2017 PREP®

Self-Assessment

Pediatrics Review and Education Program

The Self-Assessment Program of PREP® The Curriculum

PREP & Pediatric in Review (PIR) Content Specifications

The PREP covers all Content Specifications over a 5-year period. Thus, the material presented in PREP The Curriculum covers approximately 20% of the Content Specifications each year in either the PREP Self-Assessment or PIR. Therefore, in any 5-year continuous cycle, PREP The Curriculum covers the vast majority of these knowledge statements and provides participants with an educational program that is ideal for achieving lifelong learning.

Core Competency Icons

Six core competencies considered to be the foundation of high-quality medical care.

1. **I-C:** Interpersonal and Communication Skills result in effective information exchange and teaming with patients, families, and other health professionals
2. **P:** Professionalism manifested through a commitment to professional responsibilities, adherence to ethical principles, and sensitivity to a diverse patient population
3. **PBLI:** Practice-Based Learning and Improvement involves investigation and evaluation of one's own patient care, appraisal, and assimilation of scientific evidence, and improvements of patient care
4. **SBP:** Systems-Based Practice demonstrates an awareness of and responsiveness to the larger context and system of health care and effectively calls on system resources to provide care that is of optimal value
5. **S:** Safety
6. **TE:** Interdisciplinary Teams

Question 1

A 16-year-old adolescent presents to your office the day after an injury to her right ankle. She inverted her ankle when she landed after jumping to rebound a ball during a high school basketball game. She was able to bear weight after the injury, but was not able to continue playing basketball. On physical examination, you note swelling over the lateral malleolus and bruising over the lateral aspect of the heel. The ankle is tender to palpation over the anterior edge of, and just inferior to, the lateral malleolus. She has no ankle instability with ligament testing. She is able to walk with a mild right antalgic gait.

Of the following, the BEST next step in evaluation and management would be to

A. begin gradual return to basketball activities
B. begin range-of-motion exercises and wear a stirrup ankle brace
C. order magnetic resonance imaging of the right ankle
D. order radiography of the right ankle
E. place her in a walker boot to immobilize the right ankle

Correct Answer: B

The patient in the vignette suffered an inversion injury and has tenderness over the lateral ankle ligaments. Her physical examination findings are consistent with a mild ankle sprain. She should be treated with rehabilitation exercises and a stirrup brace.

The term sprain refers to an injury to a ligament. A sprain is classified as grade 1 when the ligament is stretched. A partial ligament tear is labeled as grade 2. A grade 3 injury is a complete tear of the ligament.

Ankle sprains are common injuries, particularly in athletes who participate in sports that involve frequent jumping or cutting motions while running. The anterior talofibular and calcaneofibular ligaments are the most often sprained. Individuals with lateral ankle ligament sprains typically have a history of accidental inversion of the ankle with immediate onset of pain. Common signs of ankle sprain include bruising, swelling, and antalgic gait. Physical examination should include the ankle anterior drawer test, in which the examiner stabilizes the lower leg with one hand and attempts to pull the heel forward with the other hand; laxity suggests a higher-grade ankle sprain.

The initial treatment of ankle sprain is aimed at decreasing swelling, and includes compression, ice, and elevation. Early mobilization of the joint is associated with faster recovery. Complete immobilization with a cast or removable boot should be reserved for patients who have difficulty bearing weight because of pain. A stirrup style brace allows plantarflexion and dorsiflexion of the ankle joint, allowing a more normal gait while protecting against accidental inversion. Range-of-motion exercises early in the recovery period will help prevent stiffness of the ankle joint. Once patients achieve normal range of motion, they can proceed to exercises designed to enhance strength and proprioception, followed by progression to sports-specific activities. When an athlete returns to sports, use of a support brace during play can reduce the risk of future sprains.

The patient in the vignette is not ready to return to basketball; she has swelling and altered gait and has not completed any rehabilitation. Based on the Ottawa ankle criteria, radiographs of the ankle are indicated for individuals unable to bear weight on the affected ankle or those with tenderness involving the tip or posterior aspect of the ankle malleoli. This patient does not have bony tenderness and can walk with a mild limp. The diagnosis of a mild ankle sprain can be made clinically in this case, so radiographs and advanced imaging, such as magnetic resonance imaging, are not indicated. Walker boot immobilization would increase her risk of stiffness and delayed healing.

PREP Pearls

- Ankle sprains should be treated with early mobilization, if tolerated
- Ankle support braces worn during sports can prevent ankle sprains

ABP Content Specifications(s)

- Plan the appropriate management of various sprains
- Recognize the clinical findings associated with various sprains

Suggested Readings

- Bachmann LM, Kolb E, Koller MT, Steurer J, ter Riet G. Accuracy of Ottawa ankle rules to exclude fractures of the ankle and mid-foot: systematic review. BMJ. 2003;326(7386):417. doi: http://dx.doi.org/10.1136/bmj.326.7386.417.
- McGuine TA, Brooks A, Hetzel S. The effect of lace-up ankle braces on injury rates in high school basketball players. Am J Sports Med. 2011;39(9):1840-1848. doi: http://dx.doi.org/10.1177/0363546511406242.
- Waterman BR, Owens BD, Davey S, Zacchilli MA, Belmont PJ Jr. The epidemiology of ankle sprains in the United States. J Bone Joint Surg Am. 2010;92(13):2279-2284. doi: http://dx.doi.org/10.2106/JBJS.I.01537.

Question 2

A 5-year-old girl is brought to your office with a complaint of sore throat, headache, and fever for the past 3 days. Her temperature is 39°C, and her examination is notable for pharyngeal erythema, palatal petechiae, and bilateral anterior cervical lymphadenopathy. You obtain a rapid antigen detection test for group A Streptococcus, which is positive. This is her third episode of streptococcal pharyngitis in the last 2 months.

Of the following, the MOST appropriate treatment for this patient is

A. amoxicillin for 5 days
B. benzathine penicillin G for 2 days
C. clindamycin for 10 days
D. doxycycline for 10 days
E. sulfamethoxazole/trimethoprim for 10 days

Correct Answer: C

The 5-year-old girl in this vignette has had recurrent episodes of group A streptococcal (GAS) pharyngitis. Of the options listed, a 10-day course of clindamycin is the most appropriate treatment given its activity against GAS and the correct duration of 10 days of treatment.

There are several treatment options for GAS pharyngitis. The treatment of choice for GAS is a 10-day course of oral penicillin V. Other approved treatment regimens include a 10-day course of once-a-day amoxicillin and a single dose of intramuscular benzathine penicillin G. For patients with a nonanaphylactic reaction to penicillin, a 10-day course of an oral cephalosporin is recommended. An oral macrolide or azalide is also considered an effective treatment; however, resistance rates as high as 20% have been reported with some macrolides. Clindamycin can be used as treatment for recurrent GAS pharyngitis or as a first-line agent when the patient has had an anaphylactic reaction to penicillin. Of the options given in the question, it is the only one with appropriate activity and time course for proper treatment. Fluoroquinolones, tetracyclines, and sulfonamides are not effective treatment against GAS.

There is not a consensus on the antibiotic treatment of recurrent GAS pharyngitis. It is important to determine the adherence to the previously prescribed treatment. Treatment options include retreatment with the initial antibiotic, treatment with an alternative oral agent (a narrow spectrum cephalosporin, amoxicillin-clavulanate, clindamycin, a macrolide, or an azalide), or a single dose of intramuscular benzathine penicillin G.

The most common manifestation of GAS infection is pharyngitis. This pharyngitis has an incubation period of 2 to 5 days and is most commonly seen among school age children and adolescents, peaking around 7 or 8 years of age. The infection is most commonly seen in late fall, winter, and spring. The typical clinical manifestations of GAS pharyngitis include sore throat with enlarged, exudative tonsils, tender cervical lymphadenopathy, palatal petechiae, and a strawberry tongue. The diagnosis of GAS pharyngitis requires laboratory confirmation. An appropriately obtained throat swab should be sent for rapid antigen detection or culture. The throat swab from a negative rapid antigen detection test should be sent for culture.

PREP Pearls

- Clindamycin provides coverage against group A Streptococcus; however, it is typically reserved for patients who have had anaphylactic reactions to penicillin
- Group A Streptococcus resistance to macrolides is increasing

ABP Content Specifications(s)

- Plan the appropriate management of tonsillitis/pharyngitis, including when culture results remain positive following initial therapy

Suggested Readings

- American Academy of Pediatrics. Group A streptococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:732-744.
- Langlois DM, Andreae M. Group A streptococcal infections. Pediatr Rev. 2011;32(10):423-430. doi: http://dx.doi.org/10.1542/pir.32-10-423.

Question 3

You are seeing a 6-week-old infant after a visit to an urgent care center (UCC). He was born at full term after an uncomplicated pregnancy. His mother brought him to the UCC for evaluation of congestion. His physical examination was normal and he underwent some blood tests. He was discharged and returned to your office today for follow-up.

Tests performed at the UCC showed a hemoglobin of 11.4 g/dL (114 g/L), with a normal mean corpuscular volume for age, a reticulocyte count of 0.4%, normal direct and indirect bilirubin levels, and a negative direct antibody test. The rest of the laboratory findings were unremarkable. The medical student working with you noted that the infant's hemoglobin was 15.2 g/dL (152 g/L) at birth, and asks what caused the marked drop in hemoglobin over a short period.

Of the following, the MOST accurate response to the student's question is

A. hemolytic anemia associated with maternal-fetal ABO incompatibility
B. hemolytic anemia associated with maternal-fetal Rh incompatibility
C. hemolytic anemia caused by a red blood cell membrane defect
D. physiologic anemia of infancy associated with a high erythropoietin level
E. physiologic anemia of infancy associated with a low erythropoietin level

Correct Answer: E

As the fetus develops, the erythropoietin levels rise, with the highest levels occurring in the final trimester. Erythropoiesis is directly driven by erythropoietin, and as a consequence, a significant portion of the red blood cell mass is produced in the final trimester of pregnancy. Upon birth, blood oxygen levels suddenly increase with the onset of breathing, closure of the ductus arteriosus, and transition of the newborn from the relatively hypoxic environment of the amniotic sac to oxygen-rich room air. Renal oxygen tension sensors detect this sudden rise in oxygen levels, and in response, downregulate hypoxia-inducible factors, which in turn, downregulate the production of erythropoietin. This results in a slowly decreasing hemoglobin for several weeks after birth, known as the physiologic nadir of infancy. In full-term infants, the hemoglobin typically reaches a nadir of approximately 11 g/dL (110 g/L) at 8 to 12 weeks after birth.

Other factors that can lead to anemia in the neonatal period include phlebotomy for frequent blood tests in sick neonates, a reduced lifespan for the red blood cells, and iron depletion.

A number of factors in the vignette suggest that the drop in hemoglobin is not caused by hemolysis. These include the low reticulocyte count, negative direct antibody test, and the normal direct and indirect bilirubin levels. Therefore, maternal-fetal ABO incompatibility, maternal-fetal Rh incompatibility, and red blood cell membrane defects are incorrect responses. As discussed, the rapid increase in blood oxygen levels at birth result in a drop in erythropoietin levels after birth, causing a gradual drop in hemoglobin. Thus, physiologic anemia of infancy associated with a high erythropoietin is also an incorrect option.

PREP Pearls

- The concentration of fetal erythropoietin is highest in the third trimester and rapidly drops with the sudden increase in blood oxygen levels at birth
- Low erythropoietin levels in the neonate result in a slow decrease in the hemoglobin level over the first 8 to 12 weeks after birth known as the physiologic nadir
- Nonphysiologic causes of neonatal anemia include frequent phlebotomy in sick neonates, a reduced lifespan for the red blood cells, and iron depletion

ABP Content Specifications(s)

- Recognize the laboratory findings associated with physiologic anemia of infancy

Suggested Readings

- Kett JC. Anemia in infancy. Pediatr Rev. 2012;33(4):186-187. doi: http://dx.doi.org/10.1542/pir.33-4-186.
- Roth P. Anemia in preterm infants. Pediatr Rev. 1996;17(10):370. doi: http://dx.doi.org/10.1542/pir.17-10-370.
- Strauss RG. Anaemia of prematurity: pathophysiology and treatment. Blood Rev. 2010;24(6):221-225. doi: http://dx.doi.org/10.1016/j.blre.2010.08.001.

Question 4

A 20-month-old boy is brought to your office for an influenza vaccine. He begins to play with a train set in the waiting room. When his name is called, his mother leads him to the "flu shot" room. He promptly screams, falls, and repeatedly bangs his head on the tiled floor.

Of the following, the MOST appropriate response is to

A. administer the Modified Checklist for Autism In Toddlers, Revised Edition (M-CHAT-R)
B. encourage the mother to enforce a time-out
C. escort the mother and child to a separate area until the child is calm
D. reschedule the vaccine for a later visit
E. suggest to the mother that the vaccine be given during the tantrum

Correct Answer: C
The child in this vignette is having an age-appropriate temper tantrum with associated head banging. While there are many approaches to temper tantrums, letting the child ride out the tantrum in a safe place away from others acknowledges his developmentally appropriate frustration, while minimizing exposure of unsettling noise and activity to other patients, parents, and staff. Temper tantrums are very common in typically developing children, often beginning after 1 year of age. These decrease after the child turns 3 years of age when language development allows for more functional expression of the child's frustration. Caregiver responses to temper tantrums are critical to children developing self-regulation skills to deal with everyday disappointments.

Letting a child continue the tantrum while gently acknowledging his disappointment and distracting the child with songs, funny, familiar stories, or conversation builds emotional health and resilience. Taking the child to a safe place away from others reinforces the socially undesirable nature of tantrum behaviors and allows the caregiver to support the child through the tantrum without being pressured to quickly calm the child to avoid annoying others.

Up to 20% of typically developing children will bang their heads while having a tantrum. Typical head banging does not result in serious injury. Children with autism spectrum disorders (ASD) and other developmental disabilities have more self-injurious behaviors, including head banging, than other children, but head banging associated with a tantrum in isolation is not enough to raise clinical suspicion of a developmental problem. This child should have been screened for ASD with an instrument such as the Modified Checklist for Autism-Toddlers, Revised Edition at the 18-month health supervision visit, so he does not need a repeat screen if no concern for ASD was seen then. While a time-out can be effective for some undesirable behaviors in young children, this child is probably too young and too angry for this approach. Tantrums can last for several seconds to several minutes, so it would be difficult to schedule time-outs appropriately as a response to tantrums. Moreover, a time-out would fail to acknowledge that a tantrum is a developmentally appropriate response to having to stop an enjoyable activity before the child was ready. Rescheduling the vaccine is not clinically indicated and would delay protection from influenza and may be inconvenient for the family. While the child will likely get upset after receiving the vaccine, giving the vaccine will be easier for the child and staff if done when the child is calm.

PREP Pearls

- Head banging is commonly associated with tantrums and, in isolation, is not a "red flag" for autism spectrum disorder. Typical head banging does not result in serious injury.
- Tantrums cannot be shortened or prevented with punishment.
- Tantrums are best approached with caregiver empathy and reassurance, which helps to build emotional resilience.

ABP Content Specifications(s)

- Plan the appropriate management of temper tantrums in toddlers and preschool-age children
- Plan the appropriate management of head banging in toddlers and preschool-age children

Suggested Readings

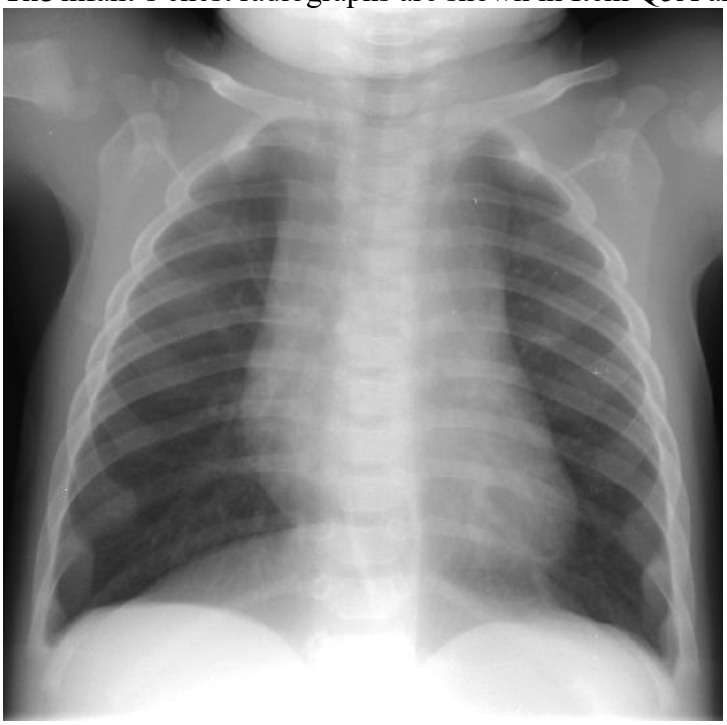
- Beers NS. Managing temper tantrums. Pediatr Rev. 2003;24(2):70-71. doi: http://dx.doi.org/10.1542/pir.24-2-70-a.
- Minshawi NF, Hurwitz S, Fodstad JC, Biebl S, Morriss DH, McDougle CJ. The association between self-injurious behaviors and autism spectrum disorders. Psychol Res Behav Manag. 2014;7:125-136. doi: http://dx.doi.org/10.2147/PRBM.S44635.

Question 5

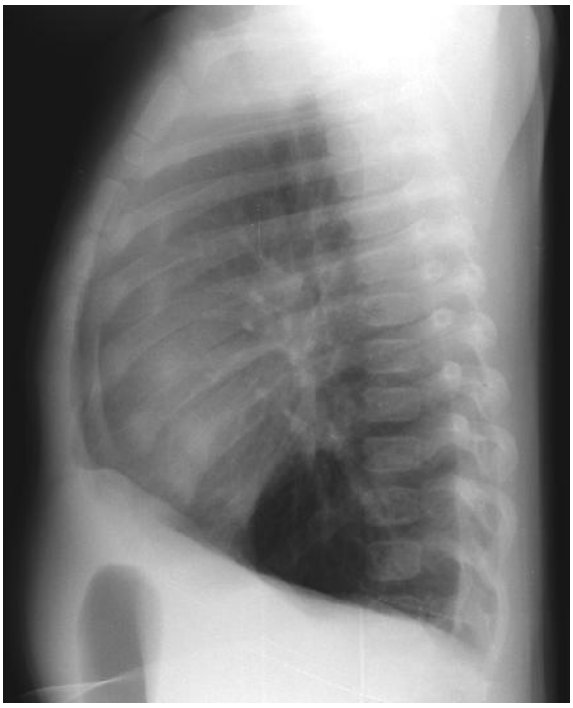
An 11-month-old male infant presents to the emergency department in March with a 2-day history of high fevers and worsening rhinorrhea, cough, vomiting, and diarrhea. He has no significant past medical history and his birth history is unremarkable. Physical examination shows an ill-appearing infant with a temperature of 39°C, respiratory rate of 45 breaths/min, heart rate of 120 beats/min, blood pressure of 90/45 mm Hg, and O2 saturation of 93% on room air. Physical examination is notable for a bulging, erythematous, nonmobile, left tympanic membrane, mild respiratory distress, clear rhinorrhea, and frequent dry cough. Auscultation of the lungs reveals diffuse wheezing with rhonchi and retractions. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	12,300/μL (12.3×10^9/L)
Lymphocytes	70%
Neutrophils	25%
Eosinophils	5%
Hemoglobin	13 g/dL (130 g/L)
Hematocrit	40%
Platelet count	210×10^3/μL (210×10^9/L)

The infant's chest radiographs are shown in Item Q5A and Item Q5B.



Item Q5A: Chest radiograph for the infant described in the vignette
Courtesy of P Lee



Item Q5B: Chest radiograph for the infant described in the vignette
Courtesy of P Lee

Of the following, the MOST likely cause of his illness is

A. Bordetella pertussis
B. human metapneumovirus
C. Mycoplasma pneumoniae
D. parainfluenza virus
E. Streptococcus pneumoniae

Correct Answer: B

The most likely cause of illness in the infant described in the vignette is human metapneumovirus (hMPV). Human metapneumovirus is second only to respiratory syncytial virus (RSV) as the cause of acute bronchiolitis in young children, and presents with high fever, cough, wheezing, tachypnea, and hypoxia. The laboratory findings and chest radiograph also point towards a viral respiratory infection. Furthermore, this infant has otitis media, which is common in children with hMPV infection and is believed to be secondary to viral induced inflammation obstructing the Eustachian tubes, allowing bacteria to more easily infect the middle ear.

Since its discovery by van den Hoogen et al in 2001, hMPV has been recognized as an important and common cause of respiratory infections in children throughout the world. Human metapneumovirus primarily circulates in the late winter and spring at the same time as, or shortly after, peak RSV activity. However, hMPV also occurs at lower rates during the rest of the year. The clinical presentation of hMPV bronchiolitis is identical to that caused by RSV.

An infant with pertussis could also present with hypoxia, but usually in the context of paroxysmal coughing fits causing cyanosis, as opposed to an oxygen requirement from alveolar disease. Also, pertussis presents with marked lymphocytosis that may be seen on the complete blood cell count and a history of the infant being unvaccinated or undervaccinated. The chest radiograph could be that of a patient with Mycoplasma pneumonia, as could the wheezing and otitis media, but Mycoplasma infections are very uncommon in children younger than 5 years of age. While parainfluenza viruses, particularly types 1 and 2, are more commonly associated with croup and stridor, type 3 can cause bronchiolitis, but is far less likely than RSV and hMPV. Streptococcus pneumoniae could cause high fever, but consolidation on the chest radiograph and a very elevated white blood cell count with a left shift should be present.

PREP Pearls

- Unlike respiratory syncytial virus (RSV), human metapneumovirus (hMPV) disease can occur year round, although it is more common in the late winter or spring.
- Human metapneumovirus bronchiolitis is clinically indistinguishable from RSV bronchiolitis.
- Otitis media is common in children with hMPV respiratory infection.

ABP Content Specifications(s)

- Understand the epidemiology of human metapneumovirus infection
- Recognize the clinical features associated with human metapneumovirus infection

Suggested Readings

- American Academy of Pediatrics. Human metapneumovirus. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:558-560.
- Schuster JE, Williams JV. Human metapneumovirus. Pediatr Rev. 2013;34(12):558-565. doi: http://dx.doi.org/10.1542/pir.34-12-558.

Question 6

A 16-month-old boy presents to the emergency department with a complaint of abdominal distention, vomiting, and irritability. There is no history of fever or diarrhea. He was born at 39 weeks of gestation by uncomplicated spontaneous vaginal delivery. He has had no surgery, and he does not take any medications. His immunizations are up to date and he is developmentally appropriate. Physical examination reveals a crying but consolable child. He is afebrile with a heart rate of 123 beats/min, blood pressure of 117/80 mm Hg (crying), respiratory rate of 37 breaths/min, and oxygen saturation of 97% on room air. His abdomen is soft and nontender, with a prominent suprapubic mass. The mass extends 4 cm above the symphysis pubis and is dull to percussion. Neurologic examination reveals normal strength and deep tendon reflexes. His laboratory results are shown:

Laboratory Test	**Patient Results**
Serum sodium	129 mEq/L (129 mmol/L)
Potassium	>6.7 mEq/L (6.7 mmol/L; moderate hemolysis)
Chloride	95 mEq/L (95 mmol/L)
Bicarbonate	13 mEq/L (13 mmol/L)
Blood urea nitrogen	93 mg/dL (33.2 mmol/L)
Creatinine	8.4 mg/dL (742 μmol/L)
Glucose	98 mg/dL (5.4 mmol/L)
Calcium	8.6 mg/ dL (2.2 mmol/L)
Phosphorus	9.0 mg/dL (2.9 mmol/L)

A cardiorespiratory monitor demonstrates normal QRS complexes and T waves.

Of the following, the MOST appropriate next step in this boy's management is

A. intravenous bolus of 3% normal saline
B. intravenous furosemide
C. nephrology consultation for urgent dialysis
D. repeat serum chemistry
E. urethral catheterization

Correct Answer: E

The boy in the vignette has acute renal failure and associated electrolyte abnormalities, for which recognition and drainage of his urinary obstruction will lead to improvement. Although he presents with severe electrolyte abnormalities and uremia, it is important to note any clinical features suggesting the underlying cause of the boy's renal failure. A dull-to-percussion suprapubic mass indicates bladder distention and possible bladder obstruction as the cause. Bladder obstruction is an uncommon cause of renal failure in children. Abdominal tumors pressing on the bladder can cause bladder outlet obstruction, leading to postrenal acute kidney injury. Identification and urgent correction of the cause of urinary obstruction is important to decrease renal injury and the risk of chronic kidney disease. Catheterization, or imaging followed by catheterization, should be performed urgently. If catheterization is difficult or imaging identifies an intravesical mass that would be a contraindication to bladder catheterization, an urgent urology or interventional radiology consultation should be requested for a urinary drainage procedure.

Urinary flow obstruction in both kidneys, or a single functioning kidney, usually presents with acute renal failure. In the presence of unilateral obstruction with 2 previously normal kidneys, the compensatory increase in glomerular filtration in the contralateral kidney prevents the development of electrolyte abnormalities associated with acute renal failure. Bladder obstruction in children is most often observed in patients with abdominal soft tissue sarcomas or posterior urethral valves. Soft tissue sarcomas are rare in children. Rhabdomyosarcoma is the most common soft tissue sarcoma of childhood. The botryoid variant (sarcoma botryoides), arising within the wall of the bladder or vagina, is seen almost exclusively in infants. Posterior urethral valves are usually identified on prenatal ultrasonography. However, boys with posterior urethral valves born to mothers who received little or no prenatal care may present later with urinary tract infection, failure to thrive, abdominal distension (from an enlarged bladder), and a poor urinary stream or voiding dysfunction (urinary frequency, daytime and nocturnal enuresis, and poor urinary stream).

Ultrasonography is safe, noninvasive, and the preferred initial imaging method for patients with acute renal failure. The presence of bladder distention or dilation of the urinary collecting system (hydronephrosis) suggests urinary obstruction, and bilateral hydronephrosis suggests obstruction in both kidneys. Hydronephrosis, unilateral or bilateral, is also seen in patients with vesicoureteral reflux; however, such patients usually present with urinary tract infections. The most common cause of congenital obstructive uropathy is ureteropelvic junction (UPJ) obstruction. Ureteropelvic junction obstruction rarely presents as renal failure, except in the case of an obstructed solitary kidney or bilateral UPJ obstruction.

Hypertonic 3% saline is indicated for the management of hyponatremia in patients with a serum sodium concentration less than 120 mEq/L (120 mmol/L) or patients with associated neurologic manifestations such as headaches, seizures, behavioral changes, obtundation, coma, and respiratory arrest. In the vignette, the boy’s hyponatremia, associated with normal neurologic findings, is secondary to renal failure and urinary obstruction leading to volume overload.

Relief of the bladder obstruction would, in this case, be indicated before the initiation of intravenous furosemide or renal replacement therapy (RRT). Intravenous furosemide is indicated for treating volume overload and hyperkalemia in patients with acute renal failure. Renal replacement therapy (eg, intermittent hemodialysis, continuous hemofiltration, and peritoneal dialysis) is considered for patients with renal failure and complications of volume overload, hyperkalemia, uremia (blood urea nitrogen > 100 mg/dL [> 35.7 mmol/L]) or symptoms associated with uremia, severe acidosis, or an inability to provide adequate nutrition. In acute renal failure, RRT is usually not considered until conservative measures have failed.

Hemolysis of red blood cells as seen in the boy's tested blood sample, can explain the elevated serum potassium results. Falsely-elevated serum potassium in such cases is not clinically significant, although a repeated serum chemistry from a nonhemolyzed venous sample would not be the best next step in management for the boy in the vignette. A blood specimen drawn without a tourniquet, a free-flowing blood draw, and avoiding cooling or prolonged storage before testing are associated with a decreased incidence of falsely-elevated potassium levels.

PREP Pearls

- Identification and drainage of urinary obstruction will lead to improvement in associated renal failure and electrolyte abnormalities.
- Identification and urgent correction of urinary obstruction is important to decrease renal injury and risk for chronic kidney disease.
- Ultrasonography is safe, noninvasive, and the preferred initial imaging method in patients with acute renal failure.
- Presence of bladder distention or hydronephrosis on ultrasonography is suggestive of urinary obstruction.
- Renal replacement therapy (eg, intermittent hemodialysis, continuous hemofiltration, and peritoneal dialysis) is considered for patients with renal failure and complications of volume overload, hyperkalemia, uremia, symptoms associated with uremia), severe acidosis, or an inability to provide adequate nutrition.

ABP Content Specifications(s)

- Formulate a differential diagnosis of urinary tract obstruction
- Understand the various causes of urinary tract obstruction

Suggested Readings

- Pathare S, Gadikota K, Baskaran C, et al. Index of suspicion: case 1—acute urinary retention in a 13-month-old boy. Pediatr Rev. 2012;33(9):427-433. doi: http://dx.doi.org/10.1542/pir.33-9-427.
- Reid-Adam J. Hyponatremia. Pediatr Rev. 2013;34(9):417-419. doi: http://dx.doi.org/10.1542/pir.34-9-417.
- Selewski DT, Symons JM. Acute kidney injury. Pediatr Rev. 2014;35(1):30-41. doi: http://dx.doi.org/10.1542/pir.35-1-30.

Question 7

A 28-year-old gravida 3, para 0 women is giving birth at 32 and 3/7 weeks of gestation. Her medical history is significant for obesity and type A1 gestational diabetes with a hemoglobin A1c of 5.4%. Prenatal ultrasonography performed at 21 weeks of gestation was unremarkable. A live born female newborn is handed to you with a spontaneous cry. Her vital signs show a heart rate of 140 beats/min, respiratory rate of 47 breaths/min, blood pressure of 58/42 mm Hg, and a temperature of 37°C. On physical examination, you note an active newborn with normal facies, no skin abnormalities, a normal S1 and S2 with no murmur, normal reflexes, and an abnormality of the newborn's upper right extremity (Item Q7).

