infancy and may be misdiagnosed with cyanotic heart disease.

Acquired methemoglobinemia is typically caused by an oxidative stress such as by environmental agents or medications. (See Appendix: Acquired Causes of Methemoglobinemia). The most common agents to induce methemoglobinemia are Dapsone and topical Benzocaine spray. Benzocaine, Lidocaine and Dapsone are common adulterants of heroine, cocaine and other drugs and cause methemoglobinemia in this context.

In pediatrics, benzocaine teething gels may induce methemoglobinemia because mucosal absorption bypasses metabolism by the liver. As stated previously, NADH methemoglobin reductase is not fully active until four months of age and γ(fetal)-hemoglobin is more readily oxidized making infants at high risk for methemoglobinemia. Infants may also develop methemoglobinemia from diarrhea, dehydration or sepsis. Premature infants, low for birth weight infants and those with underlying hematologic or pulmonary disease are at increased risk of methemoglobinemia.

CLINICAL PRESENTATION

Signs and symptoms of methemoglobinemia are caused by impaired oxygen delivery to tissues. The classic presentation is cyanosis that is unresponsive to administration of supplemental oxygen. Cyanosis occurs with 1.5 g/dL of methemoglobin (approximately 10% of hemoglobin). In contrast, 5 g/dL of deoxyhemoglobin is needed to produce cyanosis (approximately 33% of hemoglobin). Phlebotomy reveals the pathognomonic chocolate brown blood.

In addition to cyanosis, patients present with signs of tissue hypoxia including tachycardia, tachypnea, hypotension, cardiac dysrhythmias, nausea, vomiting, lethargy, confusion, coma, seizures and cardiac arrest. Presentation varies based on degree of methemoglobinemia. Patients with comorbid conditions that impair oxygen delivery such as anemia congestive heart failure and pulmonary disease may have signs and symptoms at lower levels of methemoglobin.

SIGNS AND SYMPTOMS BY METHEMOGLOBIN LEVELS*	
LEVEL	SIGNS AND SYMPTOMS
1-3%	None (normal)
3-15%	Possibly none, pulse oximeter reads low SaO_2, slate gray skin
15-20%	Chocolate brown colored blood, cyanosis
20-50%	Dizziness, syncope, headache, dyspnea, exercise, fatigue, weakness
50-70%	CNS depression, coma, seizures, dysrhythmias, metabolic acidosis (lactate)
>70%	Respiratory depression, death
*Patients with comorbidities may be symptomatic at lower levels	

DIAGNOSIS

Definitive diagnosis of methemoglobinemia is with co-oximetry (venous or arterial). Other laboratory studies may be useful such as a CBC to identify anemia, and electrolytes to identify metabolic acidosis. An anion gap metabolic acidosis (lactic acidosis) may be present due to tissue hypoxia.

CO-OXIMETRY: Co-oximetry quantifies levels of oxyhemoglobin, deoxyhemoglobin, methemoglobin and carboxyhemoglobin. Co-oximetry must be performed prior to treatment with methylene blue because methylene blue has similar absorbance characteristics to methemoglobin and the methemoglobin level will be falsely elevated. The presence of sulfhemoglobin also results in a false positive.

OXYGEN SATURATION: Standard pulse oximeter uses two wavelengths of light, deoxyhemoglobin (660 nm) and oxyhemoglobin (940 nm) to calculate the proportion of arterial hemoglobin that is oxygenated (SpO_2: p is for pulse). The presence of methemoglobin, sulfhemoglobin, carboxyhemoglobin and methylene blue interfere with this calculation. Methemoglobin absorbs light at both wavelengths. As a result, SpO_2 will typically be falsely low. SpO_2 plateaus at around 85%. However, pulse oximetry readings do not correspond to the level of methemoglobinemia. Newer pulse oximeters, which utilize eight different wavelengths of light, can correctly identify methemoglobin.

BLOOD GAS (ARTERIAL OR VENOUS): Despite cyanosis, patients with methemoglobinemia will have a normal PaO_2. PaO_2 (a is for arterial) is a measure of oxygen dissolved in plasma, and is unrelated to hemoglobin saturation. Arterial oxygen saturation (SaO_2) is the percentage of total hemoglobin that is oxyhemoglobin. The SaO_2 on an ABG is calculated using PaO_2, temperature and pH. This calculation is inaccurate in the presence of methemoglobin or carboxyhemoglobin and will result in a falsely elevated value. The difference between SaO_2 and SpO_2 is called the "Saturation gap". A saturation gap of greater than 5% is consistent with methemoglobinemia. This may help to differentiate methemoglobinemia from cyanotic heart disease where there is a consistently low SpO_2, PaO_2, SaO_2 and no saturation gap.

	SpO_2	PaO_2	SaO_2	Saturation Gap*
Methemoglobinemia	LOW	NORMAL	NORMAL	YES
Cyanotic congenital heart disease	LOW	LOW	LOW	NO
Saturation Gap = SpO_2 – SaO_2. A gap of > 5% is indicative of methemoglobinemia In both conditions, the hyperoxia test does not show a response to oxygen				

MANAGEMENT

The majority of patients with methemoglobin levels less than 10% and who are asymptomatic will require only supportive care and removal of the oxidizing agent or medication. The half-life of methemoglobin is 1-3 hours. Administration of 100% oxygen will assist in maximizing oxygenation of normal hemoglobin. Management decisions should be made in consultation with a poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.

METHYLENE BLUE: The antidote, methylene blue is indicated for patients with symptoms suggestive of oxygen deprivation which occur typically at methemoglobin levels greater than 20%, In the presence of NADPH and the enzyme NADPH methemoglobin reductase, methylene blue is reduced to leuko-methylene blue. Leuko-methylene blue is then available to donate an electron to methemoglobin converting it to the normal ferrous hemoglobin.

METHYLENE BLUE	
Mechanism	Serves as electron donor. Converts methemoglobin to normal ferrous hemoglobin
Dosing	1-2 mg/kg (maximum 50 mg) of 1% solution IV over 3-5 minutes Followed by 15-30 ml flush to minimize administration site pain May repeat dose in 30 minutes if methemoglobin level still > 20%
Onset	Rapid onset, maximal effects within 30 minutes (range 10-60 min)
Indications	Symptoms of tissue hypoxia: Chest pain, altered mental status, tachycardia, tachypnea, lactic acidosis (generally at levels > 20% in healthy patients)
Contra-indications	Known G6PD deficiency. Methylene blue is ineffective and can cause hemolysis. Methylene blue requires NADPH with is generated by G66D.
Adverse effects	May cause a transient decrease in SpO_2 due to blue color absorption at 660 nm Blue color may impede ability to identify improvement in cyanosis High doses (7 mg/kg): Chest pain, dyspnea, hemolysis Serotonin syndrome: Inhibits monoamine oxidase → ↑ Serotonin
Alternatives	Consider: Exchange transfusion, hyperbaric oxygen Dapsone: Consider Cimetidine, multi-dose activated charcoal G6PD deficiency: Ascorbic acid: 300-1000 mg/day PO divided TID

DAPSONE: Special considerations should be taken for patients taking Dapsone as it has a prolonged half-life (30 hours) and toxic intermediate metabolites. Cimetidine inhibits Dapsone metabolism resulting a decrease in methemoglobinemia. Gastrointestinal decontamination with multi-dose activated charcoal may be required in addition to methylene blue.

G6PD DEFICIENCY: Methylene blue will be ineffective in patients with known G6PD deficiency because G6PD is required to generate NADPH for methylene blue to be effective. Ascorbic acid is indicated, in preference to methylene blue, in a patient with G6PD deficiency.

Alternative therapies (exchange transfusion or hyperbaric oxygen) may be indicated if methylene blue is ineffective or contraindicated. Exchange transfusion replaces methemoglobin with normal hemoglobin
.

DISPOSITION

All patients, especially infants and younger children, who receive treatment with methylene blue should be admitted to the intensive care unit for continuous monitoring and supportive care.

APPENDIX: ACQUIRED CAUSES OF METHEMOGLOBINEMIA

ACQUIRED CAUSES OF METHEMOGLOBINEMIA		
Neonatal	Acidosis Diarrhea Low birth weight	Prematurity Sepsis
Anesthetics	Benzocaine Eutectic Mixture of Local Anesthetics (EMLA) 2.5% Lidocaine/Prilocaine	Prilocaine Lidocaine
Antimicrobials	Dapsone Sulfa-containing antibiotics (e.g. Trimethoprim/Sulfamethoxazole) Nitrofurantoin	Primaquine Chloroquine
Nitrites & Nitrates	Amyl nitrate Butyl nitrate Isobutyl nitrite Nitrates in well water Nitrites in food (Natural: most greens, vegetables, Added: cured meats)	Nitric oxide Nitroglycerin Nitroprusside Silver nitrate Sodium nitrate
Other medications	Acetaminophen Metoclopramide Phenytoin	Phenacetin Phenazopyridine (Pyridium) Flutamide
Chemicals	Aniline dyes Arsine Chlorates (Na+, K+, Barium) Chlorobenzene Copper sulfate Dinitrophenol Dinitrotoluene	Exhaust fumes Fires (denaturation) Naphthalene Naphthalene (mothballs) Paraquat/diquat Phenols Nitrochlorobenzene

NICOTINE

INTRODUCTION (ADRIANA MANIKIAN, M.D. 3/2023)
The availability of high-concentration liquid nicotine (1-30 mg/mL) for refilling e-cigarettes that comes in packaging and flavors attractive to children has increased the rate of nicotine toxicity in young children. Other sources of nicotine include: nicotine patches, gum lozenges, nasal spray and snuff. A number of non-tobacco plants (e.g. Poison Hemlock) contain alkaloids that also have a nicotinic effect. In 2015, The Child Nicotine and Poisoning Prevention Act was signed into law requiring that liquid nicotine containers used to refill e-cigarettes have child-resistant packaging. See also: PEM Guide: Toxicology: Cholinergics

PHARMACOLOGY
Nicotine toxicity can occur by inhalational, dermal, oral and mucosal exposure. Ingestion of cigarettes (1 whole or 2-3 butts) will produce toxicity in a child. The LD_{50} dose in an adult is estimated to be 0.5-1.0 mg/kg. Doses that are not problematic to an adult can produce severe toxicity and death in small children.

PHARMACOKINETICS / PHARMACODYNAMICS	
Absorption	Lungs, oral mucosa, skin, GI tract. Increased in an alkaline environment
Volume of Distribution	2.6 Liters/kg
Protein Binding	5%
Metabolism	80-90% hepatic, remainder lung/kidney
Half Life	1-2 hours, decreased with repeated exposure
Elimination	2-35% excreted unchanged in urine

PATHOPHYSIOLOGY
Nicotine mimics the effects of acetylcholine by binding to nicotinic cholinergic receptors in the brain, spinal cord, autonomic ganglia, adrenal medulla, neuromuscular junctions, and chemoreceptors of the aortic and carotid bodies.

Nicotine's effects are dose dependent. In small doses, nicotinic, cholinergic receptor agonism predominates at central nicotinic receptors in the brain, autonomic nervous system and somatic nerve fibers. At toxic doses, excessive and prolonged stimulation leads to both nicotinic and muscarinic cholinergic receptor agonism resulting in neuromuscular (nicotic) and parasympathetic (muscarinic) blockade.

CLINICAL PRESENTATION
Low doses of nicotine frequently have stimulant effects (e.g., tachycardia, hypertension). Symptoms are primarily related to sympathetic stimulation and resolve completely within 12 hours. The most common symptoms are vomiting, and infrequently agitation. Signs of central nervous system toxicity include ataxia, and at very high doses, seizures.

Toxicity is dose dependent and typically follows a biphasic pattern with early central stimulation followed by late depression. At higher doses, loss of nicotinic receptor specificity occurs and results in signs of both nicotinic and muscarinic cholinergic toxicity consistent with the cholinergic toxidrome (See Appendix: Down: bradycardia, hypotension, miosis, Wet: Vomiting, diarrhea, salivation, bronchorrhea). Death may occur within 1-2 hours with severe poisoning and is due to muscle paralysis (neuromuscular blockade similar to the effects of succinylcholine) leading to respiratory failure and cardiovascular collapse.

CLINICAL MANIFESTATIONS				
	GASTROINTESTINAL	RESPIRATORY	CARDIOVASCULAR	NEUROLOGIC
Early 0-1 hour	Nausea Vomiting Salivation Abdominal pain	Bronchorrhea Hyperpnea	Hypertension Tachycardia Pallor	Agitation Anxiety Confusion Hyperactivity
				Blurred vision Dizziness Fasciculations Headaches Seizures Tremors
Late 1-4 hours	Diarrhea	Hypoventilation Apnea	Bradycardia Hypotension Dysrhythmias Shock	Lethargy Weakness Paralysis
Nicotinic: Muscle fasciculations, paralysis (hypotonia/weakness), coma. Seizures at very high doses Muscarinic: Vomiting, diarrhea, lacrimation, salivation, bronchorrhea, broncoconstriction, bradycardia, miosis				

MANAGEMENT

Treatment is supportive and symptom driven. Consider activated charcoal for ingested nicotine patches but it is likely not to be of benefit for ingestion or dermal exposure to liquid preparation. Caregivers should were appropriate personal protective equipment and the patients skin should be wiped down to prevent further dermal exposure. Atropine can be used to manage the muscarinic toxicity. High doses may be required and should be titrated to improve airway secretions without causing anticholinergic toxicity. Management decisions should be made in consultation with your regional poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.

NOTE: Pralidoxime is not indicated in nicotine toxicity. Pesticides (Organophosphates and Carbamates) are acetylcholine esterase inhibitors. Cholinergic excess by preventing the breakdown of acetylcholine by acetylcholine esterase and increasing the concentration of acetylcholine at the neuromuscular junction. Pralidoxime, reverses the binding of acetylcholine esterase inhibitors from acetylcholine esterase and if given early, can displace the pesticide from acetylcholine esterase.

In contrast, Nicotine's effect is through direct agonism at the acetylcholine receptor and not through acetylcholine esterase so Pralidoxime will not be effective in Nicotine Toxicity.

In a patient with a cholinergic toxidrome of unclear etiology, Pralidoxime can be given. It cholinergic toxicity is known to be due to Nicotine, the Pralidoxime will be ineffective (though not likely cause harm)

MANAGEMENT OF NICOTINE TOXICITY	
Respiratory Failure	Atropine is administered for parasympathetic stimulation (muscarinic toxicity) such as excessive salivation, bronchorrhea, and bradycardia. Dose 0.02 mg/kg, repeat Q5-15 minutes doubling the dose each time to dry bronchial secretions without causing anticholinergic toxicity (fever, flushing, delirium).
	Endotracheal intubation is required for severe toxicity with respiratory failure. Succinylcholine may result in prolonged paralysis A non-depolarizing paralytic such as Rocuronium may be administered instead
Decontamination	Remove clothes and wash with soap and copious water for dermal exposures. Avoid warm water, which can cause vasodilatation and further promote skin absorption. Activated charcoal may be helpful in severe ingestion to provide removal through trans-intestinal absorption.
Seizures	Benzodiazepines
Bradycardia	Atropine 0.02 mg/kg (See dosing above in respiratory failure section)
Hypotension	Fluid resuscitation. Consider Norepinephrine or Phenylephrine for fluid refractory hypotension
Bradyarrhythmias	Atropine, Cardiac pacing
Tachyarrhythmias	Lidocaine, Magnesium sulfate, Amiodarone, Procainamide
Rhabdomyolysis	Monitor creatine kinase, urinalysis and urine for myoglobin. Fluid resuscitation to maintain urine output at a minimum of 4 ml/kg/hour in a child or 200 ml/hour in an adult. Urinary alkalinization and Mannitol may result in adverse events and should not be used (an alkaline environment increased toxicity)
Electrolyte abnormalities	Hyperkalemia, hyperphosphatemia, hypocalcemia. Hyperkalemia should be managed promptly. Hypocalcemia is typically transient and does not require treatment in the absence of tetany

APPENDIX: CHOLINERGIC TOXIDROME

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/ Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

INTRODUCTION (MICHAEL MOJICA, M.D. 8/2022)
Nonsteroidal Anti-Inflammatory Drugs (NSAIDS) are one of the most widely used class of agents and are involved in a high percentage of ingestions. (This PEM Guide does not discuss the salicylates. See PEM Guide: Toxicology: Salicylates)

PHARMACOLOGY

NSAIDS are utilized clinically for their anti-inflammatory, analgesic and antipyretic properties. They inhibit prostaglandin synthesis by blocking cyclooxygenase (COX) pathways. There are two COX pathways: COX-1 and COX-2. These are located in different tissues and increase prostaglandins responsible for a variety of functions.

COX-1 PROSTAGLANDINS	COX-2 PROSTAGLANDINS
Always Activated	Activated by Tissue Damage
Maintain Stomach Wall Integrity	Inhibit Inflammation
Maintain Renal Perfusion	Inhibit Pain
Increase Platelet Aggregation	Decrease Platelet Aggregation
	Antipyretic

The degree to which NSAIDS inhibit COX-1 and COX-2 are responsible for their clinical efficacy and adverse effects profile. Salicylates inhibit COX-1 more than COX-2. The antiplatelet effect is why they are used to prevent cardiovascular disease but is also the reason it is associated with adverse gastrointestinal and renal effects. Ibuprofen (Motrin), naproxen (Alive) and diclofenac (Voltaren) equally inhibit COX-1 and COX-2 equally. Meloxicam (Mobic) and Celecoxib (Celebrex) are selective COX-2 inhibitors. COX-2 inhibitors can increase cardiovascular risk by increasing platelet aggregation

In general, NSAIDS are rapidly absorbed and reach peak concentrations within 2 hours. Sustained-release indomethacin and enteric coated Diclofenac peak at 2-5 hours. NSAIDS exhibit a high level of protein binding, have little enterohepatic circulation, are metabolized by the liver and eliminated by the kidney.

CLINICAL MANIFESTATIONS

PRESENTING SYMPTOMS	
GI	Nausea, vomiting, epigastric pain, hemorrhage, hepatic damage
CNS	Depressed mental status, hallucinations, seizures, tinnitus
RESPIRATORY	Hyperpnea (compensation for metabolic acidosis), Apnea
METABOLIC	Anion gap metabolic acidosis
OTHER	Hypotension, acute renal injury

SYMPTOMS BASED ON AMOUNT INGESTED	
< 100 mg/kg	Typically asymptomatic
100-400 mg/kg	Symptomatic, typically within 4 hours
> 400 mg/kg	Life-threatening (6 grams in an adult)

LABORATORY TESTING

Laboratory testing is indicated for those who are symptomatic and those with a large enough ingestion to cause toxicity (> 100 mg/kg). Tests include a CBC and basic metabolic profile. A bedside glucose determination should be obtained for all patients with an altered mental status. If neurologic symptoms are present, lactate, liver function tests and a coagulation profile should be added. In patients with an intentional ingestion, acetaminophen and salicylate levels and a beta HCG (in females) should be sent. An EKG should be obtained to screen for arrhythmias due to co-ingestants or electrolyte abnormalities.

MANAGEMENT

Management of an NSAID ingestion is primarily supportive. No antidote exists. Management decisions should be made in consultation with your regional poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.

MANAGEMENT PRIORITIES	
Severe Symptoms	Unstable vital signs, altered mental status Intubation must compensate for metabolic acidosis with a higher than normal minute ventilation
GI Decontamination	Consider Activated Charcoal (1 gram/kg, max 50 grams) if the patient is alert and the ingestion has been within 1 hour (particularly for large ingestions and if the patient is symptomatic).
	Multi-dose Activated Charcoal should be considered for sustained release preparations.
	Gastric lavage is typically not indicated due to rapid absorption Hemodialysis is ineffective due to a high degree of protein binding
Gastrointestinal Symptoms	Antacids should be administered to patients with dyspepsia Anti-emetics should be administered to those who are vomiting
Seizures	Benzodiazepines
Metabolic	Sodium bicarbonate for fluid refractory metabolic acidosis Correct electrolyte abnormalities

DISPOSITION

Those with an ingestion of less than 100 mg/kg and those with an ingestion of greater the 100 mg/kg who are asymptomatic for 4-6 hours can be safely medically cleared. Ingestion of a sustained release preparation require a longer observation period. Patients with an intentional ingestion should be evaluated by psychiatry.

ADMISSION CRITERIA
Altered mental status, significant metabolic acidosis, renal dysfunction
Suicidal ideation with significant intent
Ingestion of a large amount of a sustained release preparation

OPIOIDS

INTRODUCTION (ERIC WEINBERG, M.D., 9/2020)

Substance use among adolescents and young adults is a significant cause of morbidity and mortality in the pediatric emergency population. The illicit use of prescription medications such as Vicodin and Oxycontin is an increasingly popular form of adolescent substance abuse. In 2015, the rate of deaths due to opiates exceeded that due to motor vehicle collisions for the first time. As the availability of opiates expands, many younger children are being accidentally exposed.

PHARMACOLOGY

The term opiate refers to the alkaloids derived from the opium poppy and includes morphine and codeine. The term opioid refers to an agent with results in a clinical state similar to opiates and or exerts its effect at the opioid receptors. Opioids includes naturally occurring opiates as well as synthetic and semi-synthetic agents. A semisynthetic opioid (e.g. Heroin, Oxycodone) is derived from the chemical modification of an opiate. A synthetic opioid (e.g. Fentanyl) is not derived from an opiate yet binds to an opioid receptor and exerts similar effects.

Opioid medications such as morphine, meperidine, codeine, hydrocodone, oxycodone, and propoxyphene are commonly used analgesic agents. All opioids bind to several specific opioid receptors; the most clinically relevant being the mu (OP3) receptors. Opioids also inhibit the release of many neurotransmitters in the peripheral and central nervous system. The primary effects are euphoria, analgesia and anxiolysis.

Heroin is primarily used for it's psychoactive effects. Methadone is prescribed to treat heroin addiction. Different formulations exhibit variable pharmacokinetics and are available for oral, intravenous, intramuscular, and subcutaneous administration. These agents can also be insufflated or smoked. Intravenous administration (morphine, meperidine, heroin) leads to rapid onset of effect and carries the highest risk for adverse effects.

CLINICAL MANIFESTATIONS

The management of intoxication is based on the history of exposure and the presence of clinical symptoms. The classic opioid toxidrome includes: respiratory depression, a depressed mental status and miosis (see Appendix: Toxidromes). The opiate toxidrome is similar to that of sedative hypnotics. Miosis may or may not be associated with sedative hypnotics. It is essential to distinguish between the two as a specific antidote, Naloxone, is available for opioid toxicity.

The presence of normal pupils does not exclude opioid toxicity. Meperidine results in normal pupils. In addition, co-ingestants such as sympathomimetics and anticholinergics can result in normal or dilated pupils. Hypothermia, hypotension and bradycardia may occur. Bowel sounds are typically hypoactive. Histamine release can result in bronchospasm, hives, or flushing. Seizures, rhabdomyolysis and dysrhythmias may occur with intravenous use.

DIFFERENTIAL DIAGNOSIS	
MIOSIS	BRADYCARDIA
Cholinergics, Clonidine	$Alpha_2$ adrenergic agonists
Opiates, Organophosphate	Beta adrenergic antagonist
Phenothiazines, Pilocarpine	Calcium channel antagonists
Sedative hypnotics	Cardioactive steroids (e.g. Digoxin)
	Opioids
	Organophosphates

PULMONARY: Pulmonary complications after opioid overdose include: non-cardiogenic pulmonary edema (AKA permeability pulmonary edema), aspiration pneumonia or pneumonitis and acute respiratory distress syndrome. Multiple mechanisms have been proposed for these complications. These complications have been described in opioid overdose both with and without Naloxone exposure. Acute lung injury may occur after recovery from opioid respiratory depression. This is most common with morphine, heroin and methadone. The pathophysiology is unclear and treatment is supportive. Symptoms of acute lung injury can include shortness of breath, frothy sputum, **hypoxemia and rales.**

ALTERED MENTAL STATUS: The differential diagnosis of altered mental status is extensive, including many medical conditions and toxins. The most common medical conditions to consider are intracranial hemorrhage, electrolyte abnormalities and sepsis. Frequent toxins include ethanol and sedative-hypnotics (e.g. benzodiazepines). Clonidine intoxication also presents with miosis though with a higher degree of bradycardia and hypotension. See PEM Guide: Neurology: Altered Mental Status.

ADDITIONAL TOXICITIES	
Serotonin toxicity	Meperidine, Dextromethorphan
Seizures	Meperidine, Tramadol
Arrhythmias	Loperamide: Wide complex tachycardias Methadone, Oxycodone: prolonged QT
Acetaminophen (co-ingestant)	Hydrocodone, Oxycodone

MANAGEMENT

Management decisions should be made in consultation with the regional poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.

Management of opioid toxicity includes support of oxygenation and ventilation and the delivery of the short acting opioid antagonist; Naloxone. Trauma can occur as the primary etiology of the patient's presentation or as a consequence of opioid toxicity. A bedside glucose determination is necessary for all patients with an altered mental status. An acetaminophen level should be obtained. Basic labs including a beta hcg, ethanol level and CPK may be indicated. An EKG with a prolonged QRS interval may indicate the co-ingestion of cocaine or a cyclic antidepressant. A positive urine toxicology screen for opioids doesn't not necessarily indicate an acute ingestion and false negative results can occur.

Gastrointestinal decontamination is seldom warranted as there are associated risks in a patient with a depressed mental status and an effective antidote exists. The exception would be the use of polyethylene glycol in a patient who is smuggling (body packers). Hemodialysis is ineffective due to the large volume of distribution.

Cardiopulmonary monitoring should include, respiratory rate, oxygen saturation and end tidal CO_2. Adolescent patients who are awake and alert with a respiratory rate > 12 breaths/minute and oxygen saturation > 90% after typically do not require further medical evaluation other that careful observation until symptoms resolve.

NALOXONE: If airway obstruction or respiratory failure occurs, the patient requires supplemental oxygenation and assisted ventilation. Any patient with respiratory depression and is suspected of an opioid ingestion should receive an empiric trial of Naloxone. Naloxone is a short acting competitive opioid antagonist that can be administered intravenously, intramuscularly, intranasally, sublingually, subcutaneously and endotracheally. Intravenous use is preferred. Its use can be both diagnostic and therapeutic for opioid intoxication and may preclude the need for intubation.

WEB LINK: OPIOID EMERGENCY ALGORITHM (AHA 2020)

The onset of action intravenously is 1-2 minutes with a duration of 20-90 minutes. The duration of action of Naloxone is shorter than some opioids such as methadone and the need for additional doses should be anticipated. If there is no response to Naloxone within 10 minutes, other etiologies should be considered.

DOSING: An escalating dosing scheme allows titration of sufficient Naloxone to reverse respiratory depression without precipitating withdrawal symptoms. Patients should receive an initial dose of 0.04 mg with additional doses titrated to reverse respiratory depression. Increasing to 0.4 mg, then 2 mg and then 10 mg as needed. Higher doses may be considered for high potency synthetic opioids such as Fentanyl.

The pediatric advanced life support course recommends a dose of 0.1 mg/kg with a maximum dose of 2 mg. This may be an appropriate dosing scheme in those who are opiate naive.

A continuous infusion may be required for patients with an opioid effect that outlasts the effect of a single dose of Naloxone. An infusion of 2/3 of the dose required to restore ventilation is administered per hour. There is no maximum safe dose Naloxone in the absence of symptoms of withdrawal. (Dosing recommendations based on Goldfrank's Toxicologic Emergencies 10th Edition). If respiratory depression occurs while on a Naloxone infusion a repeat bolus of ½ the initial dose can be given and the infusion restarted at a higher rate.

COMPLICATIONS: Natural withdrawal from opioids is not typically life-threatening. However, rapid, iatrogenic withdrawal can result in catecholamine surge and hemodynamic instability with the potential of myocardial ischemia and acute lung injury.
Adequate ventilatory support should be initiated prior to Naloxone administration to avoid excessive sympathetic stimulation.

Withdrawal symptoms should not be managed by administration of additional opioids. If withdrawal symptoms develop while on a continuous infusion of Naloxone, the infusion should be discontinued. If respiratory depression recurs, then the infusion may be restarted at half the initial rate.

WITHDRAWAL SYMPTOMS
Mental status: dysphoria, restlessness
Yawning, piloerection, mydriasis
Tearing, coryza, diaphoresis
Mild increases in HR, BP
Myalgias, arthralgias
Nausea, vomiting, diarrhea and abdominal cramping

DISPOSITION

A psychiatric consultation is indicated if the toxicity is a result of intended self harm. Patients presenting with toxicity due to a long acting opioid such as methadone should be hospitalized. Patients with significant opioid symptoms who have received high doses or a continuous infusion of naloxone require hospitalization. Those who respond appropriately to Naloxone without any of the above concerns may be safely discharge after an observation period of several hours.

PEDIATRIC CONSIDERATIONS

Naloxone is not recommended as part of the initial resuscitation of the neonate in the delivery room born to an opioid dependent mother (AHA: Neonatal Resuscitation (2010). This is due to the lack of demonstrated efficacy, unclear dosing and potential safety concerns (seizures, withdrawal symptoms). A Child Protective Services consultation should be considered for the infant, toddler or child who presents with opioid toxicity after a home exposure.

APPENDIX: TOXIDROMES

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is Up (agitated, ↑vital signs, mydriasis) and Wet (sweating)

TOXIDROMES

		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime

1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome

TOXIDROMES MADE SIMPLE

	Sympathomimetic	Anticholinergics	Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET

*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size

SALICYLATES

INTRODUCTION (MICHAEL MOJICA, M.D., 2/2016)
Salicylate is one of the oldest and most commonly used analgesic, antipyretic and anti-inflammatory agents. It is widely available in many forms including tablets, enteric-coated tablets, extended release tablets, pediatric chewable, analgesic ointments, and suppositories. Salicylates are frequently packaged together with other analgesics such as opiates, and are commonly found in over the counter cold medications. Salicylates can also be found in anti-diarrheal agents and Chinese herbal medications. One milliliter of methyl salicylate (Oil of wintergreen: 98% solution) is equivalent to 1.4 grams of salicylate.

The use of salicylates in pediatrics has declined significantly because of concerns of Reye syndrome, a form of hepatic encephalopathy thought to be due to the use of salicylates during a viral illness. Salicylates are still used to treat Kawasaki disease in pediatrics.

PATHOPHYSIOLOGY
Following ingestion, salicylates are rapidly absorbed from the small intestine (and to a lesser extent from the stomach), with peak plasma concentrations occurring 15-60 minutes after ingestion. In overdose, enteric coated and extended release preparations can peak at 4-6 hours. In the setting of toxic overdose, the majority of salicylates are not bound to protein in the vascular space, which increases delivery to tissues.

At therapeutic doses, the metabolism of salicylates occurs in the liver via glucuronidation, oxidation, and glycine conjugation resulting in a half life of 15-20 minutes. In a toxic overdose, these enzyme pathways become saturated and the half-life increases dramatically to up to 30 hours. Excretion is through the kidneys.

If untreated salicylate can cause derangements at the cellular and systemic level. Salicylates cause an uncoupling of oxidative phosphorylation resulting in an anion gap metabolic acidosis (lactic and pyruvic acids), hyperthermia, fluid losses and hypoglycemia. Centrally salicylates can stimulate the respiratory center causing a respiratory alkalosis and stimulate the chemoreceptor zone in the medulla causing nausea and vomiting.

CLINICAL PRESENTATION
The clinical manifestations of salicylate toxicity are dose-dependent. In adults the hallmark of salicylate overdose is a mixed acid-base picture with respiratory alkalosis and metabolic acidosis. The respiratory alkalosis predominates. The etiology of metabolic acidosis is multifactorial and includes: direct effect of salicylate (a weak acid), lactic and pyruvic acidemia, ketoacidosis and renal dysfunction. Due to limited respiratory reserve, the metabolic acidosis predominates in children

EARLY PRESENTATION
Nausea, Vomiting
Tinnitus
Tachypnea/Hyperpnea

SEVERE TOXICITY
Severe anion-gap metabolic acidosis
Altered mental status
Seizures
Non-cardiogenic pulmonary edema
Hypovolemia
Hypokalemia
Hyperthermia

PATHOPHYSIOLOGY	CLINICAL MANIFESTATIONS
Direct Effects	Gastrointestinal irritation: Nausea, vomiting Gastritis, pylorospasm Renal toxicity/failure Pulmonary edema
Uncouples Oxidative Phosphorylation (Interferes with the Krebs Cycle)	Anion gap metabolic acidosis (Lactate, pyruvate) Hyperthermia Hypovolemia, shock
Induction of Fatty acid production	Anion gap metabolic acidosis (Ketonemia)
CNS Stimulation (Early)	Hyperventilation (respiratory alkalosis) Tinnitus with mild-moderate reversible hearing loss Altered mental status (Elevated: agitation, delirium) Seizures
CNS Depression (Late)	Altered mental Status (Depressed: lethargy, coma) Vomiting (Chemoreceptor trigger Zone)
Hematologic	Hypothrombinemia, platelet dysfunction
Depletion of ATP	Paratonia (extreme muscle rigidity)

DIAGNOSTIC TESTING

In the past the Done nomogram was used to predict severe salicylate toxicity but it is no longer recommended because salicylate levels correlates poorly with clinical toxicity. Salicylate levels should be correlated with the patient's clinical condition and pH because more salicylate enters cell in an acidic environment.

DIAGNOSTIC TESTS	
ABG	Acid-base status
BMP	Acid-base status, serum glucose
Urinalysis	Urine pH, ketones
Drug levels	Salicylate, Acetaminophen, alcohol (possible co-ingestants)
Abdominal XRAY	Possible bezoar, concretions

MANAGEMENT

SUPPORTIVE CARE: Treatment of salicylate toxicity begins with an assessment and stabilization of airway, breathing, and circulation. Intubation should be avoided unless absolutely necessary because it is difficult to maintain a respiratory alkalosis and the metabolic acidosis could worsen leading to cardiac arrest. If intubation and mechanical ventilation are required then the patient should be ventilated using the same minute ventilation they were producing prior to intubation and acid-based status should be carefully monitored.

GASTRIC DECONTAMINATION: Gastric decontamination with activated charcoal (1 gram/kg) is indicated in patients who are not vomiting and have an intact airway. Activated charcoal prevents gastrointestinal absorption of salicylate and acts as "dialyze" salicylate from the bloodstream into the gastrointestinal tract. Multiple dose charcoal should be continued until plasma salicylate level is < 30-40 mg/dl and the patient is asymptomatic. Whole bowel irrigation should be considered in patients with a bezoar or concretion formation.

FLUID RESUSCITATION: Fluid losses may be due to gastrointestinal losses (vomiting and diarrhea), renal losses (diuresis) and insensible losses (fever, tachypnea, diaphoresis). Decreased CSF glucose (neuroglycopenia) may be present in the setting of a normal blood glucose. Glucose should be provided in all patients with an altered mental status.

URINARY ALKALINIZATION: Salicylate is a weak acid that can cross cellular barriers (including the blood brain barrier) easily in the uncharged state. This is increased in the setting of acidosis. Alkalinization with sodium bicarbonate traps salicylate in the non-ionized form, prevents transfer across the cell membrane and promotes renal excretion. The dose of sodium bicarbonate should be titrated to a urine pH of 8.0 with care taken to avoid severe alkalemia (maintain serum pH ≤ 7.55).

It is essential to avoid hypokalemia. Hypokalemia occurs due to movement of potassium into the cell in the setting of alkalosis. With hypokalemia, the renal tubule re-absorbs potassium in exchange for hydrogen ions. Hydrogen ions acidify the urine reducing the efficacy of alkalinization.

URINARY ALKALINIZATION
Indications: tinnitus and/or central nervous system symptoms
$NaCO_3$
Acidemia: 1-2 meq/kg bolus then infusion when corrected
Alkalemia: 3 ampules (132meg) in 1 liter D5W at 1.5-2.0 maintenance
Maintain urine pH (7.5-8.0), serum pH ≤ 7.55
Maintain normokalemia

HEMODIALYSIS: If the patient continues to deteriorate despite alkalinization with sodium bicarbonate, then hemodialysis may be necessary. Hemodialysis provides the added benefits of fluid and electrolyte correction. Exchange transfusion or peritoneal dialysis should be considered in infants too small to undergo hemodialysis.

HEMODIALYSIS INDICATIONS
Persistent CNS toxicity
Altered mental status
Cerebral edema
Focal neurologic signs
Seizures
Pulmonary edema
Renal insufficiency
Congestive heart failure
Intractable acidosis
Hepatic failure and/or coagulopathy
Salicylate level > 100 mg/dl

SEDATIVE-HYPNOTICS

INTRODUCTION (ERIC WEINBERG, M.D., 7/2016)
Substance use among adolescents and young adults is a significant cause of morbidity and mortality. Adolescents use many drugs including: marijuana, ethanol, cocaine, methamphetamine, hallucinogens, inhalants, and prescription medications. Sedative-hypnotic agents encompass a diverse group of agents. This PEM Guide is limited to a discussion of Benzodiazepines, Ethanol, and Gamma hydroxybutyrate (GHB).

BENZODIAZEPINES

Benzodiazepines such as diazepam (Valium) or alprazolam (Xanax) are commonly prescribed anxiolytic agents. Benzodiazepines are also used to treat seizures, withdrawal states (e.g. ethanol), agitation and insomnia. Flunitrazepam (aka rohypnol, “roofies”) is commonly used for drug-facilitated sexual assault (“date rape”). Its anxiolytic effects are also used to soften “coming down” after cocaine or heroin use.

Benzodiazepine (BZD) effects are mediated by gamma amino-butyric acid (GABA), the predominant inhibitory neurotransmitter in the brain. Enhanced GABA activity leads to increased sedation. Variations in the GABA receptor allow for the variable physiologic effects of these agents (sedation, hypnosis, anxiolysis, amnesia, and muscle relaxation). BZD also may decrease the effects of glutamate excitation. Activity at central and peripheral BZD receptors play an unclear role.

GAMMA-HYDROXY BUTYRIC ACID (GHB)

GHB and its analogs gamma butyroloactone (GBC) and 1,4 butanediol (BD) cross the blood-brain barrier and acts upon GHB-specific receptors. GHB serves primarily as a CNS depressant. GHB was introduced as an anesthetic agent and gained popularity with body builders as a reputed facilitator of growth hormone release. In the late 1980’s its recreational use as a euphoric and relaxant agent became more common.
Because of its early onset, amnestic properties, disinhibition and rapid clearance (avoiding later detection) it is frequently used for drug-facilitated sexual assault. It is currently a schedule III drug prescribed for narcolepsy and other sleep disorders. It is rapidly absorbed with loss of consciousness occurring within 15 minutes, peaking at 30-60 minutes and lasting 2-4 hours. There is a narrow safety margin.

ETHANOL

Ethanol (ethyl alcohol) is commonly used by adolescents and young adults, and is a contributing factor to injuries related to motor vehicle collisions, homicide, fire, drowning, and suicide attempts. It is frequently combined with other drugs. Ethanol may also be found in other products such as: mouthwash, perfumes, cooking extracts and many over the counter medications.

Ethanol’s inhibitory effects are the result of enhanced GABA transmission as well as inhibition of NMDA glutamate receptors. Ethanol is rapidly absorbed by the gastrointestinal tract (primarily duodenum and small intestines). Peak levels are seen 30-90 minutes after ingestion on an empty stomach. The average clearance is 20 mg/kg/hour though there is considerable variability.

Accidental ingestion of ethanol by young children can result in severe hypoglycemia and hypoglycemic seizures. This occurs because ethanol inhibits gluconeogenesis in children who have limited glycogen stores.

CLINICAL MANIFESTATIONS

The signs and symptoms are described by the sedative-hypnotic toxidrome (See Appendix: Toxidromes). The sedative-hypnotic toxidrome can be thought of a decrease in mental status typically with normal or decreased vital signs with normal skin (neither wet (diaphoretic) nor warm and dry. The sedative hypnotic toxidrome is very similar to the opioid toxidrome. The primary difference is that the opioid toxidrome consistently includes miotic pupils while pupil size is variable though typically normal.

Early clinical manifestations may include: slurred speech, ataxia and a depressed mental status. The hallmark of severe sedative-hypnotic intoxication is CNS depression with or without respiratory depression. The degree of CNS depression generally parallels the degree of respiratory depression.

The co-ingestion of sympathomimetics (e.g. caffeine, cocaine) can antagonize the effects of sedative hypnotics. The co-ingestion of more than one sedative hypnotic (e.g. ethanol and a benzodiazepine) can augment their effects.

BENZODIAZEPINES: Sole BZD ingestion is considered relatively safe. Respiratory depression is rare following benzodiazepine intoxication unless very large doses are ingested or a co-ingestant such as ethanol is involved.

GHB: GHB effects include: bradycardia, hypotension, coma, myoclonic jerks and rarely seizures. Stimulant effects (agitation, self-injurious behavior) may be seen early or alternating with sedative effects. The abrupt onset of coma which alternates with sympathetic surges or ends abruptly is typical of GHB.

ETHANOL: Ethanol may cause agitation, vomiting, and hypoglycemia. Tachycardia and hypotension can be seen with ethanol due to volume loss (vomiting and diuretic effects) and ethanol induced vasodilation. Infants and young children with a blood alcohol concentration of greater than 50 mg/dl have a high risk of severe hypoglycemia. The effects of ethanol may mask the sympathomimetic effects typically seen with hypoglycemia.

TOXIC ALCOHOLS: See: PEM Guide: Toxicology: Toxic Alcohols**).** Ethanol intoxication should be differentiated from intoxication from methanol and ethylene glycol as these agents have a specific antidote. Fomepizole (4 methyl pyrazole) competitively inhibits alcohol dehydrogenase. A toxic alcohol ingestion should be considered if the osmolar gap is out of proportion to that suspected with ethanol alone or if there is a delayed onset of a severe, anion gap metabolic acidosis. Isopropyl alcohol ingestion results in an increase in the osmolar gap but not a metabolic acidosis.

Osmolar gap = Measured – Calculated Osmols
Calculated osmols = {(2Na) + (GL/18) + (BUN/2.8) + (Etoh/4.6)}
Normal osmolar gap is 10-15 mmol/L H_20

DIAGNOSTIC TESTING

Diagnostic testing should be targeted to the presenting signs and symptoms. Because these are often non-specific a broad differential diagnosis should be entertained. A specific history of sedative-hypnotic use may focus the differential but the presence of co-ingestants and trauma should be carefully considered.

Blood alcohol concentration (BAC) of greater than 80 mg/dl are considered legally intoxicated. Levels can vary widely depending on: prior abuse and tolerance, rapidity of ingestion, genetics and food ingestion. In infants and children, the BAC correlates well with the degree of lethargy. Metabolic abnormalities with alcohol may include an anion gap metabolic acidosis (lactate) and decreases in many serum electrolytes (Glucose, Ca++, K+, PO4-, and Mg++).

TESTING INDICATIONS
Bedside glucose: all patients with an altered mental status or seizure
Urine toxicology screen: commonly not helpful
Serum osmolality: concern for toxic alcohol ingestion
Blood alcohol concentration: suspected ethanol intoxication or co-ingestion
Acetaminophen, salicylates, beta hcg: intended self harm
EKG: tachycardia, hypotension, pulseless, irregular heart rate
Basic metabolic profile (K+), CPK, phosphorus: muscle weakness, severe ethanol
Drug facilitated rape evidence collection kit: suspected sexual assault
XRAY, CT: signs of trauma, no improvement in clinical condition with serial exams

MANAGEMENT

Management decisions should be made in consultation with the regional poison control center. The national number for the American Association of Poison control centers is 1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.

Most sedative hypnotic patients do well with supportive care. Significant CNS and respiratory depression may require endotracheal intubation to provide ventilation and oxygenation and to protect the patient from aspiration. If miosis is presence a trial of Naloxone is appropriate. Patients should be monitored (including capnography) for respiratory depression.

Gastrointestinal decontamination with activated charcoal is of little benefit and may increase the risk of aspiration. This is particularly true for ethanol and GHB which is rapidly absorbed, frequency vomited and does not bind to activated charcoal.

Patients with ethanol toxicity and signs of volume loss should be treated with intravenous fluids. Thiamine 100 mg is recommended to treat or prevent Wernicke's encephalopathy. Thiamine is rarely indicated in the pediatric population.
Agitated, patients can be treated with low doses of benzodiazepines but should be monitored carefully for respiratory depression.

All patients should be assessed for suicidality and the need for psychiatry evaluation. Infants and children with ethanol intoxication should be evaluated for possible child abuse and neglect with consultation by child protective services.

HEMODIALYSIS: Hemodialysis can increase the removal of ethanol 3-4 fold. However, there is limited data on clinical outcomes. Hemodialysis can be considered in those with liver disease and patients without a history of chronic alcohol use with a BAC greater than 450 mg/dl.

FLUMAZENIL: Administration of flumazenil, a nonspecific benzodiazepine competitive antagonist, is only appropriate in the setting of a clinical benzodiazepine exposure (e.g. procedural sedation) associated with significant CNS and/or respiratory depression. It does not consistently reverse respiratory depression. The empiric use of flumazenil to treat respiratory and/or CNS depression following overdose of an unknown agent is not recommended because it may worsen the effects of other drugs (e.g. precipitate seizures with cyclic antidepressants). Flumazenil should not be administered to patients with possible chronic benzodiazepine use because there is a high risk of inducing withdrawal symptoms (agitation and seizures) which can be life-threatening.

DISPOSITION

Most patients with suspected sedative-hypnotic intoxication should be admitted for monitoring of respiratory and neurological status. Barbiturate and benzodiazepines may require prolonged hospitalization due to prolonged duration of effect.

Patients with uncomplicated ethanol ingestion can usually be observed and discharged after observation in an ED setting. GHB and rohypnol also have short durations of action and can typically be managed in the emergency department.

APPENDIX: SEDATIVE-HYPNOTIC TOXIDROME

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET
*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size					

SEROTONERGIC AGENTS

INTRODUCTION (MARYANN MANSOUR, 7/2017)
Serotonin syndrome is a potentially life-threatening increase in serotonergic activity in the central nervous system. Serotonin syndrome is classically defined as a triad of: mental status changes, autonomic instability and neuromuscular changes. However, there are a broad spectrum of signs and symptoms that can range from benign to lethal. Children and adolescents are at risk of intentional or accidental exposures which can lead to serotonin syndrome.

The use of Selective Serotonin Reuptake Inhibitors (SSRI's) and Serotonin Norepinephrine Reuptake Inhibitors (SNRI's) for depression and mood and behavior disorders has increased over the past twenty years as has the incidence of serotonin syndrome. Many other agents have serotonergic activity and administration of two medications with serotonergic activity is often a cause of serotonin syndrome.

SEROTONERGIC MEDICATIONS	
Analgesics	Meperidine, Tramadol, Methadone, Fentanyl, Cyclobenzaprine
Anti-Depressants	SSRI, SNRI, MAOI, Lithium, Tricyclic antidepressants
Anti-Emetics	Metoclopramide, Ondansetron
Anti-Epileptics	Valproate, Carbamazepine
Anti-Migraines	Triptans
Anti-Parkinson's	Selegiline
Anti-Psychotics	Trazadone, Buspirone
Drugs of abuse	Cocaine, MDMA, Methamphetamine, Dextromethorphan
Others	Linezolid, Methylene blue

PHARMACOLOGY
In the central nervous system serotonin modulates behavior, attention and thermoregulation. In the peripheral nervous system, over 90% of the body's serotonin can be found in the enterochromaffin cells of the gastrointestinal (GI) tract which regulates GI motility, vasoconstriction, uterine contraction and bronchoconstriction. Serotonin also promotes platelet regulation. Serotonin syndrome does not develop organically. Drug administration is needed to increase serotonin concentrations.

MECHANISM	MEDICATIONS/DRUGS
Metabolic serotonin precursor	L-Tryptophan
Inhibit serotonin metabolism	Mono-amine oxidase inhibitors (MAOI)
Increase serotonin release	Methylenedioxy-methamphetamine (MDMA), Amphetamines, Lithium
Inhibit serotonin reuptake	Cocaine, Dextromethorphan, Meperidine, SSRIs, SNRIs, Tricyclic antidepressants, Trazodone, Venlafaxine
Serotonin receptor agonists	Buspirone, LSD
Dopamine agonists	L-Dopa

CLINICAL MANIFESTATIONS

Most cases will present within 24 hours and usually within 6 hours, of a dose an ingestion or drug administration. A detailed history of prescription drugs, over the counter drugs, illicit drugs, dietary supplements, dose changes or medication scheduling changes should be obtained. Toxicity is often a result of administering a second medication with serotonergic properties to a patient already taking a serotonergic medication. In the Libby Zion case (1984), which lead to regulation of resident duty hours in New York State, Meperidine was given to a patient receiving a monoamine oxidase inhibitor.

Patients will exhibit cognitive-behavioral, neuromuscular and autonomic symptoms. The Hunter Criteria is currently the most specific diagnostic criteria for diagnosing serotonin syndrome.

SIGNS AND SYMPTOMS OF SEROTONIN SYNDROME		
COGNITIVE-BEHAVIORAL	NEUROMUSCULAR	AUTONOMIC
Agitation	Ataxia	Abdominal cramps
Anxiety	Babinski sign	Diaphoresis
Coma/Unresponsiveness	Chills	Diarrhea
Confusion	Hyperreflexia	Dilated pupils/Mydriasis
Lethargy	Muscle rigidity/hypertonia	Flushed skin
Seizures	Myoclonus	Hypertension
	Nystagmus	Hyperthermia
	Tremor	Hypotension
		Non-reactive pupils
		Salivation
		Sinus tachycardia
		Tachypnea

HUNTER SEROTONIN TOXICITY CRITERIA*	
At least one of the following in the presence of a serotonergic agent	
1	Spontaneous Clonus
2	Inducible Clonus AND [Agitation OR Diaphoresis]
3	Ocular Clonus AND [Agitation OR Diaphoresis]
4	Tremor AND Hyperreflexia
5	Hypertonic AND [Temperature > 38 C OR Inducible Clonus]
*Dunkley EJ et al., Quarterly Med J 2003 (PubMed ID: 12925718)	

DIFFERENTIAL DIAGNOSIS

It is essential to exclude other toxins that mimic serotonin syndrome. The other hyperpyrexia syndromes, neuroleptic malignant syndrome and malignant hyperthermia, are most similar to serotonin syndrome in that neuromuscular symptoms are also present. Serotonin syndrome can also present similarly to the sympathomimetic and anticholinergic toxidromes as well as CNS infection. In general, serotonin syndrome can be differentiated from other causes of agitated delirium such as in CNS infection and sympathomimetic toxicity by presence of neuromuscular activity.

DIFFERENTIAL DIAGNOSIS	
Neuroleptic Malignant Syndrome (Toxicology)	Sedative-Hypnotic withdrawal (Toxicology)
Malignant Hyperthermia (Toxicology)	Meningitis Encephalitis (Infections)
Anticholinergic Toxidrome (Toxicology)	Thyrotoxicosis (Endocrine)
Sympathomimetic Toxidrome (Toxicology)	Heat Stroke (Environmental)

DIAGNOSTIC TESTING

Serotonin syndrome is a clinical diagnosis. Serotonin levels do not correlate with clinical findings and there are no confirmatory laboratory tests. Laboratory testing should be geared toward potential complications of serotonin syndrome. Those with intentional overdose should be screened for salicylates and acetaminophen. An EKG should be obtained.

COMPLICATION	TESTING
Disseminated intravascular coagulation	Platelets, PT, PTT, fibrin split products
Rhabdomyolysis	CPK, UA, urine for myoglobin
Metabolic acidosis	BMP, ABG/VBG
Renal failure	BMP, UA
Acute respiratory distress syndrome	ABG, Chest XRAY

MANAGEMENT

Symptoms of serotonin syndrome usually resolve within 24 hours. The mainstay of treatment is discontinuation of the offending agents and supportive care. Charcoal may be considered in acute ingestions. Consultation with a toxicologist is essential (National Poison Center: (800) 222-1222)).

AUTONOMIC INSTABILITY: Autonomic instability can be difficult to treat and severe cases may exhibit dramatic changes in their blood pressure. Hypertension and tachycardia should be treated with short acting agents. Hypotension due to MAOI overdose should be treated with direct acting agents such as Epinephrine and Phenylephrine. Dopamine should not be used because it is broken down into epinephrine and norepinephrine which may lead to an exaggerated hemodynamic response. Propranolol, a 5-HT1a antagonist, has a long duration of action and may cause hypotension.

HYPERTHERMIA: Treat hyperthermia aggressively. Antipyretics are ineffective. Cooling blankets, ice packs and fans should be used. In cases of severe hyperthermia, the patient should be sedated, paralyzed and intubated to eliminate excessive muscle activity.

SEIZURES, AGITATION AND MUSCLE RIGIDITY: Seizures and agitations may be treated with benzodiazepines. Severe cases of serotonin syndrome may be treated with Cyproheptadine, a serotonin antagonist. It is only available in oral form and may be crushed and given through an orogastric or nasogastric tube. Dosing in children is 0.25 mg/kg/day divided every 6 hours. Dantrolene is ineffective and Bromocriptine may worsen serotonergic signs. Treat rhabdomyolysis with intravenous fluids. See: PEM Guide: Endocrine-Metabolic: Rhabdomyolysis

CARDIAC TOXICITY: Citalopram (Celexa) has the greatest potential for serious toxicity compared to other SSRI’s. Larger doses have the potential to cause serious cardiotoxicity. QT prolongation, QRS widening and torsades de pointes have been reported. There is a dose-dependent effect on QT prolongation which may be related to citalopram’s cardiotoxic metabolite didemethylcitalopram (DDCT). The FDA changed the dosing guidelines in 2012 with maximum daily dose of 40 mg and 20 mg in patients with established hepatic impairment. Citalopram is contraindicated in patients with QT prolongation or congenital QT abnormalities.

Escitalopram (Lexapro) is a racemic mixture of Citalopram and mimics citalopram's ability to cause serious serotonin syndrome and QTc interval prolongation. However, Escitalopram appears to have greater serotonergic toxicity and less cardiac toxicity than Citalopram.

EKG monitoring is crucial in patients with Citalopram and Escitalopram ingestion. Consider intravenous sodium bicarbonate or magnesium for QT prolongation.

MONITORING CARDIOTOXICITY: CITALOPRAM AND ESCITALOPRAM
EKG's should be repeated 1 hour and 4-6 hours post ingestion
Patients should remain on cardiac monitoring during observation period
Patients with signs of QTc or QRS prolongation, an increasing QTc interval compared to the initial ECG, or experience a dysrhythmia should be admitted for cardiac monitoring
Patients with massive ingestions (doses > 150 times the daily dose) are at greatest risk for toxicity and should be admitted for 24 cardiac monitoring
Asymptomatic patients with no EKG changes may safely be referred to psychiatry after a 4-6 hours observation period.

DISPOSITION

Moderate and severe cases of serotonin syndrome should be admitted to the intensive care unit for cardiac monitoring. Mild cases should be observed for 4-6 hours for resolution of symptoms before they are discharged to home with close follow-up. Psychiatry should be consulted for intentional ingestions.

STIMULANTS

INTRODUCTION (ERIC WEINBERG, M.D., 7/2016)
Substance use among adolescents and young adults is a significant cause of morbidity and mortality. Adolescents use many drugs including ethanol, marijuana, cocaine, methamphetamine, hallucinogens, inhalants, and prescription medications.

Cocaine, amphetamine, and amphetamine derived compounds are the most commonly used stimulants. In 2003, 9% of students reported having used cocaine in their lifetime. Over the last several years, cocaine use appears to be decreasing while methamphetamine use is rising dramatically throughout the US. This PEM Guide will focus on the acute effects of cocaine, 3,4-Methylenedioxymethamphetamine (MDMA) and methamphetamine.

All stimulants have sympathomimetic effects. These effects are indirect. The have no direct effect at adrenergic receptors but instead increase the amount neurotransmitters (Epinephrine, Norepinephrine, Dopamine and Serotonin) by increasing their release and by decreasing their reuptake. Additional effects include cardiac sodium channel blockade, serotonergic effects and an increase in central nervous system excitatory amino acids (Glutamate, Aspartate). Blockade of fast sodium channels slows conduction in axons (anesthesia) and in myocardial tissue (arrhythmias).

COCAINE
Cocaine is a short acting stimulant with local anesthetic properties. It is extracted from the leaves of the *Erythroxylon coca* plant. he desired effects are related to an increase in serotonin and include: euphoria, arousal, vigilance, alertness and self-confidence.

Cocaine can be insufflated (snorted), smoked, or injected. Crack is a purified alkaloid form of cocaine which vaporizes instead of burning, allowing it to be smoked. “Free-basing” describes the technique of heating a cocaine solution until it vaporizes, and then inhaling the fumes. When smoked or used intravenously, cocaine effects begin almost immediately and peak within several minutes. With nasal use, vasoconstriction slows absorption and effects begin in a few minutes and peak after 30 minutes.

METHYLENEDIOXYMETHAMPHETAMINE (MDMA)
MDMA is an amphetamine derivative commonly known as “Ecstasy” or “Molly” that is taken orally. It is a popular drug that is commonly used at clubs, raves, and concerts. The desired effects are: euphoria, wakefulness, empathy, disinhibition and sexual arousal. The peak effect is approximately 2 hours and lasts 4-6 hours. Minor adverse events may include: agitation, nausea, bruxism, diaphoresis and palpitations. MDMA is structural similar to do both amphetamine and serotonin.

AMPHETAMINE/METHAMPHETAMINE
Alpha-methyl-phenylethylamine (Amphetamine) and its derivatives are generically referred to as Amphetamines. The primary medical indication is for treatment of ADHD (e.g. methylphenidate). Methamphetamine (AKA crystal meth) has one more methyl group than amphetamine and can be easily synthesized from over the counter cold medications. It can be inhaled, ingested, injected intravenously and intramuscularly or applied to any mucosal surface. Duration of action can be up to 24 hours.

CLINICAL MANIFESTATIONS
Sympathomimetic symptoms include psychomotor agitation, hypertension and tachycardia and hyperthermia. The sympathomimetic toxidrome can be thought of a general ‘UP” status (increased mental status (agitation), vital signs (hypertension, tachycardia, hyperthermia) and pupils (mydriasis) and “WET” (diaphoresis). The differential diagnosis is extensive and includes both medical and toxin etiologies (see table below).

Serotonergic excess is manifested as hyponatremia and serotonin syndrome: altered mental status, autonomic dysfunction and abnormal neuromuscular activity. Hyponatremia is a result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and excess free water intake. Hyponatremia occurs in the setting of normovolemia or hypervolemia and not as a result of dehydration.

COMPARISON

Amphetamines are less likely to cause seizures, dysrhythmias and myocardial infarction when compared to cocaine but are more likely to cause psychosis including visual and auditory hallucinations. Methamphetamine causes more central nervous system effects than amphetamine. MDMA is a more potent stimulator or serotonin release than amphetamine

MAJOR COMPLICATIONS	
Metabolic	Hyperthermia: disseminated intravascular coagulation, rhabdomyolysis
	Hyponatremia: seizure, cerebral edema, herniation
	Hyperkalemia, hypocalcemia due to rhabdomyolysis
Neurologic	Altered mental status: agitation, anxiety, delirium, coma Increased motor activity: hyperthermia, rhabdomyolysis Intracranial hemorrhage, ischemic stroke, seizure
Cardiac	Hypertensive emergency, myocardial infarction, aortic dissection Arrhythmias, wide-complex tachycardia, Torsade's, prolonged QT
Gastro-intestinal	Hepatic necrosis: jaundice, vomiting, abdominal pain, Increased liver transaminases and PT/PTT
Musculo-skeletal	Rhabdomyolysis: renal failure, compartment syndrome, disseminated intravascular coagulation (DIC), hyperkalemia and hypocalcemia
Respiratory	Angioedema, bronchospasm: Due to inhalation of hot fumes Pneumothorax/mediastinum/pericardium: valsalva against a closed glottis in an attempt to avoid exhaling the drug
Gastro-intestinal	Perforated ulcers, ischemic colitis and intestinal infarction Body packing can result in intestinal obstruction
Ophtho	Closed angle glaucoma due to mydriasis Vision loss: retinal vessel vasospasm

DIAGNOSIS

The diagnosis is made by a history of ingestion or based on the characteristic findings of sympathomimetic and/or serotonin excess. A core temperature should be obtained.

A urine toxicology screen is not generally recommended. Both false negative and false positives occur. For example, metabolites may be present for a couple of days in the urine but may not indicate that the drug was taken acutely. A positive test also does not exclude the presence of co-ingestants or concomitant trauma. Testing may be helpful in suspected child abuse or neglect.

DIAGNOSTIC TESTING
Bedside glucose
Electrolytes: particularly sodium, serum osmolality, lactate
Creatine phosphokinase (CPK)
Coagulation profile
Liver function tests
Acetaminophen and salicylate levels
Troponin
Beta HCG in women of child bearing age
12 lead EKG: evidence of ischemia, arrhythmia, hyperkalemia
Chest XRAY: chest pain
Abdominal XRAY: body packers, body stuffers, free air from perforation
Consider a head CT, lumbar puncture
Urine drug screening generally not beneficial: false positives and false negatives

DIFFERENTIAL DIAGNOSIS
TOXINS
Sympathomimetics: Cocaine, amphetamine, methamphetamine, phencyclidine
Anticholinergics: Flushed, dry and warm skin rather than diaphoretic
Hyperpyrexia syndromes: serotonin syndrome, neuroleptic malignant syndrome, malignant hyperthermia – high fever with increased motor activity (tremor, clonus)
Psychiatric medications: tricyclic, monoamine oxidase inhibitors, neuroleptics, Lithium
Others: Salicylates, withdrawal from alcohol or sedative hypnotics
MEDICAL
Metabolic: Hypoglycemia, electrolyte abnormalities
Respiratory: Hypoxia, pneumothorax, pulmonary embolism
Endocrine: Hyperthyroid crisis, pheochromocytoma
Environmental: Heat related illness (exertional/nonexertional), scorpion envenomation
Infections: Sepsis, meningitis, encephalitis
CNS: Intracranial hemorrhage: subarachnoid hemorrhage, seizures
Cardiac: myocardial ischemia, aortic dissection

MANAGEMENT

Management decisions should be made in consultation with the regional poison control center. The national number for the American Association of Poison control centers is
1-800-222-1222. The NYC Poison Control Center can be reached at 212-340-4494.
The possibility of co-ingestants such as nicotine, alcohol and others should be considered.

GASTRIC ELIMINATION: Gastric elimination is generally not effective. Activated charcoal 1 gram/kg can be administered if the drug was taken orally, it has been within one hour of ingestion and the patients has a normal mental status and can protect their airway.

BENZODIAZEPINES: Benzodiazepines are the most effective treatment for many of the clinical manifestations of stimulant toxicity including: psychomotor agitation, chest pain, hypertension, hyperthermia and seizures. Benzodiazepines inhibit the release of neurotransmitters which may be more effective than peripheral antagonism of adrenergic effects.

Midazolam and Diazepam have quick onsets while Lorazepam has a slower onset.
The duration of action is longest with Lorazepam, shorter with Diazepam and shortest for Midazolam. A quick onset benzodiazepine (Midazolam, Diazepam) may be used initially. A longer acting formulation (Diazepam, Lorazepam) may be required for amphetamine toxicity which can last up to 24 hours and is less likely to be required for cocaine toxicity which lasts for only a few hours.

RHABDOMYOLYSIS: Rhabdomyolysis is a common complication of stimulant use and may require aggressive intravenous hydration, urinary alkalinization, and rarely hemodialysis.

HYPERTHERMIA: Hyperthermia is a poor prognostic factor and requires aggressive cooling.

CARDIAC: Chest pain is short-lived and benign, but about 5% of patients will have an acute myocardial infarction. This can occur in the absence of underlying heart disease, and in adolescence. The management of myocardial ischemia may include the use of benzodiazepines, aspirin, nitroglycerin, morphine and phentolamine. The differential diagnosis of chest pain includes aortic dissection and pneumothorax. For hypertension refractory to benzodiazepines a direct vasodilator (e.g. Nitroprusside. Nitroglycerine) or an alpha adrenergic antagonist (e.g. Phentolamine) is recommended.

It is generally recommended to avoid the use of beta blockers (e.g. Propranolol) and mixed beta and alpha blockers (e.g. Labetalol) for hypertension and chest pain. The theory is that blocking the beta 2 effect on vascular smooth muscle relaxation will lead to unopposed alpha stimulation resulting in worsening vasoconstriction with hypertension and coronary vasospasm. Wide complex tachycardias may respond to the use of bicarbonate.

DISPOSITION

Patients with mild symptoms on presentation who do not have evidence of end organ damage and whose symptoms resolve with a period of observation may be safely discharged.

Patients with chest pain that resolves with therapy should be observed for 8-12 hours and have serial troponin and EKG. Those with EKGs suggestive or ischemia, positive cardiac enzymes, congestive heart failure, an arrhythmia other than sinus tachycardia or persistent chest pain require admission.

Patients with hyperthermia, rhabdomyolysis and other signs of end organ damage require admission to a monitored setting. Poor prognostic factors include: coma, shock, renal failure, metabolic acidosis and temperature > 39 C.

APPENDIX: MANAGEMENT OF STIMULANT COMPLICATIONS

MANAGEMENT SUMMARY	
Airway	Succinylcholine (SUC) use can increase the duration of paralysis and duration of cocaine effects. SUC may also worsen hyperkalemia from rhabdomyolysis Rocuronium recommended: non-depolarizing muscle relaxant
Psychomotor agitation	Benzodiazepines (BZD): e.g. Diazepam 0.15 mg/kg (max 5-10 mg) May require repeated and/or increased dosing Q3-5 minutes
	Minimize stimulation e.g. quiet room
	Avoid physical restraint: Can increase temperature, rhabdomyolysis
	Amphetamine: Consider Haloperidol if refractory to BZD Cocaine: Haloperidol contraindicated, consider Propofol Haldol increases QT, decreases seizure threshold, heat dissipation
Hyperthermia	Severe: Ice water immersion
	Moderate: Cooling blankets, evaporative cooling with mist and fans
	Antipyretics likely ineffective. Fever is a result of muscle activity
	If refractory to therapy consider intubation and paralysis
Seizures	Benzodiazepines: e.g. Diazepam 0.15 mg/kg (max 5-10 mg) Avoid Phenytoin (causes sodium channel blockade)
Cardiac: Hypertension	Typically responds to benzodiazepines Refractory hypertension: Nitroprusside, Nitroglycerine, Phentolamine Maximum decrease of less than 25% of initial systolic BP Avoid beta blockers and mixed beta and alpha blockers: possible unopposed alpha adrenergic activity
Cardiac: Hypotension	Massive doses of cocaine can cause hypotension related to negative inotropy, arrhythmia and myocardial infarction Intravenous crystalloid boluses PRN Direct vasopressor. Norepinephrine or Epinephrine if fluid refractory Avoid Dopamine, indirect, requires uptake and conversion to NE
Cardiac: Chest Pain	Benzodiazepines, oxygen, nitroglycerine, aspirin, morphine Avoid beta blockers, possible unopposed alpha adrenergic activity
Cardiac: Arrhythmia	Wide complex tachycardia: Sodium Bicarbonate 1-2 meg/kg IV push, Lidocaine if refractory (type 1a,1c anti-arrhythmics contraindicated Atrial or narrow complex re-entrant tachycardia: Diltiazem
Rhabdomyolysis	Benzodiazepines for control of psychomotor agitation Urinary alkalinization with Sodium Bicarbonate 1-2 meg/kg IV push if metabolic acidosis with pH < 7.1 to prevent renal failure. Hemodialysis
Hyponatremia	Asymptomatic, mild: Fluid restriction alone Avoid unnecessary intravenous fluids
	Severe (e.g. seizures typically with Na < 120 meq/L) Hypertonic saline (3% = 513 meq/L) 100 ml over 10 minutes If symptoms persist may repeat 1-2 times Q10 minutes
Serotonin Syndrome	Benzodiazepines: e.g. Lorazepam 0.1 mg/kg (max 2 mg) Consider Cyproheptadine 12 mg PO then 2 mg Q2H or 4-8 mg Q6H

APPENDIX: STIMULANT/SYMPATHOMIMETIC TOXIDROME

Toxidromes are constellations of signs and symptoms (mental status, vital signs, examination findings) that can aid in identifying a class of agent. Two questions can be used to summarize the toxidromes; Up or Down? and Wet or Dry or Normal? Up or Down refer to mental status, vital signs and pupil size. For example, the sympathomimetic toxidrome is up (agitated, increased vital signs and mydriasis) and wet (diaphoresis).

