

# Emergency Medicine Update

# A Case-Based Review of Recent Impactful Literature

Annie Wildermuth, PhD, PA-C, EM CAQ, RD Assistant Dean & Assistant Professor Henry Jackson Foundation for the Advancement of Military Medicine Uniformed Services University About Me



Practicing EM PA-C since 2012

CAQ-EM in 2018

Educator & researcher

Launched annual EM literature update at AAPA in 2019



# Disclosures

No conflicts of interest

The views expressed herein are those of the presenter and not that of the Department of Defense, Henry M. Jackson Foundation for the Advancement of Military Medicine, or other Federal Agencies

# Learning Objectives

- 1. Recognize and discuss Lyme Disease treatment options in pediatric patients.
- 2. Analyze risk versus benefit of venous thromboembolism prophylaxis in patients with closed ankle fractures.
- 3. Provide anticipatory guidance on concussion recovery & treatment.
- 4. Discuss treatment options in spontaneous pneumothorax.
- 5. Discuss the efficacy of the PECARN criteria in detecting clinically important traumatic brain injury in pediatric patients.

### Topics



Lyme Disease



Pneumothorax



Ankle Fractures



Pediatric Head Trauma



Concussions



Facial Burns

And more...

A 5-year-old female presents to the ED in midsummer in Connecticut with a bullseye rash on her thigh. Parents report she was hiking in the woods about 7 days ago; no attached tick was visualized.

No significant PMH.

Vital signs are all within normal limits. Physical exam with lesion pictured, no focal neuro deficits, normal cardiac & MSK exam.



Which of the following is an appropriate treatment?

- a) Amoxicillin PO x 14 days
- b) Cefuroxime PO x 14 days
- c) Doxycycline PO x 10 days
- d) Any of these

#### Lyme Disease

- Ixodes tick-borne, spirochete infection caused by Borrelia burgdorferi
- 3 endemic areas
- Erythema migrans is pathognomonic, however only present in 70-80% of cases
- Other symptoms: disseminated skin lesions, neuropathy, arthritis, cardiac arrhythmias, meningitis

#### Lyme Disease Prophylaxis & Treatment

- Treatment: antibiotics (doxycycline, amoxicillin, cefuroxime, ceftriaxone, azithromycin)
- Patients <8 years & pregnant or lactating historically not prescribed doxycycline because of risk of staining permanent teeth
- Newer studies do not show this association

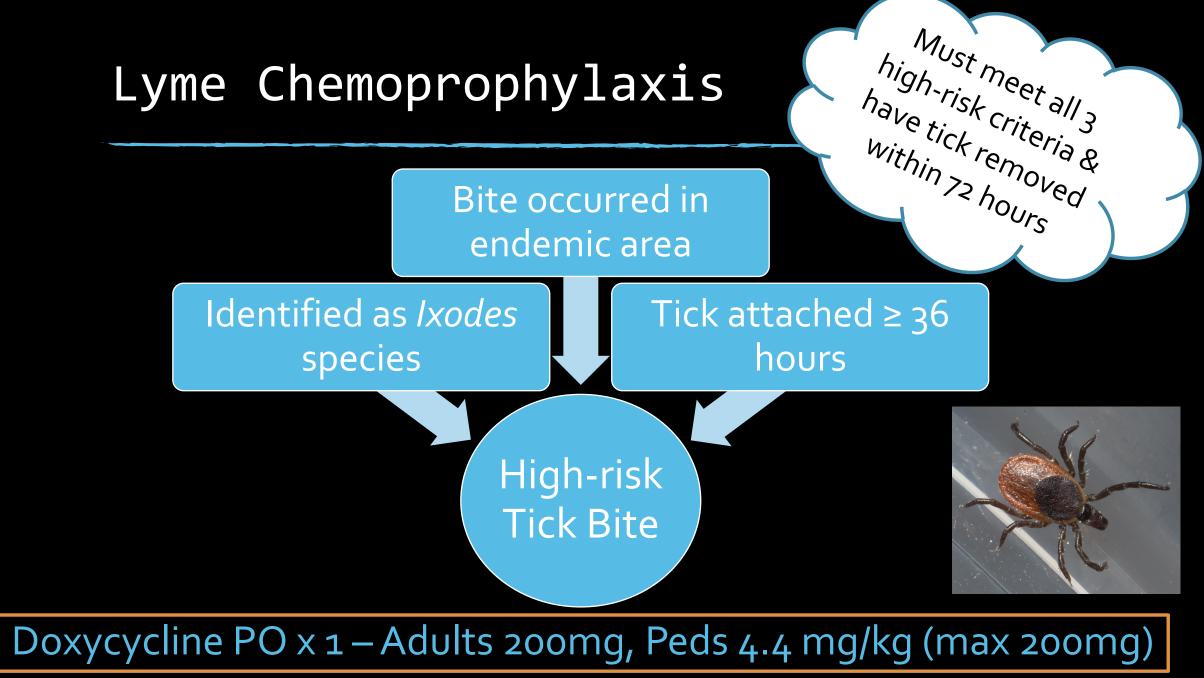
Growing consensus that doxycycline is safe in kids