Item Q7: Hand of the newborn described in the vignette
Courtesy of D Campbell

Of the following, the abnormality in development leading to this lesion is BEST described by

A. abnormal differentiation of dysplastic cells
B. complications of maternal gestational diabetes
C. germ cell mutation
D. interruption of normal development during third trimester
E. malformed extremity leading to abnormal digits

Correct Answer: D

The anomaly noted for the newborn in this vignette is caused by amniotic band syndrome (ABS). Based on current theory, ABS is caused by a sequence of events leading to an interruption of normal development of the limb tissue. In animal models, the insult leading to ABS may be a vascular insult, hypoxia, or uterine trauma. Others have hypothesized that a band of amnion constricts developing tissue, interrupting normal progression of development. The result is abnormal growth and development in the limb distal to the insult. Infants may present with fused or partially amputated digits. Most defects (77%) from ABS are identified in the arms and fingers. Typically, there is little potential for dysplastic growth in the affected limb. Initial evaluation should ensure there is no constriction of blood vessels or nerves in the affected limb. For isolated defects without constriction of blood vessels or nerves, infants should be referred to a plastic surgeon for repair and to maximize limb function.

There is no documented association between ABS and gestational diabetes. Amniotic band syndrome is not due to a germ cell mutation which would involve inheritable genetic defects. In comparison, in ABS, the defect is due to an early insult with subsequent abnormal development. There is no associated genetic abnormality.

A malformed extremity does not result in ABS. For example, infants with thanatophoric dysplasia have dramatic shortening of long bones. However, their distal extremities have normal digits. In addition, infants with ABS typically have normal limb development proximal to the insult. There is no evidence of dysplasia in tissue affected by ABS.

PREP Pearls

- Amniotic band syndrome results from interruption of the normal sequence of development during the third trimester.
- Amniotic band syndrome typically affects the arms or legs.
- Infants with amniotic band syndrome should be referred to a plastic surgeon for reconstructive surgery.

ABP Content Specifications(s)

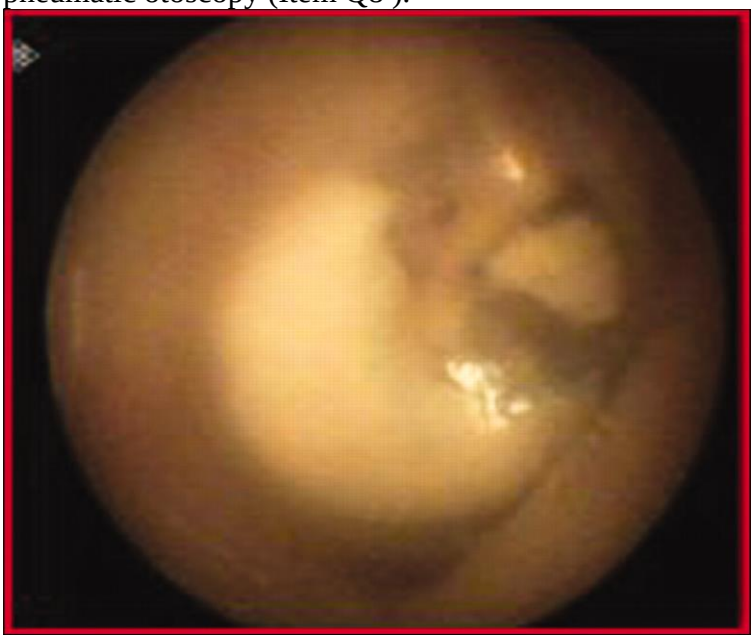
- Recognize the anatomic effects of amniotic bands

Suggested Readings

- McGuirk CK, Westgate MN, Holmes LB. Limb deficiencies in newborn infants. Pediatrics. 2001;108(4):e64. doi: http://dx.doi.org/10.1542/peds.108.4.e64.
- Slavotinek A. Dysmorphology. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:899-908.

Question 8

A 3-year-old boy is brought to your office for a routine health supervision visit. On a previsit screening form, the boy's mother indicates that he has been well with no recent illnesses and no complaints of pain. She notes that he has recently started to speak in 2-word phrases and that he uses approximately 200 spontaneous words. He seems to understand everything that his family members say to him and will follow a 2-step command. On examination, he is well appearing, cooperative, and interactive. His tympanic membranes are opaque, gray, and immobile on pneumatic otoscopy (Item Q8).



Item Q8: Tympanic membrane for the child described in the vignette.
Reprinted with permission from McConnochie KM. Potential of telemedicine in pediatric primary care.

Of the following, the MOST appropriate next step in this boy's management is

A. audiology evaluation
B. referral to an otolaryngologist for surgery
C. treatment with an intranasal corticosteroid
D. treatment with oral amoxicillin
E. watchful waiting with follow-up in 3 months

Correct Answer: A

The boy in the vignette has otitis media with effusion (OME) and expressive language delay. Audiology evaluation is the most appropriate next step in his management. Otitis media with effusion is defined as the presence of fluid in the middle ear without signs or symptoms of middle-ear inflammation. It must be distinguished from acute otitis media (AOM), in which a patient has the acute onset of middle-ear effusion with middle-ear inflammation. Middle-ear effusion is best diagnosed with pneumatic otoscopy and tympanometry may be used to confirm the diagnosis.

Otitis media with effusion may occur spontaneously as the result of AOM or associated with other conditions, including allergic rhinitis, adenoidal hypertrophy, eustachian tube abnormalities, or craniofacial anomalies. An estimated 90% of children experience OME before school age. Most episodes of OME resolve without intervention, but nearly one-third of children will have recurrence and 5% to 10% of children have persistent effusion lasting at least 1 year.

The most important potential sequelae of OME are conductive hearing loss and associated language delay. In 2004, the American Academy of Pediatrics, American Academy of Family Physicians, and American Academy of Otolaryngology-Head and Neck Surgery published joint clinical practice guidelines to assist the clinician in the diagnosis and management of OME. Children at increased risk for speech or language delay, include children with developmental delays, hearing loss independent of OME, syndromes associated with language delay, cleft palate, craniofacial anomalies, or visual impairment. These at-risk children warrant a hearing test and speech evaluation more promptly than children without any identified risk factors.

For children with OME who are not at increased risk for language delay, guidelines recommend watchful waiting and reevaluation in 3 months because the most OMEs resolve spontaneously. If OME persists longer than 3 months, or if the clinician suspects hearing loss, language delay, or learning problems, watchful waiting is not appropriate and the child should undergo hearing testing. Children with OME lasting longer than 3 months who have normal hearing should have a routine follow-up every 3 to 6 months until the OME resolves, hearing loss is identified, or structural abnormalities of the middle ear are suspected. Antihistamines, decongestants, and intranasal steroids are not effective for OME. Although antibiotics and oral corticosteroids may have short-term benefit, they do not have long-term efficacy and are therefore not recommended. Surgery may be indicated in children with hearing loss and OME lasting longer than 4 months, children at risk for language delay who have recurrent or persistent OME (regardless of hearing status), or those with OME and damage to the middle ear or tympanic membrane.

Given this boy's expressive language delay, watchful waiting is not appropriate; he warrants an audiology evaluation.

PREP Pearls

- Otitis media with effusion (OME) may occur spontaneously, be the result of acute otitis media, or associated with other conditions.
- Conditions associated with OME include allergic rhinitis, adenoidal hypertrophy, eustachian tube abnormalities, and craniofacial anomalies.
- In children with OME who are not at risk for language delay, watchful waiting with follow-up in 3 months is appropriate.
- Children with OME persisting longer than 3 months; suspected hearing loss, language delay, or learning problems; and those at risk for language delay should undergo hearing testing.

ABP Content Specifications(s)

- Plan the appropriate initial and follow-up management of otitis media with effusion in patients of various ages, including when complications occur
- Recognize conditions (including allergic rhinitis, adenoidal hypertrophy, eustachian tube abnormalities) associated with otitis media with effusion

Suggested Readings

- American Academy of Family Physicians, American Academy of Otolaryngology?Head and Neck Surgery, American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. Otitis media with effusion. Pediatrics. 2004;113(5):1412-1429. http://pediatrics.aappublications.org/content/113/5/1412.
- Gould JM, Matz PS. Otitis media. Pediatr Rev. 2010;31(3):102-116. doi: http://dx.doi.org/10.1542/pir.31-3-102.

Question 9

You are evaluating a 10-year-old female soccer player with a complaint of exercise-related dyspnea. She has no history of asthma, wheezing, or recurrent respiratory infections. Her medical history is unremarkable. The girl states that within 3 to 5 minutes of maximal exertion, she feels a shortness of breath with a choking sensation. Her mother reports that this is accompanied by noisy breathing, which on questioning, appears consistent with inspiratory stridor and expiratory wheezing. The girl's coach has noted that the girl develops a "squeaky" voice during these episodes of exercise intolerance. There is no history of cyanosis, chest pain, or loss of consciousness. On physical examination, the girl is well appearing. Her respiratory rate is 14 breaths/min and unlabored, heart rate is 66 beats/min and regular, and 3 extremity blood pressures are normal. There is no cardiac murmur. Her lungs are clear with good aeration throughout. There is no wheezing, stridor, or other adventitious sound. Her extremities are well perfused with brisk capillary refill.

Of the following, the girl's MOST likely diagnosis is:

A. extrinsic asthma
B. hypertrophic cardiomyopathy
C. laryngomalacia
D. paradoxical vocal fold dysfunction
E. vocal cord paralysis

Correct Answer: D

The girl in the vignette is most likely experiencing symptoms of episodic paradoxical vocal fold dysfunction (PVFD). Paradoxical vocal fold dysfunction and vocal cord dysfunction are terms often used interchangeably, but the term vocal cord dysfunction is less specific because it includes other vocal cord abnormalities. Patients with PVFD often present with exercise intolerance and may have been treated for asthma for many years with limited symptom relief. Patients experience episodes of dyspnea, wheezing, stridor, and/or throat tightness; these symptoms mimic those of asthma, but typically respond poorly to asthma therapies. Typically, PVFD is triggered by exertion, but episodes may occur outside of physical activity as well. Symptoms typically have an abrupt onset and resolution. Other symptoms that may help differentiate PVFD from asthma include stridor as opposed to wheezing, difficulty in inspiration as opposed to expiration, throat tightness as opposed to chest tightness, and onset of symptoms early during physical activity as opposed to late or after completion. Vocal quality or pitch may change because of narrowing of the glottis. Paradoxical vocal fold dysfunction may be present with exertional or nonexertional dyspnea in isolation. Paradoxical vocal fold dysfunction is more common than previously thought, and should be considered in patients who have dyspnea out of proportion to identifiable pulmonary disease.

Paradoxical vocal fold dysfunction is defined by adduction of the vocal cords during inspiration, or during inspiration and expiration, with preservation of a posterior region of glottic opening known as a "posterior glottic chink." For diagnostic confirmation, provocation of symptoms and direct visualization of paradoxical vocal cord movement are required. The diagnosis is often presumed and addressed based on clinical symptoms. Although flattening of the inspiratory portion of the spirometric flow volume loop has been suggested as a diagnostic sign of PVFD, this finding has not been shown to be consistent. PVFD may coexist with and complicate asthma.

Stress and psychiatric symptoms, such as anxiety, may trigger episodes of PVFD. However, 50% of affected patients have identifiable and nonpsychiatric comorbidities, which may trigger vocal cord dysfunction and make it more difficult to treat. Tobacco abuse, laryngopharyngeal reflux, sleep apnea, allergic rhinitis, and rhinosinusitis are all recognized comorbidities, and their presence should be considered and treated. The mainstay of treatment for PVFD is laryngeal control therapy. Laryngeal control therapy is also referred to as respiratory retraining therapy and is performed by a licensed speech and language therapist. This treatment, demonstrated to be effective in 95% of patients, focuses on diaphragmatic breathing and laryngeal relaxation techniques.

The girl in the vignette is exhibiting symptoms that would be atypical in character as well as timing for asthma. Although dyspnea is the most common presenting symptom of hypertrophic cardiomyopathy in children, occurring in as many as 90% of symptomatic patients, the absence of a cardiac murmur, syncope, palpitations or angina-type chest pain makes this diagnosis unlikely. However, any child with dyspnea without clear etiology may benefit from further evaluations, such as cardiac evaluation, stress testing, or pulmonary function testing. Laryngomalacia is the most common cause of neonatal stridor, and often has a positional component, with more severe respiratory compromise and stridor in the supine position.

Unilateral vocal cord paralysis suggests nerve dysfunction and most often occurs after cardiac or neck surgery. In this patient, the lack of a weakened voice or chronic stridor makes a paralyzed vocal cord unlikely. Bilateral vocal cord paralysis is associated with harsh stridor that is persistent and is associated with significant respiratory distress; in these cases, a tracheostomy will be required to maintain airway patency.

Although PVFD is the most likely diagnosis in this patient, evaluation with flexible fiberoptic laryngoscopy is recommended to rule out other laryngeal, vocal cord, or tracheal pathology. Multidisciplinary collaboration involving otolaryngology, pulmonary, speech and language pathology, and general medicine is advocated.

PREP Pearls

- Paradoxical vocal fold dysfunction (PVFD) is a common and often underrecognized etiology of exertional dyspnea.
- Paradoxical vocal fold dysfunction may be triggered, and or exacerbated, by comorbidities such as laryngopharyngeal reflux, allergic rhinitis, rhinosinusitis, or untreated obstructive sleep apnea.
- The diagnosis of PVFD may be confirmed on direct laryngoscopic visualization demonstrating adduction of the vocal cords with a classic posterior chinklike opening.

ABP Content Specifications(s)

- Plan the appropriate clinical and diagnostic evaluation of laryngeal and vocal cord disorders

Suggested Readings

- Colan SD. Hypertrophic cardiomyopathy in childhood. Heart Fail Clin. 2010;6(4):433-444. doi: http://dx.doi.org/10.1016/j.hfc.2010.05.004.
- Ledford DK, Lockey RF. Asthma and comorbidities. Curr Opin Allergy Clin Immunol. 2013;13:78-86. doi: http://dx.doi.org/10.1097/ACI.0b013e32835c16b6.
- Matrka L. Paradoxic vocal fold movement disorder. Otolaryngol Clin North Am. 2014;47:135-146. doi: http://dx.doi.org/10.1016/j.otc.2013.08.014.
- Schulze J, Weber S, Rosewich M, Eicknmeier O, Rose MA, Zielen S. Vocal cord dysfunction in adolescents. Pediatr Pulmonol. 2013;47:612-619. doi: http://dx.doi.org/10.1002/ppul.21622.

Question 10

A 3-year-old boy who is well known to your practice is brought in for complaints of not using his left arm or left leg as much over the past 3 days. He has an unrepaired atrial septal defect. He has had occasional seizures since he was 1 year of age, and takes levetiracetam. He has been in the care of grandparents this week while his parents are on vacation. The boy has not had any head injuries or seizures, and has been taking his medications regularly. There is no prior record of hemiparesis in his chart. His neurological examination shows decreased spontaneous movement of his left arm and left leg, with normal tone. His reflexes are brisk and symmetric in the upper and lower extremities. His mental status, speech, and language are normal.

Of the following, the study MOST likely to yield the diagnosis in this boy is

A. computed tomography of the head
B. echocardiogram
C. electroencephalogram
D. electromyography and nerve conduction study
E. magnetic resonance imaging of the cervical spine

Correct Answer: A
The boy in the vignette has subacute weakness of his left arm and leg. The most likely cause is a cardioembolic stroke, so of the choices, computed tomography (CT) of the head is the best study to yield a diagnosis. Although he has a history of seizures, postictal hemiparesis (also called Todd's paresis) is unlikely because the weakness has lasted for 3 days, which would be unusually long, and there is no history of recent seizure. Therefore, electroencephalogram is not the best study to make a diagnosis in this case. Cervical spine injury can cause hemiparesis, but there is no history of injury in this case. Cervical spine tumors typically cause a progressive clinical course and the examination shows asymmetric reflexes and tone, so imaging of the cervical spine is unlikely to yield a diagnosis. Nerve and muscle disorders are very unlikely to cause hemiparesis, so electromyography and nerve conduction study are not the best tests.

The cause of subacute weakness can be difficult to determine clinically. As in this case, neurological findings after an acute stroke can diminish after just a few days. A patient with a subacute stroke may appear well and findings can be subtle. Knowing that he has an unrepaired atrial septal defect should raise clinical suspicion for stroke as a cause of new hemiparesis, and evaluation should be started immediately. If magnetic resonance imaging is readily available, this could be considered instead of CT. Once embolic ischemic stroke is confirmed, there should be prompt investigation for a source. If there is any residual thrombosis in the heart or distal veins, anticoagulation therapy should be considered to prevent further emboli.

The evaluation of weakness should start with chronicity. Chronic weakness, weakness that has been present for weeks or months or longer, can be due to prior central nervous system injury or malformations, such as hypoxic ischemic encephalopathy, hemimegalencephaly, or spina bifida, or to neuromuscular causes such as myopathy or muscular dystrophy. Chronic weakness can be further divided by distribution and age. Chronic lower extremity weakness in a young child could be due to a structural abnormality such as tethered cord or a muscular disorder such as Duchenne muscular dystrophy. Chronic hemiparesis in a former premature infant may be due to periventricular leukomalacia or neonatal stroke. The clinical presentation will guide the diagnostic evaluation. In chronic weakness, it is rarely necessary to perform urgent studies. In cases where a brain or spinal cord abnormality is suspected, magnetic resonance imaging is usually the best test. If Duchenne muscular dystrophy is suspected, a serum creatine kinase level of greater than 10,000 U/L is highly specific.

Acute weakness often requires evaluation in an emergency department. The neurological examination, including distribution of weakness and assessment of reflexes, helps determine the underlying cause and the best diagnostic testing. Ascending weakness of both legs with areflexia is suggestive of Guillain-Barré syndrome, whereas acute weakness of both legs with hyperreflexia is suggestive of a spinal cord lesion such as a tumor. Clinicians should know that acute spinal cord lesions do not always present with hyperreflexia, especially in the acute phase. Magnetic resonance imaging is the best diagnostic test for suspected brain or spinal cord disorders in the medically stable child. In suspected Guillain-Barré syndrome, magnetic resonance imaging of the lumber spinal cord sometimes shows nerve root enhancement and cerebral spinal fluid studies can show elevated protein with normal white blood cell count

(cytoalbuminological dissociation). Both these studies can be normal early in the clinical course. Electromyography/nerve conductions study is also often normal early in the course of Guillain-Barré syndrome and other acute neuromuscular disorders.

PREP Pearls

- A patient with a subacute ischemic stroke may appear well and clinical findings can be subtle.
- Risk factors for stroke, such as unrepaired atrial septal defect, should raise clinical suspicion for stroke as a cause of new neurological abnormalities.

ABP Content Specifications(s)

- Differentiate the causes of acute, subacute, and chronic weakness
- Understand the benefits and limitations of neurodiagnostic tests in the evaluation of weakness

Suggested Readings

- Roach ES, Golomb MR, Adams R, et al. Management of stroke in infants and children: a scientific statement from a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young. Stroke. 2008;39(9):2644-2691. doi: http://dx.doi.org/10.1161/STROKEAHA.108.189696.
- Srinivasan J, Miller SP, Phan TG, Mackay MT. Delayed recognition of initial stroke in children: need for increased awareness. Pediatrics. 2009;124(2):e227-e234. doi: http://dx.doi.org/10.1542/peds.2008-3544.

Question 11

A 15-year-old previously healthy adolescent is brought to the emergency department with a 2-month history of fevers, fatigue, headaches, shortness of breath, and poor appetite. She has developed swelling of her face, in both arms, and around her eyes. She has not had abdominal pain, blurry vision, cough, or vomiting. She has not traveled outside of the United States.

Her vital signs show a temperature of 37°C, heart rate of 100 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 100/60 mm Hg. Her oxygen saturation is 100% on room air. On physical examination, she is well developed and well nourished. She has generalized facial and periorbital edema. She has good dentition and no oropharyngeal erythema. Pupils are 2 mm, equal, and reactive. Both jugular veins are fully distended when she is in the upright position. There is no redness or tenderness in the neck. Several enlarged lymph nodes in both axillae and supraclavicular regions are felt. She is slightly tachypneic, but breathing comfortably. Lungs and airway sounds are clear. Heart is regular with no rubs, murmurs, or gallops. Abdomen is soft, nontender, and non-distended with no hepatosplenomegaly. Her extremities are warm and well-perfused. Marked edema of both upper extremities, including the hands, is seen. Lower extremities have no cyanosis, clubbing, or edema. Neurologic examination is normal.

Of the following, the MOST likely cause of her swelling is

A. congestive heart failure
B. lymphedema
C. primary pulmonary hypertension
D. superior vena cava syndrome
E. tuberculosis

Correct Answer: D

The adolescent in this vignette likely has a malignancy, evidenced by the 2-month history of fevers, anorexia, and fatigue. The most likely answer choice is superior vena cava (SVC) syndrome, which can occur from lymphoma with an anterior mediastinal mass.

The constellation of signs and symptoms caused by the compression or obstruction of the SVC is known as SVC syndrome. Common clinical signs include facial and upper extremity swelling, jugular venous distention, headache, and air hunger. Due to obstruction of SVC drainage, affected patients are incapable of increasing cardiac output when necessary, leading to a fixed cardiac output. This results in dizziness, air hunger, and syncope with positional changes and exertion. In childhood, SVC syndrome is usually caused by anterior mediastinal masses, enlarged mediastinal lymph nodes, and occlusion of the SVC itself. Lymphoid malignancies causing anterior mediastinal masses include non-Hodgkin lymphoma, acute lymphocytic leukemia, and Hodgkin disease. Other causes of an anterior mediastinal mass include teratoma, thyroid carcinoma, and enlargement of the thymus, but are less likely to cause SVC syndrome.

A chest radiograph should be obtained in patients with suspected SVC syndrome. A characteristic widened mediastinum is suggestive of an anterior mediastinal mass (Item C11). Other causes of SVC syndrome may be more evident based on past medical history, such as indwelling vascular catheters, previous cardiac surgeries or extracorporeal membrane oxygenation, congenital diaphragmatic hernia, and ventriculoatrial shunts.

Other clinical considerations associated with SVC syndrome are related to the concomitant anterior mediastinal mass, if applicable. Respiratory symptoms are very common, and can

include air hunger, anxiety, and wheezing. Changes in position can affect these symptoms. Patients can acutely become air hungry from inability to ventilate in the supine position because of increased airway compression by the mass. Hypercapnic respiratory failure can occur due to inability to ventilate. This can occur even with a patient on mechanical ventilation. In fact, positive pressure ventilation compared to negative pressure spontaneous breathing may exacerbate derangements in ventilation, as forcing air past a fixed obstruction can be less effective than pulling air in with negative intrathoracic pressure. The SVC compression and resulting decrease in venous return can limit the capacity to increase cardiac output when the demand arises. Thus, extreme caution must be taken before intubating or anesthetizing patients with an anterior mediastinal mass.

Congestive heart failure can cause swelling, respiratory problems, and anorexia. However, the child in this vignette does not have signs of increased lower body venous pressure such as hepatosplenomegaly or lower extremity swelling, nor is there any sign of pulmonary edema. Lymphedema can cause upper extremity swelling, but it is very uncommon in a previously healthy child and does not cause respiratory symptoms. Primary pulmonary hypertension is unlikely because it generally causes cyanosis. Tuberculosis can also cause

lymphatic obstruction, difficulty breathing, and constitutional symptoms, but is not likely because of a lack of cough and travel outside the United States.

Superior vena cava syndrome can cause facial and upper extremity swelling, jugular venous distention, and inability to increase cardiac output on demand. In previously healthy children, these symptoms should raise suspicion for a malignant anterior mediastinal mass, which can be associated with life-threatening airway obstruction. Extreme caution should be exercised before providing anesthesia, sedation, or positive-pressure ventilation.

PREP Pearls

- Superior vena cava syndrome in previously healthy children is usually associated with a malignant anterior mediastinal mass.
- Extreme caution should be taken prior to sedating, anesthetizing, or initiating positive-pressure ventilation in a child with superior vena cava syndrome or anterior mediastinal mass.

ABP Content Specifications(s)

- Recognize the clinical findings associated with superior vena cava syndrome

Suggested Readings

- Aspesberro FP, Roberts JS, Brogan TV. Acute airway compromise in anterior mediastinal tumors. In: Fuhrman BP, Zimmerman JJ, eds. Pediatric Critical Care. 4th ed. Philadelphia, PA: Saunders Elsevier: 2011:212-218.
- Wan JF, Bezjak A. Superior vena cava syndrome. Emerg Med Clin North Am. 2009 May. 2009;27(2):243-255. doi: http://dx.doi.org/10.1016/j.emc.2009.01.003.

Question 12

A 16-year-old black adolescent is brought to your clinic for polyuria and polydipsia that has become bothersome over the past 2 weeks. Her mother has type 2 diabetes diagnosed at 35 years of age, and she is worried that her daughter has diabetes. The patient is otherwise healthy and is not taking any medication. Vital signs show a temperature of 37°C, blood pressure of 130/88 mm Hg, heart rate of 98 beats/min, respiratory rate of 18 breaths/min, weight of 90 kg (> 95th percentile), height of 165 cm (65th percentile), and a body mass index of 33 kg/m2 (> 95th percentile). Physical examination reveals acanthosis nigricans over the nape of her neck and both axillae. Laboratory studies are shown:

Laboratory test	**Result**
Plasma glucose	320 mg/dL (17.8 mmol/L)
Bicarbonate	28 mEq/L (28 mmol/L)
Blood urea nitrogen	12 mg/dL (4.3 mmol/L)
Creatinine	0.5 mg/dL (44 μmol/L)
Hemoglobin A1c	11%
Urinalysis	Positive glucose, negative ketones

Of the following, the BEST next step in the management of this patient is

A. 20 mL/kg of 0.9% sodium chloride intravenously
B. counsel her on healthy dietary and lifestyle changes
C. insulin therapy
D. oral metformin
E. subcutaneous exenatide

Correct Answer: C
The presentation of the patient described in the vignette is consistent with type 2 diabetes mellitus (DM). Given that her plasma glucose is greater than 250 mg/dL and hemoglobin A1c is greater than 9%, initial management with insulin is indicated. This recommendation comes from a 2013 American Academy of Pediatrics clinical practice guideline on the management of newly diagnosed type 2 DM in children and adolescents. Counseling regarding healthy dietary and lifestyle changes is also very important in the management of type 2 DM and should be initiated in conjunction with pharmacologic therapy. However, the most immediate priority is to control her blood sugar with insulin. Transition to oral metformin may be possible after achievement of initial blood sugar control, but would not be appropriate as the primary initial therapy in this case. As there is no evidence of hemodynamic instability, a bolus of intravenous fluids is not indicated. Subcutaneous exenatide, a glucagon-like peptide-1 receptor agonist, is US Food and Drug Administration-approved for type 2 DM in adults, thus it is not appropriate for use in this situation.

Distinguishing between type 1 and type 2 DM at presentation is not always straight forward. The pathophysiology of type 1 DM is autoimmune destruction of the pancreatic β cells, causing insulin deficiency. Type 2 DM requires both insulin resistance and progressive β-cell failure, so that insulin production is unable to meet the demand. In the patient in this vignette, the features that make type 2 DM more likely include: non-white race, obesity, postpubertal onset, first-degree relative with type 2 DM, acanthosis nigricans (a marker of insulin resistance), and lack of ketosis. Her borderline elevated blood pressure may be a clue to associated metabolic syndrome. Polycystic ovary syndrome and dyslipidemia are also associated with insulin resistance and the metabolic syndrome, and if present, may help to distinguish type 2 from type 1 diabetes.

Clinical features that would suggest type 1 DM include: normal or low body mass index, associated autoimmunity such as autoimmune thyroid disease, and ketoacidosis. White race is also more common in those with type 1 DM. It is important to note that there is considerable overlap among the presenting clinical features of type 1 versus type 2 DM. For example, because obesity is relatively common, type 1 DM can also occur in the setting of obesity. In addition to the clinical presentation, diabetes-associated antibodies can be helpful in distinguishing type 1 from type 2 DM. These include antibodies to insulin, islet cells, glutamic acid decarboxylase (GAD), and insulinoma-associated antigen (IA-2). Item C12 summarizes clinical features more likely to occur in type 1 versus type 2 DM. No feature is absolute and overlap exists in the clinical presentation of type 1 versus type 2 diabetes.

PREP Pearls

- Insulin therapy is indicated for the child or adolescent with newly diagnosed type 2 diabetes if the presenting glucose is greater than 250 mg/dL or the hemoglobin A1c is greater than 9%.
- Features making type 2 diabetes more likely than type 1 diabetes include non-white race, obesity, signs of insulin resistance (eg, acanthosis nigricans), insidious symptom onset, and lack of ketosis.
- Features making type 1 diabetes more likely include white race, lack of obesity, acute onset of symptoms, associated autoimmunity, ketosis, and presence of diabetes-associated antibodies.

ABP Content Specifications(s)

- Differentiate between type 1 and type 2 diabetes

Suggested Readings

- American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014;37 (Suppl 1):S81-S90. doi: http://dx.doi.org/10.2337/dc14-S081.
- Copeland KC, Silverstein J, Moore KR, et al. Management of newly diagnosed type 2 diabetes mellitus (T2DM) in children and adolescents. Pediatrics. 2013;131(2):364-382. doi: http://dx.doi.org/10.1542/peds.2012-3494.
- Dileepan K, Feldt MM. Type 2 diabetes mellitus in children and adolescents. Pediatr Rev. 2013;34(12):541-548. doi: http://dx.doi.org/10.1542/pir.34-12-541.

Question 13

You are performing the routine examination of a newborn 18 hours after birth. The baby was born at 37 2/7 weeks' gestation by routine vaginal delivery to a 38-year-old gravida 3 para 2 mother who had received good prenatal care since early in the first trimester. The pregnancy was unremarkable and maternal screening was negative for hepatitis B surface antigen, HIV, rubella, rapid plasma reagin, and direct antiglobulin (Coombs) test. Spontaneous rupture of membranes occurred at home 16 hours before delivery and clear fluid was noted. Since the mother had screened positive for group B Streptococcus vaginal colonization at 35 weeks of gestation, she received 5 million units of penicillin G on arrival at the hospital 6 hours before delivery and again 4 hours later. The mother had no fever and no signs of chorioamnionitis. The newborn's vital signs are within normal range and the physical examination reveals no abnormalities. The baby has latched on well for breastfeeding every 2 to 3 hours. One stool and 3 wet diapers have been documented. The parents are both present and are anxious for the newborn to be discharged from the hospital.