TOXIDROMES						
		Sympathomimetic[1]	Anticholinergics	Opioids/Opiates	Sedative-Hypnotics	Cholinergics
Examples		Cocaine Amphetamines	Antihistamines Cyclic Antidepressants Antipsychotics	Heroin Morphine	Benzodiazepines Barbiturates Ethanol	Organophosphate Nerve Agents Some mushrooms
Status*		UP (↑)	UP (↑)	Down (↓)	Down (↓)	Down (↓)
Mental Status		Restless Agitated, anxious Paranoia Insomnia, Mania Hallucinations Seizure	Psychosis (Mad as a Hatter) Delirium Coma Seizure Chorea	Sedation Confusion Coma	Sedation Confusion Delirium Ataxia Coma	Confusion Drowsiness Coma Seizure
Pupils		Mydriasis	Mydriasis (Blind as a bat)	Miosis	Mydriasis or Miosis Blurred vision Nystagmus	Miosis
Vital Signs	HR BP RR T	Tachycardia Hypertension Tachypnea Hyperthermia	Tachycardia Hypertension Hyperthermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia Hypotension Bradypnea, Apnea Hypothermia	Bradycardia ↑ early → ↓ late Tachypnea Hypothermia
Physical Exam		Tremor Diaphoresis Warm Skin Hyperactive bowel sounds Hyperreflexia	Dry Skin (Dry as a bone Flushed skin Red as a beet) Urinary retention (Full as a flask) Hypoactive bowel sounds		Hypoactive bowel sounds Hyporeflexia	Salivation Lacrimation Urination Defecation Emesis Bronchorrhea Muscle fasciculation Diaphoresis
Treatment		Benzodiazepine	Benzodiazepine Physostigmine (not for TCA)	Naloxone	Supportive	Atropine Pralidoxime
1. Salicylates, alcohol withdrawal and sedative-hypnotic withdrawal can mimic the sympathomimetic toxidrome						

TOXIDROMES MADE SIMPLE					
	Sympathomimetic	Anticholinergics	Opioids/ Opiates	Sedative-Hypnotics	Cholinergics
UP/DOWN	UP	UP	DOWN	DOWN	DOWN
WET/DRY NORMAL	WET	DRY	NORMAL	NORMAL	WET
*UP/DOWN: Overall increase (UP) or decrease (DOWN) in: Mental status, Vital signs and Pupil size					

TOXIC ALCOHOLS

INTRODUCTION (SEEMA AWATRAMANI, M.D., 3/2011)
The toxic alcohols include methanol, ethylene glycol and isopropanol. Most poisonings are caused by intentional ingestion by those substituting these agents for ethanol or in an attempt at suicide. Accidental ingestions occur in children particularly when the alcohols are transferred from their original containers. Inhalation (methanol) and topical exposure rarely cause toxicity. Methanol is commonly found in products such as: gasoline antifreeze, windshield wiper fluids, homemade liquor, solid fuels (e.g. Sterno) and denaturants. Ethylene glycol is found in automotive coolant and antifreeze, solvents and de-icers. (See also PEM Guide: Toxicology: Sedative-Hypnotic for a discussion of Ethanol intoxication)

Methanol and ethylene glycol cause toxicity when metabolized by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) to toxic, organic acid metabolites. Methanol is metabolized to formic acid and ethylene glycol to glycolic acid, glyoxylic acid and oxalic acid.

$$\mathit{Methanol} \xrightarrow{ADH} \mathit{Formaldehyde} \xrightarrow{ALDH} \mathit{FormicAcid} \xrightarrow{folate} CO_2 + H_2O$$

$$\mathit{Ethylene\ glycol} \xrightarrow{ADH} \mathit{Glycoaldehyde} \xrightarrow{ALDH} \mathit{Glycolic\ acid} \xrightarrow{LDH} \mathit{Glyoxylic\ acid} \longrightarrow \mathit{Oxalic\ acid}$$

METHANOL AND ETHYLENE GLYCOL

CLINICAL MANIFESTATIONS
The onset of symptoms may be delayed as methanol and ethylene glycol are metabolized to their toxic forms. Eventually an anion gap, metabolic acidosis develops. Acidemia further increases the ability of the toxic metabolites to penetrate cells, hastening clinical deterioration. Co-ingestion of ethanol may delay metabolism and onset of symptoms. Dangerous concentrations of toxic alcohols are greater than 25 mg/dl. Ingestions off greater than gram/kg may be fatal unless treated.

SIGNS AND SYMPTOMS	
METHANOL	ETHYLENE GLYCOL
METABOLIC: Tachypnea (2° metabolic acidosis)	METABOLIC: Tachypnea (2° metabolic acidosis), Tetany, Dysrhythmias (↓ Ca++ due to calcium oxalate formation)
CNS: Altered mental status/inebriation Ischemia/hemorrhage to the basal ganglia	CNS: Altered mental status/inebriation Cranial nerve deficits
VISUAL CHANGES: Central scotomata, blindness, Optic disc hyperemia, edema	RENAL CHANGES: Flank pain, Renal tubular damage from oxalic acid, Oliguria and acute renal failure

DIAGNOSIS

Ideally serum levels of the toxic alcohol should be obtained. Unfortunately, they are often not readily available. In the absence of serum levels, a number of other tests have been suggested though these have been shown to have poor sensitivity and specificity.

LABORATORY EVALUATION	
ABG, Lactate*	*Lactate levels are frequently falsely elevated in blood gas analysis. Even when elevated on serum samples the rise in lactate is not sufficient to account for the degree of acidosis.
Acetaminophen, Salicylate levels	
Amylase, Lipase (pancreatitis) (M)	
Electrocardiogram (↑QT due to ↓ Ca++) (EG)	
Electrolytes, anion gap, Ca++	
Ethanol level	
Finger stick glucose	**Fluorescein is added to antifreeze to help detect leaks
Serum methanol, ethylene glycol, isopropanol levels	
Serum Osmolality	
Urinalysis (oxalate crystals) (EG)	
Urine pregnancy test	
Urine fluorescence (Woods Lamp)**	

ANION GAP METABOLIC ACIDOSIS				
M	Methanol	P	Paraldehyde	An anion gap metabolic acidosis may not be present initially. As the toxic alcohol is metabolized to its toxic metabolic acid the anion gap increases as the osmolar gap decreases.
U	Uremia	I	Iron, Isoniazid	
D	DKA	L	Lactic acid	
		E	Ethylene Glycol	
		S	Salicylate	
Anion Gap = Na – (Cl + HCO3), Normal anion gap is 8-12				

OSMOLAR GAP		
Ethanol	Paraldehyde	Osmol Gap = Measured – Calculated osmols. Normal Osmolar Gap = 10-15 mmol/L H_20 Calculated osmols = {(2Na)+(GL/18)+(BUN/2.8)+(Etoh/4.6)} The osmol gap may be elevated early but decreases as the toxic alcohol is metabolized. A normal osmol gap does not rule out toxic alcohol ingestion
Isopropanol	Ethyl ether	
Methanol	Mannitol	
Ethylene Glycol	Renal Failure	
Acetone	Lactic Acidosis	
Trichloroethane	Alcoholic Ketoacidosis	
Hyperproteinemia	Diabetic Ketoacidosis	
Hyperlipidemia	Sepsis	

MANAGEMENT

MANAGEMENT OVERVIEW	
Assess Airway, Breathing and Circulation, Cardiac monitoring, Bedside glucose	
Consult poison control center: 212-POISONS or (800) 222-1222	
IV access with IV fluids	
	Enhance toxin elimination
	Decrease crystal deposition in the kidneys (Ethylene Glycol)
Ipecac and activated charcoal are not recommended due to:	
	Aspiration risk from CNS depression
	Alcohols are rapidly absorbed by gut and have limited charcoal binding
Nasogastric lavage may have utility within 30 minutes of ingestion	
Fomepizole: continued until serum level < 25 mg/dl	
	Likely history of toxic alcohol ingestion
	Unexplained anion gap metabolic acidosis
	Osmolar gap > 10
	Urinary Oxalate crystals (Ethylene Glycol)
	Ethylene glycol or methanol concentration > 25 mg/dl
Adjunctive therapy	
	Severe metabolic acidosis: $NaCO_3$
	Ethylene Glycol: Pyridoxine, Thiamine
	Methanol: Folate, Leucovorin
Hemodialysis	

FOMEPIZOLE (4 METHYL PYRAZOLE): Fomepizole has a high affinity for and competitively inhibits alcohol dehydrogenase. Ethylene glycol and Methanol are thus not metabolized to their respective toxic metabolic acid. It is generally preferred to ethanol because of its ease of dosing and administration, and low side-effect profile. It is costly ($1000/gm) and is unavailable at some institutions.

FOMEPIZOLE DOSING	
LOADING DOSE	15 mg/kg IV over 30 min
MAINTENANCE DOSE	10 mg/kg IV every 12 hours
	15 mg/kg IV after 48hrs

ETHANOL: Like Fomepizole, Ethanol also competitively inhibits alcohol dehydrogenase. If patients present with elevated ethanol levels and acidosis, it is unlikely that toxic alcohols are the cause of the acidosis. Treatment with ethanol aims to achieve concentrations of approximately 100 mg/dl. Ethanol levels and electrolytes need to be frequently monitored to confirm therapeutic range. Ethanol side effects include: altered mental status, loss of protective airway reflexes, hypoglycemia, phlebitis and hypotension. It is rarely used currently.

HEMODIALYSIS
Hemodialysis is used with Fomepizole or Ethanol. It enhances the removal of the parent alcohols and their metabolites and corrects acid-base abnormalities. Hemodialysis also removes Fomepizole and Ethanol. Therefore, dosing needs to be increased in the setting of dialysis. Indications for hemodialysis are controversial.

HEMODIALYSIS INDICATIONS
Refractory metabolic acidosis
Visual Complications (Methanol)
Renal Complications (Ethylene Glycol)
Persistent electrolyte abnormalities

ADJUNCTIVE THERAPY
These therapies are not an alternative to Fomepizole or Ethanol therapy. While they may have theoretical benefit, they have not been proven to effect clinical outcomes.

THERAPY ADJUNCTS

ADJUNCT	INDICATION	MECHANISM
Na bicarbonate	Severe acidosis	Enhanced elimination and decreases cell penetration of toxic metabolites. Monitor potassium
Folate	Methanol	Enhances clearance of formic acid.
Leucovorin	Methanol	Enhances clearance of formic acid.
Pyridoxine	Ethylene glycol	Enhances metabolism of ethylene glycol to glycine
Thiamine	Ethylene glycol	Enhances metabolism of ethylene glycol to alpha-hydroxy-beta ketoadipate.

ISOPROPANOL

INTRODUCTION
Unlike methanol and ethylene glycol, isopropanol (isopropyl alcohol) does not cause an anion gap metabolic acidosis. Isopropanol is metabolized by alcohol dehydrogenase to acetone. Acetone is a ketone, but not a ketoacid. Therefore, ketosis develops without acidosis. It can be found in rubbing alcohol, solvents, lacquer thinner and De-icers.

Isopropanol is a CNS depressant, similar to ethanol. Alcohols with higher molecular weights and longer carbon chains are more sedating, therefore isopropanol has an increased risk of CNS depression and coma compared to ethanol at similar concentrations. Like ethanol, isopropanol is rapidly absorbed after ingestion. In infants, dermal exposure has been noted to cause toxicity. Clinical effects usually occur 1-2 hours after exposure, earlier when compared to methanol and ethylene glycol. The elimination half-life is 2.5-8 hours.

CLINICAL MANIFESTATIONS
CNS depression can manifest in varying degrees of severity, from inebriation to coma. Steady improvement occurs with metabolism. With large ingestions, nausea, vomiting, hematemesis, and gastritis may develop. The accumulation of acetone can cause fruity-smelling breath. In rare instances, pulmonary edema, hypotension, and hemorrhagic trachea-bronchitis may be seen.

DIAGNOSIS AND EVALUATION

Suspected ingestion should be evaluated in the same manner as with Ethylene glycol and Methanol. (see above). The absence of anion gap metabolic acidosis largely distinguishes isopropanol ingestion from Ethylene glycol and Methanol. As with other toxic alcohols, an elevated osmolar gap may be present. Acetone levels can also be useful. Levels above 100 mg/dl can falsely elevate serum creatinine. Acetone metabolism can lead to elevated urine and serum ketones.

MANAGEMENT

As with ethanol overdose, treatment is mainly supportive. Frequently, asymptomatic children with accidental ingestions can be observed at home if it is confirmed that the product is isopropanol alone and if the amount is less than a mouthful. As always, poison control should be consulted.

GI decontamination is rarely indicated. Nasogastric lavage only has a role if the ingestion is recent and of large quantity. Intubation is reserved for cases involving significant CNS depression, loss of airway reflexes, or aspiration risk. Supportive care with fluid replacement is generally adequate for treatment of hypotension. Isopropanol is readily dialyzable; hemodialysis can be used for hypotension refractory to fluids and vasopressors.

There is no role for ethanol or Fomepizole therapy. Since both competitively compete for alcohol dehydrogenase they will greatly slow the metabolism of isopropyl alcohol.

COMPARISON: TOXIC ALCOHOLS					
	ONSET	OSMOLAR GAP	ANION GAP METABOLIC ACIDOSIS	FOMEPIZOLE	OTHER
Methanol	LATE	YES	YES	YES	VISUAL
Ethylene Glycol	LATE	YES	YES	YES	RENAL
Isopropanol	EARLY	YES	NO	NO	KETONES

TRAUMA

16. Neurogenic Shock — Michael Mojica, MD
17. Scrotal and Penile Trauma — Alexis Pankow, MD
18. Skull Fractures — Michael Mojica, MD
19. Thoracolumbar Spine Injuries — Michael Mojica, MD
20. Trauma Primary Survey — Michael Mojica, MD

ABDOMINAL TRAUMA: OVERVIEW

INTRODUCTION (CARRIE NG, M.D., 3/2013)
Trauma is the leading cause of morbidity and mortality in children older than one year of age, and abdominal trauma is the third leading cause of death in this age group. Children are more vulnerable than adults to intraabdominal injuries (IAI) after blunt trauma because of their immature musculoskeletal system, less overlying fat, and smaller area over which the force is distributed.

Blunt abdominal trauma can occur with seemingly minor falls, direct blows to the abdomen (e.g. bicycle handlebars) or shearing forces that may cause lacerations (e.g. head-on motor vehicle collisions). The types of injuries include but are not limited to: abdominal wall contusions, solid organ injuries, pancreatic injuries, and hollow abdominal viscera injuries.

Penetrating abdominal trauma is most frequently due to gunshot and stab wounds and is less common but more lethal than blunt IAI. These injuries include burst injuries of the liver and spleen, vascular injuries, and peritoneal perforations.

Specific abdominal injuries are discussed in the PEM Guide: Abdominal Trauma: Specific Organs. An overview to the approach to abdominal trauma follows here.

PRIMARY SURVEY

The goal of the primary survey is to rapidly identify and manage life-threatening injuries. It consists of a systematic approach using the mnemonic A-B-C-D-E for:

Airway, **B**reathing, **C**irculation, **D**isability, and **E**xposure

The following discussion focuses on the primary survey of an abdominal injury. (See also PEM Guide: Trauma Primary Survey). Intra-abdominal injuries may become apparent during the primary survey in the assessment of circulation and in particular in patients who are in shock with tachycardia, poor distal perfusion or hypotension. Intra-abdominal injury may also become apparent during the exposure phase of the primary survey. A more detailed assessment of abdominal trauma will occur during the secondary survey.

CIRCULATION: Primary survey of the circulation should assess for possible external or internal hemorrhage by evaluating the blood pressure, pulses, skin perfusion and external hemorrhage. The body compensates for diminished perfusion from significant blood loss by increasing its heart rate and peripheral vascular resistance in order to maintain the systolic blood pressure within the normal range. This is particularly true in children who can maintain blood pressure until approximately 25% of blood volume is lost but then will drop their blood pressure precipitously. The goal is to identify hemorrhagic shock in the compensatory phase before the onset of hypotension. See: PEM Guide: Trauma: Hemorrhagic Shock

CIRCULATION
ASSESSMENT
Mental status
Pulse quality (central and distal), rate, and regularity
Blood pressure, pulse pressure
Skin, color, temperature, capillary refill
Heart rhythm on cardiac monitor
Sites of external hemorrhage
MANAGEMENT
IV access: If peripheral IV difficult and hemodynamically unstable place an IO
Send blood sample for type and cross
Fluid resuscitation: PRBC 10 ml/kg or Crystalloid (NS or LR) 20 ml/kg
Give type and cross matched blood available and time permits → If not available give type specific blood → If not available give O negative blood
Initiate Massive Transfusion Protocol: PRBC FFP, Platelets ± Cryoprecipitate
Consider Tranexamic acid
Control external hemorrhage by direct compression, tourniquets
Control interval hemorrhage by pelvic binder, limit pelvic stability testing

EXPOSURE: During the exposure phase of the primary survey care must be taken to examine the abdomen for external signs of trauma (e.g. seat belt sign, handle bar signs), signs of penetrating trauma, abdominal tenderness and pelvic instability. The patient should be log rolled as a unit to examine and palpate the back and vertebral column.

SECONDARY SURVEY

The secondary survey involves obtaining the patient's history, a complete physical exam, and additional diagnostic studies as indicated (laboratory and imaging).

HISTORY: The secondary survey should include a focused history using the SAMPLE mnemonic. The mechanism of injury should be explored as it may predict patterns of injury. For example, Waddell's Triad can aid in the prediction of injury in a pedestrian struck by a motor vehicle. A pedestrian is struck first on the legs (femur in child, tibia/fibula in adults) and is thrown against the hood/windshield of the car hitting their abdomen (spleen if hit on the left and liver if hit on the right). They then hit their head on the car and are thrown hitting their head a second time. A pedestrian struck who has head and lower extremity injuries should raise suspicions of an intra-abdominal injury.

S	Symptoms
A	Allergies
M	Medications
P	Past Medical History
L	Last Meal
E	Events, Environment

PHYSICAL EXAMINATION

A secondary survey includes a complete head-to-toe examination, but only findings pertinent to abdominal injury will be discussed here. Life-threatening abdominal injuries may be occult or manifest as the following exam findings.

SECONDARY SURVEY: ABDOMINAL EXAMINATION	
Vital Signs	Hemoperitoneum may manifest as hypotension and tachycardia Normal blood pressure and pulse do not exclude IAI
Inspection	Abdominal ecchymoses, bruising, seat belt mark across the abdomen
	Abdominal distention may be due to hemoperitoneum or peritonitis. Difficult to differentiate distention due to air swallowed by a crying child. Gastric decompression may facilitate exam and decrease aspiration.
Auscultate	Absence of bowel sounds in the initial examination is not predictive. Prolonged ileus (> 4 hours) may signify pathology.
Palpation	Serial abdominal examinations. Abdominal/flank/back/pelvic tenderness.

PELVIC EXAMINATION: Evaluate pelvic stability by gently compressing the iliac wings centrally in order not to displace fracture fragments or exacerbate injuries. Repeated compressions should be avoided to avoid worsening bleeding. (See PEM Guide: Trauma: Genitourinary Trauma)

DIGITAL RECTAL EXAM (DRE): Blood on the DRE may indicate perforation of bowel, blood at the urethral meatus, or a distended bladder may represent urethral injury and bladder catheterization should be avoided until a retrograde urethrogram is obtained. There is limited utility of the digital rectal examine for guaiac testing. Absent rectal sphincter tone may indicate spinal cord injury.

RADIOLOGIC EVALUATION

FAST: The FAST Exam (Focused Assessment for Sonography in Trauma) allows for visualization of free fluid in the potential spaces but does not identify specific solid organ injury. It has reported sensitivity of up to 95% for distinguishing as little as 100 ml of fluid. It can be performed serially to increase its sensitivity. The FAST exam is a “rule in” test. A positive fast can “rules in” intra-abdominal injury but a negative FAST exam cannot “rule out” intra-abdominal. The FAST examination and the patient’s hemodynamic status can be used to determine the next steps in evaluation and treatment.

FOCUSED ABDOMINAL SONOGRAPHY IN TRAUMA (FAST*)	
1	Perihepatic (right upper quadrant: Morrison’s pouch)
2	Perisplenic (left upper quadrant)
3	Pelvic (Pouch of Douglas and retrovesicular pouch)
4	Pericardial (subxiphoid cardiac view).
5	Pulmonary views for hemothorax/pneumothorax (Extended or E-FAST)
*See: PEM Guide: Procedure: Extended FAST Exam	

MANAGEMENT BASED ON FAST AND HEMODYNAMIC STABILITY		
FAST	BP, HR, PERFUSION	MANAGEMENT
Positive	Unstable	Laparotomy
Positive	Stable	CT Scan
Negative	Unstable	?DPL or Laparotomy
Negative	Stable	Serial examination or CT*
*Consider CT: high risk mechanism or unable to assess abdominal exam		

DIAGNOSTIC PERITONEAL LAVAGE (DPL): A DPL is an invasive procedure that involves an infraumbilical abdominal incision, placement of a catheter and infusion of fluid into the abdominal cavity. It is highly sensitive but poorly specific. It also limits the usefulness of subsequent abdominal exams. DPL is rarely used and has largely been supplanted by the FAST exam and abdominal/pelvic CT. One possible indication is in children requiring immediate surgery for a non-abdominal injury when an abdominal CT scan or FAST exam are unavailable.

POSITIVE DPL
>10cc blood on initial aspirate
> 100,000 RBC/ml
> 500 WBC/ml
Gram stain (+) for bacteria
Feces, bile, vegetable fibers
Alkaline phosphatase > 6 IU/L
Amylase > 175 IU/L

PLAIN RADIOGRAPHS: A chest radiograph may show rib fractures and mediastinal air and may raise suspicion for coincident intra-abdominal injury. Free air under the diaphragm strongly suggests hollow viscous perforation. Intra-abdominal contents on the chest XRAY may suggest a diaphragmatic injury. Pelvic x-rays identify fractures.

CT SCAN: CT scan with IV contrast is the preferred diagnostic test in stable patients as it allows for the detection of specific organ injury, intraperitoneal hemorrhage, evaluation of extra-abdominal structures and the retroperitoneal space.\

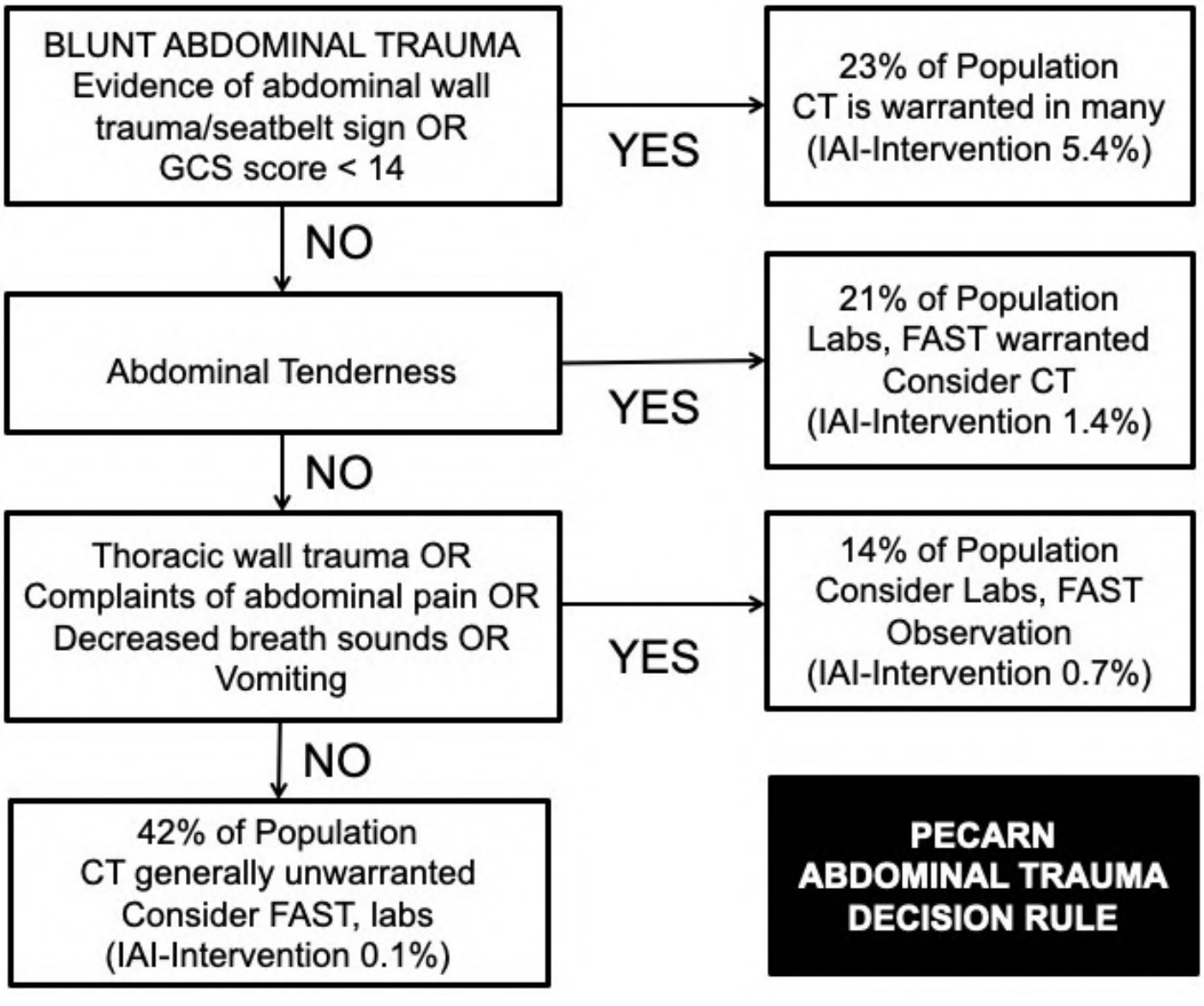
INDICATIONS FOR ABDOMINAL COMPUTED TOMOGRAPHIC SCAN
High risk mechanism of injury suggesting abdominal injury
Physical examination findings suggesting abdominal injury
Severe multisystem trauma
Significant fluid or blood requirements not explained by other injuries
Inadequate abdominal examination: Altered mental status, distracting injury
Laboratory: Hemoglobin < 10 gm/dl, UA > 50 RBC/HPF, increased AST, ALT, amylase
Positive FAST Exam in an hemodynamically stable patient
Requiring general anesthesia for another indication

LABORATORY EVALUATION

LABORATORY FINDINGS	
CBC	Initial hemoglobin and hematocrits may not reflect early blood loss. CBC establishes baseline hemoglobin and hematocrit
Type and Cross	Essential for type specific and typed and cross matched packed red blood cell transfusion (not for O (-) blood)
AST/ALT	Associated with hepatic injuries
Amylase/Lipase	Suggestive of pancreatic or hollow viscous injury
Urinalysis	Grossly bloody urine or microscopic hematuria (> 50 RBCs/HPF) suggests renal trauma
Lactate	Adequacy of perfusion

CLINICAL DECISION RULES (CDR)

In 2013, The Pediatric Emergency Care Applied Research Network (PECARN) derived a decision rule to identify pediatric patients at very low risk of intra-abdominal injury requiring intervention (Holmes, Ann Emerg Med. 2013, PubMed ID: 23375510). They identified 6 factors whose absence predicted a very low rate of intra-abdominal injury requiring intervention (Predictive value of a negative test of 99.9% 95% CI (99.7, 100%). The rule did not included laboratory tests or focused abdominal sonography for trauma as possible predictors. The rule is intended to be assistive in clinical decision making and not directive. If the rule is followed there would be a 25% reduction in the rate of CT. Unfortunately, the rate of CT could rise if all those with a positive rule were scanned. The authors provided recommendations possible management strategies based on the status of room parameters. This is a level 4 clinical decision rule. It has been derived though not yet validated



MANAGEMENT

The primary etiology of shock in the trauma patient is hypovolemic shock in in particular hemorrhagic shock from internal or external blood losses. Other causes of shock in the trauma patient include distributive (neurogenic shock), cardiogenic (myocardial contusion) and obstructive (tension pneumothorax, pericardial tamponade). The initial priorities in the management of intra-abdominal injuries is to assess hemodynamic stability, obtain intravenous access and send a type and cross in anticipation of a potential transfusion. See: PEM Guide: Trauma: Hemorrhagic Shock

HEMODYNAMICALLY STABLE: An abdominal and pelvic CT will delineate specific injuries. The majority of intra-abdominal injuries in the pediatric blunt trauma patient are managed non-operatively.

HEMODYNAMICALLY UNSTABLE: Blood should be given immediately if there is a suspicion for significant hemorrhage. Crystalloid should only be given to the hemodynamically unstable patient if blood is not immediately available. If given crystalloid should be given a 1 liter (adult) or 20 ml/kg (pediatric < 40 kg).

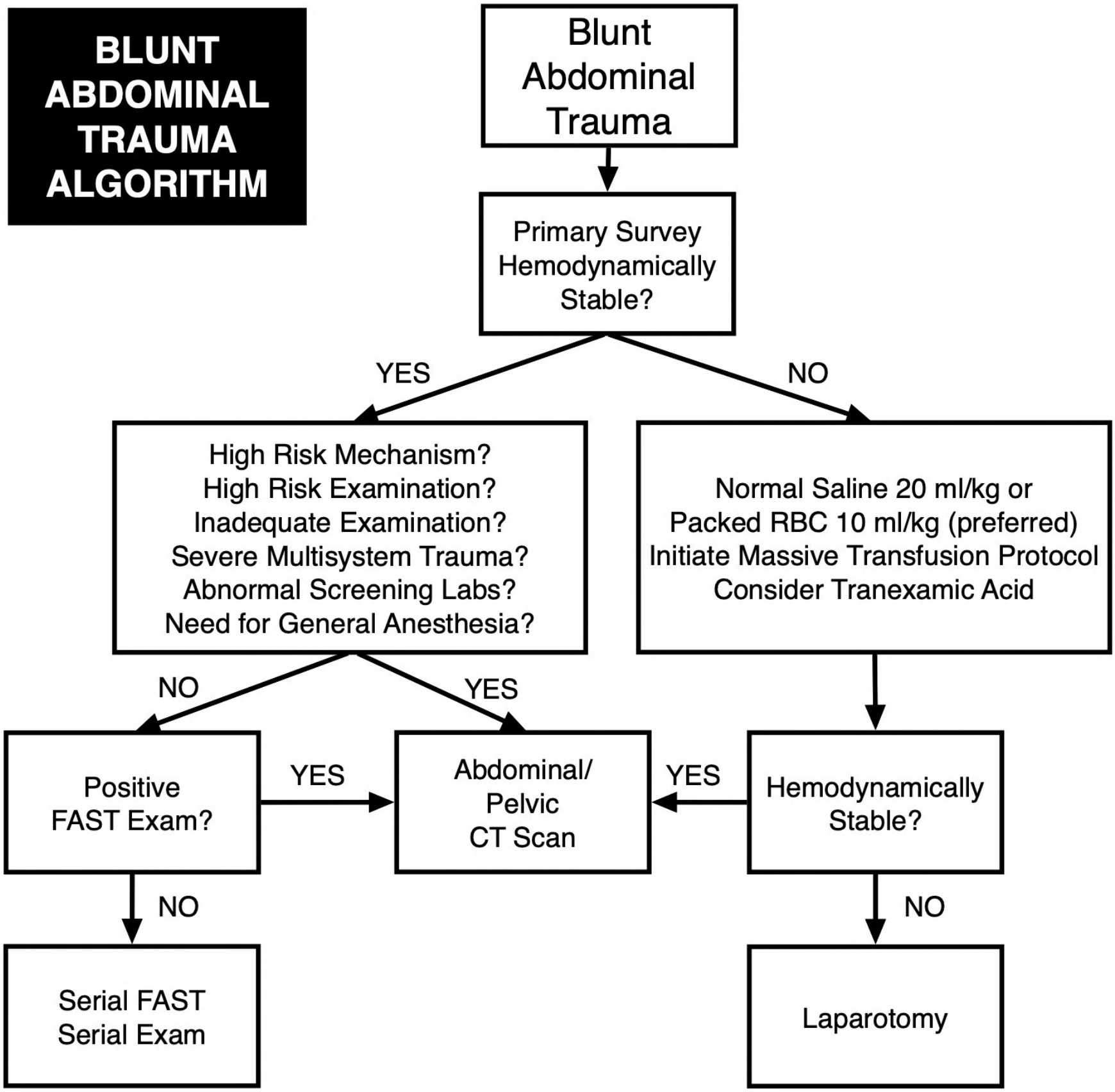
Packed RBC's are infused in preference to whole blood because whole blood needs to first be reconstituted from packed RBC's and plasma. One unit of PRBC will raise an adult's hemoglobin by 1 gm/dl or hematocrit by 3% (PRBC: 250-300 ml/unit, HCT 60%. Whole Blood: 450 ml/unit, HCT 35-40%). Pediatric blood volume is 80 ml/kg. Pediatric 10-20 ml/kg PRBC, Adult 1-2 units PRBC

Ideally, fully typed and cross-matched PRBC's are given. If time does not permit, type specific or O negative PRBC's are infused. When large volumes of blood are given a coagulopathy develops and additional blood products will be needed. Massive transfusion protocols (MTP) include platelets and fresh frozen plasma (FFP) in addition to PRBC. Some recommend a 1:1:1 ratio of PRBC, platelets and FFP.

Tranexamic acid is an antifibrinolytic that inhibits both plasminogen activation and plasmin activity, thus preventing clot break-down rather than promoting new clot formation. If a MTP is activated for trauma patients, Tranexamic acid (TXA) should be given as soon as possible and before 3 hours. It should not be started after 3 hours as the risks outweigh potentially benefits

TRANEXAMIC ACID	
Loading Dose	15 mg/kg (maximum dose 1 gram) over 10 minutes
Infusion Dose	2 mg/kg/hour (maximum dose 120 mg/hour) for 8 hours.

APPENDIX: BLUNT ABDOMINAL TRAUMA DECISION ALGORITHM



ABDOMINAL TRAUMA: SPECIFIC ORGANS

INTRODUCTION (CARRIE NG, M.D., 9/2012)
A general approach to abdominal trauma is reviewed in the PEM Guide: Abdominal Trauma: Overview. It includes a review of the primary and secondary surveys for abdominal trauma, the clinical, laboratory and imaging techniques and the urgent management. This PEM Guide will focus on the diagnosis and management of specific abdominal injuries

SOLID ORGAN INJURIES: SPLEEN	
Frequency	Most commonly injured abdominal organ
Mechanism	Includes auto-pedestrian trauma, falls, bicycle accidents
Anatomy	Highly vascular organ and has potential for morbidity and mortality if it hemorrhages into peritoneal cavity
Symptoms	Diffuse abdominal pain, with maximal tenderness in the LUQ, or L shoulder pain referred from subphrenic blood (Kehr's sign)
Diagnostic imaging	Positive FAST exam (LUQ fluid) or CT scan to identify the extent of injury
Management	Given concern for post splenectomy sepsis syndrome, non-operative treatment has largely replaced traditional treatment of splenectomy or splenorrhaphy. Non-operative management of isolated splenic injuries without blood transfusion is successful in 95% of cases.

SOLID ORGAN INJURIES: LIVER	
Frequency	Second most commonly injured, most common fatal abdominal injury
Symptoms	Diffuse abdominal tenderness secondary to hemoperitoneum with maximal tenderness in the RUQ, and occasionally right shoulder pain
Management	Non-operative management of isolated liver injuries without blood transfusion is successful in 90% of cases.

MANAGEMENT OF CHILDREN WITH ISOLATED SPLEEN OR LIVER INJURIES				
CT GRADE	I	II	III	IV
Intensive care unit days	None	None	None	1
Hospital days	2	3	4	5
Pre-discharge imaging	None	None	None	None
Post-discharge imaging	None	None	None	None
Time of restricted activity (weeks)	3	4	5	6

SOLID ORGAN INJURIES: PANCREAS	
Frequency	Most common cause of pancreatic pseudocyst in children
Anatomy	The pancreas crosses the lumbar vertebrae in the midline. A blow to the abdomen will compress the pancreas against the vertebrae
Mechanism	Injury infrequent but can occur with blunt abdominal injuries, particularly from bicycle handlebars
Presentation	Diagnosis often delayed because of nonspecific nature of complaints and physical exam findings
Symptoms	Classic triad: Epigastric pain, palpable abdominal mass, and hyperamylasemia → rarely detected in children, may develop slowly
Co-injury	Pancreas relatively well protected and commonly associated with hepatic and intestinal injuries
Diagnosis	Abdominal ultrasound and CT with contrast, but initial CT may be negative
Laboratory	Amylase normal in 30% of patients with complete pancreatic transection, amylase elevated in 14-80% of cases of blunt injury; elevated amylase suggest possibility of pancreatic involvement but absolute value does not correlate with degree of injury
Management	Gastric decompression (nasogastric/orogastric tube(, bowel rest Pseudo cyst → 25% spontaneous resolution → If persists for > 6 weeks then surgical drainage needed Severe pancreatic crush injury or transection → Immediate surgical exploration, resection, or drainage

HOLLOW ABDOMINAL VISCERA INJURIES: INTESTINAL PERFORATION	
Etiology	Most common causes are automobile-pedestrian trauma, automobile lap seat belt injuries, and child abuse
Anatomy	Involved rapid acceleration or deceleration of a structure near a point of anatomic fixation (e.g. ligament of Treitz) or trapping of a piece of bowel between two unyielding structures (e.g. lap belt and spine)
Symptoms	Fever and worsening peritonitis on serial exam suggest bowel perforation
Diagnosis	Abdominal XRAY: Only 30-50% of cases show free air
	CT: 5% of injuries are not apparent on initial CT; Rarely see pneumoperitoneum or leakage of GI contrast, must evaluate free fluid very carefully
	DPL: May demonstrate bile or amylase in the effluent and is sensitive for bowel perforations
	Laparotomy: Most perforations or transections of bowel found during laparotomy which is performed because of advancing peritonitis or unexplained persistent fever
Management	Depends on site and extent of structural injury

HOLLOW ABDOMINAL VISCERA INJURIES: DUODENAL HEMATOMA	
Frequency	Uncommon injury
Anatomy	Like the pancreas the duodenum cross the midline and can be crushed again the lumbar vertebrae with blunt trauma
Mechanism	From direct blow to epigastrium from small diameter instrument such as broom handle or toe of boot or lap belt syndrome and may cause partial or complete gastric outlet obstruction
Symptoms	Pain, bilious vomiting, and gastric distention
Diagnosis	Ultrasound or contrast upper GI series revealing duodenal
	Suspect co-Injury of the pancreas must
Management	Non-operative. NG decompression and parenteral nutrition up to 3 weeks

HEMATOBILIA	
Definition	Bleeding into the biliary passage
Co-injury	Associated with hepatic trauma caused by pressure necrosis from intrahepatic hematoma or direct injury to the biliary tree
Symptoms	Present several days after trauma with abdomen pain and upper GI bleeding
Diagnosis	Cholangiography confirms the diagnosis
Management	Embolization to achieve hemostasis and partial hepatic resection necessary if embolization fails

SEAT BELT AND AIRBAG INJURIES
Chance Fractures: Compression or flexion-distraction fractures of lumbar spine
50% associated with duodenal perforation, mesenteric disruption, transection of small bowel and bladder rupture
Normal abdominal CT does not rule out ruptured viscous
Symptoms include abdominal or flank ecchymosis in pattern of strap/belt

PELVIC TRAUMA (See: PEM Guide: Trauma: Genitourinary Trauma)

Pelvic fractures are a significant source of internal bleeding with abdominal trauma. Any patient with a major pelvic trauma should receive blood immediately in anticipation of blood loss before hematocrit results are available. Patients with open-book or other pelvic fractures with significant bleeding may be temporarily stabilized with a pelvic stabilization binder.

PENETRATING ABDOMINAL TRAUMA

Penetrating intra-abdominal injuries are much less common than blunt trauma but are more lethal. The colon and small bowel are the most commonly injured structures, followed by liver, spleen, and major vessels. The decision for laparotomy must be made quickly and broad-spectrum antibiotics such as Cefoxitin should be started.

GUNSHOT WOUNDS: >90% are associated with significant injury. Management includes a laparotomy in all gunshot wounds to the abdomen given that hollow viscera and large vessels are often involved and the liver and spleen may have burst injuries

STAB WOUNDS (ANTERIOR): Laparotomy if hemodynamic instability, peritonitis, blood in gastric aspirate or on rectal exam, pneumoperitoneum or evisceration. If hemodynamically stable, need local exploration to rule out penetration. If penetration cannot be ruled out, then exploratory laparotomy.

STAB WOUNDS (POSTERIOR): More protected by paraspinal musculature. Bleeding often tamponades in this area. Selective laparotomy common strategy, but sometimes managed non-operatively unless hemodynamic instability or peritonitis

CERVICAL SPINE TRAUMA

INTRODUCTION (ERIC WEINBERG, M.D., 8/2020)
Cervical spine injuries may involve trauma to either the cervical vertebral column, the cervical spinal cord or both. Pediatric C-spine injuries are rare occurring in approximately 1.5% of pediatric trauma patients. Only 15% of these injuries involve the spinal cord. There are many anatomic differences between the pediatric and adult cervical spine that determine the pattern of injuries seen and the interpretation of radiographs. At less than 8 years or age the fulcrum of motion is C2-C3. In those 8 years or older, the fulcrum is at C5-C6 and adult injury patterns predominate.

ANATOMIC DIFFERENCES
Cephalocervical disproportion
Facets aligned more horizontally
Weak cervical muscles
Less skeletal resistance to flexion/rotation
Increase risk of ligamentous injury/cord injury, decreased risk of fractures
In children < 3 years, 50% injuries C1-2
Incomplete closure of physes mimicking fractures

CERVICAL SPINE INJURIES
1. FRACTURES
2. DISLOCATIONS
3. SCIWORA
4. SPINAL CORD INJURY PATTERNS

1. FRACTURES
Younger children usually sustain fractures of C1 and C2. The odontoid process may become separated from body of C2. This is due to a fracture through C2 synchondrosis This may also be congenital. In older children, the most common fractures are vertebral body and arch fractures. The mechanism of injury can be used to predict the type of fracture sustained.

FRACTURE TYPE BY MECHANISM OF INJURY	
Hyperflexion	Clay shoveler’s fracture = avulsion of spinous process C6, C7 orT1
	Teardrop fracture: Anterior displacement of bony fragment of vertebral body
Hyperextension	Hangman’s fracture: Fracture of posterior neural arch of C1 or pedicles of C2
Axial Loading	E.g. Diving injuries
	Burst fractures of arch of C1 or vertebral bodies of lower C-spine
	Jefferson burst fracture: Fracture of arch of C1 and lateral displacement of C1 on C2
Rotational	Facet fracture, atlanto-axial rotary subluxation

2. DISLOCATIONS

Dislocations are more common in younger children. The most common is subluxation of C1/C2. The dislocation is usually anterior and often occurs with odontoid fractures due to disruption of broad transverse and posterior ligaments. Pseudo-subluxation typically appears as anterior slippage of C2 on C3 and less commonly with C3 on C4. This is due to the normal mobility of C2 on C3 in flexion in children less than 8 years old. Swischuk's Line is a line drawn from the spinolaminar line of C1 to C3. The spinolaminar line of C2 must be within 2mm of this line. See Appendix: XRAY Interpretation)

3. SCIWORA (SPINAL CORD INJURY WITHOUT RADIOGRAPHIC ABNORMALITY)

SCIWORA is defined as traumatic cord injury with normal plain films. It is less common than previous because injuries may be apparent using improved imaging techniques such as CT or MRI. There is a greater prevalence in younger patients secondary to elasticity of ligaments (dislocate and then spontaneously relocate).The spinal column can stretch to a greater extent than the spinal cord. Presentation may be delayed. Patients with transient or persistent weakness, numbness or paresthesias require an MRI and neurosurgical consultation even if imaging is negative.

4. SPINAL CORD INJURY PATTERNS

The spinal cord is divided into a number of pathways or tracts with specific functions. Motor tracts are descending while sensory tracts are ascending. Patterns of sensory and motor loss may aid in the identification of a lesions location.

Complete spinal cord injury results in complete bilateral loss of motor and sensory function below the level of the lesion. Incomplete spinal cord injury results in a variable pattern of sensory and motor loss that depends on the location of the lesion

INCOMPLETE SPINAL CORD SYNDROMES	
Anterior cord	Loss of motor function
	Loss of pain and/or temperature sensation
	Preservation of proprioception.
Posterior cord	Loss of proprioception
	Preservation of motor, pain temperature
Brown-Sequard (Hemisection – R or L)	Ipsilateral loss of proprioception
	Ipsilateral loss of motor function
	Contralateral loss of pain and temperature sensation.
Central cord	Motor weakness in the upper > lower extremities
	Motor weakness distal > proximal
	Sensory loss variable, sacral sensory sparing
	Pain, temperature sensation > proprioception, vibration

MANAGEMENT OF SUSPECTED C-SPINE INJURY
Immobilization
Clinical determination of the need for imaging
Selection of appropriate imaging modality
Interpretation of imaging studies: Radiologic clearance
Clinical clearance (signs and symptoms) of patients with normal radiographs
Management: Cervical spine and spinal cord injuries: Neurosurgical consultation
Management: Associated neurogenic shock (See also: PEM Guide: Trauma: Neurogenic Shock)

IMMOBILIZATION

Children have relatively larger occiputs and shorter necks resulting in flexion of the neck when in a supine position. To prevent flexion, place a pad under shoulders aligning the external auditory meatus with anterior shoulder. An appropriately sized cervical collars should be used.

CLINICAL DETERMINATION OF THE NEED FOR IMAGING: DECISION RULES

A number of clinical decision rules have been developed to aid in determination of risk of cervical spine injury. The NEXUS (Viccellio, Pediatrics. 2001, PubMed ID: 11483830) and PECARN (Leonard, Annals EM 2010, PubMed ID: 21035905) rules included children and are discussed below. The Canadian C-spine rule (Stiell, JAMA 2001, PubMed ID: 11597285) did not include patients less than 16 years of age.

NEXUS CRITERIA: NO NSAID		
NO	N	Neurologic abnormalities
NO	S	Spinal tenderness
NO	A	Alteration in mental status
NO	I	Intoxication
NO	D	Distracting injury

NEXUS: The National Emergency X-radiography Utilization Study (NEXUS) is a 5-point decision instrument than be remembered using the mnemonic “No NSAID”. If patients do not have any of the 5 criteria there is a low probability of C-spine injury. Negative predictive value of 99.8% (99.6, 100%)

PEDIATRIC NEXUS: A separate analysis of the NEXUS database including patients less than 18 years of age was published. (Viccellio Peds 2001, PubMed ID: 11483830) It included 2,160 patients (9-17 years), 817 patients (2-8 years), and 88 patients less than 2 years of age. The rule performed with a Sensitivity = 100% (88-100%) and a Negative Predictive value = 100% (99.4, 100%). Limitations of the pediatric nexus cohort include a small sample size. There were no C-spine injuries in patients less than 2 years of age and only 4 injuries in those 2-8 years of age resulting in wide confidence intervals around sensitivity. The NEXUS criteria has the potential to reduce XRAY utilization by 20% but should be used with caution in patients less than 8 years of age

PECARN DERIVATION: The PECARN Pediatric C-spine Rule was a retrospective case-control study including 504 patients with a C-spine injury. The absence of 8 factors (see table) identified those at low risk of C-spine injury with a sensitivity of 98% (96-99) and specificity of 26% (23-29). A Negative Predictive value could not be calculated due to the case-control design. The authors conclude that use of the rule has the potential to reduce in XRAY utilization by 25%. Limitations include only 27 cases less than 2 years. In addition some parameters are open to interpretation and an assessment inter-rater agreement has not possible due to its retrospective design. Though this was a multicenter study is not been externally validated.

PECARN DE NOVO: A well-designed, prospective cohort study was conducted at 4 children's hospitals that are level I trauma centers (Leonard, Pediatrics. 2019, PubMed ID: 31221898). This was a pilot study at one of the PECARN nodes to be further validated in the entire PECARN network. The goal of the study was to re-assess the criteria from the PECARN C-spine study derivation and assess new models for c-spine clearance. The study included 4,091 patients of which 74 (1.8%) had a cervical spine injury. Test characteristics were slightly better for the de novo rule than for the PECARN rule. Imaging wound potentially be reduced by 22.1% (78.2, 55.1%) for the PECARN rule and by 26.6% (78.2, 51.6%) for the De Novo rule.

INDEPENDENT PREDICTORS OF CSI: REGRESSION ANALYSIS		
PREDICTOR	PECARN MODEL[1]	DE NOVO MODEL[1]
Mechanism: High Risk MVC	1.58 (0.63, 3.97)	
Mechanism: Diving	17.60 (5.60, 55.32)	9.16 (2.41, 34.83)
Mechanism: Axial Load		2.51 (1.22, 5.16)
History: Predisposing Condition	2.02 (0.27, 15.10)	
History: Neck Pain[2]	1.65 (1.04, 2.62)	2.87 (1.50, 5.48
History: Inability to Move Neck[2]	3.77 (2.00, 7.12)	3.51 (1.72, 7.17)
Exam: Altered Mental Status	5.67 (3.54, 9.09)	2.90 (1.37, 6.12)
Exam: Intubated		10.71 (4.43, 25.91)
Exam: Limited Neck Range of Motion	1.85 (0.88, 3.90)	
Exam: Substantial Torso Injury	2.61 (1.24, 5.53)	
Exam: Respiratory Distress		5.84 (1.56, 21.88)
Exam: Focal Neurologic Deficits	2.62 (1.04, 6.63)	

GREEN = Statistically Significant, RED = Not Statistically Significant
1. Adjusted Odds Ratio (95% Confidence Interval)
2. Neck pain and inability to move neck were assessed separately. These were combined as Torticollis in the derivation of the original PECARN case-control study

RULE CHARACTERISTICS (≥ 1 RULE FACTOR PRESENT)		
	PECARN Rule[1]	De Novo Rule
Sensitivity	90.54% (83.87, 97.21%)	91.88% (85.7, 98.11%)
Specificity	45.58% (44.04, 47.12%)	50.26% (48.72, 51.81%)
PV (+) Test	2.97% (2.27, 3.68%)	3.29% (2.52. 4.06%)
PV (-) Test	99.62% (99.34, 99.90%)	99.71% (99.47, 99.94%)
LR (+) Test	1.66 (1.54, 1.80)	1.85 (1.71, 1.99)
LR (-) Test	0.21 (0.10, 0.42)	0.16 (0.07, 0.35)

1. Any of 9 factors in PECARN rule including 3 that were not statistically significant

SELECTION OF IMAGING MODALITY

The majority of pediatric patients in a Children's hospital setting have plain XRAYS to evaluated their cervical spine. In contrast, most adults are evaluated with CT. Efforts are made to limit the radiation exposure of children. A complete C-spine XRAY includes a Lateral neck, Anterior-Posterior and Open Mouth (AKA odontoid). Lateral neck XRAYS have a reported sensitivity of 73% in those less than 8 years of age and 93% in those greater than 8 years or age. Open mouth views are difficult to obtain in in children less than 5 years of age. Flexion-extension radiographs are of little value acutely because muscle spasms prevent adequate range of motion particularly if lateral and AP XRAYS are normal .

C-SPINE CT INDICATIONS*
Patients who are receiving a head CT ("One-stop scanning")
Altered mental status
Neurologic signs or symptoms consistent with a spinal cord injury
Abnormal plain XRAYS
Persistent pain and or tenderness in a patient with normal AP and Lateral XRAYS
*An MRI may be useful for identifying ligamentous and spinal cord injury.

CLINICAL CLEARANCE OF C-SPINE

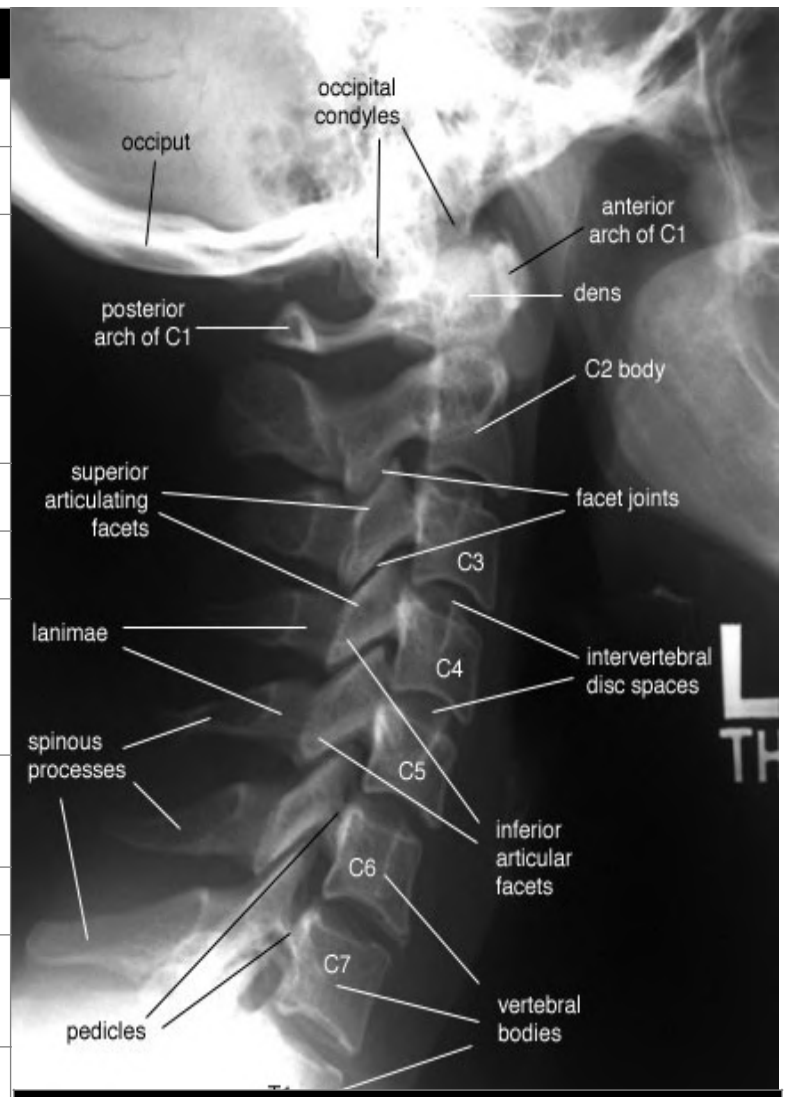
Once XRAY or CT are officially negative, or if the patient meets NEXUS criteria, carefully remove cervical collar. Have the patient actively move head laterally left and right, then superior and inferior. If the patient denies pain, weakness or paresthesias then the cervical spine is *clinically* cleared. If the patient complains of pain with movement they may have a soft issue injury. Place them in a Miami-J collar and follow up with neurosurgery.

TREATMENT OF SUSPECTED SPINAL CORD INJURY

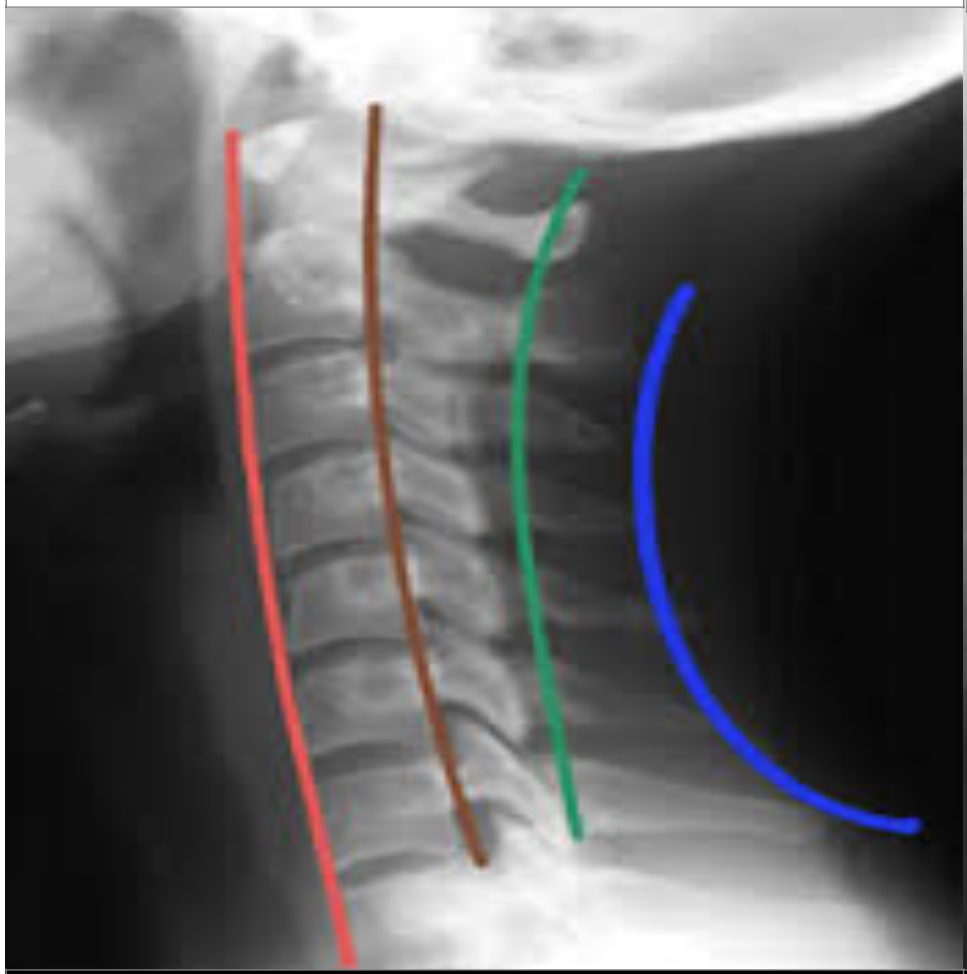
Patient should remain in a cervical collar. They may be removed from the backboard. The Congress of Neurological Surgeons issued new guidelines in 2013 on the use of corticosteroids in acute spinal cord injury (PubMed ID: 23839357). They concluded that there is no Class I or Class II medical evidence supporting the benefit of steroids in the treatment of acute spinal cord injury. There is Class I, II, and III evidence that high-dose steroids are associated with harmful side effects including death.
See: PEM Guide: Trauma: Neurogenic Shock.

APPENDIX: INTERPRETATION OF CERVICAL SPINE XRAYS

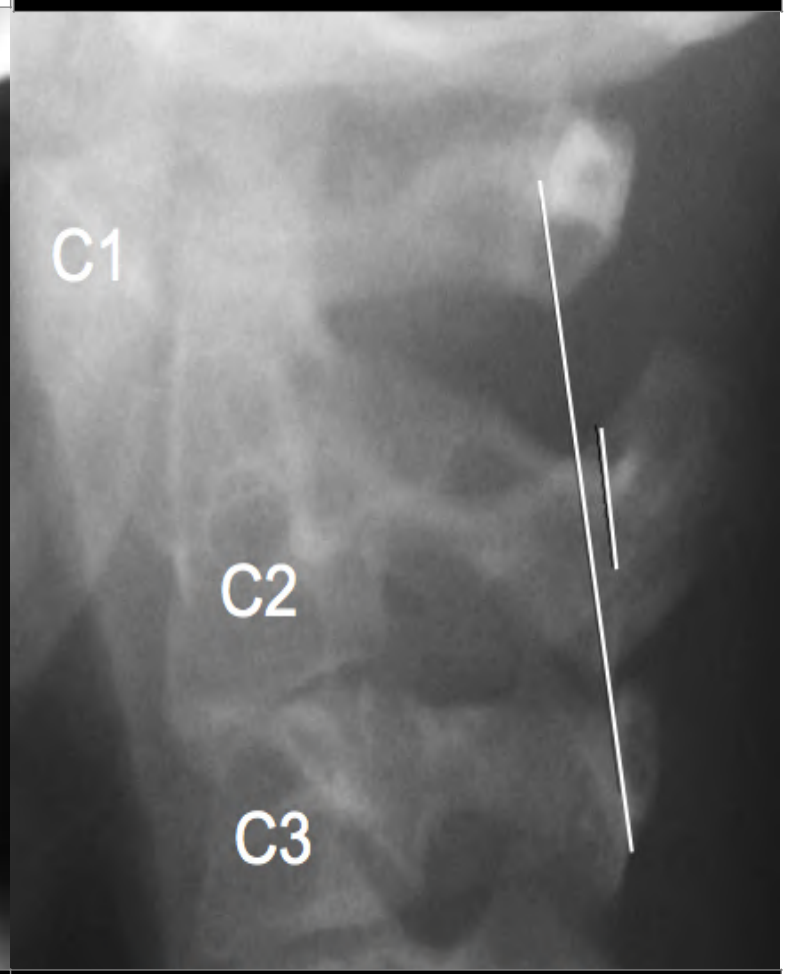
LATERAL VIEW
Adequate films must include entire C1-C7: Ideally to T1
Identifies 80% of injuries
Look for disruption of the 4 curvilinear cervical spine contour lines
Anterior vertebral body line
Posterior vertebral body line
Spinolaminar line
Line joining the tips of spinous process
Swischuk Line: Line between anterior aspects of C1 and C3 spinous process. True subluxation if line misses anterior aspect of C2 spinous process by > 2 mm
Distance between C1 and C2 (if increased consider occipito-atlantoaxial injury)
Soft Tissue Spaces
Predental space < 4-5 mm in children < 8years, < 3 mm in adults
Prevertebral space at C3/C4 < 1/3 the AP diameter of the vertebral body (< 7mm in adults)



LATERAL VIEW

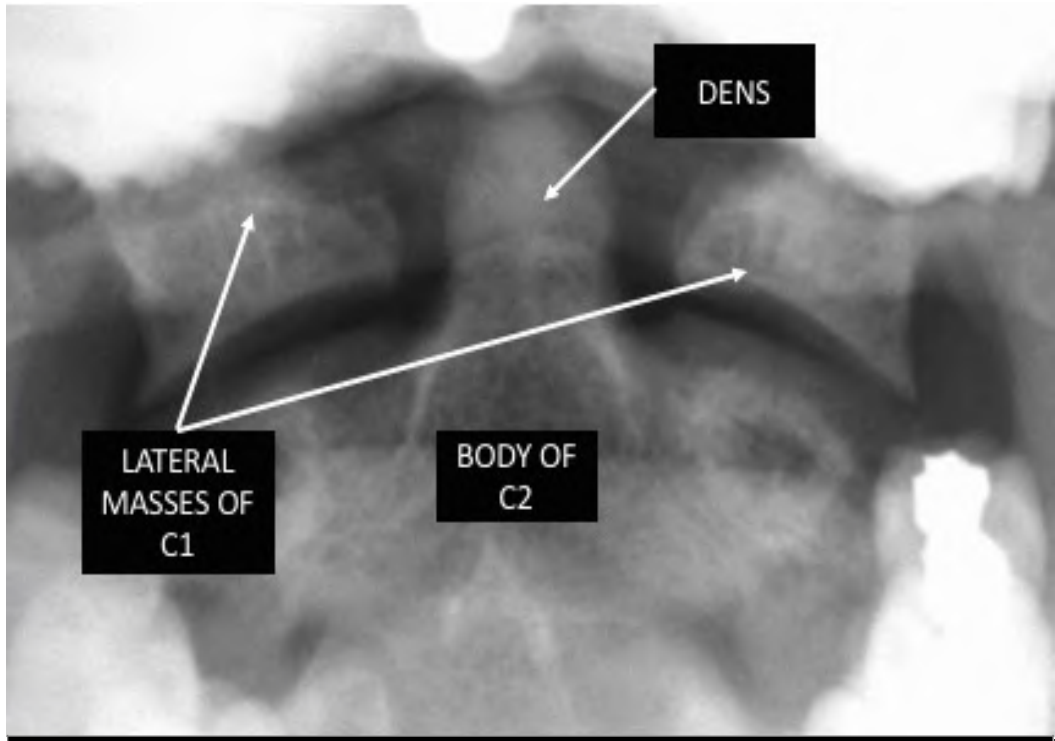


LATERAL VIEW (ALIGNMENT)



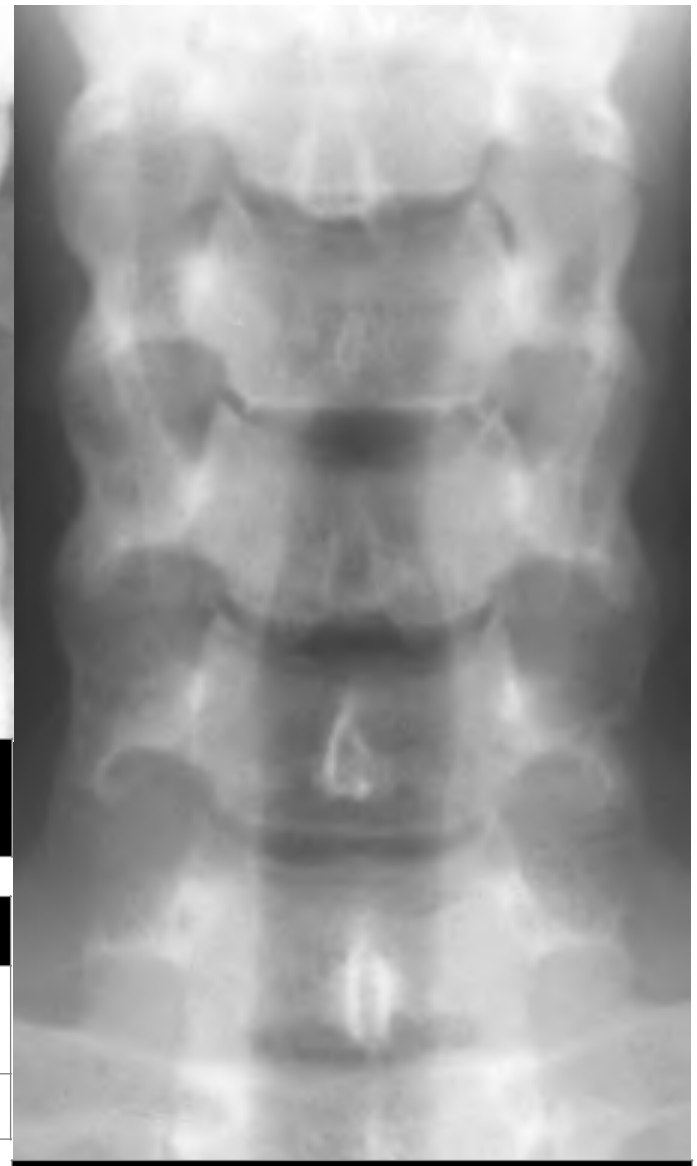
SWISCHUK LINE

OPEN-MOUTH (ODONTOID VIEW)
View lateral masses of C1 and body and odontoid process (dens) of C2
Look for odontoid fractures
Align lateral aspects of C1 with C2, symmetric spacing



ODONTOID VIEW

ANTERIOR-POSTERIOR VIEW
Check alignment of spinous processes and vertebral bodies. Consider rotary subluxation if not aligned
Can identify missed lateral mass fractures



AP VIEW

APPENDIX: PECARN C-SPINE RULE DERIVATION

PECARN PEDIATRIC CERVICAL SPINE RULE	
PARAMETER	ADJUSTED ODDS RATIO (95% CI)
Altered mental status	3.0 (2.1-4.3)
Focal neurologic findings	8.3 (5.6-12.2)
Complaint of neck pain	3.2 (2.3-4.4)
High risk motor vehicle collision	2.5 (1.8-3.6)
Diving	73 (9.6-555.6)
Substantial torso injury	1.9 (1.1-3.4)
Torticollis	1.8 (1.1-2.9)
Predisposing condition	15.6 (2.9-78.0)
Any parameter positive → XRAY	
All parameters negative → No XRAY	

PARAMETER DEFINITIONS	
Altered mental status	GCS <15 AVPU ≠ A (Alert, Voice, Pain, Unresponsive) Other findings suggestive of AMS
Focal neurologic findings	Paresthesias Loss of sensation Motor weakness Other focal neurologic findings
Complaint of neck pain	> 2 years
High risk motor vehicle collision	Head on collision Rollover Ejected from vehicle Death in the same crash Speed > 55 mph
Diving	
Substantial torso injury	Thorax including clavicles, abdomen, flanks, back, pelvis (eg rib fractures, visceral or solid organ injuries, pelvic fracture)
Torticollis	Torticollis, limited range of motion or difficultly moving the neck noted in Hx or PE
PREDISPOSING CONDITIONS Osteogenesis imperfecta Larsen syndrome Juvenile rheumatoid arthritis Juvenile ankylosing spondylitis Renal osteodystrophy Rickets	Down syndrome Klippel-Feil syndrome Achongrodysplasia Mucopolysaccharidosis Ehlers-Danlos syndrome Marfan syndrome History of CSI or cervical spine surgery

CHEST TRAUMA: PRIMARY SURVEY

INTRODUCTION (JOANNE AGNANT, M.D., 12/2022)
Thoracic trauma includes injuries to the chest wall, trachea, bronchi, lungs, heart, thoracic aorta, great vessels, esophagus, and diaphragm. Thoracic trauma in the pediatric population is relatively uncommon though many patients never reach the hospital due to the severity of the injury. In patients who do reach the hospital, most injuries do not require operative intervention other than tube thoracostomy.

Blunt thoracic injuries (85%) are more common than penetrating injuries (15%). Blunt thoracic traumas occur in motor vehicle collisions, bicycle accidents, falls, assaults and abuse. Injuries include: pulmonary contusions, pneumothorax and hemothorax, and rib ractures. Penetrating thoracic trauma occurs with gunshot and stab wounds. Injuries include: pneumothorax and hemothorax, diaphragmatic injuries, cardiac, and vascular injuries.

Children with thoracic trauma may present in respiratory or circulatory failure. Airway obstruction, external compression of the pulmonary structures, direct injury to the lung parenchyma, and chest wall injuries can cause respiratory failure.

PRIMARY SURVEY
The goal of the primary survey is to rapidly identify and manage life-threatening injuries. This PEM Guide focuses on the primary survey of thoracic injury. The secondary survey in the patient with chest trauma is covered in the PEM Guide: Trauma: Chest Trauma: Secondary Survey.

AIRWAY
ASSESS AIRWAY PATENCY, TRACHEAL LOCATION
Air exchange: Voice quality, gurgling, snoring or stridor
Causes of airway obstruction
Laryngeal or upper tracheal injury
Blood, secretions, or foreign bodies
Tracheal deviation may be seen with tension pneumothorax
MANAGEMENT
Maintain in-line cervical spine immobilization
Reposition and suction the airway
Jaw thrust maneuver if bag valve mask ventilation required
Indications for emergent intubation:
Upper respiratory obstruction
Inability to control secretions
Respiratory failure
Neurologic dysfunction with loss of protective airway reflexes
Cricothyroidotomy if ventilation is not successful
Needle thoracentesis is indicated for tension pneumothorax

BREATHING
ASSESSMENT
Respiratory rate, work of breathing, oxygen saturation
Inspect: Symmetry, adequate chest rise, neck vein fullness, tracheal position
Auscultate: Equal breath sounds, heart sounds
Palpate: Crepitus, rib fractures, flail chest
Percuss: Pulmonary parenchymal injury, air or blood in the pleural space
MANAGEMENT
High flow oxygen should be administered
Bag-valve-mask in cases of inadequate respiratory effort
Positive pressure ventilation for flail chest
Endotracheal intubation
Procedural or surgical repair as needed
Tube thoracostomy for pneumothorax, hemothorax
Needle thoracentesis is indicated for tension pneumothorax

CIRCULATION

Thoracic hemorrhage, obstruction of venous return to the heart, or direct injury to the heart can cause circulatory compromise and shock. The body compensates for significant blood loss by increasing heart rate and total peripheral vascular resistance. Pediatric patients can lose up to 25% (20 ml/kg) of their total volume (80 ml/kg) before hypotension ensues. A narrow pulse pressure may be seen. Sinus tachycardia, pulseless electrical activity and ventricular tachycardia may be seen as presenting rhythms. Patient may require surgical repair if multiple blood transfusions are needed or if laceration of hilum of the lung, a great vessel, or the heart are suspected.