### Lyme Disease Guidelines

- Infectious Diseases Society of America (IDSA) released new guidelines in 2020
- Treatment options for prophylaxis & erythema migrans in pediatric patients updated to include doxycycline
- Pediatric doxycycline dose: 4.4 mg/kg PO divided twice daily (max 200 mg/day)

#### Treatment by Disease Manifestation

Disease Manifestation	Drug	Duration
Erythema migrans	Doxycycline Amoxicillin or cefuroxime Azithromycin	10 days 14 days 7 days
Meningitis or radiculopathy	Doxycycline Ceftriaxone (IV)	14-21 days 14-21 days
Cranial nerve palsy	Doxycycline	14-21 days
Carditis	Doxycycline, amoxicillin or cefuroxime Ceftriaxone (IV)	14-21 days 14-21 days
Arthritis (initial tx)	Doxycycline, amoxicillin or cefuroxime	28 days



Lantos PM et al, 2020

Image: Robert Webster, *Pictures from Earth* 

#### Case #1 Takeaways

- Our 5-year-old had erythema migrans
- Reasonable treatment options included doxycycline, amoxicillin & cefuroxime
- Chemoprophylaxis for high risk bites is doxycycline for adults & kids PO x 1 dose
- Doxycycline <14 days likely safe for kids</li>

2020 IDSA guidelines include doxycycline as a reasonable treatment for pediatric patients

#### Case #2

A 78-year-old female presents to the ED with an ankle injury after a mechanical fall down 3 stairs.

No prior DVT/PE or recent surgery.

The patient has a closed distal fibula fracture. She is neurovascularly intact.

A below-knee, sugar tong splint is applied.



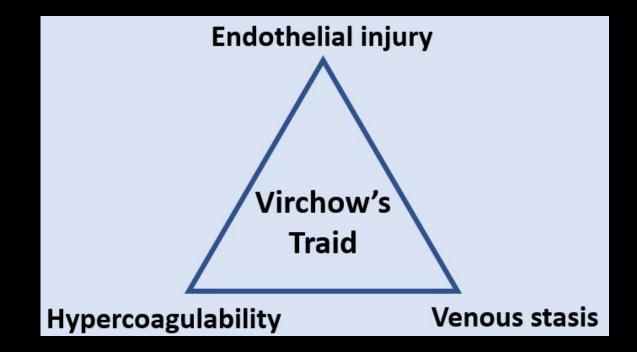
What is the biggest risk factor for venous thromboembolism (VTE) in discharged ED patients with ankle factures?

- a) Surgery in the previous 90 days
- b) Age over 65
- c) History of VTE or superficial VTE
- d) Pregnancy

# Venous thromboembolism (VTE)

- Obstructive disease hindering venous return, most frequently involving lower limbs
- Risk factors: Reduced blood flow, venous injury, hypercoagulability
- May have history of pain, redness, swelling. Exam may show edema, red/warm skin, tenderness.