Of the following, the BEST recommendation for early discharge and follow-up of this newborn is to discharge him

A. after 24 hours, with follow-up care within 24 hours
B. after 24 hours, with follow-up care within 48 to 72 hours
C. at 48 hours, with follow-up care within 48 to 72 hours
D. at 72 hours, with follow-up care within 48 to 72 hours
E. now, with follow-up care within 24 hours

Correct Answer: B
All pediatric healthcare providers need to be familiar with the American Academy of Pediatrics (AAP) recommendations for early discharge, follow-up, and management of newborns of mothers with abnormal prenatal laboratory findings. A hospital stay of less than 48 hours after delivery may be appropriate for some healthy term newborns. This newborn with a gestation of more than 37 weeks meets criteria for discharge at or after 24 hours of age, with follow-up within 48 to 72 hours. Although she screened positive for group B Streptococcus vaginal colonization, the mother received adequate intrapartum antibiotic treatment before delivery and both she and the newborn are asymptomatic.

The newborn-mother dyad in this vignette represents a common risk, group B streptococcal disease, which must be considered in determining early discharge. The US Centers for Disease Control and Prevention and AAP Committee on Fetus and Newborn and Committee on Infectious Diseases have written recommendations addressing the prevention of perinatal group B streptococcal disease and length of hospital stay for healthy term newborns. The recommendations for prevention of group B streptococcal disease include screening, indications for maternal intrapartum antibiotic prophylaxis, and management of neonates. Adequate intrapartum antibiotic prophylaxis is defined as 5 million units of intravenous penicillin or 2 g of intravenous ampicillin or cefazolin administered at least 4 hours before delivery, then 2.5 to 3.0 million units of penicillin G or 1 g ampicillin or cefazolin every 4 hours until delivery.

The duration of hospital stay for a healthy term newborn and mother should be long enough to identify problems in either, and to ensure that the mother is able to care for herself and her newborn at home. The health of both must be considered, as well as the adequacy of support systems at home and access to follow-up care. Efforts should be made to discharge both simultaneously.

Minimum criteria for discharge of a term newborn after an uncomplicated gestation, labor, and delivery include:

- term gestation (between 37 0/7 and 41 6/7 weeks')
- normal vital signs
- no physical abnormalities requiring continued hospitalization
- regular urination and passage of at least 1 stool spontaneously
- completion of at least 2 successful feedings
- no excessive bleeding from circumcision site for at least 2 hours
- clinical significance of jaundice assessed and managed according to AAP guidelines
- appropriate evaluation for sepsis in accordance with current guidelines
- review of maternal and infant screening laboratory tests (syphilis, hepatitis B surface antigen, HIV status, as well as blood type and direct Coombs test if indicated)
- hepatitis B vaccine administered as indicated by newborn's risk status
- routine screenings, including metabolic screening, hearing, and pulse oximetry according to hospital protocol and state regulations

- knowledgeable mother who demonstrates the ability and confidence to provide adequate care for her baby
- an appropriate car seat (if relevant to family transportation situation)
- addressing any social and environmental risks
- accessible health care follow-up planned for both mother and her newborn

The neonate in this vignette has met all discharge criteria, therefore the infant and mother may be discharged as early as 24 hours after birth. If the neonate is discharged before 48 hours after delivery, examination by a healthcare practitioner should take place within 48 hours.

PREP Pearls

- Minimum criteria must be met for early discharge of a newborn (< 48 hours after delivery).
- Adequate intrapartum antibiotic treatment for the prevention of group B streptococcal disease is required to meet early discharge criteria.
- The hospital stay for a healthy term newborn and mother should be long enough to identify problems in either and to ensure that the mother is able to care for herself and her newborn at home.

ABP Content Specifications(s)

- Plan the early discharge of a newborn infant, including follow-up evaluation
- Plan the management of a neonate whose mother has abnormal prenatal laboratory findings

Suggested Readings

- Benitz WE, Committee on Fetus and Newborn. Hospital stay for healthy term newborn infants. Pediatrics. 2015;135(5):948-953. doi: http://dx.doi.org/10.1542/peds.2015-0699.
- Committee on Infectious Diseases, Committee on Fetus and Newborn. Policy statement: recommendations for the prevention of perinatal group B streptococcal (GBS) disease. Pediatrics. 2011;128(3):611-616. doi: http://dx.doi.org/10.1542/peds.2011-1466.
- Goyal NK, Fager C, Lorch SA. Adherence to discharge guidelines for late-preterm newborns. Pediatrics. 2011;128(1):62-71. doi: http://dx.doi.org/10.1542/peds.2011-0258.
- Polin RA, Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics. 2012;129(5):1006-1015. doi: http://dx.doi.org/10.1542/peds.2012-0541.
- Shakib J, Buchi K, Smith E, Korgenski K, Young PC. Timing of initial well-child visit and readmissions of newborns. Pediatrics. 2015;135(3):469-474. doi: http://dx.doi.org/10.1542/peds.2014-2329.
- Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease, revised guidelines from CDC, 2010. MMWR Morbid Mortal Wkly Rep. 2010;59(RR10):1-32. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm.
- Warren JB, Phillipi CA. Care of the well newborn. Pediatr Rev. 2012;33(1):4-18. doi: http://dx.doi.org/10.1542/pir.33-1-4.

Question 14

While seeing a child in your office, his mother mentions concerns regarding her current singleton pregnancy. Her recent maternal serum screening was flagged for a very high maternal serum a-fetoprotein level of 5.5 ng/mL (5.5 μg/L). The human chorionic gonadotropin and estriol levels are normal. She is currently in her fourth month of pregnancy with accurate gestational dating.

Of the following, these test results raise concern that her unborn child MAY have

A. anencephaly
B. fetal demise
C. a neural tube defect
D. trisomy 18
E. trisomy 21

Correct Answer: C
The unborn child in the vignette likely has an open neural tube defect. Maternal quadruple serum screening in this clinical situation would demonstrate an elevated maternal serum a-fetoprotein (AFP) with normal human chorionic gonadotropin (hCG), inhibin A, and unconjugated estriol levels (μE3). Maternal quadruple screening is used in the second trimester of pregnancy between the 15th and 20th week to assess the risk that a fetus may have a chromosomal abnormality such as trisomy 21, trisomy 18, or an open neural tube defect/anencephaly. A mathematical calculation is used to find a numeric risk for certain chromosomal abnormalities or defects in the fetus by comparing known normative levels for the quadruple screen markers for that specific week of gestation with levels seen in the current pregnancy, along with considerations for maternal age, weight, race, and diabetic status.

Maternal serum AFP is an ideal biochemical marker because it is produced mostly by the fetus. a-fetoprotein leaks across exposed fetal capillaries at the site of the open defect into the amniotic fluid, then into the maternal circulation. High or low AFP levels, along with serum levels of the other markers, could be indicative of a chromosomal anomaly or a specific birth defect (Item C14). Serum levels can be difficult to interpret in cases of multiple gestation or inaccurate gestational dating. The detection rate for trisomy 21, neural tube defects, and trisomy 18 is approximately 80% with maternal quadruple screen alone, with a 5% false-positive rate. It is even higher when combined with first-trimester serum screening, cell-free fetal DNA, and targeted ultrasonography.

Item C14. Maternal Quadruple Screening Findings in Fetal Anomalies/Trisomies.

Chromosomal anomaly or birth defect	AFP	Estriol	hCG	Inhibin A
Open neural tube defect	↑	normal	normal	normal
Anencephaly	↑		↓	
Gastroschisis	↑	normal	normal	normal
Trisomy 21	↓	↓	↑	↑
Trisomy 18	↓	↓	↓	

AFP, α- fetoprotein; hCG, human chorionic gonadotropin
↑, increased levels; ↓, decreased levels

Courtesy of L. Parsley

Prenatal testing also typically includes second-trimester targeted ultrasonography that screens for birth defects and signs of chromosomal abnormalities, such as choroid plexus cysts, absent nasal bone, open neural tube defects, or echogenic cardiac foci. The combination of maternal quadruple screening along with a targeted second-trimester ultrasonography can detect an open

neural tube defect in 95% of cases. Noninvasive prenatal testing is a newer technology that uses a sample of the mother's blood to isolate fragments of the fetus's DNA to screen for trisomies and sex chromosome abnormalities, with a high detection rate. This screening test can be performed as early as 10 weeks of gestation. Diagnostic confirmation via amniocentesis or chorionic villus sampling is recommended if a screening test result is positive.

PREP Pearls

- A maternal quadruple screening result showing an elevated maternal serum α-fetoprotein (AFP) with normal human chorionic gonadotropin (hCG), inhibin A, and unconjugated estriol levels (μE3) is highly suggestive of an open neural tube defect.
- Maternal quadruple screening in pregnancy measures serum levels of AFP, unconjugated estriol, the β component of hCG, and inhibin A.
- Maternal quadruple screening is used in the second trimester of pregnancy (between the 15th and 20th week) to assess the risk of a fetal chromosomal abnormality such as trisomy 21, trisomy 18, or an open neural tube defect/anencephaly.
- If a prenatal screening test is positive for an increased risk of a chromosome abnormality, diagnostic confirmation via amniocentesis or chorionic villus sampling is recommended.

ABP Content Specifications(s)

- Understand the usefulness of maternal blood screening in prenatal diagnosis

Suggested Readings

- Canick JA, MacRae AR. Second trimester serum markers. Semin Perinatol. 2005;29(4):203-208. doi: http://dx.doi.org/10.1053/j.semperi.2005.05.011.
- Huang T, Alberman E, Wald N, Summers AM. Triploidy identified through second-trimester serum screening. Prenat Diagn. 2005;25(3):229-233. doi: http://dx.doi.org/10.1002/pd.1115.
- Rose NC, Mennuti MT. Maternal serum screening for neural tube defects and fetal chromosome abnormalities. West J Med. 1993;159(3):312-317. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1011344/pdf/westjmed00073-0082.pdf.

Question 15

A father brings his 11-year-old daughter to your office for a health supervision visit. His daughter began puberty at a young age, and he asks you whether there will be any social, behavioral, or academic impact associated with her early pubertal development.

Of the following, the MOST accurate response is that young girls like his daughter often have

A. better academic performance
B. better conduct in school
C. decreased risk for early sexual initiation
D. no risks associated with early development
E. poor body image

Correct Answer: E

Adolescence is the period of development between the onset of puberty and adulthood. Adolescent development can be divided into 3 major components: physical, cognitive, and psychosocial. Physical changes include an increased rate of linear growth and the development of secondary sexual characteristics, which typically begin between ages 8 and 13 years in girls and 9 and 14 years in boys. The primary task of cognitive development is the transition from concrete to abstract thinking. The psychosocial development of adolescence involves the achievement of a mature self-identity, mature sexuality, and independence. Development of a healthy self-identity is pivotal because a negative self-identity has been linked to adverse consequences, such as poor interpersonal relationships, risky behaviors, and depression.

The timing of the physical changes of puberty can have an impact on the development of a sense of self. Early pubertal changes in girls have been associated with lower self-esteem and poor body image. Early maturing girls tend to have lower academic achievement, evidenced by lower high school grade point averages and a higher incidence of course repetition. Adolescents who experience puberty earlier than their peers have an increased risk of depression, anxiety, psychosomatic symptoms, drug use, truancy, and sexual initiation.

PREP Pearls

- Psychosocial developmental during adolescence involves the achievement of a mature self-identity, mature sexuality and independence.
- Early pubertal changes in girls have been associated with lower self-esteem and poor body image.

ABP Content Specifications(s)

- Understand the effect of rapid body changes on an adolescent's sense of self
- Understand features associated with an adolescent's search for identity

Suggested Readings

- Downing J, Bellis MA. Early pubertal onset and its relationship with sexual risk taking, substance use and anti-social behaviour: a preliminary cross-sectional study. BMC Public Health. 2009;9:446. doi: http://dx.doi.org/10.1186/1471-2458-9-446.
- Golub MS, Collman GW, Foster PM, et al. Public health implications of altered puberty timing. Pediatrics. 2008;121 Suppl 3:S218-S230. doi: http://dx.doi.org/10.1542/peds.2007-1813G .
- Hazen E, Schlozman S, Beresin E. Adolescent psychosocial development. Pediatr Rev. 2008;29(5):161-168. doi: http://dx.doi.org/10.1542/pir.29-5-161.
- Sherer S, Radsik M. Psychosocial development in normal adolescents and young adults. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. Neinstein's Adolescent and Young Adult Health Care: A Practical Guide. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:38-42.

Question 16

A 15-year-old adolescent is brought to your office with concerns about poor school performance. He complains of difficulty concentrating and remembering facts needed for tests. His parents report that he seems more anxious recently and have observed that he has been intermittently eating larger meals and snacks. They are concerned about his sleep as they have noticed his eyes to appear red. There have been no significant changes at home. He has been a healthy adolescent who has done well in school in previous years.

Of the following, the BEST next step in management is to

A. ask the family to keep a record of your patient's sleep habits
B. direct the family to request an Individualized Education Program
C. give the family Vanderbilt questionnaires for his teachers to complete
D. interview your patient separately and ask about drug use
E. provide the family with contact information for counseling services

Correct Answer: D
The differential diagnosis for poor school performance in an adolescent includes possible illicit drug use. Although other reasons for academic underachievement are conceivable, the constellation of behavioral and physical symptoms in the patient in this vignette who is otherwise healthy and had previously done well in school is consistent with marijuana use. This includes decreased concentration, increased anxiety, increased hunger, and red eyes. Interviewing the patient separately and asking about drug use is the best next step in management for the patient in this vignette.

Marijuana is the most commonly used illegal substance in the United States and worldwide. Derived from the cannabis plant, marijuana's primary active component is delta-9-tetrahydrocannabinol (THC). Selective cannabis plant breeding has increased the THC content of marijuana, making marijuana more potent today than in the past. Marijuana's street names include pot, grass, dope, ganja, MJ, and hemp. Marijuana can be smoked in a variety of forms (eg, cigarettes, pipes, cigars) or can be mixed with food and ingested (eg, brownies, candies). Marijuana's effects occur within seconds of smoking and 30 to 90 min after ingestion. The peak is 15 to 30 min after smoking and 2 to 3 hours after ingestion. Effects last up to 4 hours after smoking and up to 12 hours after ingestion.

Marijuana produces various physiologic results. The cardiovascular outcomes are most consistent and include the sympathomimetic effects of tachycardia and increased blood pressure. Palpitations, abnormal orthostatic responses, and peripheral vasodilation may also occur. Regular marijuana smoking can produce respiratory problems and can decrease pulmonary function. The harmful chemicals and carcinogens in marijuana smoke increase the risk of respiratory tract cancer and lung damage. Marijuana's other physiologic effects may include conjunctival injection, nystagmus, dry mouth, slurred speech, hunger, and ataxia.

Neurobehavioral consequences of marijuana use include poor executive function, decreased concentration, memory impairment, distorted perception, drowsiness, and impaired cognition. These effects interfere with learning and school performance. By impairing judgment, coordination, and reaction time, marijuana increases risk-taking behaviors (eg, unprotected sex, drug use) and injuries (eg, motor vehicle accidents). Some marijuana users may experience anxiety and panic attacks. Mental health problems such as anxiety, depression, and schizophrenia may worsen with heavy use.

Other reasons for academic problems in this patient are possible. While sleep disturbance, clarified from a record of the patient's sleep habits, is possible and may coexist with marijuana use, other symptoms such as increased hunger make it unlikely as the primary cause for this patient's academic underachievement. Next, an Individualized Education Program is essential in providing for special education services for a student with learning disability or other eligible condition. Children with learning disabilities tend to present before high school, making learning disability less likely in this patient. Eligibility under "other health impaired" could be considered should this patient have attention-deficit/hyperactivity disorder (ADHD). Vanderbilt questionnaires are helpful in the assessment of a student with possible ADHD, which may be

considered for this patient's difficulty with concentration and poor school performance. However, ADHD is also less likely, given the patient's prior academic success and that his symptoms are accompanied by other clinical features such as increased hunger and red eyes. While counseling services could be helpful in addressing the adolescent's drug use and difficulty with school, providing the family with contact information for these services would not be the next best step in management. The next step would be to interview the adolescent separately about possible drug use.

Illicit drug use should be considered in the differential diagnosis of an adolescent with new onset academic underachievement. Marijuana is the most commonly used illicit drug and has negative immediate and long-term behavioral and health consequences. Early consideration of marijuana use may identify and prevent harm to adolescent users.

PREP Pearls

- Illicit drug use should be considered in the differential diagnosis of an adolescent with new onset academic underachievement.
- Marijuana is the most commonly used illicit drug and has negative immediate and long-term behavioral and health consequences.
- Marijuana's physiologic effects include tachycardia, increased blood pressure, decreased pulmonary function, increased risk of lung cancer, conjunctival injection, nystagmus, dry mouth, slurred speech, hunger, and ataxia.
- Neurobehavioral consequences of marijuana use include poor executive function, decreased concentration, memory impairment, distorted perception, drowsiness; impaired cognition, judgment, and coordination; and reaction time.
- Mental health problems such as anxiety, depression, and schizophrenia may worsen with heavy use of marijuana.

ABP Content Specifications(s)

- Recognize the major behavioral consequences of marijuana use/abuse
- Identify the major physiologic consequences associated with marijuana use/abuse

Suggested Readings

- Ammerman S, Ryan S, Adelman WP, Committee on Substance Abuse, Committee on Adolescence. Technical report: the impact of marijuana policies on youth: clinical, research, and legal update. Pediatrics. 2015;135(3):e769-e785. doi: http://dx.doi.org/10.1542/peds.2014-4147.
- Neuspiel DR. Marijuana. Pediatr Rev. 2012;33(7):333-334. doi: http://dx.doi.org/10.1542/pir.33-7-333.
- Wong GS. Cannabis (marijuana): acute intoxication. UpToDate. Available online only with subscription.

Question 17

A 17-year-old female soccer player is brought to the emergency department (ED) following a head injury that occurred while she was playing in a soccer game. Approximately 20 minutes ago, she collided head-to-head with another player while she was running and fell to the ground. Her mother, who accompanied her daughter to the ED, tells you that she had a very brief loss of consciousness (less than 15 seconds) immediately following the injury and that she has seemed "dazed" since it occurred. She vomited once about 10 minutes ago.

A review of the patient's medical history indicates that she has no significant past medical or surgical history, takes no medications, has no allergies, and has had no prior head injuries.

In the ED, the patient is sleepy, but answers all questions appropriately and follows instructions. When you ask her about her current symptoms, she states: "My head still hurts, but it is starting to feel a little better now." Her vital signs are within normal limits. On physical examination, her pupils are equal in size and reactivity. She has a 3 x 4 cm area of ecchymosis near the center of her forehead, but no hematomas or step-offs on palpation of her entire forehead and scalp. There are no focal deficits on a complete neurologic examination, although she tells you that she feels tired and wants to lie down again after you ask her to walk back and forth across the room. The remainder of the physical examination is unremarkable.

Of the following, the MOST appropriate next step in the management of this patient is to

A. admit her to the hospital for 24-hour observation
B. continue to observe her in the emergency department
C. discharge her home with her mother now
D. obtain neurosurgical consultation
E. order computed tomography of the brain

Correct Answer: B
The adolescent girl in the vignette presents for evaluation after sustaining a closed head injury associated with a very brief loss of consciousness. Though she complains of headache and feels sleepy in the emergency department (ED), her symptoms have begun to improve since her injury occurred only 20 minutes ago. She has no focal deficits on neurologic examination. Continued clinical observation is the most appropriate next step in her management.

Head injury is the leading cause of death and disability in pediatric trauma victims. While most children sustaining head trauma have only minor injuries, a small number will have more serious injuries, with the potential for clinical deterioration and significant sequelae. All providers of pediatric care must understand how to appropriately evaluate and initially manage those children and adolescents who present after sustaining head trauma.

Pediatric head injuries account for over 600,000 ED visits and presumably an even larger number of visits and calls to primary care providers each year. Most closed head injuries in children result from falls, motor vehicle collisions, automobile versus pedestrian accidents, bicycle-related injuries, and sports-related injuries. The majority of pediatric closed head injuries are minor, though some can be life-threatening; more than 3,000 deaths related to head trauma occur in US children annually. Pediatric providers are challenged with identifying the relatively small number of children at high risk for intracranial complications and clinical deterioration after closed head trauma from the many who are at very low risk. Clinical symptoms are neither completely sensitive nor specific for significant injury.

Computed tomography (CT) of the brain is a rapid and accurate way to identify intracranial injuries in children after head trauma. There is consensus that patients identified as high risk for intracranial injury should undergo early noncontrast CT of the brain for evidence of intracranial hemorrhage, midline shift, or increased intracranial pressure. However, widespread use of this diagnostic modality has downsides; these include exposure of the brains of developing children to ionizing radiation, identification of minor lesions or incidental findings with unclear clinical importance, the need for sedation for younger or uncooperative pediatric patients, and significant increases in healthcare costs. The goal of pediatric providers should be to identify children with clinically important intracranial injury after head trauma, while limiting unneeded radiographic imaging in children at low risk.

Recent studies, including a very large multicenter study conducted through the Pediatric Emergency Care Applied Research Network (PECARN), have yielded validated clinical decision rules that can help to provide a useful clinical framework for determining which children are at higher (as well as at very low) risk for clinically important brain injuries after head trauma. Based on the findings of the PECARN study, the risk of clinically important traumatic brain injury is estimated at more than 4% for children with a Glasgow coma scale score of 14, other signs of altered mental status, palpable skull fracture, or signs of basilar skull fracture. Thus, CT of the brain is recommended for these children.

For those children meeting the following criteria, the risk of clinically important traumatic brain injury has been determined to be extremely low (< 0.05%) and thus brain CT is not recommended:

- Normal neurologic examination findings
- Normal mental status
- Normal behavior as noted by caregiver
- No loss of consciousness
- No vomiting
- No severe headache
- No evidence of skull fracture (no nonfrontal scalp hematoma for children younger than 2 years of age)
- No signs of basilar skull fracture
- No high-risk mechanism
- No concern for inflicted injury

For children in the "intermediate" risk category (for example, those with history of isolated loss of consciousness, isolated headache, isolated vomiting, and certain isolated scalp hematomas in infants older than 3 months of age but no alteration of mental status or signs of skull fracture), the PECARN guidelines recommend that the decision to perform brain CT versus clinical observation only should be made based on additional clinical factors, such as the presence of single versus multiple intermediate risk factors, age younger than 3 months, worsening symptoms or signs after ED observation, physician experience, and parental preference. The patient in the vignette would fall into this "intermediate" risk category, but she is already showing clinical improvement over the short timeframe since her injury occurred.

Clinical observation before the decision to obtain brain CT allows providers to selectively image only those patients whose symptoms worsen or fail to improve. The PECARN study investigators found that brain CT utilization was lower among children who were observed following closed head trauma without a higher rate of clinically significant traumatic brain injuries, especially if their symptoms improved during the observation period. In one study of children who sustained minor closed head injuries, ED observation time was associated with a time-dependent decrease in brain CT rate, without delaying identification of significant traumatic brain injuries.

While a period of continued observation is warranted for the patient described in the vignette given that she has intermediate risk for significant traumatic brain injury as defined by the PECARN clinical decision rule, her symptoms are improving within just a few minutes of her injury. Immediate admission to the hospital for a 24-hour period is unnecessary at this time. While there is no definite consensus regarding the optimal observation period for children following minor closed head injury, some experts have recommended an observation period of 4 to 6 hours. For the patient in the vignette, hospitalization for a prolonged period of clinical observation is not likely to be needed if her symptoms continue to improve and therefore is not the best next step in her management at this time.

Discharging the patient home with her mother immediately without further clinical observation for continued improvement in symptoms is not the best next step in management based on the PECARN clinical decision guidelines.

As the patient is displaying no focal neurologic deficits, is only at intermediate risk for a clinically significant traumatic brain injury, and is already displaying clinical improvement, neurosurgical consultation is not warranted at this time.

While immediately obtaining a CT brain for the patient in the vignette is an option, clinical observation before obtaining CT brain would be the best next step in management given that her symptoms are quickly improving and that she has a nonfocal neurologic examination. Clinical observation will most likely prevent this patient from exposure to the health risks and costs associated with brain CT.

PREP Pearls

- While computed tomography (CT) of the brain is a rapid and accurate way to identify intracranial injuries in children after head trauma, use of this diagnostic modality has downsides, including exposure to ionizing radiation, identification of minor lesions or incidental findings with unclear clinical importance, the need for sedation for younger or uncooperative pediatric patients, and significant increases in healthcare costs
- The goal of pediatric providers should be to identify children with clinically important intracranial injury after head trauma to prevent deterioration and secondary brain injury, while limiting unneeded radiographic imaging in children at low risk.
- For patients falling into the “intermediate risk” category for intracranial injury, observing patients clinically before obtaining computed tomography of the brain allows providers to selectively image only those whose symptoms worsen or fail to improve.

ABP Content Specifications(s)

- Plan the appropriate diagnostic evaluation of closed-head injury and brief loss of consciousness
- Plan the appropriate physical and laboratory evaluation of head injury, including serial evaluations of the patient’s status
- Recognize the immediate life-threatening complications of closed-head trauma

Suggested Readings

- 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. Lancet. 2009;374(9696):1160-1170. doi: http://dx.doi.org/10.1016/S0140-6736(09)61558-0.
- Schonfeld D, Fitz BM, Nigrovic L. Effect on the duration of emergency department observation on computed tomography use in children with minor blunt head trauma. Ann Emerg Med. 2013;62(6):597-603. doi: http://dx.doi.org/10.1016/j.annemergmed.2013.06.020.

- Schunk JE, Schutzman SA. Pediatric head injury. Pediatr Rev. 2012;33(9):398-411. doi: http://dx.doi.org/10.1542/pir.33-9-398.
- Wing R, James C. Pediatric head injury and concussion. Emerg Med Clin North Am. 2013;31(3):653-675. doi: http://dx.doi.org/10.1016/j.emc.2013.05.007.

Question 18

A 4-year-old boy with acute lymphocytic leukemia presents to the oncology clinic for laboratory evaluation. He is currently receiving consolidation chemotherapy. His mother informs you that 9 days ago he was in contact with a child who has now been diagnosed with varicella. Her son has not had varicella in the past. His serologic test results are not available.

Of the following, the BEST next step in management is to administer

A. acyclovir
B. ganciclovir
C. intravenous immune globulin
D. varicella vaccine
E. varicella-zoster immune globulin

Correct Answer: E
For the patient described in the vignette, administration of varicella-zoster immune globulin would be the best next step in management. Passive immunoprophylaxis after exposure to varicella is indicated in individuals likely to develop infection if exposed and likely to have complications if they develop infection. Severe disease can occur in immunocompromised hosts and complications can include bacterial superinfection, pneumonitis, hepatitis, and encephalitis.

The clinical manifestations and epidemiology of varicella have been altered with routine vaccination. In unvaccinated individuals, varicella manifests as a generalized vesicular rash with at least 250 lesions in various stages of development (Item C18). Vaccinated individuals who experience breakthrough disease have far fewer lesions (median of less than 50) that can be maculopapular instead of vesicular. As a result of routine vaccination, the illness peaks at 10 to 14 years of age.

Item C18: Varicella rash in an unvaccinated child. Reprinted with permission from Kimberlin DW, Brady, MT, Jackson, MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL American Academy of Pediatrics; 2015.

After primary infection, varicella-zoster virus remains latent in sensory ganglia. Reactivation of disease leads to herpes zoster or shingles. Herpes zoster is typically a vesicular rash distributed over 1 to 3 dermatomes and can be associated with local pain or neuralgia. In immunocompromised patients, however, herpes zoster can become a disseminated infection, with lesions in multiple dermatomes and organ involvement.

Candidates for immunoprophylaxis include immunocompromised patients, certain neonates, and pregnant women. Immunocompromised patients include individuals with a congenital or acquired T-lymphocyte immunodeficiency, neoplasms affecting the bone marrow or lymphatic system, those who have received a hematopoietic stem cell transplant, and those receiving immunosuppressive therapy including prednisone at a dose of 2 mg/kg per day or more for 14 days.

While varicella-zoster immune globulin should be given as soon as possible after exposure, limited data suggest there may be efficacy up to 10 days after exposure. Prior to 2012, immune globulin was administered only up to 96 hours after the exposure. Given the revision in the allowable time frame for administration, the patient in the vignette who was exposed 9 days ago would still be a candidate for varicella-zoster immune globulin. Based on expert opinion, intravenous immune globulin can be used for candidates as passive immunoprophylaxis if the varicella-specific formulation cannot be obtained.

Acyclovir can also be used for postexposure prophylaxis, starting at 7 days after exposure, when passive immunoprophylaxis is not available. Of note, acyclovir may modify disease in healthy children, though data are lacking regarding its efficacy in immunocompromised children. While ganciclovir is effective against varicella-zoster virus, it is typically used for disease due to cytomegalovirus. Additionally, ganciclovir has poor oral bioavailability and therefore is not used as an oral agent for prophylaxis.

When an individual lacking immunity is exposed to a person with varicella but does not meet criteria for receipt of immunoglobulin, varicella vaccine can be used for postexposure prophylaxis if the individual is 12 months of age or older and the vaccine is not contraindicated. If using vaccine, it must be given up to 5 days after exposure.

PREP Pearls

- Passive immunoprophylaxis after exposure to varicella is indicated in immunocompromised patients, certain neonates, and pregnant women.
- Varicella-zoster immune globulin should be given as soon as possible after exposure or up to 10 days after exposure to varicella.
- For individuals that are nonimmune and exposed but otherwise do not meet criteria for immunoprophylaxis, varicella vaccine can be used if the individual is 12 months of age or older and the vaccine is not contraindicated.

ABP Content Specifications(s)

- Understand the relationship between varicella and herpes zoster infection
- Plan appropriate control measures to prevent the spread of varicella and herpes zoster
- Understand the epidemiology of varicella-zoster virus
- Recognize the clinical features associated with varicella and herpes zoster infections in normal and immunocompromised children of various ages

Suggested Readings

- American Academy of Pediatrics. Varicella-zoster virus infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:846-860.
- US Centers for Disease Control and Prevention. Updated recommendations for use of VariZIG- United States, 2013. MMWR Morbid Mortal Wkly Rep. 2013;62(28):574-576. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6228a4.htm.

Question 19

A 6-month-old female infant is brought to your office by her mother with concerns about her difficulty in passing stools. The girl's mother reports that she had normal passage of meconium and passed stools well until 1 month ago when rice cereal was introduced. Her stools are now described as formed, difficult, and painful to pass. You prescribe lactulose. The girl's mother is concerned that her daughter will become dependent on this treatment, and asks how it works.