CIRCULATION
ASSESSMENT
Mental status
Pulse quality (central and distal), rate, and regularity
Blood pressure
Skin, color, temperature, capillary refill
EKG: Rhythm disturbances, electrical alternans (pericardial tamponade)
MANAGEMENT
Intravenous access and fluid resuscitation
Send blood sample for type and cross
Fluid resuscitation: PRBC 10 ml/kg or if not available Crystalloid (NS or LR) 20 ml/kg
Type and Cross matched OR Type specific OR type O blood
Massive Transfusion Protocol: PRBC, FFP, Platelets (1:1:1) ± Cryoprecipitate
Consider Tranexamic Acid
Needle thoracentesis: Pulseless electrical activity due to tension pneumothorax
Tube thoracostomy: Hemothorax, pneumothorax
Pericardiocentesis: Pulseless electrical activity due to cardiac tamponade
Thoracotomy: Emergency Department versus Operative
See PEM Guide: Trauma: Hemorrhagic Shock

DISABILITY
Assess mental status: AVPU, GCS
Maintain cervical immobilization
Consider the possibility of SCIWORA (spinal cord injury without radiologic abnormality) in children. The use of cervical spine CT scans may identify injuries that would not have been seen on plain XRAYS in the past.
Signs of herniation: Posturing, dilated pupils, hypertension and bradycardia
Elevate the head of the bed 30 degrees: Hypertonic Saline, Mannitol
Controlled hyperventilation to increase cerebral perfusion pressure
Evaluate for any focal neurologic deficits; thoracolumbar spinal injuries may occur with severe chest trauma

EXPOSURE
Assess for external signs of injury including abrasions, ecchymoses, lacerations, crepitus, and tenderness. Lack of these findings does not exclude significant injury (i.e. pulmonary and cardiac contusions)
Thoracic trauma in children is an indicator of multisystem injury
Log roll the patient while maintaining cervical spine immobilization to fully assess for injuries to the back and flank

SIGNS OF LIFE-THREATENING CHEST INJURY			
	TENSION PNEUMOTHORAX	HEMOTHORAX	CARDIAC TAMPONADE
Breath Sounds	Decreased (Ipsilateral)	Decreased (Ipsilateral)	Normal
Percussion	Hyperresonant	Dull	Normal
Trachea	Shift (Deviation) (Contralateral)	Midline	Midline
Neck Veins	Distended	Flat	Distended
Heart Sounds	Normal	Normal	Muffled

PRIMARY SURVEY: CHEST INJURY MANAGEMENT	
INJURY	TREATMENT
Tension pneumothorax	Needle thoracentesis
Open pneumothorax	3-Sided dressing
Flail chest	Positive pressure ventilation
Massive hemothorax	Chest tube, transfusion
Cardiac tamponade	Pericardiocentesis
The pulmonary component of the extended fast exam can identify many of the injuries requiring urgent treatment. See PEM Guide: Trauma: Extended FAST Examination	

SPECIFIC LIFE-THREATENING THORACIC INJURIES

TENSION PNEUMOTHORAX
Clinical diagnosis reflecting air under pressure in the pleural space. Causes a shift of the mediastinum and compression of the great vessels and contralateral lung reducing systemic venous return to the heart
Children are at greater risk of tension pneumothorax due to greater compliance of the mediastinal structures
Common signs and symptoms: chest pain, shortness of breath, respiratory distress, tachycardia, hypotension, tracheal deviation, unilateral absence of breath sounds, neck vein distention, pulseless electrical activity and cyanosis (late manifestation)
E-FAST indicates absence of lung sliding, stratosphere and lung point signs
Treatment should not be delayed pending radiologic confirmation
MANAGEMENT: Immediate needle decompression Chest Tube placement Children: Midclavicular line in the 2nd ICS, Adults: Just anterior to the Midaxillary line in the 5th ICS.

OPEN PNEUMOTHORAX (SUCKING CHEST WOUND)
Result of penetrating trauma
Air preferentially enters during inspiration through a large defect in the chest wall compromising lung expansion
MANAGEMENT: Promptly close with a sterile 3-sided occlusive dressing (best done when patient is in full expiration). Patient will need a chest tube inserted as soon as possible to prevent development of a tension pneumothorax. Respiratory Distress is an indication for intubation and positive pressure ventilation

MASSIVE HEMOTHORAX
Rapid accumulation of more than 1,500 ml of blood in an adult-sized adolescent or greater than or equal to 1/3 of a child’s blood volume in the chest cavity (Estimated blood volume of approximately 80 ml/kg)
Most commonly caused by penetrating wound through systemic or hilar vessels
May occur from blunt trauma from rib fractures lacerating lung or other vascular structures
Respiratory distress, tachycardia, hypotension, decreased breath sounds on affected side
Adult studies indicate thoracic ultrasound is comparable to chest XRAY
Blood within the pleural cavity may tamponade a significant bleeding source within the chest and evacuation may cause additional bleeding.
Thoracostomy is indicated for continued bleeding (greater than 1-2 ml/kg/hour), inability to expand lung, or retained blood
MANAGEMENT: Large caliber intravenous lines and PRBC transfusion followed by tube thoracostomy. (See PEM Guide: Trauma: Chest Tube)

FLAIL CHEST
Disruption of normal chest wall movement due to 2 or more adjacent rib fractures. Paradoxical movement of the chest occurs. The flail chest segment is drawn in during inspiration.
Restricted chest wall movement and underlying lung injury lead to hypoxia
Tenderness and crepitus at fracture sites, external signs of injury are often absent
Clinical signs and Chest XRAY findings may be normal
Ventilation/perfusion mismatch and respiratory failure develop later
Frequently associated with pulmonary contusions
MANAGEMENT: Initial therapy includes positive pressure ventilation, humidified 0_2, fluid resuscitation, and analgesia

CARDIAC TAMPONADE
A blood filled pericardial sac compromises venous return. This leads to decreased ventricular filling and decreased stroke volume. Cardiac output is reduced leading to cardiogenic shock.
More commonly caused by penetrating trauma
Beck's Triad: Venous pressure elevation (JVD), decline in arterial pressure, and muffled heart sounds (not always present)
Chest XRAY may show an enlarged cardiothymic silhouette
EKG may show low voltage QRS complexes, electrical alternans
E-FAST is a rapid and accurate method of imaging the heart and pericardium
MANAGEMENT: Pericardiocentesis can be both diagnostic and therapeutic. Definitive therapy includes surgery for examination of the heart and repair of injury (See PEM Guide: Cardiology: Pericardiocentesis**)**

TRAUMATIC ASPHYXIA
Result of sudden compression of the thorax, upper abdomen or both (e.g., run over by a motor vehicle). The accompanying Valsalva maneuver, inspiration against a closed glottis, occurs in response to a sudden startle.. The combination results in in a sharp rise in intrathoracic pressure with venous hypertension of the head and neck and rupture of venules and capillaries
Clinical examination findings included facial edema, cyanosis, petechiae and subconjunctival hemorrhages.
Associated Life-Threatening injuries: Requires a complete primary survey
Facial fractures: Bleeding, airway obstruction Pulmonary contusions: Impaired oxygenation Tracheobronchial tree, lung, thoracic blood vessel laceration: Hemopneumothoraces Rib/Sternal fractures: Injury to thoracic and mediastinal structures Cardiac: Hemopericardium, dysrhythmia, pump failure Upper Abdomen: Spleen, liver lacerations, intestinal perforation Neurologic: Ischemia, anoxia, cerebral edema due to prolonged increasedvenous pressure
Immediate brain imaging in those with neurologic injury
MANAGEMENT: Oxygen delivery, reduce intracranial pressure, increasing cerebral perfusion. Provide supplemental oxygen and maintain euvolemia. Intubation, mechanical ventilation and osmotic agents (Mannitol or hypertonic saline) may be required for cerebral edema. Therapy for life-threatening thoracic injuries also takes precedence.

PENETRATING CHEST TRAUMA

Pneumothorax and hemothorax are the most common injuries associated with penetrating chest trauma. These are typically managed with chest tube placement. The “cardiac box” is defined as the region medial to the nipples, below the clavicles, and superior to the costal margin. Penetrating trauma to the cardiac box may injure the great vessels, heart, trachea, or esophagus. The mortality rate and need for surgical intervention are much higher for these injuries.

OPERATIVE THORACOTOMY: INDICATIONS (ATLS 2018)				
	ADULT		CHILD[1]	
Penetrating Injury to the Cardiac “Box”	<u>Anterior</u> Medial to Midclavicular Line	<u>Posterior</u> Medial to scapula border	<u>Anterior</u> Medial to Midclavicular Line	<u>Posterior</u> Medial to scapula border
Chest Tube Output: Initial	> 1,500 ml		> 25 ml/kg	
Chest Tube Output: Ongoing	> 200 ml/hour for 2-4 hours		> 5 ml/kg/hour	
Clinical Status	Hemodynamically Unstable Despite Transfusion		Hemodynamically Unstable Despite Transfusion	
1. Pediatric blood volume approximately 80 ml/kg				

ED THORACOTOMY: Thoracotomy in the ED may be indicated in the patient with a penetrating thoracic injury, signs of life and acute loss of pulses in the ED or just prior to ED arrival. Pediatric data is limited. Survival after blunt trauma in patients without signs of life is rare and ED thoracotomy shouldn’t be attempted in these patients.

EMERGENCY DEPARTMENT THORACOTOMY: GOALS	
1	Pericardial blood evacuation to relieve cardiac tamponade
2	Direct control of intrathoracic hemorrhage that may cause exsanguination
3	Open cardiac massage
4	Cross clamping of the descending aorta to decrease infra-diaphragmatic blood loss and increase brain and heart perfusion

SURVIVAL AFTER ED THORACOTOMY		
	ADULTS	CHILDREN
Penetrating Trauma	8.8-11.2%	10.2%
Blunt Trauma	< 2%	1.6%

SECONDARY SURVEY

The secondary survey involves patient history, a complete physical examination, and additional diagnostic studies (i.e. upright CXR, CT, sonography) or therapeutic procedures (i.e. needle decompression). Injuries identified and managed in the secondary survey are reviewed in the PEM Guide: Trauma: Chest Trauma: Secondary Survey.

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CHEST TRAUMA: SECONDARY SURVEY

INTRODUCTION (JOANNE AGNANT, M.D., 7/2011)
Thoracic trauma includes injuries to the chest wall, trachea, bronchi, lungs, heart, thoracic aorta and great vessels, esophagus, and diaphragm. Thoracic trauma in the pediatric population is relatively uncommon though many patients never reach the hospital due to severity of the injury. In patients who do reach the hospital, most injuries do not require operative intervention other than tube thoracostomy.

Blunt thoracic injuries (85%) are more common than penetrating injuries (15%). Blunt thoracic traumas occur in MVC and bicycle accidents, falls, assaults and abuse. The types of injuries include lung contusions, pneumothorax and hemothorax, and fractures. Penetrating thoracic trauma occurs with gunshot and stab wounds. These injuries include pneumothorax and hemothorax, diaphragmatic injuries, cardiac, and vascular injuries.

Children with thoracic trauma may present in respiratory or circulatory failure. Airway obstruction, external compression of the pulmonary structures, direct injury to the parenchyma, and chest wall injuries can cause respiratory failure.

PRIMARY SURVEY
The goal of the primary survey is to rapidly identify and manage life-threatening injuries.
See: PEM Guide: Trauma: Chest Trauma: Primary Survey

PRIMARY SURVEY: LIFE THREATENING THORACIC INJURIES	
Tension pneumothorax	Needle thoracentesis, Tube thoracostomy
Open pneumothorax	3-sided dressing, Tube thoracostomy
Flail chest	Positive pressure ventilation
Massive hemothorax	Tube thoracostomy, Aggressive fluid resuscitation
Cardiac tamponade	Pericardiocentesis

SECONDARY SURVEY
The secondary survey involves patient history, a complete physical examination, and additional diagnostic studies (i.e. upright CXR, CT, sonography) or therapeutic procedures.

CHEST XRAY FINDINGS	
Pneumothorax	Absence of peripheral lung markings, mediastinal shift
Hemothorax	Fluid at the costophrenic angle, dependent opacity
Rib fractures	Cortical discontinuity
Pulmonary contusion	Non-anatomic infiltrates
Vascular injury	Widened mediastinum. Apical capping
Tracheal-bronchial injury	Pneumomediastinum, Pneumopericardium
Pericardial tamponade	Enlarge cardiothymic silhouette
Diaphragmatic injury	Air overlying lung, air fluid level

SIMPLE PNEUMOTHORAX/HEMOTHORAX
Definition: Air entering the potential space between the visceral and parietal pleura
Etiology: Both penetrating and blunt trauma
Symptoms: Asymptomatic, pleuritic chest pain, tachypnea, severe respiratory distress
Examination: Decreased breath sounds, crepitus, hyper-resonance on affected side
Chest XRAY: Upright, expiratory CXR aids if patient is stable
E-FAST: Absence of lung sliding, lung point sign
MANAGEMENT: If the pneumothorax is small and patient is asymptomatic, hospital observation and administration of 100% 0_2 is indicated. Tube thoracostomy is indicated (4^{th} or 5^{th} ICS anterior axillary line) in the symptomatic patient, any patient receiving positive pressure ventilation (including those going to the OR) or those requiring air transports. A simple pneumothorax can be converted to a tension pneumothorax if positive pressure ventilation is applied prior to chest tube insertion.

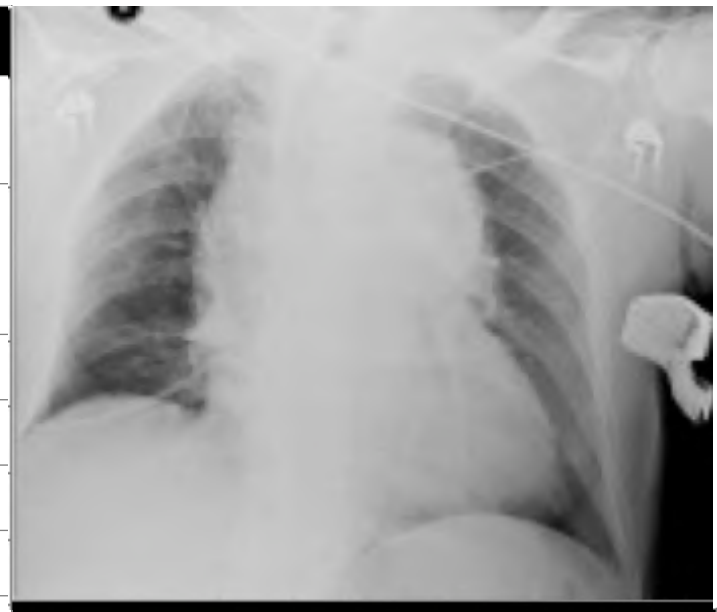
See: PEM Guide: Trauma: Extended FAST Examination
See: PEM Guide: Trauma: Chest Tube

PULMONARY CONTUSION
Pulmonary contusion is the most common thoracic injuries in children.
Because the pediatric chest wall is very compliant, force is transmitted to the underlying parenchyma resulting in hemorrhage (contusion). The presence of rib fractures indicates a great degree of force in the pediatric patient.
Initially chest XRAY may be normal. A chest CT may be more sensitive. Findings include irregular infiltrates that do not follow anatomic landmarks
MANAGEMENT: Significant or multiple pulmonary contusions can result in hypoxia and require positive pressure ventilation. Close observation is required in mild contusions for possible deterioration in respiratory status. Fluid restriction is helpful to avoid pulmonary edema.

TRACHEOBRONCHIAL TREE INJURY
Rare in children, high mortality rate
Associated with crush injury to the chest or acceleration/deceleration forces
Presents with cyanosis, hemoptysis, tachypnea, subcutaneous emphysema, tension pneumothorax, persistent air leak, inability to re-expand the lung after tube thoracostomy
In a stable patient, chest CT can help confirm the diagnosis and identify other injuries
Confirmed by bronchoscopy
MANAGEMENT: Surgical consultation is warranted early if suspected. Be cautious of endotracheal intubation, which can convert a partial tracheal tear into a complete one

BLUNT CARDIAC INJURY (MYOCARDIAL CONTUSION)
Direct blunt trauma to anterior chest may produce cardiogenic shock
Patient may present with tachycardia, chest pain and anterior chest wall tenderness
There is a potential for significant dysrhythmias and hypotension
May result in sudden death (commotio cordis)
MANAGEMENT: Inotropic agents may help improve contractility. If a pericardial tamponade is suspected, pericardiocentesis is indicated. Evaluation includes a 12-lead EKG. Troponins are sensitive indicator of myocardial injury. Symptomatic patients should receive an echocardiogram. Transesophageal echocardiogram has been shown to be more sensitive than a transthoracic echo

TRAUMATIC AORTIC DISRUPTION
Laxity of mediastinal fixation allows organs to shift which may result in aortic injury
Clinical signs and symptoms may include chest or back pain, hypotension, paraplegia, anuria, absent or diminished femoral pulses, or excessive chest tube bleeding
Radiographic findings may include:
Widened mediastinum
Obliteration of the aortic knob
Deviation of the trachea to the right
Depression of left mainstem bronchus
Elevation of right mainstem bronchus
Obliteration of space b/w pulmonary artery and aorta
Deviation of esophagus to the right
Widened para-tracheal stripe or paraspinal interfaces
Fracture of the first or second rib or scapula
Helical CT is 100% sensitive and specific and indicated for stable patients. A transesophageal echocardiogram performed in the OR may be diagnostic in an unstable patient.
MANAGEMENT: Requires immediate surgical repair



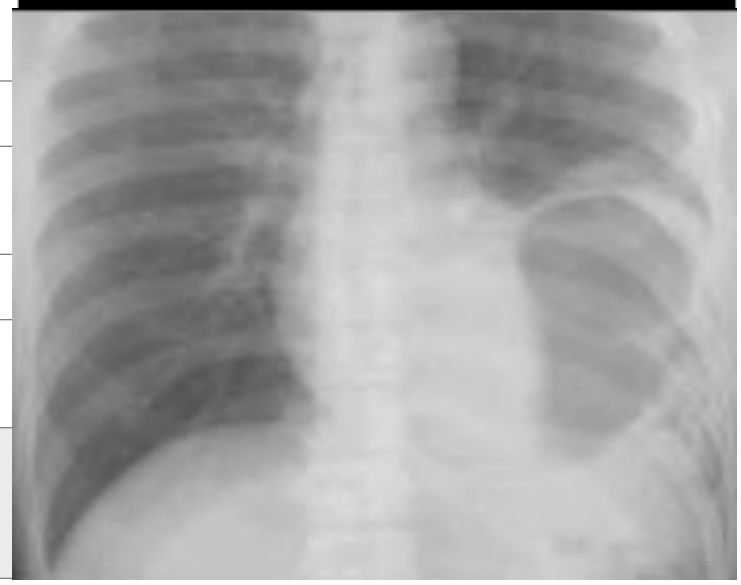
WIDENED MEDIASTINUM

See: PEM Guide: Trauma: Extended FAST Examination
See: PEM Guide: Cardiology: Pericardiocentesis

TRAUMATIC DIAPHRAGMATIC INJURY

Most frequently caused by blunt force injury; often associated with lap belts
Presents abdominal pain and/or respiratory distress
Exam may be normal or may show decreased BS, respiratory distress, and scaphoid abdomen
CXR normal in 30-50% of diaphragmatic hernias
CXR may show bowel gas pattern in the lungs, a displaced nasogastric tube, or an elevated hemi-diaphragm
MANAGEMENT**:** A nasogastric tube allows decompression of the stomach and decreases the risk of aspiration of vomit or swallowed blood. Treatment is by operative repair

DIAPHRAGM RUPTURE (L)



BLUNT ESOPHAGEAL RUPTURE

Most commonly caused by penetrating injury
Should be considered in any patient with:
Left pneumothorax or hemothorax without a rib fracture
History of severe blow to the lower sternum or epigastrium, in pain or shock out of proportion to apparent injury
Particulate matter in chest tube after blood clears
Mediastinal air
Complications include mediastinal sepsis and death
Confirm with contrast studies and/or esophagoscopy
MANAGEMENT: Treatment consists of wide drainage of the pleural space and mediastinum with direct repair of injury via thoracotomy. Patients will require volume resuscitation, nasogastric tube placement, and antibiotics (coverage for gram-positive, gram-negative, and anaerobic organisms).

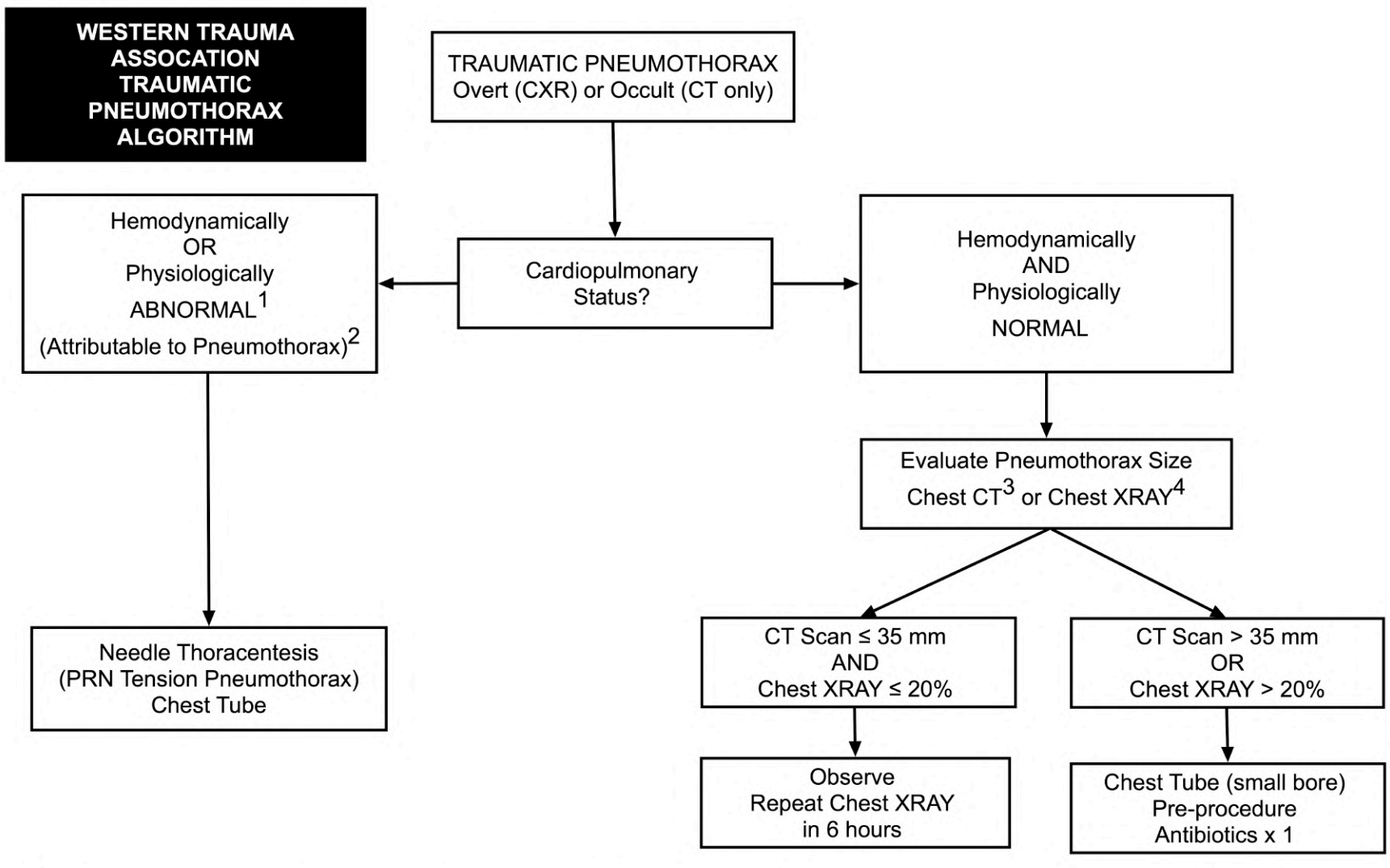
RIB FRACTURES

Uncommon in young children because of increased compliance in the pediatric thoracic rib cage due to greater cartilage content and greater elasticity of bones
Suggests a high energy force; often associated with severe underlying organ injury including pulmonary contusions
Posterior rib fractures are typically associated with intentional injury
Dedicated Rib XRAYS are more sensitive than a Chest XRAY
MANAGEMENT: Isolated rib fractures are managed conservatively with analgesia. A flail chest requires positive pressure ventilation

CHEST TUBE (THORACOSTOMY)

INDICATIONS (DAVID KESSLER, M.D., 1/2022)
Indication for tube thoracostomy include significant pneumothorax, hemothorax and pleural effusion (empyema, chylothorax). Recommendation are evolving as new evidence becomes available. An increase in the use of CT has resulted in an increase in occult pneumothorax (seen on CT but not seen on Chest XRAY). Evidence suggest that patients with occult pneumothoraxes or undergoing positive pressure ventilation, may not require chest tubes and that observation is a suitable alternative. In addition, recent recommendations (ATLS 2018) are for the placement of small-bore chest tubes (Inaba 2012, J Trauma Acute Care Surg, PubMed ID: 22327984). See also PEM Guide: Respiratory: Spontaneous: Pneumothorax, PEM Guide: Trauma: Chest Primary Survey and PEM Guide: Trauma: Chest Trauma: Secondary Survey.

There has also been a trend in the use of alternatives to chest tube placement to reduce their morbidity. Alternatives may be considered in patients who are: asymptomatic and have small collections. Pigtail catheters have been shown equal efficacy for pneumothorax with less pain the tradition chest tubes (Kulvatunyou, Br J Surg 2014., PubMed ID: 24375295). Pig tail catheters have also shown efficacy for hemothorax and hemopneumothorax (Bauman, World J Surgery 2018, PubMed ID: 28795207). Alternative techniques are listed in the table below.



1. Persistent HR > 120, RR > 30, Systolic BP < 90, Base deficit > 4
2. Unlikely attributable if < 1 cm on CT or XRAY
3. CT: Radial Line (mm): Perpendicular to chest wall to the largest air pocket on axial view (See appendix)
4. Chest XRAY: Collin's method (See appendix)

WTA, J Trauma Acute Care, 2021, PubMed ID: 34538823

ALTERNATIVE CHEST TUBE TECHNIQUES
Observation followed by serial exam and chest XRAY
Pleurocentesis (catheter aspiration)
Modified Seldinger technique with a pigtail catheter or Heimlich valve
Chest tube placement with trocar (higher risk of injury) or over a bougie
Operative thoracotomy, video assisted thorascopic surgery (VATS)

CONTRAINDICATIONS

There are no absolute contraindications. Patients with a tension pneumothorax with cardiopulmonary compromise (tension pneumothorax physiology) require needle decompression by needle thoracentesis. Given the difficulty in reaching the pleural space in patients with extensive soft tissue, a finger thoracostomy is frequently recommended in patients in pulseless electrical activity with suspected tension pneumothorax (VIDEO LINK: FINGER THORACOSTOMY). Relative contraindications to chest tubes may include bleeding diathesis, pleural adhesions and complex or loculated collections.

PROCEDURE: NEEDLE THORACENTESIS	
Equipment	Performed with an angiocatheter attached to a fluid-filled syringe.
	Unfortunately, standard safety angiocatheters cannot be directly attached to syringe. A syringe can be attached to a catheter from a central line kit.
	In the adult, a 3.5-inch needle is recommended to ensure penetration of the overlying soft tissue. No pediatric recommendations for length.
Anatomic Landmarks	Children: Midclavicular line in the 2nd intercostal space.
	Adults: Just anterior to the midaxillary line in the 5th intercostal space
Procedure	The needle is advanced perpendicular to the chest wall over the superior border of the lower rib to avoid damaging the neurovascular bundle located under the inferior border of the upper rib.
	The plunger of the syringe should be retracted during catheter advancement. Air will bubble into the syringe when the needle penetrates the parietal pleura.
	Angiocath is advanced into intrapleural space and retract the needle.
	Secure the angiocath with tape. Attach the angiocath to an IV tubing extension set and place the distal end of the tubing into a bottle of saline. This prevents air from being drawn into chest when the diaphragm contracts. It also provides an outlet for intra-pleural air so that tension does not recur as air reaccumulates.

VIDEO LINK: LIFE IN THE FAST LANE

VIDEO LINK: THREE KINGS TENSION PNEUMOTHORAX SCENE

TENSION PNEUMOTHORAX: PHYSICAL EXAM	
Vital Signs	Tachycardia*, hypotension, pulseless electrical activity
Respiratory	Tachypnea*, increased work of breathing*, cyanosis
Breath Sounds	Decreased (Ipsilateral)*
Percussion	Hyper-resonant (Ipsilateral)*
Trachea Position	Shift (Deviation) (Contralateral)
Neck Veins	Distended
Heart Sounds	Normal or displaced (Contralateral)
*May also been seen with moderate-large simple pneumothorax (without tension)	

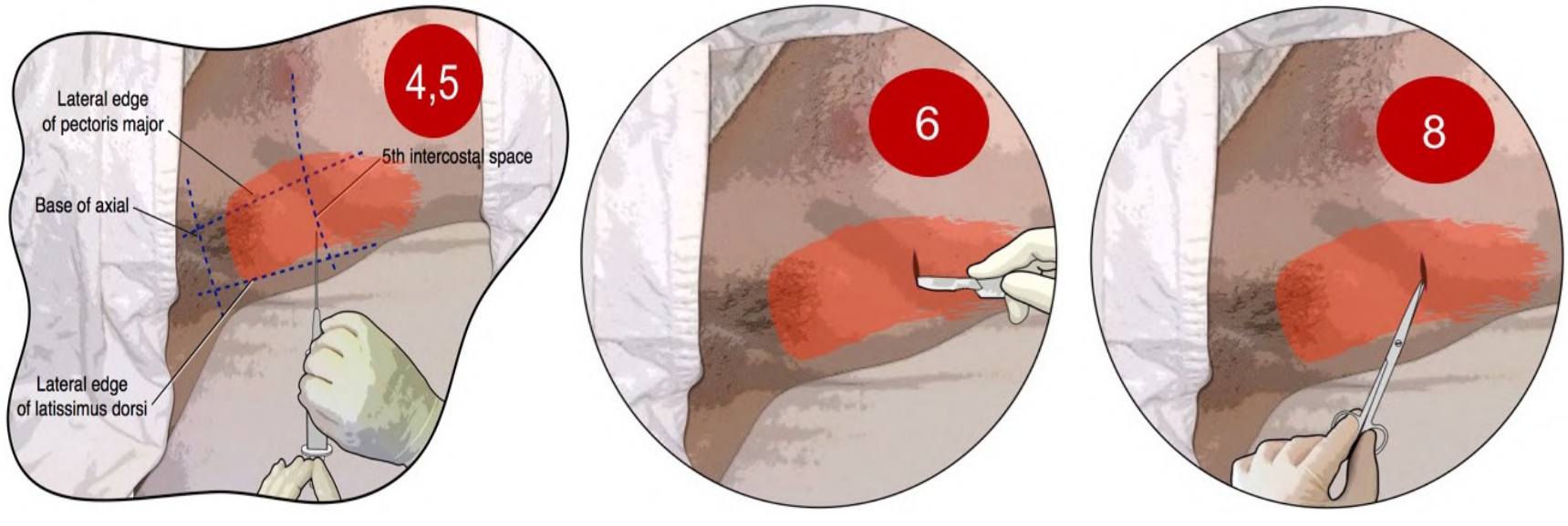
ANATOMIC LANDMARKS

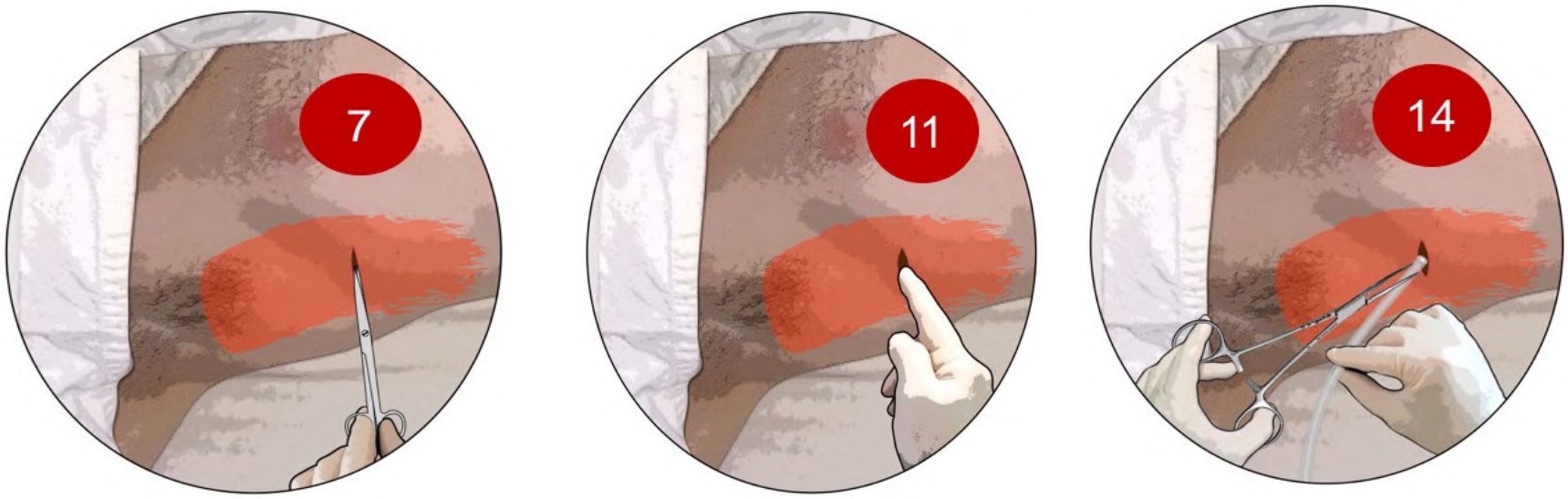
Emergency department chest tube placement is typically at the 4th/5th intercostal space in the mid-axillary line though other landmarks may be appropriate.

EQUIPMENT	CHEST TUBE SIZE*		
Use universal precautions, drape, antiseptic	AGE	WEIGHT	SIZE
1% Lidocaine with Epinephrine if awake	Premature	3 kg	10-14 F
Scalpel	0-6 months	3.5 kg	12-18 F
Large Kelly clamp	6-12 months	7 kg	14-20 F
Small clamp (for clamping the distal end of tube)	1-3 years	10-12 kg	12-24 F
Chest tube	4-7 years	16-18 kg	20-25 F
Silk suture with straight needle, scissors	8-10 years	24-30 kg	28-32
Vaseline Gauze, regular gauze, tape	Adult	> 30 kg	28-32
Pleural drainage system	*ATLS 2018 Recommendations		

PROCEDURE: SELDINGER TECHNIQUE	
1	Identify anatomic landmarks, prepare, anesthetize area
2	Make a small incision over desired intercostal space, above rib
3	Insert the needle into the pleural space, aspirate air/fluid
4	Insert guide wire through introducer needle and into the pleural space
5	Guide the wire apically (air) or inferior/posterior (fluid)
6	Pass the dilator(s) over the wire. Don’t lose wire in pleura cavity!
7	Remove the dilator and pass chest tube into pleural space
8	Remove guide wire
9	Connect chest tube to pleural drainage system

PROCEDURE: STANDARD SURGICAL TECHNIQUE	
1	Cardiac monitor, consider procedural sedation
2	Use universal precautions, gown, mask, gloves. Use sterile technique
3	Have patient place their arm over their head to expose the lateral chest wall
4	Locate the 4th/5th intercostal space in the mid-clavicular line
5	Inject Lidocaine over lower rib, then through muscle and into the pleura
6	Make a 2-3 cm incision over lower rib, down to bone in the intercostal space below and tunneling up to the desired intercostal space to avoid air leaks
7	Blunt dissect superiorly with Kelly clamp toward the intercostal space
8	With the clamp in closed position, push clamp through pleura over the inferior rib to avoid injury to the neurovascular bundle that parallels the lower rib margin.
9	This may require considerable force. Hold the Kelly clamp close to the distal end to avoid inserting the clamp further than necessary into the pleural space
10	Open the Kelly clamp in the plane parallel to the ribs to further open the pleura wide enough to allow chest tube passage
11	Insert a finger into the pleural space to confirm proper position
12	Clamp the distal end of chest tube with a small clamp
13	Clamp the Kelly clamp over the proximal end of the chest tube
14	With aid of Kelly and finger, guide chest tube:
	a. Apically, medially and anteriorly for air
	b. Apically, medially and posteriorly for fluid
15	Advance the tube sufficiently to ensure that the holes are within pleural cavity
16	Connect to pleural drainage system
17	Suture to skin, apply Vaseline gauze, dressing
18	Obtain a chest XRAY and look for condensation to confirm correct placement
RED numbers correspond to the labelled illustration below Steps 1-11 constitute a finger thoracostomy	

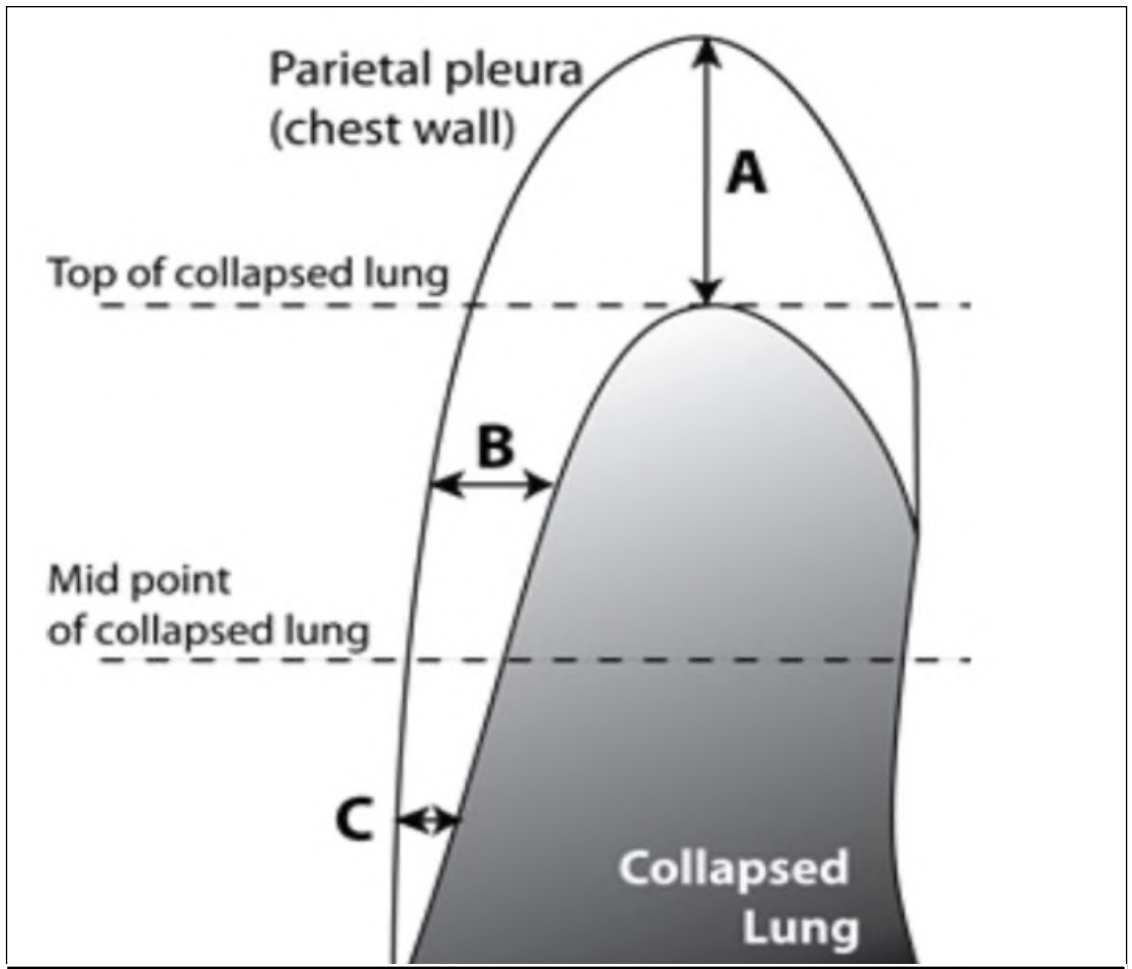




ANTIBIOTICS: Antibiotic prophylaxis has been shown to decrease the rates of empyema and pneumonia associated with chest tube placement (Ayoub, Trauma Surg Acute Care Open 2019, PubMed ID: 30899791). Ideally, antibiotics should be administered prior to the procedure but should be delay the procedure in those with cardiopulmonary compromise attributable to the pneumothorax. At present, the optimal duration or dosing of antibiotics is unknown.

COMPLICATIONS	
Hemodynamic instability	Evacuation of a large hemothorax may results in hemodynamic instability if the hemothorax served to tamponade further bleeding into the pleural space. Administer blood components prior to the evacuation of massive hemothorax
Mal-positioning of the tube	25% of chest tubes are malpositioned (intrafissural, intraparenchymal, or subcutaneous). The majority of these malpositions may not be diagnosed by CXR and may only identified by CT
Re-expansion pulmonary edema	Patients with a large pneumothorax/pleural effusion and those who have a pneumothorax for a few days are at risk for re-expansion pulmonary edema (RPE). This risk does not appear to be reduced by attempts at limiting re-expansion. The hallmark is cough with frothy sputum. A chest XRAY may reveal near total opacification on the affected side. Treatment is supportive with oxygen and assisted ventilation (non-invasive or mechanical) as required.
Tension pneumothorax	A tension pneumothorax may occur if there is a persistent air leak from the lung and the chest tube is occluded or misplaced. Correction of occlusion, correcting the location of a misplaced tube or needle thoracentesis may be indicated

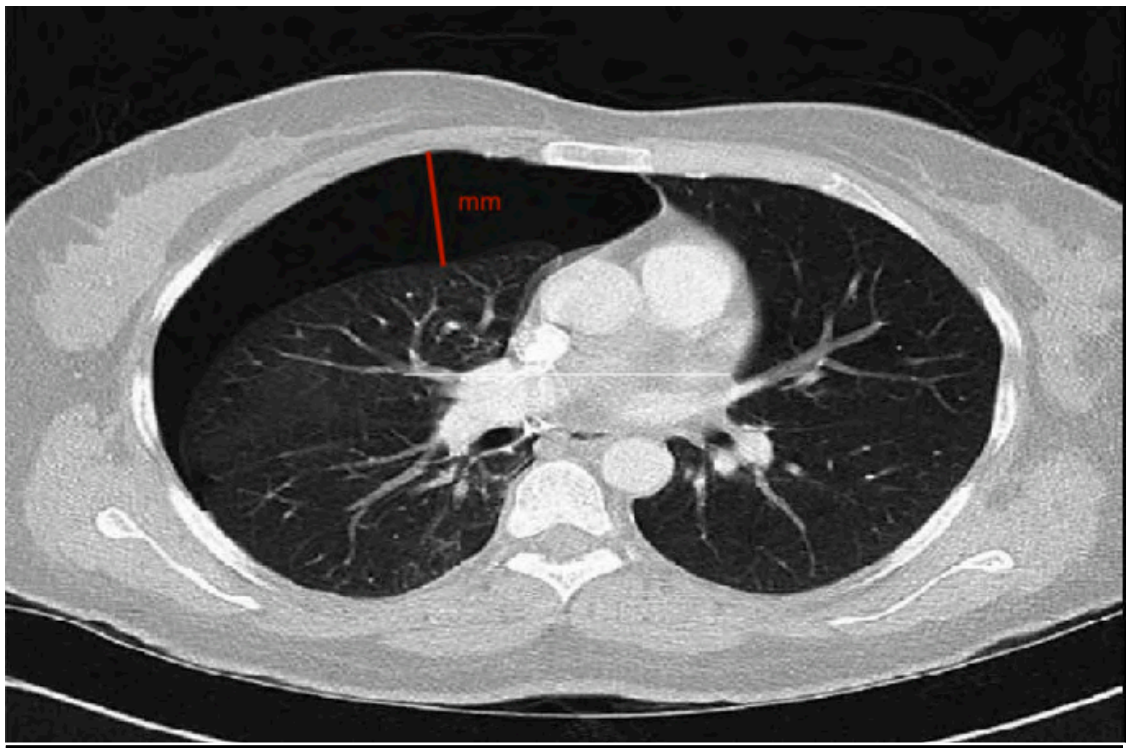
APPENDIX: ASSESSMENT OF PNEUMOTHORAX SIZE



CHEST XRAY (LATERAL)

Chest XRAY(%)
= 4.2 + 4.7(A + B + C)
(A, B, C in centimeters)

Collins CD, Lopez A, Mathie A, Wood V, Jackson JE, Roddie ME. Quantification of pneumothorax size on chest radiographs using interpleural distances: regression analysis based on volume measurements from helical CT. AJR Am J Roentgenol. 1995 Nov;165(5):1127-30., PubMed ID: 7572489



CHEST CT (AXIAL)

Line (in millimeters): Drawn perpendicular to the chest wall to the largest air pocket on the axial view

CONCUSSION

INTRODUCTION (MARY GRADY, M.D. 4/2022)
Concussion is broadly defined as a disturbance of normal brain function resulting from a biomechanical force. Concussion is a form of traumatic brain injury Concussion is the historical term representing low-velocity injuries that cause brain ‘shaking’ resulting in clinical symptoms and that are not necessarily related to an observable pathological injury. It is helpful to think of concussion as a process that may last from days to weeks and not the initial traumatic event. Importantly, concussion can occur without a loss of consciousness and without a direct blow to the head as with a whiplash injury.

The underlying pathophysiology of concussion is unclear but is thought to be due to the rapid acceleration/deceleration of the brain causing compressive, tensile and shearing forces to neurons and axons. This results in axonal injury, metabolic derangement, and alterations in neurotransmission.

Critical periods in development are particularly sensitive to brain insult, resulting in longer duration of symptoms, more variable symptoms, and prolonged recovery. Adolescents are more vulnerable to poor outcomes from concussion compared to adults. Little evidence exists for the preadolescent patient with a concussion.

SPORTS RELATED CONCUSSION DEFINITION*	
A traumatic brain injury induced by biomechanical forces. Common features that may define the nature of a concussive head injury include:	
1	Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an ‘‘impulsive’ force transmitted to the head.
2	Concussion typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, symptoms and signs may evolve over a number of minutes to hours.
3	Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.
4	Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course. However, it is important to note that in some cases symptoms may be prolonged.
*International Consensus Statement on Concussion 2016, PubMed ID: 28446457.	

DIAGNOSIS
Clinical signs and symptoms, although highly variable, are manifestations of neuronal dysfunction. Most symptoms of concussion occur within 6-24 hours of injury, although other symptoms, especially memory and cognitive symptoms, may not become apparent for several days when activities are re-introduced.

GOALS OF INITIAL ASSESSMENT AND MANAGEMENT	
1	Identify urgent neurologic emergencies
2	Identify and treat neurologic sequelae
3	Prevent further symptomatology through graduated cognitive and physical rest

Patients presenting to the ED after head injury are typically referred because of concerns for conditions other than concussion, such as cervical spine injury, skull fracture, or intracranial hemorrhage. Initial evaluation of a patient with suspected concussion should include evaluation for cervical spine injury (PEM Guide Trauma: Cervical Spine Injury) and traumatic brain injury (PEM Guide: Trauma: Head Trauma).

After initial assessment has ruled out severe head trauma or spinal injury, evaluation for concussion includes: mechanism of injury, symptoms, and physical exam findings with special attention to ocular tracking, balance and neuropsychiatric evaluation. The most common symptom of concussion is headache. Deficits in the vestibulo-spinal system, such as errors in balance testing, are the most specific physical exam findings. Eye-tracking testing commonly detects deficits in the vestibulo-ocular system as well.

PRESENTING SYMPTOMS	
SOMATIC SYMPTOMS	COGNITIVE SYMPTOMS
Headache (#1)	Difficulty concentrating
Nausea/Vomiting	Difficulty remembering
Dizziness, balance disturbance	Confusion, disorientation
Sensitivity to light or sound	Feeling slowed down, slow reaction times
Blurry vision	Emotional lability, irritability
Sleep disturbance, insomnia	Depressed, anxious
Fatigue	Amnesia (anterograde, retrograde)

CONCUSSION ASSESSMENT TOOLS: Standard assessment tools such as the Sport Concussion Assessment Tool version 3 (WEB LINK: SCAT-3) or the Standard Assessment for Concussion (WEB LINK: SAC)can be helpful in diagnosis of concussion. However, these tests are most useful when compared to baseline testing. Additionally, they are time consuming and rarely used in ED assessment. A version of the Center for Disease Control's has been modified for Emergency Department use. (WEB LINK: Acute Concussion Evaluation (ACE) Tool**).**

NEUROIMAGING: Imaging is indicated in patients with severe or progressively worsening symptoms. The PECARN head trauma rule for those older than 2 years (See Appendix: PECARN Head Trauma Rule) can be used to assess the risk of clinically important traumatic brain injury (ciTBI). In a patient older than two years of age, a Glasgow Coma Scale of less than 15, signs of an altered mental status or signs of basilar skull fracture are associated with a risk of ciTBI of 4.3% and are considered indications for neuroimaging. Patients without any of the 3 high-risk factors and who have a history of loss of consciousness or vomiting or a severe mechanism of injury or severe headache are at intermediate risk of ciTBI (0.9%). They may be imaged or observed. Those without any of the six predictors have a risk of ciTBI of 0.05% and do not require imaging.

MRI is more sensitive for small contusions, petechial hemorrhage, axonal injury and small extra-axial hematomas though the presence of injuries not typically visualized on CT scan are unlikely to affect management. Use of MRI will avoid the radiation exposure associated with CT. In patients without signs or symptoms suggestive of clinically important traumatic brain injury, clinicians should not routinely use of CT, MRI, skull XRAY, single photon emission CT or serum biomarkers to support the diagnosis of concussion (CDC, JAMA Pediatrics 2018, PubMed: 30193284).

PERSISTENT POST-CONCUSSIVE SYMPTOMS

Persistent post-concussive symptoms are defined as persistence beyond 4 weeks of at least 3 symptoms compared with state of being prior to injury. Most children do not show significant difficulties that last more than 1 to 3 months. Recovery is unique in each patient.

A multicenter, prospective cohort study was designed to identify predictors of persistent post-concussion symptoms. (Zemeck, JAMA, 2016, PubMed ID: 26954410). The study included 2,500 patients (Derivation 1,700, Validation 800) ages 5-18 years who presented within 48 hours of acute head injury. The study included evaluation with the ED ACE, SCAT 3 and the Balance Error Scoring System (VIDEO LINK). Follow up occurred at 28 days post injury. 30% of patients had persistent symptoms. The study identified 9 predictors of persistent post concussive symptoms.10.5% of patients with a score of 0-3, 30.4% of patients with a score of 4-8 and 61.7% of patients with a score of 9-12 had persistent post-concussive symptoms respectively.

CLINICAL RISK SCORE: PERSISTENT POST-CONCUSSION SYMPTOMS		
Age group (years)	5-7 years	0
	8-12 years	1
	13-18 years	2
Sex	Male	0
	Female	2
Prior concussion, Symptom duration	No prior concussion, duration < 1 week	0
	Prior concussion, duration ≥ 1 week	1
Physician diagnosed Migraine	No	0
	Yes	1
Answering questions slowly	No	0
	Yes	1
Balance Error Scoring System Tandem stance (Number of errors)	0-3	0
	≥ 4 or unable to undergo testing	1
Headache	No	0
	Yes	1
Sensitivity to noise	No	0
	Yes	1
Fatigue	No	0
	Yes	2
Low Risk: 0-3, Moderate Risk: 4-8, High Risk: 9-12		

MANAGEMENT

There is a paucity of prospective data to inform the management of concussion and the existing guidelines are typically consensus based. The management of non-sports related concussions can likely be managed according to sports-oriented guidelines.

Patients should refrain from any strenuous physical or cognitive activity for a minimum of 24 hours. In school age children, a “Return to Learn” protocol takes priority over a “Return to Play” protocol. Children should return to full school function prior to re-introducing sports participation.

RETURN TO LEARN: Returning to school and cognitive activities should follow a step-wise progression from complete rest to full cognitive activities. Students should not return to school on the day of injury and a period of reduced activity for at least 24 hours is often recommended. Rest includes any activities that require concentration such as cellular phone, television and computer use and video games.

Some individuals may progress rapidly while others, especially those with eye tracking deficits, will progress more slowly back to full school participation. Students may participate in school with mild symptoms, but school participation should not make symptoms significantly worse.

A clinical trial included 125 patients, 12-25 years of age, presenting to the ED within 24 hours of sustaining a concussion (Macnow, JAMA Peds 2021, PubMed ID: 34491285). Patients were randomized to the screen time permitted group (n=66, median reported screen time 630 minutes) and the screen time abstinent group (n=59), median reported screen time of 130 minutes) for 48 hours after injury. Patients in the screen time abstinent group had a higher rate of symptom resolution (Post-concussive Symptom Scale Score ≤ 3) over the 10 day study period (Hazard Ratio: 0.51, 95% CI (0.29, 0.90)) and a significantly lower median time to recovery (3.0 days vs 3.5 days). The primary limitations are reliance on self-reporting and that only 36% of patient completed all 3 screen time surveys.

ACADEMIC ACCOMMODATIONS
Gradual return on modified schedule (leave of absence, half day, late arrival etc.)
Supervised breaks as needed in a quiet place
Preprinted teacher's notes
Additional time for assignments
Excuse nonessential work (don't add make-up work and new work)
Additional help and tutoring as needed
No testing until tolerating a full day then untimed testing

RETURN TO PLAY: After completing "Return to Learn" protocol, the "Return to Play" recommendations can be initiated. This first step in process should not begin until the patient is asymptomatic and not taking any medications that may mask symptoms. Medications that are safe in the treatment of concussion are acetaminophen and non-steroidal anti-inflammatory drugs.
The return to play plan may need to be prolonged for young children and those with risk factors for prolonged symptoms. Children who are not given adequate time to rest and heal after injury are much more likely to have prolonged symptoms (post-concussion syndrome).

Second impact syndrome is a rare but dangerous condition in which an athlete who has not completely recovered from concussion returns to play and suffers a second head injury. This results in massive swelling in the brain, and in severe cases, herniation and death.

The consensus statement on concussion in sport (October 2016), (Brit J Sports Med 2017, PubMed ID: 28446457) makes the following statement regarding rest after concussion: "The basis for recommending physical and cognitive rest is that rest may ease discomfort during the acute recovery period by mitigating post-concussion symptoms and/or that rest may promote recovery by minimizing brain energy demands following concussion. There is currently insufficient evidence that prescribing complete rest achieves these objectives. After a brief period of rest during the acute phase (24-48 hours) after injury, patients can be encouraged to become gradually and progressively more active while staying below their cognitive and physical symptom-exacerbation thresholds (i.e., activity level should not bring on or worsen their symptoms). It is reasonable for athletes to avoid vigorous exertion while they are recovering. The exact amount and duration of rest is not yet well defined in the literature and requires further study."

A clinical trial pediatric patients (n=88) with acute concussion randomized patients to "strict rest" for 5 days and "usual care" defined as 1-2 days of rest and then a gradual return to activities. (Thomas, Pediatrics 2015, PubMed ID: 25560444). The strict rest group reported more daily post-concussive symptoms and slower symptom resolution. There was no difference in neurocognitive or balance outcomes.

A prospective, multicenter cohort study including 2,413 pediatric participants with concussion was designed to determine the association of early return to physical activity (< 7 days) on the rate of persistent post-concussive symptoms at 7 and 28 days' post injury (Grool, JAMA 2016, PubMed ID: 27997652). Early physical activity was associated with lower risk of persistent symptoms (28.7%) compared to those with no physical activity (40.1%)(Risk Difference: 11.4%, 95% CI (5.8, 16.9%)). It is important to note that this is an observational study and that those returning early to physical activity may be those who were less symptomatic though propensity scoring was utilized to account for these differences.

A clinical trial including randomized 113 adolescents with a sports related concussion to sub-symptoms threshold daily aerobic exercise daily for up to 20 minutes or a prescribed daily stretching program (Leddy, JAMA Pediatrics 2019, PubMed ID: 30715132). The median time to recovery was shorter in the sub-symptom threshold aerobic exercise group (13 days, IQR (10, 18.5 days) than in the placebo-stretching group (17 days, IQR (13, 23 days). The authors also report a statistically significant difference with lower daily symptom severity scores over time in the aerobic exercise group. Finally, the rate of delayed recovery (> 30 days) was higher in the stretching group (n=7, median 58 days, IQR (36, 62 days) compared to the aerobic exercise group (n=2, median 50 days, IQR (46, 54 days) though this difference was not statistically significant.

RETURN TO PLAY GUIDELINES		
PHASE	REHABILITATION	FUNCTIONAL EXERCISE
1	No activity	Complete physical and cognitive rest
2	Light aerobic activity	Walking, swimming, stationary bicycle
3	Sport specific	Running drills in soccer
4	Non-contact	More complex drills, may start resistance training
5	Full contact practice	With medical clearance, normal training activities
6	Return to play	Normal game play

- Should not return to play the same day as the injury.
- Must be medically cleared prior to initiating the plan.
- Must be symptom free before progressing to the next stage.
- If symptoms are experienced, rest until resolved and then return to previous stage.
- If symptoms persist for more than 24 hours should contact physician

DISPOSITION

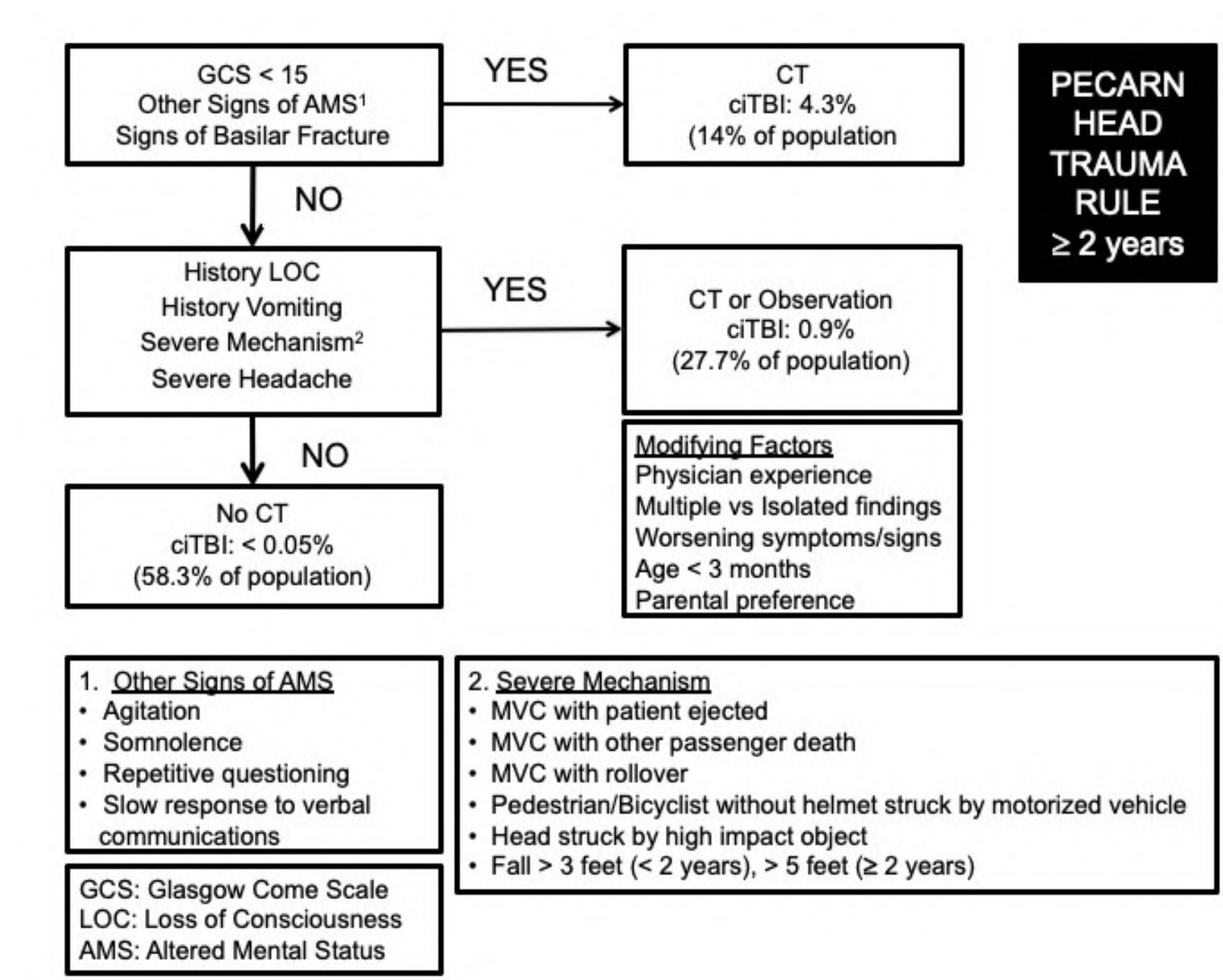
A number of valuable resources for patients and their families are available on the CDC Head Up for Youth Sports Site. Introduction of a standardized ACE discharge instruction instrument improved the rate of patient follow up and adherence to recommendations (Zuckerbraun et al. Pediatrics 2014, PubMed ID: 24616361).The CDC Acute Concussion Evaluation (ACE) Care Plan can be used as discharge instructions.

DISCHARGE INSTRUCTIONS
Warning signs of more serious injury
Description of injury and expected course of symptoms and recovery
Instructions on how to monitor post concussive symptoms
Management of cognitive and physical activity/rest
Instructions regarding return to play/recreation and school
Clear clinician follow-up instructions

INDICATIONS FOR REFERRAL TO A CONCUSSION SPECIALIST
The symptoms worsen at any time
The symptoms have not gone away after 10-14 days
Patient has a history of multiple concussions
Patient has a history of risk factors for prolonged recovery: Migraines, depression, mood disorders, anxiety, learning disabilities, ADHD

APPENDIX A: PECARN HEAD TRAUMA RULE (≥ 2 YEARS)

(Kupperman et al, Lancet 2009 PubMed ID: 19758692)



APPENDIX B: CDC MANAGEMENT RECOMMENDATIONS (2018)

CDC: CONCUSSION MANAGEMENT RECOMMENDATIONS 2018*	
13A	Observe more restrictive physical and cognitive activity during the first several days after mild traumatic brain injury (mTBI)
13B	Resume a gradual schedule of activity that does not exacerbate symptoms.
13C	Offer an active rehabilitation program of progressive reintroduction of non-contact aerobic activity that does not exacerbate symptoms,
13D	Return to full activity when return to premorbid performance if they have remained symptom free at rest and with increasing levels of physical exertion
14	Assess the extent and types of social support (emotional, informational, instrumental, and appraisal) available to children with mTBI
15A	Should counsel the student and family regarding the process of gradually increasing the duration and intensity of academic activities as tolerated
15B	Return-to-school protocols should be customized based on the severity of post- concussion symptoms in children
15C	If prolonged symptoms that interfere with academic performance, school-based teams should determine the student's need for additional educational supports
15D	Post-concussion symptoms and academic progress should be monitored by the student, family, health care professionals, and school teams
15E	The provision of educational supports should be monitored and adjusted until the student's has returned to preinjury levels
15F	For prolonged symptoms and academic difficulties despite an active treatment approach, should refer for a formal evaluation by a specialist in pediatric mTBI.
16A	In the ED should consider a head CT in children with severe headache, when associated with other risk factors and worsening headache
16B	Children undergoing observation periods for headache with acutely worsening symptoms should undergo emergent neuroimaging
16C	Should offer nonopioid analgesia (Ibuprofen or Acetaminophen) for headache
16D	Should not administer 3% hypertonic saline
16E	Refer children with chronic headache after mTBI for multidisciplinary evaluation and treatment, with consideration of analgesic overuse as a contributory factor
17	Refer children with subjective or objective evidence of persistent vestibulo-oculomotor dysfunction to a program of vestibular rehabilitation
18A	Should provide guidance on proper sleep hygiene methods
18B	If sleep problems emerge/continue despite appropriate sleep hygiene measures, may refer children with mTBI to a sleep disorder specialist
*CDC, JAMA Pediatrics 2018, PubMed: 30193284 (Only ED Relevant Recommendations Included)	

DENTAL AND ORAL TRAUMA

INTRODUCTION (JOANNE AGNANT, M.D., 1/2023)
Dental emergencies are relatively common in the emergency department. Every year, up to 50% children will sustain a dental injury. Patients continue to seek care from the ED because 1. dental problems exist in the context of other injuries, 2. lack of access to after-hours dental care, and 3. assumed cost of dental care. In light of this, ED physicians must know what complaints require urgent dental consultation, outpatient referral, or expectant management.

Dental assessment involves a rapid assessment and stabilization of the airway, breathing and circulation. It is important to ensure airway patency. The most common cause of airway obstruction in a child with facial injuries is the accumulation of blood in the oral cavity and pharynx. Check for possible tooth aspiration. A fractured mandible may cause tongue to fall posteriorly and create obstruction. It is important to achieve hemostasis. Important historical features include: time of trauma, immunization history and endocarditis risk factors. See also: PEM Guide: Trauma: Facial Fractures (for a review of mandibular and maxillary fractures)

CLINICAL EVALUATION

EXTRA-ORAL EXAMINATION
INSPECTION
Symmetry of the face
Swelling, color, quality of skin
Lacerations, hematomas, ecchymosis, foreign bodies, or ulcerations
Mandibular deviation
Lip competency
PALPATION
Palpation of TMJs: equal movement of both sides without major deviations
Infra-orbital rims palpated to ensure continuity to inner canthus of eye
Palpate zygoma to nose for crepitus, mobility or depression
Examine the mandible for discontinuity, mobility, swelling, or point tenderness
Examine the maxilla for discontinuity, mobility, swelling, or point tenderness
Assess for paresthesias/numbness, of lips, nose, and cheeks

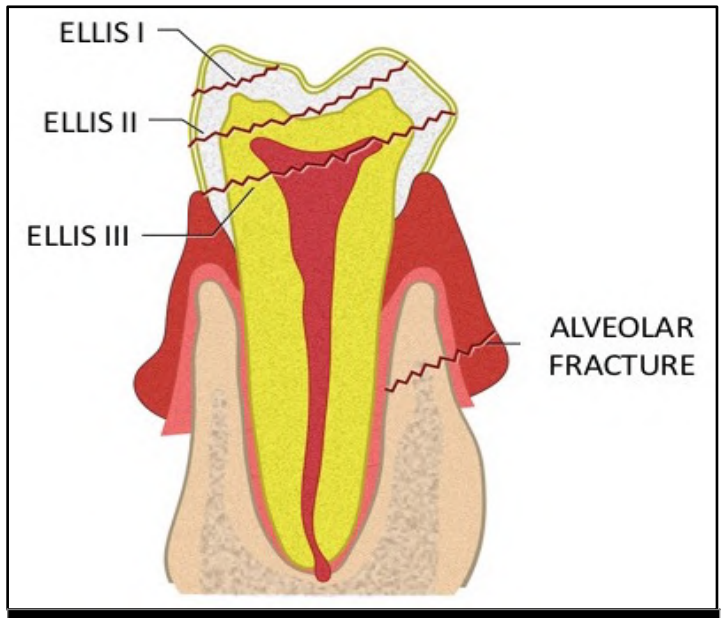
TRAUMATIC DENTAL INJURIES
Management of dentoalveolar trauma depends on the extent of tooth and alveolar involvement, the degree of development of the apex of the tooth, and the age of the patient. In injuries in younger patients, especially those who are <12 years of age, the pulp of the anterior teeth is quite large and dental fractures involving the pulp are common. Fortunately, in this age group, the apex of the root also is usually incompletely formed, providing for greater pulpal regenerative capability. With age, more dentin is formed. Thus, in older patients, the pulp chamber may be very small and pulpal exposure highly unlikely. Involvement of the root of the tooth compromises the attachment apparatus (periodontal ligament) and makes it difficult to restore the tooth to function.

INTRA-ORAL EXAMINATION
INSPECTION
Lips, gingiva, buccal mucosa, floor of the mouth, tongue, and palate
Hematomas or mucosal ecchymoses: suggestive of mandibular fracture
Malocclusion: traumatically displaced teeth, mandible fracture
PALPATION
Alveolar ridge: all 4 quadrants (swelling, discontinuity, or mobility)
Palate: swelling or tenderness
Masseter muscle
Tongue: dorsal, ventral, & lateral surfaces and floor of mouth
Teeth-mobility, tenderness to percussion, fracture

Fracture class can be identified by the patient's symptoms and visualization of exposed dentin, which is a creamy yellow color compared with the whiter enamel. The thickness of remaining dentin determines the rate of pulpal contamination. Greater than 2 mm of remaining dentin is felt to offer some protection to the pulpal tissue. Microorganism contamination of the pulp, oral irritants, or desiccation from mouth breathing initiates an inflammatory process in the pulpal tissue. A delay in treatment increases the likelihood of pulpal necrosis and likelihood of infection.

The exposed dentin should be covered to decrease pulpal contamination. A glass ionomer dental cement can be applied to the dried exposed dentin. Referral to a dentist within 24 hours is mandatory to best ensure tooth vitality.

Careful attention should be paid to identifying fractures of



ELLIS FRACTURES

ELLIS CLASS DENTAL FRACTURES			
CLASS I	CLASS II (70%)	CLASS III	ALVEOLAR/ROOT
Enamel only	Dentin exposed	Pulp exposed	Coronal segment may be displaced/mobile
Non-sensitive	Sensitivity to hot/cold	Painful Bleeding from core of tooth	Tenderness to percussion
Non-emergent; can smooth sharp corners	Place dressing over exposed dentin for thermal & chemical insulation	Immediate treatment needed to avoid pulpal necrosis	Immediate dental for XRAY, reduction and splinting
Referral to dentist for aesthetic repair	Dentist within 24-48 hours Save fragment in water for possible bonding	Oral analgesics; Definitive Rx: root canal or tooth extraction Monitor for abscess	Upper 1/3 (Apical): Monitor Lower 2/3: Extraction

the root as they can be clinically obscure. Dental radiographs from several angles may be necessary to identify these fractures. Healing of stabilized root fractures has been reported; thus, current recommendations are to reposition the coronal segment to its original position, confirm that position by radiograph and then stabilize with a flexible splint (See Appendix: Dental Splinting). Referral to a dentist within 24 hours is essential as splinting for a minimum of 4 weeks is required.

Avulsion of a primary tooth in a child does not require repair. If an adult tooth is avulsed it should be rinsed but not scrubbed and then should be transported in Hanks balanced salt solution (e.g. Save-a-Tooth) or milk. In an older, cooperative child it may be replaced in the socket. Alternatively, in can be placed under the parents tongue. Dental XRAYS may be required to identify an alveolar fracture.