Treatment aims to prevent pulmonary embolism, usually with anticoagulation



#### Venous Thromboembolism in Patients Discharged from the ED with Ankle Fractures

#### Retrospective cohort study

Propensity score matched to 2 controls (finger wounds and wrist fractures) to compare relative hazard of VTE

90-day incidence of VTE among splinted, discharged ankle fractures was 1.3%

These patients had a 5.7-6.3-fold increased hazard compared to controls

Factors Associated	Hazard Ratio; 95%
with VTE	Confidence Interval (CI)
Age >65	HR 1.18 95% CI 1.00-1.39
History of VTE or	HR 5.18
superficial VTE	95% CI 4.33-6.20
Recent admission	HR 1.33 95% Cl 1.05-1.68
Recent non-ankle	HR 1.58
fracture surgery	95% Cl 1.30-1.93
Subsequent ankle	HR 1.80
fracture surgery	95% CI 1.48-2.20

Incidence of VTE in this study was overall low, but ankle fractures with immobilization did increase risk

Literature is unclear exactly which patients would benefit from thromboprophylaxis

Our patient was >65 and thus at even higher risk for VTE associated with her splinted ankle fracture

In most patients, risk of thromboprophylaxis outweighs benefit; however, it may be worth considering in patients with prior DVT/PE

VTE should be in the differential diagnosis for splinted anklefracture patients returning with leg redness or pain.

#### Case #3



A 13-year-old female presents to the ED following a head injury sustained in her soccer game today. She bumped heads with another player going for the ball. No LOC; she was pulled from play.

Initial nausea resolved. Current HA & "tired feeling". No neck pain, vision changes, or gait changes.

VS WNL. Patient seems tired. Bruising/swelling on forehead Neurologic exam WNL. You diagnose the patient with a concussion.

What anticipatory guidance do you provide for sports-related concussion?

- a) Strict bedrest
- b) Mostly rest w/ minimal activity allowed
- c) Subthreshold aerobic exercise
- d) Stretching

# Early Subthreshold Aerobic Exercise for Sport-Related Concussion: a RCT

- 103 patients, age 13-18, within 10 days of sports-related concussion
- 20 mins. of: stretching (placebo) vs. subthreshold aerobic exercise on bike or treadmill
- No intervention until at least 48 hours post-injury
- Results:
  - Aerobic exercise asymptomatic at median of 13 days
  - Stretching asymptomatic at median of 17 days
  - P= 0.009
  - Lower incidence of delayed recovery in aerobic exercise (P = 0.08)

- Our patient demonstrated persistent symptoms of concussion with no indication of moderate or severe TBI
- Advised 48 hours of rest followed by 20-mins sub-threshold, low-intensity aerobic exercise

Short duration, low intensity aerobic exercise may hasten sports concussion recovery in adolescents.

A 22-year-old male presents to the emergency department with sudden onset dyspnea 20 minutes ago. No hemoptysis or fever. He smokes a pack daily.

RR of 22, SpO2 95% on RA, BP 120/80, HR 90

Hyperresonant to percussion with absent breath sounds over the left lung fields.

CXR reveals an approximately 50% left-sided pneumothorax (PTX). The patient has no history of PTX.

# Does this patient require procedural intervention to manage his pneumothorax?

- a) Yes all moderate-to-large pneumothoraxes requires it
- b) Maybe it can resolve with conservative treatment
- c) No because of his age and stability, intervention is not needed

### Treatment of Spontaneous Pneumothorax

- Spontaneous pneumothorax is common in adults; over 1/3 of cases are primary
- Most common treatment is interventional drainage and chest tube placement
- Chest tube placement is painful & often requires hospitalization
- Adverse effects include organ injury, bleeding, infection, and need for additional surgery

# Conservative vs. Interventional Treatment for Spontaneous Pneumothorax

- Open-label, multicenter, noninferiority trial of 316 patients randomized to immediate intervention vs. conservative management group
- Followed up at 1-3 days, 2 weeks, 4 weeks, 8 weeks with a CXR if not previously resolved
- Primary outcome: complete radiographic resolution within 8 weeks
- Numerous secondary outcomes, including adverse events, reoccurrence within 12 months, & patient satisfaction