Of the following, the mechanism of action of this treatment is as a(n)

A. bulking agent
B. chloride channel activator
C. osmotic
D. prebiotic
E. stimulant

Correct Answer: C
The mechanism of action of lactulose is as an osmotic agent. The treatment of constipation involves the use of behavioral, dietary, and medical therapies. Medical therapy may include various medications, each with a different mechanism of action (Item C19A). Prebiotics, sugars that help to support an active and healthy gut microbiome, are not currently the standard of care for the treatment of constipation. The differential diagnosis of constipation varies by age (Item C19B).

Item C19A. Medications for the Treatment of Constipation.

Class	Medication(s)	Mechanism of Action
Osmotic laxative	Lactulose Magnesium hydroxide Polyethylene glycol 3350 Sorbitol Sodium phosphate	Poorly absorbed ions or molecules create an osmotic gradient, drawing water into the intestines.
Stimulant laxative	Bisacodyl Castor oil Senna	Increases peristalsis in the colon, and fluid and electrolyte secretion in the distal small bowel and colon
Stool softener	Docusate sodium	Acts as a surface-active agent to facilitate the interaction of water with the stool
Chloride channel activator	Lubiprostone	Activates chloride channels on the small intestinal mucosa, increasing chloride rich intestinal fluid secretion that increases luminal water content
Lubricant	Mineral oil	Softens and lubricates
Bulking agent	Fiber Methylcellulose Psyllium	Increases stool bulk and water in the stool

Courtesy of C. Waasdorp Hurtado

Item C19B. Differential Diagnosis of Constipation.

Age	Differential for Constipation
0-12 months	Anal malformation Anterior displacement of the anus Cystic fibrosis Decreased muscle tone Hirschsprung disease Hypercalcemia Hypokalemia Hypothyroidism Imperforate anus with fistula Medication side effect Mitochondrial disorders Neuromuscular disorder Neuronal intestinal dysplasia Spinal abnormality
>12 months	Anterior displacement of the anus Celiac disease Decreased muscle tone Developmental delay Functional constipation (>95%) Gluten sensitivity Heavy-metal poisoning Hirschsprung disease Hypercalcemia Hypokalemia Hypothyroidism Imperforate anus with fistula Medication side effects Mitochondrial disorders Neuronal intestinal dysplasia Physical or sexual abuse

Courtesy of C. Waasdorp Hurtado

To appropriately manage constipation, it is important to identify the underlying etiology. Appropriate management should address dietary changes, behavioral modification, medical management, and parental education. Dietary recommendations include maximizing fiber, increasing the consumption of poorly absorbed carbohydrates (prune and pear juice), and ensuring appropriate fluid intake for age. Fiber should be increased with a blend of both soluble and nonsoluble fiber. The recommended daily intake is 5 + age (in years) grams. Many children have significant behavioral issues surrounding toileting, including withholding. To maximize the

likelihood of success, the physician and family should create a stooling regimen. Reward charts may be helpful. Toilet sitting after meals maximizes the benefit of the gastrocolic reflex, and is achievable for most families. If needed, medical management can be added by selecting the appropriate medication from Table C19A, based on the severity of the constipation. Finally, education of parents plays an enormous role in successful treatment.

PREP Pearls

- Lactulose is an osmotic agent used to treat constipation.
- Constipation has a broad differential diagnosis that differs between infants and children.
- Dietary management plays a significant role in the successful management of constipation.

ABP Content Specifications(s)

- Formulate an age-appropriate differential diagnosis in a patient with constipation
- Plan the appropriate management of a patient with constipation
- Understand the action of laxatives, stool softeners, and lubricants in a patient with constipation

Suggested Readings

- Auth MK, Vora R, Farrelly P, Baillie C. Childhood constipation. BMJ. 2012;345:e7309. doi: http://dx.doi.org/10.1136/bmj.e7309.
- Hoekman DR, Benninga MA. Functional constipation in childhood: current pharmacotherapy and future perspectives. Expert Opin Pharmacother. 2013;14(1):41-51. doi: http://dx.doi.org/10.1517/14656566.2013.752816.
- Langer JC. Hirschsprung disease. Curr Opin Pediatr. 2013;25(3):368-374. doi: http://dx.doi.org/10.1097/MOP.0b013e328360c2a0.
- Stewart ML, Schroeder NM. Dietary treatments for childhood constipation: efficacy of dietary fiber and whole grains. Nutr Rev. 2013;71(2):98-109. doi: http://dx.doi.org/10.1111/nure.12010.

Question 20

An 18-month-old girl presents to your office for a health supervision visit. Her parents express concern that the girl toe walks on the left side and has an unusual gait. They first noticed this 3 months ago when she began walking. The girl was delivered at term and has appropriately met all developmental milestones. She has been well, other than experiencing several "colds" over the past few months. On physical examination, the child's muscle tone is normal. She has limited abduction and internal rotation of the left hip, and her left leg appears to be shorter than the right. On observation of her gait, you note toe walking on the left side.

Of the following, the BEST next step in evaluation would be to obtain

A. a complete blood cell count and C-reactive protein test
B. magnetic resonance imaging of the brain
C. radiographs of the hip and pelvis
D. scanogram radiographs to determine leg lengths
E. ultrasonographic images of the hips

Correct Answer: C
The combination of apparent leg length discrepancy, abnormal gait, and decreased hip range of motion in a young child, in the absence of constitutional symptoms, suggests a dislocated hip. Hip radiographs should be obtained for the child in this vignette to evaluate hip joint morphology.

Developmental dysplasia of the hip (DDH) refers to deficient development of the hip joint. Children with mild dysplasia may have subtle radiographic findings, such as flattening of the acetabulum and clinically normal hips. In more severely affected children, the hip is subluxed or dislocated. Affected hips are typically unstable on physical examination in the newborn period. In rare cases, physical examination and ultrasound are normal in young infants, and dysplasia is identified later. Risk factors for DDH include female sex, firstborn status, breech presentation, family history, and oligohydramnios. Positional musculoskeletal deformities (eg, metatarsus adductus, congenital torticollis) may also be associated with DDH.

On physical examination, children with a dislocated hip have a positive Galeazzi sign; with the knee and hip flexed, the thigh will appear shorter on the affected side because of the superior position of the femoral head. In infants, the Ortolani and Barlow maneuvers are used to detect hip instability. For both maneuvers, the hip and knee are flexed to 90 degrees, with the hip adducted. In the case of a dislocatable hip, the Barlow maneuver, which applies posterior pressure to the knee while maintaining hip adduction, will cause the examiner to feel a “clunk” as the hip shifts posteriorly. With the Ortolani maneuver, the examiner abducts the hip. The test result is positive when the examiner can feel a dislocated hip clunk back into place. Infants and children with DDH typically exhibit limited hip abduction, especially in the case of a dislocated hip that cannot be reduced.

Ultrasonography is the preferred imaging method to evaluate the hip in young infants before ossification of the femoral head. However, ultrasonographic screening for dysplasia before the age of 6 weeks results in a high rate of false-positive results. Radiographs are more helpful once the ossific nucleus of the femoral head is visible, which occurs at about 5 or 6 months of age. This would be the preferred imaging method for the child in the vignette. Laboratory evaluation for the presence of infection or inflammatory arthritis would be appropriate for a child with a more acute presentation and with systemic symptoms. Magnetic resonance imaging of the brain, presumably to look for injury associated with cerebral palsy, would not be indicated given the child’s normal gross motor development and tone. A scanogram includes simultaneous bilateral anteroposterior radiographs of the hips, knees, and ankles, alongside a metal ruler, to accurately measure leg length. A leg-length discrepancy would explain the child’s gait, but not the limited hip motion.

PREP Pearls

- For an ambulatory child, a unilateral toe-walking gait and limited hip range of motion suggests a hip dislocation.
- Ultrasonography is the preferred imaging method to evaluate hip dysplasia in a child younger than 5 to 6 months.
- Radiographic evaluation is the preferred imaging method to evaluate hip dysplasia in a child older than 6 months

ABP Content Specifications(s)

- Plan the appropriate diagnostic evaluation of developmental dysplasia/subluxation of the hip in patients of various ages
- Recognize the clinical findings associated with developmental dysplasia/subluxation of the hip

Suggested Readings

- Nemeth BA, Narotam V. Developmental dysplasia of the hip. Pediatr Rev. 2012;33(12):553-561. doi: http://dx.doi.org/10.1542/pir.33-12-553.
- Sarwark JF, LaBella CR. Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014: 650 pp.

Question 21

A 6-year-old girl is brought to your office with an itchy rash. The rash started on her right upper arm 2 days ago and spread to her right lower leg this morning. She was playing outside in the park several days ago. She has had no fevers and has otherwise been well. On examination, your patient has several linear streaks of vesicles on her right arm (Item Q21) and right lower leg

Item Q21 : Rash described in the vignette. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology.A quick Reference Quide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012

Of the following, you are MOST likely to tell her parents that

A. keeping the rash covered will help prevent spread to other people
B. oral steroids are indicated with the rash being in 2 different locations
C. swimming should be avoided until all lesions have crusted over
D. topical steroids are sufficient treatment
E. treatment with oral acyclovir will shorten the duration of the rash

Correct Answer: D
The girl in this vignette has allergic contact dermatitis. Of the options given, the most appropriate one is to tell her parents to apply topical corticosteroids. Allergic contact dermatitis, such as the rhus dermatitis illustrated in Item C21 , is a T-cell mediated hypersensitivity reaction caused by the exposure of the skin to a particular antigen. Common antigens associated with allergic contact dermatitis include jewelry (especially jewelry containing nickel), clothing, shoes, henna tattoo dyes, and plants. Rhus dermatitis is caused by poison ivy, poison sumac, or poison oak, and typically presents as linear streaks of vesicles in areas where the plant has come into contact with the skin. This rash is intensely pruritic and the treatment is mainly aimed at reducing the itch and discomfort associated with the rash. Treatment consists of cool compresses, as well as medium-to-high dose topical corticosteroids. An oral antihistamine is often also used to decrease the pruritus.

In addition to treatment with steroid creams and antihistamines, it is important to eliminate any potential further exposure to the antigen. Patients should be advised to use soap and water to remove any remaining antigen on the skin and under the fingernails. Clothes should also be washed, as any remaining antigen could lead to the development of new areas of dermatitis.

The fluid from the ruptured vesicles does not cause a spread of the dermatitis; therefore, the rash does not need to be covered up and children do not need to avoid swimming in pools. Oral steroids are often used to treat rhus dermatitis when there are large reactions that lead to swelling around the eyes or genitals. Oral steroids are not indicated when the rash leads only to mild swelling. The vesicular rash associated with rhus dermatitis is not associated with varicella or herpes viruses and treatment with acyclovir is not appropriate.

PREP Pearls

- Topical steroids are the mainstay of treatment for contact dermatitis; oral steroids are indicated only when there are large reactions around the eyes or the genitals.
- Fluid from ruptured vesicles in rhus dermatitis does not lead to additional areas of skin being affected.

ABP Content Specifications(s)

- Recognize the clinical findings associated with contact dermatitis

Suggested Readings

- Chiu YE, Dickey BZ. Contact dermatitis. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:3150-3152.
- Yoo K-Y, Langevin KK, Craft N. Papulosquamous eruptions. In: Berkowitz, CD, ed. Berkowitz's Pediatrics: A Primary Care Approach. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:821-825.

Question 22

You are seeing a 13-month-old boy in your office for the first time, after his family recently moved to the United States. He was born at term after an uncomplicated pregnancy. He is the third child born to these parents. Their first 2 children are girls who are healthy and thriving. They report that this child has been "sickly" almost from birth. He has had multiple episodes of otitis media, recurrent oral ulcers, several skin abscesses especially in the perianal region, and was hospitalized twice for pneumonia. On physical examination, the boy's growth is lower than the third percentile for weight and at the tenth percentile for height. The results of a complete blood cell count taken in the office are shown

Laboratory Test	**Patient Result**
White blood cell count	11,000/μL (11.0×10^3/L)
Neutrophils	72%
Lymphocytes	23%
Monocytes	3%
Eosinophils	1%
Basophils	1%
Platelet count	245×10^3/μL (245×10^9/L)

Of the following, the test MOST likely to reveal the boy's diagnosis is

A. colonoscopy for evidence of inflammatory bowel disease
B. gene sequencing for cystic fibrosis mutations
C. gene sequencing for severe congenital neutropenia
D. lymphoblast evaluation by flow cytometry
E. phagocyte oxidative burst by flow cytometry

Correct Answer: E
The child in the vignette has a medical history replete with stigmata associated with an abnormality of the innate immune system, and in particular, of the neutrophil. These include recurrent oral ulcers, repeated invasive bacterial illnesses, and poor growth. Given the normal absolute neutrophil count found on the complete blood cell count (CBC), neutrophil dysfunction should be considered. The most common disorder of neutrophil function is chronic granulomatous disease (CGD), a defect caused by a failure to produce oxygen radicals needed to kill phagocytosed microorganisms. The gold standard for diagnosing CGD is testing the phagocyte oxidative burst with flow cytometry.

Chronic granulomatous disease occurs in both X-linked and autosomal recessive forms. The X-linked form is by far the most common and is caused by a mutation in the CYBB gene that results in a dysfunctional gp91 protein. The most common autosomal form of CGD is caused by a mutation in the NCF1 gene on chromosome 7, resulting in a dysfunctional p47 protein. CGD most often presents with recurrent abscesses, in particular caused by Staphylococcus aureus. It can also present with invasive fungal infections, usually with Aspergillus.

Other rarer disorders of neutrophil function exist. Leukocyte adhesion deficiency represents a group of genetic disorders that result in the failure to express proteins necessary for the normal trafficking of leukocytes to areas of infection. Without the ability to leave the bloodstream and enter an area of infection, the leukocytes are unable to contain infections. The resulting phenotype can be very similar to CGD.

Frequent bacterial infections in a young child, especially of the skin, lung, and sinus, should raise concern for an underlying immunodeficiency. The immune system can be divided into: (1) the innate immune system, comprising barriers such as skin and mucosal membranes, and phagocytes, such as the neutrophil, macrophage, and natural killer cell; and (2) the adaptive immune system comprising B and T lymphocytes and their subsets. Generally, abnormal viral infections suggest a deficiency of the adaptive immune system, whereas frequent bacterial or fungal infections suggest a deficiency of the innate immune system.

Although children with inflammatory bowel disease (IBD) can present with oral ulcerations, the recurrent bacterial infections in this vignette are not consistent with IBD, so colonoscopy would not be the diagnostic test of choice. Children with newly diagnosed cystic fibrosis often present with pneumonias and failure to thrive, but mucosal ulcerations and skin infections are not typically associated with cystic fibrosis. The frequent bacterial infections described in the vignette could represent a clinical manifestation of severe neutropenia, such as that seen in severe congenital neutropenia or cyclic neutropenia. However, the CBC has a normal number of neutrophils, essentially ruling out severe congenital neutropenia. Children with leukemia are at risk for invasive infections; however, the CBC exhibited no lymphoblasts, and the normal hemoglobin and platelet count do not suggest bone marrow dysfunction. Thus, testing for lymphoblasts with flow cytometry would not be indicated in this scenario.

PREP Pearls

- A defect of the innate immune system should be suspected in a child presenting with frequent bacterial infections.
- Chronic granulomatous disease (CGD) is the most common disorder of neutrophil function.
- The gold standard for diagnosing CGD is testing of the phagocyte (neutrophil) oxidative burst by flow cytometry.

ABP Content Specifications(s)

- Recognize the clinical presentation of chronic granulomatous disease
- Plan and interpret the results of laboratory evaluation in a patient with chronic granulomatous disease

Suggested Readings

- Esfandbod M, Kabootari M. Images in clinical medicine: chronic granulomatous disease. N Engl J Med. 2012;367(8):753. doi: http://dx.doi.org/10.1056/NEJMicm1106350.
- Holland SM. Chronic granulomatous disease. Hematol Oncol Clin North Am. 2013;27(1):89-99. doi: http://dx.doi.org/10.1016/j.hoc.2012.11.002.
- Newburger PE. Disorders of neutrophil number and function. Hematology Am Soc Hematol Educ Program. 2006;2006(1):104-110. doi: http://dx.doi.org/10.1182/asheducation-2006.1.104.

Question 23

A new medication to treat Kawasaki disease (KD) is reported in a single journal publication. While you are admitting a patient with KD today, the family asks you if the new medication can be used instead of intravenous immunoglobulin. You agree to review the single report and discuss the evidence with them. The study included 50 pediatric patients ranging in age from 18 months to 7 years who were offered the new drug, which is not derived from blood products. No complications or treatment failures were reported. The study had no age or disease severity control cases. It is not clear how certain the diagnosis of KD was for the treated patients. You classify the data as a case series.

Of the following, the MOST accurate statement you can make in this situation is that

A. a cohort study would be preferable to a randomized control study
B. a large case series could determine treatment effectiveness
C. a randomized control study would not offer any advantage
D. there is clear evidence of selection bias
E. there is not enough evidence to recommend the new drug

Correct Answer: E
The single study available, a case series, does not provide enough evidence to recommend the new drug. A case series, case-controlled series, or cohort study may show an association between patients and response to a new medication, but cannot be used to state causality. These study designs are considered observational. We also cannot be sure whether this study had a selection bias because the process used for subject selection is unknown. If there were selection bias, such as all patients offered the new therapy were from one clinical practice, results might have been affected.

The hierarchy for study design, in terms of ability to use the data to change clinical practice, places a randomized controlled trial at the highest level. A well-designed, randomized control study of the medication referred to in the vignette might have demonstrated a cause-and-effect response to the new medication. Randomized control trials have practical and ethical limits. Exposure to more than minimal risk in a vulnerable population such as children, especially if there is no clear benefit to the subject, is not feasible. This risk definition would include the use of a placebo when the alternative treatment option is generally thought to be of benefit or if a placebo would deprive the patient of the usual standard medical care. In that setting, a well-constructed observational study may be needed.

The selection of the control population in a randomized control study is crucial. In this study design, a control population that receives placebo treatment is different from one that receives routine medical management. An example of a well-designed randomized, multicenter, placebo-controlled trial is the study protocol using 40% dextrose gel in newborns to prevent hypoglycemia. In this trial, infants at risk for hypoglycemia were randomized online to receive either dextrose gel or placebo before breastfeeding. The primary outcome was the need for admission to the neonatal intensive care unit. Such a study design would enable investigators to draw a conclusion of causation if there were a decrease in the frequency of admissions to the neonatal intensive care unit for hypoglycemia.

Effective study designsare ethical and protective of patients, especially those who are vulnerable such as children. Randomized controlled studies are the gold standard for evaluating a new intervention’s effect, but may not always be possible. Observational studies can be conducted before randomized control studies; they provide preliminary data and can show associations but not causality.

PREP Pearls

- Randomized controlled studies can provide evidence for causality.
- Observational studies, including case series and case control studies, can demonstrate association but not causality.

ABP Content Specifications(s)

- Understand the uses and limitations of controlled clinical trials
- Understand the uses and limitations of randomized clinical trials
- Understand the validity hierarchy for study design and study type

Suggested Readings

- Concato J, Shah N, Horowitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med. 2000;342(25):1887-1892. doi: http://dx.doi.org/10.1056/NEJM200006223422507.
- Grady C. Ethical principles in clinical research. In: Gallin JI, Ognibene FP, eds. Principles and Practice of Clinical Research. 3rd ed. Waltham, MA: Elsevier; 2012:19-30.
- Harding JE, Hegarty JE, Crowther CA, et al. Randomized trial of neonatal hypoglycemia prevention with oral dextrose gel (hPOD): study protocol. BMC Pediatr. 2015;15:120. doi: http://dx.doi.org/10.1186/s12887-015-0440-6.
- Johnson LL. Design of observational studies. In: Gallin JI, Ognibene FP, eds. Principles and Practice of Clinical Research. 3rd ed. Waltham, MA: Elsevier; 2012:207-22.
- Mann CJ. Observational research methods: research design II—cohort, cross sectional, and case-control studies. Emerg Med J. 2003;20(1):54-60. doi: http://dx.doi.org/10.1136/emj.20.1.54.
- Stoney CM, Johnson LL. Design of clinical studies and trials. In: Gallin JI, Ognibene FP, eds. Principles and Practice of Clinical Research. 3rd ed. Waltham, MA: Elsevier; 2012:225-242.

Question 24

A 6-week-old female infant is brought to your office for concern for an eye infection. Her parents report that her left eye is “more watery” than the right. Her mother saw some golden-colored crust on her eyelashes this morning. Her eye has never appeared red, and the parents have seen only clear fluid from the eye. She is otherwise well, eating appropriately, and not excessively fussy.

Of the following, the BEST next step in management for her condition is

A. nasolacrimal duct massage
B. referral to an ophthalmologist
C. systemic antibiotics
D. topical antibiotics
E. warm compresses to the affected eye

Correct Answer: A

The infant described in this vignette most likely has nasolacrimal duct stenosis (dacrostenosis), a condition affecting up to 20% of newborns. It commonly presents with excessive tearing, most frequently unilateral, but sometimes bilateral. Resolution without surgical treatment occurs in 90% of infants by 1 year of age. The recommended first-line treatment is nasolacrimal duct massage several times per day. Massage involves a caretaker using a clean finger to place firm pressure over the lacrimal sac, stroking downward. Frequent warm compresses to the eye have been historically recommended, but evidence of effectiveness is limited.

Complications of dacrostenosis can include acute dacryocystitis, which presents as erythema over the lacrimal sac with associated cellulitis. This is a medical emergency, requiring systemic antibiotics to cover methicillin-resistant Staphylococcus aureus, if prevalent in the community, and involvement of an ophthalmologist. Chronic dacryocystitis can cause persistent mucopurulent drainage from the eye that can be treated with topical antibiotics. Dacryocystocele presents as a firm, bluish mass below the medial canthus in the first few weeks of life and requires urgent referral to an ophthalmologist.

Dacrostenosis that persists after 6 months of age can be treated by an ophthalmologist with in-office lacrimal duct probing. Since most cases resolve spontaneously, some ophthalmologists prefer to wait until after 1 year of age to perform lacrimal duct probing under general anesthesia. Both approaches are clinically effective; in-office probing at younger ages has been shown to be equally or more cost-effective, with earlier relief of symptoms, compared to probing at an older age under general anesthesia.

PREP Pearls

- Dacrostenosis should not routinely be treated with topical antibiotics
- Frequent downward massage is the best recommended treatment for dacrostenosis.
- Ninety percent of cases of dacrostenosis resolve by 1 year of age without surgical intervention.

ABP Content Specifications(s)

- Recognize the clinical findings associated with obstruction of the nasolacrimal duct
- Plan the appropriate management of obstruction of the nasolacrimal duct

Suggested Readings

- Schnall BM. Pediatric nasolacrimal duct obstruction. Curr Opin Ophthalmol. 2013;24(5):421-424. doi: http://dx.doi.org/10.1097/ICU.0b013e3283642e94.
- Wong RK, VanderVeen DK. Presentation and management of congenital dacryocystocele. Pediatrics. 2008;122(5):e1108-e1112. doi: http://dx.doi.org/10.1542/peds.2008-0934.

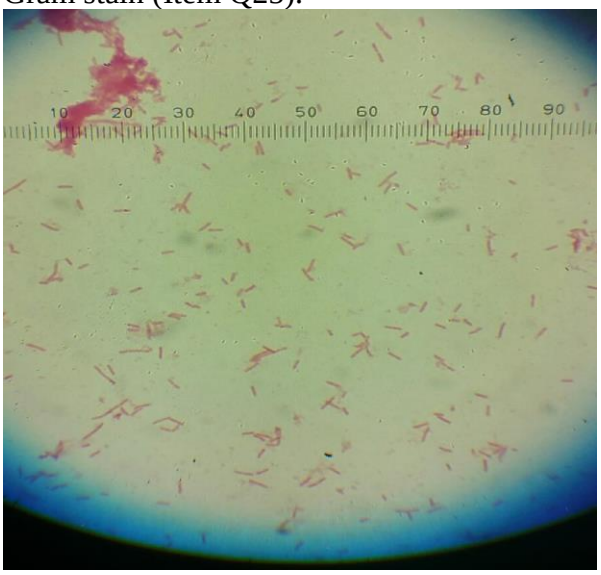
Question 25

An 18-year-old young woman presents to your office with a 4-day history of left ear pain and swelling. She reports no recent trauma or insect bites to the ear, but did have a new piercing along the upper pinna about 1 week ago. Her past medical history is significant only for seasonal allergies. Physical examination shows an uncomfortable young woman complaining of 8 out of 10 pain in her left ear and left lateral neck. Vital signs show a temperature of 37°C, respiratory rate of 18 breaths/min, heart rate of 95 beats/min, and blood pressure of 125/65 mm Hg. Her left ear is impressively swollen, hot, erythematous, and tender along the helix; there is fluctuance with an earring embedded in the swelling. Left postauricular swelling is also seen. There is no lymphadenopathy and she has full range of motion in her neck. The left tympanic membrane and external auditory canal appeared normal.

Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	10,400/μL (10.4 x 10^9/L)
Lymphocytes	30%
Neutrophils	66%
Monocytes	1%
Hemoglobin	13 g/dL (130 g/L)
Hematocrit	40%
Platelet count	369 x 10^3/μL (369 x 10^9/L)

When the earring is removed, about 3 mL of pus is expressed. The pus is sent for culture and Gram stain (Item Q25).



Item Q25: Gram stain of the pus described in the vignette. Courtesy of P Lee

Of the following, the BEST choice for initial therapy is

A. ceftriaxone
B. ciprofloxacin
C. mupirocin
D. trimethoprim-sulfamethoxazole
E. vancomycin

Correct Answer: B
The best choice for initial therapy for the young woman in the vignette is ciprofloxacin. At first glance, she has what may appear to be a straightforward ear abscess, but due to location and association with piercing of the ear helix (ie, a "high piercing"), this is more consistent with a suppurative auricular perichondritis. The perichondrium is a layer of connective tissues surrounding all of the body's cartilage except the cartilage in joints. Since cartilage is avascular, it is dependent on the perichondrium for its nutrients and oxygen. When an infection from a piercing through cartilage occurs, the subsequent inflammation and pus that results can separate the perichondrium from the cartilage and lead to aseptic and/or septic necrosis, resulting in permanent loss or deformity of the outer ear. While Staphylococcus aureus remains an important cause of perichondritis, Pseudomonas aeruginosa is the usual pathogen involving piercing of the helix of the ear. Pseudomonas from the external ear canal, where it is commonly found, or from nonsterile water may inadvertently get into the piercing, creating an insidious, progressively destructive infection.

The Gram stain in this example shows gram-negative rods, confirming that Pseudomonas, not the less common Staphylococcus, is the pathogen that needs to be treated. Vancomycin, which has activity only against gram-positive organisms, would be the antibiotic of choice for S aureus, but would not be appropriate for Pseudomonas. Mupirocin and trimethoprim-sulfamethoxazole, which are also used against S aureus, have some gram-negative activity, but not against Pseudomonas. Also, mupirocin is topical and systemic intravenous antibiotics are necessary to treat perichondritis. Third-generation cephalosporins have good gram-negative activity, but many of them, including ceftriaxone, are ineffective against Pseudomonas. Of the choices listed, ciprofloxacin, a fluoroquinolone, is the only antibiotic with excellent Pseudomonas coverage. It can penetrate into the cartilage, making it a frequent first-line agent for perichondritis.

A multidisciplinary team, including otorhinolaryngology, surgery, and plastic surgery, may be necessary for incision and drainage of the abscess, removal of necrotic tissue, and reconstruction and revision of the deformed ear that often results.

PREP Pearls

- Piercings of the upper ear helix may cause a suppurative perichondritis, frequently caused by Pseudomonas aeruginosa, instead of Staphylococcus aureus.
- Systemic treatment with an antipseudomonal agent like ciprofloxacin is required.
- Surgical drainage, debridement, and reconstruction of the ear may be necessary.

ABP Content Specifications(s)

- Recognize the risk factors for the development of pseudomonal infections
- Recognize the clinical manifestations of pseudomonal infections and manage appropriately

Suggested Readings

- American Academy of Pediatrics. Escherichia coli and other gram-negative bacilli (septicemia and meningitis in neonates). In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:340-342 .
- Davidi E, Paz A, Duchman H, Luntz M, Potasman I. Perichondritis of the auricle: analysis of 114 cases. Isr Med Assoc J. 2011;13(1):21-24. http://www.ima.org.il/FilesUpload/IMAJ/0/38/19428.pdf.

Question 26

You are called to the emergency department to evaluate a 2-month-old infant presenting with new-onset seizures. The patient has a 4-day history of vomiting and diarrhea. He was born to an 18-year-old primigravida woman by normal vaginal delivery. He has been exclusively formula-fed since birth. The infant is afebrile with a heart rate of 160 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 80/40 mm Hg. His physical examination is significant for dry mucous membranes and capillary refill of more than 3 seconds. The remainder of his physical examination is unremarkable.

Of the following, the laboratory findings MOST likely to be seen in this patient are

A. high urine sodium, high urine osmolality, high serum osmolality
B. high urine sodium, low urine osmolality, high serum osmolality
C. high urine sodium, low urine osmolality, low serum osmolality
D. low urine sodium, high urine osmolality, low serum osmolality
E. low urine sodium, low urine osmolality, low serum osmolality

Correct Answer: D
The infant in the vignette presents with clinical features of dehydration and a history of vomiting, tachycardia, dry mucous membranes, and prolonged capillary refill. The presentation of seizures in a patient with dehydration suggests an associated electrolyte abnormality. This infant most likely has low urine sodium, high urine osmolality, and low serum osmolality.

Serum sodium is an indicator of water balance, which in turn is reflected in the serum osmolality.

The formula for calculating serum osmolality is:

$$Serum\ osmolality = 2\ \times serum\ sodium + \frac{glucose}{18} + \frac{BUN}{2.8}$$

The contribution of glucose and blood urea nitrogen (BUN) to serum osmolality is minimal. The normal serum concentrations of glucose (60–100 mg/dL [3.3–5.5 mmol/L]) and BUN (10–20 mg/dL [3.6–7.1 mmol/L]) contribute less than 10 mOsm/kg to total serum osmolality. Therefore, 2 × serum sodium approximates the serum osmolality. Thus, it follows that hyponatremia usually reflects hyposmolality and hypernatremia represents hyperosmolality.