SOFT TISSUE LACERATIONS

The soft tissues, which include, the tongue, lips, and gingiva are highly vascular. Most bleeding will stop with direct pressure and, if not, careful suturing. One must clean, debride, and examine the oral mucosa for foreign bodies. Occasionally, dental XRAYs may be indicated. A mandible CT is indicated if a mandibular fracture is suspected. Suspicion of a maxillary fracture (Le Fort classification) requires a facial CT.

In general, most intraoral mucosal lacerations will heal by themselves; however, they should be repaired if they are gaping (typically wider than 2 cm) or if flaps are present.

PERIODONTAL INJURIES					
CONCUSSION	SUBLUXATION	LATERAL LUXATION	INTRUSION	EXTRUSION	AVULSION
No displacement No mobility	Angled forward or backward +/- mobility	Angled laterally +/- mobility	Displaced into socket +/- mobility	Displaced incompletely out of socket +/- mobility	Displaced completely out of socket
Percussion sensitive	Percussion sensitive +/- Malocclusion		May not be visible (false appearance of avulsion)		Missing tooth
Non-emergent; NSAIDS Soft Diet	NSAIDS, soft diet	Realign & immobilize w/ splint asap	Rx: Extract vs spontaneous re-eruption		Re-implant avulsed permanent teeth ASAP Best if 15-30m
Dental referral Good prognosis	Dental Follow-up Dental consult for possible immobilization Monitor for pulp necrosis	Firm, gentle pressure usually will reposition tooth Dental consult or referral within 24 hours Monitor for pulp necrosis	Primary tooth: Dental F/U for imaging of the proximal tooth. Permanent tooth: Urgent follow-up. Monitor for pulp necrosis	Primary tooth: Extract if aspiration risk Permanent tooth: Emergent dental for splinting Monitor for pulp necrosis	Primary tooth: Do not replace Permanent tooth: Rinse gently replace immediately Dentist for immobilization

LIP LACERATIONS

Lip lacerations are a potential cosmetic problem. Careful closure is essential in lacerations involving the vermilion border. Alignment of the border is important and the border should be sutured first. The portion of the laceration extraoral to the wet–dry line of the lip and involving the skin of the face should be closed with 6-0 non-resorbable monofilament. Because of the musculature of the lips, any deep laceration requires closure of the deep layers using a 4-0 or 5-0 resorbable suture material to decrease the likelihood of the wound edges opening on removal of the suture.

As with any laceration involving the face or other aesthetic areas, sutures should be removed as early as possible, generally in 3-5 days, to decrease iatrogenic scarring from the suture material. Careful daily cleansing of the wound and application of a triple-antibiotic ointment makes suture removal easier and improves the aesthetic results. Controversy concerning closure of through-and-through lip laceration exists. Some advocate leaving the intraoral portion of the laceration open. Others advocate that mucosal lacerations greater than1 cm be repaired. Generally, the intraoral component should be repaired first, and then, the extraoral laceration should be cleansed and irrigated aggressively. Prophylactic antibiotics such as penicillin are typically indicated.

TONGUE LACERATIONS
Control bleeding with pressure and gauze.
Small lacerations with good approximation do not require repair.
Close if: they gape widely, actively bleed, are flap-shaped or penetrate through the tongue
Tongue lacerations may be repaired with 4-0 absorbable sutures
Topical anesthesia or regional blocks can be used (i.e. lingual block)
A bite block may be useful to prevent bites to health care providers
Procedural sedation may be required for an uncooperative patient

EMERGENT DENTAL/ORAL SURGERY CONSULT
Avulsed permanent teeth for splinting
Lateral luxation with malocclusion
Extrusion > 3 mm
Ellis III fractures
Alveolar ridge fractures
Root fractures

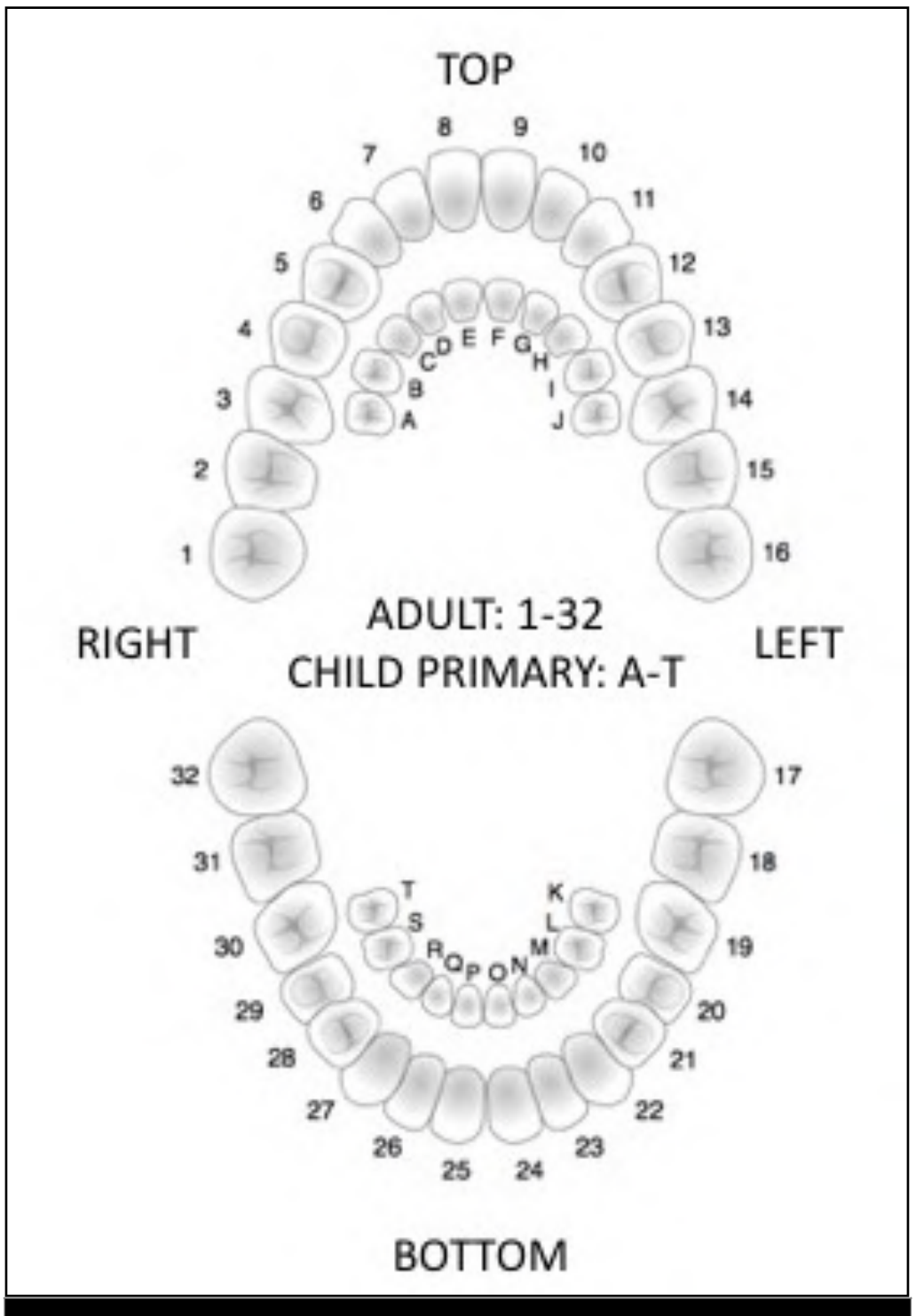
DENTAL PROCEDURE EQUIPMENT
Cement liquid & powder
Cheek retractor
Topical anesthetic: Orabase/Benzocaine
Syringe 25 & 18 in
Lidocaine (local)/Bupivacaine
Cotton rolls/gauze/
Q-tips/tongue blades
Saline flush; Flex suction tip
Hank’s solution/EMT tooth saver
Laminated mixing paper
Base & catalyst

APPENDIX: DENTAL SPLINTING

EMERGENCY DENTAL SPLINTING: PERIODONTAL PASTE PROCEDURE	
Definition	Tooth is stabilized and supported by attaching it to uninjured neighboring teeth
	Promotes regeneration of the periodontal ligaments avoiding fusion of the tooth and alveolar bone (ankylosis)
	Promotes regeneration of cementum, the calcified coating of the teeth, that is required for viability
Indications	Reimplantation of avulsed permanent teeth, repositioned luxated or extruded teeth, crown-root fractures, alveolar fractures
Contra-indications	Injured primary teeth Permanent teeth with minimal instability
Types	a. Periodontal pastes (most common, simplest) b. Composite adhered mesh ribbons c. Wire composite splints
Procedure	1. Clean and dry the injured tooth, adjacent teeth and gingiva (or the paste will not stick)
	2. Position the injured tooth in anatomic position
	3. Mix equal amounts of the periodontal base and catalyst with a tongue depressor for 30-60 seconds until it thickens
	4. Scoop up the mixed paste with a tongue depressor and submerge it in a basin with water
	5. With wet gloves (to avoid sticking), role the paste in to a ribbon shape
	6. Apply the mixed periodontal paste to the anterior of the injured and adjacent teeth and gingiva. Work the paste into the spaces between the teeth.
	7. It may be necessary to apply the paste to the posterior surface of the teeth to improve stability for some injuries
	8. Avoid getting the paste over the occlusal or biting surface of the tooth
Follow-up Care	Follow up with a dentist within 24 hours
	Oral antibiotics (a primary complication is infection)
	Soft diet
VIDEO LINK: DENTAL SPLINTING	

APPENDIX: TOOTH NUMBERING

PERMANENT TOOTH ERUPTIONS	
Central Incisors	7-8 years
Lateral Incisors	8-9 years
Cuspids	11-12 years
Bicuspids	10-11 years
Second Bicuspids	10-12 years
First Molars	6-7 years
Second Molars	12-13 years
Third Molars	17-21 years



PRIMARY AND ADULT TEETH

EXTENDED FAST EXAM

(FOCUSED ABDOMINAL SONOGRAPHY IN TRAUMA)

INTRODUCTION (DAVID KESSLER, M.D., 12/2018)

Focused abdominal sonography for trauma (FAST) was one of the earliest applications of point of care ultrasound in the emergency department setting and remains one of the most common bedside studies performed with ultrasound. It is typically utilized in the trauma setting to help identify certain types of internal bleeding. Blood in the abdominal compartment (hemoperitoneum) or pericardial space (hemopericardium) appears anechoic or black on ultrasound. In the extended FAST exam examination, assessment of pneumothorax and hemothorax are included. The FAST exam is typically performed at the end of the primary survey. See: PEM Guide: Trauma: Trauma Primary Survey, PEM Guide: Trauma: Abdominal Trauma Overview)

FAST: BENEFITS
Non-invasive
Uses no ionizing radiation
Can be performed in unstable patient (who can't be transported to CT)
Can be repeated multiple times
Children are easier to image than adults
FAST: CAUTIONS
A negative FAST does not rule out intra-abdominal injury. Repeat if high clinical suspicion
Children are more likely than adults to have solid organ injury without bleeding
At least 250 ml of is blood required before it is apparent on ultrasound
Clotted blood (1-4 hours) is of variable echogenicity
Free fluid does not necessarily indicate blood, e.g. ascites, ruptured cyst
Does not identify bowel, diaphragm or retroperitoneal injuries
Might not change management, regardless of findings
Low grade injuries (I or II) are usually managed conservatively, even with bleeding
More severe injuries are usually managed with embolization, necessitating CT

PERFORMANCE

The test performance of the FAST exam in pediatrics has been variable. The test performance is dependent on user training and experience. In addition, the FAST examination is subject to spectrum bias. A population with a large amount of blood will have a higher sensitivity than a population with less blood.

A 2018 Cochrane meta-analysis including 1,384 children from 10 studies founds a pooled sensitivity for point of care sonography of 62%, 95% CI (47, 75%) and specificity of 91%, 95% CI (81, 96%). In contrast, in 8,635 adults from 34 studies the pooled sensitivity was 74%, 95% CI (65, 81%) and specificity of 96% (94, 98%). The authors concluded that "with regard to abdominal trauma, a negative point of care sonography exam does not rule out injuries and must be verified by a reference test such as CT. This is of particular importance in pediatric trauma, where the sensitivity of point of care sonography is poor" (Stengel, Cochrane Database Syst Rev. 2018, PubMed ID: 30548249).

The clinical utility of FAST in children is debated. A multicenter study at 14 level I pediatric trauma centers (Calder, J Trauma Acute Care Surg. 2017, PubMed ID: 28590347). included 2,188 children less than 16 hears of age. The test characteristics are presented in the table below.

TEST CHARACTERISTICS: PATIENTS WITH BOTH A FAST AND A CT		
	INTRA-ABDOMINAL INJURY	INTRA-ABDOMINAL INJURY REQUIRING INTERVENTION
Prevalence	28.5%	7.9%
Sensitivity	27.8% (19.9, 37.5%)	44.4% (27.6, 62.7%)
Specificity	91.4% (87.2, 94.3%)	88.5% (84.5, 91.6%)
Predictive Value (+) Test	56.3% (42.3, 69.3%)	25.0% (14.9, 38.8%)
Predictive Value (-) Test	76% (70.8, 80.6%)	94.9% (91.7, 96.9%)
Likelihood Ratio (+) Test	3.2 (1.9, 5.4)	3.86 (2.29, 6.51)
Likelihood Ratio (-) Test	0.79 (0.69, 0.90)	0.63 (0.45, 0.88)

A randomized trial including 925 hemodynamically stable children at a single level I pediatric trauma center compared FAST exam to “standard care”. There was no difference in the primary outcome of CT utilization (FAST: 52.4%, Standard Care: 54.6%, Risk Difference: -2.2, 95% CI (- 8.7, 4.2%), Holmes, JAMA 2017, PubMed ID: 28609532). 44.8% of patients with a negative FAST exam had a CT. Indications for CT were not provided. There was also no difference between the two groups in the secondary outcomes of the rate of laparotomy, admission or admission to the ICU.

Data suggests that the FAST it is much more accurate in hypotensive or otherwise symptomatic patients. For example, a hemodynamically unstable patient with a grossly positive FAST exam could go straight to laparotomy, bypassing CT. The utility of the FAST examination in hemodynamically stable pediatric patients remains unclear.

INDICATIONS
Need for urgent evaluation of blunt or penetrating trauma patient where rapid determination of intra-abdominal bleeding or pneumothorax is needed
May be used to re-evaluate a trauma patient serially

CONTRAINDICATIONS
The primary survey should precede the FAST examination
The FAST exam should not delay definitive diagnostic or therapeutic interventions

EQUIPMENT
Ultrasound machine, preferably with curvilinear, mid or lower frequency probe (for better penetration), ultrasound gel.

COMPLICATIONS
Incorrect diagnosis. False positive results leading to overuse of CT scans. False negative results leading to a delay in injury identification and definitive care.

E-FAST QUESTIONS
Hemopericardium?
Hemoperitoneum?
Hemothorax?
Pneumothorax?
ANSWERS: Yes, No, Indeterminate

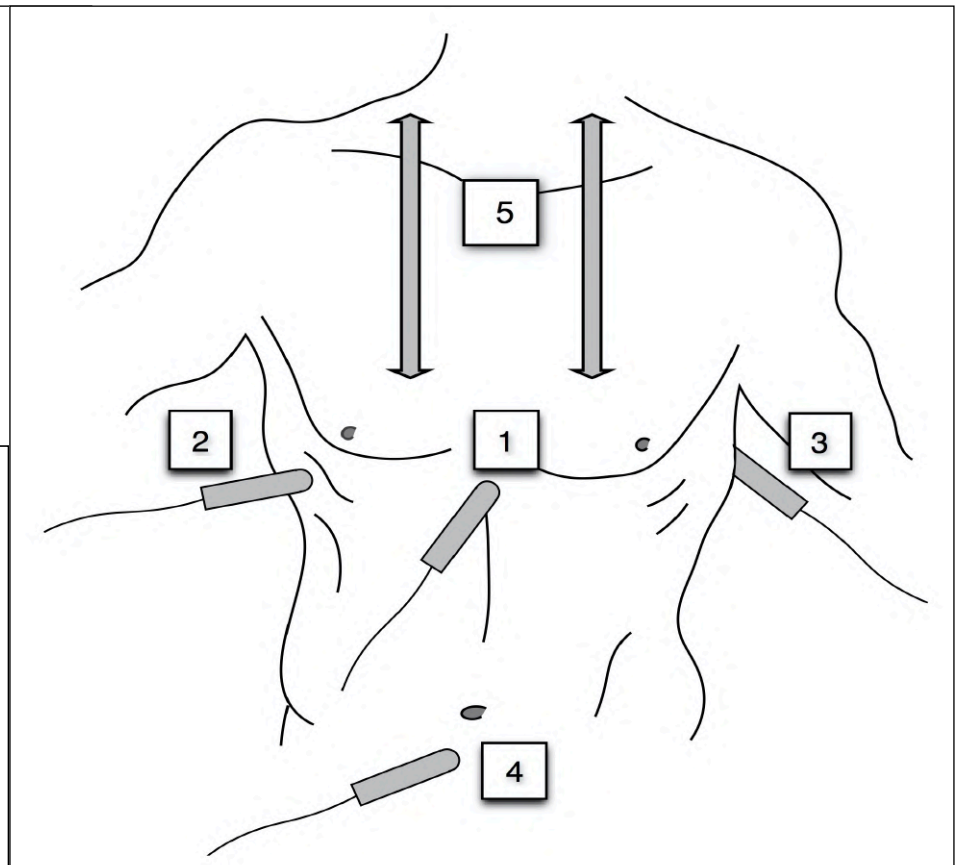
APPROACH

1. There are 4 views for the standard FAST exam, and many recommend an extended FAST or “E-FAST” that also involves examining the lung for pneumo/hemothorax.
2. Some start with the sub-xiphoid view because it is the most immediately life threatening if hemopericardium is detected. This is also the most sensitive view (will be positive with the least amount of blood).
3. The most common site of blood in adults is the right upper quadrant view (Morrison’s pouch). In children, the pelvic/bladder view is more commonly positive.
4. Trendelenburg position (head down, feet up) will improve visualization in the RUQ and LUQ. Reverse Trendelenburg position (head up, feet down) will improve visualization in the pelvis.

FAST
1. SUB-XIPHOID* (CARDIAC)
2. MORRISON’S POUCH (RUQ)
3. SPLENO-RENAL RECESS (LUQ)
4. SUPRAPUBIC (PELVIS)

*ALTERNATE: PARASTERNAL LONG AXIS

EXTENDED FAST: ABOVE WITH
5. EVALUATION FOR LUNG SLIDING (EVIDENCE OF PNEUMOTHORAX



PROBE PLACEMENT

1. SUB-XIPHOID VIEW (CARDIAC)

1A. SUB-XIPHOID VIEW (CARDIAC)

Subxiphoid view with marker dot to the right and probe at 15 degrees to the plane of the patient (parallel to the abdominal wall). Angle towards the right shoulder

Use the liver as a sonographic window to visualize the heart. If there is a lot of stomach or bowel gas, move the probe slightly to the right in order to use more of the liver as acoustic window.

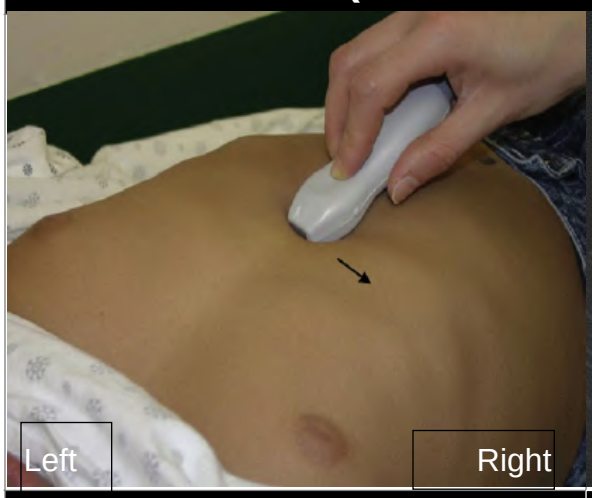
Cardiac tamponade: right ventricular collapse

1B. PARASTERNAL LONG AXIS VIEW (CARDIAC): ALTERNATIVE

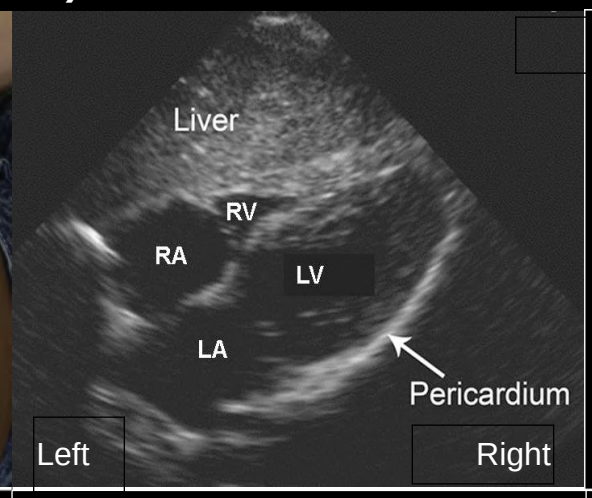
The transducer is placed just lateral to the sternum at the 3-4th intercostal space and is oriented with the probe marker toward the patient's left hip/right shoulder (4:00 / 11:00 o'clock position), perpendicular to the patient's chest wall.

Fluid anterior to the transverse aorta indicates pericardial fluid. Posterior to the aorta is pleural fluid

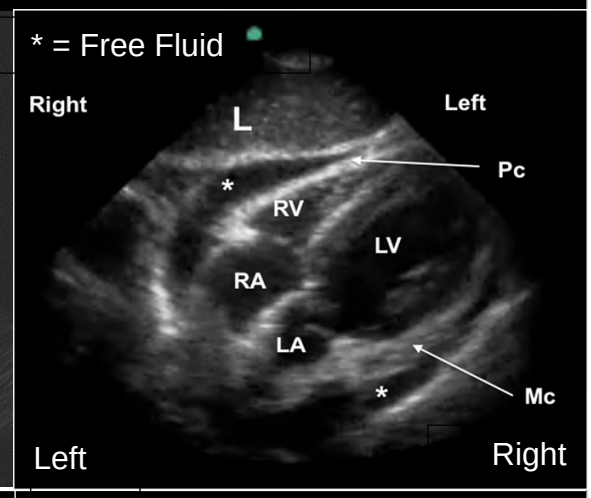
CARDIAC VIEW (SUB-XIPHOID)



POSITION



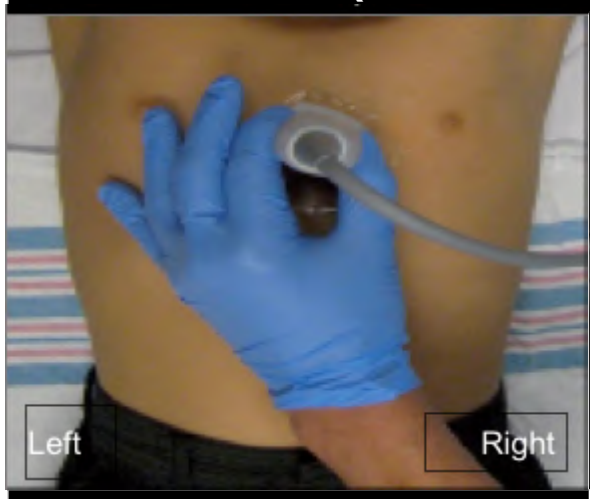
NORMAL



ABNORMAL

VIDEO LINK: SONOSITE: FAST: SUBXIPHOID

CARDIAC VIEW (PARASTERNAL LONG AXIS)



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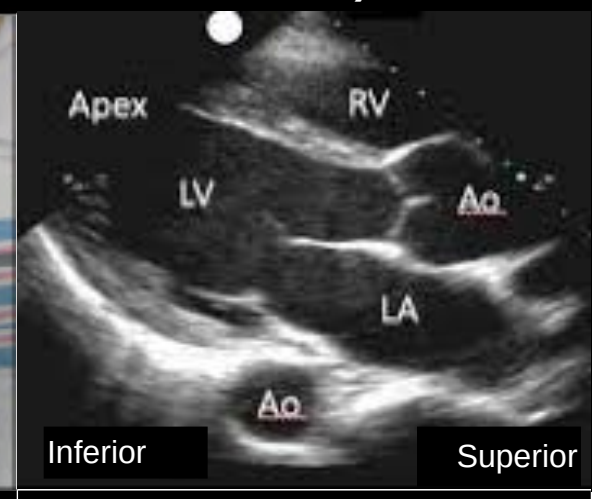
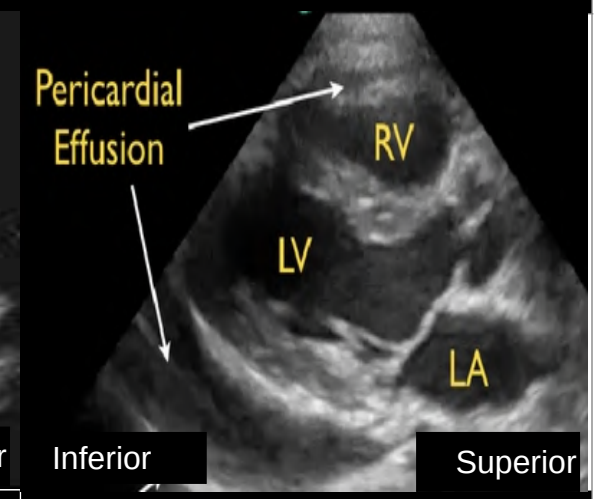


NORMAL



ABNORMAL

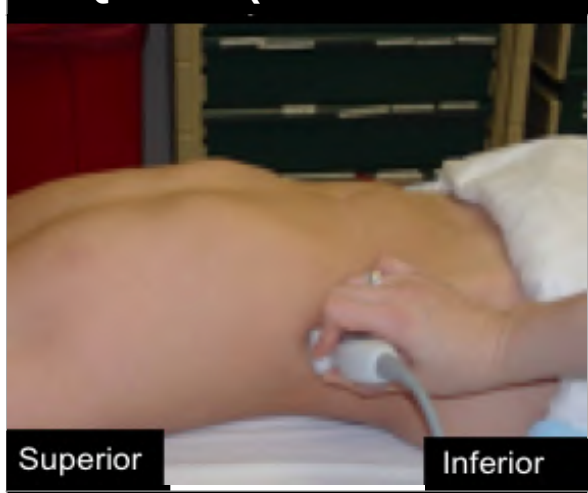
VIDEO LINK: SONOSITE: FAST: PARASTERNAL LONG AXIS VIEW

2. MORRISON’S POUCH (RIGHT UPPER QUADRANT)

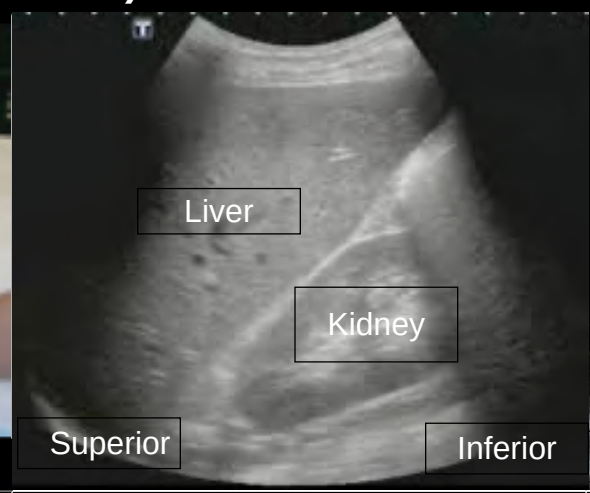
MORRISON’S POUCH (RIGHT UPPER QUADRANT)
Most common location of blood in adults
Positioning Children: Anterior axillary line at the 7-9th intercostal space
Positioning Adults: Mid-axillary line at the 8-10th intercostal space
Trendelenburg position (head down, feet up) may improve visualization. Avoid if suspicion of intracranial injury.
The marker dot oriented toward posterior axillary line (obliquely: between adjacent ribs). This improves visualization of the space above and below the diaphragm and avoids rib shadows.
Rock the probe up and down to visualize the lower pole of the liver and kidney. This is the first location of fluid accumulation as it is the most posterior.
Diaphragm and sub-phrenic space. In the supine position, hemothorax can be detected with a sensitivity and specificity in the high 90’s. May detect as little as 20 ml of fluid (Supine chest XRAY > 175 ml, Upright chest XRAY > 50-100 ml). Positive spine sign above the diaphragm indicates hemothorax. Spine Sign: The vertebra can normally be visualized above the diaphragm. The absence of vertebra above the diaphragm indicates fluid (hemothorax, pleural effusion, pulmonary contusion, severe pneumonia) in the pleural space

VISUALIZE	IDENTIFY
Morrison’s pouch	Hemoperitoneum between liver and kidney
Inferior pole of kidney	Hemoperitoneum
Sub-phrenic space	Hemoperitoneum between diaphragm and liver
Pleural space	Pneumothorax, hemothorax

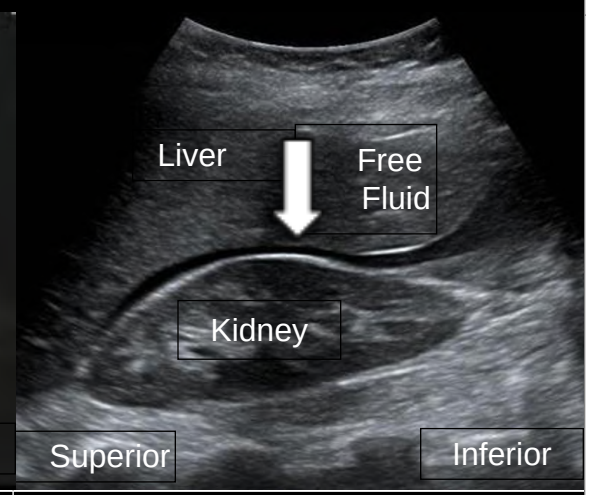
RUQ VIEW (MORRISON’S POUCH)



POSITION



NORMAL



ABNORMAL

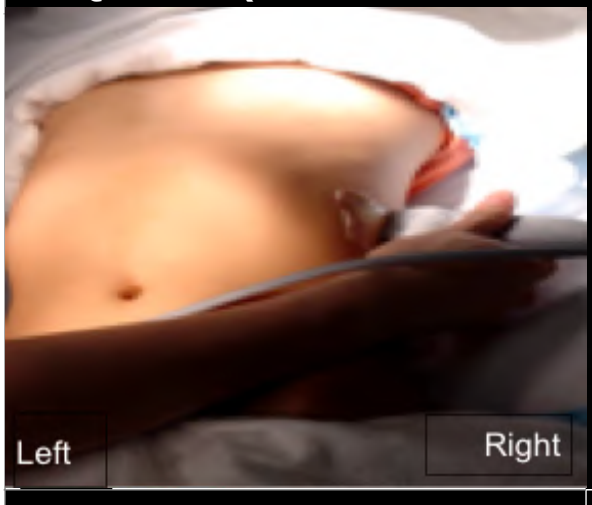
VIDEO LINK: SONOSITE: FAST: RUQ

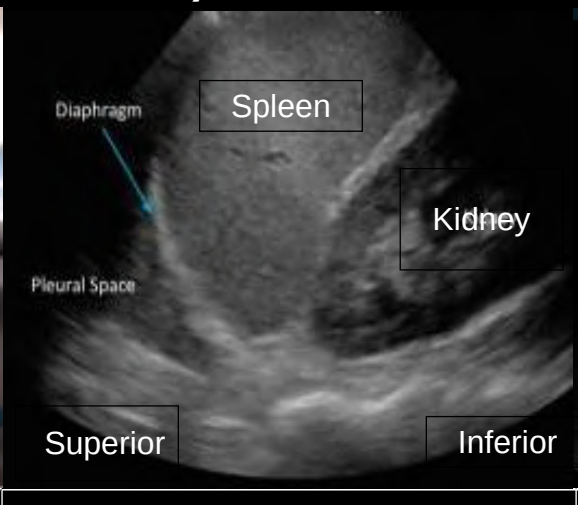
3. SPLENO-RENAL RECESS (LEFT UPPER QUADRANT)

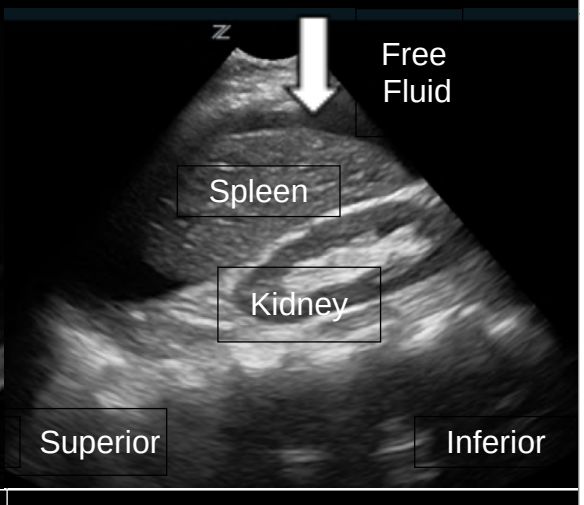
SPLENO-RENAL RECESS (LEFT UPPER QUADRANT)
This is the most difficult view to obtain. The left kidney is higher and more posterior
Positioning Children: 5-7th intercostal space, very posterior (post axillary line)
Positioning Adults: 7-9th intercostal space, very posterior (post axillary line)
In the LUQ view you typically need to hold the probe lower to the table (with your knuckles practically touching the table) and around one to two finger breadths more superiorly than on the right side.
Trendelenburg position (head down, feet up) may improve visualization. Avoid if suspicion of intracranial injury.
May need to move the probe in several intercostal spaces to visualize the entire recess and the diaphragm.
If you cannot visualize the entire sub-phrenic region in LUQ, the study is incomplete and may lead to false negatives.
Blood tends to accumulate in the sub-phrenic area first (due to obstruction from the phrenico-colic ligament) and not in the spleno-renal recess. Always scan the diaphragm.
In adolescents and adults, blood from LUQ will overflow more to the RUQ and R paracolic gutters rather than in the pelvis. Therefore, the RUQ is the most common site for fluid collection with both liver and spleen injury.

VISUALIZE	IDENTIFY
Space between spleen/kidney	Hemoperitoneum
Inferior pole of the kidney	Hemoperitoneum
Sub-phrenic space	Hemoperitoneum between diaphragm and spleen
Pleural space	Pneumothorax, hemothorax

LUQ VIEW (SPLENO-RENAL RECESS)





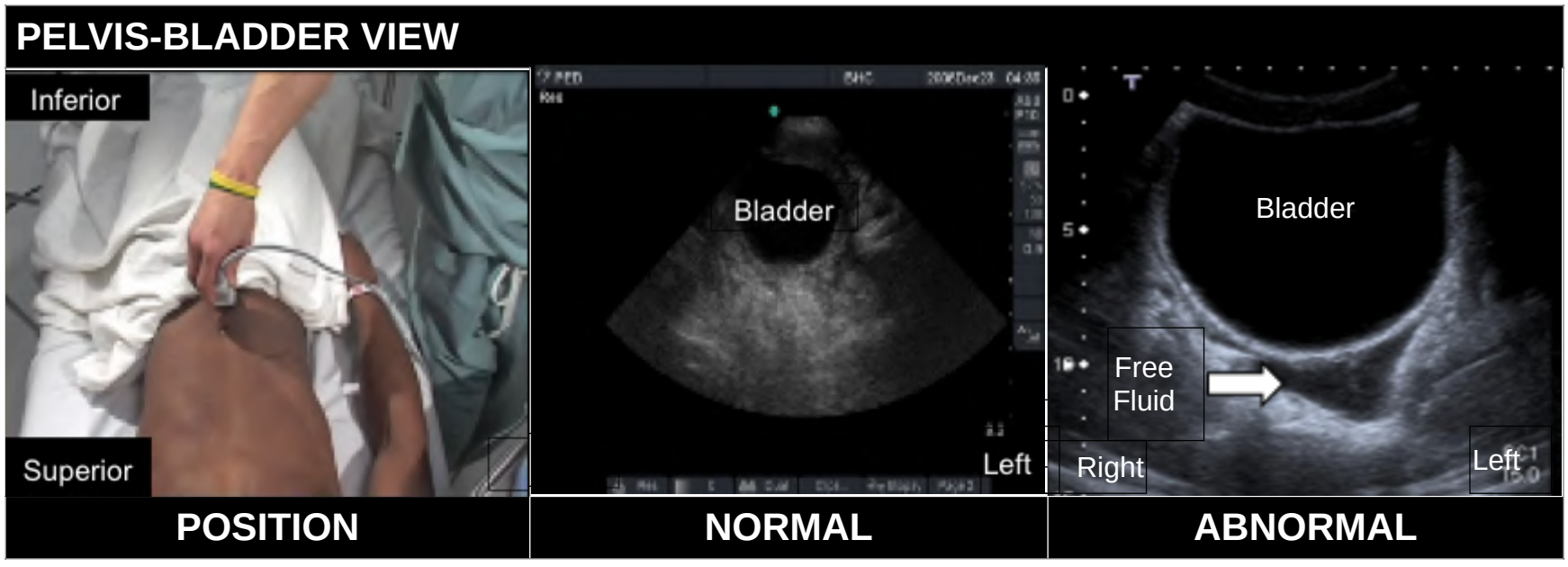


POSITION	NORMAL	ABNORMAL

VIDEO LINK: SONOSITE: FAST: LUQ

4. PELVIS / BLADDER VIEW

PELVIS / BLADDER VIEW
Most common location of fluid in children
Best with urine in the bladder to serve as an acoustic window
A slight reverse Trendelenburg position (head up, feet down) improves visualization
Turn the gain down a bit to see fluid better. Posterior enhancement of fluid filled structures (the bladder in this case) can mask free fluid.
Probe positioning: 1-2 cm above symphysis in both transverse and sagittal views
Sagittal view: Female: Uterus above the bladder, Male: Prostate inferior (to the right on screen).
Transverse view: Scan from superior to inferior looking for free fluid anterior or posterior to the bladder. Both the uterus and prostate (and seminal vesicles) are under the bladder (angle down until you see them). Seminal vesicles can be confused with free fluid. They can be distinguished from fluid because they are only seen on the transverse view and not the sagittal view. If the bladder is over-distended, it may compress the free fluid posteriorly and displace it laterally. Don't forget to look at the sides of the bladder on transverse view. The prostate may be hypoechoic and should not be confused with free fluid.
Location of free fluid. Most common site of free fluid in children. Pouch of Douglas in females. Retro-vesicular pouch in males.



VIDEO LINK: SONOSITE: FAST: PELVIS (MALE)

VIDEO LINK: SONOSITE: FAST: PELVIS (FEMALE)

5. LUNG EXAMINATION FOR PNEUMOTHORAX

Lung ultrasound has been found to be more sensitive (SN 95%, NPV 100%) than chest XRAY in identifying pneumothorax in the supine trauma patient and can be performed rapidly at the bedside.

The probe is place in the midclavicular line oriented in the vertical position with the marker dot to the patient's head.

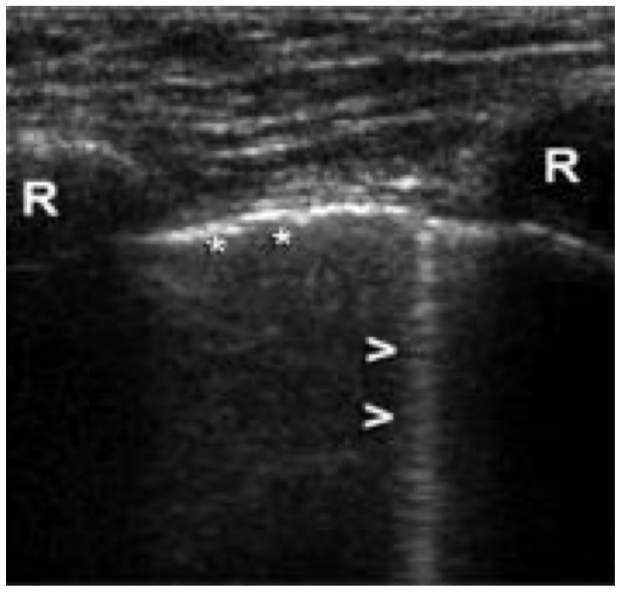
FINDINGS CONSISTENT WITH PNEUMOTHORAX	
1	Absence of lung sliding
2	Absence comet tail artifact (i.e. B lines)
3	Presence of "lung point" sign
4	In m-mode: Absence of the "sandy beach" or "waves on the "beach sign"
5	In m-mode: Presence of the "bar code" or "stratosphere"

Lung sliding indicates that the parietal pleura of the chest wall and visceral pleura of the lungs are contiguous and moving together as the lungs expand and contract with ventilation. This is seen as a moving shimmering white line. The absence of lung sliding may also be seen with apnea, chronic (e.g. fibrosis) or inflammatory pleural adherence (e.g. ARDS), atelectasis and one-lung intubation (absence of lung sliding on side of non-ventilated lung).

The lung point sign occurs when an area of lung sliding is adjacent to an area without lung sliding. This occurs at the junction of normal pleural approximation and a pneumothorax and is typically seen with a small to moderate pneumothorax

Comet tail artifact or B lines are oriented perpendicular to the pleura (due to visceral pleura intralobular septae). They are rare in children. These are absent in the presence of pneumothorax.

COMET TAIL ARTIFACT



R = Rib

* Pleural line

> Comet tail artifact

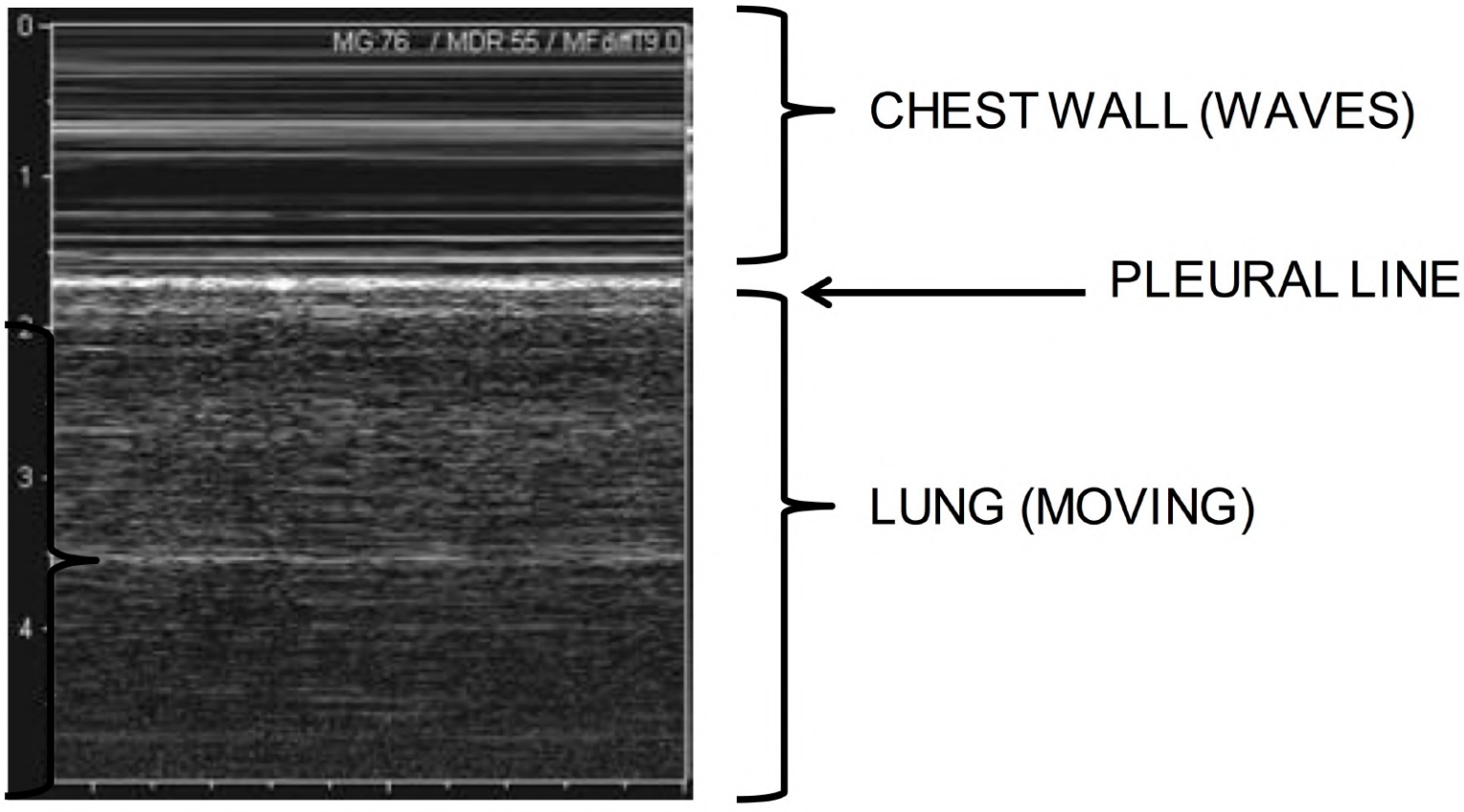
VIDEO LINK: SONOSITE: FAST PNEUMOTHORAX

ESTIMATING PNEUMOTHORAX SIZE	
Small	Lung sliding not visible anteriorly only in supine position
Moderate	Lung Sliding not visible at the mid-axillary line
Large	Lung Sliding not visible at the posterior-axillary line

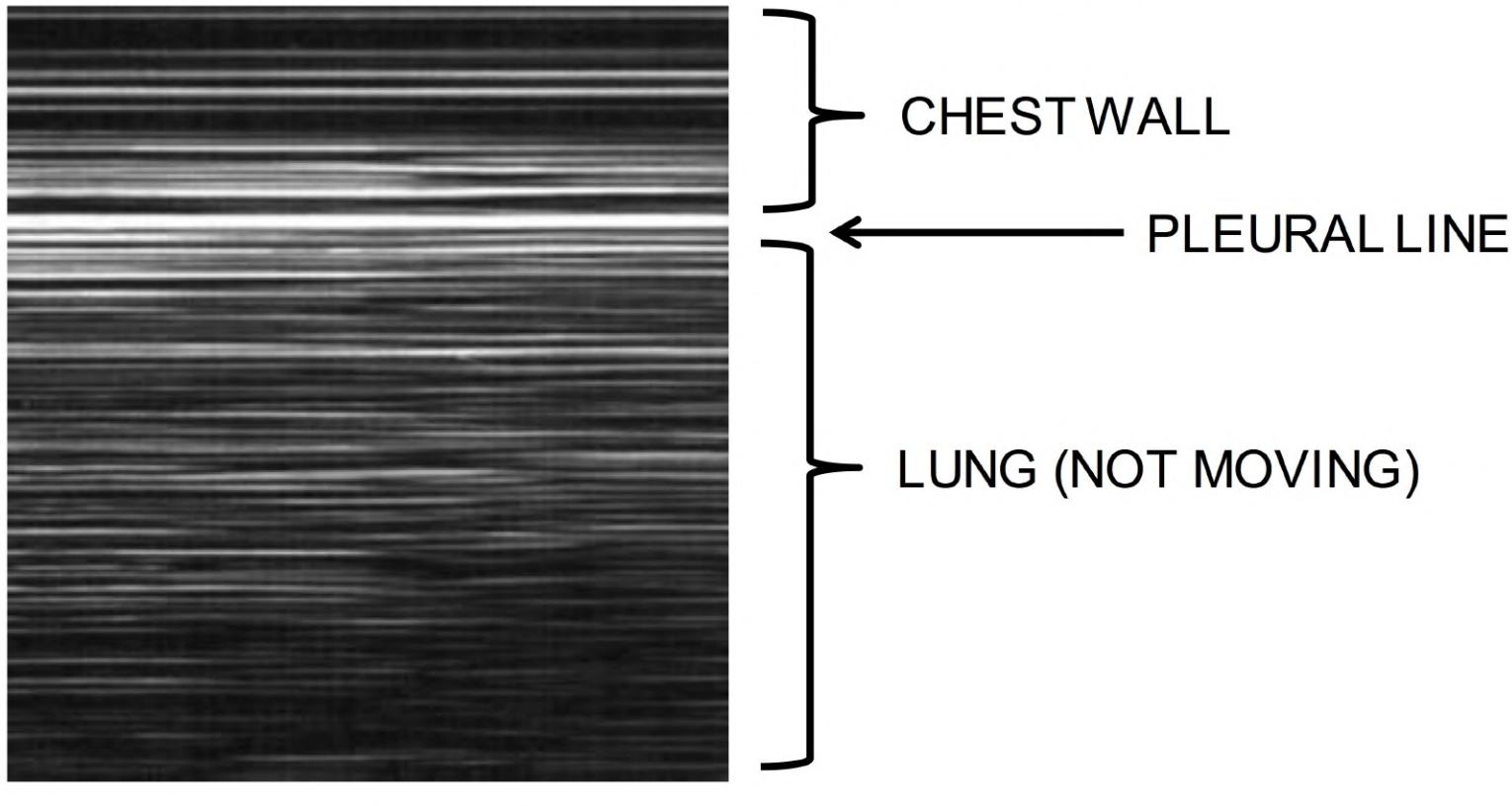
M MODE

In a normal patient, the upper half of the image in m-mode is the non-mobile chest wall and the lower half of the image is the mobile lung. Normal lung sliding will result in a grainy image below (the beach of the sandy beach sign) while the non-mobile chest wall results in a wavy appearance.

WAVY OR SANDY BEACH (NORMAL)

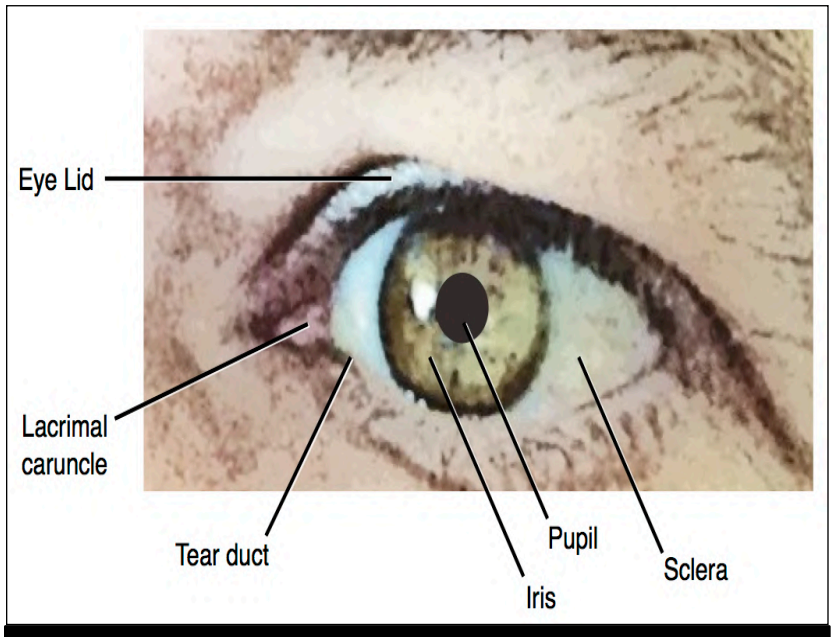


STRATOSHERE SIGN OR BAR CODE (PNEUMOTHORAX)

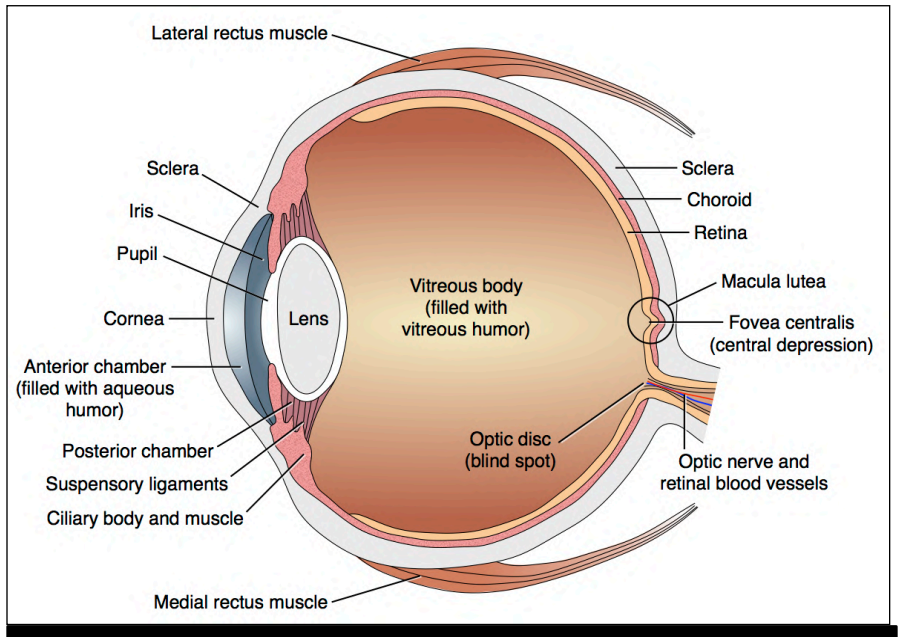


EYE TRAUMA

INTRODUCTION: (JOANNE AGNANT, MD, 8/2020)
Ophthalmologic complaints in the emergency department represent 3% of all visits. The ED physician must be prepared to diagnose and manage eye trauma and determine the need for ophthalmologist consultation. The following will provide the framework for the evaluation and management of common traumatic eye injuries that may be encountered in the pediatric emergency department.



EYE ANATOMY (EXTERNAL)



EYE ANATOMY (CROSS-SECTION)

TRAUMATIC INJURIES TO THE EYE*	
Eyelid lacerations	Lens dislocation
Subconjunctival hemorrhage	Vitreous hemorrhage
Corneal abrasions	Retinal detachment
Foreign body	Globe rupture
Chemical burns	Retrobulbar hemorrhage
Hyphema (aqueous hemorrhage)	Orbital fracture
Traumatic iritis	
*Listed from anterior to posterior anatomically	

MANAGEMENT OF PEDIATRIC EYE TRAUMA: GENERAL PRINCIPLES	
1	Manage life-threatening systemic illness or CNS trauma before eye trauma
2	Ensure the structural integrity of the globe (rule out a ruptured globe)
3	Check the vision in both the injured and uninjured eye.
4	When in doubt, seek ophthalmology consultation.

INITIAL EVALUATION	
HISTORY	PHYSICAL EXAMINATION*
Mechanism: Blunt, penetrating	Eyelids, orbits, surrounding tissue
Visual acuity: Past and present	Anterior: Sclera, cornea, conjunctiva, ant chamber
Pain: Location, severity	Pupils: Shape, size, reactivity
Foreign body sensation	Extraocular movements
Photophobia	Posterior (fundoscopy): Retina, optic discs
Contact lens use (current)	Fluorescein
Visual acuity, visual fields	Slit lamp, intraocular pressure
*Visual acuity in the injured eye should be assessed before proceeding with the rest of the exam. The examination of the eye must be attempted in a stepwise, anatomic approach beginning with inspection of periorbital tissues and eyelids, to the anterior surface of the eye, to the evaluation pupillary reflexes, extra-ocular movements, and fundoscopic exam.	

VIDEO LINK: SLIT LAMP EXAMINATION

CHEMICAL BURNS

When a child has a clear history of a noxious substance coming in contact with the ocular surface, it is important to determine whether the substance is an acid, an alkali, solvents, detergents, or irritants. Alkali injuries tend to be much more severe as they can cause aggressive tissue necrosis. It is also important to determine whether particulate matter may have been deposited on the ocular surface.

Medical management involves immediate ocular lavage, even before visual acuity testing. Ophthalmology consultation can be called while lavage is ongoing.

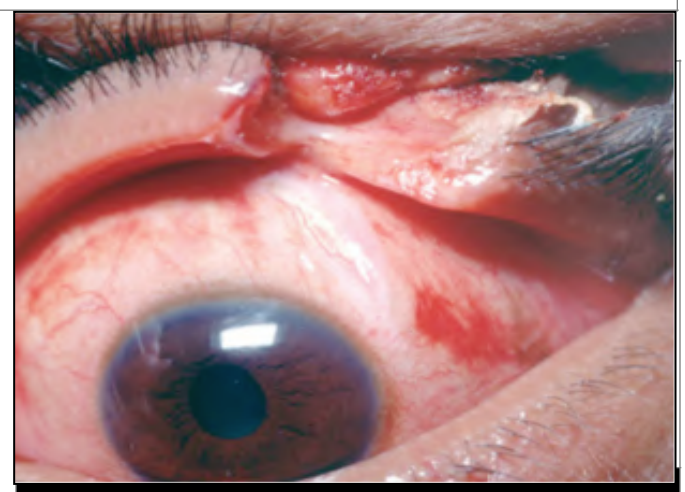
OCULAR LAVAGE	
1	Apply topical anesthetic drops along the medial canthus
2	Particulate matter can be removed with a cotton-tipped sway
3	An irrigation system can be constructed by attaching a saline bag to IV tubing, which attaches to an oxygen nasal cannula. A Morgan lens may also be used, if available
4	Secure the nasal cannula prongs over the patient's nasal bridge
5	Retraction of the upper and lower eyelids will allow for a more thorough inspection
6	Irrigate with normal saline or Ringers lactate for 20-30 min Goal is to irrigate to neutral pH: 7.0 (normal eye pH)

VIDEO LINK: OCULAR LAVAGE

EYELID LACERATIONS

Eyelid lacerations must prompt further evaluation for possible underlying injury to the eye.

A CT scan of orbit should be obtained prior to repair in cases of significant orbital trauma or when a foreign body or a ruptured globe is suspected. Tetanus prophylaxis should be considered.



EYELID LACERATION

EYELID LACERATIONS: INDICATIONS FOR OPHTHALMOLOGY CONSULTATION
Full-thickness perforation of lid
Ptosis
Involvement of lid margin: May interfere with tear retention
Possible damage to tear drainage system (medial canthus)
Tissue avulsion
Globe injury

CORNEAL AND CONJUNCTIVAL INJURY

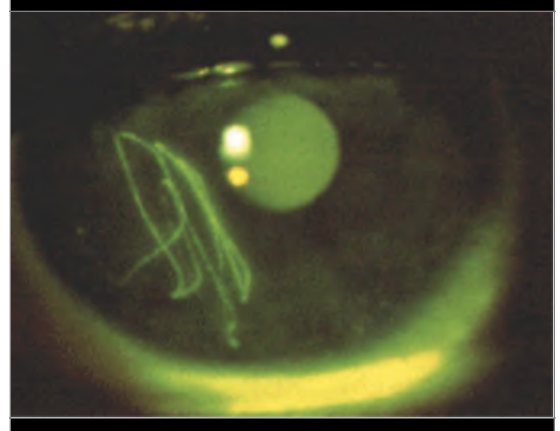
A corneal abrasion results from disruption of the corneal epithelium either due to trauma, contact lens, infection or a foreign body. The term keratitis refers to inflammation of the cornea.

It may present with pain, photophobia, excessive tearing, a foreign body sensation, and resistance to opening of the eyes.

On exam, conjunctival injection may be present. A topical anesthetic can be placed in the eye prior to fluorescein exam. A fluorescein exam is necessary to identify corneal epithelial defects. Improvement of symptoms with application of a topical anesthetic is often diagnostic. A slit lamp exam will facilitate the identification of small lesions.

The goal of treatment is pain control, prevention of infection, and promoting rapid healing of corneal epithelium. Topical antibiotics can be applied to prevent infection and artificial tears for comfort.

CORNEAL ABRASION



A vertical, linear corneal abrasion may be seen with a foreign body affixed to the inner eyelid

Larger corneal abrasions and those involving the visual axis should be seen on the following day by ophthalmology. The patient should be instructed to seek ophthalmologic care if pain or foreign body sensation continues for more than 2 to 3 days, or if there is increasing pain and redness.

Contact Lens wearers are at increased risk of complications, including corneal ulcers and infection with resistant organisms (i.e. pseudomonas, serratia).

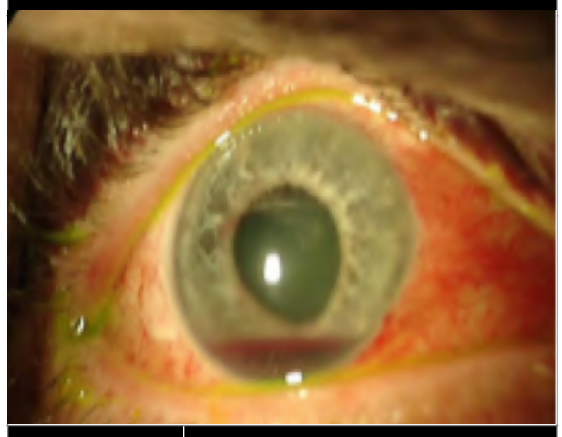
HYPHEMA

Blood in the anterior chamber of the eye is a sign of severe ocular trauma. Trauma damages vessels in the eye, causing blood to leak into the anterior chamber and leads to increased intraocular pressure. Bleeding stops when a clot forms. Re-bleeding risk is highest on days 3-5 when the clot weakens. Symptoms include pain and blurred vision.

The size of the hyphema is directly proportional to the incidence of secondary glaucoma. Patients with sickle cell and sickle cell trait are at increased risk of acute angle glaucoma.

An ophthalmology consultation is indicated as well as hospital admission. Management includes bed rest with head elevated at 45 degrees. This position helps allow blood within the anterior chamber to settle inferiorly, thus allowing clearance of the visual axis, improvement of vision, and a better ocular exam.

HYPHEMA



GRADE	ANTERIOR CHAMBER
1	< 1/3
2	1/3 to 1/2
3	1/2 to less than total
4	Total (“eight ball”)

Medical management includes atropine, epsilon-aminocaproic acid (AMICAR) analgesics (no aspirin or NSAIDS) and anti-emetics as needed to avoid vomiting with spikes in intraoccqular pressure.

Surgical evacuation of the hyphema may be indicated if vision deteriorates significantly, the entire anterior chamber becomes filled with blood, a substantial clot persists for 7 days, or the IOP is persistently elevated despite optimized medical therapy.

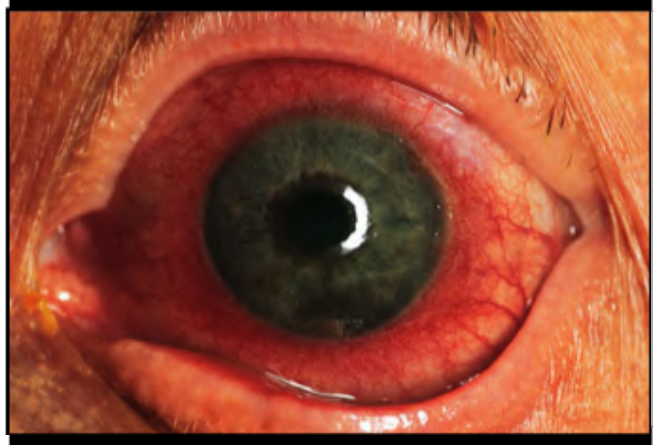
TRAUMATIC IRITIS

Inflammation within the anterior chamber of the eye may present 24 to 72 hours after blunt trauma to the eye. One should consider the possibility of iritis in children who have unilateral, sudden onset of pain, photophobia, and redness.

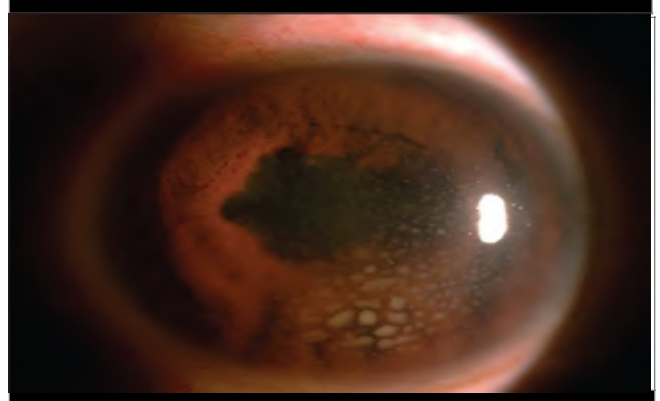
Physical examination reveals a miotic pupil and perilimbal injection. The ring of redness surrounding the cornea is known as ciliary flush.
Definitive recognition of traumatic iritis requires a slit lamp exam, revealing aqueous flare and cells. The term uveitis refers to inflammation of the iris, choroid of the eye and the ciliary body.

Ophthalmology consultation should be obtained in the diagnosis and management of this condition. Medical management often includes the use of topical steroids and cycloplegics (to help reduce pain and photophobia associated with papillary constriction associated with this inflammation). Topical steroids should never be prescribed except in consultation with an ophthalmologist.

UVEITIS



MIOSIS, CILIARY FLUSH



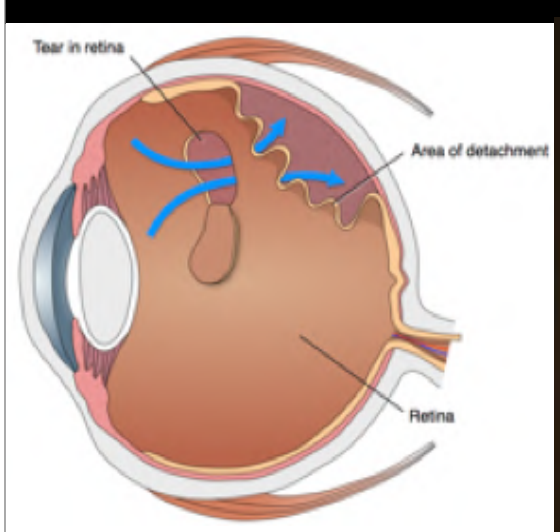
CELLS IN ANTERIOR CHAMBER

RETINAL DETACHMENT

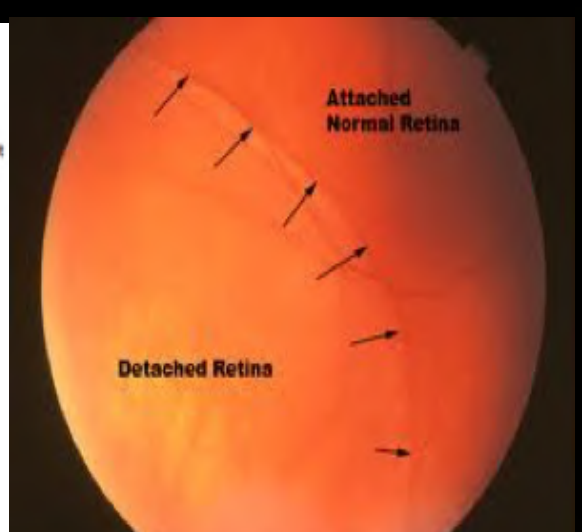
Retinal detachment is characterized by the separation of the retina from the underlying retinal epithelium. Common symptoms include new floaters, squiggly lines, or cobwebs that appear abruptly, associated with visual field loss.

Point of care ultrasound can be used to diagnosis a retinal detachment, A dilated examination by an ophthalmologist is required for diagnosis and possible surgical repair.

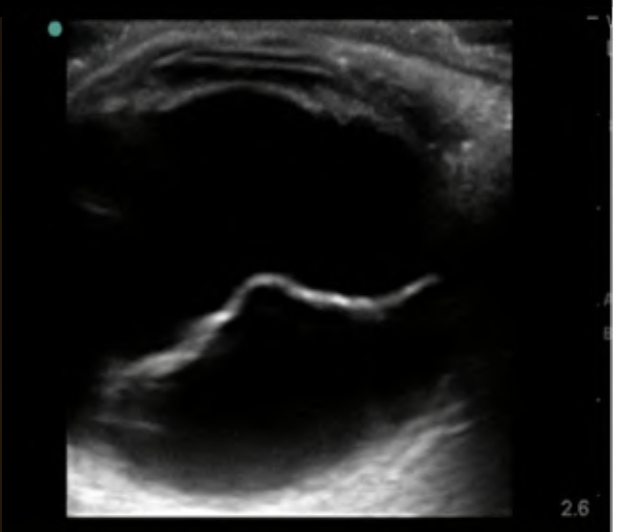
RETINAL DETACHMENT



ANATOMY



FUNDOSCOPY

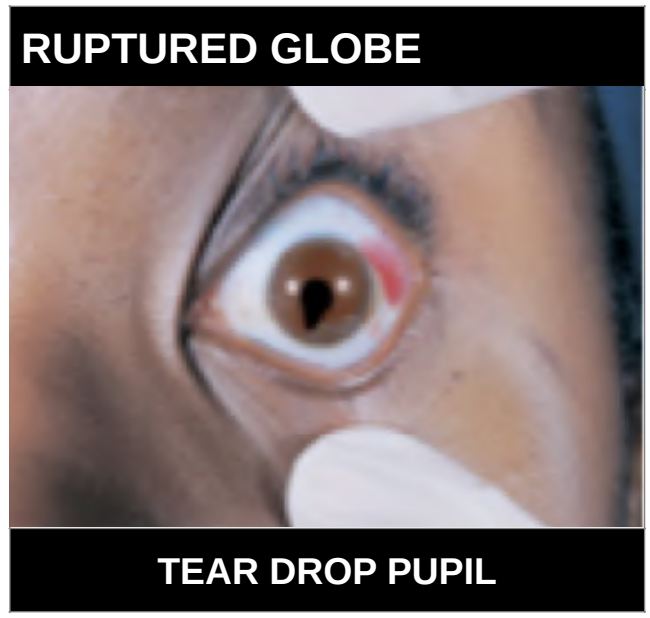


ULTRASOUND

RUPTURED GLOBE

A ruptured globe occurs when the integrity of the sclera or cornea is disrupted, either penetrating or blunt trauma.

A teardrop pupil or hyphema may be present on examination. If the history or examination indicates a globe rupture is a possibility, it is important to avoid putting pressure directly on the eye. The globe can be visualized by placing the examiner's thumbs on the infra-orbital and supra-orbital rims and separating the lids.



The goal of management is to limit intra-ocular pressure to avoid causing extrusion of eye contents. Once a ruptured globe is suspected, further ocular examination should be stopped. An eye shield (not an eye patch) should be placed.
The patient should be kept calm with the head of the bed at 45 degrees.

An orbit CT will identity the globe rupture as well as a foreign body and fractures. The physician can consider sedation, analgesics, antiemetic, antibiotics, and tetanus, while awaiting an emergent ophthalmology consultation.