#### Conservative vs. Interventional Treatment for Spontaneous Pneumothorax

Outcome	Interventional (N=154)	Conservative (N=162)	Non-inferiority
Resolution within 8 weeks	129 / 131 (98.5%)	118 / 125 (94.4%)	P=0.02
Outcome	Interventional (N=154)	Conservative (N=162)	Hazard Ratio (95% CI)
Radiographic resolution in days (IQR)	16 (12-26)	30 (25-54)	0.49 (0.39 – 0.63)
Outcome	Interventional (N=154)	Conservative (N=162)	Risk Difference (95% Cl)
Any adverse event - no. (%)	41 (26.6)	13 (8.0)	18.6 (10.5 – 26.7)
Serious adverse event – no. (%)	19 (12.3)	6 (3.7)	8.6 (2.7-14.6)
Recurrence within 12 mos. – no. (%)	25 / 149 (16.8%)	14 / 159 (8.8%)	8.0 (0.5 – 15.4)

Patient satisfaction was higher with conservative management.

- Our patient was stable with a moderate size pneumothorax; conservative treatment was an option
- Several limitations; results are modest and statistically fragile

Conservative management of moderate-to-large primary spontaneous pneumothorax may be noninferior to interventional management



An 18-month-old infant presents to the ED after falling off the couch 2 feet onto the floor and hitting his head 1 hour ago.

No LOC. The patient is acting normally, per dad.

Vital signs normal. Patient acting appropriately for age. No neuro deficits. No palpable skull fractures or hematomas.



How do you decide on neuroimaging in these cases?

- a) Clinical gestalt
- b) Clinical prediction rule
- c) Presence of LOC
- d) Image every kid with blunt head trauma

### Pediatric Blunt Head Trauma

800,000 children present to ED with blunt head trauma annually in U.S.

Majority of children present with minor head trauma (GCS 14-15)

Of those with minor head trauma who undergo CT, most have no findings

Minimizing radiation exposure and/or risks of sedation is important What to do? PECARN

PECARN Algorithms for Minor Head Trauma: Risk Stratification Estimates from a Prospective PREDICT Cohort Study

Secondary, prospective, multicenter analysis of 15,163 children with GCS of 14 or 15

Calculated clinically important TBI (ciTBI) rates for each PECARN risk category

#### Very Low Risk Groups

• o% risk of ciTBI in both groups

#### Intermediate Risk Groups

- Children 2+: All 4 risk factors highest risk (25%); combination of severe mechanism and severe headache 2<sup>nd</sup> highest (7.7%)
- Children <2: Insufficient data

#### High Risk Groups

- Children <2: highest risk factor was signs of palpable skull fracture
- Children 2+: greatest risk factor was signs of basilar skull fracture

Risk estimates of ciTBI for each PECARN algorithm risk group were consistent with original PECARN study

Our patient was in very-low-risk category; no CT ordered after shared decision making with parent

PECARN algorithm is a helpful clinical decision tool in pediatric blunt head trauma with a GCS of 14-15.

#### Case #6

A 41-year-old male presents to the ED after a house fire.

HR 130, RR 25, SpO2 90% RA. He has singed facial hair, carbonaceous sputum, and hoarseness, but no overt facial burn.

Total body surface area (TBSA) burned 65%.



Which exam finding is most associated with inhalation injury?

- a) Hoarseness
- b) Burned nostril hair
- c) Cough
- d) Shortness of breath
- e) Abnormal chest x-ray

# Inhalation injury

Smoke inhalation is common in patients exposed to fires

- Damage is due to heat (to level of larynx) and chemical byproducts (airways, alveoli, or both)
- Important to elucidate if exposure was due to flames, smoke, and/or chemicals.
- Airway can become rapidly edematous, mucous production increases, bleeding is possible

Current guidelines advise endotracheal intubation for facial burn patients & consideration of early intubation for patients with physical exam findings concerning for inhalation injury.