Hyponatremia and hypernatremia are common dyselectrolytemias that indicate disorders of water balance, and may be associated with changes in total body sodium. The renal response to a decreased effective circulating volume (dehydration) is to increase reabsorption of salt and water, thereby increasing effective circulatory volume. This leads to a low urinary sodium concentration (< 20–25 mEq/L [20–25 mmol/L]). Urine sodium is therefore an indicator of intravascular volume status, and low urine sodium (< 20–25 mEq/L [20–25 mmol/L]) suggests decreased perfusion, even in patients without clinical features of dehydration. Edematous patients (nephrotic syndrome, cirrhosis, congestive heart failure) with an overall increase in total body volume, but a decreased effective circulatory volume will also have a low urinary sodium concentration. It is important to note that in patients with underlying renal disease (renal dysplasia, acute glomerulonephritis) and in those receiving diuretic therapy, urinary sodium is not a good indicator of effective circulatory volume.

A patient with diarrhea and dehydration may present with a low, normal, or elevated serum sodium concentration. The balance of compensatory responses, thirst, and antidiuretic hormone (ADH) secretion influences their serum sodium level. Hyponatremia will occur when gastrointestinal losses are replaced with excess free water. Hyponatremia secondary to improper formula preparation must be considered in any infant with a low serum sodium concentration and a history of inadequate weight gain.

Hypernatremic dehydration with gastrointestinal losses is seen when water intake is decreased as in patients who do not get enough free water. Patients with developmental delay or infants dependent on caregivers for fluid intake are at increased risk for hypernatremic dehydration. Hypernatremic dehydration with serum hyperosmolality secondary to gastrointestinal losses is associated with low urine sodium and urine hyperosmolality. The resultant serum hyperosmolality leads to fluid shifts from the intravascular to the extravascular compartment.

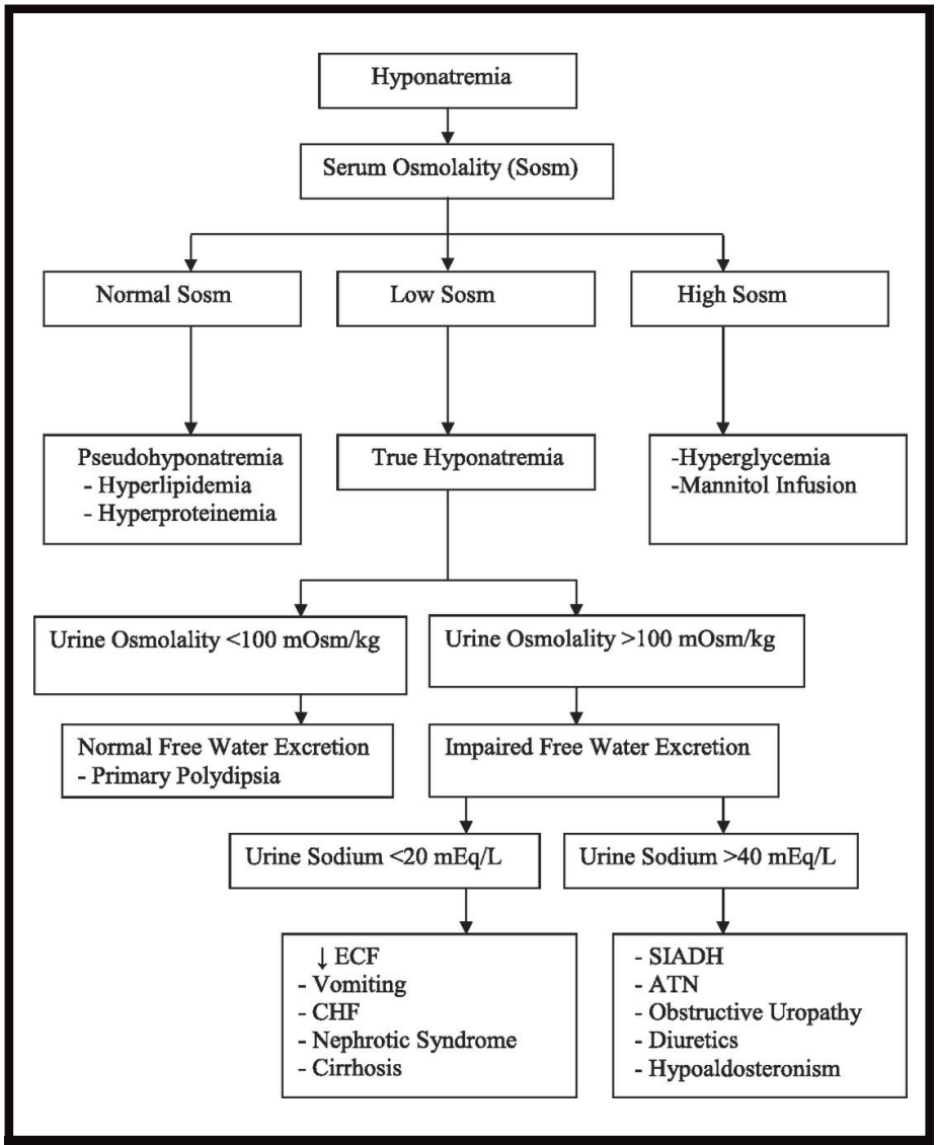
Thus, these patients will present with less marked clinical features of dehydration compared with those with hyponatremia (Item C26A, Item C26B).

Item C26A. Pathogenesis of Common Disorders Leading to Hyposmolarity or Hyponatremia.

Solute Depletion (↓ Solute + Water retention)		Solute Dilution (↑ TBW ± solute depletion)		
Renal solute losses (Urine sodium > 40 mEq/L)	• Diuretics • Mineralocorticoid deficiency • Salt-losing nephropathy • Solute diuresis (eg, mannitol, hyperglycemia)	↓ Renal free water excretion	↑Proximal tubular reabsorption (Urine sodium < 20 mEq/L)	• Cirrhosis • Congestive heart failure • Nephrotic syndrome
			↑ water permeability of collecting tubule (Urine sodium >40 mEq/L)	• Glucorticoid deficiency • SIADH
Nonrenal solute losses + water replacement (Urine sodium < 20 mEq/L)	• Blood loss • Gastrointestinal (vomiting, diarrhea) • Skin (burns, sweating)	Normal renal water excretion	• Primary polydipsia	

↑, increased; ↓, decreased; TBW, total body water; SIADH, syndrome of inappropriate antidiuretic hormone

Adapted and reprinted with permission from Jain A. Body fluid composition. *Pediatr Rev.* 2015;36:141-152.



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ITEM C26B: Diagnostic algorithm for a patient with hyponatremia.
ATN, acute tubular necrosis; CHF, congestive heart failure; ECF, extracellular fluid; SIADH, syndrome of inappropriate antidiuretic hormone.

A high urine sodium concentration and low serum osmolality is seen in patients with the syndrome of inappropriate ADH secretion (SIADH). Urine osmolality in SIADH is inappropriately elevated compared with serum osmolality. This is because ADH secretion in these patients is increased, leading to increased water absorption by the renal tubules. This results in increased total body water and hyponatremia, but with normal total body sodium and

sodium excretion. Patients with SIADH do not present with the typical clinical features of dehydration or volume overload.

Patients with primary polydipsia may also present with low serum and urine osmolality. In rare cases, water intake may exceed the ability of the kidneys (> 10–15 L/day) to excrete free water, resulting in symptomatic hyponatremia. Patients with excessive thirst due to polyuria typically respond with increased water intake and their serum sodium concentration is usually normal or borderline low because renal excretion of excess free water compensates for the increased intake.

The other response choices in the vignette are associated with increased serum osmolality or hypernatremia (Item C26C). Polyuria is characterized by an increased total urine volume leading to free water loss, resulting from an underlying defect in water balance. Patients with polyuria present with the excretion of large volumes of dilute urine (low urine osmolality), as seen in diabetes mellitus (osmotic diuresis), diabetes insipidus (ADH disorders), and psychogenic polydipsia. Patients with diabetes insipidus may present with recurrent episodes of hypernatremic dehydration. Urine sodium concentration in patients with polyuria is variable, depending on the effective circulating volume, which is regulated by thirst and access to fluids.

Item C26C. Pathogenesis of Common Disorders Leading to Hyperosmolarity or Hypernatremia.

Water Depletion		Solute Excess
↓Total TBW and normal total body sodium	Sodium and water losses ↓TBW > ↓Solute	↑ Solute ↑TBW
Renal free water losses	*Renal losses*	*Salt supplementation*
• Low urine osmolality/urinary sodium variable • Decreased AVP secretion (central diabetes insipidus) • Decreased AVP action (nephrogenic diabetes insipidus)	• Low or normal urine osmolality • Urinary sodium > 20 mEq/L • TN/intrinsic renal disease • Postobstructive diuresis • Osmotic diuresis (hyperglycemia) • Diuretics (loop, thiazide)	• Urinary sodium > 20 mEq/L • Sodium chloride • Sodium bicarbonate • Hyperaldosteronism
Increased nonrenal losses	*Nonrenal losses*	
• Increased urine osmolality • Urinary sodium < 20 mEq/L • Pulmonary (hyperventilation, tachypnea) • Internal insensible losses	• Urinary sodium < 20 mEq/L • Gastrointestinal (vomiting, diarrhea) • Skin (burns, sweating, phototherapy)	
Low water intake		
• Decreased availability (infants, cognitive impairment) • Hypodipsia (osmoreceptor dysfunction)		

↑, increased; ↓, decreased; AVP, arginine vasopressin; TBW, total body water; TN, tubular necrosis

Adapted and reprinted with permission from Jain A. Body fluid composition. *Pediatr Rev.* 2015;36:141-152

Hypernatremia associated with increased total body sodium will present with increased urine sodium and urine osmolality. Increased total body sodium is seen in primary hyperaldosteronism, or the ingestion of sodium chloride or sodium bicarbonate. Hypernatremia occurring with sodium and water losses is associated with an increased urine sodium and low urine osmolality, as seen in patients with intrinsic renal disease, osmotic diuresis, or diuretic therapy. If such

patients have restricted access to free water, their total body water deficit will exceed renal sodium losses, leading to hypernatremia.

PREP Pearls

- Hyponatremia or hypernatremia indicate disorders of water balance that may be associated with changes in total body sodium.
- Urine sodium is an indicator of intravascular volume status and low urine sodium (< 20–25 mEq/L [20–25 mmol/L]) suggesting decreased perfusion even in patients without clinical features of dehydration
- High urinary sodium and low urinary and serum osmolality are seen in patients with syndrome of inappropriate antidiuretic hormone (ADH) secretion.
- Patients with polyuria present with the excretion of large volumes of dilute urine (low urine osmolality), as seen in diabetes mellitus (osmotic diuresis), diabetes insipidus (ADH disorders), and psychogenic polydipsia.

ABP Content Specifications(s)

- Recognize the clinical findings associated with water intoxication in patients of various ages

Suggested Readings

- Jain A. Body fluid composition. Pediatr Rev. 2015;36(4):141-152. doi: http://dx.doi.org/10.1542/pir.36-4-141.
- Reid-Adam J. Hyponatremia. Pediatr Rev. 2013;34(9):417-419. doi: http://dx.doi.org/10.1542/pir.34-9-417.

Question 27

You are in your local community hospital reviewing discharge instructions with the mother of a 38-week-gestation male neonate. The mother is an 18-year-old gravida 1 para 0 woman with no medical or obstetrical problems. The neonate was born via spontaneous vaginal delivery and has been breastfeeding and formula feeding well. He is being discharged home on the second day of life. The mother asks how to care for the umbilical cord.

Of the following, the BEST recommendation to address the mother's concern is

A. allow the cord to dry without intervention
B. apply triple antibiotic ointment to the cord
C. clean the cord with alcohol
D. place triple dye on the cord prior to discharge
E. wash the cord with soap and water daily

Correct Answer: A

In the past, various bactericidal agents have been applied to umbilical cords in an effort to decrease the incidence of omphalitis, an infection of the umbilical cord that can rapidly evolve into necrotizing fasciitis. Omphalitis is a rare complication affecting less than 1% of all neonates born in the United States. However, it is associated with rates of morbidity and mortality as high as 85%. Omphalitis may be caused by multiple organisms, including skin-associated gram-positive bacteria, those associated with maternal vaginal tract such as Streptococcus agalactiae, and less commonly, gram-negative bacteria.

A randomized trial comparing air drying the umbilical cord to application of triple dye at birth with subsequent application of alcohol showed no difference in the incidence of omphalitis. Based on this data, caregivers of neonates born in hospitals should be instructed to leave umbilical cords dry without additional treatment, as is the recommendation for the neonate in this vignette.

Triple antibiotic ointment has not been studied in relation to umbilical cord care. Cleaning the umbilical cord with isopropyl alcohol or soap and water does not change the risk of omphalitis. In addition, using alcohol on the umbilical cord may delay cord separation.

Triple dye (brilliant green, proflavine hemisulphate, and crystal violet) decreases the rate of colonization with gram-positive and gram-negative bacteria. However, use of triple dye does not decrease the risk of omphalitis or death. In addition, triple dye is typically applied immediately after birth and not at the time of hospital discharge.

PREP Pearls

- In the developed world, the umbilical cord should remain dry after birth without additional treatment.
- Application of isopropyl alcohol to the umbilical cord does not decrease the incidence of omphalitis.

ABP Content Specifications(s)

- Plan appropriate umbilical cord care

Suggested Readings

- Imdad A, Bautista RMM, Senen KAA, Uy MEV, Mantaring JB III, Bhutta ZA. Umbilical cord antiseptics for preventing sepsis and death among newborns. Cochrane Database Syst Rev. 2013;5:CD008635. doi: http://dx.doi.org/10.1002/14651858.CD008635.pub2.
- Janssen PA, Selwood BL, Dobson SR, Peacock D, Thiessen PN. To dye or not to dye: a randomized, clinical trial of a triple dye/alcohol regime versus dry cord care. Pediatrics. 2003;111(1):15-20. doi: http://dx.doi.org/10.1542/peds.111.1.15.

Question 28

A 6-year-old previously healthy, fully immunized boy is brought to your office by his mother. He has had a cough and runny nose for 1 week and developed fever yesterday. Today, the boy is complaining of neck pain, resists turning his head to the side, is refusing to eat, and will only take small sips of water. On physical examination, the boy is tired appearing with a temperature of 40.3°C, heart rate of 130 beats/min, respiratory rate of 45 breaths/min, and oxygen saturation of 98% by pulse oximetry. His lung fields are clear with good aeration. He has tender anterior cervical lymphadenopathy, torticollis, and his posterior oropharynx appears erythematous. The remainder of his physical examination is within normal limits.

Of the following, the test MOST likely to confirm this boy's diagnosis is

A. anteroposterior and lateral chest radiographs
B. blood culture
C. lateral neck radiograph
D. lumbar puncture
E. throat culture

Correct Answer: C
The boy in the vignette has a retropharyngeal abscess that could be visualized on lateral neck radiography as abnormally thickened prevertebral soft tissue. Contrast-enhanced computed tomography is sometimes necessary to differentiate between a retropharyngeal abscess and retropharyngeal cellulitis. Chest radiographs, blood cultures, cerebrospinal fluid analyses, and throat cultures do not typically aid in the diagnosis of a retropharyngeal abscess.

Retropharyngeal abscesses occur most commonly in younger children, typically through lymphatic spread. Initial symptoms are nonspecific and insidious. Children may have a preceding upper respiratory infection, followed by fever, sore throat, and decreased oral intake. They may develop neck stiffness or pain, and as symptoms progress, tachypnea, drooling, or stridor. Physical examination may reveal enlarged and/or tender cervical lymph nodes. Laboratory evaluation usually shows an increased white blood cell count and signs of inflammation, but blood cultures are unlikely to reveal a causative organism. Medical management with empiric antibiotics is effective in up to 25% of patients; refractory cases require surgical management.

In contrast, peritonsillar abscesses are most common in adolescents and young adults. These abscesses are caused by infection of the potential space between the palatine tonsil and the tonsillar capsule. Symptoms include fever, sore throat, muffled or “hot potato” voice, and dysphagia, leading to decreased oral intake. Patients may experience pain referred to the ipsilateral ear and may also have trismus. Physical examination findings include soft palate edema on the affected side, resulting in medial displacement of the tonsil and deviation of the uvula. Diagnosis is suggested with ultrasonography or computed tomography and confirmed on needle aspiration. Treatment includes surgical drainage and antibiotic therapy.

Item C28 compares retropharyngeal abscess and peritonsillar abscess.

Item C28. Comparison of Retropharyngeal Abscess and Peritonsillar Abscess.

	Retropharyngeal Abscess	Peritonsillar Abscess
Most Common Age	<6 y	20-40 y
History	• Fever (gradual onset) • Sore throat • Dysphagia • Stridor • Symptoms of upper respiratory infection	• Fever • Sore throat • Dysphagia • Ipsilateral otalgia
Physical Examination	• Tachypnea • Neck pain or stiffness • Drooling • Cervical lymphadenopathy • Retropharyngeal mass	• Trismus • Muffled "hot potato" voice • Cervical lymphadenitis • Ipsilateral palatal edema • Contralateral uvular deviation
Etiology	• Polymicrobial, primarily - *Streptococcus pyogenes* - *Staphylococcus aureus*	• Aerobes - *Streptococcus pyogenes* - *Staphylococcus aureus* - *Haemophilus influenzae* - *Neisseria species* • Anaerobes - *Fusobacterium* - *Peptostreptococcus* - *Prevotella* - *Bacteroides*
Diagnosis	• Inspiratory lateral neck radiograph • Contrast-enhanced CT	• Needle aspiration • Ultrasonography (transcutaneous or intraoral) • Contrast-enhanced CT or magnetic resonance imaging
Treatment	• Medical (successful alone in 25% of cases) • Antibiotic coverage for staphylococcal and streptococcal infections with or without surgical incision and drainage • CT-guided needle aspiration	• Aspiration or surgical incision and drainage AND • Antibiotics (10-14 d)—Cover aerobes and anaerobes
Complications	• Aspiration pneumonia due to abscess rupture • Poststreptococcal glomerulonephritis • Rheumatic fever • Local extension • Airway obstruction	• Aspiration pneumonia due to abscess rupture • Poststreptococcal glomerulonephritis • Rheumatic fever • Carotid sheath rupture hemorrhage and death

CT, computed tomography.

Reprinted with permission from Gereige R, Cunill-DeSautu B. Throat infections. *Pediatr Rev*. 2011;32(11):459-469.

PREP Pearls

- Retropharyngeal abscesses present with the insidious onset of symptoms including fever, sore throat, neck stiffness, and in more severe cases, tachypnea, drooling, and stridor.
- Retropharyngeal abscesses are most common in children younger than 6 years of age.
- Lateral neck radiographs of retropharyngeal abscesses show thickened prevertebral soft tissues.
- Peritonsillar abscesses, most common in adolescents and young adults, present with fever, sore throat, muffled voice, and dysphagia.
- Ultrasonography or computed tomography is useful in making the diagnosis of peritonsillar abscesses.

ABP Content Specifications(s)

- Recognize the clinical findings associated with peritonsillar abscess
- Recognize the clinical findings associated with retropharyngeal abscess

Suggested Readings

- Brook I. Microbiology and management of peritonsillar, retropharyngeal, and parapharyngeal abscesses. J Oral Maxillofacial Surg. 2004;62(12):1545-1550. doi: http://dx.doi.org/10.1016/j.joms.2003.12.043.
- Gereige R, Cunill-De Sautu B. Throat infections. Pediatr Rev. 2011;32(11):459-469. doi: http://dx.doi.org/10.1542/pir.32-11-459.
- Grisaru-Soen G, Komisar O, Aizenstein O, Soudack M, Schwartz D, Paret G. Retropharyngeal and parapharyngeal abscess in children-epidemiology, clinical features and treatment. Int J Pediatr Otorhinolaryngol. 2010;74(9):1016-1020. doi: http://dx.doi.org/10.1016/j.ijporl.2010.05.030.

Question 29

You are seeing a 6-year-old boy for a new patient visit. He was born at term, after an uncomplicated pregnancy, to a primigravida mother. His birthweight was 3.0 kg. He required supplemental oxygen in the first 24 hours after birth for transient tachypnea of the newborn, but did not require intubation or ventilatory support. Since 2 months of age, the boy has had a persistent cough, described as mucousy in quality but nonproductive. He has also had chronic otitis media, requiring 2 sets of myringotomy tubes, and persistent purulent nasal drainage. In an attempt to ameliorate his symptoms, the boy has been treated for asthma, gastroesophageal reflux, and allergic rhinitis without effect. There is no history of failure to thrive or malodorous stools. Prior evaluation demonstrated dextrocardia and polysplenia.

On physical examination, the boy is active and playful. His heart rate is 80 beats/min and his respiratory rate is 22 breaths/min, with oxygen saturation of 97% in room air. There is purulent rhinitis and postnasal drip. His oropharynx is otherwise clear. Myringotomy tubes are in place with serous drainage bilaterally. His neck is supple, with shotty cervical lymphadenopathy. Breath sounds are mildly coarse with fine crackles at the left lower lobe. He has no wheezing or stridor. The boy's abdomen is soft and nontender. The liver edge is palpable at the right costal margin, nontender, and of normal size. His extremities are warm and well perfused with 1+ digital clubbing bilaterally. There is no cyanosis.

Of the following, the MOST likely diagnosis for this child is

A. cystic fibrosis
B. immunodeficiency
C. primary ciliary dyskinesia
D. tracheoesophageal fistula
E. tracheomalacia

Correct Answer: C
The boy in the vignette has a clinical history and symptoms that are most suggestive of a diagnosis of primary ciliary dyskinesia (PCD). The classic clinical phenotype of PCD includes a history of neonatal respiratory distress in more than 80% of affected individuals, daily nasal congestion, and wet cough, starting in the early neonatal period, and chronic otitis media and sinus disease beginning in early childhood. Patients with PCD typically demonstrate an obstructive pattern of lung disease starting in early childhood; bronchiectatic changes may be seen on computed tomography. Approximately 50% of patients with PCD have laterality defects. Kartagener syndrome includes the triad of chronic sinusitis, bronchiectasis, and situs inversus totalis. Situs ambiguus syndromes, including heterotaxy, isomerism, and congenital heart defects, are strongly associated with symptoms suggestive of PCD. The term immotile cilia syndrome is no longer used because at least 30% of patients with PCD demonstrate normal ciliary ultrastructure and normal or near-normal ciliary waveform. The diagnosis of PCD can be challenging. Use of nasal nitric oxide measurements is emerging as a potentially sensitive and noninvasive tool for the diagnosis of PCD in patients with suggestive clinical findings. At present, nasal nitric oxide remains a research tool.

Digital clubbing, as seen in the boy in the vignette, is the enlargement of the distal segments of the fingers or toes. This enlargement creates an abnormal convexity of the distal phalanx. Digital clubbing may be diagnosed by the presence of the Schamroth sign, in which the normal diamond-shaped window seen when dorsal surfaces of the terminal phalanges of opposite index fingers are apposed is absent. Alternatively, the phalangeal depth ratio may be used; the ratio of the distal phalangeal depth to interphalangeal depth of the index finger is recorded, with a ratio of more than 1.0 indicating clubbing.

Clubbing may be hereditary or idiopathic, but most often represents an underlying medical condition. Various diseases are associated with digital clubbing. Commonly associated pulmonary diseases include cystic fibrosis (CF), primary ciliary dyskinesia, bronchiectasis, and interstitial lung disease. Clubbing may also be encountered in nonpulmonary diseases such as cyanotic congenital heart disease, inflammatory bowel disease, hepatic cirrhosis, and HIV.

Digital clubbing is associated with hypoxemia and appears to increase in correlation with hypoxemia severity and chronicity.The pathogenesis of digital clubbing remains unclear. Proposed mechanisms include dilation of peripheral vessels, local deposition of platelet clusters, or stimulation of connective tissue growth. Dysregulated expression of vascular endothelial growth factor A and platelet-derived growth factor in a hypoxemic vascular bed have been implicated as causes for the development of digital clubbing.

Patients with CF will typically have a wet cough and evidence of obstructive lung disease. However, the patient with CF is more likely to demonstrate symptoms of pancreatic insufficiency, including malodorous stools and failure to gain weight. Liver disease is often present in patients with CF. Situs ambiguous, polysplenia, and chronic nasal drainage are not associated with CF.

Immunodeficiency and tracheoesophageal fistula (TEF) are both known causes of bronchiectasis, due to chronic infection and pulmonary aspiration, respectively. Both disorders may escape detection for prolonged periods, and a high index of suspicion is required for diagnosis. Although relatively uncommon, the diagnosis of H-type TEF is often delayed because of the absence of esophageal atresia. Pneumonia and/or sinopulmonary infections may recur with both immunodeficiency and TEF, but laterality defects are uncommon.

Tracheomalacia is a common cause of chronic or recurrent wheezing and cough. The quality of the cough is typically harsh and brassy, unlike the wet, productive cough of CF and ciliary dyskinesia. A monophonic wheeze may be heard on auscultation. Inspiratory crackles, chronic nasal drainage, and chronic otitis are not expected clinical findings.

PREP Pearls

- The finding of digital clubbing suggests an underlying medical condition.
- The classic clinical phenotype of primary ciliary dyskinesia (PCD) includes a history of neonatal respiratory distress in more than 80% of affected individuals, daily nasal congestion, and wet cough, starting in the early neonatal period, and chronic otitis media and sinus disease beginning in early childhood.
- Primary ciliary dyskinesia is often unrecognized; this may result in delayed diagnosis, delays in access to optimal therapies, and disease-associated morbidity and mortality
- A significant proportion of individuals with heterotaxy syndromes have symptoms suggestive of PCD.
- Kartagener syndrome includes the triad of chronic sinusitis, bronchiectasis, and situs inversus totalis.

ABP Content Specifications(s)

- Recognize disorders commonly associated with digital clubbing

Suggested Readings

- Al Subie H, Fitzgerald DA. Non-cystic fibrosis bronchiectasis. J Pediatr Child Health. 2012;48(5):382-388. doi: http://dx.doi.org/10.1111/j.1440-1754.2010.01871.x.
- Atkinson S, Fox SB. Vascular endothelial growth factor (VEGF)–A and platelet derived growth factor (PDGF) play a central role in the pathogenesis of digital clubbing. J Pathol. 2004;203:721-728. doi: http://dx.doi.org/10.1002/path.1565.
- Knowles MR, Daniels LA, Davis SD, Zariwala MA, Leigh MW. Primary ciliary dyskinesia: recent advances in diagnostics, genetics and characterization of clinical disease. Am J Respir Crit Care Med. 2013;188(8):913-922. doi: http://dx.doi.org/10.1164/rccm.201301-0059CI.
- Paton JY, Bautista DB, Stabile MW, et al. Digital clubbing and pulmonary function abnormalities in children with lung disease. Pediatr Pulmonol. 1991;10:25-29. doi: http://dx.doi.org/10.1002/ppul.1950100106.
- Shapiro AJ, Tolleson-Rinehart S, Zariwala MA, Knowles MR, Leigh MW. The prevalence of clinical features associated with primary ciliary dyskinesia in a heterotaxy population: results of a web-based survey. Cardiol Young. 2015;25(4):752-759. doi: http://dx.doi.org/10.1017/S1047951114000912.

Question 30

A 15-year-old adolescent is brought to your clinic after he had a convulsion at home 2 days ago. His mother tells you she heard a loud thumping noise, and when she went to check on him, he was convulsing on the bedroom floor. This lasted about 2 minutes. He was seen in an urgent care clinic and no acute abnormalities were found. He tells you he has had quick twitching movements of his shoulders and upper extremities, particularly in the morning for the past year. There is no family history of tremor or seizures. His neurological examination shows an anxious adolescent with bilateral upper extremity tremulousness when his arms are outstretched. There are no other abnormal movements. His physical examination is otherwise unremarkable. He and his mother ask to start a medication to treat this problem.

Of the following, the BEST medication to treat this patient's underlying problem is

A. fluoxetine
B. lorazepam
C. phenytoin
D. propranolol
E. valproate

Correct Answer: E
The patient in the vignette has juvenile myoclonic epilepsy (JME). Juvenile myoclonic epilepsy is a lifelong seizure disorder, so treatment should be started after the diagnosis is made. Of the choices, valproate is the best medication to treat juvenile myoclonic epilepsy.

Lorazepam is used acutely to stop prolonged or repetitive seizures, but it is not an appropriate long-term anticonvulsant for JME. Phenytoin, oxcarbazepine, and carbamazepine can worsen seizures in JME, so these medications should be avoided. Fluoxetine is not a treatment for epilepsy, however, anxiety and depression are common comorbidities in patients with epilepsy and these diagnoses should be considered if symptoms are present. The adolescent in the vignette seems anxious and has tremulousness that is likely to be from anxiety. Propranolol is not the best medication choice for this patient, as the lack of a rhythmic tremor of his upper extremities and the lack of family history of tremor make a diagnosis of essential tremor or familial tremor unlikely. If an essential or familial tremor were present, treating JME would take precedence.

Juvenile myoclonic epilepsy starts in adolescence with upper extremity myoclonic jerks on awakening; eventually, the person has a generalized tonic-clonic seizure. Some people with JME had absence seizures as a younger child. The diagnosis of JME is based on the presence of these clinical features, an electroencephalogram showing the characteristic pattern of a 4 to 6 Hz spike and slow wave discharges in an otherwise typically developing adolescent. In typical cases, brain imaging is not indicated.

PREP Pearls

- Juvenile myoclonic epilepsy is diagnosed based on the clinical features of myoclonic jerks of the upper extremities on awakening and generalized tonic-clonic seizures, and in some cases, a history of absence seizures.
- Juvenile myoclonic epilepsy has a characteristic electroencephalogram pattern of 4 to 6 Hz spike wave discharges.
- Valproate is a first-line anticonvulsant for juvenile myoclonic epilepsy; phenytoin, oxcarbazepine, and carbamazepine can exacerbate seizures in this syndrome and should be avoided.

ABP Content Specifications(s)

- Recognize the clinical findings associated with juvenile myoclonic epilepsy, and manage appropriately

Suggested Readings

- Camfield CS, Camfield PR. Juvenile myoclonic epilepsy 25 years after seizure onset: a population-based study. Neurology. 2009;73(13):1041-1045. doi: http://dx.doi.org/10.1212/WNL.0b013e3181b9c86f.
- Sidhu R, Velayudam K, Barnes G. Pediatric seizures. Pediatr Rev. 2013;34(8):333-342. doi: http://dx.doi.org/10.1542/pir.34-8-333.