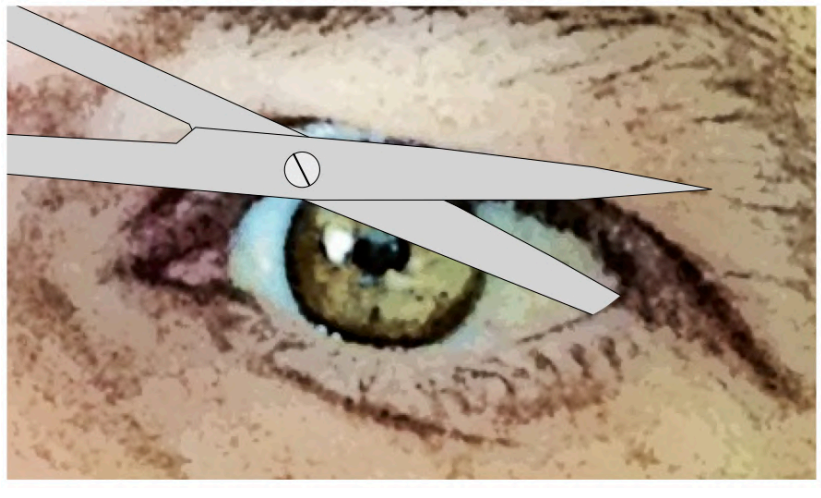
TRAUMATIC RETROBULBAR HEMORRHAGE

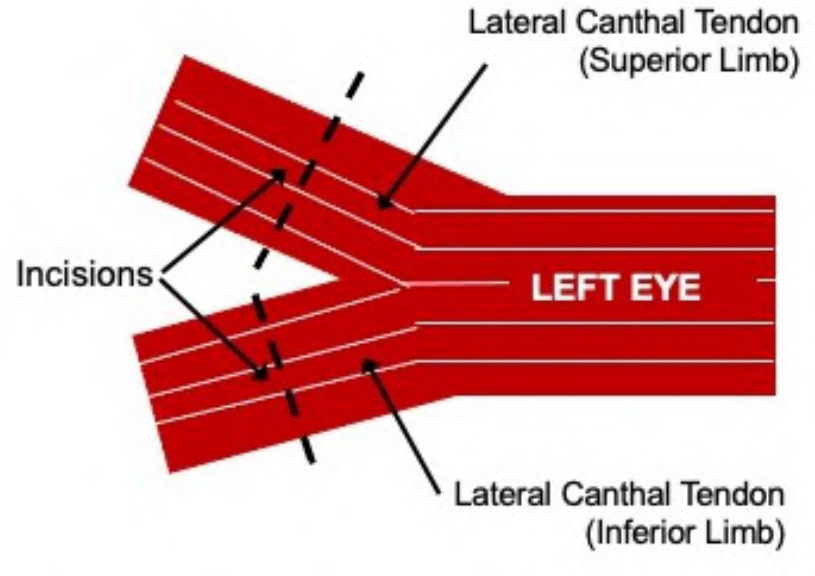
A retrobulbar hemorrhage may present with history of pain and decreased vision. Proptosis may be present on physical exam. Increase pressure in the orbit may result in an orbital compartment syndrome. An emergency lateral canthotomy may be required to reduce intraocular pressure.

If an emergency lateral canthotomy is not indicated then CT of the orbits and ophthalmology consultation is indicated. Medical management is aimed at decreasing intra-ocular pressure. Treatment options include Diamox (a carbonic anhydrase inhibitor), a topical B-blocker, and/or a hyperosmotic agent.

LATERAL CANTHOTOMY INDICATIONS
Decreased visual acuity
Proptosis
IOP > 40 mmHg

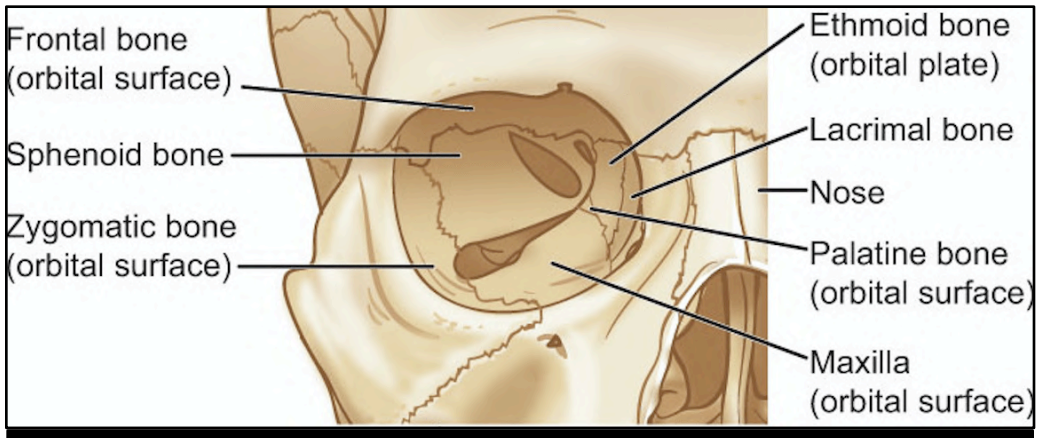
VIDEO LINK: LATERAL CANTHOTOMY





ORBITAL FRACTURES

The orbital walls consist of several bones. The inferior and medial walls are the most fragile and therefore the most commonly fractured. Fractures of the frontal, ethmoid, sphenoid and maxillary bones disrupt the integrity of the underlying sinuses. Other complications of orbital fractures include extraocular muscle entrapment, globe injury, infraorbital nerve injury and retrobulbar hematoma. Patient may present with pain, local tenderness, and diplopia.

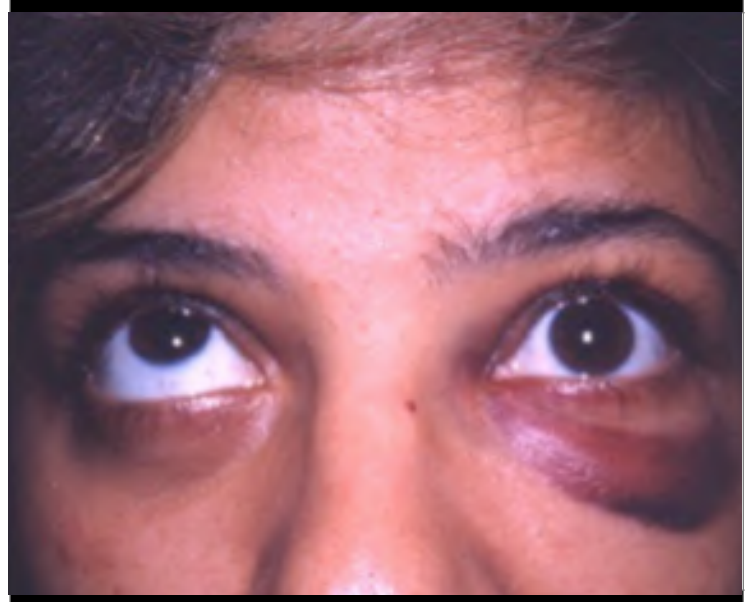


ORBIT ANATOMY (BONES)

Orbital floor (inferior wall) fractures may entrap the inferior rectus muscle limiting upward gaze. Orbital floor fractures may also damage the infraorbital nerve leading to numbness of the ipsilateral lower eyelid, nose and upper lip. Orbital medial wall fractures can entrap the medial rectus muscle leading to diplopia, enophthalmos and restricted lateral gaze. The lateral wall is the least commonly fractured.

A CT scan of the orbits is required to delineate the extent of injury. Ophthalmology should be consulted. Isolated orbital fractures are typically treated with antibiotics and nasal decongestants. Patients should be cautioned to not blow their nose. Close follow up with a facial surgery consultant (e.g. Plastic surgery, ENT, Ophthalmology) should be arranged.

ORBIT FRACTURE



UPWARD GAZE PARALYSIS AND ENOPHTHALMOS (LEFT)

PHYSICAL EXAMINATION: ORBIT FRACTURE
Enophthalmos: Sunken globe
Proptosis: Protruding globe (retrobulbar hemorrhage)
EOM entrapment → Upward and/or lateral gaze palsy
Subcutaneous emphysema
Infraorbital Nerve: ↓ sensation to the ipsilateral lower eyelid, cheek and upper lip
Palpable step-off along orbital rim

FACIAL FRACTURES

INTRODUCTION (ELLEN DUNCAN, MD, PHD, 8/2020)
Maxillofacial trauma include fractures of the frontal, orbital, zygoma, maxillary and mandibular bones, as well as injury to the overlying soft tissue and underlying structures (e.g. sinus fractures). This PEM Guide reviews mandibular, maxillary, nasal and frontal bone fractures. See also:
PEM Guide: Trauma: Dental and Oral Trauma
PEM Guide: Trauma: Eye Trauma (Orbital fractures)

The trauma primary survey (Airway, Breathing, Circulation, Disability, and Exposure) should be prioritized in children with significant facial trauma. The airway and cervical spine are most commonly affected, and advanced airway management is often required. This should be considered a difficult airway situation. Concomitant hemorrhage, airway edema, and/or backwards displacement of the tongue can cause airway obstruction. Airway management should be performed by the most experienced clinician and may require anesthesiology and surgical airway consultation (See PEM Guide: Airway Procedures: Difficult Airway, PEM Guide: Airway Procedures: Cricothyrotomy). The cervical spine should be immobilized. A direct blow to the chin can result in hyperextension or hyperflexion of the neck. Some fractures (e.g. midface fractures) are associated with a high rate of intracranial injury.

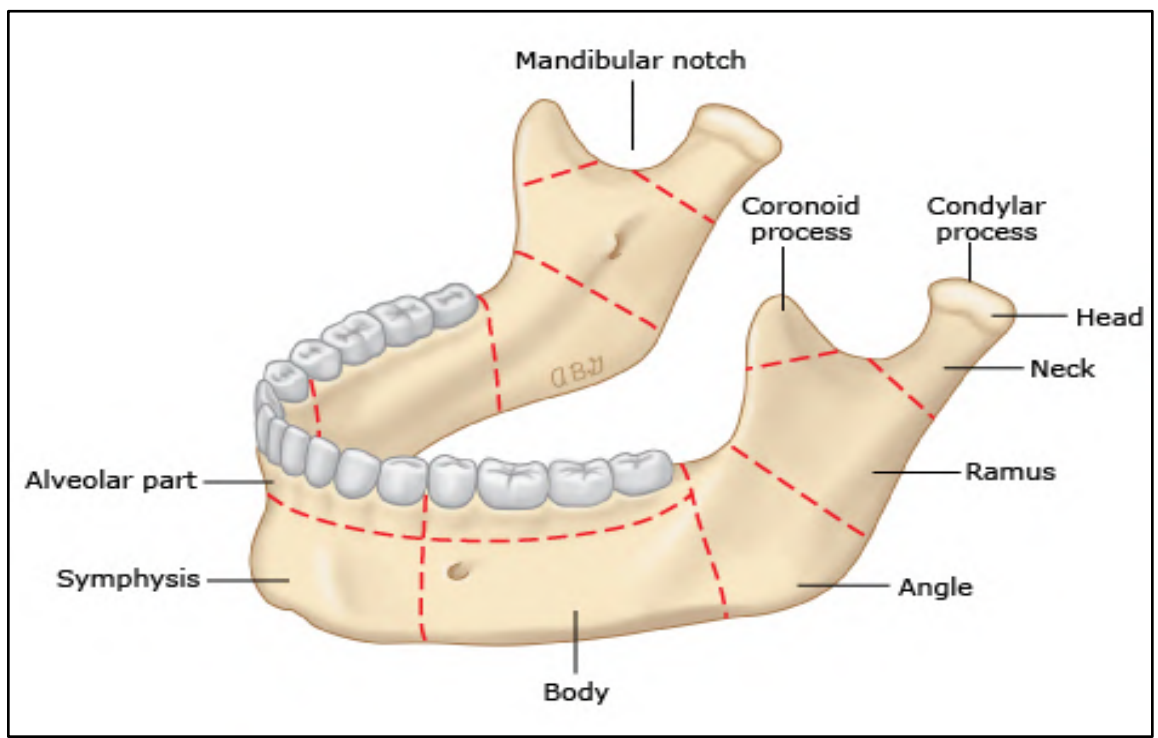
MANDIBULAR FRACTURES

INTRODUCTION
In adolescents mandibular angle fractures are the most common. Mandibular condyle process fractures are the most common pediatric mandible fractures in children. Because of the thickness and elasticity of the condyle process, fractures are less common in infants and young children, and when they do occur, they are more likely to be incomplete (greenstick) and less likely to be comminuted. Motor vehicle collisions (MVC) are the most common mechanism of injury in infants, children, and adolescent females. In adolescent males, MVC and assaults are the most common mechanisms.

ANATOMY
The mandible is U-shaped. The coronoid and condylar processes articulate with the glenoid fossa at the base of the temporal bone to form the temporomandibular joint (TMJ).

The inferior alveolar nerve (a branch of the mandibular nerve, which is the V3 branch of the trigeminal nerve) provides sensory innervation to the lower lip and chin.

The mylohyoid branch of the inferior alveolar nerve provides inconsistent sensory innervation of the chin and regions just lateral to it. The mental branch of the inferior alveolar nerve provides sensory innervation from the lower lip to the labiomental fold and occasionally to the chin as well.



MANDIBLE ANATOMY

CLINICAL ASSESSMENT

Injuries associated with mandibular trauma include facial and intraoral soft tissue injuries, dental injuries, TMJ dislocation, and parotid gland injury. Multi-trauma patients may also have cervical spine and intracranial injuries. These associated injuries are more common in infants and young children with mandibular fractures due to the higher degree of force required to fracture the mandible in this age group. A complete examination of the head, neck, and intraoral cavity (including the floor of the mouth) should be completed.

CLINICAL ASSESSMENT	
HISTORY	PHYSICAL EXAMINATION
Difficulty opening or closing mouth	Dental trauma: Fractures, gingival lacerations
New malocclusion	Facial swelling and bruising
Numbness to lower lip or chin	Failed tongue depressor test[1]
Pain: Ear, TMJ	Lacerations: Face, tongue, mouth floor, chin
Pain: Mandible, dental	Lateral or posterior mandible deviation
Pain with chewing	Malocclusion, gross malalignment
	Preauricular/TMJ swelling/tenderness
[1]WEB LINK: CORE EM: TONGUE DEPRESSOR TEST	

IMAGING

Patients without malocclusion, pain, or tenderness, and with a negative tongue depressor test and normal range of motion of the mandible are at very low risk of mandibular fractures and usually do not require imaging. CT of the facial bones and mandible with 3-D reconstruction is the imaging study of choice in those not meeting the above criteria. Panoramic X-rays (Panorex) are better suited to identify associated dental fractures, though these should be performed in conjunction with CT and are not routinely available in many EDs. Simple radiographs of the mandible are less helpful because of its U shape and overlap of adjacent bony structures; furthermore, in children, tooth buds can obscure fractures and the cortex is underdeveloped. Because of associated injuries, CT scan of the cervical spine and head may be warranted.

TYPES OF MANDIBULAR FRACTURES	
LOCATION	CONSIDERATIONS
Body and symphysis	Children may have bilateral injury of the anterior mandible as well as greenstick fractures of the posterior jaw
Angle	Combined angle and condylar fractures requires operative reduction and internal fixation; fractures threatening tooth growth should be reduced and fixed
Condyle	Condylar injury can be produced by forceful chin trauma; in children there is often deviation *away from* the injury because of joint swelling and/or hematoma formation

MANAGEMENT

TRAUMA PRIMARY SURVEY: Assessment and management of airway, breathing, circulation, disability, and exposure should be prioritized. The cervical spine should be immobilized. Falling onto the chin or a direct blow to the chin can result in hyperextension or hyperflexion of the neck.

AIRWAY AND CERVICAL SPINE: Airway management in the patient with a mandibular fracture can be difficult due to hemorrhage, swelling, limited mouth opening, jaw displacement, and the need to maintain immobilization of the cervical spine. In addition, concomitant airway edema, hemorrhage, and posterior displacement of the tongue can cause airway obstruction.

This should be considered a difficult airway situation and managed by the most experience provider. Definitive airway management may require anesthesiology and/or surgical airway, and these teams should be called early. Equipment for alternate intubation techniques and cricothyrotomy should be prepared (See PEM Guide: Airway Procedures: Difficult Airway, PEM Guide Airway Procedures: Cricothyrotomy).

Significant intraoral hemorrhage in the supine patient can lead to aspiration and may require log rolling the patient to the side for suctioning while maintaining cervical spine immobilization. If possible, the patient should be placed in a sitting position. Packing of the oral cavity with radiologically marked gauze may be required to tamponade bleeding after intubation. Foreign bodies such as fractured or avulsed teeth should be removed either manually or with a large bore suction catheter.

FRACTURE MANAGEMENT: Otolaryngology or oral and maxillofacial surgery (OMFS) consultation is required for all mandibular fractures. The primary goal of management is reduction and stabilization of any bony fragments to allow for proper alignment and healing. Mandibular fractures can disrupt bony growth and must be addressed quickly, as fast bony healing can make reduction difficult in children, even in as little as five days after the injury. (Sharma, Int J Clin Ped Dentistry 2019, PubMed ID: 25206104).

Fracture management is based on the type and location of the fracture and the patient's stage of dental development. Incomplete or nondisplaced fractures in very young children are managed with soft diets only. Children 6-8 years of age with mixed dentition development (both primary and secondary teeth) and with minimal occlusive changes may be managed with a soft diet or 2-arched bars is required for multiple or more severely displaced fractures.

ANTIBIOTICS: Antibiotics should be administered to patients with open or multiple fractures and those with dental injuries.

MAXILLARY FRACTURES

INTRODUCTION: Midface fractures can involve the area between the orbital rim and the maxillary alveolar ridge. Midface fractures can be life-threatening for many reasons (airway obstruction, facial instability, intracranial injury, cervical spine injury) and can also lead to significant disability (speaking, chewing, breathing, seeing) and cosmetic defects. Severe injuries typically occur in the setting of MVCs and assaults. Contact sports also result in a high proportion of injuries.

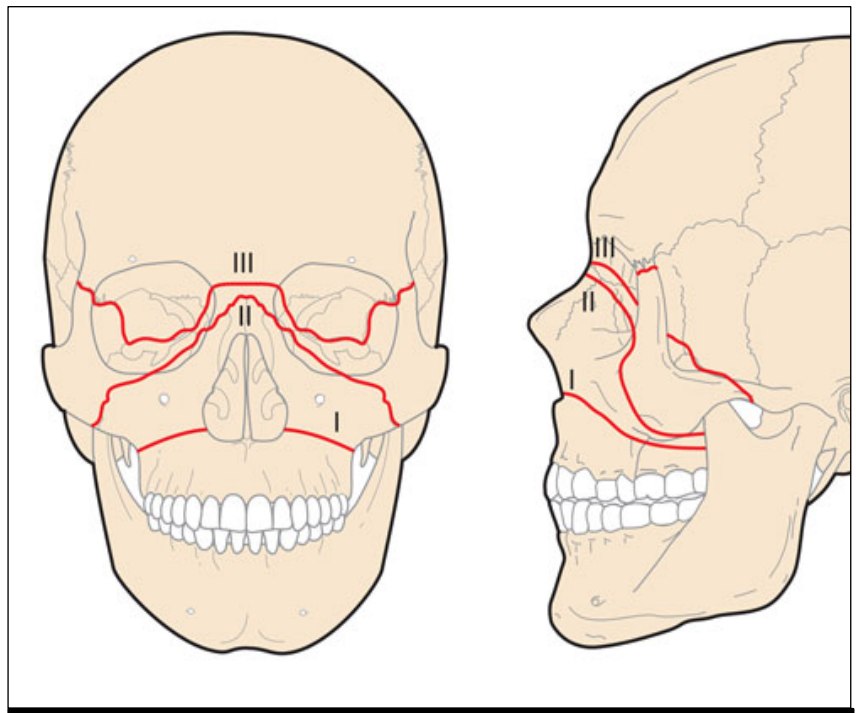
Midface fractures are uncommon in pediatric patients and are especially rare in younger children. Le Fort fractures are almost never seen in patients younger than 2 years of age, because children have small, flat faces, and younger children without pneumatized sinuses are less likely to fracture. Non-erupted teeth also protect the maxilla and mandible. Zygomatic complex fractures are often greenstick fractures.

ANATOMY

Facial anatomy is complex. It is essential to understand the bony structure of the face and underlying structures as well as the motor and sensory innervation. The only joint in the face is the TMJ. Significant bleeding can occur due to the high vascularity of the face.

ZYGOMA FRACTURES. The zygoma are prominent and superficial, and are frequently fractured due to assault. In addition to the zygomatic arch, the zygoma encompasses the inferior and lateral walls of the orbit and the superior and lateral walls of the maxillary sinus. Tripod fractures involve the zygoma, lateral orbital wall, and maxilla.

FACIAL BONES	
EXTERNAL	INTERNAL
Frontal	Sphenoid
Nasal	Ethmoid
Zygoma	Lacrimal
Maxilla	Vomer
Mandible	Temporal



LE FORT FRACTURES

SENSORY: TRIGEMINAL NERVE (CN V)		MOTOR	
Ophthalmic (V1)	Upper 1/3 Face	Eye movements	CN: III, IV, VI
Maxillary (V2)	Middle 1/3 Face[1]	Facial muscles	CN: VII
Mandibular (V3)	Lower 1/3 Face	Mastication	CN: V
		Palate movement	CN: X, IX

[1]The infraorbital nerve is a branch of the maxillary branch (V1) of the trigeminal nerve. It exits the infraorbital foramen in the midline of the infraorbital ridge and provides sensory innervation of the ipsilateral lower eyelid, cheek, nose & upper lip

LE FORT FRACTURE CLASSIFICATION			
CLASS	FRACTURE	LOCATION	MECHANISM
Le Fort I	Horizontal	1. Pterygoid plate[1] 2. Lateral nasal opening 3. Upper alveolar plate (dental roots)	Downward injury to maxillary alveolar rim Separates body of maxilla from pterygoid plate, nasal septum
Le Fort II	Pyramidal	1. Pterygoid plate[1] 2. Inferior orbital rim 3. Nasal bridge 4. Lacrimal bones	Blow to lower or mid maxillary area Results in mobility of the hard palate and nose but not the eyes
Le Fort III	Transverse	1. Pterygoid plate[1] 2. Zygomatic arch 3. Medial, inferior and lateral orbit	Impact to nasal bridge or upper maxilla Craniofacial dissociation

[1]Of the sphenoid bone

CLINICAL MANIFESTATIONS

Associated injuries include facial injuries as well as intraoral soft tissue and dental injuries. Multi-trauma patients may have cervical spine and intracranial injuries. A thorough examination includes:

1. Observation: Symmetry, swelling, ecchymosis, lacerations
2. Palpation: Step-off, crepitus, mobility (bones, TMJ, teeth)
3. Assessment of motor and sensory function: Cranial nerve evaluation
4. Adjacent structures: Eye, nasal and oral cavities, dentition and auditory canal

CLINICAL ASSESSMENT	
HISTORY	PHYSICAL EXAMINATION
Anosmia	Dental trauma: Fractures, gingival lacerations
Difficulty opening or closing mouth	Ear: Lac, hemotympanum, CSF, battle sign
Eye: Abnormal/double vision	Enophthalmos, ↓ extraocular muscle
Inability to breathe through the nose	Facial bone instability[2], tenderness, crepitus
Nasal: Epistaxis, congestion	Facial swelling and bruising
New malocclusion	Increased intercanthal distance (separation)
Numbness: Infraorbital nerve[1]	Lacerations: Face, chin
Pain: Ear, TMJ	Lacerations: Tongue, mouth floor, palate
Pain: Mandible, dental	Malocclusion
[1]Acute numbness likely represents nerve injury. Numbness that develops later likely represents adjacent swelling with nerve compression [2]Grasp upper teeth or alveolar ridge in the midline, gently attempt to move the maxilla anteriorly and posteriorly	

IMAGING

CT scan of the face with 3-D reconstruction is the imaging study of choice. Plain X-rays are poorly sensitive and have little utility. CT of the head and cervical spine may also be warranted.

MANAGEMENT

TRAUMA PRIMARY SURVEY: Assessment and management of airway, breathing, circulation, disability, and exposure issues should be prioritized. The cervical spine should be immobilized.

AIRWAY AND CERVICAL SPINE: Airway management in the patient with a midface fracture can be difficult due to hemorrhage, swelling, limited mouth opening, inability to make a secure seal with a bag-valve-mask, and the need to maintain immobilization of the cervical spine. In addition, concomitant airway edema, hemorrhage, and posterior displacement of the tongue can cause airway obstruction.

This should be considered a difficult airway situation and managed by the most experience provider. Definitive airway management may require anesthesiology and/or surgical airway, and these teams should be called early. Blind nasotracheal intubation is contraindicated due to high risk of intracranial intubation. Equipment for alternate intubation techniques and cricothyrotomy should be prepared (See PEM Guide: Airway Procedures: Difficult Airway, PEM Guide Airway Procedures: Cricothyrotomy).

Significant intraoral hemorrhage in the supine patient can lead to aspiration and may require log rolling the patient to the side for suctioning while maintaining cervical spine immobilization. If possible, the patient should be placed in a sitting position. Packing of the oral cavity with radiologically marked gauze may be required to tamponade bleeding after intubation. Foreign bodies such as fractured or avulsed teeth should be removed either manually or with a large bore suction catheter.

FRACTURE MANAGEMENT: Otolaryngology or oral and maxillofacial surgery (OMFS) consultation is required for all midface fractures. (Morales, *J Craniofac Surg* 2010, PubMed ID: 20647837, Yu, J Craniofac Surg. 2011, PubMed ID: 21772207). Ophthalmology consultation is required for ocular involvement. Neurosurgery consultation is required for fractures with CSF leakage. Non-displaced and minimally displaced fractures generally do not require operative repair.

ANTIBIOTICS: The utility of antibiotic prophylaxis is unclear. Some recommend antibiotics if there are significant soft tissue injuries, fractures into a sinus, or intraoral/dental injuries.

NASAL FRACTURES

INTRODUCTION

Nasal fractures are common. They can be associated with midface fractures, fractures of the ethmoid and sphenoid sinuses, and frontobasal fractures, Epistaxis is common in nasal injuries because of the abundance of vasculature. Younger children's noses are more cartilaginous and less protuberant, and are therefore less likely to be injured. However, missed nasal trauma can cause deformity, septal deviation, and nasal airway obstruction. Injuries are typically related to a direct blow to the nose (MVC, sports, assaults).

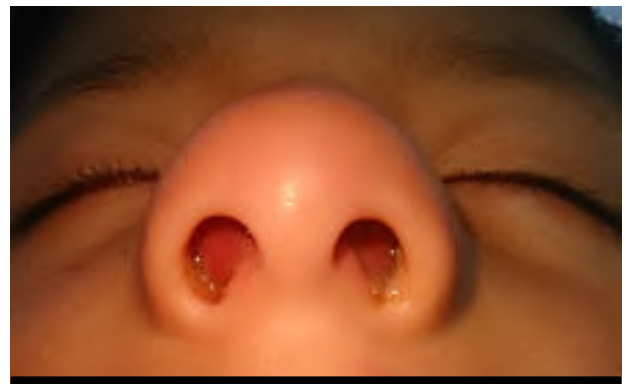
ANATOMY

The nasal bone is pyramid-shaped with two segments that join in the midline.

ANATOMY: ADJACENT STRUCTURES	
Superior	Nasal part of the frontal bone
Medial	Opposite segment of the nasal bone
Lateral	Frontal process of the maxilla
Inferior	Nasal cartilage
Posterior	Perpendicular plate of ethmoid bone and septal cartilage

NASAL INJURIES			
INJURY	IMPACT	RESULT	NOTES
Nasal bone Fracture ± Septal injury	Lateral	Simple, Linear fracture	Deviation: No ± Greenstick fractures
	Midface	Naso-orbitoethmoid fractures	See below
	Lateral + Midline	Septal fractures	Deviation: Yes
Naso-orbitoethmoid fracture	High impact to central face	Separation of nasal bones from medial walls of the orbits and the frontal bone and infraorbital rim (traumatic telecanthus)	Increased inner canthal distance
		Open book fractures (infants): Separation of nasal bone segments in the midline	
Septal	Trauma to nasal septum	Hematoma: Blood collection adjacent to septal cartilage Septal deviation, perforation	Hematoma → Avascular necrosis → Saddle deformity

SEPTAL HEMATOMA
Epistaxis
Blue or red swelling with deviation of the nasal septum
Boggy, compressible swelling with nasal obstruction
Mass doesn’t reduce after topical vasoconstrictor



SEPTAL HEMATOMA (RIGHT)

CLINICAL ASSESSMENT

It is important to determine the injury mechanism and timing as well as whether the injury is limited to the nose or involves adjacent structures. Naso-orbitoethmoid fractures can be associated with intracranial injury. Patients should be asked about bloody or clear drainage; the latter may represent cerebrospinal fluid rhinorrhea. Patients should also be asked about nasal obstruction and vision changes.

PHYSICAL EXAM	
Inspection	Depression (posterior), deviation (lateral) of nasal bridge, laceration, swelling, ecchymosis, inner canthal distance, periorbital ecchymosis
Palpation	Mobility, step off, crepitus, tenderness
Nasal cavity	Patency (air flow), CSF rhinorrhea, hemorrhage
Septum	Epistaxis, deviation, perforation
Adjacent	Frontal bone, eye/orbits, maxilla, dental, oral cavity, mandible

DIAGNOSIS

Isolated nasal fractures can be diagnosed clinically, and X-rays are of limited utility.

CT SCAN: INDICATIONS
Adjacent injuries: Frontal, orbit, ethmoid, maxilla, zygoma
Type: Naso-orbital-ethmoid fractures, open-book fractures, Le Fort fractures
High-force mechanism or injury
CSF rhinorrhea

PLAIN XRAYS NOT INDICATED IF (ALL REQUIRED)
Tenderness and/or swelling is limited to the bridge of the nose only AND
Nares are patent to airflow bilaterally AND
No bony step-off or crepitus to palpation AND
No significant nasal deviation (lateral) or depression (posterior) AND
No septal hematoma, deviation, or perforation

MANAGEMENT

As with mandibular and maxillary fractures, the trauma primary survey with particular attention to the airway and cervical spine takes precedence. Nasogastric tubes and nasotracheal intubation are contraindicated in patients with nasal trauma because of the risk of placing the tube intracranially. Initial management consists of pain control, control of epistaxis, efforts to reduce/minimize swelling, and treatment of soft tissue injuries.

Epistaxis can be controlled with direct pressure (compressing the nasal alae for 3-5 minutes) or topical vasoconstrictors if direct pressure is insufficient. Nasal packing may be required for refractory epistaxis.

NASAL TRAUMA: ENT CONSULTATION
Septal hematoma, deviation, perforation
Associated orbital, sinus, maxillary fractures
Significant deformity: Deviation, depression
Complex lacerations
Persistent epistaxis
Newborns with obstruction/deviations (obligate nasal breathers)

DISPOSITION

Patients with simple nasal fractures can be discharged with pain control, ice, elevation of the head of the bed, and ENT follow up within 3-5 days. At that point, swelling will have subsided and a better assessment of cosmetic and functional issues can take place. Parents should be advised to bring a recent pre-injury photo to the visit for comparison.
Anterior nasal packing may be required for refractory epistaxis and after incision and drainage of a septal hematoma. Patients with packing should follow up with ENT for packing removal and re-evaluation in 2-3 days.

Antibiotics with coverage for *Staphylococcus aureus*, *Streptococcus pneumoniae*, group A beta-hemolytic *Streptococcus*, and non-typable *Haemophilus influenzae* are indicated after septal hematoma incision and drainage and for those with significant external soft tissue injuries.

FRONTAL BONE FRACTURES

The frontal bone is the densest facial bone and therefore requires a great deal of force to fracture. Frontal fractures can therefore be associated with significant craniofacial and intracranial injury. Frontal bone fractures in the area of the frontal sinus are described as anterior table (pre-sinus) and posterior table (post sinus).

Isolated anterior table fractures are usually stable but can be associated with significant cosmetic deformity and should be followed closely by facial plastics or neurosurgeon.

The posterior table is adherent to the dura and fractures can be associated with CSF leakage and pneumocephalus. Posterior table fractures can also be associated with intracranial and cervical spine injury. Posterior table fractures require neurosurgery consultation and are frequently prescribed antibiotics.

GENITOURINARY TRAUMA

INTRODUCTION (ALEXIS PANKOW, M.D. 5/2018)
Patients may present with genitourinary (GU) trauma from a variety of mechanisms. Identification of these injuries is essential as they can be overlooked in the setting of multi-trauma. In particular, pelvic fractures may be the source of major hemorrhage. This PEM Guide reviews major GU injuries including injuries to the kidneys, ureters, bladder, urethra and pelvis. See: PEM Guide: Trauma: Penile and Scrotal Injuries.

Major GU injuries may be identified during the primary survey. Injuries resulting in major bleeding can present with hemorrhagic (hypovolemic) shock during circulatory assessment. Examination of external signs of abdominal or back trauma can be identified during the exposure phase of the primary survey. Injuries may also be identified during the secondary survey. For example, a careful examination of the perinuem and genital exam may reveal blood at the urethral meatus or perineal eccymosis/lacerations, In addition, bedside testing may reveal hematuria and the extended focused adominal assessment in trauma (E-FAST) may reveal intraperitoneal bladder rupture. It is important to note that the E-FAST exam will not identify retroperitoneal bleeding due to pelvic fractures.

DIAGNOSTIC STUDIES
Urinalysis: >50 WBC/HPF
Pelvic XRAY
Point of Care FAST examination
Retrograde urethragram (suspected urethral injury)
Cystoscopy (suspected bladder injury)
CT scan of abdomen and pelvis

Gross of microscopic hematuria may be present with a GU injury. Patients with physical exam findings or mechanism of injury suspicious for GU trauma should have imaging regardless of urinalysis results. Urologic Injury has been found in patients without hematuria and hematuria found in patients with no injury.

1. RENAL INJURY

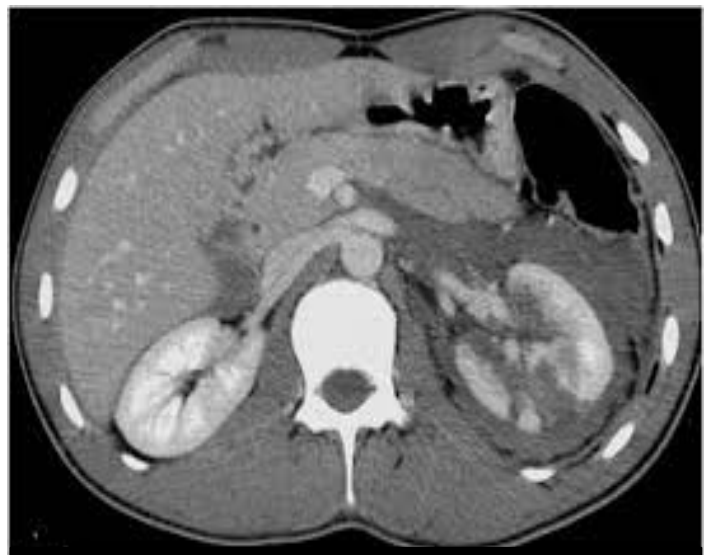
Children have larger kidneys in relation to abdomen size and less perinephric fat and musculature to protect the kidney. These factors predispose them to renal injuries. Renal injuries may occur from motor vehicle collisions, lower rib fractures, and direct blows. General signs of renal injury include abdominal tenderness, rigidity, paralytic ileus, and hypovolemic (hemorrhagic) shock. More specific indicators of renal injury may include flank tenderness, hematoma or mass.

Hematuria may be present with renal injury but the degree of hematuria does not correlate with the severity of injury. In addition, the absence of hematuria does not preclude the presence of a renal injury. Gross hematuria or microscopic hematuria with greater than 50 RBC/HPF should prompt evaluation for kidney injury in trauma patient.

CT imaging can be used to: determine the degree of renal parenchymal injury, evaluate the presence of nonviable tissue, demonstrate extravasation and perirenal collections, and diagnose pedicle injuries. The diagnostic accuracy of the CT scan for renal injuries has been reported to be as high as 98%.

Ultrasonography is readily available and can be performed at the bedside. Despite these benefits it is not widely accepted in identifying renal injuries. The E-FAST exam will not identify retroperitoneal fluid collections. The sensitivity in demonstrating renal injury is only 70% compared to 98% with CT. Pulsed-flow duplex Doppler ultrasound can assess renal arterial and venous flow and may represent the most immediate means of screening for renal pedicle injury.

A one shot intravenous pyelogram (IVP) could be utilized to identify renal injury in the hemodynamically unstable patient who could not tolerated a delay to obtain a CT scan of the abdomen and pelvis or when a CT scan is not available. Delayed excretion, extravasation and nonvisualization of calices on an IVP indicates renal injury



CT: RENAL FRACTURES (L)

AAST* GRADING OF RENAL INJURIES		
I	Contusion	Microscopic or gross hematuria, urologic studies normal
	Hematoma	Subcapsular, non-expanding without parenchymal laceration
II	Hematoma	Non-expanding peri-renal hematoma confined to renal retroperitoneum
	Laceration	<1.0 cm parenchymal depth of renal cortex without urinary extravasation
III	Laceration	>1.0 cm parenchymal depth of renal cortex without collecting system rupture or urinary extravasation
IV	Laceration	Parenchymal laceration extending through renal cortex, medulla, and collecting system
	Vascular	Main renal artery or vein injury with contained hemorrhage
V	Laceration	Completely shattered kidney
	Vascular	Avulsion of renal hilum which devascularizes kidney
*The American Association for the Surgery of Trauma		

Angiography can be useful to both diagnosis ongoing bleeding and to perform embolization if required. Grade 2 and 3 injuries require hospitalization for 24 hours at a minimum because the risk of bleeding is high within that time frame. Management includes intravenous hydration, antibiotics, serial hematocrits and serial examinations.

Grade 4 and 5 require admission with serial hematocrit and surgical repair. Patient who continue to bleed will require more urgent surgical intervention with many grade 5 injuries progressing to nephrectomy.

2. URETERAL INJURY

Ureteral injury can result from a deceleration force. It should be considered in patients with transverse fracture of lumbar vertebrae, pelvic fracture, lower rib fracture, splenic laceration and liver laceration. Penetrating trauma can rarely cause ureteral injury. The onset of symptoms may be delayed. Hematuria is not a reliable sign. The urinalysis may be normal in up to 30% of cases.

INDICATORS: URETERAL INJURY
Fever
Pain
Palpable urinoma
Pyuria
Bacteriuria
Fistula
Hematuria

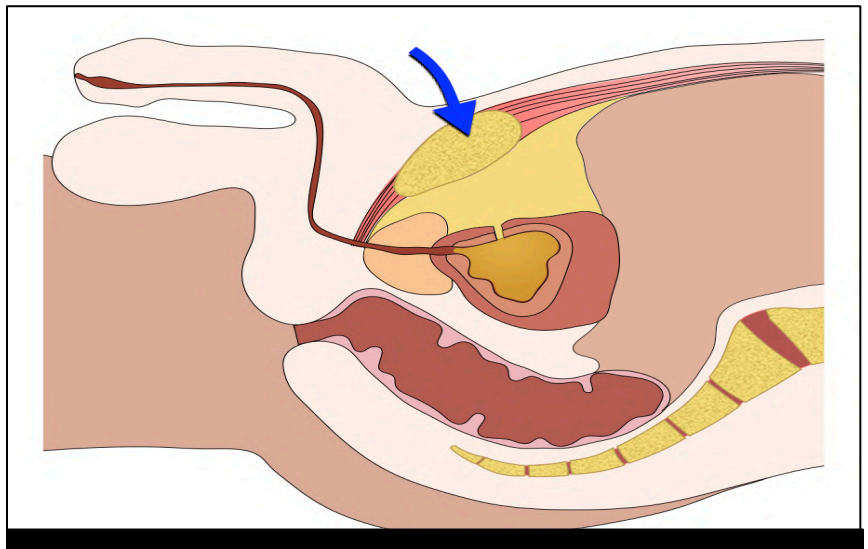
Management of ureteral injuries depends on the degree of injury and timing of diagnosis. Stents are used for partial tears or avulsions. Complete tears presenting in the first 10 days undergo surgical repair. Complete tears presenting after 10 days undergo urinary diversion with a delayed definitive repair.

3. BLADDER INJURY

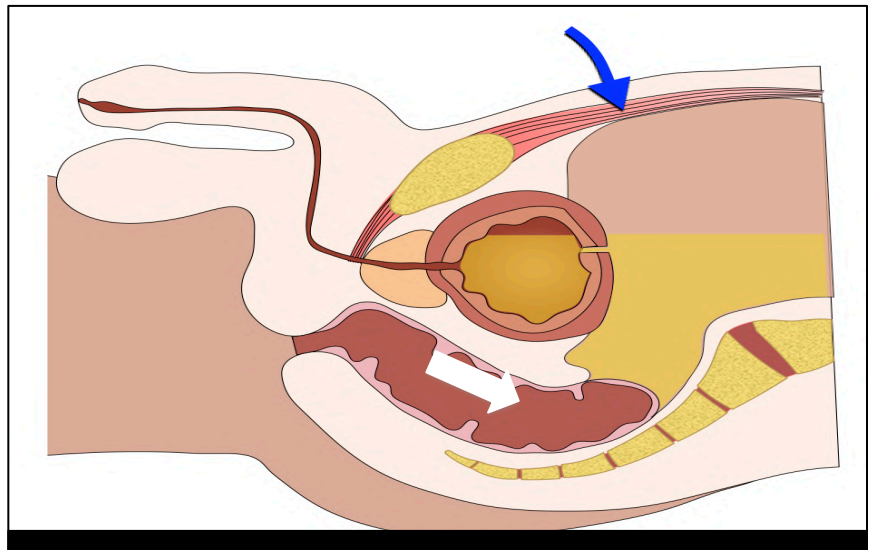
Bladder injuries are more likely to occur when the bladder is full. The weakest point of the bladder is at the dome. The bladder in children is higher in the abdominal cavity and more likely to be injured.

Urinalysis will identify gross or microscopic for hematuria. Gross hematuria is reliable sign of bladder injury. Hematuria is present in nearly 100% of cases of significant bladder trauma. However, it is nonspecific as it can be seen with both urethral and renal injuries as well. Microscopic hematuria is more commonly associated with less severe injury such as a bladder contusion. Pelvic XRAY and CT will identify pelvic fractures that may result in bladder trauma.

The diagnosis of bladder injury is made with retrograde cystography if no signs of urethral injury are present. Cystoscopy is contraindicated if signs of urethral injury such as blood at the urethral meatus or perineal hematoma are present. Bladder rupture may be extraperitoneal (most common) or intraperitoneal. Extraperitoneal bladder rupture requires catheterization for urine drainage to assist healing. Suprapubic drainage can be used for patients with urethral injuries. Intraperitoneal bladder rupture requires surgical repair. Treatment is supportive for bladder contusions. A Foley catheter can be placed to keep bladder from overextending.



EXTRAPERITONEAL BLADDER RUPTURE (FROM A PELVIC FRACTURE)

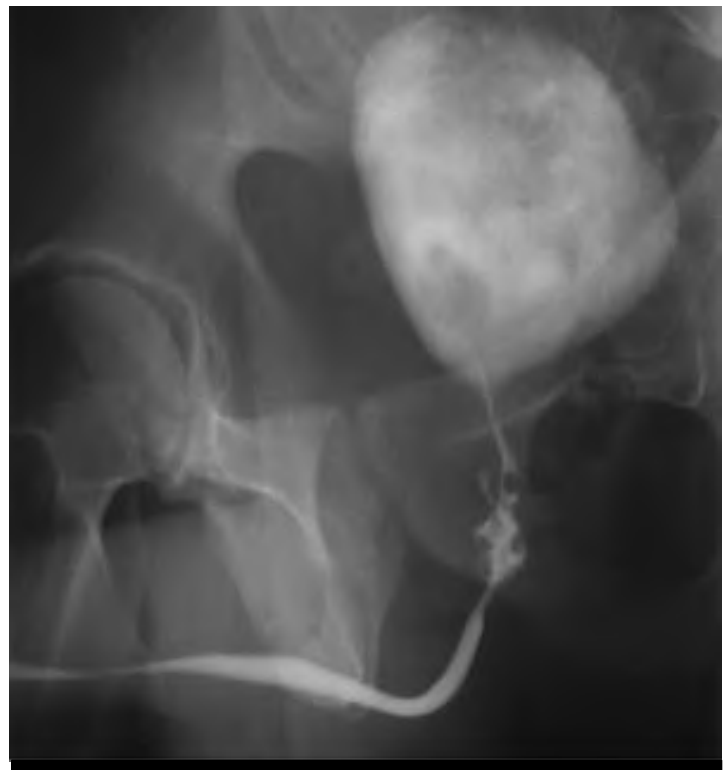


INTRAPERITONEAL BLADDER RUPTURE (FROM A BLOW TO THE ABDOMEN)

4. URETHRAL INJURY

Symptoms of urethral injury include difficulty voiding and hematuria. Signs of urethral injury include: blood at the urethral meatus and perineal/periurethral swelling or ecchymosis. The digital rectal examination for a “high riding” prostate has not been demonstrated to be sensitive or specific. In a trial of healthy volunteers 25% had a non-palpable prostate. It is not longer recommended in the 2018 ATLS Guidelines

Urethral catheterization is contraindicated if there is a suspicion of urethral injury. Instead, a retrograde urethrogram should be performed (most commonly by a urologist or trauma surgeon). A catheter is placed in the tip of the urethra, the balloon is inflated with 1.0-1.5 cc and die is injected under fluoroscopic guidance to determine urethral integrity. Urethral rupture is managed with stenting of the urethra, suprapubic drainage or surgery depending on the extent of the injury. Antibiotic prophylaxis for urinary tract infection is recommended



RETROGRADE URETHROGRAM
(DEMONSTRATING URETHRAL RUPTURE)

CLASSIFICATION OF URETHRAL INJURIES		
I	Contusion	Blood at the urethral meatus. Normal urethrogram (without extravasation)
II	Stretch	Elongation of the urethra without extravasation on urethrography
III	Partial	Extravasation of contrast at injury site with contrast visualized in the bladder
IV	Complete	Extravasation of contrast at injury site without visualization in the bladder. < 2 cm of urethral separation
V	Complete	Complete transection with >2 cm urethral separation, or extension into the prostate or vagina

CONTRAINDICATIONS TO FOLEY CATHETER PLACEMENT*
Inability to void
Unstable pelvic fractures
Blood at the urethral meatus
Scrotal hematoma
Perineal hematoma, ecchymosis or laceration
*Factors associated with urethral injury or indications for a retrograde urethrogram

5. PELVIC FRACTURES

Pelvic fractures can lead to life threatening hemorrhage. Hemorrhage from pelvic fractures comes from 4 potential sources: 1. The surface of fractured bones, 2. the presacral pelvic venous plexus, 3. pelvic arterial injury and 4. extra-pelvic sources (1 and 2 account for 85% of pelvic bleeding). Unstable pelvic fractures involve 2 fractures of the pelvic ring and are associated with a high morbidity and mortality. Hemodynamically instability is not necessarily related to pelvic instability. The pelvic volume is approximately 1.5 liters. However, this is increased with disruption of the pelvic ring. Disruption of the pelvic ring results in the inability to tamponade ongoing blood losses. Pelvic fractures cause bleeding into the retroperitoneal space and as a result will not be identified by a FAST exam.

EXAMINATION: Since pelvic fractures are a result of high-energy impact they are often associated with other injuries. Associated injuries include hemorrhage from liver or splenic lacerations, spinal cord injury, chest injury, abdominal injuries, head injuries and extremity injuries.

Local injuries as a direct result of the fracture occur frequently. Associated genitourinary trauma is seen in 11-12% of pelvic fractures. “Open” pelvic fractures involved the GI tract (rectum), GYN tract (vagina) and GU tract (bladder, urethra).

CLINICAL INDICATORS OF PELVIC FRACTURES
Laceration to the perineum, vagina, rectum, buttocks
Ruptured urethra: Blood at the meatus, scrotal hematoma
Limb abnormalities: Limb length discrepancy, rotation deformity
Pelvic instability: Compression distraction maneuver if indicated (see below)

In patients with signs of pelvic fractures, manipulation of the pelvis may dislodge clots and precipitate hemorrhage. Assessment of pelvic instability should not be performed in patients with shock and an obvious pelvic fracture. Using the compression-distraction maneuver, the hips are held at the iliac crests at the anterior superior iliac spines and pressure is placed first medially then posteriorly. The pelvis is considered unstable if it moves in either direction. This should only be performed once to minimize bleeding.

IMAGING: Pelvic fractures can be identified with plain XRAYS. CT scans of the abdomen and pelvis can identify retroperitoneal hemorrhage and pelvic injuries that are difficult to assess clinically and are the gold standard for identification of pelvic fractures and associated injuries. There are multiple pelvic fracture classification schemes.

Pediatric bones have a thicker periosteum and are more pliable than adult bones with relatively stronger ligaments. As a result, avulsion fractures and isolated pelvic ring fractures are more common in the pediatric population. Significant force is required to disrupt the posterior ring.

MODIFIED TORODE AND ZIEG CLASSIFICATION OF PELVIC FRACTURES		
I	Avulsion Injury	Caused by forceful muscle contraction Most common site at the anterior iliac spine (sartorius muscle insertion)
II	Iliac Wing Fracture	Lateral compression fracture on the side of injury
III	Simple Ring Fracture	Symphysis pubis diastasis or superior and inferior pubic rami fractures
IV	Unstable Ring Disruption	Double ring breaks. Open book deformity: Fracture of pubic diastasis and anterior sacroiliac joint disruption

MANAGEMENT: Pelvic fracture management is guided by the patient’s hemodynamic status and the fracture classification. In general, the management of those who are hemodynamically stable is determined by the results of a CT angiogram of the pelvis and the presence of ongoing bleeding. Interventional radiology embolization may preclude the need for operative intervention.

The management of those who are hemodynamically unstable due to hemorrhagic shock included the administration of blood products. Activation of a massive transfusion protocol and Tranexamic acid may be required. Hemorrhage control can be obtained through stabilization of the pelvic ring with external, medial counter pressure at the level of the greater trochanter with a pelvic binder or bed sheet. Persistent hypotension despite these interventions requires operative intervention for pelvic packing.

VIDEO LINK: CORE EM: PELVIC BINDER APPLICATION

PELVIC FRACTURE MANAGEMENT: HEMODYNAMICALLY UNSTABLE
Placement of pelvic binder over greater trochanters (sheet if binder not available)
Fluid resuscitation: Single bolus of crystalloid: 1 Liter (adult), 20 ml/kg (child) Only if blood products are not immediately availabl
PRBC: 1 unit (adult), 10 ml/kg (child)
Initiate massive transfusion protocol
Tranexamic Acid: Yes, in adults, limited pediatric data
?REBOA (Resuscitative Endovascular Balloon Occlusion of the Aorta): Zone III
Operative intervention: Trauma surgery: Pelvic packing
Operative intervention: Orthopedics: Internal fixation
Interventional radiology: Embolization (approximately 15% amenable)
Each of the above steps implies ongoing hemodynamic instability after the preceding steps have been accomplished. If initial steps are successful at correcting hemodynamic instability a CT pelvic angiogram can be obtained

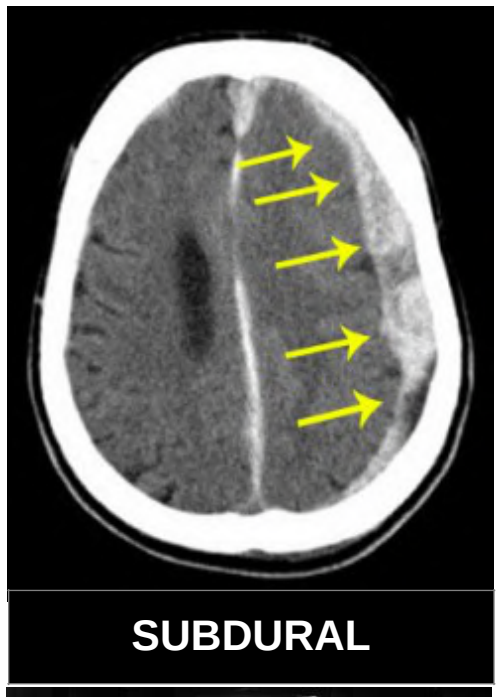
HEAD TRAUMA

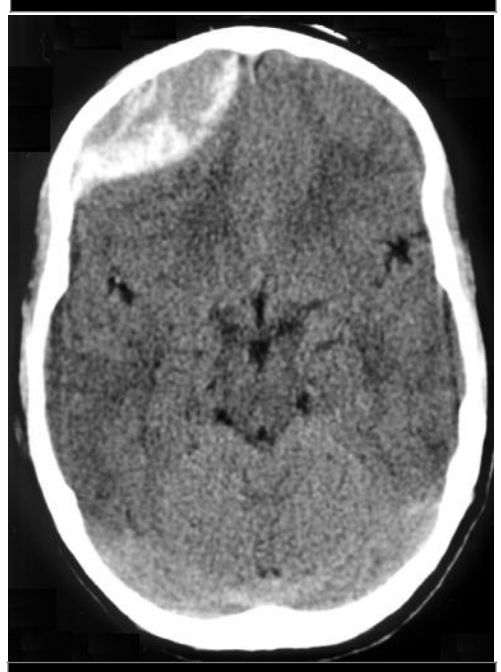
INTRODUCTION (RACHEL KOWALSKY, M.D. MPH, 10/2019)
The term “head trauma” is used to describe a spectrum of injuries. The goal is to determine which patients are at risk of intracranial injury and therefore would benefit from neuroimaging. (See also PEM Guide: Trauma: Concussion, PEM Guide: Child Protection: Child Abuse and Neglect for a discussion of non-accidental head trauma).

Subdural hematomas are more common than epidural hematomas. They are associated with underlying cortical injury and result in poor outcomes. The extracranial blood follows the brain contours on the head CT.

Epidural hematomas present typically with a loss of consciousness and less commonly with a lucent interval (a period of normal consciousness follow by a decreased mental status). Epidural hematomas represent arterial bleeding (the middle meningeal artery runs below the pterion or point of junction of frontal, parietal, temporal, and sphenoid bones). The extracranial blood forms a lenticular shape on head CT.

Diffuse axonal injury occurs due to axonal shearing results in edema and punctate hemorrhage. Presentation may be delayed for a few hours. Coma without an extracranial hematoma or brain parenchymal injury is more likely to represent diffuse axonal injury. Diffuse swelling is seen on head CT (loss of gyri, compression of ventricles).


SUBDURAL


EPIDURAL

DIAGNOSIS
The evaluation of a patient with head trauma involves an assessment of the mechanism of injury, patient symptoms and physical examination findings. The focus of the evaluation is to identify those at risk for intracranial injury who require neuroimaging. This should be balanced with the risks of radiation exposure and procedural sedation if needed. Mental status in children can be assessed with age-specific versions of the Glasgow Coma Scale (See Appendix). The physical exam can identify signs of basilar skull fracture and increased intracranial pressure .

The Pediatric Emergency Care Applied Research Network (PECARN) has derived and validated clinical decision rules (See Appendix) to identify those at low risk of clinically important traumatic brain injury (PECARN, Lancet 2009, PubMed ID: 19758692). Patients with non-trivial head trauma and a Glasgow Coma Scale of greater than or equal to 14 were enrolled (< 2 years, n=8,502, ≥ 2 years, n=25,283). The negative predictive value for the < 2-year-old rule was 99.9%, 95% CI (99.88, 99.999%). The negative predictive of the ≥ 2-year-old rule was 99.95%, 95% CI (99.9, 99.99%). These values indicate a very low risk of traumatic brain injury in those without any of the six risk factors for each age cohort identified. With the age groups and the validation and derivation sets combined, 0.02% or 1 in 5,000 with clinically important traumatic brain injury would have been missed by the rules (See Appendix A for rule parameters).

Fast MRI has been evaluated as a radiation-free substitute for CT scan. A single center study assessed the feasibility and accuracy of fast MRI using a gradient recall echo (which is more sensitive for blood) in pediatric patients in which a CT was obtained as part of their ED trauma evaluation (Lindberg, Pediatrics. 2019, PubMed ID: 31533974). The MRI completion rate was 99.1% (223/225 attempted). 8/223 (3.6%) were sedated for a non-head trauma indication). The procedure time for these patients was 365 seconds, IQR (340, 392 seconds) for MRI compared to 59 seconds, IQR (52, 78 seconds) for CT.

The sensitivity of MRI was 92.8%, 95%CI (86.3, 96.8%). This sensitivity did not meet the authors criteria for clinical acceptability. The specificity was 96.2%, 95%CI (90.5, 99.0%) though an equivocal MRI counted as a negative MRI for the test characteristic calculations. 1 of the 8 cases missed by MRI (a subarachnoid hemorrhage) met PECARN criteria for clinically important traumatic brain injury. 6 injuries were missed on CT but identified by MRI. In addition, there were 4 cases with an equivocal CT in which MRI definitively excluded a subdural.

The primary applicability concern is the availability of MRI is a clinically relevant time frame. 19% of consented patients did not have an MRI. This was primarily due to unavailability prior to discharge. Use of FAST MRI would require collaboration with our radiology, trauma and neurosurgery colleagues.

SIGNS OF INCREASED INTRACRANIAL PRESSURE (ICP)
Headache
Vomiting
Papilledema
Decorticate posturing
Transtentorial herniation: Brain transverses tentorium at the level of the incisura
Ipsilateral fixed, dilated pupil due to 3rd cranial nerve compression
Contralateral hemiparesis
Foramen magnum herniation: Cerebellar tonsils, brainstem
Depressed consciousness
Cushing’s Triad: Bradycardia, hypertension, irregular respirations

SIGNS OF BASILAR SKULL FRACTURE
Battle sign: Bruising over the mastoid
Raccoon eyes: Periorbital ecchymosis
Hemotympanum: Blood in the middle ear behind the tympanic membrane
Hearing loss
Facial nerve paralysis
CSF otorrhea or rhinorrhea

MANAGEMENT: GENERAL

MANAGEMENT OF HEAD TRAUMA	
AIRWAY & CERVICAL SPINE	If a C-spine injury is suspected, 1. Apply a cervical collar or manual inline stabilization. 2. Use the jaw-thrust maneuver to open the airway. 3. Use a log-roll maneuver when turning the patient.
BREATHING	Hyperventilation (PCO_2 of 30-35 mmHg) to increase cerebral perfusion pressure for signs of impending herniation
CIRCULATION	Assess for hypertension and bradycardia as signs of increased ICP The goal is to maintain cerebral perfusion pressure. Hypotension: Transfuse PRBC, initiate massive transfusion protocol Vasoconstrictor's may be indicated in neurogenic shock
DISABILITY	Assess mental status using AVPU or the Age-appropriate Glasgow Coma Scale. (Appendix B) Assess for signs of herniation (e.g. dilated fixed pupil)
EXPOSURE	Examine for signs of penetrating head trauma Assess for signs of basilar skull fracture

MANAGEMENT: INCREASED INTRACRANIAL PRESSURE

The Monroe-Kellie Doctrine indicates that intracranial volume is a constant, made up of brain (70%), blood (10%), CSF (10%) and interstitial fluid (10%). With the addition of volume (hemorrhage, edema), compensatory mechanisms will maintain ICP. For example, swelling compresses the ventricles decreasing the intracranial volume of CSF.

In addition, cerebral vasoconstriction increases cerebral perfusion pressure. This manifested by the increased blood pressure seen in Cushing's triad (the bradycardia is as a result of hypertension). When the limits of compensatory mechanisms are met intracranial pressure (ICP) will increase.

Conceptually, the management of increased ICP has been replaced by management of cerebral perfusion pressure (CPP). (CPP = Mean Arterial Pressure (MAP) – ICP)). An increase in ICP will result in a decrease in CPP unless MAP increases. A decrease in CPP will result in cerebral ischemia and edema (secondary brain injury) further increasing ICP.

The mainstay of therapy is to maintain optimal mean arterial pressure and respiratory support to ensure adequate oxygenation and perfusion. Further management may require consultation with a pediatric intensivist and/or pediatric neurosurgeon.

MANAGEMENT: TRAUMATIC BRAIN INJURY: ↑ INTRACRANIAL PRESSURE	
Positioning	Head of bed up to 30 degrees. Neutral head/neck position. (maximizes cerebral venous return)
Temperature	Avoid hyperthermia: Antipyretics, cooling blanket, Cerebral metabolic demand ↑ 5% for each ↑ 1°C Recent evidence suggests that cooling is ineffective
Sedation and Analgesia	Balanced to maintain blood pressure and ability to assess neurologic status
Systolic Blood Pressure	Maintain mean arterial pressure > 5% for age Do not restrict fluids if poor perfusion or hypotension PRBC > Crystalloid for poor perfusion Consider vasoconstrictor for neurogenic shock
Controlled Hyperventilation	Consider brief periods hyperventilation (PCO_2 30-35) for signs of herniation. Otherwise normal PCO_2
Mannitol (20%)*	Dose: 0.5-1.0 grams/kg over 10-20 minutes Avoid in the hypotensive patient: Diuretic effect may decrease intravascular volume
Hypertonic Saline (3%)	Bolus Dose: 5 ml/kg over 20 minutes Infusion Dose: 0.1-1.0 ml/kg/hour Benefit of increasing intravascular volume
Anticonvulsants	Keppra (Levetiracetam): 20 mg/kg IV Indications: >1 seizure, seizure > 1 hour post injury or severe intraparenchymal brain injury
Neurosurgery	Decompressive craniectomy
*"Although mannitol is commonly used in the management of raised ICP in pediatric TBI, no studies meeting inclusion criteria were identified for use as evidence for this topic." Mannitol has not been subjected to contemporary controlled clinical trials versus placebo, other osmolar agents, or other therapies in children". Brain Trauma Foundation Guidelines, Pediatr Crit Care Med. 2019, PubMed ID: 30830015)	

RECOMMENDATIONS: HYPERVENTILATION	
ATLS (2018)	Prophylactic hyperventilation is not recommended. In general, maintain PCO_2 at approximately 35 mmHg
	Brief periods of hyperventilation (PCO2 25-30 mmHg) for signs of herniation while other treatments are initiated.
Brain Trauma Foundation Guideline (Adult 2016)	Prolonged prophylactic hyperventilation with PCO_2 of 25 mm Hg is not recommended.
	Hyperventilation is recommended as a temporizing measure for the reduction of elevated ICP
	Hyperventilation should be avoided during the first 24 h after injury when cerebral blood flow is often reduced critically.
Brain Trauma Foundation Guideline (Peds 2019)	Prophylactic severe hyperventilation to a PCO_2 < 30 mm Hg in the initial 48 hours after injury is not suggested.
	If hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia is suggested.

RECOMMENDATIONS: HYPEROSMOLAR THERAPY	
ATLS (2018)	Mannitol or hypertonic saline for signs of herniation. No difference in controlling ICP. Neither lowers ICP in hypotensive patient
	Mannitol 1 gram/kg over 5 minutes
	Hypertonic saline (3 or 23.4%) preferred in hypotensive patients (no diuresis)
Brain Trauma Foundation Guideline (Adult 2016)	Mannitol is effective for control of raised ICP at doses of 0.25 to 1 g/kg body weight.
	Arterial hypotension (systolic blood pressure < 90 mm Hg) should be avoided.
	Restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial causes.
Brain Trauma Foundation Guideline (Peds 2019)	Bolus hypertonic saline (3%) is recommended in patients with intracranial hypertension. Recommended effective doses for acute use range between 2 and 5 mL/kg over 10-20 min.
	Continuous infusion hypertonic saline is suggested in patients with intracranial hypertension. Suggested effective doses as a continuous infusion of 3% saline range from between 0.1 and 1.0 mL/kg of body weight per hour. The minimum dose needed to maintain intracranial pressure ICP < 20 mm Hg is suggested.
	Bolus of 23.4% hypertonic saline is suggested for refractory ICP. The suggested dose is 0.5 mL/kg with a maximum of 30 mL.

RECOMMENDATIONS: PROPHYLACTIC ANTICONVULSANT	
ATLS (2018)	Prophylactic use of phenytoin or valproate is not recommended for preventing late (> days) post-traumatic seizures
	Phenytoin is recommended to decrease early (< 7 days) post traumatic seizures when the overall benefits is felt to outweigh the complications associated with such treatment (can inhibit brain recovery)
Brain Trauma Foundation Guideline (Adult 2016)	Prophylactic use of phenytoin or valproate is not recommended for preventing late PTS.
	Phenytoin is recommended to decrease the incidence of early PTS (within 7 d of injury), when the overall benefit is thought to outweigh the complications associated with such treatment. However, early PTS have not been associated with worse outcomes.
	At the present time there is insufficient evidence to recommend levetiracetam compared with phenytoin regarding efficacy in preventing early post-traumatic seizures and toxicity.
Brain Trauma Foundation Guideline (Peds 2019)	Prophylactic treatment is suggested to reduce the incidence of early (within 7 d) PTS.
	At the present time there is insufficient evidence to recommend levetiracetam over phenytoin based on either efficacy in preventing early PTS or toxicity.

WEBLINK: Brain Trauma Foundation Guideline (Peds 2019)

WEBLINK: Brain Trauma Foundation: Guideline (Adult 2016)

DISPOSITION

Patients with severe traumatic brain injury should be admitted to a pediatric intensive care unit. However, those with mild traumatic brain injury who require admission for observation may not require ICU admission. A clinical decision rule has been derived and internally validated in pediatric patients (n=839) with mild traumatic brain injury and intracranial injury on CT to identify clinical and imaging factors associated with neurosurgical intervention or intubation for greater than 24 hours (PECARN, JAMA Pediatr., PubMed ID: 28192567). The CHILDA Score included clinical and radiologic variables associated with a need for ICU admission. Using a score of > 0 for ICU admission, 51.3% could have potentially avoided ICU admission. Using a score of > 2 for ICU admission, 65.4% could have potentially avoided ICU admission.

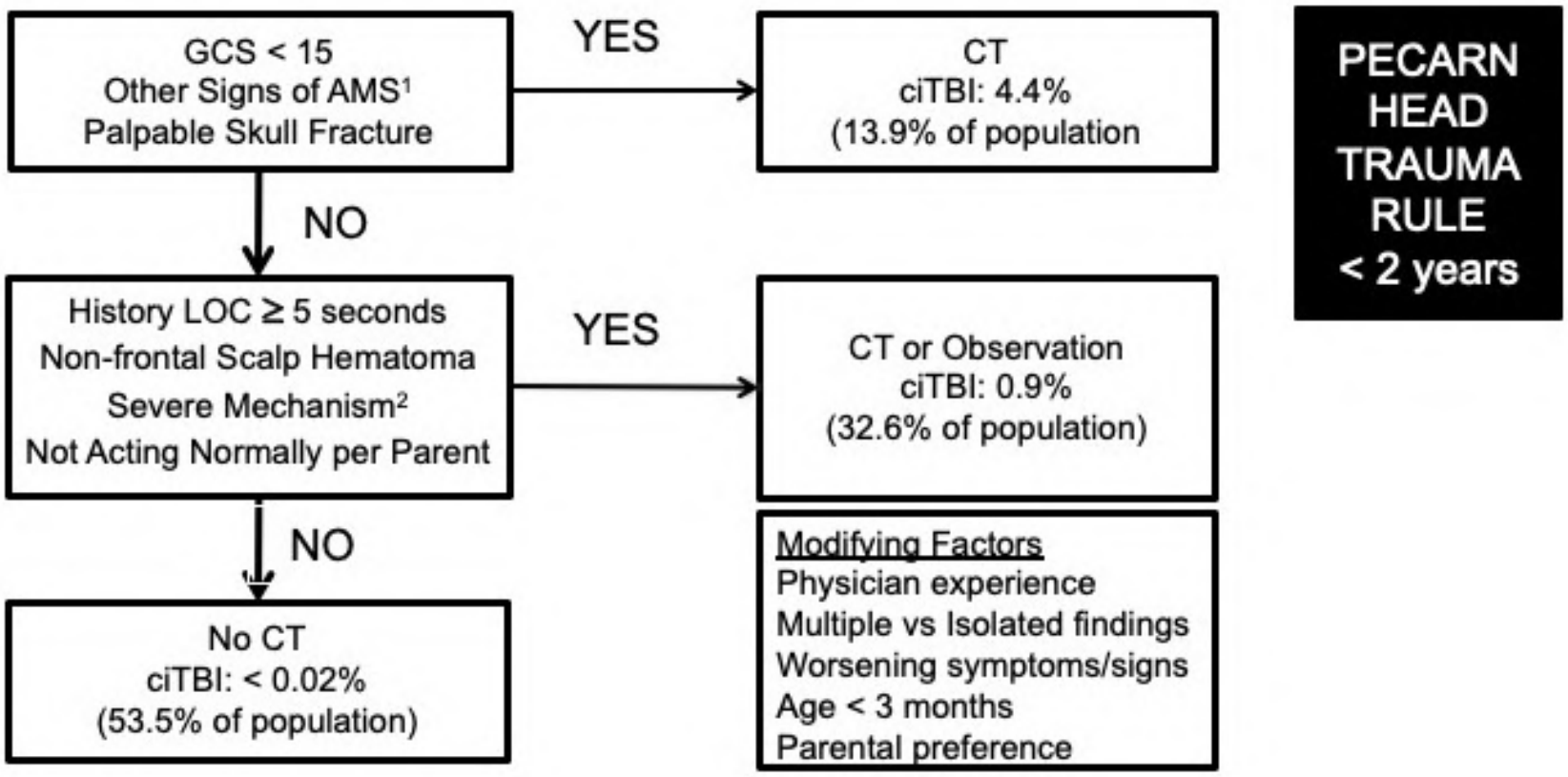
This is a level IV decision rule. It has been derived only or validated only in split samples, large retrospective databases or by statistical methods. The rule requires further validation before it can be applied clinically

CHILDREN'S INTRACRANIAL INJURY DECISION AID (CHILDA) RISK SCORE			
VARIABLE	ODDS RATIO (95% CI)	BETA	POINTS
Depressed Skull Fracture	6.5 (3.7, 11.4)	1.9	7
Midline Shift	6.8 (3.4, 13.8)	1.9	7
Epidural Hematoma	3.4 (1.8, 6.2)	1.2	5
GCS 13	1.6 (0.82, 3.1)	0.46	5
GCS 14	3.4 (1.5, 7.4)	1.2	2
Score Range: 0-24 points			

CHILDA RISK SCORE TEST CHARACTERISTICS		
	ICU Admit for SCORE > 0	ICU Admit for SCORE > 2
Sensitivity	93.2% (84.7, 97.7%)	86.3% (76.3, 93.2%)
Specificity	55.5% (51.9, 59.0%)	70.4% (67.0, 73.6%)
Predictive Value Positive	16.6% (13.2, 20.6%)	21.7% (17.1, 26.9%)
Predictive Value Negative	98.8% (97.3, 99.6%)	98.2% (96.7, 99.1%)
Avoid ICU admission	51.3%	65.4%

APPENDIX A: PECARN HEAD TRAUMA RULES

(Kupperman, Lancet 2009, PubMed ID: 19758692)



APPENDIX B: NEUROLOGIC ASSESSMENT

GLASGOW COMA SCALE				
	< 1 YEAR	>1 YEAR		
Eye Opening	Spontaneous	Spontaneous		4
	To Verbal Command	To shout		3
	To Painful	To Painful		2
	No response	No response		1
Motor Response	Spontaneous	Obeys Commands		6
	Localizes Pain	Localizes Pain		5
	Withdraws to Pain	Withdraws to Pain		4
	Flexion-Decorticate	Flexion-Decorticate		3
	Extension-Decerebrate	Extension-Decerebrate		2
	No Response	No Response		1
	< 2 YEARS	2-5 YEARS	> 5 YEARS	
Verbal	Smile/Coos Appropriately	Appropriate Words/ Phrases	Oriented	5
	Cries and is Consolable	Inappropriate Words	Confused / Disoriented	4
	Persistent Inappropriate crying and/or screaming	Persistent Cries Screams	Inappropriate Words	3
	Grunts, Agitated or Restless	Grunts	Incomprehensible Sounds	2
	No Response	No Response	No Response	1

AVPU CLASSIFICATION	
A	Alert
V	Responds to Voice Stimuli
P	Responds to Painful Stimuli
U	Unresponsive to all Stimuli

HEMORRHAGIC SHOCK

INTRODUCTION (MICHAEL MOJICA, MD, 11/2020)
The primary etiology of shock in the trauma patient is hypovolemic shock due to internal or external hemorrhage. Rarer causes of shock in the trauma patient include distributive shock (neurogenic shock due to injury to the thoracic sympathetic ganglion chain), cardiogenic shock (myocardial contusion) and obstructive shock (tension pneumothorax or pericardial tamponade).