Positive Signs on Physical Exam are Not Always Indications for Endotracheal Tube Intubation in Patients with Facial Burn

Retrospective analysis of 335 facial burn patients with & without intubation in ED

121 patients intubated in ED, including all patients with total body surface area (TBSA) >60% even without signs of inhalation injury

Only 60.3% of patients found to have inhalation injury on bronchoscopy

Independent risk factors for inhalation injury

Shortness of breath (p=0.027)

High TBSA (p=0.001)

Non-predictive risk factors for inhalation injury

Hoarseness

Burned nostril hair

Cough

GCS Score

Laboratory examinations

Abnormal CXR findings

Our patient was intubated due to concern for inhalation injury & need for airway protection

Conventional physical exam findings may not predict inhalation injury & need for intubation

Airway protection may be needed in patients with facial burns without inhalation injury

In facial burns, shortness of breath & high TBSA are significant predictors of inhalation injury.



A 12-year-old male presents to the ED with suspicion of a wood splinter in his palm.

No visible sign of splinter on exam. Diffuse abrasions present. Patient has mild tenderness to palpation of his thenar eminence.

No neurovascular injury patterns.

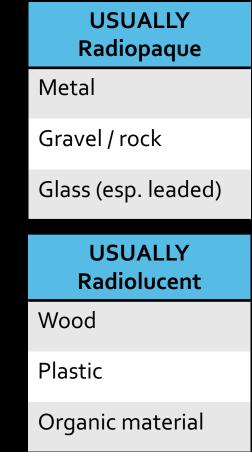


## What is the best way to identify this potential foreign body?

- a) X-ray
- b) Ultrasound
- c) CT
- d) No identification necessary

## Soft Tissue Foreign Bodies (FB)

- Very problematic easily missed & common cause of litigation
- Can cause infection, hypersensitivity reactions, severe inflammation
- Imaging necessary for suspected FB not identified on exam
- Radiopaque vs. radiolucent is not binary



## Ultrasonography in Soft-tissue FB Detection: a Phantom Study

740 chicken breasts prepared as phantoms (100 as controls)

FB: glass, porcelain, plastic, wood, pencil tip, chicken bone, iron, walnut, fishbone, rose thorn, cactus thorn, staples, pellets

Sensitivity >82.5% for all objects EXCEPT cactus thorn

Specificity > 90% for all objects EXCEPT cactus thorn

As the size of the FB increased, sensitivity increased





Cacti & associated thorns are the worst

Surgery consult / exploration indicated for suspected FB not identified on imaging

We ultrasounded our patient's hand – positive for 2 cm wood splinter, removed at bedside

Ultrasonography is a valuable adjunct to identifying soft tissue foreign bodies.

## A few other important/cool emergency medicine studies...

#### Bacteremia From a Presumed Urinary Source in Hospitalized Adults with Asymptomatic Bacteriuria

- Cohort study of 11,590 patients in 68 hospitals admitted with asymptomatic bacteriuria (ASB)
  - Primary outcome: prevalence of bacteremia from a presumed urinary source
  - 72.2% (n=8364) received antimicrobial treatment for UTI
  - 1.4% (n=161) had bacteremia from a presumed urinary source
  - 0.7% (n=17) of patients with AMS and no signs of infection developed bacteremia
- Multivariate analysis: male sex, hypotension, 2+ SIRS criteria, urinary retention, fatigue, log of serum leukocytosis, pyuria were associated with bacteremia
  - No single factor associated with more than 2% risk of bacteremia
  - If 2% or higher risk was a cutoff for empiric antibiotics, 78.4% of antibiotic exposures would have been avoided

Bacteremia from a presumed urinary source is rare in ASB.

Association of Tramadol vs. Codeine Prescription Dispensing with Mortality and Other Adverse Outcomes

Retrospective, population-based, propensity score-matched cohort study

Tramadol vs. codeine new prescriptions on mortality and adverse clinical outcomes in outpatients

New prescription of tramadol was significantly associated with a higher risk of all-cause mortality, cardiovascular events, and factures compared to codeine Outcomes (n=368,960 patients; 184,480<br/>propensity matched pairs)TramadolCodeineAll-Cause Mortality (per12.865.59