Question 31

An 8-year-old girl has been in the intensive care unit for 2 weeks after suffering a devastating neurologic injury from a ruptured arteriovenous malformation. Despite several aggressive therapies, her neurologic status has worsened. She currently has reactive pupils and breathes over the ventilator, but has no purposeful movements, response to voice or stimuli, and no cough or gag reflex. She has developed anuric renal failure, but does not yet meet criteria for emergent dialysis. You anticipate life-threatening fluid overload, hyperkalemia, and acidosis to develop within 2 or 3 days. Oxygen saturation is 100% on FiO2 of 0.4 on the ventilator. The child's parents wish to continue aggressive therapies, including dialysis, even though the brain injury is devastating and refractory to all treatments. You have brought up withdrawal of support for the first time, but the parents believe the child would have wanted to remain alive as long as possible. Critical care medicine, nephrology, neurosurgery, neurology, palliative care medicine, and religious services have all been involved in her care.

Of the following, the BEST next step is to

A. conduct multidisciplinary family meeting
B. consult hospital ethics committee
C. obtain cerebral blood flow scan
D. place a dialysis catheter
E. remove the endotracheal tube

Correct Answer: A

The child in this vignette has suffered an irreversible neurologic injury and withdrawal of life-sustaining medical therapies (LSMT) is reasonable. Furthermore, she would likely require dialysis, an invasive therapy, to keep her alive past the next few days. Since the family is not interested in withdrawal of support at the moment and there are several subspecialists involved, the best option is to conduct a multidisciplinary family meeting.

The American Academy of Pediatrics (AAP) released a policy statement in 1994 that was last reaffirmed in 2012 which discussed limitation of LSMT. Physicians must provide families with relevant risks and benefits of available options and to provide specific recommendations, as opposed to offering a "menu" of choices. For this girl, there are few benefits to continuing LSMT because of the particularly poor neurologic prognosis. Quality of life is a concept fraught with value judgment. However, society generally views those who lack the most basic cognitive functions and the capability of perceiving their surroundings to be in a persistent vegetative state and have a low quality of life. The medical team should give families adequate time to consider these risks and benefits. At the time point described in the vignette, the family would like to prolong life as long as possible. However, this is the first time withdrawal of LSMT has been introduced. For that reason, a multidisciplinary approach outlining the status and needs of the child and the family may effectively inform the medical decision makers. Physicians are not obligated to provide any treatment thought to be unlikely to benefit the patient. Even though decisions to actively withdraw LSMT should be made with the family's agreement, physicians cannot be forced to provide futile care. Children should generally be allowed to participate in their own medical decision-making when possible, and mature and emancipated minors may be able to make their own decisions. Even though the family in this vignette believes the child would have wanted to live as long as possible, she had not likely reached the cognitive status to have made that determination in an informed manner. Lastly, decisions for children who have not reached that capacity should be made based on the best interest standard, which provides that decisions should be based on the relative risks and benefits of the treatment to the child. Benefits to children can include prolongation of life beyond simple biological existence without consciousness, improved quality of life, increased physical pleasure, increased emotional enjoyment, and increased intellectual satisfaction.

Although ethics committees can be helpful in informing hospital policies and to give guidance in unusual circumstances, the scenario in the vignette has not yet reached that point. The medical team has introduced the idea of withdrawal of LSMT for the first time. Obtaining a cerebral blood flow scan can be helpful in the diagnosis of brain death if the clinical examination is equivocal, but the child does not meet brain death criteria because breathing over the ventilator requires brainstem activity. To proceed with invasive therapies in a patient who has a poor chance of any meaningful neurologic outcome is futile care. Placing a dialysis catheter with the intention of performing dialysis may prolonging life, but it is an invasive therapy that would lead to futile care. Although removal of the endotracheal tube and withdrawal of LSMT is reasonable, the medical team should provide adequate time for the family to make informed decisions. At the moment of the vignette, the family wishes to continue aggressive therapies. Providing them more

information regarding the risks and benefits of the options and adequate time to consider the options would most likely lead to decisions made in the best interest of the child and family.

For this girl who has suffered a devastating, irreversible neurologic injury whose parents are not willing to withdraw LSMT the first time the option is introduced, a multidisciplinary meeting may best inform the family and provide more time for them to make a decision in her best interest.

PREP Pearls

- Physicians are not obligated to provide futile care, which includes prolonged or invasive therapies on patients who are not likely to derive benefit from them.
- Withdrawal of life-sustaining medical therapies should occur with agreement from the medical decision makers, after they have been allowed adequate time to make a fully informed decision.

ABP Content Specifications(s)

- Recognize and apply ethical principles when caring for a patient who is in a persistent vegetative state
- Recognize and apply ethical principles regarding the issue of medical futility
- Recognize and apply ethical principles involving palliative care and pain management
- Recognize and apply ethical decision-making when caring for critically ill patients

Suggested Readings

- Burns JP, Mitchell C, Outwater KM, et al. End-of-life care in the pediatric intensive care unit after the forgoing of life-sustaining treatment. Crit Care Med. 2000;28(8):3060-3066.
- Committee on Bioethics. Guidelines on forgoing life-sustaining medical treatment. Pediatrics. 1994;93(3):532-536. http://pediatrics.aappublications.org/content/93/3/532.
- Mercurio MR, Maxwell MA, Mears BJ, Ross LF, Silber TJ. American Academy of Pediatrics Policy Statements on Bioethics. Pediatr Rev. 2008;29(3):e15-e22. doi: http://dx.doi.org/10.1542/pir.29-3-e15.
- Zawistowski CA, DeVita MA. A descriptive study of children dying in the pediatric intensive care unit after withdrawal of life-sustaining treatment. Pediatr Crit Care Med. 2004;5(3):216-223. doi: http://dx.doi.org/10.1097/01.PCC.0000123547.28099.44.

Question 32

A 14-year-old adolescent is seen for a routine preparticipation evaluation to play volleyball. She has no significant past medical history and has no current concerns. On physical examination, she has multiple enlarged cervical lymph nodes (1 to 2 cm) on the left side of her neck that are firm and fixed. She also has a 3 to 4 cm, firm, fixed anterior neck mass just left of midline (Item Q32). The remainder of the physical examination is unremarkable.

Item Q32: Neck mass as seen for the adolescent described in the vignette. Reprinted with permission from Osipoff JN, Wilson TA. Consultation with the specialists. Pediatr Rev. 2012;33(2):75-81.

Of the following, the test MOST likely to establish the diagnosis is

A. complete blood cell count
B. computed tomography of the neck
C. fine-needle aspiration of the neck mass
D. thyroid-stimulating hormone level
E. ultrasonography of the thyroid gland and regional lymph nodes

Correct Answer: C
The patient described in the vignette has papillary thyroid carcinoma (PTC) presenting with a thyroid nodule and associated cervical lymphadenopathy. While ultrasonography is the preferred imaging modality to characterize thyroid nodules and risk of malignancy, the diagnosis of thyroid cancer can not be made by appearance on ultrasonography alone. In this case, ultrasonography of the thyroid gland and regional lymph nodes is indicated, but will not make a diagnosis. Due to size greater than 1 cm, the nodule in the patient in this vignette warrants fine-needle aspiration under ultrasonographic guidance. This procedure is the gold standard for preoperative diagnosis of thyroid cancer and is the best option to establish a diagnosis in this patient. Indications for ultrasonography-guided fine-needle aspiration include a nodule 1 cm or greater or a nodule 0.5 cm or greater if other risk factors for malignancy are present on history, physical examination, or ultrasonography. The final diagnosis requires surgical pathology. A thyroid-stimulating hormone level is also indicated in the evaluation of a thyroid nodule to determine if the nodule is hyperfunctioning, but is usually normal in PTC and would not be diagnostic. Computed tomography of the neck can be useful to evaluate potential neck metastasis, but would not be diagnostic of PTC and could delay I-131 therapy because of the iodine load of the contrast material. A complete blood cell count would not likely provide additional diagnostic information.

Papillary thyroid carcinoma is the most common thyroid cancer type in both children and adults. Papillary thyroid carcinoma is more aggressive in childhood compared to adulthood, but survival is better. Follicular thyroid carcinoma and medullary thyroid carcinoma are rare in pediatric patients. Medullary thyroid carcinoma has 100% penetrance in those with multiple endocrine neoplasia (MEN) types 2A and 2B, which are inherited in an autosomal dominant pattern. Pheochromocytoma and hyperparathyroidism are other components of MEN, in addition to a Marfanoid body habitus and mucosal neuromas in type 2B.

As in the patient described in the vignette, an incidentally found thyroid nodule is a common presentation of thyroid cancer in children. About 25% of thyroid nodules in children and adolescents are malignant, versus about 5% in adults. Nodules that are firm, irregular, fixed, or show microcalcifications or irregular margins on ultrasonography confer increased risk for malignancy. Abnormal cervical lymph nodes on palpation or by ultrasonography suggest regional metastases to the neck. Thyroid cancer can also present with abnormal cervical lymphadenopathy without an obvious palpable thyroid nodule. In this situation, diffuse thyroid enlargement may be present.

When evaluating a patient with a thyroid nodule, important aspects of the history include radiation exposure to the thyroid, such as treatment for childhood cancer, and a family history of thyroid cancer or other features of MEN. Careful physical examination of the thyroid and cervical lymph nodes should be undertaken, as well as for findings consistent with MEN2B. Further evaluation should include a thyroid-stimulating hormone level, thyroid ultrasonography, and referral to a subspecialist experienced in the evaluation and management of pediatric thyroid nodules

PREP Pearls

- Exposure to ionizing radiation to the thyroid is a risk factor for development of thyroid carcinoma.
- Thyroid nodules 1 cm or greater, or 0.5 cm or greater if other risk factors for malignancy are present, should be evaluated by ultrasonography-guided fine-needle aspiration.
- Medullary thyroid carcinoma has 100% penetrance in those with multiple endocrine neoplasia types 2a and 2b.

ABP Content Specifications(s)

- Recognize the clinical features associated with thyroid carcinoma

Suggested Readings

- Francis GL, Waguespack SG, Bauer AJ, et al. Management guidelines for children with thyroid nodules and differentiated thyroid cancer. Thyroid. 2015;25(7):716-759. doi: http://dx.doi.org/10.1089/thy.2014.0460.
- Jatana KR, Zimmerman D. Pediatric thyroid nodules and malignancy. Otolaryngol Clin North Am. 2015;48(1):47-58. doi: http://dx.doi.org/10.1016/j.otc.2014.09.005.
- Osipoff JN, Wilson TA. Consultation with the specialist: thyroid nodules. Pediatr Rev. 2012;33(2):75-82. doi: http://dx.doi.org/10.1542/pir.33-2-75.

Question 33

You are called to the newborn nursery to evaluate a neonate born with localized bullae and erosion of the skin on the feet and lower extremities (Item Q33).

Item Q33: Findings for the neonate described in the vignette. Reprinted with permission from Johr RH, Schachner LA. Neonatal dermatologic challenges. Pediatr Rev.1997; 18(3):86-94

This appropriate-for-gestational-age male neonate was delivered at term by spontaneous vaginal delivery to a 25-year-old gravida 2 para 1 mother. The baby's mother received routine prenatal care without complications. Spontaneous rupture of membranes with clear fluid occurred 12 hours before delivery. The mother had no signs or symptoms of chorioamnionitis. Other than the skin lesions, the neonate is well appearing. On physical examination, his temperature is 37°C, heart rate is 140 beats/min, and respiratory rate is 50 breaths/min. There is no abnormality of the mucous membranes or nails.

Of the following, the test MOST likely to confirm your suspected diagnosis is a/an:

A. anti-Ro/SSA testing
B. Darier sign
C. Gram stain of bullous fluid
D. polymerase chain reaction for herpes simplex virus DNA
E. skin biopsy of a bullous lesion

Correct Answer: E
The newborn in this vignette has lesions typical of epidermolysis bullosa (EB). Skin biopsy of a bullous lesion is the test most likely to confirm the suspected diagnosis. Epidermolysis bullosa should be suspected in neonates with blistering lesions or skin erosions without other etiology. It is important to distinguish the clinical findings associated with EB from other conditions; therefore, a comprehensive examination is imperative. The maternal, obstetric, and family history may offer important information toward identifying the diagnosis.

Epidermolysis bullosa is a heterogeneous group of inherited disorders with epithelial fragility, characterized by bullous lesions that develop spontaneously or in response to mild or moderate trauma. Bullae are defined as blistering lesions 0.5 to 1 cm in diameter. The overall incidence of EB is 1 in 50,000 births. Neonates typically present with localized absence of skin, usually of the lower extremities. Onset in infancy or childhood presents with recurrent blistering or skin erosions.

The major types of EB are identified based on the structural level of skin cleavage. In EB simplex, blistering occurs in the epidermis and healing occurs without scarring. In junctional EB, blistering occurs in the lamina lucida of the dermal-epidermal junction and leads to atrophic scarring. The cleavage plane in dystrophic EB is below the lamina densa in the papillary dermis and also leads to scarring. More than 30 subtypes have been defined. Skin biopsy of an induced blister with examination by immunofluorescence microscopy is the key to diagnosis.

The newborn in this vignette most likely has EB simplex, localized, the most common subtype of EB. In this subtype, the lesions are mainly limited to involvement of the palms and soles. Although clinical onset is usually at birth or during early infancy, lesions may not appear until adolescence or early adulthood. Bullae occur with mild-to-moderate frictional trauma and heal without scarring. There is mild or no mucosal involvement (25%), and nail involvement is rare. The course of disease is chronic; blistering tends to decrease with age, reticulated pigmentation may occur on the arms and trunk, and hyperhidrosis is common. The inheritance pattern is autosomal dominant. Lifespan is usually normal.

The differential diagnosis of bullous lesions in a newborn includes several potentially serious infectious and noninfectious conditions. Maternal history may be helpful in making the diagnosis, but not conclusive. The rash of neonatal lupus erythematosus is characterized by scaly atrophic plaques that may occur in conjunction with cardiac symptomatology, most commonly congenital heart block. Anti-Ro/SSA and anti-La/SSB testing may provide a diagnosis in these cases. Darier sign, the classic finding in cutaneous mastocytosis, is the development of localized urticaria, erythema, or bullae after rubbing, scratching, or stroking the skin or skin lesions that are heavily infiltrated with mast cells. The presentation of impetigo neonatorum ranges from bullous impetigo to scalded skin syndrome. Impetigo neonatorum may occur as early as the second or third day after birth, with vesicles, pustules, or bullae on a normal or erythematous base. Bullae are typically tense and leave a red, denuded, oozing area when ruptured. Gram stain

of bullous fluid, typically demonstrating Staphylococcus aureus, aids in the diagnosis of these cases. Grouped vesicles, crusts, and erosions on an erythematous base suggest herpes simplex virus, and a DNA polymerase chain reaction test will confirm the diagnosis.

PREP Pearls

- Epidermolysis bullosa (EB) should be suspected in neonates presenting with blistering lesions or skin erosions without other etiology.
- The major types of EB are identified based on the structural level of skin cleavage.
- Skin biopsy of an induced blister with examination by immunofluorescence microscopy is the key to diagnosis of EB.

ABP Content Specifications(s)

- Recognize the clinical findings associated with epidermolysis bullosa

Suggested Readings

- Johr RH, Schachner LA. Neonatal dermatologic challenges. Pediatr Rev. 1997;18(3):86-94. doi: http://dx.doi.org/10.1542/pir.18-3-86.
- Paller AS, Mancini AJ. Bullous disorders of childhood. Hurwitz Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood and Adolescence. 4th ed. Philadelphia, PA: Saunders Elsevier; 2011:303-320.

Question 34

A couple whose first child has trisomy 21 presents to your office with their newborn who also has physical features suggestive of trisomy 21, including epicanthal folds, upslanting palpebral fissures, a flat midface, small low-set ears, short neck, protruding tongue, and a left transverse palmar crease. Rapid fluorescence in situ hybridization analysis confirms trisomy 21. Family history reveals a maternal second cousin with trisomy 21 as well. The newborn's karyotype confirms the presence of a Robertsonian translocation between chromosomes 14 and 21. The parents ask about the risk of trisomy 21 occurring in their next pregnancy. You counsel the parents about the recurrence risk, as it appears likely the translocation is inherited from the mother.

Of the following, the MOST accurate response regarding recurrence risk for Down syndrome from this type of translocation would be

A. higher if inherited from the mother
B. lower if inherited from the mother
C. risk increases with advanced maternal age
D. 50% with each live birth
E. 100% with each live birth

Correct Answer: A

The recurrence risk for trisomy 21 is higher in a subsequent pregnancy if the translocation is inherited from the mother. A carrier of a Robertsonian translocation (Item C34) involving the 14 and 21 chromosomes has only 45 chromosomes. Chromosomes 14 and 21 are absent and are replaced by the translocation chromosome. There are 6 possible outcomes in this situation for a gamete and 3 of the 6 are not viable for live offspring. The 3 remaining situations that can result in live offspring include the following: normal, balanced translocation carrier, or unbalanced translocation carrier with trisomy 21. In theory, one would think the recurrence risk would be 33% regardless of the parent from whom the infant inherits it, but it is not. Numerous population studies have confirmed that the recurrence risk for trisomy 21 in this situation is dependent on which parent has the balanced translocation. If inherited from the mother, the risk is 10% to 15%. If inherited from the father, the risk is 1% to 2%. Importantly, the risk of trisomy 21 caused by translocation or partial trisomy is unaffected by maternal age.

If a parent has a 21:21 balanced translocation, it is thought to originate as an isochromosome. This is a chromosome produced by transverse splitting of the centromere so that both arms are from the same side of the centromere (either two short arms [p] or two long arms [q]). This scenario has 2 possible outcomes, a chromosome with a double dose of chromosome 21 genetic material or a complete lack of chromosome 21 genetic material, which is not viable. Therefore, the chance of recurrence if the parent is a 21:21 balanced translocation carrier is 100%. It is therefore important to confirm the etiology when a newborn presents with trisomy 21. A rapid fluorescence in situ hybridization analysis may be used initially as a relatively fast diagnostic tool for suspected trisomy 21, but it must be followed by karyotyping for etiologic diagnosis and recurrence risk. If karyotyping reveals an unbalanced translocation as the reason for the trisomy 21, then cytogenetic analysis of both parents is recommended to determine the recurrence risk.

It is widely recognized that in cases of trisomy 21 caused by 3 complete copies of chromosome 21, the risk increases with maternal age, most significantly after 35 years of age. If a woman younger than 35 years of age has a child with trisomy 21 resulting from 3 complete copies of chromosome 21, her recurrence risk for another child with trisomy 21 is 1%.

PREP Pearls

- The risk for trisomy 21 with a Robertsonian translocation 14:21 inherited from an infant's mother is 10% to 15%, but only 1% to 2% if inherited from the father.
- The recurrence risk for an unbalanced translocation, if inherited, is unaffected by parental age.
- Most cases of trisomy 21 result from meiotic nondisjunction yielding 3 complete copies of chromosome 21, rather than a translocation. This risk increases with maternal age, most significantly after age 35 years

ABP Content Specifications(s)

- Understand the risk factors of having another child with trisomy 21 when the mother is a balanced translocation carrier

- Understand the risk factors associated with subsequent pregnancies when an infant is born with a translocation chromosome abnormality

Suggested Readings

- Epstein CJ. Down syndrome (trisomy 21). In: Valle D, Beaudet AL, Vogelstein B, et al, eds. The Online Metabolic and Molecular Bases of Inherited Disease. New York, NY: McGraw-Hill; 2016.
- Ludman MD, Gilbert F, Hirschhorn K. Risk of recurrence of chromosomal abnormalities. Pediatr Rev. 1984;6(5):141-149. doi: http://dx.doi.org/10.1542/pir.6-5-141.
- Rare Chromosome Disorder Support Group. Robertsonian translocations. Rare Chromosome Disorder Support Group website. http://www.rarechromo.org/information/other/robertsonian%20translocations%20ftnw.pdf.

Question 35

A 14-year-old adolescent girl presents to your office with a 2-week history of a white, malodorous vaginal discharge. She had menarche at 12 years of age and her last menstrual period was 3 weeks ago. She states that she is not sexually active. On physical examination, you note a milky, white vaginal discharge, with an otherwise normal examination. You suspect that she has bacterial vaginosis.

Of the following, the finding that BEST supports your suspected diagnosis is a

A. Gram stain showing gram-negative diplococci
B. negative whiff test
C. Nugent score of 3
D. vaginal pH of less than 4.0
E. wet mount with greater than 20% clue cells

Correct Answer: E
Bacterial vaginosis (BV) accounts for approximately 40% to 50% of all cases of symptomatic vaginal discharge in women of reproductive age. Bacterial vaginosis is characterized by an overgrowth of anaerobic bacteria, particularly Gardnerella vaginalis, which replace the normal vaginal flora, Lactobacillus species. Clinical symptoms of BV typically include a thin, homogenous white-gray malodorous, "fishy," vaginal discharge. Less commonly, pruritus and vaginal or vulvar erythema and irritation may be present. Many females with BV may be asymptomatic. The relationship between sexual activity and BV is not clearly understood. Although BV is more common among sexually active women, it has been reported among those who have never had sex.

Bacterial vaginosis can be diagnosed clinically using the Amsel criteria, which requires the presence of 3 of the following:

1. homogeneous, thin, white discharge that adheres to the vaginal walls
2. greater than 20% clue cells on microscopy
3. vaginal pH greater than 4.5
4. release of a fishy amine odor with the addition of 10% potassium hydroxide to a drop of vaginal discharge (ie, positive whiff test)

Bacterial vaginosis can also be diagnosed with the Gram stain using the Nugent scoring system, which assesses for the presence of large gram-positive rods, small gram-variable rods, and curved gram-variable rods. A Nugent score of 7 to 10 shows a few lactobacilli and a predominance of Gardnerella/Bacteroides and curved gram-negative rods and is consistent with BV.

The presence of gram-negative diplococci would be suggestive of Neisseria gonorrhoeae.

The recommended treatment regimen for BV, according to the 2015 Sexually Transmitted Diseases Treatment Guidelines published by the US Centers for Disease Control and Prevention, is metronidazole 500 mg orally twice a day for 7 days or metronidazole gel 0.75%, 5 g intravaginally once a day for 5 days or clindamycin cream 2%, or 5 g intravaginally at bedtime for 7 days.

PREP Pearls

- Bacterial vaginosis accounts for approximately 40% to 50% of all cases of symptomatic vaginal discharge among women of reproductive age.
- Bacterial vaginosis can be diagnosed clinically using the Amsel criteria by the presence of 3 of the following:
- homogeneous, thin, white discharge that adheres to the vaginal walls
- greater than 20% clue cells on microscopy
- vaginal pH greater than 4.5
- release of a fishy amine odor with the addition of 10% potassium hydroxide to a drop of vaginal discharge (ie, positive whiff test)

ABP Content Specifications(s)

- Recognize the clinical findings associated with bacterial vaginosis

Suggested Readings

- Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the United States, 2001-2004: associations with symptoms, sexual behaviors, and reproductive health. Sex Transm Dis. 2007;34(11):864-869. doi: http://dx.doi.org/10.1097/OLQ.0b013e318074e565.
- Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. J Clin Microbiol. 1991;29(2):297-301. http://jcm.asm.org/content/29/2/297.long.
- O'Brien G. Bacterial vaginosis. Pediatr Rev. 2008;29(6):209 -211. doi: http://dx.doi.org/10.1542/pir.29-6-209.
- Sha BE, Chen HY, Wang QJ, Zariffard MR, Cohen MH, Spear GT. Utility of Amsel criteria, Nugent score, and quantitative PCR for Gardnerella vaginalis, Mycoplasma hominis, and Lactobacillus spp. for diagnosis of bacterial vaginosis in human immunodeficiency virus-infected women. J Clin Microbiol. 2005;43(9):4607-4612. doi: http://dx.doi.org/10.1128/JCM.43.9.4607-4612.2005.
- Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015;64(RR03):1-137. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6403a1.htm.

Question 36

An 8-year-old boy is brought to your office for a health supervision visit. His parents inform you that he was recently evaluated by his school and determined to qualify for an Individualized Education Program under intellectual disability. They have brought his aptitude test assessment report that shows a verbal IQ score of 63, performance IQ score of 65, and full scale IQ of 64. His adaptive skill scores are 65 in communication, 62 in daily living skills, 67 in motor skills, and 66 in socialization. The parents would like to know what to expect for his future as an adult.

Of the following, you would tell them that their son will MOST likely

A. be employable with intermittent support
B. read at a middle school grade level
C. require an adult residential facility
D. require frequent supervision for safety
E. require support for basic self-care skills at home

Correct Answer: A

Most measures of cognitive and adaptive skills have a mean of 100 and a standard deviation (SD) of 15. Scores at least 2 SDs below the mean (< 70) in both cognitive and adaptive measures are in the intellectual disability (ID) range. The levels of severity correspond to the number of SDs from the mean: mild (2 to 3 SDs; score of 55 to 70), moderate (3 to 4 SDs; score of 40 to 55), severe (4 to 5 SDs; score of 25 to 40), and profound (> 5 SDs; score < 25). The patient in this vignette has scores that are between 2 to 3 SDs below the mean on both measures of intelligence and adaptive functioning, placing him in the mild range of ID. People with mild ID can be employed with possible occasional need for support.

Intellectual disability, previously known as mental retardation, is a chronic condition with onset during the developmental period. Significant impairment in both cognitive abilities and adaptive functioning are required for diagnosis.

Cognitive abilities include the ability to reason, plan, solve problems, think abstractly, learn, and use appropriate judgment. IQ tests compare an individual's performance on standardized tests of cognitive abilities (eg, verbal, visual-spatial, problem-solving) with same-age peers. Commonly used IQ tests include the Wechsler intelligence scales (eg, Wechsler Preschool and Primary Scale of Intelligence [2.5-7.5 years], Wechsler Intelligence Scale for Children [6-16 years], Wechsler Adult Intelligence Scale [16-90 years]). Global developmental delay may be a more appropriate term to use until 5 years of age, when IQ tests become more reliable and predictive.

Adaptive skills are those that allow a person to self-manage and perform everyday tasks for independent living in the areas of communication, interpersonal relationships, self-care, home and community living, health, safety, recreation, work, and functional academics (eg, money management). Adaptive functioning can be divided into the conceptual domain (eg, reasoning, practical knowledge), social domain (eg, social judgment, interpersonal communication skills), and practical domain (eg, personal care, vocational skills, accessing transportation). It is measured by standardized tests such as the Vineland Adaptive Behavior Scales and the Adaptive Behavior Assessment System. For a diagnosis of ID, at least 1 domain is impaired such that support is needed for the individual to function.

Test scores have been de-emphasized in the latest version of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. IQ test scores have been removed from the criteria, but are still considered important approximations of conceptual functioning. Adaptive functioning in real-life situations does not always correspond with intellectual capacity; therefore, clinical assessment with a greater focus on adaptive functioning has been stressed. Severity is determined by deficits in adaptive functioning, and treatment plans should be developed to address those needs.

The prevalence of ID is approximately 1% to 2%. The majority (85%) of those with ID have mild ID. Children with mild ID are typically identified when they are unable to keep up academically in school. They can achieve academic skills to the sixth grade level. Adults with mild ID can live and work independently with some possible need for intermittent support.

Children with moderate ID (10% of those with ID) may learn up to the third grade level, but as adults, will require support and supervision for work and daily living. Children with more severe forms of ID are typically identified in the first few years after birth due to delays in motor and language development. They require assistance and supervision for their self-care, daily needs, and safety during childhood and adulthood. Item C36 outlines expectations for adaptive function with different levels of ID.

Item C36. Levels of Intellectual Disability and Expectations for Adaptive Function.

Level of ID	Self-help Skills	Academic Skills	Living Arrangements	Employment
Mild	Independent in personal care and activities of daily living	Up to sixth grade; some difficulties with planning and money management	Independent living with possible need for intermittent support	Independent employment with possible need for intermittent support
Moderate	Can care for personal needs and activities of daily living, but often requires prompts or reminders	Up to third grade; difficulty understanding time and money	Supportive living such as in a group home in the community	Supported, supervised unskilled or semiskilled work
Severe	Needs support for personal care and activities of daily living	Limited; possible recognition of critical words (eg, stop)	Needs supervision at all times	Sheltered work may be possible with ongoing assistance
Profound	Dependent on others for personal care and activities of daily living	May use objects in a goal-directed fashion	Needs nursing care	Typically not employable

Courtesy of Y. Liu

Expectations for the 8-year-old boy in this vignette with mild ID are independence in his living and employment circumstances, with some occasional assistance needed when there are special circumstances or challenges. He would read up to the sixth grade level and be able to accomplish his daily living and self-care tasks without need for support or supervision for his safety. The other options presented are typical of people with more severe levels of ID.

Recognizing the potential needs of a child with ID according to the severity level of his ID and his deficits in adaptive functioning allows the primary care provider to engage parents in a discussion about the child's future. The earlier that support can be given to developing communication, learning, and adaptive skills, the better the progress towards maximizing the child's present and future independence.

PREP Pearls

- Significant impairment in both cognitive abilities and adaptive functioning are required for diagnosis of intellectual disability (ID).
- Most measures of cognitive and adaptive skills have a mean of 100 and a standard deviation (SD) of 15. Scores at least 2 SDs below the mean (< 70) in both cognitive and adaptive measures are in the ID range.
- The majority (85%) of those with ID have mild ID. Children with mild ID are typically identified when they are unable to keep up academically in school.

- Adaptive functioning in real-life situations does not always correspond with intellectual capacity. Severity is determined by deficits in adaptive functioning and treatment plans should be developed to address those needs.

ABP Content Specifications(s)

- Distinguish between mild and moderate intellectual disabilities with regard to the potential for educational and independence/vocational achievement

Suggested Readings

- American Psychiatric Association. Neurodevelopmental disorders (intellectual disabilities). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA: American Psychiatric Publishing; 2013:33-41.
- Shea SE. Intellectual disability (mental retardation). Pediatr Rev. 2012;33(3):110-121. doi: http://dx.doi.org/10.1542/pir.33-3-110.