This PEM Guide focuses on hemorrhagic shock in the trauma patient, but management principles also apply to the patient with gastrointestinal hemorrhage, bleeding from a ruptured ectopic pregnancy and maternal hemorrhage at delivery.

CLINICAL ASSESSMENT
An increase in heart rate and vasoconstriction compensate for blood loss. These compensatory changes result in the clinical manifestations of hemorrhagic shock. Signs and symptoms of shock include deficits in central and peripheral perfusion.

Tachycardia increases cardiac output (CO = HR x SV) and is the earliest, measurable sign of shock. Vasoconstriction increases blood pressure by 1. increasing systemic vascular resistance and by 2. increasing cardiac output by increasing venous return to the right heart with an increase in stroke volume. Vasoconstriction shifts blood flow from the skin, muscle and viscera to the brain, heart and kidneys. This is manifested clinically by poor distal perfusion (compensated shock) before hypotension occurs (hypotensive shock). This is particularly true in children who may lose up to 45% of their blood volume before hypotension occurs. Tachycardia and poor distal perfusion (weak peripheral pulses, pale/mottled and/or cold extremities and prolonged capillary refill) are ominous signs in a pediatric trauma patient and should be assessed and treated promptly.

CLINICAL FINDINGS IN SHOCK		
CENTRAL	COMPENSATED SHOCK	HYPOTENSIVE SHOCK
Blood Pressure	Normal	Decreased
Central Pulses	Normal	Weak
Mental Status	Normal	Decreased
PERIPHERAL	COMPENSATED SHOCK	HYPOTENSIVE SHOCK
Peripheral Pulses	Weak	Weak
Extremities	Cool, Pale	Cold, Mottled
Capillary Refill	> 2 seconds	> 2 seconds

HEART RATE (BEATS/MINUTE)			
AGE	AWAKE	MEAN	SLEEPING
< 3 months	85-205	140	80-160
3 months-2 years	100-190	130	75-160
2 years-10 years	60-140	80	60-90
> 10 years	60-100	75	50-90

HYPOTENSION*		
CATEGORY	AGE	SYSTOLIC BP (mmHg)
Term neonates	< 1 month	< 60
Infants	1-12 months	< 70
Children	1-10 years	< 70 + (2 x Age in years)
Adolescent	> 10 years	< 90
*< 5th Percentile of Systolic Blood Pressure for Age		

TRAUMATIC SHOCK CLASSIFICATION (ATLS MANUAL: 10th EDITION (2018))				
	CLASS I	CLASS II (MILD)	CLASS III (MODERATE)	CLASS IV (SEVERE)
Blood Loss	≤ 15%	15-30%	30-40%	> 40%
Heart Rate	Normal	Normal or ↑	↑	↑↑
Blood Pressure	Normal	Normal	Normal or ↓	↓↓
Pulse Pressure	Normal	↓	↓	↓
Respiratory Rate	Normal	Normal	Normal or ↑	↑
Urine Output	Normal	Normal	↓	↓↓
Mental Status (GCS)	Normal	Normal	↓	↓
Base Deficit	-2, 0	-6, -2	-10, -6	-10 or less
BLOOD NEEDED?	MONITOR	POSSIBLE	YES	MASSIVE TP

SHOCK INDEX, PEDIATRIC ADJUSTED (SIPA)				
Age	Heart Rate	Systolic BP	Abnormal	Risk of Blunt Injury
4–6 years	65–110	90–110	> 1.22	22.0%
7–12 years	60–100	100–120	> 1.00	25.1%
13-16 years	55–90	100–135	> 0.90	32.0%
SIPA predicts mortality in children (4-16 years) with blunt trauma,(>16yrs: NL= 0.5-0.7) SIPA = Maximum Heart Rate Minimum Systolic Blood Pressure WEB LINK: MDCALC: SIPA, Acker, J Pediatr Surg. 2015, PubMed ID: 25638631				

LABORATORY TESTING

The most essential laboratory test in the trauma patient is a type and cross. An elevated lactate (metabolic acidosis) is a marker for anaerobic metabolism due to poor perfusion. Laboratory tests in the patients requiring blood products should include serial monitoring of CBC, PT/PTT/INR, fibrinogen and electrolytes, specifically serum K^+, ionized Ca^{++}.

Thromboleslastography (TEG) and Rotational Thromboleslastography (ROTEM) are tests that may allow for more specific monitoring of coagulopathy and can target the need for specific blood products. A 2015 Cochrane Review concluded that “We are unable to offer advice on the use of global measures of hemostatic function for trauma based on the evidence on test accuracy identified in this systematic review. This evidence strongly suggests that at present these tests should only be used for research.” (Hunt, Cochrane Database of Systemic Reviews 2015, PubMed ID: 25686465).

IMAGING

The Extended Focused Abdominal Sonography in Trauma (E-FAST) examination can be used at the bedside to rapidly identify blood in the abdominal and thoracic cavities and in the pericardial space (See PEM Guide: Trauma: E-FAST). In the hemodynamically stable patient, CT can identify both the source of internal bleeding and the extent of injury to inform the need for operative management.

MANAGEMENT

Damage control resuscitation (also known as balanced or hemostatic resuscitation) is a trauma management strategy with the goals of rapid restoration of normal cardio-vascular status while avoiding coagulopathy, acidosis and hypothermia. Evidence for the use of many of the interventions described below in the pediatric population is very limited.

Initial management priorities are to assess hemodynamic stability, obtain intravenous access, send a type and cross in anticipation of a potential blood product transfusion and if indicated by the primary survey, correction of obstructive shock with needle thoracentesis for tension pneumothorax or pericardiocentesis for cardiac tamponade)(See PEM Guide: Cardiology: Pericardiocentesis).

Localizing and stopping the source of bleeding is an essential first step in restoring perfusion. Techniques to control internal hemorrhage include surgical intervention, embolization and application of a pelvic blinder. Control of external hemorrhage can be obtained with direct compression or tourniquet application.

MANAGEMENT OVERVIEW	
IV Access	IV access x 2. Intraosseous access if intravenous not attainable
Establish Weight	Medication and blood product dosing, equipment selection
Initial Labs	T&Cross, VBG/Lactate, CBC, INR/PT/PTT, Fibrinogen, BMP, iCal
Ongoing Labs	VBG/Lactate, CBC, PT/PTT/INR, Fibrinogen, BMP (K+), iCal
Monitoring	Continuous vital signs monitoring (including temperature)
Re-warming	Warm fluids/blood products, warm blankets, remove wet clothing
Crystalloid	As necessary until blood available, avoid dilutional coagulopathy
Blood	Early blood product administration
MTP	PRBC, FFP, Platelets, 1:1:1 ± Cryoprecipitate
Tranexamic Acid	Administer within 3 hours of injury if MTP activated

FLUID RESUSCITATION: Severe injury with hemorrhage results in a coagulopathy due to consumption of coagulation factors. In addition, large volumes of crystalloid or blood will result in a dilutional coagulopathy. Large volumes of crystalloid or blood increase intravascular pressure and may also lead to an increase in the rate of bleeding. Fluid resuscitation before the control of bleeding must balance the competing goals of restoration of organ perfusion and avoidance of coagulopathy that can occur with fluid resuscitation. Hypotensive resuscitation (permissive hypotension) is an attempt to balance these goals. Lower intravascular pressure may also limit ongoing bleeding by allowing blood vessels to spasm and clot. This approach is not applicable to severely head injured patients in which maintaining cerebral perfusion is the priority or to those with spinal cord injury.

1. CRYSTALLOID INFUSION: Recent recommendations are to provide blood as soon as possible in the unstable patient and avoid high volumes of crystalloid. Recommendations for crystalloid in the adult patient (> 40 kg) has been reduced to 1 liter. Pediatric crystalloid dose is unchanged at 20 ml/kg (ATLS Manual 2018). In a multi-center, prospective observational study including 712 children in traumatic hemorrhagic shock as evidenced by an elevated pediatric adjusted shock index, the provision of more than one bolus of crystalloid was associated with a statistically significant increased odds of ventilator use more than 3 days (2 boluses: aOR 3.18 95% CI (1.25, 8.04), > 2 boluses: aOR 3.88, 95% CI (1.39, 10.8)), ICU length of stay more than 6 days (2 boluses: aOR 2.38, 95% CI (1.01, 5.62), > 2 boluses (aOR 8.53, 95% CI (3.43, 21.3) and hospital length of stay more than 14 days (2 boluses: 2.95, aOR 95% CI (1.34, 6.51), > 2 boluses: a OR 6.41, 95% CI (2.74, 14.9). There was a dose-response effects with higher odds for more than 2 boluses compared to 2 boluses. However, there was no increase in the primary outcome of survival to hospital discharge. (Polites, J Trauma Acute Care Surg 2020, PubMed ID: 32251263)

2. BLOOD TRANSFUSION: PRBCs are infused in a bolus of 10 ml/kg in the pediatric patient. Packed red blood cells (PRBC's) are infused in preference to whole blood because whole blood needs to first be reconstituted from packed RBC's and plasma. There is combat evidence that whole blood may be preferable to packed red blood cells but recent recommendations have not yet incorporated this evidence (Weymouth, J Emerg Med 2019, PubMed ID: 30904380).

A 70 kg male has a blood volume of approximately 5 liters. A child's blood volume is 70-80 ml/kg. One unit of PRBCs will raise an adult's hemoglobin by 1 gm/dl and hematocrit by 3%. Ideally, and if time permits, fully typed and cross-matched PRBC's is preferred followed by type specific, uncross-matched PRBC's. Type O PRBC's are given in an emergency. Type O negative PRBCs should be prioritized for women of child bearing age to prevent Rh isoimmunization. PRBCs should be warmed to prevent hypothermia.

PRODUCT	VOLUME/UNIT	HEMATOCRIT
PRBC	250-300 ml/unit	60%
Whole blood	450 ml/unit	35-40%

3. MASSIVE TRANSFUSION PROTOCOLS: A massive transfusion is generally defined as the need of more that 10 units of PRBC's in the first 24 hours or 4 units within the first hour of injury in an adult patient. Massive transfusion protocols include platelets, fresh frozen plasma (FFP) and cryoprecipitate in addition to PRBCs typically in a 1:1:1 ratio of PRBCs to Platelets to FFP. The goal is to reverse and prevent coagulopathy.

MASSIVE TRANSFUSION PROTOCOL (PEDIATRIC): PACK CONTENTS												
PRODUCT	5-10 kg			10-30 kg			30-50 kg			> 50 kg		
Pack Number	#1	#2	#3	#1	#2	#3	#1	#2	#3	#1	#2	#3
PRBC (units)	1	1	1	2	1	1	3	2	2	5	5	5
Thawed Plasma (units)	1	1	1	2	1	1	3	2	2	4	4	4
Single Donor Platelets (u)	1	0	0	1	0	0	1	0	0	1	1	1
Cryoprecipitate (units)	0	5[1]	5[2]	0	5[1]	5[2]	0	5[1]	5[2]	5[3]	5[3]	5[3]
1. If available with pack #2, 2. If not available with pack #2, 3. When ordered Bellevue Trauma Slot: 2 units O (-) PRBC, 2 units O (+) PRBC, 2 units FFP												

MASSIVE TRANSFUSION PROTOCOL (BELLEVUE): ONGOING BLEEDING	
INDICATION	PRODUCT
INR > 1.5	FFP: 20 ml/kg
Fibrinogen < 100 mg/dl	Cryoprecipitate: 5 ml/kg
Platelets < 50 x 10^9/L	Platelets: 10 ml/kg
Ionized Calcium < 4 mg/dL	Calcium Chloride (10%): 10 mg/kg (0.1 ml/kg)* Calcium Gluconate (10%): 200 mg/kg (0.2 ml/kg)*
Tranexamic Acid	Within 3 hours of injury (After 3 hours Risks > Benefits) 15 mg/kg (max 1 g) loading dose over 10 minutes then 2 mg/kg (max 120 mg) per hour for 8 hours.
*Do not give Calcium and blood products in the same IV line	

ABC (ASSESSMENT OF BLOOD CONSUMPTION) SCORE (ADULT)
Penetrating Mechanism of Injury
(+) FAST EXAM
Systolic Blood Pressure 90 mmHg
Heart Rate ≥ 120 beat per minute
≥ 2 of the 4 criteria predicts the need for multiple transfusions Nunez, J Trauma 2009, PubMed ID: 19204506

TRANEXAMIC ACID: Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine. It inhibits fibrinolysis by blocking the lysine binding sites on plasminogen. Tranexamic acid has proven effective in reducing blood transfusions in a variety of surgical (e.g. maternal hemorrhage) and non-surgical (e.g. gastrointestinal) situations.

The CRASH-2 Trial was a multinational, randomized clinical trial including over 20,000 adult trauma patients suspected of having active hemorrhage (CRASH-2 Trial, Lancet 2010, PubMed ID: 20554319). Patients were randomized to a saline placebo or to a 1 gram loading dose of Tranexamic acid over 10 minutes followed by a 1 gram infusion over the next 8 hours. Tranexamic acid was shown to have a statistically significant survival benefit. There was a 1.45%, 95% CI (0.5, 2.4%), reduction in all-cause mortality and a 0.8% 95% CI (0.2, 1.5%) reduction in death due to bleeding in the Tranexamic acid group. No statistically significant difference was found for fatal and non-fatal vascular occlusive events, the need or amount of transfusion and the need for surgery.

A retrospective, cohort study of a Japanese pediatric trauma registry used propensity scoring to pair pediatric trauma patients who received Tranexamic acid to those who did not (n=1,914 pairs) (Maeda, Ped Crit Care Med. 2018, PubMed ID: 30199511). The purpose of the study was to assess adverse events associated with Tranexamic in the pediatric population. The study used a composite outcome of adverse events defined as thromboembolism or seizure or renal dysfunction. Adverse events were statistically higher in the Tranexamic acid group (0.6%) compared to the No Tranexamic acid (0.1%) (Risk Difference: 0.5%, 95% CI (0.1, 0.9%). When individual outcomes were assessed, there was a higher rate of seizures in the Tranexamic acid group (0.37%) than in the non-Tranexamic acid group (0.0%)(Risk Difference: 0.37%, 95% CI (0.10, 0.64%). There were no statistically significance differences in the rate of thromboembolism (Risk Difference: -0.05% (-0.23, 0.12%)), renal dysfunction (Risk Difference: 0.16% (-0.02, 0.33%)) or in-hospital mortality (Risk Difference: -0.26% (-0.83, 0.31%)).

A retrospective, cohort study included 776 combat injured pediatric patients of which 66 received Tranexamic acid (PED-TRAX Trial, J Trauma Acute Care Surg 2014, PubMed ID: 25423534). Patients who received TXA were significantly sicker with higher injury severity scores, hypotension, acidosis, and coagulopathy. After correcting for potential confounding variables, Tranexamic acid use was independently associated with decrease in mortality (Odds Ratio: 0.27; 95% (CI not interpretable). The Pediatric Emergency Care Applied Research Network (PECARN) is planning a multicenter, randomized trial of the safety and efficacy of Tranexamic acid in pediatric trauma patient.

TRANEXAMIC ACID DOSING	
Loading Dose	15 mg/kg (maximum dose 1 gram) over 10 minutes
Infusion Dose	2 mg/kg/hour (maximum dose 120 mg/hour) for 8 hours

TOURNIQUETS: External bleeding can often be stopped with direct pressure at the site of bleeding. Blind clamping of a blood vessel can damage adjacent nerves and should be avoided. Extremity tourniquets have proven life-saving in both combat situations and civilian mass casualty events. The Stop the Bleed Coalition (WEB LINK: STOP THE BLEED COALITION), is a joint venture of the American College of Surgeons (ACS), The ACS Committee on Trauma, the Hartford Consensus, Department of Defense and the Department of Homeland Security. It provides training and sells bleeding control kits with components (tourniquets and hemostatic dressings) similar to those used by the military.

VIDEO LINK: COMBAT APPLICATION TOURNIQUET

REBOA: REBOA is Resuscitative Endovascular Balloon Occlusion of the Aorta. A catheter is placed in the femoral artery using Seldinger technique and the balloon is inflated in one of three locations in the aorta (see table below). REBOA limits subdiaphragmatic hemorrhage distal to the balloon and improve blood pressure proximal to the balloon. The indications and contraindications for REBOA have not been conclusively established and are evolving as new evidence becomes available. The main complication of REBOA is ischemia/reperfusion injury distal to the balloon inflation.

REBOA BALLOON INFLATION ZONES	
ZONE	BALOON LOCATION
I	Origin of the left subclavian to the coeliac artery
II	Coeliac artery to the most caudal renal artery
III	Most caudal renal artery to the aortic bifurcation

An observational study using a trauma and acute care surgery registry compared REBOA (n=83) to resuscitative thoracotomy (n=202) in adults. (Brenner, J Am Coll Surg 2018, PubMed ID: 29421694). Survival beyond the ED was 62.6% in the REBOA and 44.1% in the resuscitative thoracotomy group (Risk Difference: 18.6%, 95% CI (5.8, 30.3%). Survival to discharge was 9.6% in the REBOA group and 2.5% in the resuscitative thoracotomy group (Risk Difference: 7.2%, 95% CI (1.5, 15.3%). Of note, the results are based on a univariate analysis and not on a regression analysis including other confounding predictors of survival. The authors caution that “considerable additional study is required to definitively recommend REBOA for specific subsets of injured patients.” Specifically, clinical trial data and pediatric data are lacking.

VIDEO LINK: PROCEDURE VIDEO
(Prytime Medical Catheter available at Bellevue)

PROCEDURES WITH RISK OF CARDIOVASCULAR INSTABILITY: Some procedures may worsen a tenuous cardiovascular status leading to hypotension or traumatic arrest. For example, a massive hemothorax may tamponade bleeding. Chest thoracotomy and evacuation of blood in the pleural cavity may exacerbate hemorrhage. Similarly, the presence of a penetrating object (e.g. knife) can also tamponade bleeding. Removal of the object may exacerbate hemorrhage. Endotracheal intubation and positive pressure ventilation increase intrathoracic pressure and decreases venous return to the right side of the heart and ultimately decreases cardiac output. These procedures should be delayed, when feasible, until restoration of normal vital signs and perfusion.

ED RESUSCITATIVE THORACOTOMY: Children requiring cardiopulmonary resuscitation in the field with return of spontaneous circulation will have 50% neurologically intact survival (ATLS 10th Edition). Children who received CPR for more than 15 minutes prior to ED arrival or who present with fixed pupils are Typically non-survivors. ATLS concludes “for pediatric trauma patients who arrive in the trauma bay with continued CPR of long duration, prolonged resuscitative efforts are not beneficial.”

The ACS National trauma data bank (2013-16) was assessed for indications and outcomes of pediatric patients less than 16 years of age who underwent ED thoracotomy within 30 minutes of arrival. 114 patients were identified with a mean age of 10.3 ± 4.7 years. 69% were male and 56% had penetrating trauma. Overall mortality was 88% for penetrating trauma and 94% for blunt trauma. Mortality rates and indications were similar among pediatric, adult and mixed trauma center designations. There were no survivors (0/53) among those who arrived without signs of life. The authors concluded that “regardless of injury mechanism, ED thoracotomy is not appropriate in children without signs of life on arrival. Pediatric guidelines are needed to increase awareness of the poor outcomes and limited indications for ED thoracotomy.” (Prieto, J Trauma Acute Care Surg. 2020, PubMed ID: 33017132).

ED THORACOTOMY RECOMMENDATIONS: PULSELESS IN ED

Signs of Life[1]	Mechanism	Adult Recommendation[2]	Pediatric Recommendation[3]
Yes	Penetrating: Thoracic	Strong YES[4]	Strong YES
No	Penetrating: Thoracic	Conditional YES[5]	Conditional NO[6]
Yes	Penetrating: Extra-thoracic	Conditional YES	Conditional YES
No	Penetrating: Extra-thoracic	Conditional YES	Conditional NO
Yes	Blunt	Conditional YES	Conditional YES
No	Blunt	Conditional NO	Conditional NO

1. Pupillary response, spontaneous ventilation, presence of carotid pulse, palpable or measurable or blood pressure, extremity movement, or cardiac electrical activity.
2. Eastern Trauma Assoc, J Trauma Acute Care Surg 2015, PubMed ID: 26091330
3. Prieto, J Trauma Acute Care Surg. 2020, PubMed ID: 33017132
4. Desirable consequences clearly outweigh undesirable consequences
5. Desirable consequences probably outweigh undesirable consequences
6. Undesirable consequences probably outweigh desirable consequences

LACERATION REPAIR

INTRODUCTION (ERIC WEINBERG M.D., 9/2018)
Children constitute a significant proportion of patients who present to emergency departments for care of traumatic injuries. Over one third of injuries in children will involve a laceration. The phases of wound healing include: inflammatory, proliferative (collagen deposition) and remodeling.

WOUND REPAIR GOALS
1. Restoration of skin integrity
2. Acceptable cosmetic and functional outcome
3. Prevention of infection

MECHANISM OF INJURY	
The type of force inflicting the injury determines the wound's infection and scarring potential. Three types of mechanical forces are shearing, tension, and compression.	
1	Shearing injuries such as those obtained with a knife have little devitalization of the wound edges and therefore, there is less potential for infection.
2	Tension injuries such as an avulsion or flap occur when a blunt object strikes the skin at an angle less than 90^0. There is usually more devitalized tissue at the wound edges with possible vascular compromise, resulting in a higher risk for infection and more difficult repair.
3	Compression injuries from blunt trauma at an angle of 90^0 cause the most tissue damage with the most devitalization, resulting in the highest risk for infection and poor cosmetic outcome.

CLINICAL ASSESSMENT

INITIAL ASSESSMENT
Airway, breathing and circulation should be assessed and stabilized.
Significant bleeding should be controlled as part of the primary survey.
a. Direct pressure or temporary use of a sphygmomanometer proximal to the wound for less than two hours will achieve hemostasis.
b. Don't blindly clamp an artery. It risks injury to adjacent nerves
The secondary survey should be completed in a systematic fashion before focusing on wound repair so that other major injuries will not be missed

HISTORY
Mechanism of injury
Time of injury
Possibility of a foreign body
Environment (possible contaminants)
Medical history
Tetanus vaccination status

PHYSICAL EXAMINATION
Location: Length, depth, potential penetration of adjacent structures (e.g. joint)
Type of wound: Extent of devitalized tissue
Neurovascular status distal to the wound
Tendon function: Range of motion
Bone tenderness, crepitus, or deformity
Anesthetized wound: Completion of the exam, foreign bodies

IMAGING

Radiographs may identify underlying fractures and localize radiopaque foreign bodies. Point of care ultrasound may be useful to identify both radiopaque and non-radiopaque foreign bodies.

CONSULTATION

Patients with vascular, nerve, bony or tendon injuries should be referred to surgical specialists for possible repair in the operating room.

WOUND PREPARATION

ANESTHESIA
A local anesthetic can be infiltrated directly into the wound (not surrounding the wound)
Lidocaine is used at a maximal dose of 3-5 mg/kg without Epinephrine and 5-7 mg/kg with Epinephrine
It is traditionally taught to avoid Epinephrine for lacerations in an end artery circulation (fingers, toes, pinna, nose, and penis). Data from patients who accidentally inject themselves with an epinephrine auto-injector does not demonstrate adverse effects and does not support restricting epinephrine use in digits.
Pain of administration may be diminished by slow administration avoiding tissue distention, warming and buffering with NaHCO3
Alternatively, a Lidocaine containing gel (e.g. LET (Lidocaine, Epinephrine, Tetracaine)) can use applied to a wound for 30-45 minutes prior to wound cleansing.
Depending on the cooperation and age of the patient, procedural sedation or proper restraint of the patient may be necessary.
The combination of a topical anesthesia and a tissue adhesive results in a needless procedure and can obviate the need for procedural sedation.

WOUND CLEANSING
High pressure saline irrigation effectively removes most foreign material. Studies have demonstrated that the use of tap water does not increase infection rates.
The skin around the wound should be cleaned. Chlorhexidine or Povidone-Iodine solution can be used to clean the periphery of the wound. Povidone-Iodine should not be used in the wound itself because of its potential to increase infection by damaging tissues.
Surrounding hair should be clipped and not shaved to avoid creating additional points of entry for infection.

WOUND CLOSURE

There are a variety of wound closure techniques. These include sutures, adhesive strips, staples, tissue adhesives and the hair apposition technique for scalp lacerations. The same basic principle applies to each of these techniques. The skin edges should be approximated to allow normal wound healing to take place. Deeper lacerations may require a layered approach with deep sutures and dermal sutures.

TIMING OF WOUND CLOSURE
PRIMARY CLOSURE
Immediate wound closure is the most common approach for pediatric lacerations.
The main reason to not close a laceration is to prevent infection.
Although the laceration should ideally be closed within six hours, low infection risk wounds can be closed even up to 12 to 24 hours after injury. Wounds of the face heal best with primary closure even up to 24 hours after injury due to good blood flow.
SECONDARY CLOSURE (OR INTENTION)
The wound is left open and allowed to heal by granulation. Some examples of wounds that may require secondary closure are infected ulcers and animal bites.
TERTIARY CLOSURE (AKA DELAYED PRIMARY CLOSURE)
Wounds are left open for several days (typically 5 days) and then closed after the risk of infection has decreased.
This method is not commonly used in pediatric patients, but is a possible option for heavily contaminated wounds such as blast, crush, or bite injuries.

SUTURE SELECTION	
Absorbable (e.g. Gut)*	Not to be removed: Deep sutures, mucous membranes
Non-Absorbable (e.g. Nylon)	To be removed: Cutaneous
Braided vs Monofilament	Braided sutures limit knot slippage but promote Inflammation. The converse is true for monofilament
Size	Large sutures are stronger and are preferred on areas under tension (e.g. knee) Small sutures result in better cosmesis

*Rapidly dissolving sutures (e.g. Fast Absorbing Gut) on the face and extremities have been shown to have similar cosmetic outcomes to non-absorbable sutures that are removed. They are particularly helpful for wounds in children for which suture removal would be problematic (e.g. would require sedation). They also avoid the need for a follow-up visit (Karounis, Acad Emerg Med. 2004, PubMed ID: 15231459

SUTURE ALTERNATIVES	
Tissue adhesives (Cyanoacrylate (Dermabond)	The wound should be cleaned and dried. Apply the adhesive in layers allowing the first layer to dry before the next is applied. Tissue adhesives can be used to approximate superficial lacerations that are not under tension or in hairy areas. For deep lacerations, deep inverted sutures can be used to approximate the deep tissue and tissue adhesive to approximate the superficial tissue.
Staples	Typically used for areas where cosmesis is not a concern such as the scalp
Others	Others: Wound adhesive strips, hair apposition technique

IMMOBILIZATION: Splint wounds in areas of motion or tension. For example, a volar forearm/hand splint could be used to limit motion for a laceration to a dorsal metacarpophalangeal joint.

INFECTION PROPHYLAXIS

ANTIBIOTICS: Systematic prophylactic antibiotics are not routinely recommended, if proper wound irrigation and debridement take place in a timely manner. There may be certain situations where prophylactic antibiotics (first generation cephalosporin or penicillinase resistant penicillin) may be useful.

A large, multicenter study found an overall wound infection rate of 69/2,663 or 2.6% 95% CI (2.0-3.3) (Quinn, EM J, 2014, PubMed ID: 23314208). They found that patients with wound infections were more likely to assess their wound as having poor cosmesis and more likely to seek a scar revision. They found no difference in infection rate between those with wounds sutured before or after 12 hours though there were only 72 patients whose wounds were sutured after 12 hours. Factors associated with an increased rate of infection are listed in the table below. The authors suggest that these wounds, with an infection rate between 5-10%, could be targeted for prophylactic antibiotics.

WOUNDS AT HIGH RISK OF INFECTION*	ODDS RATIO (95% CI)
Non head or neck laceration	2.5 (1.4, 4.5)
Diabetes	3.1 (1.2, 8.0)
Wound length > 5 cm	2.4 (1.4, 4.0)
Moderate of heavily contaminated wounds	1.9 (1.0, 3.3)
*This study excluded bite wounds	

ANTIBIOTIC INDICATIONS
Contaminated wounds
Lacerations involving the hand or perineum
Animal or human bites
Deep puncture wounds

TETANUS PROPHYLAXIS				
	CLEAN. MINOR WOUNDS		ALL OTHER WOUNDS[1]	
History	Td[2]	TIG[3]	Td[2]	TIG[3]
< 3 doses	YES	NO	YES	YES
≥ 3 doses	NO[4]	NO	NO[5]	NO
1: Wounds contaminated by dirt, feces, soil, saliva, Puncture wounds, avulsions. Wounds from missiles, crushing, burns, frostbite				
2: For children < 7yrs – DTaP or DT recommended, > 7 yrs Td recommended				
3: Tetanus Immune Globulin 250 Units IM				
4: Yes if > 10 years since last dose				
5: Yes if > 5 years since last dose				

DISPOSITION

DISCHARGE INSTRUCTIONS
Patients and parents should be advised to keep the wound clean and dry for the first 24 hours in order to allow bridging of the wound to take place (neoepithelialization).
Coverage with a non-adhesive bandage for 12-24 hours can promote healing.
A large scab impedes proper approximation of the wound edges and results in a poorer cosmetic outcome.
After 24 hours they should wash at least daily with gentle soap and water
Apply an antibiotic ointment after washing
Do not apply any petroleum-based ointments to wounds closed with tissue adhesives which can dissolve
Analgesics such as Acetaminophen or Ibuprofen can be taken for pain
Patients and parents should be advised to return for wound dehiscence or signs of infection such as: fever, increased pain, redness or swelling or purulent discharge from the wound or red streaks proximal to the wound (lymphangitis)
After the tissue adhesive dissolves or the sutures are removed it is advisable to use a sunscreen to avoid hyperpigmentation of the wound.
The complete healing of the wound may take 6 months to a year as new collagen is deposited and remodeled.

SUTURE REMOVAL: The timing of suture removal is a balance between the potential for scarring and tensile strength of the healing wound.

SUTURE REMOVAL TIME FRAME	
Face	3-5 days
Skin not under tension	7 days
Scalp	7-10 days
Skin under tension (e.g. elbows, knees)	14 days

APPENDIX: SUTURE TECHNIQUES

BASIC WOUND REPAIR TECHNIQUE
Personal protective equipment: Minimum of gloves, mask with eye shield
Anesthetize the wound: Lidocaine, LET
Irrigate the wound; Approximately 10 ml per centimeter. More if grossly contaminated
Explore the wound for foreign bodies, damage to underlying tissues
Load the suture onto the needle driver.
Hold the forceps in your non-dominant hand. Gently pick up tissue
The first stitch should bisect the wound.
If there is tension, it may be best to come out within the wound with the first bite and then take a second bite through the opposite wound edge.
Apply gentle pressure on the suture ends to approximate the wound edges
Instrument tie: 2 loops for the first knot, 1 loop for subsequent knows. Total 4-5 knots
Slide the knot to either side to avoid it sitting in the wound margin
Continue suturing the laceration by bisecting the remainder of the wound
Clean the skin surrounding the wound
Apply antibiotic ointment and a non-adherent dressing
Splint the area if necessary

VIDEO LINK: DUKE SUTURE SKILLS COURSE

VIDEO LINK: LACERATION REPAIR.COM

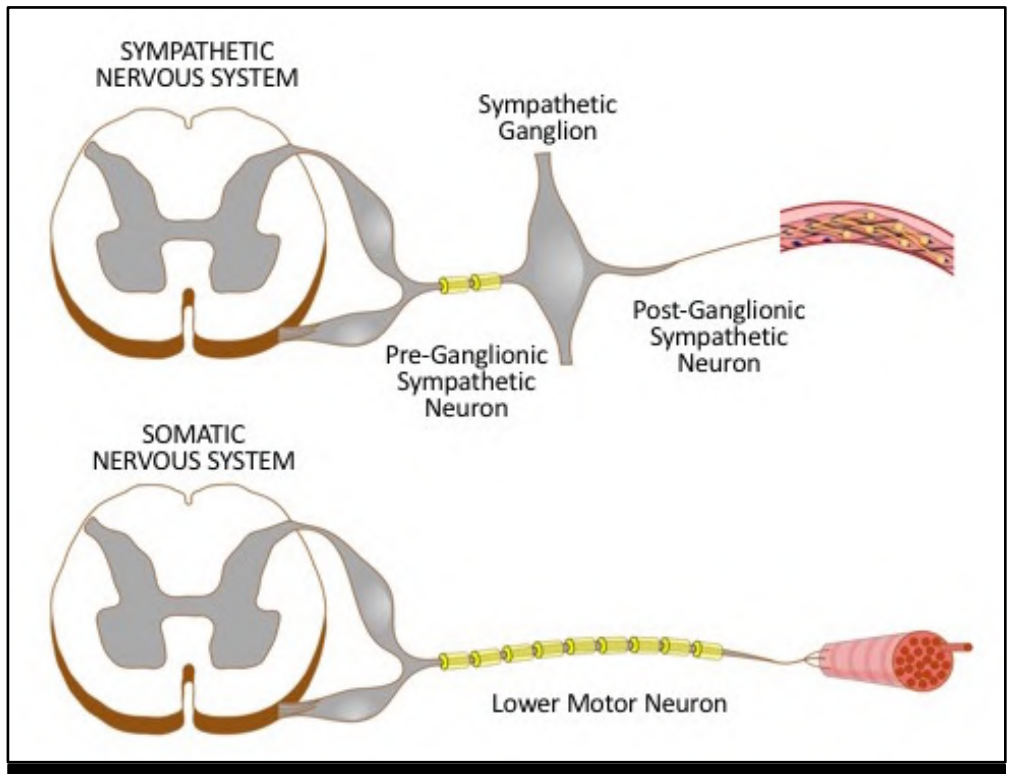
NEUROGENIC SHOCK

INTRODUCTION (MICHAEL MOJICA, M.D., 7/2020)
The terms neurogenic shock and spinal shock are often used interchangeably though they represent distinct entities. Neurogenic shock occurs due to injury to the sympathetic ganglion chain and is manifested by hypotension and bradycardia due to disruption of sympathetic function. The loss of sympathetic function results in unopposed parasympathetic function. Less than 20% of patients with cervical cord injury have neurogenic shock.

Spinal shock is not a true form of shock. The term refers to transient flaccid areflexia that may occur after spinal cord injury. It is thought to be due to a concussion of the spinal cord and may resolve as swelling improves. Spinal shock may last for several hours to several weeks post injury. See also PEM Guide: Trauma: Cervical Spine Injuries, PEM Guide: Resuscitation: Circulation: Shock Overview.

ANATOMY
The somatic nervous system consists of an upper motor neuron which synapses in the spinal cord with a lower motor neuron. The sympathetic nervous system consists of an upper motor neuron which synapses in the spinal cord.

In contrast to the somatic nervous system, the sympathetic system exits the spinal cord from T1-L2 to synapse with a series of ganglion located anterior and lateral to the spinal cord. The preganglionic neuron exiting the spinal cord synapses in the ganglion with the post ganglionic neuron which joins with the peripheral nerve. Though the ganglion arises from T1-L2, the upper ganglion extends proximally to provide cervical innervation and the lower ganglion extends distally to provide innervation of the lower lumbar and sacral regions.



NERVOUS SYSTEM ANATOMY

SYMPATHETIC NERVOUS SYSTEM: PRIMARY FUNCTIONS	
Eye	Dilation (mydriasis)
Salivary, sweat glands	Increased secretions
Heart	Increases rate (Chronotropy) and stroke volume (Inotropy)
Blood vessels	Vasoconstriction ($Alpha_1$), vasodilation ($Beta_2$)
Gastrointestinal	Decrease secretions and motility. Sphincter constriction
Genitourinary	Ejaculation (Parasympathetic: Erection)
Adrenal	Increase secretion of Epinephrine

PRIMARY SURVEY: NEUROGENIC SHOCK

AIRWAY: High cervical injuries may lead to airway obstruction due to local hematoma and swelling. Immobilization of the spine should be maintained.

BREATHING: The phrenic nerve arises from the C3-5 level. Lesions at the C5 level or higher lead to diaphragmatic paresis or paralysis. Thoracic or higher lesions may lead to respiratory distress due to paralysis of intercostal muscles (T1-12). Patients with suspected spinal cord injury in the cervical or thoracic areas should be monitored closely for respiratory insufficiency. Signs of impending respiratory insufficiency may include: tachypnea, decreased oxygen saturation, up trending end-tidal CO_2 and abdominal breathing. Those requiring intubation should be considered a difficult airway due to the need to maintain cervical immobilization. Concomitant thoracic trauma is common.

CIRCULATION: Damage to a significant proportion of the sympathetic nervous system may occur with lesions at the T6 level or higher. Injury disrupts sympathetic regulation of vascular tone (vasoconstriction) and heart rate (tachycardia) leading to unopposed parasympathetic activity (vasodilation and bradycardia).

1. HYPOTENSION: In the trauma patient, hypotension should first be considered to be due to

	NEUROGENIC SHOCK	HEMORRHAGIC SHOCK
BLOOD PRESSURE	Low	Low
PULSE PRESSURE	Wide	Narrow
HEART RATE	Normal or Low	High
PULSE	Bounding*	Weak
CAPILLARY REFILL	Flash*	Prolonged
SKIN TEMPERATURE	Warm*	Cold
*Warm shock initially, can progress to cold shock if persistent or worsens		

hypovolemic shock. Only after a thorough evaluation for internal or external hemorrhage should neurogenic shock be considered.
Neurogenic shock is a type of distributive shock. However, neurogenic shock includes elements of hypovolemic shock and cardiogenic shock as well. Vasodilation results in a relative hypovolemia (think: same amount of fluid in larger pipes). Bradycardia and reduced stroke volume can decrease cardiac output.

Patients should be positioned flat or with the head of the bed down to promote venous return. Typically, there is poor response to fluid resuscitation with approximately one-third of patients requiring vasopressors. For fluid refractory hypotension administer a vasoactive infusion with vasoconstrictive properties (vasopressor: $alpha_1$ activity) and chronotropic and inotropic properties ($beta_1$ agonist). Recommended agents include: Epinephrine, Norepinephrine, Dopamine and Phenylephrine.

There is no conclusive evidence supporting one vasopressor over another. Some recommend avoiding phenylephrine (a pure alpha agonist) in patients with bradycardia due to its potential for reflex bradycardia. The pediatric advance life support course (2015) recommends Norepinephrine and Epinephrine. In adults, it is recommended to titrate vasopressors to maintain a mean arterial pressure (MAP) of 85-90 mmHg.

MEDICATION: CLASSIFICATION			
Class	Medication	Action	Shock Indication
Inopressors	Epinephrine	Low: $Beta_1$ > $Alpha_1$ High: $Alpha_1$ > $Beta_1$	Cardiogenic (Low BP), Anaphylactic, Septic
	Norepinephrine	$Alpha_1$ > $Beta_1$	Septic, Neurogenic
	Dopamine	Dop → $Beta_1$ → $Alpha_1$	Post Resuscitation?
Vasopressors	Phenylephrine	$Alpha_1$	Neurogenic (HR)
	Vasopressin	V_I, V_2	Septic

ADRENERGIC VASOACTIVE MEDICATIONS: CARDIOVASCULAR EFFECTS							
	Dose	$Alpha_1$	$Beta_1$	$Beta_2$	DOP	SVR	CO
Epinephrine: Low	0.05-0.3 mcg/kg/min	1+	3+	1+	0	No▲,↓	↑
Epinephrine: High	> 0.3 mcg/kg/min	3+	2+	1+	0	↑	↑
Norepinephrine	0.05-2.0 mcg/kg/min	3+	2+	0	0	↑	No▲,↑
Phenylephrine	0.1-0.5 mcg/kg/min	3+	0	0	0	↑	No▲,↑
Dopamine: Low	0.5-2.0 mcg/kg/min	0	1+	0	2+	No▲	↑
Dopamine: Mod	5-10 mcg/kg/min	1+	2+	0	2+	↑	↑
Dopamine: High	10-20 mcg/kg/min	2+	2+	0	2+	↑↑	No▲
Dobutamine	2-10 mcg/kg/min	1+	3+	2+	0	↓	↑

a. EPINEPHRINE: Epinephrine has potent $beta_1$ and moderate $beta_2$ and $alpha_1$ activity. Epinephrine's response is dose dependent. At low doses, the $beta_1$ activity predominates increasing cardiac output. $Alpha_1$ (vasoconstriction) and $beta_2$ (vasodilation) have offsetting effects on systemic vascular resistance at low doses. At high doses, $alpha_1$ activity (vasoconstriction) predominates increasing systemic vascular resistance. High dose would be indicated for neurogenic shock. Splanchnic vasoconstriction is more common with Epinephrine than with Norepinephrine or Dopamine. See Appendix: Push Dose Epinephrine

b. NOREPINEPHRINE: Norepinephrine has potent $alpha_1$ activity and modest $beta_1$ activity. Alpha induced vasoconstriction can cause a reflex bradycardia that can offset the tachycardia due to $beta_1$ activity. Norepinephrine does not increase heart rate to the same extent as Epinephrine and Dopamine. Norepinephrine is indicated in normal/high cardiac output states with low systemic vascular resistance (distributive shock). It is recommended as the first line agent for neurogenic shock by some sources.

c. PHENYLEPHRINE: Phenylephrine is selective for $alpha_1$ receptors resulting in potent vasoconstriction. Vasoconstriction increases systemic vascular resistant and increases ventricular afterload with a decrease in cardiac output. It can also lead to reflex bradycardia. Phenylephrine is indicated in neurogenic shock without bradycardia.

d. DOPAMINE: The response to Dopamine is dose dependent. Doses less than 5 mcg/kg/min (AKA renal-dose) act at dopamine receptors to improve splanchnic blood flow. The clinical significance of this effect is unclear. At doses of 5-10 mcg/kg/min $beta_1$ activity predominates and at 10-20 mcg/kg/min $alpha_1$ activity predominates.

Dopamine is associated with a higher risk of tachydysrhythmias. In addition, it has both direct and indirect adrenergic effects. It indirectly increases the release of Epinephrine and Norepinephrine. This limits its efficacy in catecholamine depleted patients. Low dose Dopamine causes a diuresis. This can worsen hypovolemia and falsely indicate adequate urine output.

2. BRADYCARDIA: Bradycardia is due to the loss of compensatory tachycardia that should occur with hypotension and due to unopposed vagal stimulation. Treatment is with atropine or a vasopressor with beta receptor activity. Phenylephrine should be avoided in the patients with bradycardia due to its potential for reflex bradycardia. Transcutaneous pacing may be required for refractory bradycardia with cardiopulmonary compromise (hypotension, signs of shock, altered mental status).

DISABILITY: The preganglionic sympathetic neurons are located in the lateral aspect of the spinal accord (intermediolateral cord) adjacent to the spinothalamic tract (ascending sensory) and corticospinal tracts (descending motor). Physiologic loss of motor and sensory function distal to cord injury is common. Signs and symptoms include: flaccid paralysis, loss of sensation, loss of bowel/bladder function, absent reflexes and priapism.

Preganglionic axons exiting the spinal cord join in network of prevertebral and paravertebral ganglia. Postganglionic axons exit the ganglia and extend with the peripheral nerves and blood vessels to innervate their end organs. Damage to the ganglia or postganglionic sympathetic system due to thoracic trauma may occur without spinal cord injury so that neurogenic shock can be seen without signs of motor or sensory dysfunction.

Horner’s syndrome (ipsilateral ptosis, miosis, anhidrosis) may occur. The contralateral pupil will be larger and can be confused with a “blown” pupil. However, it will be reactive.

The Congress of Neurological Surgeons issued new guidelines in 2013 on the use of corticosteroids in acute spinal cord injury (PubMed ID: 23839357). They concluded that there is no Class I or Class II medical evidence supporting the benefit of steroids in the treatment of acute spinal cord injury. There is Class I, II, and III evidence that high-dose steroids are associated with harmful side effects including death.

EXPOSURE: Thermoregulation governed by the sympathetic nervous system is disrupted. Patients are typically hypothermic but may be febrile. They may require warming or cooling.

IMAGING	
Cervical Spine Injury	Cervical spine CT
Spinal cord injury	MRI
Thoracic trauma	Chest XRAY, Chest CT

APPENDIX: PUSH-DOSE PRESSORS: EPINEPHRINE

PUSH DOSE PRESSORS	
Definition	Small bolus doses of vasoactive agents to support blood pressure
History	Used anesthesiologists in the OR for many years
	Recently, more common in the ED and ICU settings
Indications	Bridge the time until a vasoactive infusion is available
	Expected short lived ↓ BP: e.g. after RSI, during procedural sedation
Adverse Events	Incorrect preparation → ↓ dose (ineffective),↑ dose (adverse events)
	Must label syringes appropriately to avoid dosing errors
Pediatric Dose	Weight base concentration: 1 mcg/kg/ml and dosed in 1 ml aliquots
Adult Dose	Standard Concentration: 10 mcg/ml and dosed in 1 ml aliquots
Other	Norepinephrine and Phenylephrine can also be used in push doses

EPINEPHRINE DOSING: NEW CONCENTRATIONS				
	CONCENTRATION		PEDIATRIC DOSING	
Route	Old	New	mg/kg	mL/kg
Intravenous	1:10,000	0.1 mg/mL	0.01	0.1
Intramuscular	1:1,000	1 mg/mL	0.01	0.01

PUSH-DOSE EPINEPHRINE: STANDARD PREPARATION (ADULT)	
Epinephrine (0.1 mg/ml)	Code Dose: 1 mg = 100 mcg = 10 ml
Normal Saline	9 ml Normal Saline
Preparation	1 ml of Epinephrine (0.1 mg/ml) + 9 ml of NS = 10 ml
Concentration	0.01 mg/ml (10 mcg/ml)
Dosing	0.5-2 ml (5-20 mcg) Q2-4 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION (PEDIATRICS)	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 10 mcg/kg = 0.1 ml/kg
Normal Saline	Normal Saline to total 10 ml
Preparation	0.1 ml/kg + NS to total 10 ml
Concentration	0.01 mg/kg/ml = 1 mcg/kg/ml
Dose	1 ml Q2 minutes PRN to target MAP
Kinetics	Onset: 1 minute, Duration 5-10 minutes

PUSH-DOSE EPINEPHRINE: WEIGHT-BASED PREPARATION: 20 KG CHILD	
Epinephrine (0.1 mg/ml)	Code Dose: 0.01 mg/kg = 0.2 mg, 10 mcg/kg = 200 mcg 0.1 ml/kg = 2 ml
Preparation	2 ml of Epinephrine (0.1 mg/ml) + 8 ml of NS = 10 ml
Preparation (concentration)	200 mcg/10 ml = 20 mcg/ml = 1 mcg/kg/ml
Dosing	1 ml (20 mcg or 1 mcg/kg) Q2 minutes PRN
Infusion Comparison	0.5-1.0 mcg/kg/min (10-20 mcg/min) Push-dose: 1 ml = 20 mcg (1/10th code dose) Equals: 0.5 mcg/kg/min x 2 min, 1.0 mcg/kg/min x 1 min

APPENDIX: PEDIATRIC MEAN ARTERIAL PRESSURE (1-10 YRS)

PEDIATRIC MEAN ARTERIAL PRESSURE (BASED ON PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
1	5th	30	35	33	37	34	37	36	39	37	40
	50th	49	53	52	54	53	55	54	57	56	58
	95th	69	71	70	72	72	73	73	74	74	76
2	5th	35	39	38	41	39	42	40	42	41	44
	50th	54	57	56	58	57	59	59	60	60	62
	95th	73	75	75	76	76	77	77	78	79	80
3	5th	39	42	41	44	42	44	44	46	45	47
	50th	58	60	60	61	61	62	62	64	64	65
	95th	77	78	78	79	80	80	81	81	82	83
4	5th	42	45	43	46	46	47	47	47	48	49
	50th	61	63	63	65	64	65	66	65	67	67
	95th	79	80	82	82	83	83	84	84	86	85
5	5th	45	46	47	48	49	49	49	50	51	52
	50th	63	64	66	66	67	67	68	68	69	69
	95th	82	82	84	83	85	85	87	86	88	87
6	5th	47	49	49	50	50	51	52	52	53	54
	50th	66	66	67	68	69	69	70	67	71	71
	95th	84	84	86	85	87	86	88	87	90	89
7	5th	51	50	50	51	52	52	53	53	54	55
	50th	67	68	69	69	70	70	72	71	73	72
	95th	83	85	88	87	89	88	90	89	92	90
8	5th	50	52	53	52	54	54	55	55	56	56
	50th	69	70	71	70	72	71	73	72	75	74
	95th	87	81	89	88	91	89	92	90	93	91
9	5th	51	53	53	54	55	55	56	56	58	57
	50th	70	71	72	71	73	73	75	74	76	75
	95th	88	89	91	89	92	90	93	91	94	93
10	5th	52	54	55	55	56	56	56	57	59	59
	50th	71	72	73	73	75	74	75	75	77	76
	95th	90	90	92	90	93	92	94	93	96	94

Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40
Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55

CONTINUED ON NEXT PAGE →

APPENDIX: PEDIATRIC MEAN ARTERIAL PRESSURE (11-17 YRS)

PEDIATRIC MEAN ARTERIAL PRESSURE (BASED ON PERCENTILE OF HEIGHT)											
Height%→		5th		25th		50th		75th		95th	
Age	BP%	M	F	M	F	M	F	M	F	M	F
11	5th	54	55	57	56	57	57	58	59	59	60
	50th	72	73	74	74	75	75	76	76	78	78
	95th	91	91	92	92	94	93	95	94	96	95
12	5th	54	57	57	58	58	58	60	60	61	61
	50th	73	75	75	75	77	76	78	78	79	79
	95th	92	92	94	93	95	94	96	95	98	97
13	5th	56	58	57	59	59	60	60	61	61	62
	50th	75	76	76	77	77	78	79	71	80	80
	95th	93	94	95	94	96	95	97	97	99	98
14	5th	59	60	59	60	61	61	62	62	63	64
	50th	75	77	78	78	79	79	80	80	82	81
	95th	91	95	96	96	97	97	99	98	100	99
15	5th	58	61	61	61	62	62	63	63	64	64
	50th	77	78	79	79	80	80	82	81	83	82
	95th	96	91	98	97	99	98	100	99	102	100
16	5th	90	61	62	62	63	63	65	63	66	66
	50th	79	79	81	90	82	81	83	82	85	84
	95th	98	96	99	98	101	99	102	100	104	101
17	5th	63	61	63	62	65	63	67	65	69	66
	50th	81	79	83	80	84	81	85	82	87	84
	95th	100	96	102	98	103	99	104	100	106	101
Pediatric MAP (5th percentile at 50th height percentile) = 1.5 x Age (years) + 40 Pediatric MAP (50th percentile at 50th height percentile) = 1.5 x Age (years) + 55											

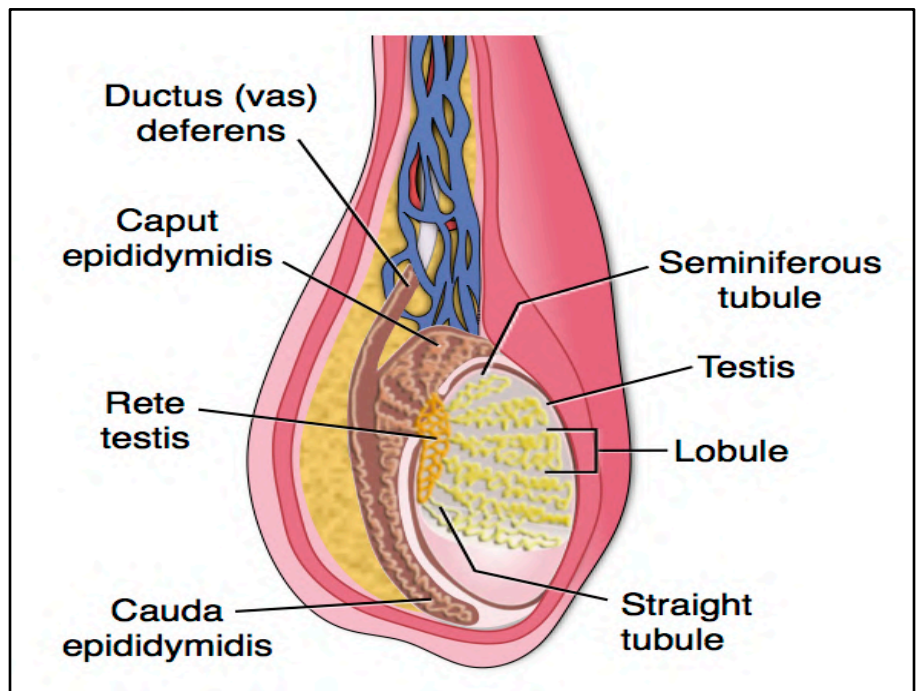
Haque IU, Zaritsky AL.
Analysis of the Evidence for The Lower Limit of Systolic and Mean Arterial Pressure in Children
Pediatr Crit Care Med. 2007 Mar;8(2):138-44., PubMed ID: 17273118

SCROTAL AND PENILE TRAUMA

INTRODUCTION (ALEXIS PANKOW, M.D., 11/2014)

Patients present with genitourinary trauma from a variety of mechanisms. Evaluation of these injuries is essential as they can be overlooked particularly when in the setting of multi-trauma. This PEM Guide reviews injuries to the penis and scrotum. For a review of injuries to the kidneys, ureters. bladder, urethra and pelvis see also PEM Guide: Trauma: Genitourinary Trauma. On occasion patients with a non-traumatic cause of scrotal pain such a testicular torsion may present with a history of minor trauma. For a review of non-traumatic causes of scrotal pain see PEM Guide: Genitourinary Trauma.

The initial evaluation of a patient with trauma to the scrotum and penis involves a careful examination to determine if a more serious injury such as a pelvic fracture or urethral injury is present and then a focused examination of the scrotum, penis and surrounding area.



SCROTAL ANATOMY

PHYSICAL EXAMINATION
FOCUSED SCROTAL EXAM
Skin inspection: Defects, laceration, bruising, swelling
Testicle: Lie (orientation), tenderness, integrity (intact?)
Location of swelling
Cremasteric reflex
Transillumination
PENILE EXAM
Palpable defect
Blood at the meatus
OTHER
Palpation of the inguinal canal: Swelling, adenopathy
Palpation of the femoral vessels
Penetrating trauma: Location of entrance, exit wounds

SCROTAL INJURIES

1. Scrotal Hematoma (Hematocele)
2. Testicular Dislocation
3. Testicular Rupture
4. Testicular Fracture
5. Intratesticular Hematoma

INTRODUCTION

The majority of scrotal trauma is due to blunt trauma. Typically this is a result of an assault, motor vehicle accident or sports related trauma. The primary mechanism of injury is crushing of the testicles against the pubic symphysis or between the thighs. Blunt scrotal trauma can result in testicular rupture, fracture, dislocation or torsion, as well as intra-testicular and extra-testicular hematomas, intratesticular pseudo-aneurysms, and hematoceles. Scrotal and epididymal hematomas, epididymal fracture and rupture, and traumatic epididymitis can also occur.

Patients typically present with severe scrotal pain and nausea. The degree of scrotal swelling and ecchymosis does not always correlate with the severity of testicular injury. Ultrasound is necessary to assess the morphology and vascularity of the testes.

SCROTAL ULTRASOUND QUESTIONS	
1	Is there blood flow to the testes?
2	Is the tunica albuginea intact?
3	Where is the hematoma? Hematocele (scrotal), subscapular or intratesticular

Urology consultation is required for non-trivial injuries. Scrotal injuries can result in an increase in intratesticular pressure and decrease is testicular blood flow. Testicular ischemia and necrosis can occur.

SURGERY INDICATIONS	
1	Pronounced scrotal hematoma (hematocele)
2	Suspected testicular rupture
3	Decreased testicular blood flow.

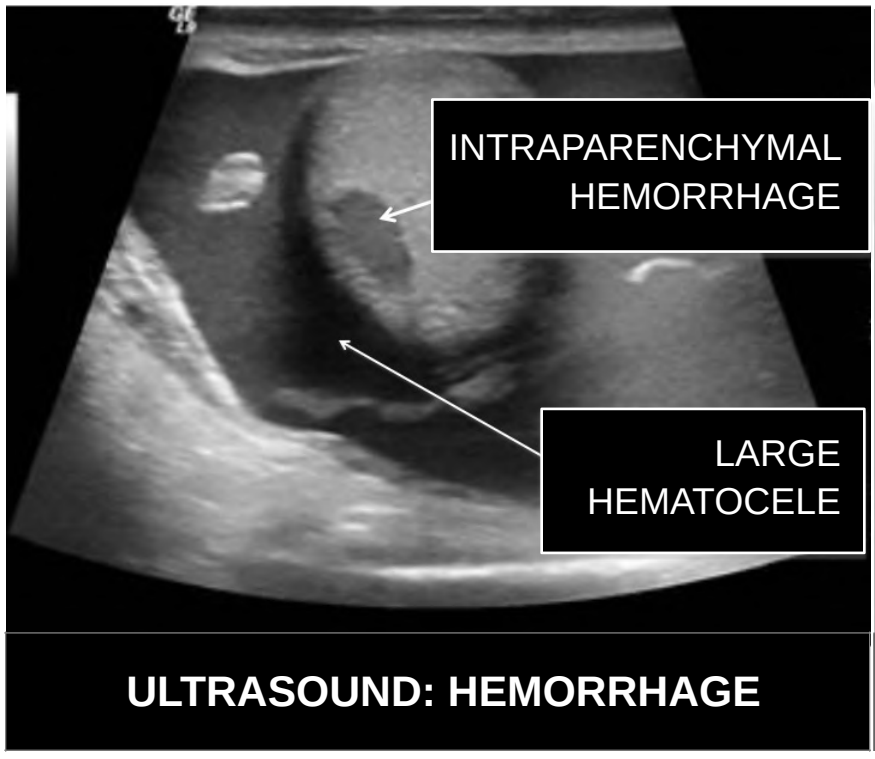
1. SCROTAL HEMATOMA (HEMATOCELE)	
Definition	Blood within the layers of the tunica vaginalis (extra-testicular)
	Most common finding after blunt trauma
Pathology	Large hematoceles can cause reduced blood flow
Diagnosis	Ultrasound: Acute hematocele appears echogenic (see image below)
Treatment	Small hematomas with normal flow: bed rest, NSAIDS, scrotal support
	Large hematomas with/without decrease blood flow require surgery

2. TESTICULAR DISLOCATION	
Definition	Testicle displaced into the abdomen
Exam	Empty Scrotal sac
Diagnosis	Ultrasound or CT scan
Treatment	Surgical repair

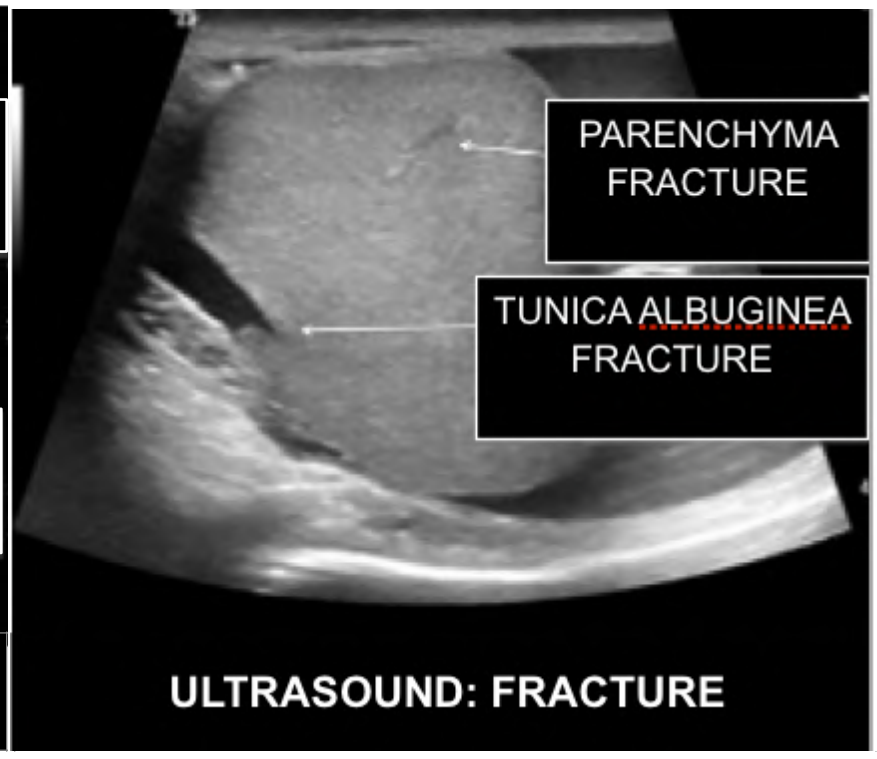
3. TESTICULAR RUPTURE	
Definition	A tear of the tunica albuginea
Pathology	Associated with a tear of the tunica vasculosa which can result in loss of vascularity to a portion or the testes
Exam	Loss of scrotal folds (due to swelling)
Diagnosis	Ultrasound: Integrity of the tunica albuginea, irregular contour
Treatment	Early surgical repair: Salvage rate > 90% within 3 days

4. TESTICULAR FRACTURE	
Definition	A break or discontinuity in the testicular parenchyma
Pathology	Can occur with or without disruption of the tunica albuginea
Diagnosis	Ultrasound: Linear hypoechoic and avascular fracture line within testis
Treating	Debridement along the avascular fracture line

5. INTRATESTICULAR HEMATOMA	
Definition	Hematoma within the testicular parenchyma ear isoechoic
Diagnosis	Ultrasound: Appear isoechoic
Treatment	Small hematoma without rupture or fracture are treated non-operatively
	Large hematomas can increase intratesticular pressure resulting in ischemic necrosis and testicular atrophy and are drained surgically



ULTRASOUND: HEMORRHAGE



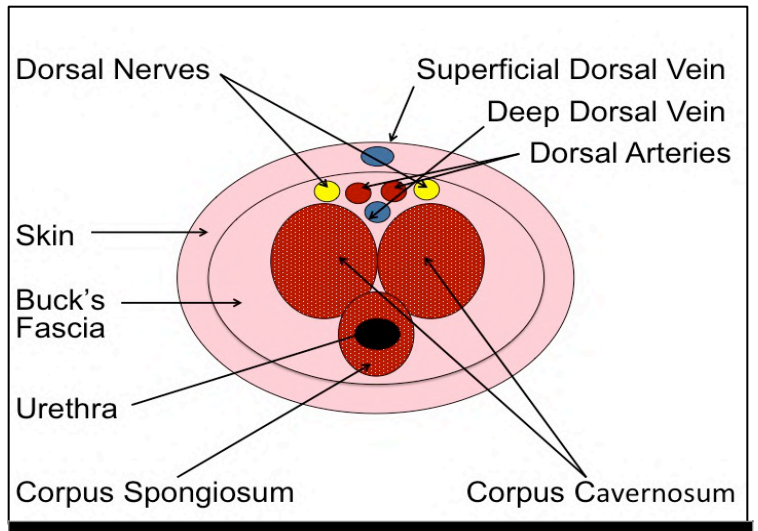
ULTRASOUND: FRACTURE

PENILE INJURIES

1. Penile Fracture
2. Penile Zipper Entrapments
3. Penile Penetrating Injury
4. Penile Hair Tourniquets
5. Urethral Injuries

INTRODUCTION

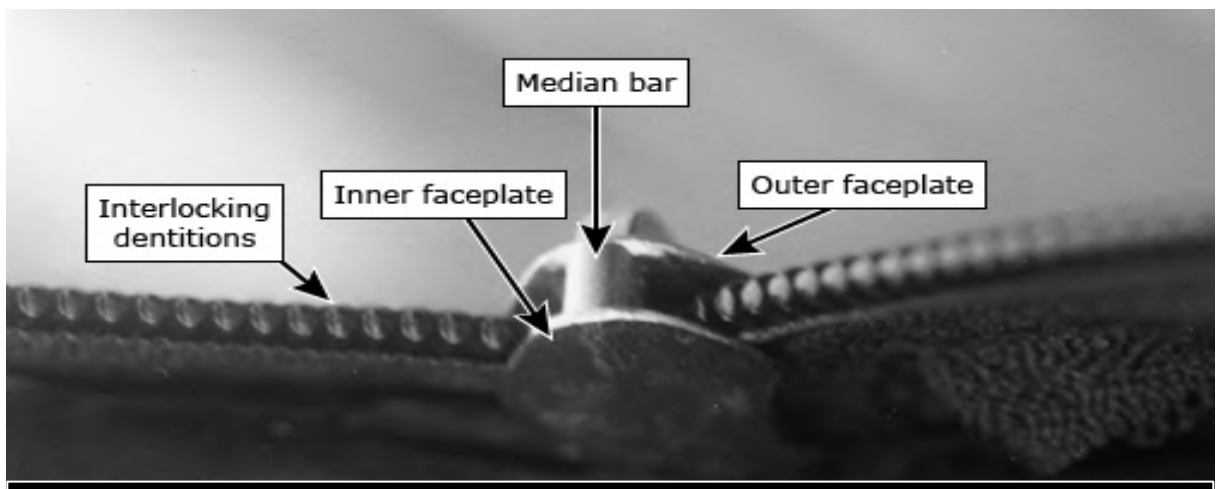
Penile injuries are often accompanied by other more serious injuries. Most non-trivial injuries require urology consultation and surgical repair. (See appendix: Dorsal Penile Nerve Block)



ANATOMY: CROSS SECTION

1. PENILE FRACTURE	
Definition	Rupture of corpus cavernosum
Pathology	Sudden blunt trauma or lateral bending of erect penis
	Urethral injury more common if both corpus cavernosum involved
Diagnosis	History and exam findings, MRI if equivocal
Treatment	Compression and analgesia. Surgical repair often required

2. PENILE ZIPPER ENTRAPMENTS	
Common with uncircumcised skin (foreskin)	
Local anesthesia, dorsal penile block (see appendix) or procedural sedation PRN	
Removal as soon as possible by a variety of techniques	
1	Cut the median bar of the zipper
2	Cut the zipper dentition and release zipper from the rear
3	Use a screwdriver to apply torque between the inner and outer faceplate
4	Mineral oil to the skin and apply traction
5	Surgical removal with incision or emergent circumcision



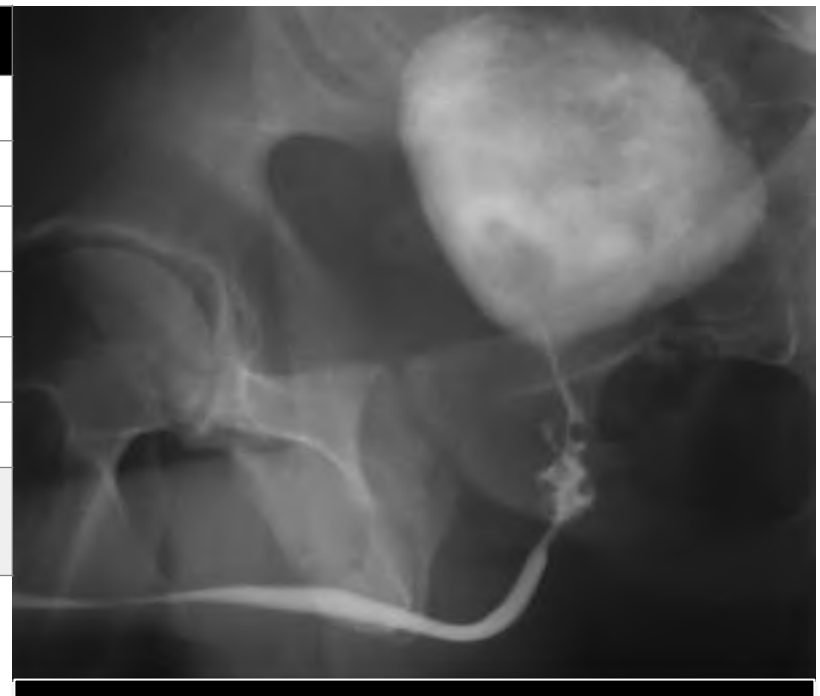
ZIPPER PARTS

3. PENETRATING PENILE INJURY	
Mechanism	Gun shots, stab wounds, impalement
Pathology	Disruption of the corpus cavernosum can create an expanding penile hematoma, copious bleeding, palpable corporal defects
Rectal Exam	High riding prostate neither sensitive nor specific. Not recommended
Diagnosis	Retrograde urethrogram if blood at the meatus. Avoid catheterization
Treatment	Urology consult for emergent surgical intervention

4. PENILE HAIR TOURNIQUETS	
May transect the neurovascular bundle, urethra or corpus if not removed promptly	
Constriction of the area distal to the band leads to decreased venous and lymphatic drainage, which then causes edema. Ischemia can lead to necrosis	
Incisional Technique	INDICATION: Preferred when marked edema, constricting band not visualized, has been epithelialized, or if other attempts fail
	PROCEDURE: A longitudinal incision is made perpendicular to the strand in order to avoid neurovascular bundles. A dorsal penile nerve block and or sedation may be required
Unwrapping Technique	INDICATION: Utilized if there is minimal edema and there is a clear view of the constricting fibers and its free end
	PROCEDURES: The end of the hair is grabbed with a forceps and the constricting bands can be unwrapped. Multiple attempts may be required, but poses the least risk
Depilatory Creams	INDICATION: Depilatory creams used when the skin remains intact. Depilatory creams are painless, work well for hair, but not thread.
	PROCEDURE: Apply for 3 to 10 min then wash with soap and water
Blunt Probe Technique	INDICATION: Other techniques are unsuccessful
	PROCEDURE: A blunt probe or metal ear curette can be wedged in under the constricting. With the probe protecting the underlying skin, the hair is cut against the surface of the probe.