All-Cause Mortality (per 1,000 person years)	12.86	5.59
Cardiovascular events (per 1,000 person years)	9.97	8.62
Fractures (per 1,000 person years)	12.07	8.08
Risk of Falls	No significant difference	
Delirium	No significant difference	
Constipation	No significant difference	
Opioid Abuse / Dependence	No significant difference	
Sleep Disorders	No significant difference	

# Early Restrictive or Liberal Fluid Management for Sepsis-Induced Hypotension (CLOVERS trial)

- Multicenter unblinded superiority trial of restrictive fluids vs. liberal fluids for 24 hours
- Restrictive fluid group = more vasopressors Liberal fluid group = fluids before vasopressors
- Randomization occurred within 4 hours after patients met criteria for sepsis-induced hypotension
- Primary outcome: death before discharge home by day 90



# Early Restrictive of Liberal Fluid Management for Sepsis-Induced Hypotension (CLOVERS trial)

- Death before d/c home by 90 days:
- Restrictive 109 (14%)
- Liberal 116 (14.9%)
- P=0.62
- Similar adverse events between groups

Restrictive fluid strategy did not result in significantly lower or higher mortality than liberal fluid strategy

<b>Baseline Patient Characteristics &amp; Intervention Data</b>			
	Restrictive (N=782)	Liberal (N=781)	
Age	59.1 (±16.0)	59.9 (±15.9)	
SOFA Score	3.4±2.8	3.5±2.7	
Systolic BP mm Hg	93.2±12.0	93.8±12.2	
Median volume of IVF given before randomization	2050 (1500-2457)	2050 (1371-2442)	
% of patients receiving vasopressors before randomization	21%	18%	
Median IVF given during 1 <sup>st</sup> 6 hours post-randomization	500 mL	2300 mL	
Cumulative median IVF given in 24 hours post-randomization	1267 mL	3400 mL	
% of patients receiving vasopressors after randomization	59%	27%	

Utility of Serum Lactate on Differential Diagnosis of Seizure-like Activity: a Systematic Review & Meta-analysis

Transient loss of consciousness (TLOC) presents frequently to the ED; etiology is often unclear

Primary outcome: serum lactate level difference between a patient with generalized tonic-clonic seizures (GTCS) vs. other forms of TLOC

Eight studies, 1,348 total patients

Serum lactate levels in GTCS significantly higher than TLOC from any other cause (p=0.004)

Serum lactate level  $\geq$  2.4 mmol/L (normal 0.5-2.2 mmol/L) allowed differentiation between GTCS and non-GTCS & can be a valuable differentiating tool but not used for definitive diagnosis

Serum lactate likely to remain elevated for 2 hours post-GTCS

## Key Points

- Current IDSA guidelines include doxycycline as a reasonable treatment for pediatric patients
- VTE should be in the differential diagnosis for splinted ankle-fracture patients returning with leg redness or pain
- Short duration, low intensity aerobic exercise may hasten sports concussion recovery in adolescents
- Conservative management of moderate-to-large primary spontaneous pneumothorax may be non-inferior to interventional management
- The PECARN algorithm is a helpful clinical decision tool in pediatric blunt head trauma with a GCS of 14-15
- In facial burns, shortness of breath & high TBSA are significant predictors of inhalation injury
- Ultrasonography is a valuable adjunct to identifying soft tissue foreign bodies