Question 37

A 16-year-old previously healthy adolescent girl is brought to the emergency department (ED) by emergency medical services after having a seizure during a concert she was attending with friends. Her friends reported to the paramedics that she "seemed normal" at the beginning of the concert. Approximately 1 hour later, she began to seem anxious, shaky, and confused. She complained of feeling "hot and sweaty." Thirty minutes after that, she seemed more confused, began shaking uncontrollably, and then fell to the ground, prompting her friends to call 911. When the paramedics arrived, she was actively seizing, with stiffening of all extremities, generalized twitching of her face, and drooling. Intravenous lorazepam was administered, with resolution of the seizure activity.

On arrival to the ED, the patient is breathing spontaneously, but is responsive only to painful stimuli. Her heart rate is 150 beats/min, blood pressure is 160/95 mm Hg, respiratory rate is 22 breaths/min, rectal temperature is 38.9°C, and pulse oximetry is 95% (room air). Her pupils are 5 mm in diameter, equal, and sluggishly reactive. Her skin is diaphoretic. There are no signs of traumatic injury on physical examination.

One of the patient's friends confided to the paramedics that "she may have tried some drugs" that a man at the concert had offered her.

Of the following, the substance MOST likely to be responsible for the symptoms and clinical findings in this patient is

A. ethanol
B. heroin
C. lysergic acid diethylamide (LSD)
D. marijuana
E. synthetic cathinone ("bath salt")

Correct Answer: E
The adolescent girl in the vignette presents with a constellation of findings including altered sensorium, tremulousness, tachycardia, hypertension, hyperpyrexia, mydriasis, diaphoresis, and generalized seizure activity following suspected exposure to an illicit substance. The substance most likely to be responsible for these findings is synthetic cathinone ("bath salt"), an amphetamine analog. All pediatric providers should recognize the major physiologic and behavioral consequences associated with amphetamine use, including the clinical findings associated with acute intoxication.

Historically, amphetamines have been utilized in medicine to treat conditions including nasal congestion, fatigue, narcolepsy, attention deficit/hyperactivity disorder, and obesity (to promote weight loss). Though they have played a significant role in medicine over the years, these substances have also had a long history of being abused in the United States and worldwide. Abuse of illicit amphetamine-like substances including methamphetamine, ecstasy (also known as 3,4-methylene-dioxymethamphetamine, or MDMA), and synthetic cathinones among US youth has been increasing in prevalence in recent decades. Specifically, abuse of synthetic cathinones (ie, "bath salts") emerged in Europe around 2009 and spread to the United States in 2010. These compounds are typically sold as tablets or white powders, marketed as "bath salts" or "plant food," in a variety of venues, including "head shops," gas stations, and convenience stores. Despite the disclaimer on their packaging that these substances are "not intended for human consumption," they are widely sold and used as "legal" drugs of abuse in the United States.

Amphetamines and amphetamine-like substances are potent activators of adrenergic receptors in both the central and peripheral nervous system. Signs of sympathetic hyperstimulation characterize amphetamine intoxication. These signs include tachycardia, hypertension, hyperpyrexia, mydriasis, and diaphoresis. Central nervous system effects may include anxiety, agitation, combativeness, and even seizures. Other clinical effects may include the musculoskeletal system (myoclonus, tremors), kidneys, and gastrointestinal system. In severe cases of amphetamine intoxication, lethal arrhythmias, hyperthermia, and intracranial hemorrhage may occur.

Clinical management of acute amphetamine intoxication should focus on supporting and protecting the airway, maintaining adequate ventilation and oxygenation, and ensuring adequate perfusion to the brain and other vital organs. While there is no specific antidote available to reverse amphetamine toxicity, benzodiazepines such as diazepam or lorazepam are first line for treating psychomotor agitation and seizures arising from amphetamine toxicity; these agents are also beneficial in alleviating amphetamine-induced hypertension and hyperthermia. Activated charcoal is effective at binding amphetamines and amphetamine-like stimulants and should be administered within the first 1 to 2 hours following a significant oral amphetamine ingestion, provided that the patient's airway is adequately protected.

Ethanol is a central nervous system (CNS) depressant that may initially result in exhilaration and loss of inhibition, but causes ataxia, slurred speech, lack of coordination, somnolence, and eventually extreme lethargy and coma as serum concentrations rise. Patients with acute ethanol intoxication would typically display CNS depression rather than the CNS excitation displayed by the patient in the vignette. Furthermore, hypertension and hyperpyrexia are not typical clinical features of ethanol intoxication.

Classic clinical features of intoxication with heroin, an illicit opioid, would include central nervous system depression, respiratory depression, and miosis ("pinpoint pupils"). The patient in the vignette does not exhibit any of these clinical findings.

Intoxication with lysergic acid diethylamide (LSD) may produce clinical manifestations that closely resemble those of amphetamine intoxication. Patients may display signs of sympathetic stimulation, including mydriasis, hypertension, tachycardia, and hyperpyrexia, following ingestion of LSD. However, exposure to LSD typically results in a psychedelic state, in which patients experience euphoria, visual perceptual distortions (hallucinations), an altered sense of time, and even psychosis following ingestion.

While intoxication with marijuana may result in the clinical finding of altered sensorium and may also cause tachycardia and hypertension, the degree of CNS agitation and the ultimate seizure activity displayed by the patient in the vignette would not be expected sequelae of marijuana intoxication.

PREP Pearls

- Signs of sympathetic hyperstimulation characterize amphetamine intoxication. These signs include tachycardia, hypertension, hyperpyrexia, mydriasis, and diaphoresis. Central nervous system effects may include anxiety, agitation, combativeness, and seizure activity.
- Clinical management of acute amphetamine intoxication should focus on supporting and protecting the airway, maintaining adequate ventilation and oxygenation, and ensuring adequate perfusion to the brain and other vital organs.
- Benzodiazepines such as diazepam or lorazepam are first line for treating psychomotor agitation and seizures arising from amphetamine toxicity; these agents are also beneficial in alleviating amphetamine-induced hypertension and hyperthermia.
- Activated charcoal is effective at binding amphetamines and amphetamine-like stimulants and should be administered within the first 1 to 2 hours following a significant oral amphetamine ingestion, provided that the patient's airway is adequately protected.

ABP Content Specifications(s)

- Recognize the major behavioral consequences of amphetamine use/abuse
- Identify the major physiologic consequences associated with opioid use/abuse, including those associated with the various means of administration
- Recognize the clinical findings associated with an acute amphetamine intoxication, and manage appropriately

Suggested Readings

- Arnold TC, Ryan ML. Acute amphetamine and synthetic cathinone ("bath salt") intoxication. UpToDate. Available online only with subscription.
- Capriola M. Synthetic cathinone abuse. Clin Pharmacol. 2013;5:109-115. doi: http://dx.doi.org/10.2147/CPAA.S42832.
- Spiller HA, Ryan L, Weston RG, Jansen J. Clinical experience with and analytical confirmation of "bath salts" and "legal highs" (synthetic cathinones) in the Unites States. Clin Toxicol (Phila). 2011;49(6):499-505. doi: http://dx.doi.org/10.3109/15563650.2011.590812.
- Stremski E, Gummin DD. Amphetamines. In: Erickson TB, Ahrens WR, Aks SE, Baum CR, Ling LJ, eds. Pediatric Toxicology: Diagnosis and Management of the Poisoned Child. New York, NY: McGraw-Hill; 2004: 375-382.

Question 38

A 5-year-old girl presents to your clinic for evaluation of fever for 7 days. She recently returned from Pakistan where she travelled with her parents to visit family. She did not receive pre-travel vaccinations. Vital signs show a temperature of 38.7°C, respiratory rate of 30 breaths/min, heart rate of 120 beats/min, and blood pressure of 105/65 mm Hg. On physical examination, she has abdominal tenderness and hepatosplenomegaly. Laboratory data are shown:
Laboratory test

Laboratory test	**Result**
White blood cell count	17,000/μL (17.9×10^9/L)
Hemoglobin	9.2 g/dL (92 g/L)
Platelet count	87×10^3/μL (87×10^9/L)
Segmented neutrophils	80%
Lymphocytes	20%
Aspartate aminotransferase	230 U/L
Alanine aminotransferase	250 U/L

Of the following, the test that is MOST likely to establish the diagnosis in this child is

A. abdominal ultrasonography
B. blood culture
C. hepatitis panel
D. urine culture
E. viral nasal wash

Correct Answer: B
The study most likely to establish the diagnosis for the girl in this vignette is a blood culture. In a traveller returning from Pakistan, typhoid fever must be considered as an etiology, given that Salmonella typhi infections are endemic in resource-limited countries, especially in Asia. In typhoid fever, stool cultures are often negative, thus negative stool tests do not exclude this diagnosis.

Infections due to Salmonella typhi are distinct compared to nontyphoidal Salmonella infections. Nontyphoidal Salmonella typically cause enteritis, though invasive infections including bacteremia, osteomyelitis and meningitis can occur. In contrast, Salmonella typhi is more likely to cause invasive infections than enteritis. The main reservoirs for non-typhoidal Salmonella include birds, mammals, reptiles, or amphibians. Infections occur either via food contamination or direct contact with infected animals. In contrast, Salmonella typhi is identified only in human hosts.

Abdominal ultrasonography may reveal hepatosplenic enlargement in the setting of typhoid fever, among other etiologies of fever of unknown origin, though this would not specifically identify the diagnosis. In cases of fever of unknown origin suspected to be due to cat scratch disease, however, abdominal ultrasonography can aid with diagnosis, given that characteristic hepatosplenic lesions can often be seen.

Given that the child in the vignette has transaminitis, infection due to a hepatitis virus is a consideration. However, the clinical scenario is more fitting with typhoid fever given the prolonged fever and absence of emesis, diarrhea, and jaundice.

Urine should be evaluated in cases of fever of unknown origin, though there is nothing in this scenario to invoke the urinary tract. Likewise, the child in the vignette has not demonstrated respiratory symptomatology, therefore, a nasal wash for a virus is unlikely to prove useful.

Of note, the patient in this vignette should have received pre-travel vaccinations, including typhoid vaccine. While not completely protective, typhoid vaccine certainly enhances resistance against infection.

PREP Pearls

- Consider typhoid fever as an etiology in individuals that have travelled to resource-limited countries where Salmonella typhi infections are endemic.
- Nontyphoidal Salmonella infections typically cause enteritis and more rarely invasive infections, whereas Salmonella typhi is more likely to cause invasive infections than enteritis.
- Typhoid vaccine should be offered to patients traveling to endemic regions, as it enhances resistance against infection.

ABP Content Specifications(s)

- Understand the epidemiology of typhoidal and nontyphoidal Salmonella species
- Recognize the clinical features associated with typhoidal and nontyphoidal Salmonella infection

Suggested Readings

- American Academy of Pediatrics. Salmonella infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:695-702 .
- Christenson J. Salmonella infections. Pediatr Rev. 2013;34(9):375-383..

Question 39

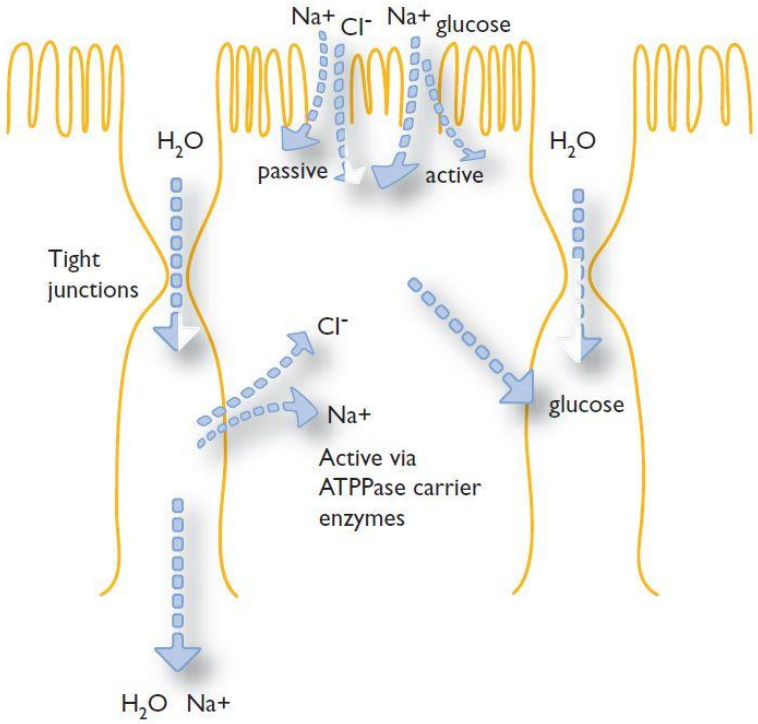
You are supervising a resident who is caring for a 3-year old boy who presented to your urgent care center. The boy's mother states that he was healthy until 2 days ago when he developed fever, nausea, vomiting, and diarrhea. His vomiting has decreased in the past 24 hours, but his diarrhea continues with 7 to 9 large, liquid bowel movements daily. The boy's temperature is 37.8°C, heart rate is 116 beats/min, and respiratory rate is 30 breaths/min. On physical examination, he is ill appearing, pale, and has tacky mucous membranes. The resident asks about the recommended approach to management of this child's hydration. The literature shows a clear advantage to oral rehydration. You discuss the mechanism of action of this treatment with the resident.

Of the following, the transporter that is MOST critical to this treatment's mechanism of action is

A. sodium bicarbonate
B. sodium fructose
C. sodium glucose
D. sodium potassium adenosine triphosphatase
E. sodium potassium chloride

Correct Answer: C

The mechanism of action of oral rehydration solutions (ORS) involves the sodium-glucose transporter, which cotransports one sodium with one glucose (Item C39A). Water then follows by diffusion because of the concentration gradient of the sodium. There are many versions of ORS, each varying in carbohydrate and electrolyte concentration. ORS are significantly better than other oral fluid options for rehydration because of the relatively low carbohydrate load and elevated sodium and potassium levels that maximize hydration while minimizing osmotic loads that drive diarrhea. Studies have demonstrated increased safety, more rapid recovery, and cost effectiveness with the use of ORS compared with intravenous fluid hydration. Mild to moderately dehydrated patients who are able to take in the fluid without emesis should receive ORS. Patients with diarrhea do well with ORS because of the low osmotic load and excellent absorption. Item C39B details the composition of ORS.



Item C39A: Mechanisms of water absorption in the intestinal mucosa Reprinted with permission from Yu CE, Lougee DA, Murno JR. Module 6. Dehydration and Diarrhea. In Children and Disasters. American Academy of Pediatrics. Elk Grove Village, IL 2011 (6):pg18

Item C39B. Composition of Oral Rehydration Solutions (ORS).

ORS	Carbohydrate (g/L)		Sodium mEq/L	Potassium mEq/L	Osmolarity mOsm/L
WHO	Glucose	20	90	20	310
WHO reduced osmolarity	Glucose	13.5	75	20	245
Pedialyte®	Glucose Fructose	25	45	20	250
Gatorade®	Fructose Sucrose Glucose	58	20	3	330
Apple juice	Fructose Sucrose Glucose	Variable	2	0	680
Water	None	0	0	0	0-18

Courtesy of C. Waasdorp Hurtado

The sodium potassium adenosine triphosphate transporter, also known as the Na+/K+ pump, actively pumps sodium out of, and potassium into, cells. Adenosine triphosphate is used to move both electrolytes against their concentration gradients.

The sodium potassium chloride (NKCC) transporter is a membrane transport protein with 2 forms that move sodium, potassium, and chloride in and out of the cell in the same direction. NKCC1 is found in all fluid-secreting organs, such as the kidney, where it helps in the reabsorption of sodium, potassium, and chloride. NKCC2 is found in nephrons in cells of the thick ascending limb of the loop of Henle, where it aids in the reabsorption of sodium.

The sodium bicarbonate transporter mediates the coupled movement of Na^+ and HCO_3^- across plasma membranes, and is vital in maintaining tissue pH levels.

Fructose transportation is typically independent of sodium, via the Glut-5 transporter.

PREP Pearls

- The sodium glucose transporter improves hydration through diffusion of water due to increased sodium concentration.
- Oral rehydration solutions (ORS) are the best rehydration products.
- Because of a low osmotic load and their electrolyte content, ORS help to minimize diarrhea and stabilize electrolyte levels.
- Oral rehydration solutions with low sodium levels are less effective.

ABP Content Specifications(s)

- Understand the role of oral rehydration solutions in the treatment of acute diarrheal dehydration
- Understand the differences between and the rationale for the composition of oral rehydration solutions

Suggested Readings

- Guarino A, Dupont C, Gorelov AV, et al.The management of acute diarrhea in children in developed and developing areas: from evidence base to clinical practice. Expert Opin Pharmacother. 2012;13(1):17-26. doi: http://dx.doi.org/10.1517/14656566.2011.634800.
- Rouhani S, Meloney L, Ahn R, Nelson BD, Burke TF. Alternative rehydration methods: a systematic review and lessons for resource-limited care. Pediatrics. 2011;127(3):e748-e757. doi: http://dx.doi.org/10.1542/peds.2010-0952.
- Unger CC, Salam SS, Sarker MS, Black R, Cravioto A, El Arifeen S. Treating diarrhoeal disease in children under five: the global picture. Arch Dis Child. 2014;99(3):273-8. doi: http://dx.doi.org/10.1136/archdischild-2013-304765.

Question 40

A 4-year-old boy presents to your office for evaluation of possible leg-length discrepancy. His mother noticed that his left knee seemed a little higher than the right when she was toweling him off after a bath. The boy's medical history is significant for Kawasaki disease at 18 months of age, and a left femur fracture at 2 years of age that was treated with cast immobilization. The boy's mother is concerned because a maternal uncle had a leg-length difference and walked with a limp. On physical examination, you measure from the anterior superior iliac crest to the medial malleolus and note that the left leg is 1 cm longer than the right. Hip range of motion is full and symmetric.

Of the following, the MOST accurate statement is that this physical finding likely

A. does not require follow-up evaluation
B. is the result of a genetic condition
C. is the result of the patient's history of femur fracture
D. is the result of the patient's history of Kawasaki disease
E. will require surgical intervention

Correct Answer: C
The boy in the vignette has a leg-length discrepancy that is most likely the result of posttraumatic overgrowth after his femur fracture. Overgrowth is most common in children between the ages of 4 and 7 years, with an average increase of 1 cm. Fractures of the femur have the highest risk of overgrowth. Although overgrowth typically occurs during the first 2 years after injury, affected children should be followed intermittently until growth is complete to make sure the leg-length discrepancy does not continue to increase. This child's length discrepancy is not currently an indication for surgery, but this could change as he grows. The boy in the vignette has no history or other indication of a genetic condition.

Kawasaki disease does not cause leg-length discrepancy. There are many causes of leg-length discrepancy. Congenital limb deficiencies (eg, fibular hemimelia), physeal damage caused by trauma or infection, vascular insufficiency, and neurologic conditions (eg, polio, cerebral palsy) can cause shortening of a limb.

Overgrowth syndromes (eg, Beckwith-Wiedemann), increased vascular perfusion after infection or with inflammatory arthritis, and posttraumatic overgrowth can cause lengthening of a limb. Idiopathic leg-length differences of 1 cm or more are present in one-quarter to one-third of the adult population.

Children and adolescents with leg-length discrepancy may exhibit alterations in gait. On physical examination, comparison of the distances from the anterior superior iliac spine to the ipsilateral medial malleolus on each leg can provide an estimate of the discrepancy. However, differences in muscle bulk, coronal plane alignment, and bone torsion can lead to inaccurate results. A scanogram, which includes simultaneous bilateral anteroposterior radiographs of the hips, knees, and ankles alongside a metal ruler, can provide more accurate measurement of limb-length discrepancy.

Limb-length discrepancy tends to increase proportionally with growth, for most etiologies. For example, a 3-year-old child with a 1-cm leg-length difference will likely exhibit a difference of close to 2 cm at skeletal maturity, when the limbs are twice as long. Discrepancies estimated to be less than 2 to 2.5 cm at skeletal maturity are generally managed with small shoe lifts. Children with leg-length discrepancy predicted to be between 2 and 5 cm at skeletal maturity are generally candidates for epiphysiodesis, stopping growth early in the long leg by putting small metal plates over the physes around the knee. For larger discrepancies, more complicated leg lengthening surgeries may be indicated. Because surgical intervention may eventually be needed, children with leg-length discrepancies should be assessed periodically until skeletal maturity.

PREP Pearls

- The risk of posttraumatic overgrowth is highest in children between the ages of 4 and 7 years with a history of femur fracture.
- Limb-length discrepancy tends to increase proportionally with growth.

ABP Content Specifications(s)

- Recognize the clinical findings associated with leg length discrepancy

Suggested Readings

- Halanski MA, Noonan KJ. Limb-length discrepancy. In: Weinstein SL, Flynn HM, eds. Lovell and Winter's Pediatric Orthopaedics. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1341-1387.
- Sarwark JF, LaBella CR. Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014: 650 pp.

Question 41

A 7-year-old healthy boy comes to your office for his annual well child visit. The parents have previously refused any vaccines, but are now requesting to have him vaccinated. The parents agree to vaccinate him "with everything that he needs."

Of the following, the vaccines MOST likely to be administered at this visit are

A. DTaP, hepatitis A, hepatitis B, IPV, MMR, varicella
B. DTaP, hepatitis A, hepatitis B, IPV, MMR, PCV13, varicella
C. Td, hepatitis A, hepatitis B, IPV, MMR, varicella
D. Tdap, hepatitis A, hepatitis B, IPV, MMR, varicella
E. Tdap, hepatitis A, hepatitis B, IPV, PCV13, varicella

Correct Answer: D

Of the options listed for the unimmunized 7-year-old boy in the vignette, the most appropriate immunizations for him to receive at this time are Tdap, hepatitis A, hepatitis B, IPV, MMR, and varicella. DTaP is not administered to patients older than 6 years of age; Tdap is used, as it has lower doses of diphtheria toxoid and acellular pertussis toxoid, which makes it less likely to cause adverse reactions in older children and adults. The PCV13 and Hib vaccines are not administered to healthy children after 59 months of age. The currently recommended immunization schedule for previously unimmunized children are shown in Item C41A and Item C41B.

Item C41A. Recommended Immunization Schedule For Previously Unimmunized Children 7 to 18 Years of Age.

Tdap	Unimmunized children or children who have not completed the DTaP series should receive Tdap as their first dose in the catch-up series; future doses to complete the series should be Td
Hepatitis A	2 doses required, separated by 6 months
Hepatitis B	3 doses required; the second dose must be at least 4 weeks from the first dose, and the third dose must be at least 8 weeks from the second dose and at least 16 weeks from the first dose
MMR	2 doses required, with the doses separated by at least 4 weeks
Varicella	2 doses required, with the doses separated by at least 12 weeks; if the child is 13 years of age or older, the doses may be separated by only 4 weeks
HPV	First dose may be given as early as 9 years of age; minimum of 4 weeks in between dose 1 and dose 2; minimum of 12 weeks in between doses 2 and 3; dose 3 must be at least 24 weeks after dose 1
MCV4	First dose at 11 to 12 years of age; requires a booster dose at 16 years of age; if the first dose is given at 13 to 15 years of age, the booster dose should be given at 16 to 18 years of age, with a minimum of 8 weeks between doses; if the first dose is given at 16 years of age or later, a booster dose is not required
IPV	Requires 3 doses, with at least 4 weeks between first dose and second dose; minimum of 6 months between second dose and third dose

Courtesy of D. DeBlasio

Item C41B. Recommended Immunization Schedule For Previously Unimmunized Children Younger Than 72 Months of Age.

DTaP	Can receive first DTaP dose as early as 6 weeks; should receive 3 doses separated by 4 weeks; minimum of 6 months between fourth and fifth dose; if fourth dose is given at 4 years of age or older, fifth dose is not needed
IPV	Can receive first IPV as early as 6 weeks; should receive 3 doses separated by at least 4 weeks; fourth IPV dose must be given at least 6 months after third dose at a minimum age of 4 years; if third dose is given at 4 years of age or older, fourth dose is not needed
Hepatitis A	Requires 2 doses, separated by 6 months; minimum age for the first dose is 12 months
Hepatitis B	Requires 3 doses; the second dose must be at least 4 weeks from the first dose, and the third dose must be at least 8 weeks from the second dose and at least 16 weeks from the first dose. The minimum age for the third dose is 24 weeks.
MMR	Requires 2 doses; the minimum age for the first dose is 12 months. The second dose recommended to be given at 4 to 6 years of age, must be least 4 weeks after the first dose.
Varicella	Requires 2 doses; the minimum age for the first dose is 12 months. The second dose recommended to be given at 4 to 6 years of age, must be at least 3 months after the first dose.
Rotavirus	Minimum age for first dose is 6 weeks; first dose must be administered by age 14 weeks and 6 days and series must be completed by age 8 months.
PCV13	Minimum age for the first dose is 6 weeks. The total number of doses and spacing of doses depends on the patient's age at the various doses. An infant may require as many as 4 doses if he/she receives 3 doses prior to the age of 12 months or as few as 1 dose if the first dose is given at age 24 months or older.
Hib	Minimum age for the first dose is 6 weeks. The total number of doses and spacing of doses depends on the patient's age at the various doses. An infant may require as many as 4 doses if he/she receives 3 doses prior to the age of 12 months or as few as 1 dose if the first dose is given at 15 months of age or older.

Courtesy of D. DeBlasio

PREP Pearls

- For children 7 years of age or older who are unimmunized or who have not completed the DTaP series, the first dose in the catch-up series should be Tdap.
- Hib and PCV13 vaccine are not routinely given to healthy children after 59 months of age.

ABP Content Specifications(s)

- Plan an immunization schedule for a child or adolescent who begins receiving immunizations late or whose immunizations are delayed

Suggested Readings

- American Academy of Pediatrics. Lapsed immunizations. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:37-38.
- US Centers for Disease Control and Prevention. Catch-up immunization schedule. US Centers for Disease Control and Prevention website. http://www.cdc.gov/vaccines/schedules/hcp/imz/catchup.html. Updated January 28, 2015.

Question 42

A previously well 16-year-old adolescent girl who is a varsity athlete presents to the emergency department with new-onset exercise intolerance. Four days earlier, she competed successfully at a high school track meet. Over the next few days, her stamina during practice decreased and on the day of presentation, she became winded while climbing a flight of stairs. She has no other symptoms. Her last menstrual cycle ended 2 weeks ago and was normal in duration and intensity. She denies having seen any blood in her urine or stool. On physical examination, she is afebrile, with a heart rate of 123 beats/min and a blood pressure of 110/76 mm Hg. She appears pale and fatigued, has slightly icteric sclera, and a grade 2/6 systolic murmur. Her examination is otherwise unremarkable.

Laboratory results are shown:

Laboratory Test	Patient Result
White blood cell count	11,000/μL (11×10^9/L)
Hemoglobin	3.9 g/dL (39 g/L)
Mean corpuscular volume	95 fL
Platelet count	455×10^3/μL (455×10^9/L)
Reticulocyte count	35%

Of the following, the MOST appropriate next steps in management are to perform

A. a chest radiograph, an echocardiogram, and a serum B-type natriuretic peptide level, and start a milrinone drip
B. a direct antibody test, start prednisone, and transfuse the least incompatible packed red blood cell unit
C. flow cytometry testing for lymphoblasts, start allopurinol and intravenous fluids at twice maintenance
D. hemoglobin electrophoresis, start penicillin, and transfuse a sickle-negative packed red blood cell unit
E. a stool guaiac test and consult gastroenterology to perform colonoscopy

Correct Answer: B
Autoimmune hemolytic anemia (AIHA) is a true hematologic emergency. Rapid diagnosis and initiation of therapy can be life-saving. The adolescent girl in the vignette presents with signs and symptoms that strongly suggest AIHA. In particular, her tachycardia, fatigue, and exercise intolerance are likely due to hypoxemia of an acute onset. The laboratory results show a severe, normocytic anemia with a marked reticulocytosis, suggesting a destructive process rather than a red blood cell (RBC) production failure. The reticulocyte count increases as the renal oxygen tension sensors detect a drop in oxygen-carrying capacity caused by the anemia. In response, they upregulate hypoxia-inducible factors, which in turn upregulate the production of erythropoietin, driving erythropoiesis.

The most appropriate next steps in her care would be to order a direct antibody test (DAT) and begin emergent management. The DAT will be positive if there are circulating antibody-coated RBCs. It is important to note that in instances of brisk hemolysis from AIHA, the antibody-coated cells may be destroyed so quickly that the DAT is paradoxically negative. Management of severe, life-threatening AIHA requires the emergent transfusion of a "least-incompatible" unit of packed RBCs, rapid initiation of immune suppression with corticosteroids, and ultimately identification of the autoantibody. The blood bank will perform compatibility testing on a number of units of packed RBC to determine which is least likely to be hemolyzed by the offending antibody.

Although the fatigue, tachycardia, and exercise intolerance would be consistent with heart failure, the severe anemia and reticulocytosis are not. Echocardiography and serum B-type natriuretic peptide level would be noncontributory in this scenario, and the initiation of a milrinone drip in this patient would not be appropriate.

Patients with sickle cell disease can present with hyperhemolytic crises associated with severe anemia and reticulocytosis. It would be highly unusual, however, for a 16-year-old patient who has been previously well to have a severe hemolytic crisis as her initial presentation of sickle cell disease.

Although inflammatory bowel disease can lead to severe anemia secondary to iron deficiency and the anemia of chronic inflammation, the sudden onset of symptoms and the severity of the anemia suggest that inflammatory bowel disease is not the cause of the anemia in this scenario. The mean corpuscular volume would have been low in iron-deficiency anemia, and the reticulocyte count would be low in anemia of chronic inflammation.

The patient's complete blood cell count exhibited no lymphoblasts, and the normal platelet number does not suggest bone marrow dysfunction. Thus, testing for lymphoblasts with flow cytometry and initiating therapy for leukemia would not be warranted in this scenario.

PREP Pearls

- Autoimmune hemolytic anemia (AIHA) is a life-threatening hematologic emergency.
- Sudden onset of fatigue, pallor, scleral icterus, and tachycardia should immediately raise suspicion for AIHA.
- A reticulocyte count and direct antibody test can be diagnostic for AIHA.

ABP Content Specifications(s)

- Recognize aspects of a patient's medical history that may suggest hemolytic anemia
- Plan the appropriate diagnostic evaluation of acute-onset anemia
- Recognize the clinical findings associated with autoimmune hemolytic anemia

Suggested Readings

- Sackey K. Hemolytic anemia: part 1. Pediatr Rev. 1999;20(5):152-159. doi: http://dx.doi.org/10.1542/pir.20-5-152.
- Sackey K. Hemolytic anemia: part 2. Pediatr Rev. 1999;20(6):204-208. doi: http://dx.doi.org/10.1542/pir.20-6-204.
- Teachey DT, Lambert MP. Diagnosis and management of autoimmune cytopenias in childhood. Pediatr Clin North Am. 2013;60(6):1489-1511. doi: http://dx.doi.org/10.1016/j.pcl.2013.08.009.