5. URETHRAL INJURY	
History	Difficulty voiding and hematuria
Exam	Blood at the meatus and perineal/periurethral swelling or ecchymosis. A “high riding” prostate on rectal exam is neither sensitive or specific.
Diagnosis	Urethral catheterization is contraindicated if urethral injury is suspected
	Retrograde urethrogram: A catheter is placed in the tip of the urethra, the balloon is inflated with 1.0-1.5 ml and dye is injected under fluoroscopic guidance to determine urethral integrity.
Treatment	Urethral rupture is managed with stenting of the urethra, suprapubic drainage or surgery depending on the extent of the injury. Antibiotic prophylaxis for urinary tract infection is recommended

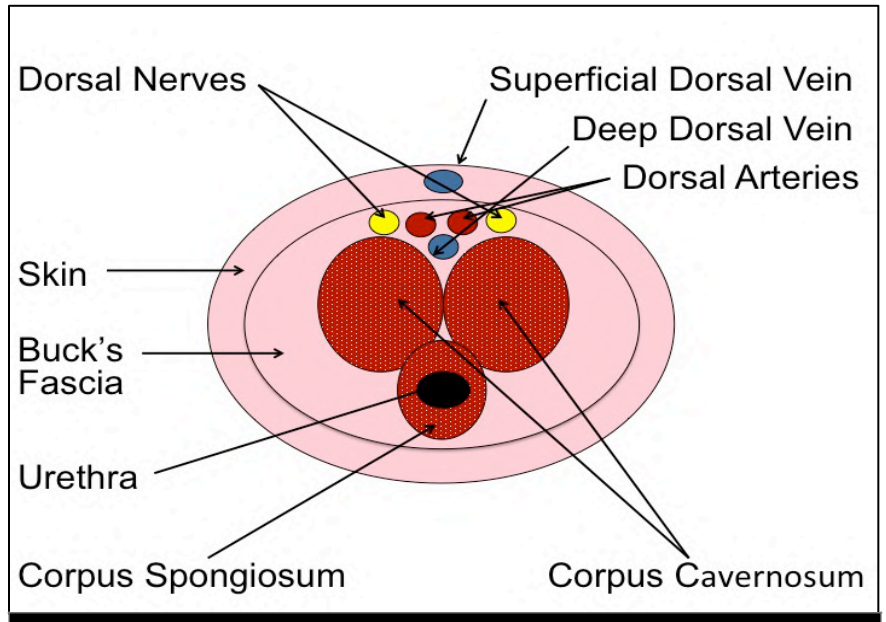
INDICATORS OF URETHRAL INJURY*
Inability to void
Unstable pelvic fractures
Blood at the urethral meatus
Scrotal hematoma
Perineal hematoma, ecchymosis or laceration
Digital rectal exam with high riding prostate
*Foley catheter placement contraindicated *Diagnosis: Retrograde urethrogram



RETROGRADE URETHROGRAM
(DEMONSTRATING URETHRAL RUPTURE)

APPENDIX: DORSAL PENILE NERVE BLOCK

ANATOMY
The penis is innervated by the pudendal nerve (S2-S4). This nerve divides into the right and left dorsal nerves of the penis that pass under the pubis symphysis to travel just below the Buck fascia to supply the sensory innervation to the penis. The penile shaft is composed of 3 erectile columns, the 2 corpora cavernosa and 1 corpus spongiosum. These erectile columns are enveloped by fascial layers, which include nerves, lymphatics, and blood vessels. All are covered by skin.



ANATOMY: CROSS SECTION

INDICATIONS
Dorsal slit procedure for paraphimosis reduction
Paraphimosis Reduction
Repair of penile lacerations
Release of penile skin entrapped in zippers

CONTRAINDICATIONS
Suspected testicular torsion
Skin infection at the site of injection

EQUIPMENT	
1	Antiseptic solution: Povidone-iodine or Chlorhexidine
2	Gauze
3	Sterile drapes
4	Topical anesthetic cream (EMLA or LMX)
5	Local anesthetic: 1% Lidocaine without Epinephrine
6	3 or 5 ml syringe
7	16 and 27 gauge needles

PROCEDURE: PATIENT PREPARATION
Obtain informed consent
Parenteral analgesia with or without sedation is recommended
Topical anesthetic cream such as EMLA or LMX is recommended (for 45 minutes)
Apply a generous amount of antiseptic solution to the penis and scrotum
Soak 4 x 4 gauze in antiseptic solution. Clean the glans and shaft of the penis
Create a sterile field with drapes

PROCEDURE: DORSAL PENILE NERVE BLOCK
The right and left dorsal penile nerves are blocked proximally at the base of the penis
Use a 27 gauge needle to raise skin wheals at the 2 o’clock and 10 o'clock positions
Slowly insert the needle through the center of each skin wheal.
Needle is directed toward the center of the shaft, to a depth of about 0.5 cm or until loss of resistance is felt (the needle is within Buck’s fascia)
Aspirate to ensure that the needle is not in a blood vessel
If > 10 kg slowly inject about 2 mL of local anesthetic on each side
If < 10 kg inject 0.2-0.4 mL of 1% Lidocaine using a 30-g needle. Maximum 4.5 mg/kg

COMPLICATIONS
Bleeding: Most bleeding can be easily controlled with direct pressure
Failure to achieve adequate anesthesia
Skin sloughing: More common with distal injections and when epinephrine is used
Infection: Rare. Prophylactic antibiotics are not recommended

SKULL FRACTURES

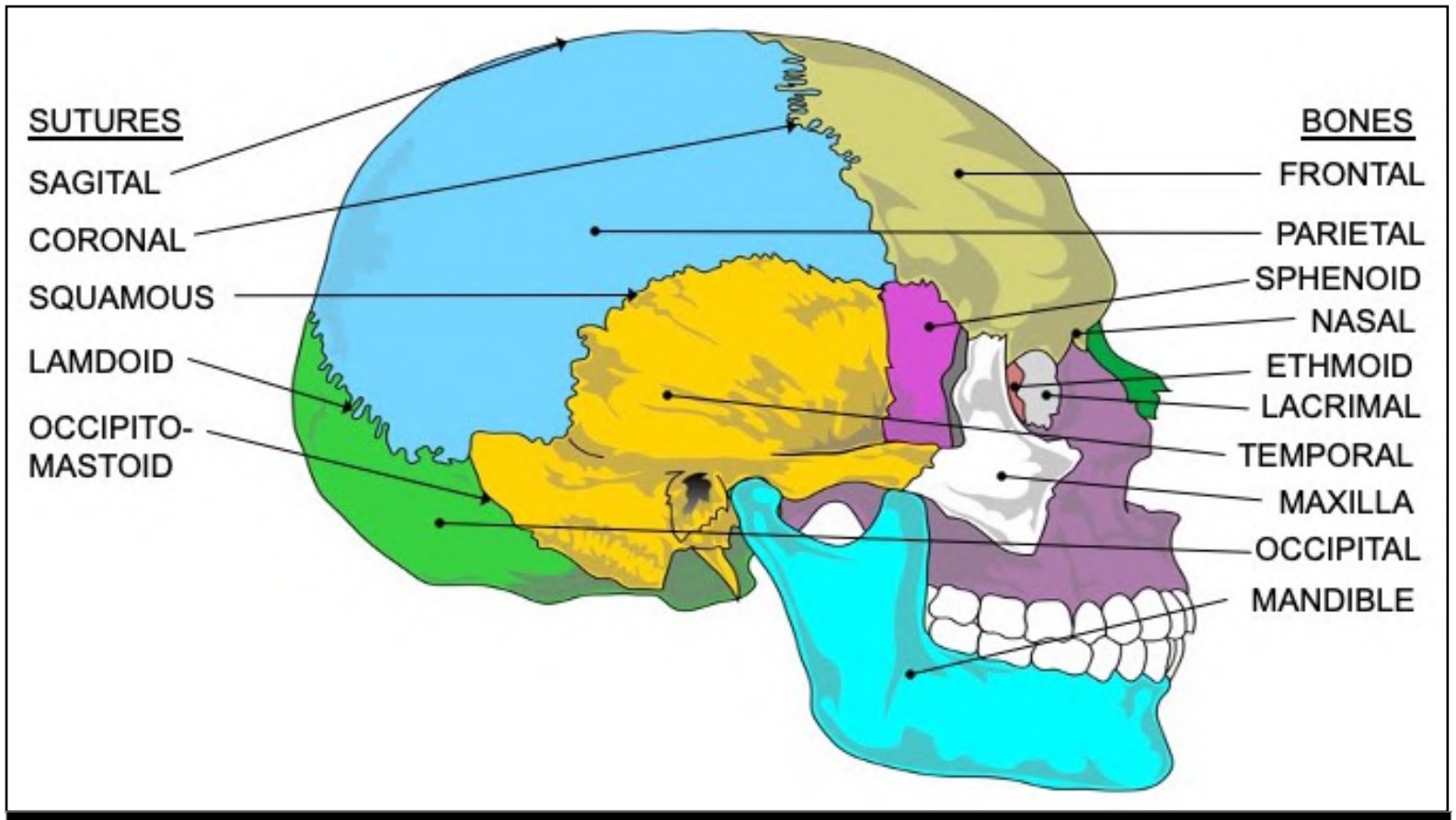
INTRODUCTION (MICHAEL MOJICA, MD, 12/2022)
Skull fractures are typically the result of a direct blow to the head from falls, sports and motor vehicle collisions. Fractures as a result of falls are the most common cause in younger children while motor vehicle collisions and assaults are more common in older children and adolescents. Skull fractures are more common in infants and toddlers due to thinner bones, higher head to torso ratio and weaker neck musculature. It is essential to consider intentional injury in infants and toddlers with skull fractures. Multiple fractures and occipital fractures are most often associated with intentional injury. (See also PEM Guide: Child Protection: Child Abuse and Neglect).

The primary clinical concern in patients with a skull fracture is the high rate of associated intracranial injury. 15-30% of skull fractures are associated with traumatic brain injury (See also: PEM Guide: Trauma: Head Injury).

SKULL FRACTURE: COMPLICATIONS
Intracranial injury: Subdural, epidural, parenchymal injury
Meningitis: Open fractures, basilar skull fractures with CSF leak
Subgaleal hematoma: May be large enough to cause anemia.
Seizures
Venous sinus thrombosis
Late: Growing fractures: Diastatic (separated) fractures

ANATOMY
Fractures typically originate from the site of impact. Skull fractures can be classified as fractures of the flat (calvarial) bones (parietal, temporal, frontal, occipital) and fractures of the skull base (basilar skull fractures). Basilar skull fractures include fractures involving the sphenoid, maxillary and palatine bones as well as portions of the occipital and temporal bones. Open fractures (AKA communicating fractures) between the extracranial and intracranial spaces increase the risk of CNS infection.

Flat bone fractures occur more frequency to the parietal bone followed by frontal, occipital and temporal in decreasing frequency. Flat bone fractures can be further classified by fracture type (linear, comminuted or depressed) or by the presence of external communication (open or closed). Linear skull fractions are most common. Comminuted fractures typically represent a higher degree of force than linear fractures. Depressed fractures can lacerate the dura and are associated with an increased risk of intracranial injury. Temporal bone fractures have the highest risk of mortality due to injury to the underlying middle meningeal artery and epidural hematoma formation, Frontal fractures occur more frequently in young child due the protuberance of the forehead relative to the face and may involve the frontal sinus, orbit and base of the skull. Occipital fractures may involve the underlying venous sinus



SKULL ANATOMY: BONES AND SUTURES

CLINICAL MANIFESTATIONS

The goal of the initial assessment is to identify those with clinically important intracranial injuries requiring intervention. This includes a trauma primary and secondary survey. Assess for symptoms suggestive of intracranial injury (alerted mental status, persistent vomiting). A thorough history should include an assessment of the mechanism of injury and symptoms immediately post and subsequent to the injury. This includes loss of consciousness, seizures, altered mental status, headache and vomiting. Delayed presentations and mechanisms not consistent with a child's developmental abilities should rase concern for intentional injury. An accurate history of the mechanism of injury may not be provided in intentional injury.

HISTORY: SEVERE MECHANISM OF INJURY (PECARN[1])
Motor Vehicle Collision: Rollover, passenger death or ejection
Un-helmeted bicyclist/pedestrian struck by a motorized vehicle
Head struck by a high impact object
Fall from height > 3 feet (< 2 years), > 5 feet (2 years)
1. PECARN excluded penetrating trauma

After the initial neurologic assessment for life-threatening injuries, complete a careful neurologic exam of the head and face. Simultaneously palpate both sides of the skull at the same location to identify asymmetry. Palpate for a bone step off or depression. Examine lacerations over fractures of the scalp and upper face (frontal bone) for signs of an open fracture. Identify signs of a basilar skull fracture (see below).

PHYSICAL EXAMINATION
Trauma primary, secondary survey: Generalized trauma, signs of intentional injury
Altered mental status: Glasgow Coma Scale, Alert, Verbal, Pain, Unresponsive
Head/Neck exam: Bruising/Lacerations, CSF leakage, cranial nerve exam

A retrospective analysis of a data set from the National Emergency X-Radiography Utilization Study (NEXUS) II Head CT validation study at 4 Emergency Departments in the US assessed the accuracy of physical examination in identifying skull fractures in children (Akie Ann Emerg Med. 2022, PubMed ID: 36328857). In the population as a whole, the sensitivity of physical exam findings for all skull fractures was low (18.5%, 95% CI (11.6, 28.3%) as was the sensitivity of physical exam findings for depressed or basilar skull fractures on CT (11.1%, 95% CI (3.1, 32.85)). Sensitivity was also low (< 35%) in the populations with minor injuries, significant injuries and those requiring neurosurgical intervention for both all skull fractures and depressed or basilar skull fractures. However, it is unclear that the poor sensitivities for physical exam are due to missed exam findings or the absence of exam findings in those with skull fractures (62.4% (53/85) of skull fractures did not have scalp hematomas).

SUSPECTED INTENTIONAL INJURY: Skin is the most common organ injured in child abuse. Identify cuts, scrapes, bruises (ecchymosis), lacerations, burns, bites, redness, and swelling. Typical abusive injuries include unusual locations (inner thighs, cheeks, buttocks, lower back), patterned bruises/burns, multiple injuries, and different stages of healing. The TEN4-FACESp bruising clinical decision rule for children less than 4 years of age with at least one bruise on a comprehensive skin exam includes, age, location of bruise, frenulum injury and patterned bruises (Pierce, JAMA Netw Open. 2021, PubMed ID: 33852003)). TEN-4FACESp had a sensitivity of 95.6%, 95% (93.0, 97.3%) and specificity of (87.1%, 95% CI (85.4, 88.6%)) for child abuse. Identification of any of the predictors in the rule should prompt further evaluation for child abuse including imaging.

TEN4-FACESp: BRUISING IN CHILDREN < 4 YEARS OF AGE[1]			
T	Torso[2]	F	Frenulum
E	Ear	A	Angle of the jaw (mandible)
N	Neck	C	Cheeks (fleshy)
4	Any bruise 4.99 months of age	E	Eyelids
		S	Subconjunctival
		p	Patterned bruises[3]
1. Positive response to any predictor signals the need for further evaluation 2. Torso: Chest, abdomen, back, buttocks and genitourinary area 3. Patterned Bruises: Bite, loop, hand slap, squeeze, grab, multilinear			

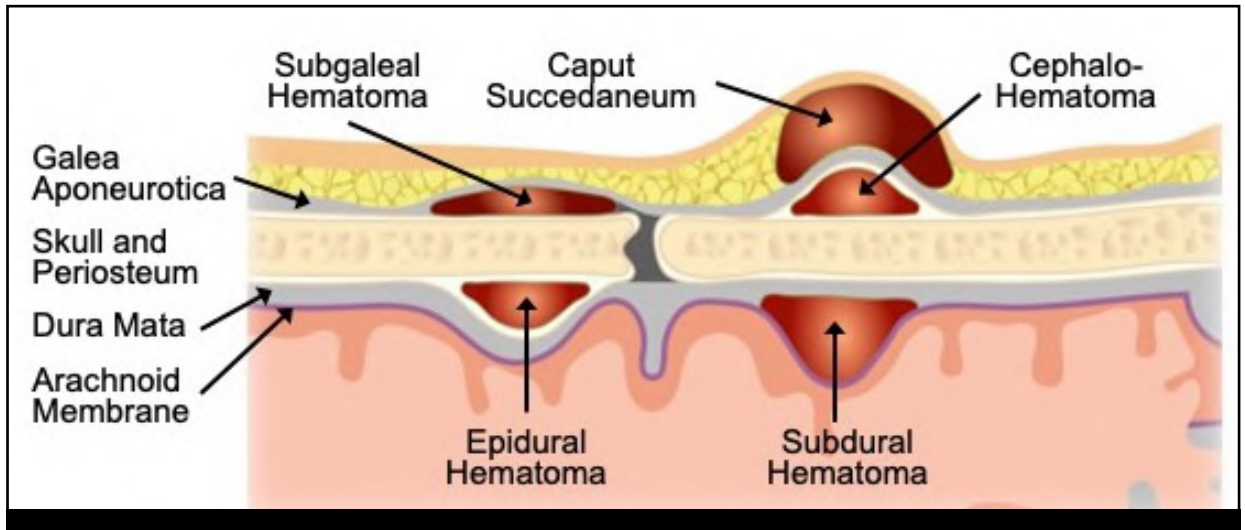
SCALP HEMATOMAS: Skull fractures are most commonly associated with localized pain and swelling. Overlying scalp hematomas are common. In the PECARN head trauma rule for those less than two years of age, a palpable skull fracture was an indication for head CT and a non-frontal, scalp hematoma was associated with a higher rate of clinically important brain injury (PECARN, Lancet 2009, PubMed ID: 19758692).

In the less than 2-year-old PECARN cohort, 28.7% (2,998/10,463) had an isolated scalp hematoma (PECARN, Annals EM 2014, PubMed ID: 24635991). Traumatic brain injury (TBI) on CT occurred in 8.8%, 95% CI (6.6, 11.4%). Younger age, a non-frontal hematoma, larger hematoma size and a severe mechanism of injury were independent predictors of TBI on CT. Clinical important TBI (ciTBI) occurred in 0.4% (1 in 250), 95% CI (0.2, 0.7%) with an isolated scalp hematoma. No patients with ciTBI died or required neurosurgery.

The infant scalp score was derived and validated using the PECARN data set for use in infants with acute, blunt head trauma with an isolated scalp hematoma. The sensitivity and negative predictive value for both ciTBI and TBI on CT at cutoffs of ≥5 and ≥4 were 100%. However, the lower limits of the 95% confidence interval for sensitivity were wide due to the small sample size of patients with TBI and ciTBI. The specificity and positive predictive value were substantially lower. Use of an ISS 4 as an indication for CT would not miss any patients with TBI on CT or ciTBI but could increase the CT rate (36% 52%). Use of an ISS 5 as an indication for CT would miss 3 patients with TBI but no patients with ciTBI and would slightly decrease the CT rate (36% 32%).

INFANT SCALP SCORE (ISS)		
Age (months)	Hematoma Size	Hematoma Location
12 (0 points)	None (0 points)	Frontal (0 points)
6-11 (1)	Small (1)	Occipital (1)
3-5 (2)	Medium (2)	Temporal/Parietal (2)
0-2 (3)	Large (3)	
Score Range: 0 (lowest risk) to 8 (highest risk) Since only infants < 1 year were included in this study, the lowest ISS was 1 Score calculated for the largest hematoma if more than 1 was present		

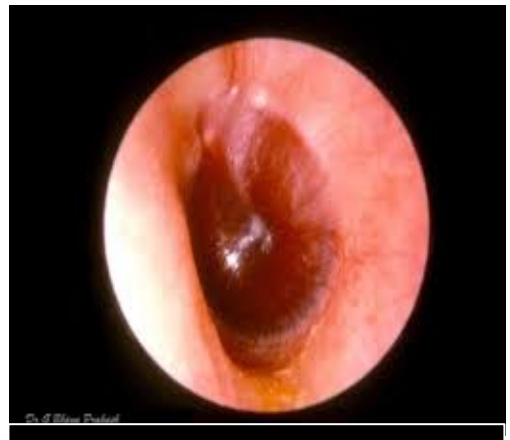
SCALP LAYERS	
S	Skin
C	Connective Tissue
A	Aponeurosis
L	Loss Connective Tissue
P	Periosteum



HEMATOMA LOCATION

BASILAR SKULL FRACTURES: Basilar skull fractures are less common than flat bone fractures. Basilar skull fractures may be complicated by cranial nerve involvement (particularly the facial nerve as in travels through the base of the temporal bone), sinus fractures and CSF leakage. CSF leakage occurs in approximately 2% of patients is associated with an increased risk of meningitis. “Ring” or “Halo: sign can be used to assess for the presence of CSF mixed with blood. CSF separates on paper as a ring (or halo) around the blood. This may also be seen with mucous, tears, saline and water mixed with blood.

BASILAR SKULL FRACTURES: PHYSICAL EXAMINATION	
Hemotympanum	Blood behind the tympanic membrane (see picture above)
Racoon Eyes	Subcutaneous bleeding around the orbit
Battle Sign	Subcutaneous bleeding around the mastoid process
CSF Otorrhea	CSF leak from the ear
CSF Rhinorrhea	CSF leak from the nose
Cranial Nerve Deficits	VI, VII, VII most common e.g. facial paralysis, hearing loss, anosmia, vertigo and tinnitus



HEMOTYMPANUM

Cranial nerve deficits occur in approximately one-quarter of basilar skull fractures with residual deficits occurring in approximately half of those. Hearing loss occurs in approximately 50% of children with basilar skull fractures. Sensorineural loss occurs as a result of cochlear injury. Conductive hearing may be due to tympanic membrane perforation, hemotympanum or injury to the ossicles.

GROWING SKULL FRACTURES: Fractures with diastasis (separation) and a dural tear may continue to enlarge due to protuberance of herniated brain, leptomeningeal cysts or dilated ventricles. Comminuted and diastatic fractures have a higher risk of growing skull fractures (Lopez, Plastic and Recon Surg 2020, PubMed ID: 32332544). These are most common in those less than 3 years of age. They may present as a persistent skull defect, localized swelling that increases in size over time or neurologic deficits due to compression of underlying brain.

FRONTAL BONE FRACTURES: The frontal bone is the densest facial bone and therefore requires a great deal of force to fracture. Frontal fractures can therefore be associated with significant craniofacial and intracranial injury. Frontal bone fractures in the area of the frontal sinus are described as anterior table (pre-sinus) and posterior table (post sinus). Isolated anterior table fractures are usually stable but can be associated with significant cosmetic deformity and should be followed closely by facial plastics or neurosurgeon. The posterior table is adherent to the dura and fractures can be associated with CSF leakage and pneumocephalus. Posterior table fractures can also be associated with intracranial and cervical spine injury. Posterior table fractures require neurosurgery consultation and are frequently prescribed antibiotics.

IMAGING

A non-contrast head CT identifies both skull fractures and traumatic brain injury. If a basilar skull fracture is suspected, temporal bone CT with fine cuts should be included. MRI is less sensitive in detecting skull fractures, is not readily available and may require prolonged sedation. Skull XRAYS are less accurate in identifying skull fractures than head CT and are neither sensitive nor specific in predicting traumatic brain injury (Dunning, Arch Dis Child 2004, PubMed ID: 15210499).

NON-CONTRAST HEAD CT: INDICATIONS (PECARN) [1]		
	< 2 years	2 years
Major CT	GCS <15	GCS <15
	Altered Mental Status	Altered Mental Status
	Palpable Skull Fracture	Signs of Basilar Skull Fracture
Minor CT or Observation	Loss of Consciousness > 5 sec	Loss of Consciousness
	Non-frontal Hematoma	Vomiting
	Severe Mechanism	Severe Mechanism
	Not Acting Normally Per Parents	Severe Headache
1. Patients with suspected intentional injury should undergo imaging		

Point of care ultrasound can also be used to identify skulls fractures in patients in which there is not a concern for intracranial injury. A systematic review of 7 prospective studies included 925 patients of which 28.8% (229/925) had a skull fracture (range 10-77%) (Alexandridis, EM J 2022, PubMed ID: 33273039).The study demonstrated a pooled sensitivity of 91%, 95% CI (83, 97%), Specificity of 96%, 95% CI (94, 97%), Predictive Value (+) Test 88%, 95% CI (84, 92%) and a Predictive Value of (-) Test of 97%, 95% CI (95, 98%). It is important to note that the skull fracture may not be at the site of the scalp hematoma. Wider scanning can improve sensitivity.

MANAGEMENT

Social work, child protective service and child protection consultation should be involved in all patients with suspected intentional injury.

The majority of isolated, linear skull fractures do not require intervention. Young infants and those who are symptomatic may warrant inpatient observation. Neurosurgical intervention may be required for frontal bone fractures (particularly involving the frontal sinus), depressed skull fractures with greater than one bone table width or associated intracranial injury and open fractures that require washout and exploration and prophylactic antibiotics (including anti-staphylococcal coverage)

Basilar skull fractures are typically managed non-operatively. Surgery may be required for facial nerve entrapment or middle ear injury. A nasogastric tube is contraindicated in patients with basilar skull fractures. Patients with a CSF leak require close follow-up with neurosurgery and should be advised to return for signs and symptoms of meningitis. There is no evidence to support the use of prophylactic antibiotics. Those with a CSF leak for more than a week may require antibiotics and surgical intervention (e.g. a lumbar drain to reduce intrathecal pressure or operative fistula repair).

Depressed skull fractures should be managed in concert with neurosurgery. Depressed skull fractures that are not associated with intracranial injury, are depressed less than 5-10 mm and are located in non-cosmetically important areas may be managed non-operatively. Short term anti-epileptic prophylaxis with Fosphenytoin/Phenytoin or Levetiracetam may be considered to prevent seizures within one week of injury. Long term seizure prophylaxis is ineffective and not recommended.

NEUROSURGICAL CONSULTATION
Depressed skull fracture
Basilar skull fracture, if CSF leak consult ENT as well
Linear skull fracture with > 3mm separation (diastatic)
Skull fractures associated with traumatic brain injury
Open skull fractures, including fractures involving a sinus, pneumocephalus
Growing skull fractures

DISPOSITION

In a meta-analysis including 6,646 children with an isolated skull fracture, only 1 patient required neurosurgery (Bressan, Annals EM 2017, PubMed ID: 29174834). In the PECARN combined cohort, 350 patients had an isolated linear skull fracture of which 57.4% were admitted. Of the 62 patients who underwent repeat imaging, 5 had new findings and none required neurosurgery (PECARN, Pediatrics 2015, PubMed ID: 25780067). The authors concluded that ““hospital admission for neurologically normal children with isolated linear skull fractures after minor blunt head trauma for monitoring is typically unnecessary.”

In a PECARN sub-study, 1.3% of patients had signs of basilar skull fracture and/or basilar skull fracture on CT. 28.7% of those with signs of a basilar skull fracture had basilar skull fracture on CT. Those with an isolated basilar skull fracture on CT had no adverse outcomes (0.0%, 95% CI (0.0, 1.4%)(PECARN, Annals EM 2016, PubMed ID: 27471139).

DISCHARGE CRITERIA
No significant extracranial injuries
No intracranial injury
Normal neurologic examination and mental status
No concern for child abuse
Reliable caretakers who are able to return with the child if necessary

DISCHARGE INSTRUCTIONS
Close observation for the first 24 hours
Follow-up with primary care provider in 1-2 days
Follow-up with neurosurgery in 1 week
Avoid participation in physical activities that pose a risk for re-injury until cleared
Seek medical attention: Does not awaken, unusually sleepy, seizure, persistent vomiting, difficulty with coordination, confusion, change in vision

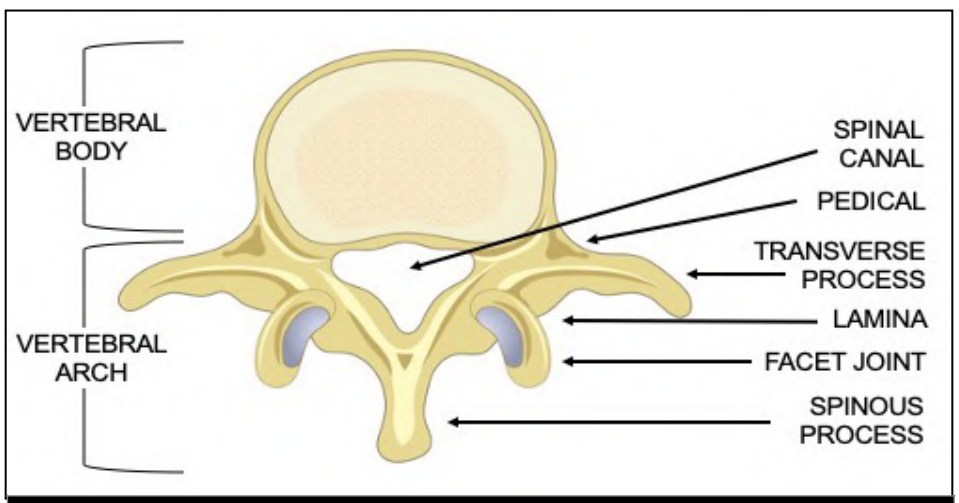
THORACOLUMBAR SPINE INJURIES

INTRODUCTION (MICHAEL MOJICA, MD, 3/2020)
Thoracolumbar (TL) spine injuries are typically associated with severe blunt trauma such as motor vehicle collisions and falls from height. These injuries are less common in the pediatric population due to the greater elasticity and compressibility of the pediatric spine. In the adolescent period, TL fractures increase as the musculature and ligamentous attachments mature. Cervical spine injuries are more common than thoracolumbar spine injuries. In children, this is due to weaker support by the neck musculature and ligaments because the relatively larger head serves as a lead point for flexion and extension and (See: PEM Guide: Trauma: Cervical Spine Injuries). When present, thoracolumbar spine injuries should trigger an evaluation for adjacent injuries to the thoracic and/or abdominal cavities.

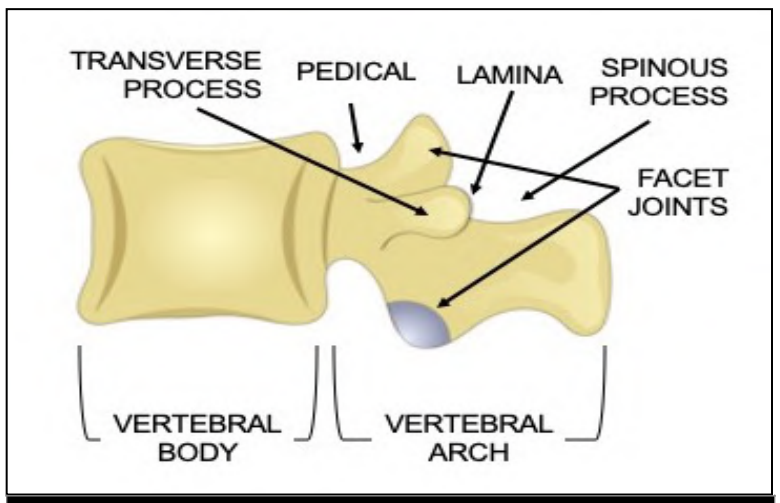
ANATOMY
An understanding of thoracolumbar injuries requires a review of the complex bone and ligamentous anatomy of the pediatric spine.

PEDIATRIC ANATOMIC DIFFERENCES	
Facets aligned more horizontally	Allow for dislocation, rotation
Weaker paraspinal musculature	Less anatomic support → ↑ Mobility
Ligamentous laxity	Increase risk of spinal cord injury without fracture
Incomplete closure of physes	Serves as a point of fracture (weaker than bone)

VERTEBRAL ANATOMY: Each vertebrae consists of an anterior vertebral body and a posterior arch. The arch consists of, from anterior to posterior, the pedicles, transverse processes, lamina and spinous process. The vertebral bodies articulate with the intervertebral disks and at the facet joints. Ligamentous anatomy is discussed below.



VERTEBRA: TRANSVERSE



VERTEBRA: SAGITTAL

SPINE REGIONS: The thoracolumbar spine is divided into three regions, the upper spine, transition spine and lower spine. These regions differ in their mobility (mobile vs immobile) and their shape (kyphotic vs straight vs lordotic). These mechanical differences result in changes in their likelihood of fracture and the types of injuries encountered.

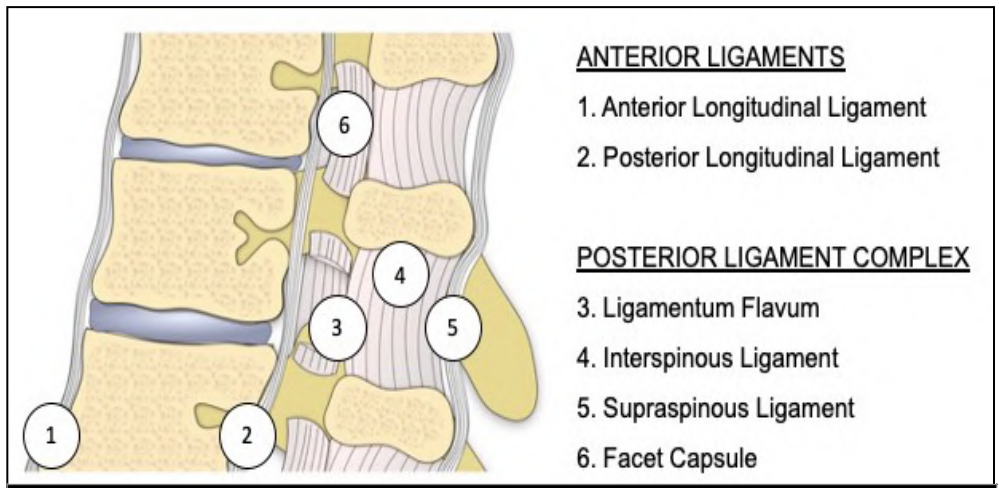
1. UPPER SPINE (T2-T10): This is a relatively immobile zone because of its articulation with the ribs and through the ribs with the sternum. It is consequently less likely to fracture. Due to the normal kyphosis, the center of gravity is anterior to the spine and compression injuries tend to occur anteriorly.

2. TRANSITION SPINE (T10-L2): This region represents a transition from the kyphosis and stability of the upper spine and lordosis and mobility of the lower spine. It is the region that is most commonly injured because it serves as a fulcrum between the immobile upper spine and mobile lower spine.

3. LOWER SPINE (L3-SACRUM): This is a relatively mobile zone. Due to the normal lordosis, the center of gravity is posterior to the spine. With flexion, the spine straightens and burst fractures result. It is the also the most common location for axial loading injuries.

ANTERIOR LIGAMENTS: Anterior ligaments include the anterior longitudinal and posterior longitudinal ligaments which attach to the anterior and posterior vertebral bodies respectively.

POSTERIOR LIGAMENTS: The posterior ligament complex (PLC) consists of four ligaments that stabilize the thoracolumbar spine against the forces due to our anterior center of gravity. Two ligaments limit flexion of the spine; the supraspinous ligament and the interspinous ligaments. The ligamentum flavum attaches to the lamina of each vertebra. It is thick and broad and is responsible for the “pop” felt when the needle enter the spinal canal during lumbar puncture in older patients. The facet capsule on the articulating surfaces protects against rotational forces.



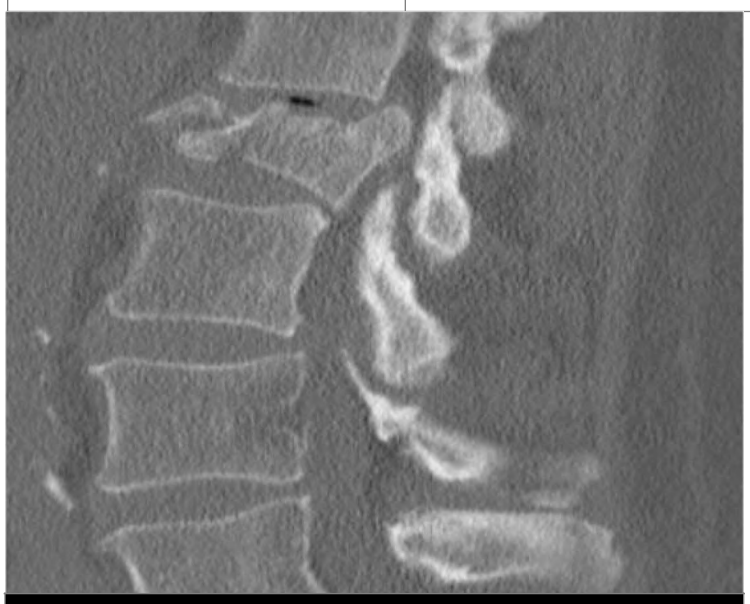
VERTEBRAL LIGAMENTS

POSTERIOR LIGAMENT COMPLEX		
LIGAMENT	CONNECTION	LIMITS
Supraspinous	Tips of spinous process	Flexion
Interspinous	Body of spinous process (weak)	Flexion
Ligamentum Flavum	Lamina of each vertebral (strong)	Anterior subluxation
Facet capsule	Articular surface	Rotation

FRACTURE CLASSIFICATION

The most common injuries of the pediatric lumbosacral spine include compression fractures and spinous process fractures. Compression fractures often occur from sports trauma or fall and are considered stable fractures. Other fractures include flexion-distraction injuries, apophyseal fractures, and process fractures.

FRACTURE TYPES	
Compression	Loss of vertebral body height or endplate disruption (1 column: Anterior)
	Less severe that burst: Anterior compression (wedging), stable fracture
	More common at the thoracolumbar junction
	Due to axial load in flexion
Burst	Require more force. Axial load or lateral flexion
	Entire vertebral body, anterior arch (2 columns: Anterior, Middle)
	± Retropulsion of the posterior vertebral body into the canal
	Vertical fracture through the posterior arch
	More frequently associated with neurologic injury
Translational or Rotational	Vertebral body displaced or rotated in relation to another
	Often due to shearing force or torsion
	Translation: Anterior-Posterior (Lateral XR), medial (AP XR)
Distraction	Vertebrae are pulled apart (distracted)
	High risk of spinal cord injury
	Often with compression on the side opposite the distraction
Chance Fracture	Seat Belt Fractures: Lap without shoulder belt, ± seat belt sign
	Flexion → Compression (anterior), distraction (posterior)
	Horizontal fracture through vertebrae, vertebral arch (3 column, unstable)
	Thoracolumbar > Lumbar (L2, 3 most common)
	High incidence of intra-abdominal injury: Pancreas, bowel
Ring Apophysis Fractures	Unique to the immature spine
	AKA Slipped vertebral apophysis injury, Typically L4, L5
Process Fractures	Isolated fractures of the transverse or spinous process
	Typically managed non-operatively



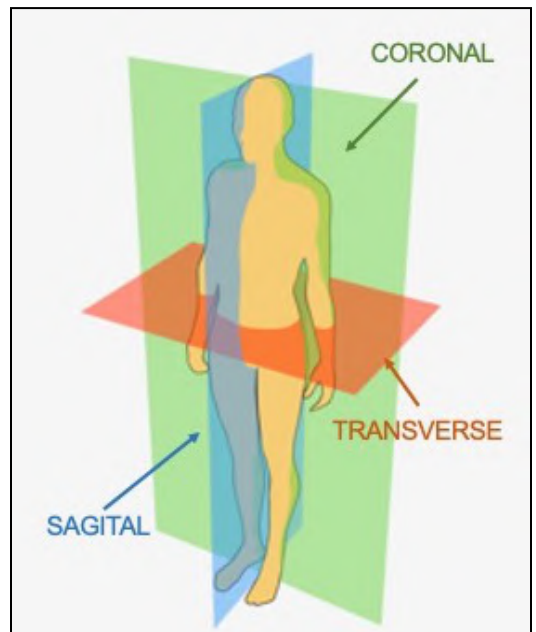
LUMBAR BURST FRACTURE
(WITH VERTEBRAL BODY RETROPULSION)

CLINICAL ASSESSMENT

The primary survey takes precedence in the trauma patient (PEM Guide: Trauma: Primary Survey). Life-threatening injuries identified in the primary surveyed should be addressed first. Spinal immobilization should be maintained until an unstable spine injury is excluded by clinical or radiologic evaluation. Thoracolumbar injuries can be identified during the disability (neurologic) or exposure segments of the primary survey or during the secondary survey.

HISTORY: Assessment for thoracolumbar injuries should include the mechanism of injury, the location and type of pain, the presence of neurologic symptoms and symptoms of associated injury (abdominal, thoracic). Risk factors for injury include fall for a height of greater than 10 feet, an axial load to the head or base of the spine and high-speed motor vehicle collisions. Pain is frequency described as a non-radiating, stabbing or aching. Neurological symptoms can include paresthesias and weakness below the level of injury or urinary retention.

EXAM: Examination is neither sensitive nor specific in identifying TL spine injury. The patient should be log-rolled in order to examine the spine. A back board can be removed if present. Identify areas of abrasion, bruising or tenderness, a gap between the spinous process or areas of step-off (difference in the relative transverse position of adjacent spinous processes). A complete neurologic exam should be conducted with attention to motor and sensory levels. Mobility of the spine should be assessed for those without indications for imaging. The spine can move in the sagittal plane (flexion, extension), in the coronal) plane (right and left lateral bending) and in the transverse plane (right and left rotation).



BODY PLANES

IMAGING

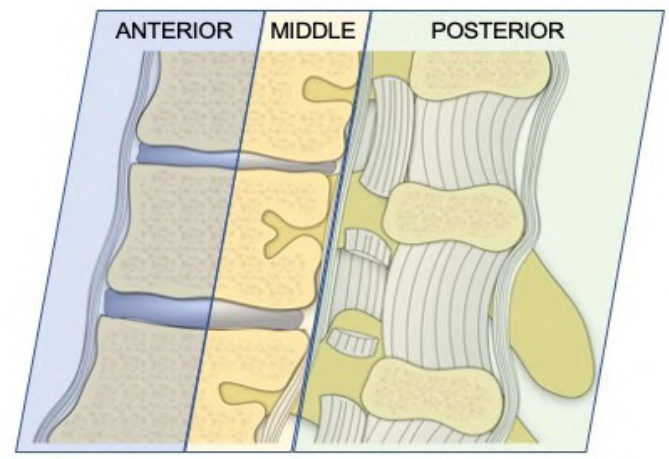
Imaging decisions should be made in conjunction with our trauma, radiology, neurosurgery and orthopedic colleagues.The adult literature favors CT because of its higher sensitivity. Plain XRAYs may be obtained in low risk patients. If a pediatric patient has no neurologic abnormalities and an abdominal or thoracic CT is not indicated for other reasons, then XRAY may be a sufficient screening tool. CT involves a 10-fold higher radiation exposure and may identify injuries without clinical significance. Abnormal XRAYS should be followed by CT to better delineate the extent of injury. The presence of one spine fracture warrants imaging of the entire spine. MRI should be obtained when there is suspicion of neurologic and/or ligamentous injury or if CT identifies an injury that is highly associated with spinal cord involvement. WEB LINK: PEDIATRIC TL SPINE XRAY INTERPRETATION).

IMAGING INDICATIONS	
HIGH FORCE MECHANISM	SIGNS OF TL SPINE INJURY
Automobile vs Pedestrian	Bruising, hematoma, step-off of TL spine
Ejection from a vehicle	Focal pain or tenderness of TL spine
Fall > 10 feet (3 meters)	Neurologic deficit consistent with TL injury
Forceful direct blow to TL spine	OTHER
Gunshot wound to the trunk	Fractures: Cervical spine, calcaneus
Moderate-High speed MVC	GCS < 15, intoxication[1]
Penetrating spine trauma	Painful distracting injury[1]
Unenclosed vehicle (motorcycle, ATV)	Severe multisystem injury
1. With mechanism or complaint/examination consistent with TL spine injury	

MANAGEMENT

Assessment of fracture stability, the need for neurologic decompression and the potential for long term healing guide the need for surgical intervention with the goals of preventing further neurologic injury or worsening deformity. As a general rule, injuries involving the posterior ligament complex Injuries require surgery to prevent poor healing. The spinal cord is divided into 3 columns (Table. Image below). Involvement of more than the anterior column defines an unstable fracture. The thoracolumbar injury classification and severity score (TLICS) was derived by the Spine Trauma Study Group and has been externally validated (Table below). It can also be used to determine the need for surgical intervention and has been validated in children (Dawkins, Neurosurgery 2019, PubMed ID: 30189030).

Most pediatric thoracolumbar spine fractures can be managed conservatively. For example, bracing of simple compression and burst fractures can allow for earlier mobilization. However, a meta-analysis of bracing compared to no bracing for thoracolumbar spine injuries found no significant differences in pain, return to work, spinal cord function improvement, or instrumentation failure. In addition, the overall complication rate was also higher in the bracing group (Skoch, World Neurosurgery 2016. PubMed ID: 27262651).

THREE-COLUMN MODEL		
Anterior	Anterior 2/3 of vertebral body Anterior 2/3 of intervertebral disc Anterior longitudinal ligament	
Middle	Posterior 1/3 of vertebral body Posterior 1/3 of intervertebral disc Posterior longitudinal ligament	
Posterior	Posterior to the posterior longitudinal ligament Pedicles, lamina, spinous process, facet joints and articular processes Posterior ligamentous complex	
Unstable Injury: More than anterior column involved (2 or 3 columns		

THORACOLUMBAR INJURY CLASSIFICATION AND SEVERITY SCORE (TLICS)		
CATEGORY	INJURY	SCORE
Morphology (XRAY or CT)	Compression	1
	Burst	2
	Translational or Rotational	3
	Distraction	4
Posterior Ligament Complex (MRI)	Intact	1
	Suspected	2
	Confirmed	3
Neurologic Status (Physical Exam)	Intact	0
	Nerve root	2
	Complete cord	2
	Incomplete cord	3
	Cauda equina	3
Score < 3: No surgery, Score 4: Surgeons discretion, Score > 4: Likely surgery		

SPINAL CORD INJURY

The spinal cord ends to the L1/L2 region. The cauda equina extends below that level. Spinal cord injury can be due to transection, contusion, compression, distraction and vascular compromise.Patients with transient or persistent weakness, numbness or paresthesias with normal XRAY or CT findings require an MRI to identify spinal cord or ligamentous injury and neurosurgical should be consulted.

SCIWORA (Spinal Cord Injury With-Out Radiographic Abnormality): SCIWORA is defined as traumatic spinal cord injury with normal plain films. SCIWORA is almost exclusively seen in those less than 8 years of age. It is less common than previous thought because injuries may be apparent using improved imaging techniques such as CT or MRI that are not present on plain film. Greater elasticity and compressibility of the pediatric spine allows for vertebrae to dislocate and then spontaneously relocate and for forces to be transmitted to the spinal cord without injuring the spine.

STEROIDS: The Congress of Neurological Surgeons issued guidelines in 2013 on the use of corticosteroids in acute spinal cord injury (PubMed ID: 23839357). They concluded that there is no Class I or Class II medical evidence supporting the benefit of steroids in the treatment of acute spinal cord injury. However, there is Class I, II, and III evidence that high-dose steroids are associated with harmful side effects including death.

TRAUMA PRIMARY SURVEY

INTRODUCTION (MICHAEL MOJICA, M.D., 5/2018)
Trauma and injury are the leading cause of death and disability in children greater than one year of age in the United States. Approximately 22 million children are injured each year.

Blunt injury accounts for approximately 90% of pediatric trauma. Mechanisms include: motor vehicle collisions, falls, bicycle injuries, and child abuse.

Penetrating injury, which primarily includes stabbings and gunshot wounds, accounts for approximately 10% and occurs more commonly during adolescence.

The timing of trauma related deaths is trimodal. The first peak is within minutes and results from severe injuries such as aortic rupture. The second peak is from 30 minutes to a few hours. This time period is often referred to as the “golden hour”. The focus of the advance trauma life support course (ATLS) is to prevent deaths and further injury during this time period. The third peak occurs days to weeks later due to sepsis or multi-organ failure in those with severe injuries.

PEDIATRIC CONSIDERATIONS
Children have proportionally larger heads in relation to body mass which makes them more susceptible to head injuries. Their occiput is more prominent until 10 years of age, resulting in neck flexion in the supine position. This needs to be taken into account when positioning the head for airway management and cervical spine immobilization.

Children have shorter necks that support a relatively heavier weight than adults and have incomplete bony development. This predisposes them to cervical spine fractures, dislocations and spinal cord injury without radiographic abnormality (SCIWORA). Recent reports using CT scan suggest that the incidence of SCIWORA may be over-estimated.

The pediatric thorax has greater pliability due to less muscle mass and more flexible ribs. This allows a blunt force to be transmitted to underlying organs. This makes rib fractures less common in children but they are more susceptible to pneumothoraxes and pulmonary and abdominal organ contusions. A flexible mediastinum increases the risk of tension pneumothorax when a pneumothorax is present.

In the abdomen, the spleen and liver are in a more anterior and caudal position. In addition, they are less protected because of poorly developed abdominal musculature. As a consequence, these organs are more prone to injury.

Lastly, the pediatric skeleton sustains injuries due to the presence of physes or growth plates. These areas of bone growth are weaker than surrounding bone predisposing them injury. A child is more likely to sustain a fracture while the same mechanism of injury would cause a ligament injury (sprain) in an adult.

EVALUATION OF THE PEDIATRIC TRAUMA PATIENT
The evaluation of the critically injured patients does not allow for an extensive history, physical examination or diagnostic testing. The 3 underlying concepts of ATLS include.
1. Treat the greatest threat to life first.
2. The lack of a definitive diagnosis should not delay treatment.
3. A detailed history is not necessary to begin the evaluation.

If advanced notification is provided
1. Identify and notify key personnel and assign roles
2. Estimate medication doses, fluid bolus volume, and equipment sizes

DIRECTED HISTORY: A*M*P*L*E		
A	Allergies	Egg and/or soy allergy may preclude Propofol use
M	Medications	Medications metabolized by the cytochrome P450 enzyme pathway (e.g. anticonvulsants and psychotropic medications), may interfere with pharmacokinetics of some sedatives
P	Past medical history	Relevant hospitalizations Prior sedation or anesthesia-related adverse events Patient/family history of anesthesia complications
L	Last meal	Timing, contents (liquids, solids)
E	Existing medical status	Conditions predisposing to airway obstruction or pulmonary compromise, Pregnancy status, Vital signs

PRIMARY SURVEY

The first priority is a rapid assessment with the goal of rapidly identifying and managing life threatening injuries. The sequence: Airway with cervical spine immobilization, Breathing, Circulation, Disability and Exposure should guide the primary survey.

A: AIRWAY WITH CERVICAL SPINE PROTECTION
B: BREATHING AND VENTILATION
C: CIRCULATION WITH HEMORRHAGE CONTROL
D: DISABILITY (NEUROLOGIC STATUS)
E: EXPOSURE (UNDRESS) AND ENVIRONMENT (TEMPERATURE) CONTROL

If a life-threatening injury is identified then it should be appropriately managed before moving on to the next stage of the primary survey.

PRIMARY SURVEY: LIFE THREATENING INJURIES	
Airway	Airway Obstruction, tracheobronchial tree injury
Breathing	Tension pneumothorax, open pneumothorax, massive hemothorax
Circulation	Cardiac tamponade, traumatic circulatory arrest

A: AIRWAY WITH CERVICAL SPINE PROTECTION

AIRWAY
ASSESS: AIRWAY PATENCY, TRACHEAL LOCATION
Air exchange/phonation: Voice quality, gurgling, snoring, and stridor
Causes of airway obstruction: Tongue, blood, secretions, foreign bodies
Oral/dental trauma: Mandible, maxillary fractures
Laryngeal or upper tracheal injury
Tracheal deviation may be seen with tension pneumothorax
Neck swelling, masses
MANAGEMENT
Maintain in-line cervical spine immobilization (not traction)
Jaw thrust maneuver for positioning the airway (not head tilt/chin lift)
Clear any obstruction with suction
Indications for emergent intubation:
Upper respiratory obstruction
Inability to control secretions including bleeding
Respiratory failure
Neurologic dysfunction with loss of protective airway reflexes
Cricothyroidotomy may be indicated if ventilation is not successful
A needle thoracentesis is indicated for tension pneumothorax

B: BREATHING AND VENTILATION

BREATHING
ASSESSMENT
Assess: Respiratory rate, work of breathing, oxygen saturation
Inspect: symmetry, chest rise, neck vein fullness, tracheal position, open chest wounds
Auscultate: Breath sounds, heart sounds
Palpate: Crepitus, rib fractures, flail chest
Percuss: Pulmonary parenchymal injury, air/blood in the pleural space
E-FAST: Thoracic: Pneumothorax/hemothorax, Subxiphoid: Cardiac tamponade
MANAGEMENT
High flow oxygen should be administered
Bag-valve-mask ventilation in cases of inadequate respiratory effort
Endotracheal intubation
Positive pressure ventilation for flail chest, significant pulmonary contusion
If suspicious of a tension pneumothorax, perform needle decompression
Tube thoracostomy for hemothorax or pneumothorax
Pericardiocentesis for cardiac tamponade

SIGNS OF LIFE THREATENING CHEST INJURY: COMPARISON			
	TENSION PNEUMOTHORAX	HEMOTHORAX	CARDIAC TAMPONADE
BREATH SOUNDS	Decreased (Ipsilateral)	Decreased (Ipsilateral)	Normal
PERCUSSION	Hyper-Resonant	Dull	Normal
TRACHEA	Shift (Contralateral)	Midline	Midline
NECK VEINS	Distended	Flat	Distended
HEART SOUNDS	Normal	Normal	Muffled
TREATMENT	Needle Thoracentesis Chest Tube	Chest Tube	Pericardiocentesis

C: CIRCULATION WITH HEMORRHAGE CONTROL

CIRCULATION
ASSESSMENT
Mental status
Pulse quality (central and distal), rate, and regularity
Blood Pressure, pulse pressure
Skin, color, temperature, capillary refill
EKG: Rhythm disturbances (particularly with blunt chest trauma)
External hemorrhage
E-FAST: Intra-abdominal injury, hemothorax/pneumothorax, cardiac tamponade
MANAGEMENT
Intravenous access and fluid resuscitation
Send blood specimen for type and cross
Fluid resuscitation: Crystalloid: normal saline 20 ml/kg (child < 40kg), 1 liter (adult)
If unresponsive to crystalloid give packed RBC 10 ml/kg (child), 1 unit (adult)
PRBC Priority: Type and cross matched > Type specific > O negative
Massive transfusion protocol: PRBC, FFP, platelets (1:1:1), consider Tranexamic acid
Needle thoracentesis: Tension pneumothorax
Pericardiocentesis: Cardiac tamponade
Tube thoracostomy: Massive hemothorax
Thoracotomy: ED versus operating room
Control of external hemorrhage: Direct compression, no blind clamping, ?tourniquets

TRAUMATIC SHOCK CLASSIFICATION (ATLS 2018)				
	CLASS I	CLASS II (MILD)	CLASS III (MODERATE)	CLASS IV (SEVERE)
Blood Loss	≤ 15%	15-30%	30-40%	> 40%
Heart Rate	Normal	Normal or ↑	↑	↑↑
Blood Pressure	Normal	Normal	Normal or ↓	↓↓
Pulse Pressure	Normal	↓	↓	↓
Respiratory Rate	Normal	Normal	Normal or ↑	↑
Urine Output	Normal	Normal	↓	↓↓
GCS	Normal	Normal	↓	↓
Base Deficit	-2, 0	-6, -2	-10, -6	-10 or less
RX BLOOD?	MONITOR	POSSIBLE	YES	MASSIVE TP

D: DISABILITY (OR NEUROLOGIC STATUS)

DISABILITY
ASSESSMENT
Level of consciousness by the AVPU method or Glasgow coma scale (specify category scores for eye opening, motor, verbal)
Pupillary size and reactivity
PECARN head trauma rule to assess risk of clinical important traumatic brain injury
Hypertension, bradycardia and irregular respirations (Cushing's Triad): due to increased intracranial pressure
Signs of basilar skull fracture: Raccoon's eyes, battle sign, hemotympanum, cerebral spinal fluid rhinorrhea, facial nerve paralysis (temporal bone fracture)
Signs of spinal cord injury: neurogenic shock (distributive): widened pulse pressure, bounding pulses, flash capillary refill, warm, flushed extremities
MANAGEMENT
Maintain cervical spine immobilization
Rapid sequence intubation for airway protection
Controlled hyperventilation PCO_2 30-35 mmHg for impending herniation
Elevate head of bed to 30 degrees for signs of increased intracranial pressure
Mannitol: 0.25 - 1.0 gram/kg over 10-20 min for impending herniation
Neurogenic shock: Fluid resuscitation, Atropine (bradycardia), Vasoconstrictor

AVPU CLASSIFICATION	
A	Alert
V	Responds to Voice Stimuli
P	Responds to Painful Stimuli
U	Unresponsive to All Stimuli

GLASGOW COMA SCALE (ADULT)		
Eye Opening	Spontaneous	4
	Verbal Stimuli	3
	Painful Stimuli	2
	No Response	1
Motor Response	Obeys Commands	6
	Localizes Pain	5
	Withdraws to Pain	4
	Flexion: Decorticate	3
	Extension: Decerebrate	2
	No Response	1
Verbal Response	Oriented	5
	Confused/Disoriented	4
	Inappropriate Words	3
	Incoherent	2
	No Response	1

E: EXPOSURE (UNDRESS), ENVIRONMENT (TEMPERATURE)

Undress the patient completely and do a rapid physical exam, including the back and buttocks (by log rolling with the cervical spine supported). After the exam cover the patient (blanket) to prevent hypothermia.

Trauma scores are used as triage tools and to predict mortality. There is no trauma score that is universally accepted. The Revised Trauma Score (RTS) is most frequently used and includes an assessment of vital signs and Glasgow Coma Scale (LINK: MD CALC). However, the vital signs categories used in the RTS do not apply to children and the verbal component of the Glasgow coma scale requires modification to be applied to children. While the RTS is easy to determine, it tends to under triage children.

The Pediatric Trauma Score (PTS) serves as a checklist to ensure that all critical components have been assessed. The PTS is inversely related to mortality. A score above 8 has a mortality rate of 0%. Approximately 25% of pediatric trauma patients will have a score of less than 8 and should be triaged to a pediatric trauma center.

PEDIATRIC TRAUMA SCORE			
	+2	+1	-1
Size	> 20 kg	10-20 kg	< 10 kg
Airway	Normal	Oral/Nasal Airway Oxygen	Intubated Cricothyrotomy
Systolic Blood Pressure	> 90 mm Hg Good pulses/perfusion	50-90 mm Hg Carotid/Femoral Pulses Palpable	< 50 mm Hg Weak/No Pulses
Level of Consciousness	Awake	Obtunded/Any Loss of Consciousness	Coma Unresponsive
Skeletal	None seen or suspected	Single Closed	Open or Multiple
Open wound	None visible	Contusion/Abrasion Laceration < 7 cm, not through fascia	Tissue loss, Any gun shot or stab wound through fascia
Tepas, J Pediatric Surgery 1987, PubMed ID: 3102714			

SECONDARY SURVEY

Once the primary survey is complete, life-threatening injuries identified, and resuscitation started, move on to the secondary survey. The secondary survey is a timely and thorough head-to-toe examination. In addition to the examination, a more complete history is obtained, laboratory studies are sent, radiographic studies obtained and problems identified. Procedures such as nasogastric tube and Foley catheter placement can be completed at this time. Subspecialty consultation and disposition decisions can usually be made at this time.

APPENDIX: PEDIATRIC GLASGOW COMA SCALE

GLASGOW COMA SCALE				
	< 1 YEAR	>1 YEAR		
Eye Opening	Spontaneous	Spontaneous		4
	To Verbal Command	To Shout		3
	To Painful	To Painful		2
	No Response	No Response		1
Motor Response	Spontaneous	Obeys Commands		6
	Localizes Pain	Localizes Pain		5
	Withdraws to Pain	Withdraws to Pain		4
	Flexion-Decorticate	Flexion-Decorticate		3
	Extension-Decerebrate	Extension-Decerebrate		2
	No Response	No Response		1
	< 2 YEARS	2-5 YEARS	> 5 YEARS	
Verbal	Smile/Coos Appropriately	Appropriate Words/ Phrases	Oriented	5
	Cries and is Consolable	Inappropriate Words	Confused/Disoriented	4
	Persistent Inappropriate Crying and/or Screaming	Persistent Cries Screams	Inappropriate Words	3
	Grunts, Agitated or Restless	Grunts	Incomprehensible Sounds	2
	No Response	No Response	No Response	1

VASCULAR ACCESS

CENTRAL VENOUS ACCESS

INTRODUCTION (DAVID KESSLER, M.D., 10/2016)
In most emergency situations, peripheral venous access is the appropriate first step for resuscitation. This includes large gauge peripheral intravenous or intraosseous catheters for fluid resuscitation and medication delivery. Once peripheral access has been secured, central venous access may still be desired for its unique advantages in treating certain conditions. Central venous access allows for the delivery of both caustic and critical medications in addition to central venous pressure monitoring and venous sampling in critically ill patients.

INDICATIONS
Need for medication delivery that can only or best be given through a central line
Desire for central venous pressure monitoring, or central venous blood sampling
Need for large volume blood exchange or dialysis

CONTRAINDICATIONS
1. Bleeding disorders: Abnormal coagulation, thrombocytopenia
2. Infection of the overlying skin

EQUIPMENT
Central Venous Catheter Kit (needle introducer, wire, dilator, scalpel, catheter)
Povidone-iodine or Chlorhexidine
Sterile gloves, mask, hat, eye shield, gown, sterile drapes
Lidocaine and syringe/needle
Saline flushes
3.0 Silk sutures
Hemostat, scissors
Sterile gauze or other occlusive dressing

COMPLICATIONS: Complications vary by site and can be grouped into those associated with placement and those associated with use.

COMPLICATIONS
Infection (femoral is highest risk)
Bleeding, puncture of adjacent artery
Pneumothorax, pneumopericardium, cardiac rupture (subclavian, internal jugular)
Air embolism (subclavian, internal jugular)
Damage to adjacent nerves, structures (e.g thoracic duct injury)
Arrhythmias (subclavian, internal jugular)
Loss of guide wire internally, catheter malposition
Arrhythmia (subclavian, internal jugular)
Thrombophlebitis/thrombosis

PROCEDURE STEPS

1. Informed Consent, procedural sedation plan (if needed)
2. Place patient on a cardiac monitor
3. Choose catheter size and length based on age and insertion site (see table below)
4. Localize the needle insertion site. Ultrasound, if available, should be used to directly identify the vein and guide needle insertion during the procedure (See Appendix)

CENTRAL VENOUS CATHETER SELECTION: DIAMETER (FR) / LENGTH (CM)						
	INTERNAL JUGULAR		FEMORAL		SUBCLAVIAN	
0-6 months	3 Fr	6-7.3 cm	3 Fr	15.7-19.1 cm	3 Fr	5.5-6.6 cm
6 months-2 years	3 Fr	7.3-9.2 cm	3-4 Fr	19.1-24.2 cm	3 Fr	6.6-8.3 cm
3-6 years	4 Fr	9.2-11.8 cm	4 Fr	24.2-31.4 cm	4 Fr	8.3-10.7 cm
7-12 years	4-5 Fr	11.8-15 cm	4-5 Fr	31.4-39.9 cm	4-5 Fr	10.7-13.5 cm
Adolescent/Adult	5-8 Fr	17.3 cm	5-8 Fr	46.3 cm	5-8 Fr	15.7 cm

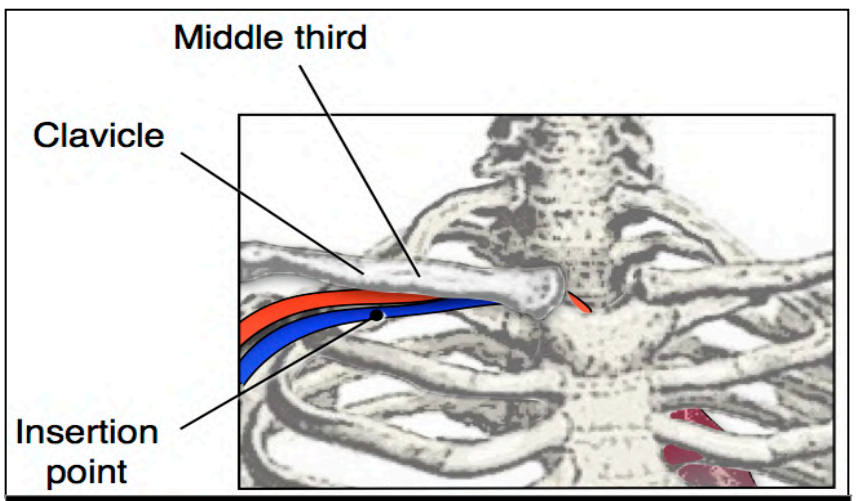
VEIN SELECTION: Typically, it is easier to obtain access via the right internal jugular and subclavian veins. Acute angles on the left versus where vessels connect to the central circulation. Subclavian access is more difficulty and more likely to result in complication for infants under 1 year of age. Femoral access is associated with a higher rate of infection, dislodgment and patient discomfort.

VEIN IDENTIFICATION: ANATOMIC LANDMARK METHOD	
Femoral	Anterior thigh, medial to femoral artery, 1-2 cm below inguinal ligament
Internal jugular	Angle of mandible to mid clavicle, crosses sternocleidomastoid
Subclavian	Immediately below clavicle in mid-clavicular line
Umbilical**	1 vein (thin walled, floppy), 2 arteries (thick walled, round)

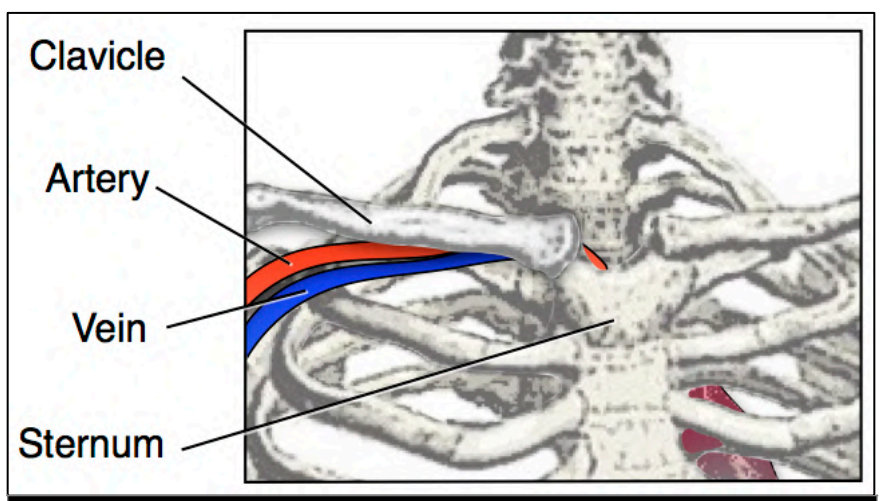
* While the landmark method provides general localization, there is significant anatomic variation. Direct visualization of the vein with ultrasound is recommended (See appendix)
**See PEM Guide: Procedures: Umbilical Vein Cannulation

4A. SUBCLAVIAN

1. Place patient in Trendelenburg position
2. Palpate clavicle for site of bend (junction of lateral and medial portions)
3. Aim needle towards bend in clavicle, walk needle beneath bone while aspirating



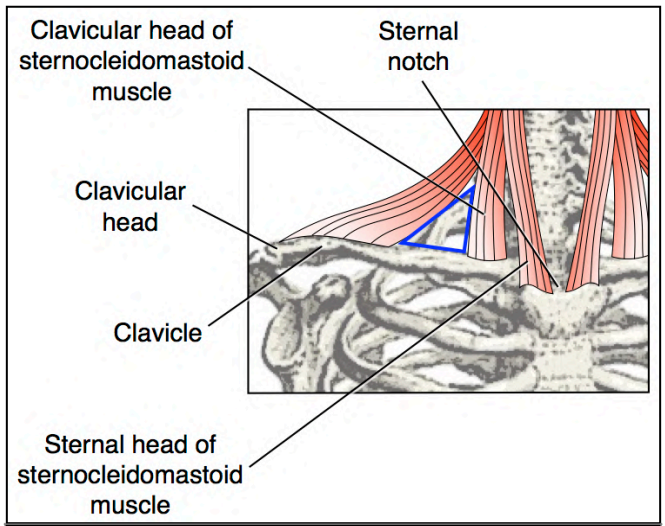
SUBCLAVIAN: LANDMARKS



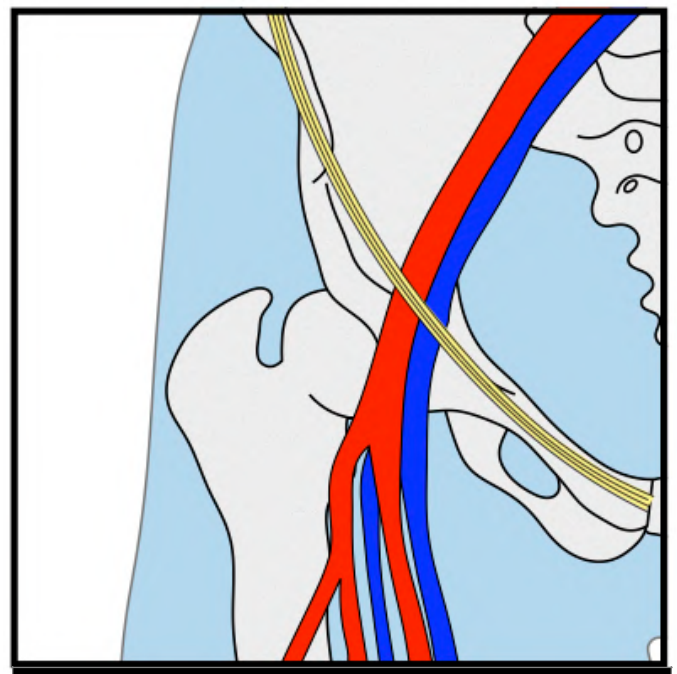
SUBCLAVIAN: VESSELS

4B. INTERNAL JUGULAR

1. Place patient in Trendelenburg position
2a. Midneck approach (most common): Apex of triangle formed by heads of the sternocleidomastoid muscle bone and clavicle.
2b. Superior approach: medial to medial head of sternocleidomastoid
2c. Inferior approach: medial to the clavicular head of the sternocleidomastoid
3. Palpate carotid artery and enter skin laterally to pulse aiming toward the ipsilateral nipple with needle.