#### Questions: anne.Wildermuth.ctr@usuhs.edu



#### References

- Lantos PM, Rumbaugh J, Bockenstedt LK, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease. Clin Infect Dis. 2021;72(1):e1-e48. doi:10.1093/cid/ciaa1215
- 2. Waheed SM, Kudaravalli P, Hotwagner DT. Deep Vein Thrombosis. [Updated 2023 Jan 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507708/
- 3. Grewal K, Atzema CL, Sutradhar R, et al. Venous Thromboembolism in Patients Discharged From the Emergency Department With Ankle Fractures: A Population-Based Cohort Study. *Ann Emerg Med*. 2022;79(1):35-47. doi:10.1016/j.annemergmed.2021.06.017
- 4. Campbell EA, Wilbert CD. Foreign Body Imaging. [Updated 2022 May 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK470294/</u>
- 5. Leddy JJ, Haider MN, Ellis MJ, et al. Early Subthreshold Aerobic Exercise for Sport-Related Concussion: A Randomized Clinical Trial. JAMA Pediatr. 2019 Apr 1;173(4):319-325. doi: 10.1001/jamapediatrics.2018.4397.
- 6. Guskiewicz KM, Register-Mihalik J, McCrory P, et al. Evidence-based approach to revising the SCAT 2: introducing the SCAT3. *Br J Sports Med.* 2013 Apr;47(5):289-93. doi: 10.1136/bjsports-2013-092225.
- 7. Brown SGA, Ball EL, Perrin K, et al. Conservative versus Interventional Treatment for Spontaneous Pneumothorax. *N Engl J Med.* 2020;382(5):405-415. doi:10.1056/NEJM0a1910775
- 8. Halverson M, Servaes S. Foreign bodies: radiopaque compared to what?. *Pediatr Radiol*. 2013;43(9):1103-1107. doi:10.1007/s00247-013-2660-y

## References, continued

- 9. Tok S, Kadioglu E. Ultrasonography in soft-tissue foreign-body detection: a phantom study. *Pol J Radiol*. 2021;86:e496-e499. Published 2021 Aug 21. doi:10.5114/pjr.2021.108879
- 10. Bressan S, Eapen N, Phillips N, et al. PECARN algorithms for minor head trauma: Risk stratification estimates from a prospective PREDICT cohort study. *Acad Emerg Med*. 2021;28(10):1124-1133. doi:10.1111/acem.14308
- Kuppermann N, Holmes JF, Dayan PS, et al. Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study [published correction appears in Lancet. 2014 Jan 25;383(9914):308]. Lancet. 2009;374(9696):1160-1170. doi:10.1016/S0140-6736(09)61558-0
- 12. Shubert J, Sharma S. Inhalation Injury. [Updated 2022 Jun 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513261/
- 13. Clark C, Ledrick D, Moore A. Facial Burns. [Updated 2022 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559290/
- 14. Huang RY, Chen SJ, Hsiao YC, et al. Positive signs on physical examination are not always indications for endotracheal tube intubation in patients with facial burn. *BMC Emerg Med.* 2022;22(1):36. Published 2022 Mar 8. doi:10.1186/s12873-022-00594-9
- 15. Li Y, Pang AW, Zeitouni J, Zeitouni F, Mateja K, Griswold JA, Chong JW. Inhalation Injury Grading Using Transfer Learning Based on Bronchoscopy Images and Mechanical Ventilation Period. *Sensors*. 2022; 22(23):9430. https://doi.org/10.3390/s22239430
- National Heart, Lung, and Blood Institute Prevention and Early Treatment of Acute Lung Injury Clinical Trials Network, Shapiro NI, Douglas IS, et al. Early Restrictive or Liberal Fluid Management for Sepsis-Induced Hypotension. N Engl J Med. 2023;388(6):499-510. doi:10.1056/NEJM0a2212663

### References, continued

- Advani SD, Ratz D, Horowitz JK, et al. Bacteremia From a Presumed Urinary Source in Hospitalized Adults With Asymptomatic Bacteriuria. *JAMA Netw Open*. 2024;7(3):e242283. Published 2024 Mar 4. doi:10.1001/jamanetworkopen.2024.2283
- 22. Xie J, Strauss VY, Martinez-Laguna D, et al. Association of Tramadol vs Codeine Prescription Dispensation With Mortality and Other Adverse Clinical Outcomes. *JAMA*. 2021;326(15):1504-1515. doi:10.1001/jama.2021.15255
- 23. Patel J, Tran QK, Martinez S, Wright H, Pourmand A. Utility of serum lactate on differential diagnosis of seizure-like activity: A systematic review and meta-analysis. *Seizure*. 2022;102:134-142. doi:10.1016/j.seizure.2022.10.007
- Nass RD, Zur B, Elger CE, Holdenrieder S, Surges R. Acute metabolic effects of tonic-clonic seizures. *Epilepsia Open*. 2019;4(4):599-608. Published 2019 Oct 22. doi:10.1002/epi4.12364