INTERNAL JUGULAR VEIN



FEMORAL VEIN

4C. FEMORAL

1. Palpate femoral pulse in inguinal region and insert needle medially to pulse.

PROCEDURE STEPS (STEPS 5-16)	
5	Prep the site in sterile fashion with povidone iodine and sterile drapes
6	In an awake child, inject the site with Lidocaine to provide local anesthesia.
7	Prepare catheter by flushing all ports with normal saline
8	Attach 10cc syringe to introducer needle, insert into skin while drawing back on the plunger. Advance slowly until syringe fills with blood from vein
9	Disconnect syringe. Hold pressure at skin and insert guide-wire into needle hub
10	Advance guide-wire slowly until clearly several centimeters within vein. If subclavian or internal jugular line being placed, monitor EKG for ectopic beats and pull the wire back until they disappear. If resistance is felt at any point do not force guide-wire, reattach syringe and reassess for proper location of needle
11	Secure guide-wire at skin with fingers and carefully remove needle introducer.
12	Thread dilator over guide-wire and insert into vein. If difficult to advance the dilator, use scalpel to make nick in skin for 1-3 mm above dilator.
13	Continue to stabilize guide-wire at skin and remove dilator.
14	Thread catheter over guide-wire and place in up to hub. Aspirate and flush all hubs to check function. Do not let go of the guidewire
15	Suture line in place using 3.0 silk sutures simple interrupted knots through skin proximally to the plastic base and passing needle through openings in the catheter base. Apply sterile dressing.
16	Chest x-ray to confirm proper placement (subclavian or internal jugular). Listen to chest to assure bilateral breath sounds. Catheter should rest at junction of SVC and right atrium.

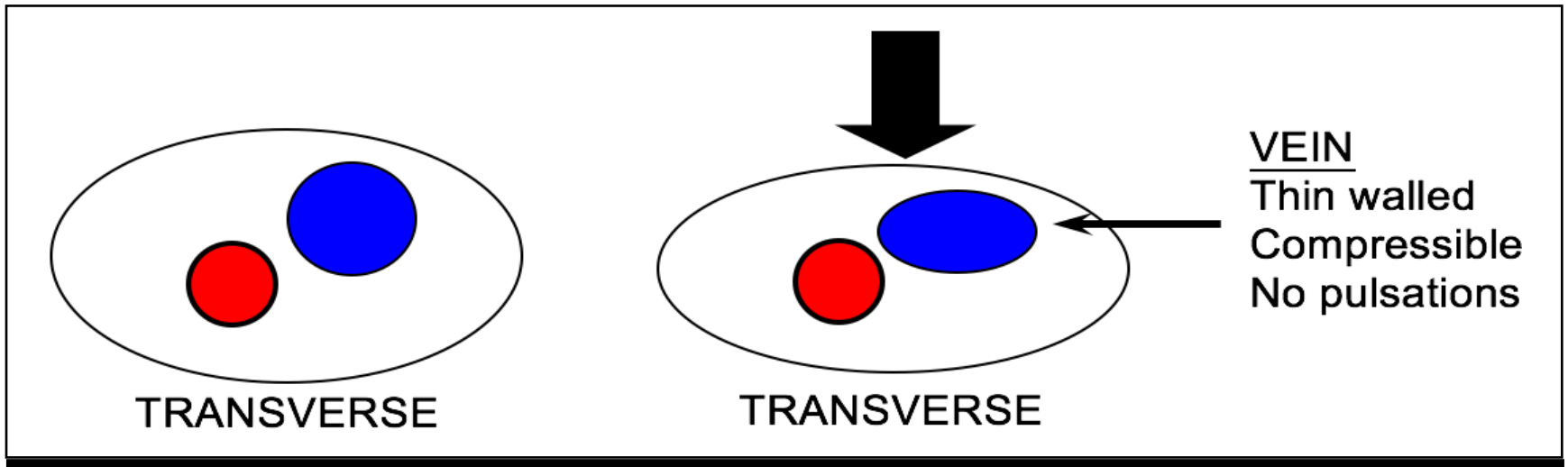
APPENDIX: ULTRASOUND GUIDED CENTRAL VENOUS ACCESS

Ultrasound guidance during central venous cannulation can increase success rates and decrease complications. (See also PEM Guide: Procedures: Ultrasound Guided Peripheral Venous Access). Ultrasound allows clear identification of the target vessel as well as adjacent arteries, nerves, and other structures. The Agency for Healthcare Research and Quality (AHRQ) recommends ultrasound guidance for central venous access on their top ten patient safety practices.

This appendix reviews the technique for ultrasound guided cannulation of the internal jugular vein but the technique may be applied to cannulation of the femoral vein and subclavian vein as well. The mnemonic EASE for Examine, Anesthetize, Stick and Ensure correct placement outlines the procedural steps involved. Identification of the appropriate vein for cannulation can begin with the landmark approach for each vessel discussed previously. Ultrasound can then further refine vein identification. Equipment and complications for each technique have been reviewed previously.

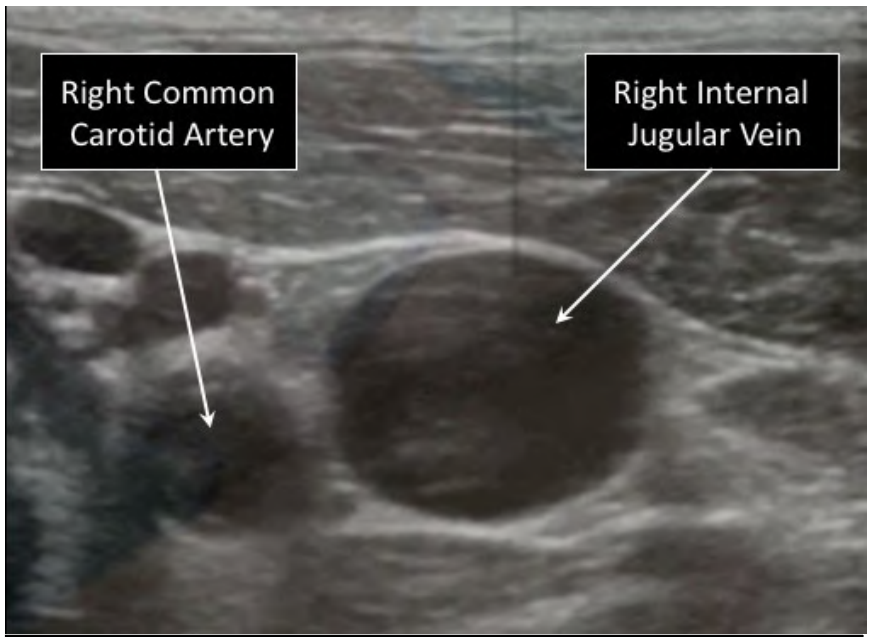
VEIN IDENTIFICATION

Scan the area with the linear probe in a transverse axis. This will allow for cross-sectional view and will help identify the larger and more superficial veins. In general, the veins are thin walled structures that are easily compressible by minimal pressure with ultrasound probe and do not pulsate. Doppler and M-mode can be used to confirm pulsations.



VEIN IDENTIFICATION

1. EXAMINE
Ensure that you are in a position of comfort (bed elevated, sitting if desired)
It is helpful to align your visual axis so that the needle insertion site and ultrasound screen can be visualized simultaneously
Place the patient in 15 degrees of Trendelenburg to optimize vessel diameter
Ultrasound with a linear high resolution transducer. Use the vascular preset
Place probe in a transverse position on the neck distal to the needle insertion site
Probe marker to patient's left side, corresponding to the marker on ultrasound screen
Determine: vessel patency, diameter, degree of collapse with respiration and compression, overlap with the internal carotid artery, and depth from the skin
A size of less than 0.7 cm is a risk factor for unsuccessful venous cannulation
Locate a position with minimal overlap with internal carotid artery to reduce the chance of inadvertent arterial puncture.



CAROTID ARTERY & JUGULAR VEIN

2. ANESTHETIZE
Local anesthesia to ensure patient comfort/cooperation and reduce complications
Prepared site with the standard sterile technique
Apply ultrasound gel to the probe and place a sterile cover on the probe. Ensure there are no air bubbles between the probe face and inner surface of sterile sheath
Apply sterilized ultrasound gel to the outside of the sterile cover for scanning

3. STICK
Adjust probe so that the internal jugular vein is in the center of the ultrasound field
Needle angled at 40 to 60 degrees. Enters skin 1 cm back from the ultrasound probe
Looking at the patient's neck and the needle during adjustments in needle position
Advancing the needle in small (1cm) increments.
Visualize needle trajectory on ultrasound screen. Observe continuously for blood "flashback" in the syringe. Avoid the mistake of through-and-through vessel puncture
Needle tip will be seen on the screen to "indent" the wall of the internal jugular vein
If blood flashback obtained, guide wire can be passed through the needle into vein
If confident that the guide wire is located within the vein, the dilator can be used to prepare a path for the catheter.
After dilation of the soft tissues and vein, the catheter can be passed into the vessel.

4. ENSURE (CORRECT PLACEMENT)
Direct visualization of guide wire location within the vein confirms proper placement
Additionally, central venous pressure measurements can confirmation catheter placement prior to use
Chest XRAY should be used to rule out procedure-related pneumothorax

INTRAOSSEOUS ACCESS

INTRODUCTION (ADRIANA MANIKIAN, M.D., 12/2020)
In young children, venous access in emergency situations may be difficult to obtain, particularly if circulation is compromised. Central venous access may take a long time to achieve. This could delay delivery of emergency medications or resuscitative fluids. Intraosseous (IO) cannulation is a fast and safe alternative method of vascular access for delivery of drugs, fluids and blood products. An IO line can be easily placed within 30–60 seconds, and requires minimal equipment. IO cannulation has also been used recently in non-resuscitation situations in patients with difficult access (e.g. Sickle cell disease)

The IO route delivers medications and fluids into the bone marrow venous plexus, and then through emissary veins to the peripheral and then the central circulation.
Any medication used in an intravenous form can be delivered via the IO line, including Epinephrine, Atropine, Lidocaine, Calcium, Potassium, Anticonvulsants, inotropes, muscle relaxants, and Adenosine. Infusions of crystalloids, colloids, blood products, Dopamine, Dobutamine, are also successfully accomplished. An IO line is a high resistance system and drugs and fluids should be delivered via infusion pump with a pressure infusion bag or manual push. Medication delivery should be followed by a rapid saline flush.

NOTE: This PEM Guide reviews IO access using the EZ IO device because it is available at our institutions. The authors have no financial interests in the product.

INDICATIONS
Need for urgent fluid, medications when other venous access cannot be rapidly Obtained. Examples: Status epilepticus, cardiopulmonary arrest, trauma requiring rapid sequence intubation
IO cannulation has also been used recently in non-resuscitation situations in patients with difficult access (e.g. Sickle cell disease)

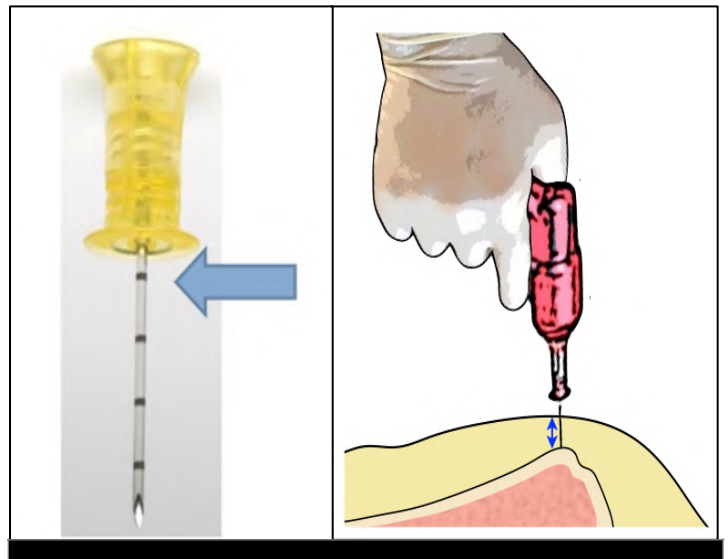
CONTRAINDICATIONS
Trauma (e.g. fracture) to bone being used
Previous unsuccessful attempt at IO on same bone in the previous 48-hours
Infection overlying site of placement
Hardware (prosthetics, fracture plate) at site of placement
Inability to identify anatomic landmarks

EQUIPMENT
Povidone–iodine or chlorhexidine
Sterile gloves and drapes
Drill device (such as EZ IO) with appropriate size needle.
10 cc syringe with saline flush

EZ-IO NEEDLE SELECTION			
COLOR	LENGTH	WEIGHT	INSERTION SITE TISSUE DEPTH
RED	15 mm	3-38 kg	Minimal Tissue
BLUE	25 mm	≥ 39 kg	Too Much Tissue (> 10 mm)
YELLOW	45 mm	≥ 39 kg	Excessive Tissue (> 25 mm) or Humerus site
A needle requires 5 mm to ensure adequate insertion into the bone. A 15 mm needle would be inadequate at a site with > 10 mm of soft tissue			

In obese patients, the ability to palpate the tibial tuberosity can be used as a surrogate measure of soft tissue depth. It is recommended that if the tibial tuberosity is palpable then a 25 mm needle will be adequate at the tibial site but a 45 mm needle should be used in the humerus. If the tibial tuberosity is not palpable then a 45 mm needle should be used at every site (Kehrl, Amer J EM, 2016, PubMed ID: 27344097).

In general, the red needle is of little utility except for neonates. Place the needle through the skin to the level of the bone. The proximal black line on the needle should be visible. If the line is not visible, then the needle may be too short to reach the marrow cavity and a larger needle should be utilized.

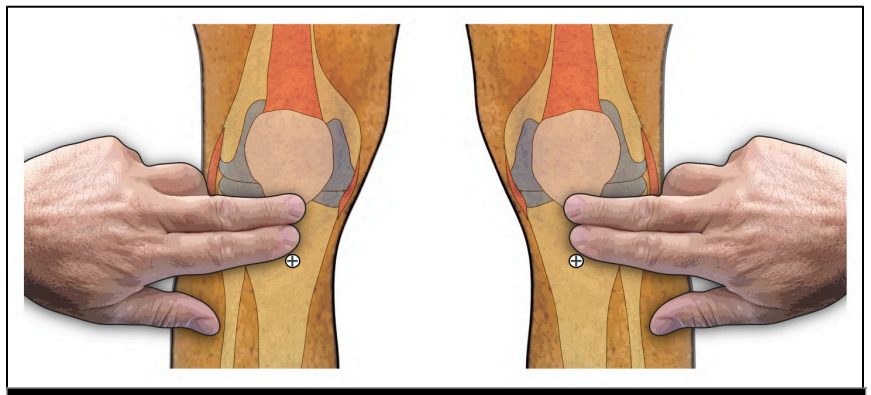


NEEDLE DEPTH

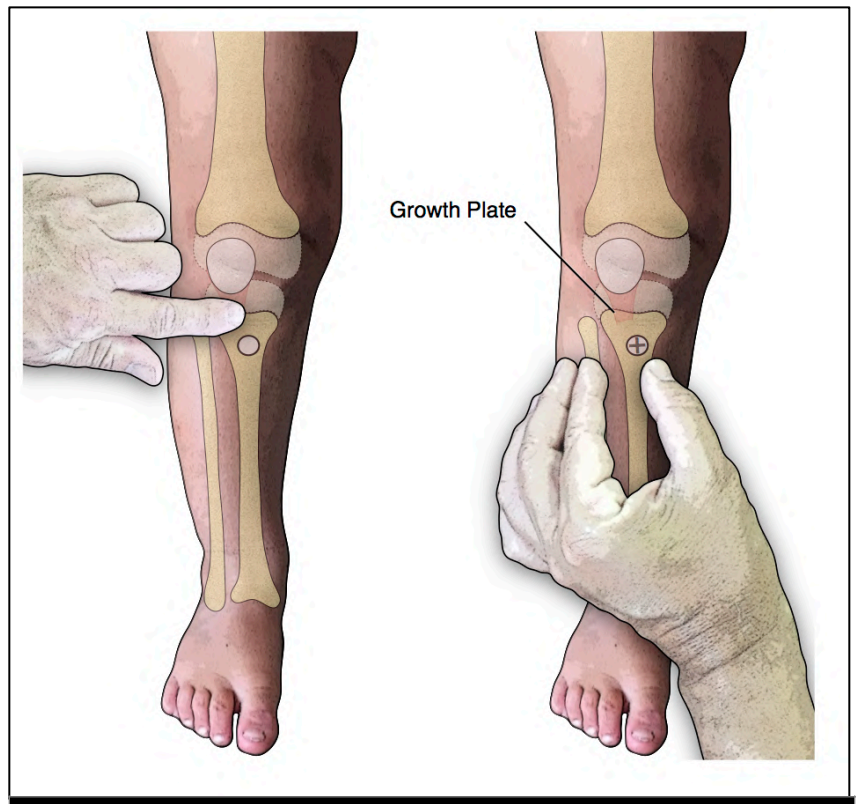
COMPLICATIONS
Fracture
Compartment syndrome (proximal tibial placement)
Skin necrosis
Osteomyelitis
Extravasation
Systemic infection
< 1% rate of serious complications

ANATOMIC LANDMARKS		
	ADULT	PEDIATRIC
Proximal humerus	YES (PREFERRED)	YES
Proximal tibia	YES	YES (PREFERRED)
Distal tibia	YES	YES
Distal femur	NO	YES

PROXIMAL TIBIA (anteromedial aspect): The classic site of insertion is 1–3 fingerbreadths below and medial to the tibial tuberosity on the flat surface of the tibia. Data suggests that placement may be more successful just medial to the tibial tuberosity without moving distally. The needle is placed at a 90-degree angle to the bone to avoid damaging the physis superiorly.

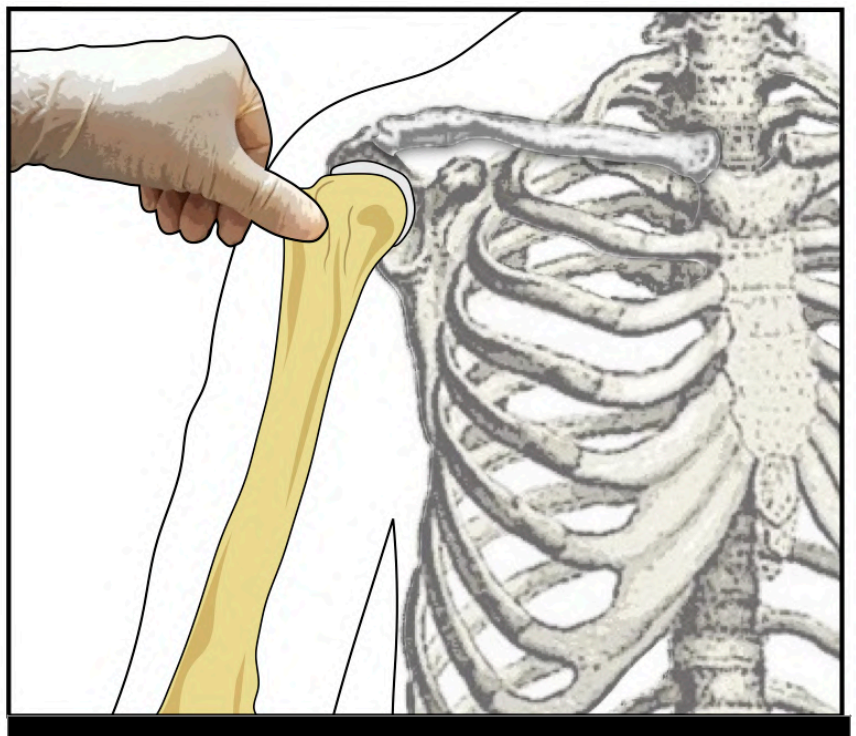


TIBIA: PALPATION (ADULT)

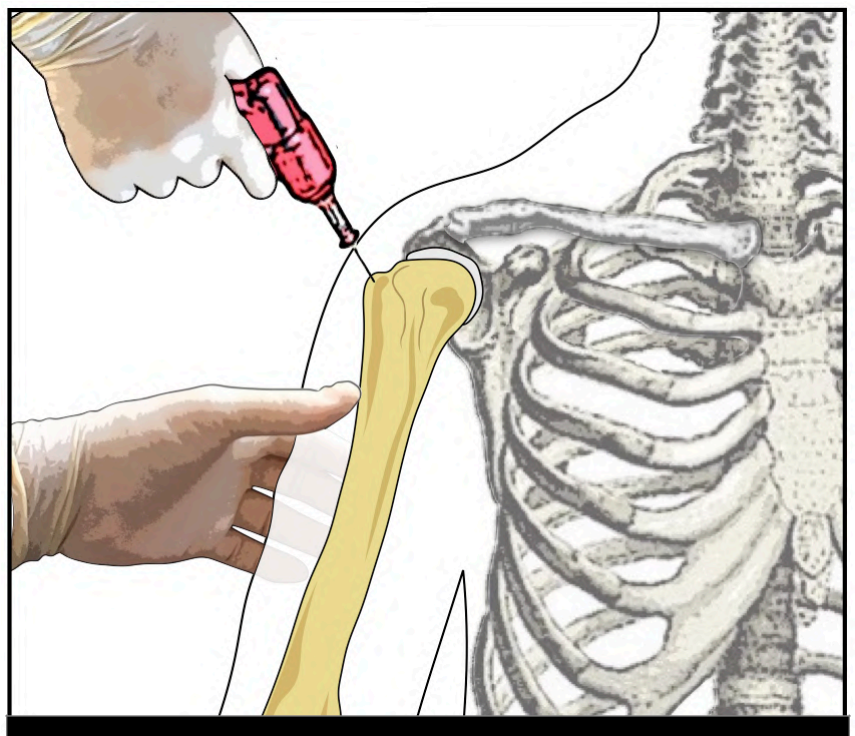


TIBIA: PALPATION (CHILD)

PROXIMAL HUMERUS (HEAD): The humerus should be rotated medially to avoid damage to the bicep's tendon in the intertubercular grove. This can be achieved by flexing the elbow to 90 degrees and placing the hand over the abdomen with the upper arm adducted to the thorax. Alternatively, this can also be achieved with the arm adducted to the patient's side with the forearm hyper-pronated with the thumb side of the hand facing the stretcher. In adults the proximal humeral head is the preferred site. The needle is placed at angle of 45 degrees medial to the sagittal plane and aimed inferiorly at a 45-degree angle (see illustrations below). Flow rate up to 5 liters per minute can be achieved. Medications and fluids can be in the central circulation via the subclavian vein in less than 3 seconds.

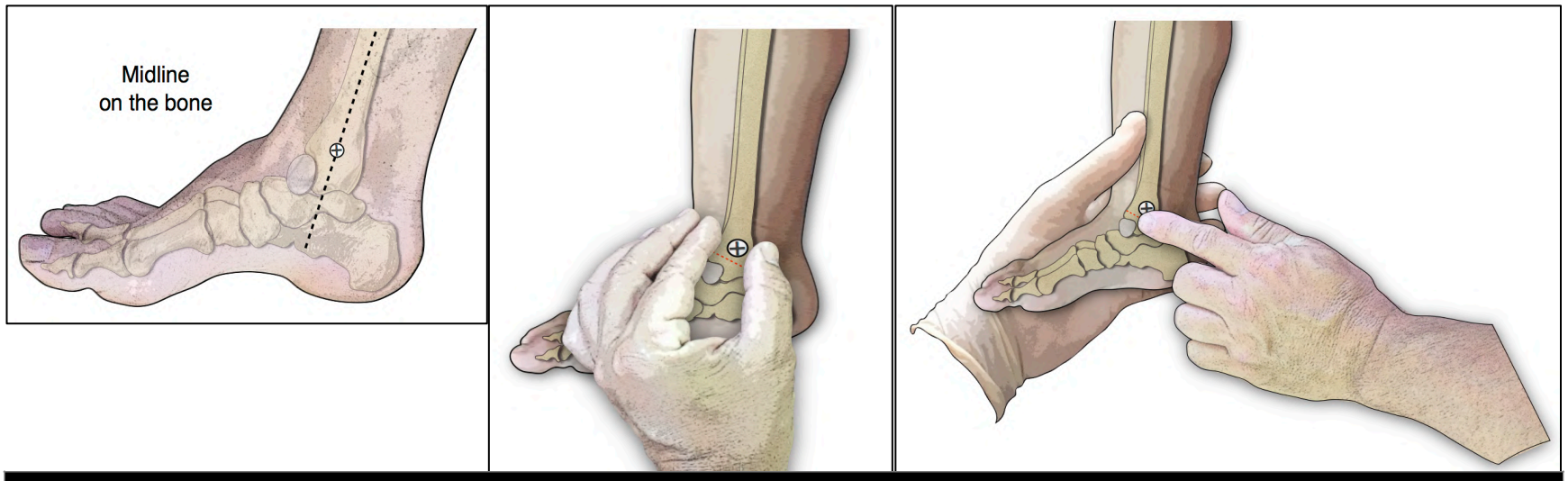


HUMERAL HEAD: PALPATION

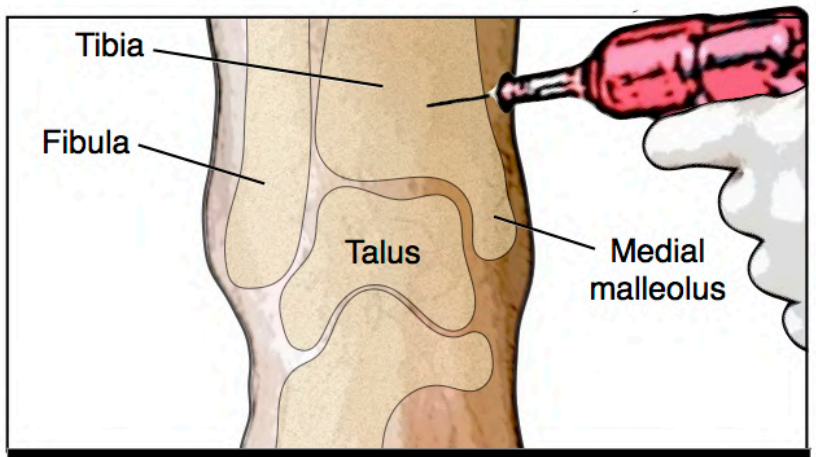


HUMERAL HEAD: INSERTION

DISTAL TIBIA (MEDIAL MALLEOLUS): The insertion site is located approximately 1-2 cm (pediatric) or 3 cm (adult) proximal to the most prominent aspect of the medial malleolus. Palpate the anterior and posterior borders of the tibia to assure that your insertion site is on the flat center aspect of the bone. The needle is placed at a 90 degree angle the bone to avoid damaging the physis inferiorly.



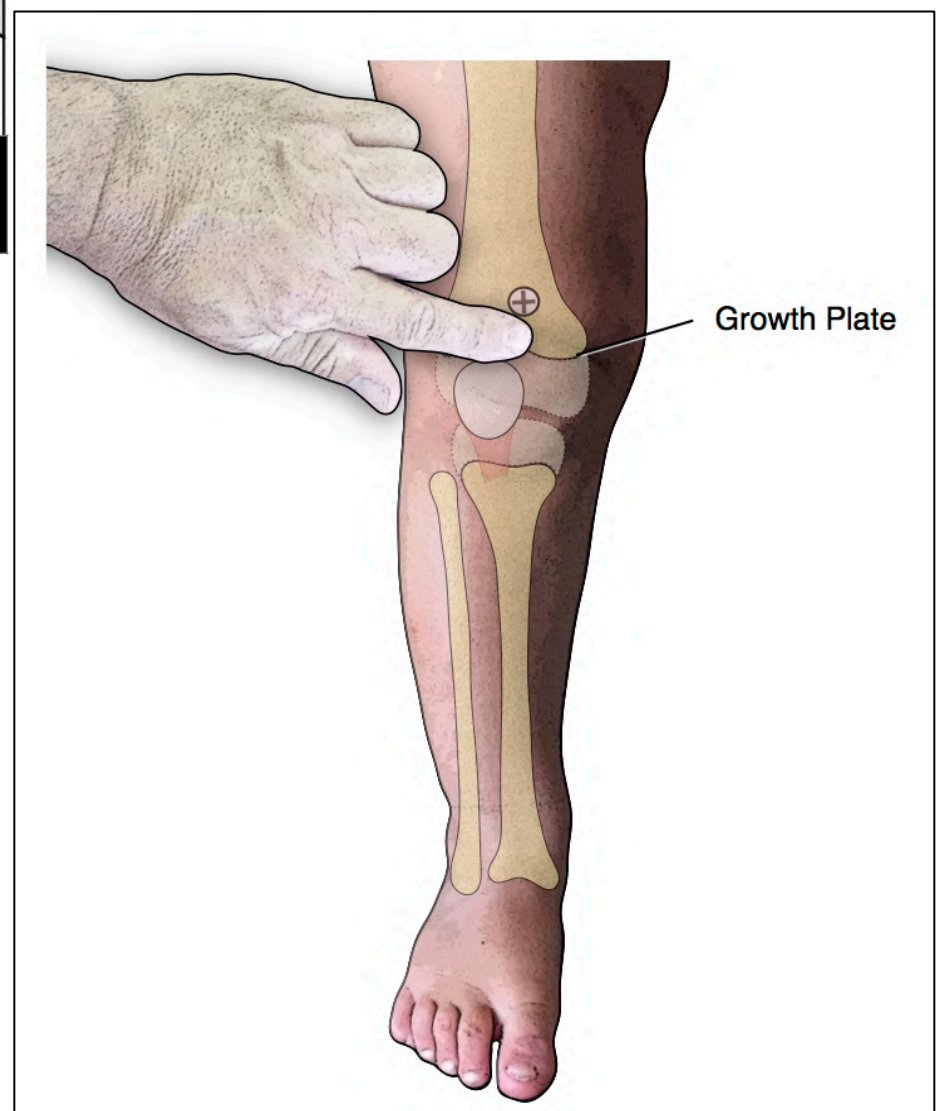
MEDIAL MALLEOLUS: PALPATION



MEDIAL MALLEOLUS: INSERTION

VIDEO LINK: PEDIATRIC IO ACCESS

DISTAL FEMUR (PEDIATRICS ONLY): The leg should be fully extended. The insertion site is just proximal to the patella (maximum 1 cm) and approximately 1-2 cm medial to midline of the femur. This site is proximal to the distal femoral epiphysis. The needle is placed at a 90-degree angle the bone to avoid damaging the physis.



DISTAL FEMUR (PEDIATRICS ONLY)

PROCEDURE: INTRAOSSEOUS PLACEMENT	
INDICATIONS	Need for urgent fluid, medications when other venous access cannot be rapidly obtained. Examples: Status epilepticus, cardiopulmonary arrest, trauma requiring rapid sequence intubation
	IO cannulation has also been used recently in non-resuscitation situations in patients with difficult access (e.g. Sickle cell disease)
CONTRA-INDICATIONS	Trauma (e.g. fracture) to bone being used Previous unsuccessful attempt at IO on same bone in the previous 48-hours Infection overlying site of placement Hardware (prosthetics, fracture plate) at site of placement Inability to identify anatomic landmarks
IDENTIFY LANDMARKS	Pediatric: Proximal tibia (preferred) Adult: Proximal humerus (preferred) Other: Distal femur (pediatrics only), distal tibia (medial malleolus)
PREPARE SITE	Support the extremity to be used in the correct position and prepare the site in a sterile fashion with Povidone iodine and sterile drapes.
IO NEEDLE SELECTION	RED (15 mm) = 3-38 kg and minimal soft tissue depth at insertion site BLUE (25 mm) ≥ 39 kg or > 10 soft tissue depth YELLOW (45 mm) ≥ 39 kg and > 20 soft tissue depth or site is proximal humerus
PLACEMENT	Advanced the needle with the drill device activated. This should take a minimal of pressure. Avoid compressing the hub of the needle into the underlying skin.
ASPIRATE	Unscrew the needle cap, remove the stylet and aspirate with a 10 ml syringe. This sample may be used for labs studies such as bedside glucose, type/screen. The inability to aspirate does not necessarily indicate incorrect placement.
FLUSH UNCONSCIOUS	Flush the line rapidly with 5 to 10 ml (adult) or 2-5 ml (pediatric) of normal saline. A rapid flush displaces bone marrow making the infusion easier.
FLUSH CONSCIOUS	IO needle may be placed with minimal pain. The flush results in significant pain. Provide analgesia to awake patients. Lidocaine can be instilled as follows
	Prime the EZ-Connect extension set with lidocaine (approximately 1.0 ml)
	Lidocaine 2%: Initial dose 40 mg (adult), 0.5 mg/kg (max 40 mg) (pediatric)
	Slowly infuse over 2 minutes. Allow lidocaine to dwell for 1 minute
	Flush with 5-10 ml (adult) or 2-5 ml (pediatric) of normal saline
	Slowly infuse Lidocaine at ½ of the initial dose over 1 minute. This subsequent dose allows for analgesia of pain fibers made accessible by the saline flush
	May repeat Lidocaine PRN or consider systemic analgesia.
CONFIRM PLACEMENT	Successful insertion is indicated by:
	a. Fluid administration without swelling to surround tissue due to extravasation
	b. Fluid or medication administration with relative ease (some resistance is normal)
	c. Needle remains upright in the bone without support
SECURE	Secure with tape and support with a bulky dressing or EZ-IO attachment device
INFUSE	An IO line has high resistance. Deliver drugs/fluids by IV pump with a pressure infuser bag or manual push. Follow bolus medication with a saline flush.
REMOVAL	Remove as soon other IV access is established IO should not be used for longer than 24 hours due to risk of osteomyelitis.

ULTRASOUND GUIDED PERIPHERAL VENOUS ACCESS

INTRODUCTION (ADRIANA MANIKIAN M.D., 8/2019)
Obtaining peripheral venous access in children is difficult. This is particularly true for infants and toddlers and those with chronic medical conditions requiring frequent intravenous access. Traditional intravenous placement is associated with an overall 75% first attempt success rate but only 50% success in those with difficult venous access (Curtis, CMAJ 2015, PubMed ID: 25897047). A pediatric Difficult Intravenous Access (DIVA) Score of greater than 4 is associated with a 50% first attempt success rate (Yen K, Pediatr Emerg Care. 2008, PubMed ID: 18347490). Ultrasound allows for direct visualization and cannulation of the vein and could decrease the number of peripheral venous access attempts and the need for more invasive venous access such as intraosseous access and central venous lines.

A 2019 randomized clinical trial including 165 pediatric patients with difficulty venous access compared ultrasound guided peripheral venous access to traditional peripheral venous access (Vinograd, Ann Emerg Med 2019., PubMed ID: 31126618). The first attempt success risk difference was 39.6%, 95% CI (25.5, 51.5%) higher in the ultrasound guided group. This corresponds to a number needed to treat of 2.5 (1/0.396). For every 2.5 patients for which USPIV is used, 1 additional patient will have a successful IV placed on the first attempt compared to traditional peripheral intravenous placement.

PEDIATRIC DIVA SCORE			
Vein Visibility	Visible = 0		Not Visible = 2
Vein Palpability	Palpable = 0		Not palpable = 2
Age	>= 36 months = 0	12-35 months = 1	< 12 months = 3
Prematurity	NO = 0		YES = 3
Skin shade	Light = 0	Dark = 1	
A score of 4 or more had a more than 50% likelihood of first attempt failure			

INDICATIONS
1. Failed attempts in PVL placement using conventional technique
2. Known or anticipated difficult PVL placement in patients without visible or palpable veins (or DIVA score ≥ 4)

EQUIPMENT
Use standard sterile techniques and universal precautions required for peripheral vein cannulation
Consider topical anesthesia with EMLA, LMX or vapocoolant spray
Angiocatheters of various size and length (longer required for deeper veins)
Tourniquet, Occlusive dressing (e.g. Tegaderm or /Duofilm)
Sterile ultrasound gel or Surgilube
High frequency linear ultrasound probe – standard 5-12 MHz or Hockey stick SLA used for small children and tight spaces such as neck (smaller footprint) Provides high resolution images of superficial layers of the soft tissue
Ultrasound Machine: use vascular preset to maximize visualization of vessels

PATIENT POSITIONING

The patient should be in a supine position with the forearm and arm extended and the volar aspect of the forearm and arm exposed when attempting cannulation of the forearm, antecubital or deep brachial veins.

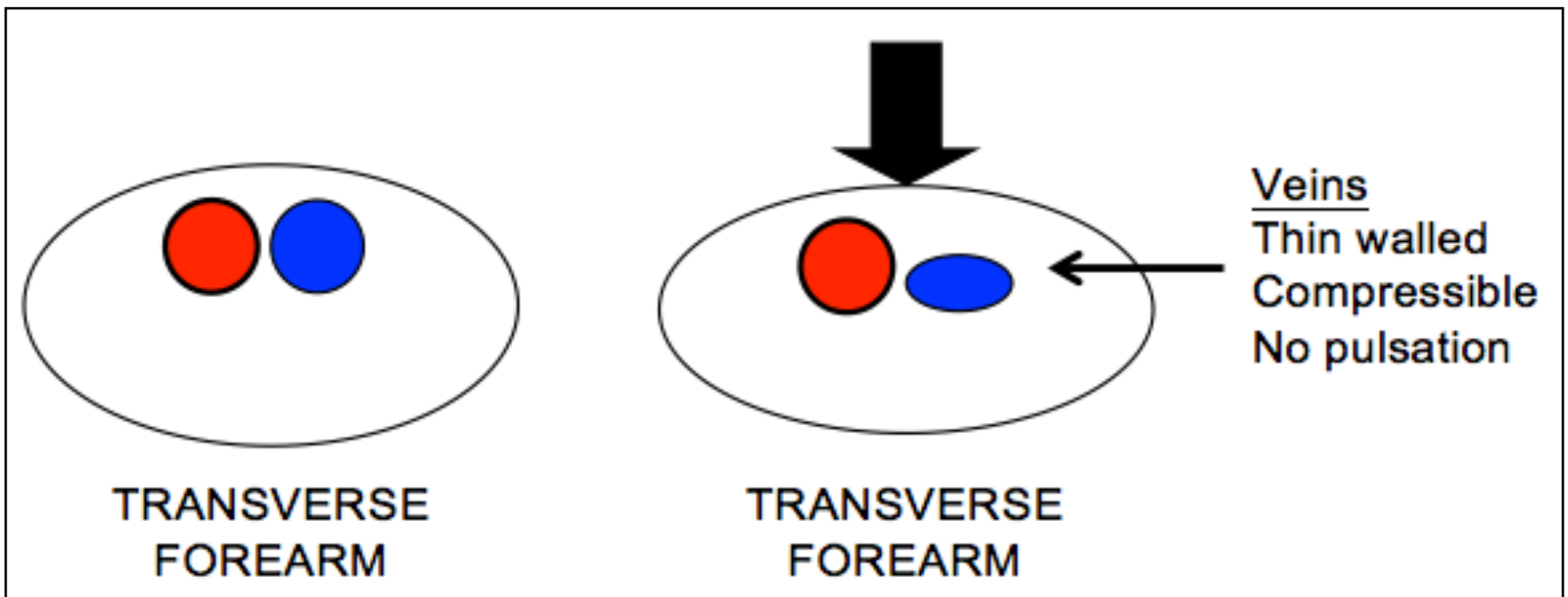
Younger children may not cooperate with the procedure and may require a papoose or other means of restraint. They may prefer to be held by their parents. When available, child life specialist assistance should be sought.

PROBE ORIENTATION

Start scanning the area of interest with the linear probe oriented in the transverse plane of the extremity and with the probe's marker dot to the patient's right (or your left). If you are using the hockey stock probe, the marker is at the tip of the probe. This orientation will produce an image on the ultrasound screen with identical orientation as the structures of the extremities. Left sided (in relationship to the operator) structures will appear on the left side of the screen and will correspond to the orientation of the marker dot. This will allow right or left movements on the display to correspond to the right or left movement of the probe or needle and makes it more intuitive.

VEIN IDENTIFICATION

Place a tourniquet above the area of interest. Scan the area with the linear probe in a transverse axis. This will allow for cross-sectional view of the extremities and will help identify the larger and more superficial veins. In general, the veins are thin walled structures that are easily compressible by minimal pressure with ultrasound probe and do not pulsate.



VEIN IDENTIFICATION

VEIN SELECTION

When you are looking for a vein to be used for cannulation, note the depth (look at the centimeter marks on the right of the screen) and the size of the vein. In general, larger and more superficial veins may be easier to access. A study in adult demonstrated that veins > 6 mm in diameter had much higher success rate than those ≤ 3 mm. There was no successful cannulation in veins ≥ 1.6 cm deep. The size rather than the depth of the vein is a better predictor for success. Larger veins are better to use even if they are a little deeper. Always take into account the depth of the vein when choosing the length of the angiocatheter – the deeper the vein, the longer the angiocatheter should be. The deep brachial and cephalic veins are generally not used for peripheral access so should be available for cannulation.

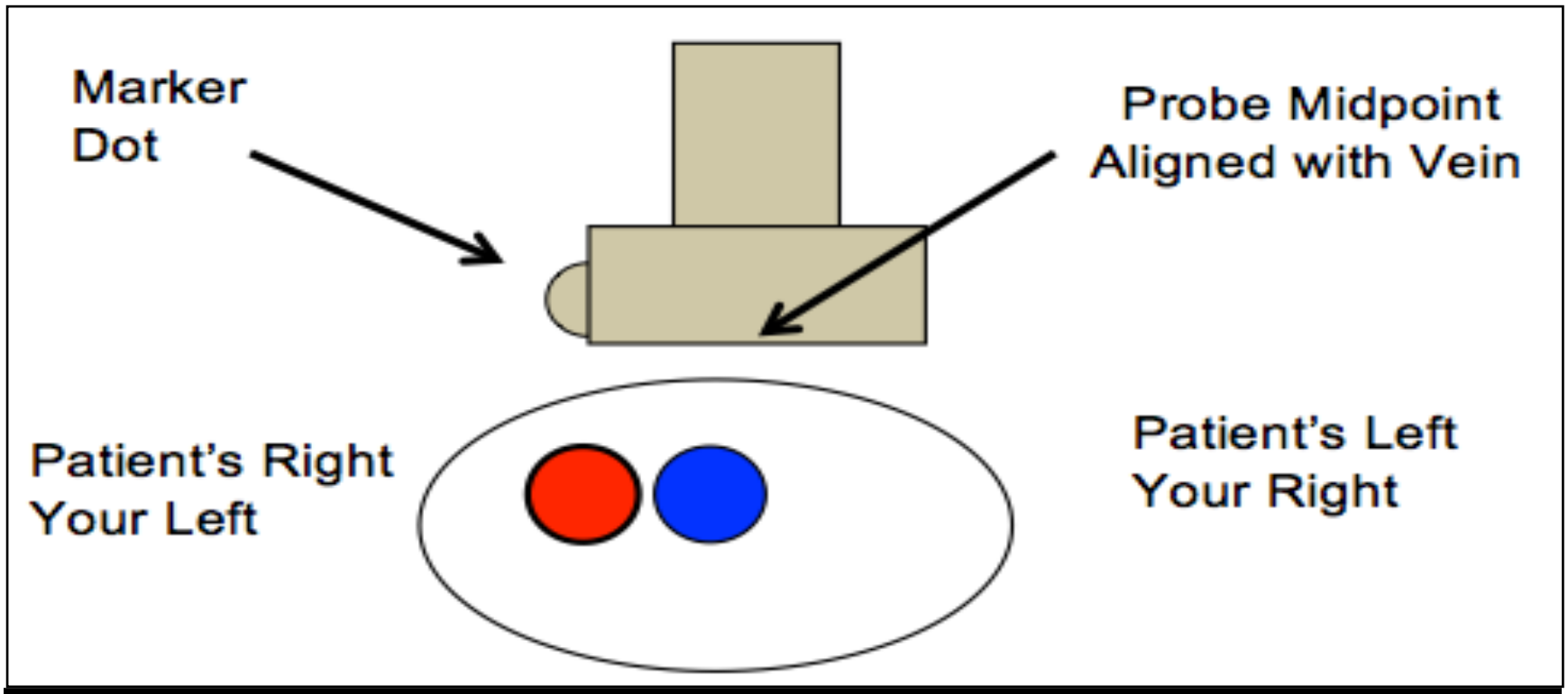
Once you identify the vein for cannulation, turn the probe in the longitudinal axis and identify the long view and the trajectory of the vein. If you are using the long axis during cannulation, make sure the marker dot is facing you and is adjacent to the puncture spot. This will allow you to follow the movement of the needle much more easily. (See longitudinal technique below)

In young children, you may not be able to both visualize the vein with the ultrasound and place the angiocatheter at the same time (dynamic technique) due to patient movement. In these circumstances, you may need to mark the location and the direction of the vein, note the depth, and then perform the cannulation without direct ultrasound visualization (static technique).

PROCEDURE

Both the transverse and longitudinal techniques can be performed with one or two operators. In single operator technique, 1 person performs the ultrasound identification and visualization of the vein using the non-dominant hand to hold the probe, while performing the cannulation with the dominant hand. With two operators, one holds the probe in the desired plane and the other performs the cannulation.

TRANSVERSE TECHNIQUE: Transverse technique is usually easier to learn and master, and may be the first step in learning how to perform the procedure. Transverse approach will allow you to adjust the medial-lateral trajectory of the more easily.



PROBE ORIENTATION

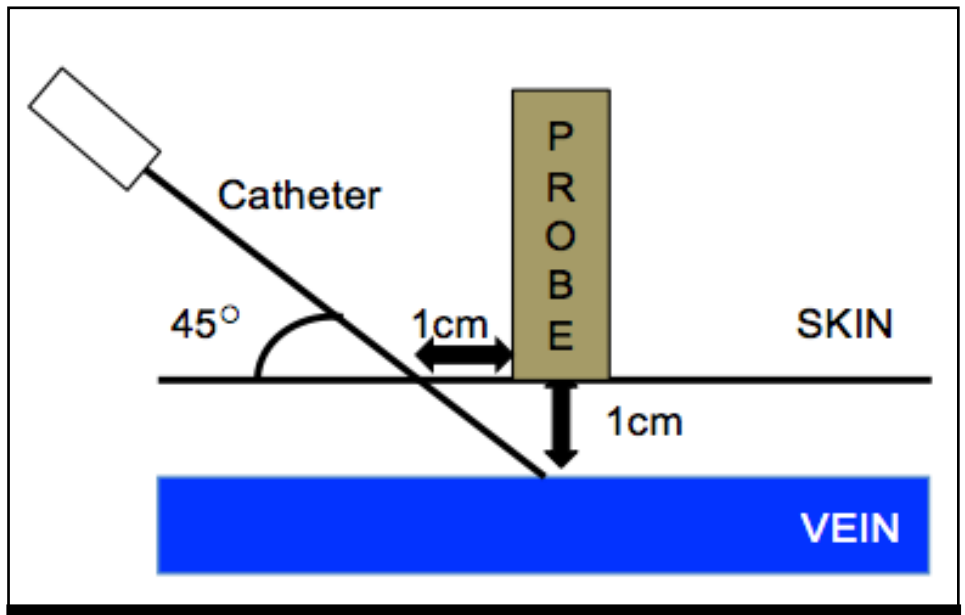
Follow the above steps to for vein identification and selection for cannulation. The probe is in a transverse axis and the marker dot of the standard linear probe or the tip of the hockey stick probe (SLA) is to your left (the patient's right). The middle of the probe is aligned over the vein (there is usually a middle needle marker on the linear probe). Adjust the depth of the image until the vein is about the middle of the ultrasound screen.

Once you identify the vein and are ready for cannulation, penetrate the skin distal to the probe at a 45-degree angle and start inserting the needle. The start point of the skin penetration should be about the same distance from the probe as the depth of the vessel. If the vein is 0.5 cm deep, start the cannulation at about 0.5 cm from the probe. As you advance the needle, start tilting or advancing the probe proximally slowly and gently in the same direction as the needle advancement to follow the position of the needle tip at all times. The tip will appear as reverberation artifact – multiple concentric bright short lines starting from the tip of the angiocatheter (called also "ring down" artifact).

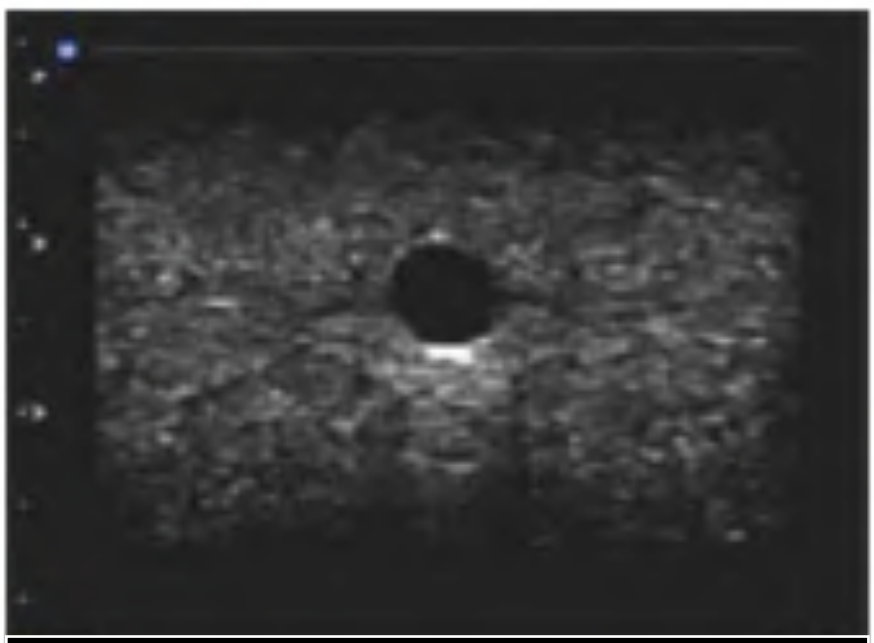
NEEDLE PUNTURE SITE

The catheter should enter the skin at a 45 degree angle at a distance from the probe equal to the depth of the vein. The catheter length should be greater that the hypotenuse of the imaginary triangle to avoid dislodgement of the catheter.

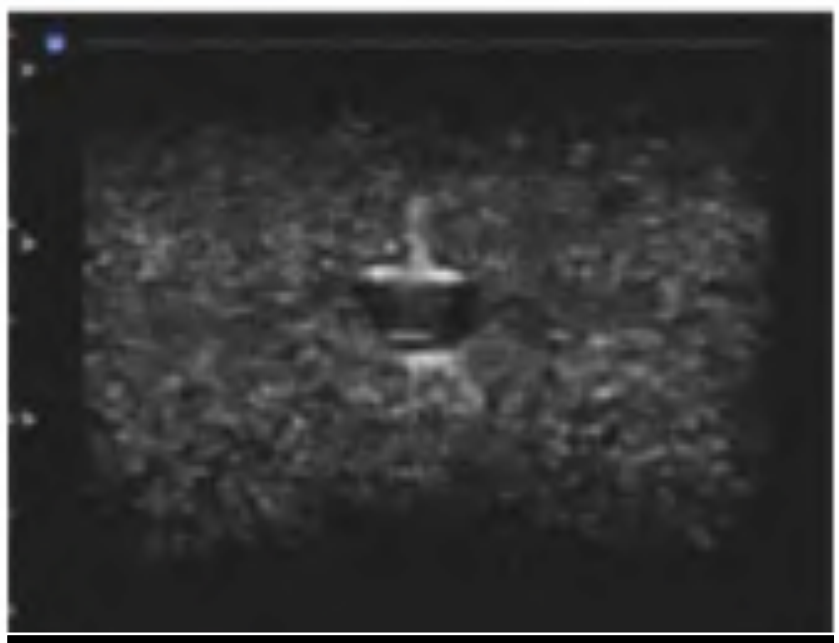
As the needle reaches the anterior wall of the vein, there will be downward tenting of the wall. Once the wall is punctured, the tenting will disappear, you will see the needle tip in the middle of the vessel and a blood return in the angiocatheter reservoir.



CATHETER ADVANCEMENT



VEIN: TRANSVERSE

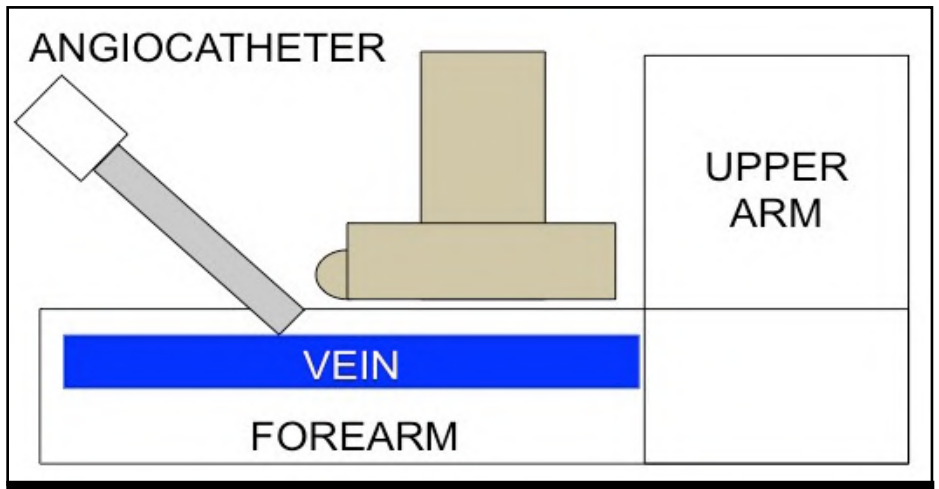


TENTING/RING SIGN

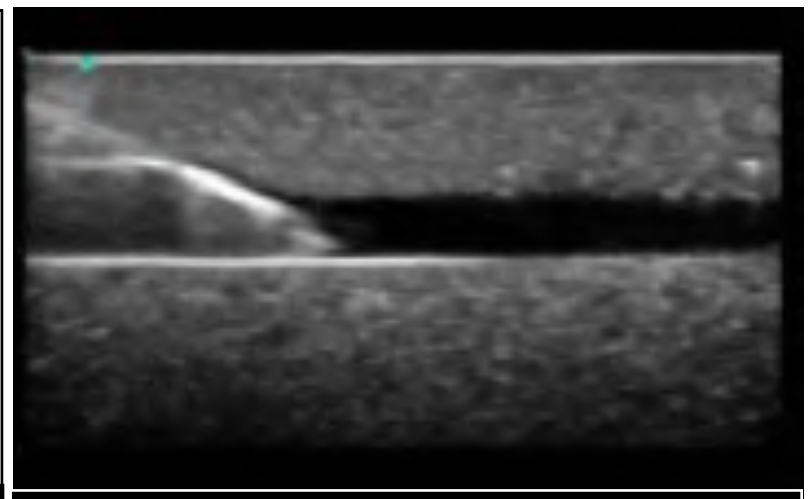
In order to confirm the position of the tip, you may want to perform the “wiggle” test – wiggle the needle, and if the tip is inside the vessel, that will produce wiggling of the tip freely inside the vein and the tissue above it, but not below it. If the needle is not moving in the lumen, this suggest that the tip had pierced the posterior wall of the vessel and is under the vein, which you can confirm by turning the probe in the long axis. If this is the case, pull the needle back until you can visualize the tip inside the vessel on long axis or if you have a positive wiggle test on transverse.

Now that you confirmed appropriate position of the tip, you flatten the angle at which the angiocatheter is held and advance the catheter another 1-2 mm to assure the entire needle is inside of the vein. Then advance the catheter and remove the needle and proceed as usual to secure the line.

LONGITUDINAL TECHNIQUE:This technique requires significant experience and perfect alignment of the probe with the plane and trajectory of the vein. Patient cooperation and steady hands are essential. Anchor your hand on the patient's extremity and keep your hand very still in order not to lose the site of the vein.



CATHETER TIP IN THE VEIN



CATHETER TIP IN THE VEIN

Identify the vein for cannulation using the transverse technique. Once the vein is identified, turn the probe in long axis to align with the long axis of the vein. It is more intuitive to direct the marker dot toward the puncture site (toward the operator). With this orientation, you will see the appearance of the needle on the left side of the screen and will correspond to the marker dot on the screen, and will make further adjustment of the needle more intuitive.

Puncture the skin just distal to the probe at 30-45 degree and follow the needle tract as it advances through the soft tissue. You will see the angiocatheter as long hyper echoic structure. Once you reach the vessel wall, you will note tenting of the wall and when the needle penetrates the vessel. The tenting will disappear and you will see blood flash back. Decrease the angle or insertion and advance another 1-2 mm to ensure that a significant part of the needle is inside the vein. Remove the needle and advance the catheter and follow as the catheter advances through the lumen of the vessel until its final position.

With this technique, you should see the entire needle and the tip at all times as you advance it. If you see the vein but cannot see the needle and its tip, it is lateral to the vein. Do not advance the needle any further, instead pull back and redirect until you see the needle.

The longitudinal technique has the advantage of being able to follow the position of the catheter in the vessel, while this is not possible with the transverse technique. However, you can always convert the transverse to longitudinal axis once you penetrate the vein to confirm tip position and be able to follow the path of the catheter.

To confirm intravascular placement keep the probe in a long axis and flush the catheter with saline: you will see bubbles coming out of the end of the catheter. This will only happen if the catheter is positioned within the lumen of the vein.

VIDEO LINK: CORE EM: US GUIDED PERIPHERAL INTRAVENOUS CATHETER

COMPLICATIONS AND PITFALLS

The most common problem with US guided PVL placement is overly deep placement or through and through penetration of the vein. This is more common with the transverse technique as needle tip visualization is more challenging. Use the probe advancing / tilting technique to visualize the tip until appropriate position is achieved. Keeping an eye on the tip all the time will help to prevent puncturing of the posterior wall of the vein.

If the catheter cannot be flushed easily, confirm placement in longitudinal axis as described before. If unsure, do not use the line and remove the catheter.

Occasionally, an artery instead of a vein is cannulated. You can assess this by applying color Doppler and if the catheter is in an artery, the flow in that vessel will be pulsatile. The blood return will also be pulsatile. Remove the line immediately upon detecting the problem.

When using the deeper veins, always use longer catheters. Even if you confirm the position of the catheter inside the vein, movement of the extremity may dislodge standard shorter catheter. This is particularly important for obese patients, both children and adults, or if deeper veins such as the brachial vein are used.

PROCEDURE PEARLS

Make yourself comfortable. Adjust the bed and table height so that you do not have to bend or stoop. If you prefer, you can sit.

Make sure the extremity is placed on a completely horizontal plane, so that the US probe and the needle are placed in a true vertical position, therefore images and needle movements are in a vertical and not oblique plane.

Place the US monitor directly in front of you, so that all you have to do is look straight ahead while working. It is very important to have the angiocatheter, the US probe and the US machine screen aligned in front of you. Ideally, once you penetrate the skin, you only look at the monitor while advancing and adjusting the angiocatheter.

UMBILICAL VEIN CATHETERIZATION

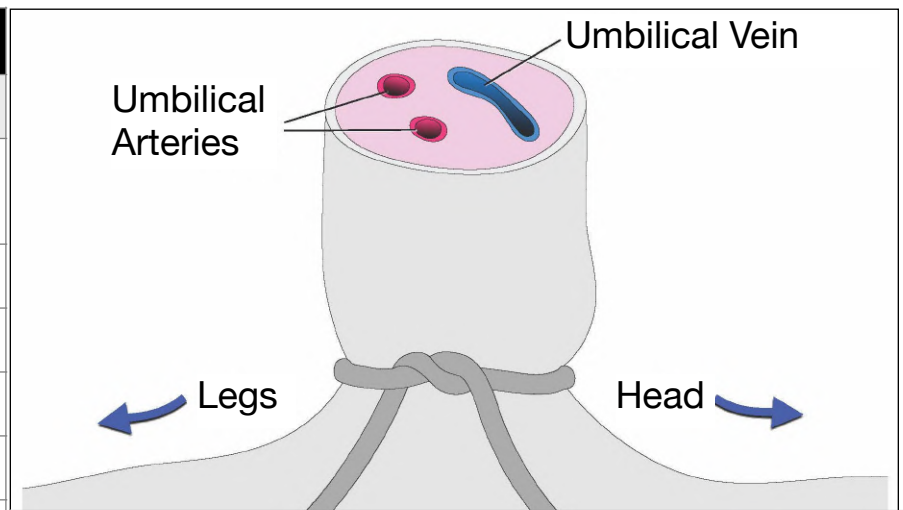
INTRODUCTION (DANA SUOZZO, M.D., 6/2020)
In neonates, peripheral blood vessels are both friable and difficult to access. The umbilical vein provides reliable and quick access to the central circulation in term neonates until 10 days of age and in preterm neonates until 7 days of age. The umbilical vein flows through the ductus venosus into the hepatic sinusoids and from there to the inferior vena cava and the right heart. Ease of placement is facilitated by direct visualization of the vein in cross section. This PEM Guide focuses on emergency umbilical venous catheterization (UVC) in the emergency department. The procedure for UVC and umbilical artery catheterization in the neonatal intensive care unit or delivery room differs from that described here.

UVCs can be placed emergently in the ED setting for administration of fluids, medication (e.g. Epinephrine) and blood products (See PEM Guide: Resuscitation: Neonatal Resuscitation). Unlike intraosseous access, the umbilical catheter provides reliable access for blood sampling.

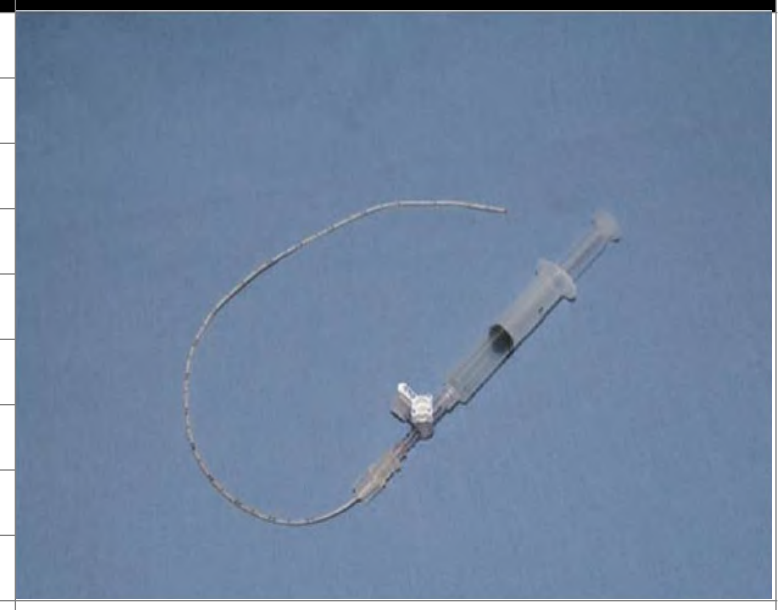
UMBILICAL VENOUS CATHETERIZATION
INDICATIONS
Unstable condition requiring prolonged resuscitation
Multiple failed attempts at peripheral vascular access
Extreme volume loss requiring crystalloid or blood products
Administration of Epinephrine (preferred over the endotracheal route)
CONTRAINDICATIONS
Infection: Omphalitis, peritonitis or necrotizing enterocolitis.
Anatomic abnormalities of the umbilicus: Omphalocele, Gastroschisis

ANATOMIC LANDMARKS

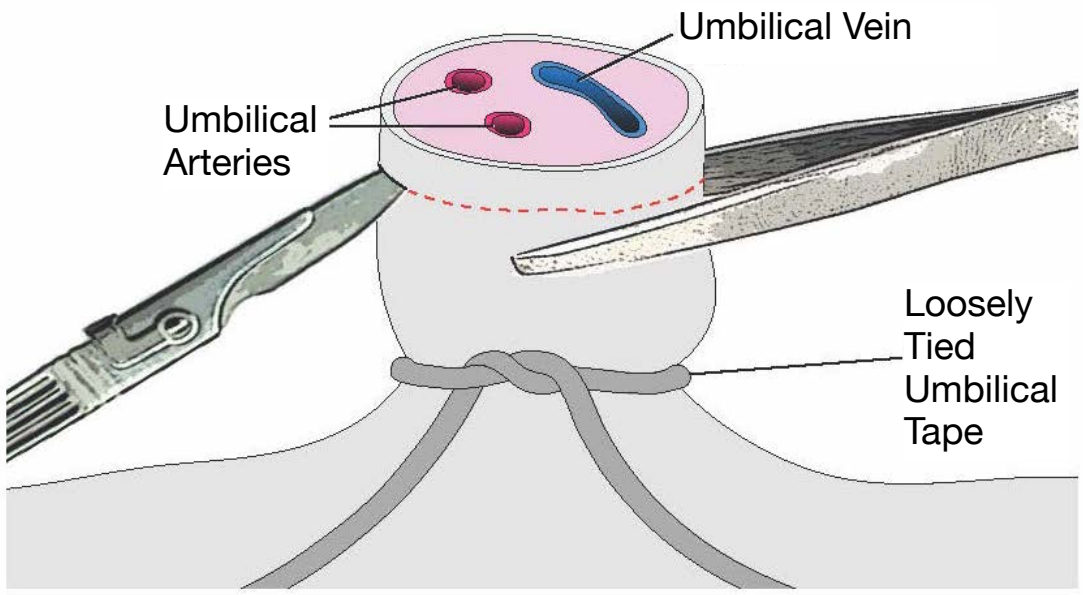
UMBILICAL VESSEL IDENTIFICATION		
	VEIN	ARTERY
Position	Superior 12 o'clock	Inferior 4 and 7 o'clock
Number	1	2*
Shape	Irregular, ovoid	Round
Size	Large	Small
Wall	Thin	Thick
Lumen	Large	Small
*0.05% with a single umbilical artery		



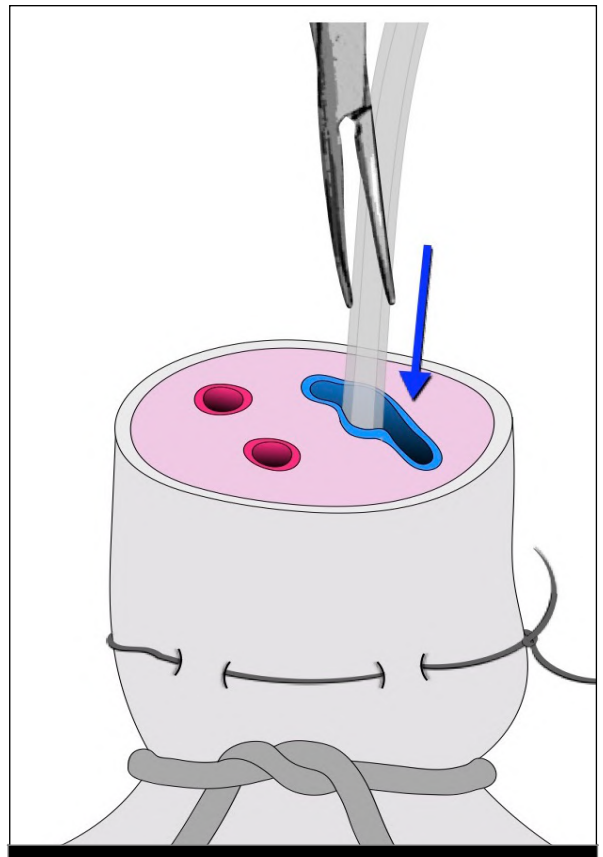
IDENTIFY UMBILICAL VEIN

EQUIPMENT		
Infant radiant warmer		
Sterile gloves, gown, mask w/face shield or goggles		
Sterile drapes		
Antiseptic solution (Chlorhexidine or Povidone-iodine)		
Umbilical tape or suture material		
Forceps		
11 blade scalpel or scissors		
3 ml syringe		
Three-way stopcock		
Single Lumen Umbilical Catheter	3.5 French (< 3.5 kg) 5.0 French (≥ 3.5 kg)	3 ml Syringe 3-way Stopcock Umbilical Catheter (flushed with sterile saline)
Normal saline for flush		
Gauze, tape, Tegaderm		

PROCEDURE STEPS	
1	Put on personal protective equipment
2	Have assistant immobilize the infant’s extremities if necessary
3	Cover the area with sterile drapes
4	Prepare umbilical cord with an antiseptic solution
5	Place a loose tie of umbilical tape around the base of the cord. The tie should be tight enough to control bleeding but not tight enough to impede passage of the catheter. The tie can be tightened if there is excessive bleeding after you cut the cord. Alternatively, a purse string suture can be used.
6	Attach a 3.5 French (< 3.5 kg) or 5 French (≥ 3.5 kg) umbilical catheter to a 3-way stopcock that is attached to a 3-ml syringe. Flush the catheter and both ports of the 3-way stopcock with normal saline
7	Using sterile technique, resect the cord in cross section with a scalpel below the clamp (if present) and 1-2 cm above the umbilical tie at the base of the cord
8	Identify the umbilical vein: It is cephalad in the cord, single, thin walled, irregular shaped with a large lumen
9	Dilating forceps may be used to overcome vessel spasm prior to catheter passage
10	Gently insert catheter into the umbilical vein. Never force the catheter. The course of the vein will be toward the heart. Providing gentle traction on the umbilical cord with forceps and twisting the catheter slowly may facilitate passage.
11	Continue inserting the catheter to the 3 to 4 cm mark. Check for blood return at this point by opening the stopcock to the syringe and gently aspirating.
	In the emergency department, the tip of the catheter should be located only a short distance into the vein, at the depth at which blood is first able to be aspirated. If the catheter is inserted farther, there is a risk of infusing solution or medication directly into the hepatic vessels causing cellular damage. Formulas for the depth of the catheter are not for emergency department use.
12	Secure catheter with tape, Tegaderm



STEP 7: RESECT THE DISTAL CORD



STEP 10: INSERT CATHETER

COMPLICATIONS*
Pericardial effusion
Pericardial tamponade
Cardiac arrhythmias
Pneumopericardium
Perforation of the peritoneum
Perforation of the colon
Air embolization
*Most commonly associated with incorrect position