Question 43

A 4-year-old boy is admitted to the hospital with a 6-day history of fever, with a temperature of up to 40°C and a 3-day history of red cracked lips, nonpurulent conjunctivitis, and swollen hands and feet. On physical examination the boy is very irritable. His heart rate is 130 beats/min and his blood pressure is 90/56 mm Hg in the right arm. The boy has an erythematous, nonvesicular rash on his trunk and a 2-cm left cervical lymph node. On auscultation, his lungs are clear and there is no murmur or gallop. There is no hepatosplenomegaly and he is well perfused. The remainder of his examination is unremarkable.

Of the following, the BEST next step in the evaluation and management of this patient is to

A. administer intravenous (IV) ceftriaxone after obtaining blood cultures
B. administer IV immunoglobulin 2 g/kg over 12 hours
C. administer low-dose aspirin orally at 5 mg/kg per day
D. administer prednisone orally at 2 mg/kg per day
E. restrict fluids to two-thirds of the maintenance rate

Correct Answer: B
The boy in the vignette has clinical manifestations that meet the criteria for a diagnosis of Kawasaki disease. He has fever for 5 days, red cracked lips, nonpurulent conjunctivitis, swollen hands and feet, a rash, and an enlarged cervical lymph node. This syndrome is a vasculitis, and patients may develop coronary artery aneurysms (CAA). Compared with children treated with aspirin alone, the addition of intravenous immunoglobulin (IVIG) has been shown to reduce the risk of CAAs from 25% to 2%. A single dose of IVIG (2 g/kg over 10-12 hours) is most efficacious when given within 10 days of the onset of fever. A second dose is recommended if fever persists for 36 hours after the first dose.

High-dose aspirin (80 mg/kg per day orally in 4 divided doses) is recommended while the patient is febrile; once the child's fever has abated, the dose is lowered to 3 to 5 mg/kg per day for 6 to 8 weeks. Longer low-dose aspirin treatment is recommended in those with coronary artery abnormalities. Patients with large CAAs may require additional anticoagulation.

Kawasaki disease has not been shown to be a bacterial process, therefore, a blood culture and intravenous ceftriaxone would not be indicated.

Steroids have been shown to be useful in patients with more severe disease, carditis, or persistent fever after IVIG dosing. They may be beneficial in the initial phase of treatment as well, but not as a substitute for, or before, IVIG. Initially, there was concern that CAAs worsened with administration of steroids, but this has not been supported in subsequent studies and may have been a reflection of these patients being the most ill. The recommended dose of intravenous methylprednisolone has varied from 30 mg/kg per day to 1 to 2 mg/kg per day. New agents such as infliximab have been administered in cases of IVIG resistance, with encouraging results.

Fluid restriction would not be the best first intervention for the boy in this vignette. For a febrile child with normal cardiac function, administration of IVIG and maintenance of hydration would be recommended. If the child were acutely ill with evidence of shock and carditis on echocardiography, fluid resuscitation and IVIG with fluid balance closely regulated in an intensive care unit would be required.

PREP Pearls

- Kawasaki syndrome is a clinical diagnosis.
- Early diagnosis and treatment with intravenous immunoglobulin can markedly decrease the development of coronary artery aneurysms.
- High-dose aspirin (80 mg/kg per day orally in 4 divided doses) is recommended while the patient is febrile; once the child's fever has abated, the dose is lowered to 3 to 5 mg/kg per day for 6 to 8 weeks.

ABP Content Specifications(s)

- Plan the appropriate management of Kawasaki disease

Suggested Readings

- Eleftheriou D, Levin M, Shingadia D. Management of Kawasaki disease. Arch Dis Child. 2014;99(1):74-83. doi: http://dx.doi.org/10.1136/archdischild-2012-302841.
- Son MB, Gauvreau K, Burns JC, et al. Infliximab for intravenous immunoglobulin resistance in Kawasaki disease: a retrospective study. J Pediatr. 2011;158(4):644-649. doi: http://dx.doi.org/10.1016/j.jpeds.2010.10.012.
- Son MBF, Newburger JW. Kawasaki disease. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:1209-1214.
- Sundel RP, Baker AL, Fulton DR, Newburger JW. Corticosteroids in the initial treatment of Kawasaki disease: report of a randomized trial. Pediatrics. 2003;142(6):611-616. doi: http://dx.doi.org/10.1067/mpd.2003.191.
- Zhu BH, Lv HT, Sun L, et al. A meta-analysis on the effect of corticosteroid therapy in Kawasaki disease. Eur J Pediatr. 2012;171(3):571-578. doi: http://dx.doi.org/10.1007/s00431-011-1585-4.

Question 44

An 8-year-old boy is brought to your office for a health supervision visit. His parents report that school is "OK." Their son "works so hard," spending several hours per night on math homework, and has struggled to achieve average or low-average grades since first grade. His English grades are above average. The child reports that math is "boring" and he does not enjoy it. He participates successfully in other activities, including Boy Scouts, choir, and basketball. He sleeps well, approximately 9 hours per night. His mother reports that when he was 5 years of age, he participated in a research study where he underwent IQ testing. His parents were told his IQ was "above average."

Of the following, the MOST appropriate next step for this child is to

A. administer Vanderbilt attention-deficit/hyperactivity disorder scales
B. encourage his parents to request an evaluation for eligibility for special education from the school
C. reassure his parents that his academic performance is likely to improve if they provide more assistance with homework
D. refer him to a child psychiatrist
E. refer him to a tutoring program

Correct Answer: B
The child in this vignette likely has a learning disorder (LD). Approximately 8% of US school-aged children have an LD. Signs of an LD include achieving mediocre grades in the context of a disproportionate amount of time on homework. Reporting that school is boring or not enjoyable may be masking anxiety about school performance. His success in other activities outside of school and the ability to focus on homework suggest that the child does not have attention-deficit/hyperactivity disorder (ADHD) or a behavioral problem. While Vanderbilt scales may be a part of a comprehensive evaluation for an LD, ADHD is not the most likely cause of this patient's relatively disappointing school performance. Children with learning disabilities often have IQs in the normal range, so this patient's previous IQ test result does not exclude an LD.

Learning disorders are treated within the school context, in compliance with the Individuals with Disabilities Education Act (IDEA). Under IDEA, school officials are required to provide timely evaluations of students when a concern is noted and parents or teachers request testing. Parents should request this testing in writing. If an LD is found, school officials then create an Individualized Education Plan (IEP) to provide services, such as tutoring or modifying the curriculum, according to the specific LD found. Referring for private testing can be problematic: neuropsychological testing is expensive and patient insurance often does not cover such testing, waits for appointments can be long and can delay treatment, and school officials are not required to consider private testing when structuring an IEP. Referral to a tutoring program without an evaluation for an LD misses the opportunity to tailor a tutoring plan in accordance with the specific disorder.

PREP Pearls

- Learning disorders should be suspected when the effort spent on homework is out of proportion to school achievement.
- Children with learning disorders often have normal IQs.
- An assessment by special education staff at the child's school in accordance with the Individuals with Disabilities Education Act is the best recommended initial approach for a suspected learning disorder.

ABP Content Specifications(s)

- Evaluate the cognitive and behavioral developmental progress/status of a child at 6 to 12 years of age

Suggested Readings

- Floet AMW, Scheiner C, Grossman L. Attention-deficit/hyperactivity disorder. Pediatr Rev. 2010;31(2):56–69. doi: http://dx.doi.org/10.1542/pir.31-2-56.
- Rimrodt SL, Lipkin PH. Learning disabilities and school failure. Pediatr Rev. 2011;32(8):315-324. doi: http://dx.doi.org/10.1542/pir.32-8-315.

Question 45

A disoriented 16-year-old adolescent is brought by emergency medical services to the emergency department. According to his parents, he had been to a party with his friends the night before, but had returned early complaining of not feeling well and gone to bed. During the night, he vomited multiple times, which the parents had attributed to alcohol use. This morning, the parents found him in bed, lying in diarrhea, and confused. Past medical history is significant only for an open fracture of his right radius and ulna 1 week ago that required a 2-day hospitalization for orthopedic surgical pin placement. After discharge, he has been taking his father's baby aspirin and mother's naproxen for ongoing pain and discomfort, but otherwise is doing well.

Physical examination shows a young male adolescent, oriented only to person. His temperature is 39°C, respiratory rate is 22 breaths/min, pulse is 115 beats/min, and blood pressure is 88/54 mm Hg. Physical examination shows his pupils to be equal, round, and reactive to light and accommodation. He has dry mucous membranes, clear lung fields, normal heart sounds, and a soft abdomen. His right arm is in a plaster cast and there is good capillary refill in the fingers. He is moving spontaneously, but following commands with difficulty. He has strong pulses in his extremities, but they appear to be tender to palpation. His skin is very warm, with diffuse macular erythema.

Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	18,100/μL (18.1 x 10^9/L)
Neutrophils	80%
Lymphocytes	15%
Monocytes	3%
Eosinophils	2%
Hemoglobin	13.8 g/dL (138 g/L)
Hematocrit	42%
Platelet count	125 x 10^3/μL (125 x 10^9/L)
Sodium	140 mEq/L (140 mmol/L)
Potassium	4.5 mEq/L (4.5 mmol/L)
Chloride	100 mEq/L (100 mmol/L)
Bicarbonate	22 mEq/L (22 mmol/L)
Glucose	72 mg/dL (4 mmol/L)
Blood urea nitrogen	25 mg/dL (8.9 mmol/L)
Creatinine	1.5 mg/dL (133 μmol/L)
Creatine kinase	690 U/L (11.5 μkat/L)

Of the following, the clinical investigation MOST likely to establish a diagnosis is

A. electrocardiogram
B. Gram stain and culture from the right arm fracture site
C. head computed tomography
D. liver function tests
E. urine toxicology screen

Correct Answer: B
The clinical investigation most likely to establish a diagnosis for the adolescent in the vignette is a Gram stain and culture from the right arm fracture site. Arrhythmia, infection, head injury, metabolic derangement, and toxins are all potential causes for acute mental status changes. However, based on the history, physical examination, and laboratory values for this adolescent, the best explanation for these findings is staphylococcal toxic shock syndrome (TSS).

Toxic shock syndrome is a potentially life-threatening multisystem disease caused by a bacterial exotoxin. Toxic shock syndrome was first reported in 1978 in a series of children. In the 1980s, a large number of cases occurred in young women using absorbent tampons, creating awareness of TSS in association with menstruation. However, the etiology in around half of TSS cases is nonmenstrual and secondary to other causes, including surgical and postpartum wound infections, burns, and as a complication of infections such as influenza, sinusitis, osteomyelitis, and enterocolitis. Toxic shock syndrome toxin-1 (TSST-1) produced by Staphylococcus aureus (both methicillin-susceptible S aureus [MSSA] and methicillin-resistant S aureus strains) is responsible for TSS in over 90% of menstrual cases and at least half of nonmenstrual cases. Other toxins, including other staphylococcal enterotoxins (A-E, H) as well as streptococcal pyogenic exotoxins A and B, can cause TSS. The US Centers for Disease Control and Prevention has clinical criteria for staphylococcal TSS:

- Fever > to 38.9°C (102°F)
- Rash (typically diffuse erythroderma)
- Desquamation (commonly palms/soles 1 to 2 weeks after the onset of symptoms)
- Hypotension (systolic blood pressure less than fifth percentile for age for children younger than 16 years of age, ≤ 90 mm Hg for ≥ 16 years of age)
- Multisystem involvement (in 3 or more organ symptoms):

    - Gastrointestinal – vomiting or diarrhea at onset of illness
    - Musculoskeletal – severe myalgias at onset of illness or creatine phosphokinase (CPK) greater than twice the upper limit of normal
    - Mucocutaneous – vaginal, oropharyngeal, and/or conjunctival hyperemia
    - Renal – blood urea nitrogen (BUN) or creatinine greater than twice the upper limit of normal, or urine with greater than 5 white blood cells/high power field without a urinary tract infection
    - Hepatic – total bilirubin or aspartate aminotransferase/alanine aminotransferase greater than twice the upper limit of normal
    - Hematologic – platelet count less than 100 x 10^3/μL (100 x 10^9/L)
    - Central nervous system (CNS) – altered mental status without focal neurologic signs when afebrile and normotensive

- Negative results on the following tests or serology , if obtained:

- Blood, throat, or cerebrospinal fluid cultures (blood culture may be positive for S aureus)
- Rocky Mountain spotted fever, leptospirosis, or measles

Diagnosis of staphylococcal TSS is primarily based on clinical criteria, and not the isolation of S aureus. While 80% to 90% of wound and mucosal cultures are positive for S aureus in TSS patients, less than 5% of blood cultures are positive.

This adolescent in the vignette fulfills all of the acute criteria for staphylococcal TSS: he is febrile, with diffuse erythroderma, is hypotensive, and has evidence of gastrointestinal, musculoskeletal, renal, hematologic, and CNS involvement. A cardiac arrhythmia might account for his hypotension, elevated CPK, and elevated BUN/creatinine. However, it would not explain his fever or normal cardiac examination. Central nervous system pathology such as increased intracranial pressure could account for fever and confusion, but not his laboratory findings. Hepatic encephalopathy from metabolic disturbances or drugs is usually diagnosed clinically, with support from liver biopsy and liver function tests. Certain drugs such as heroin, cocaine, phencyclidine, and amphetamines can be responsible for both mental status changes and rhabdomyolysis, as well as the elevated CPK, BUN, and creatinine. However, these toxidromes present with normothermia, hypertension, and dark urine.

PREP Pearls

- Staphylococcus aureus can cause toxin-mediated disease resulting in staphylococcal food poisoning, staphylococcal scalded skin syndrome, and toxic shock syndrome (TSS).
- Half of TSS cases are not associated with menstruation and about half of pediatric TSS cases occur in children younger than 2 years of age.
- A positive culture for S aureus is not required for the diagnosis of staphylococcal TSS.

ABP Content Specifications(s)

- Recognize the clinical features associated with Staphylococcus aureus infection
- Plan the appropriate diagnostic evaluation of Staphylococcus infection

Suggested Readings

- American Academy of Pediatrics. Staphylococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:715-732.
- DeVries AS, Lesher L, Schlievert PM, et al. Staphylococcal toxic shock syndrome 2000-2006: epidemiology, clinical features and molecular characteristics. PLoS One. 2011;6(8):e22997. doi: http://dx.doi.org/10.1371/journal.pone.0022997.
- Smit MA, Nysquist AC, Todd JK. Infectious shock and toxic shock syndrome diagnoses in hospitals, Colorado, USA. Emerg Infect Dis. 2013;19(11):1855-1858. doi: http://dx.doi.org/10.3201/eid1011.121547.

Question 46

You are supervising a resident who is seeing a 7-year-old boy with a solitary kidney, diagnosed in utero, for a health supervision visit. The boy was recently seen at an urgent care center for viral gastroenteritis with mild dehydration. His interim history since his last routine visit, 1 year ago, has otherwise been unremarkable. The boy's weight is 22 kg (50th percentile) and height is 122 cm (50th percentile). His physical examination is normal.

Urgent care laboratory results include normal complete blood cell counts and electrolytes results, as well as the findings shown:

Laboratory Test	
Blood urea nitrogen	46 mg/dL (16.4 mmol/L)
Creatinine	0.7 mg/dL (61.8 μmol/L)

Urinalysis findings are negative for blood and protein with a 1.030 specific gravity.

You order renal ultrasonography that demonstrates a solitary left kidney with compensatory hypertrophy. The left kidney has increased echogenicity consistent with medical renal disease. There is no hydronephrosis or other dilation of the urinary system. These findings are unchanged from those seen 2 years ago. While reviewing the laboratory and ultrasonography results with you, the resident asks about the effect of chronic kidney disease on glomerular filtration rate (GFR).

Of the following, the MOST accurate statement is that

A. blood urea nitrogen and serum creatinine levels can be used interchangeably in diagnosing decreased GFR
B. GFR in individuals with a single functioning kidney is half the normal rate
C. some patients with chronic renal failure have a normal GFR
D. a stable GFR indicates stable chronic kidney disease
E. there is an exact correlation between the number of functioning nephrons and GFR

Correct Answer: C
Glomerular filtration rate (GFR) is a measure of kidney function and is indicative of disease stage in a patient with chronic kidney disease (CKD). Glomerular filtration rate represents the ultrafiltration of plasma across the glomerular capillary and correlates with the number of functioning nephrons. Glomerular filtration rate is not a good indicator of the loss of functioning nephrons, as seen in CKD, because of the compensatory increased function in the remaining nephrons. Therefore, a patient with a single functioning kidney with half the number of functioning nephrons may have a normal GFR because of the compensatory hyperfiltration in the functioning nephrons. These single kidneys appear larger on renal ultrasonography because of hypertrophy of the functioning nephrons. With progressive glomerular injury, as the GFR decreases, the rise in serum creatinine is counteracted by increased tubular secretion of endogenous creatinine, leading to no or minimal increase in serum creatinine.

The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical practice guidelines define the diagnosis of CKD in children by the presence of 1 of the following criteria:

GFR less than 60 mL/min per 1.73 m2 for more than 3 months, with implications for health regardless of whether other CKD markers are present.
GFR greater than 60 mL/min per 1.73 m2 that is accompanied by evidence of structural damage or other markers of functional kidney abnormalities, including proteinuria, albuminuria, renal tubular disorders, or pathologic abnormalities detected on histology or inferred with imaging
The KDIGO guidelines also stage CKD in children (> 2 years of age) for risk stratification:

- G1: Normal GFR (≥ 90 mL/min per 1.73 m2)
- G2: GFR between 60 and 89 mL/min per 1.73 m2
- G3a: GFR between 45 and 59 mL/min per 1.73 m2
- G3b: GFR between 30 and 44 mL/min per 1.73 m2
- G4: GFR between 15 and 29 mL/min per 1.73 m2
- G5: GFR of less than 15 mL/min per 1.73 m2

The progression of CKD from stages G1 to G3a, accompanied by minimal initial elevation in serum creatinine, indicates a major decrease in GFR. With subsequent progression of CKD, a marked increase in serum creatinine indicates only a small decrease in GFR. Increasing proteinuria, albuminuria, and/or new-onset or worsening hypertension is indicative of progressive CKD despite a stable GFR (diagnostic criterion 2).

Although blood urea nitrogen (BUN) also varies inversely with GFR, it is a less reliable marker than creatinine. Forty to 50% of the urea in the glomerular filtrate is reabsorbed by the tubules. This tubular reabsorption is enhanced in hypovolemic states associated with decreased effective

circulating volume. In addition, enhanced urea production with elevated BUN is seen with high protein diets, tissue injury (trauma, gastrointestinal bleeding), or high-dose corticosteroids. These conditions lead to BUN/serum creatinine ratio of more than 20 (normal, 10–15). Conditions associated with variable urea production in patients with renal injury and tubular urea reabsorption are seen frequently.

PREP Pearls

- Serum creatinine and glomerular filtration rate (GFR) are not good indicators of the loss of functioning nephrons because of the compensatory increased function in the remaining nephrons and increased tubular secretion of endogenous creatinine.
- The early stages of progression of chronic kidney disease (CKD) are accompanied by minimal elevation in serum creatinine, but a major decrease in GFR.
- Increasing proteinuria, albuminuria, and/or new-onset or worsening hypertension is indicative of progressive CKD despite a stable GFR (especially in the early stages of CKD).
- Variable urea production in patients with renal injury and tubular urea reabsorption make blood urea nitrogen a less reliable marker for GFR than creatinine.

ABP Content Specifications(s)

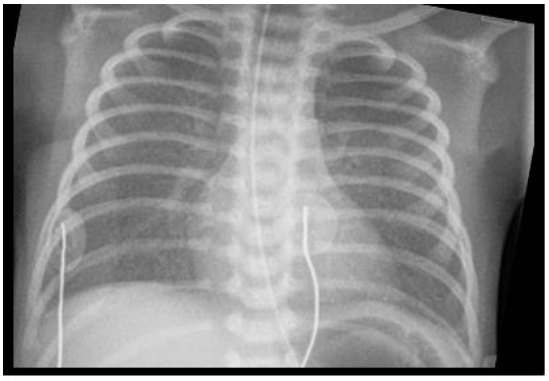
- Recognize age-related changes in renal tubular function
- Recognize age-related changes in glomerular filtration rate and their impact on the serum creatinine concentration

Suggested Readings

- Kidney Disease Improving Global Outcomes, National Kidney Foundation. KDIGO 2012: Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-163. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf.
- National Kidney Foundation. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification: part 5, evaluation of laboratory measurements for clinical assessment of kidney disease 5. National Kidney Foundation website. http://www2.kidney.org/professionals/KDOQI/guidelines_ckd/p5_lab.htm.

Question 47

A 31-week-gestation female neonate is admitted to the neonatal intensive care unit. She was born to a 32-year-old gravida 1, para 0 mother with a history of chronic hypertension. Due to severe preeclampsia, the neonate was delivered by cesarean delivery after the mother received 1 dose of betamethasone. Her birth weight was 1,350 g. In the delivery room, the neonate required positive pressure ventilation for 30 seconds due to poor respiratory effort. On admission, vital signs show a temperature of 36.7°C, heart rate of 176 beats/min, respiratory rate of 72 breaths/min, and a blood pressure of 46/25 mm Hg. On physical examination, she has mild intercostal retractions and nasal flaring with decreased breath sounds throughout. She is currently receiving nasal continuous positive airway pressure with FiO2 of 50%. Her chest radiograph (Item Q47) shows bilateral ground glass opacities.



Of the following, the MOST likely diagnosis is

A. pneumonia
B. pneumothorax
C. pulmonary hypoplasia
D. pulmonary sequestration
E. transient tachypnea of the newborn

Correct Answer: A

Of the responses given, pneumonia is the most likely diagnosis for the neonate in this vignette. The chest radiograph for this neonate shows bilateral homogenous pulmonary opacities. Radiographically, respiratory distress syndrome (RDS) appears identical to pneumonia caused by group B Streptococcus (GBS). For this reason, newborns with respiratory distress syndrome with risk factors for infection should be treated with antimicrobial therapy. Approximately 10% of newborns with GBS infection in the first 6 days after birth present with pneumonia. Other less common causes of early onset sepsis with respiratory manifestations include Listeria monocytogenes, Mycobacterium tuberculosis, and herpes simplex virus.

Respiratory distress syndrome is a disease of premature neonates born before 37 weeks of gestation due to inadequate surfactant production. The incidence of disease increases with decreasing gestational age. Maternal antenatal steroid administration within 7 days of delivery reduces the risk of RDS in premature neonates. Neonates with RDS present with grunting respirations, central cyanosis, and respiratory distress. At a cellular level, lack of adequate surfactant production decreases lung compliance, causing microatelectasis. Chest radiographs shows poor lung expansion and a homogenous ground glass appearance and air bronchograms. Symptomatic neonates may be treated with exogenous surfactant based on clinical signs and symptoms. Treatment with exogenous surfactant in premature neonates is associated with lower rates of death, pneumothorax, pulmonary interstitial emphysema, and bronchopulmonary dysplasia. Typically, endogenous surfactant production by type II pneumocytes is adequate to support pulmonary function by 2 to 3 days of life.

Pneumothorax describes air that has moved from the lung parenchyma into the space between the lung and rib cage. It may be visible on chest radiograph as a lucency at the heart border or lung base. Pneumothorax is not apparent on the chest radiograph for the infant in this vignette.

In pulmonary hypoplasia, lungs on radiography appear normal in size. However, with significant hypoplasia, ventilation and oxygenation are impaired, requiring mechanical ventilation. There is often a prenatal history of oligohydramnios with postnatal pulmonary hypoplasia. Pulmonary hypoplasia is unlikely in the neonate in this vignette.

Bronchopulmonary sequestration is a congenital malformation of lung development. A portion of lung tissue is disconnected from the main bronchial tree and has a separate blood supply. It appears on chest radiograph as a hyperdense region or cystic lesion. Clinically, most infants with bronchopulmonary sequestration are asymptomatic. No similar abnormality is noted on the chest radiograph shown.

Transient tachypnea of the newborn (TTN) typically appears on chest radiograph as increased pulmonary fluid markings. There is a delayed transition in Na-K transporters in the lung from influx to efflux of fluid postnatally. Neonates may have significant respiratory distress with an oxygen requirement. Transient tachypnea of the newborn typically resolves within the first 24 hours of life. Management includes respiratory support with continuous positive airway pressure

and oxygen therapy as needed. There is no clear association between long-term morbidity and TTN.

PREP Pearls

- Respiratory distress syndrome can look identical to group B streptococcal pneumonia on chest radiograph.
- Respiratory distress syndrome is a disease of premature neonates with an incidence inversely proportional to gestational age.
- Other less common causes of early onset sepsis with respiratory manifestations include Listeria monocytogenes, Mycobacterium tuberculosis, and herpes simplex virus.

ABP Content Specifications(s)

- Differentiate respiratory distress syndrome from congenital pneumonia in a newborn infant
- Recognize the characteristic clinical and radiographic appearance of respiratory distress syndrome in a newborn infant, and manage appropriately

Suggested Readings

- Engle WA, Committee on Fetus and Newborn. Surfactant-replacement therapy for respiratory distress in the preterm and term neonate. Pediatrics. 2008;121(2):419-432. doi: http://dx.doi.org/10.1542/peds.2007-3283.
- Stoll BJ, Hansen NI, Sanchez PJ, et al. Early onset neonatal sepsis: the burden of group B streptococcal and E. coli disease continues. Pediatrics. 2011;127(5):817-826. doi: http://dx.doi.org/10.1542/peds.2010-2217.
- Warren JB, Anderson JM. Core concepts: respiratory distress syndrome. NeoReviews. 2009;10(7):e351-e361. doi: http://dx.doi.org/10.1542/neo.10-7-e351.

Question 48

An 18-month-old girl is brought to your office for a health supervision visit. The father mentions that the family recently completed renovations on their home, which was originally built in 1925. Since she is at risk of lead exposure, you recommend that the girl have a blood lead level drawn at the visit today. Her father is resistant. You discuss with him the risks of lead toxicity, as well as the presentation of children with lead exposure.

Of the following, the MOST common sign or symptom seen in children with this type of exposure is

A. anemia
B. constipation
C. learning disability
D. none
E. vomiting

Correct Answer: D
Lead toxicity can cause constipation, abdominal pain, growth failure, hearing loss, seizures, encephalopathy, learning disability, renal disease, and microcytic anemia. However, the vast majority of children with elevated lead levels are asymptomatic.

Children are at greater risk for lead toxicity than adults because of oral exploration, enhanced gastrointestinal absorption, preferential deposition of lead in soft tissues as opposed to bone, and increased permeability of the blood-brain barrier. The peak age for lead toxicity is between 18 and 30 months of age. There are sociodemographic and racial disparities in lead exposure and lead poisoning, with African-American children, immigrants, international adoptees, publicly insured children, and those living in urban or poor neighborhoods disproportionately affected.

One common source of lead exposure is lead-based paint. Use of this type of paint was banned in the United States in 1977, but home disrepair or renovation can disrupt the paint already present and create lead-laden dust. Other sources of lead exposure include stagnant water in lead-containing pipes, soil contaminated by leaded gasoline, and certain folk remedies, imported foods, and candies.

It is important to be aware of other common environmental toxins. Home renovation can increase the risk of asbestos exposure, if insulation or older ceiling materials are disrupted without proper containment. Certain parental hobbies and occupations, such as soldering or automobile repair, increase the risk of toxin exposure for children in the household. Agricultural families may be exposed to various pesticides that have been shown to have deleterious health effects in cases of preconception, prenatal, or childhood contact.

PREP Pearls

- Children with elevated blood lead levels are typically asymptomatic.
- Home renovation can lead to asbestos and lead exposure.
- Parental occupational toxin exposures can affect children.

ABP Content Specifications(s)

- Know the potential exposures that result from a parent's occupation that directly or indirectly affect the health of their children
- Identify the common exposures and health problems associated with home renovation and repair

Suggested Readings

- Chandran L, Cataldo R. Lead poisoning: basics and new developments. Pediatr Rev. 2010;31(10):399-406. doi: http://dx.doi.org/10.1542/pir.31-10-399.
- Council on Environmental Health. Pesticide exposure in children. Pediatrics. 2012;130(6):e1757-e1763. doi: http://dx.doi.org/10.1542/peds.2012-2757.
- Karr C. Addressing environmental contaminants in pediatric practice. Pediatr Rev. 2011;32(5):190-200. doi: http://dx.doi.org/10.1542/pir.32-5-190.

Question 49

An 11-year-old boy presents for evaluation of persistent cough. The cough has been present for 8 weeks, is dry and harsh in quality, and is notably worse immediately before bedtime. He has had no fever, nasal drainage, headache, or vomiting. He has missed multiple school days because of his cough. A chest radiograph obtained 2 weeks ago was interpreted as normal. No improvement was seen with a short-acting b-agonist, nonsedating antihistamine, antibiotic, or oral steroid administration. While you are obtaining the history from the parents, the child appears mildly anxious. You also note that his cough appears to lessen while he is playing games on his mobile phone.

On physical examination, the boy is afebrile. His respiratory rate is 12 breaths/min and unlabored. His nasal turbinates are normal without drainage, and his oropharynx is clear without postnasal drip, erythema, or cobblestoning. The boy's lungs are clear, with no wheezing, stridor, or differential aeration. Cardiac rhythm is normal without murmur. His abdomen is soft, nontender, and nondistended without organomegaly. Extremities are warm and well perfused without clubbing, cyanosis, or edema. There is no rash.

Of the following, the MOST likely cause for this boy's cough is

A. bronchitis
B. foreign body aspiration
C. gastroesophageal reflux disease
D. habitual cough
E. sinusitis

Correct Answer: D

Cough accounts for approximately 16 million physician visits per year in the pediatric population. Cough is a protective reflex that clears mucus and debris from the airway. The most frequent cause of cough is an uncomplicated viral illness, and may last as long as 6 to 8 weeks. An average 10-year-old child will have 5 to 8 respiratory illnesses each year, with younger children likely to have even more. Most children with cough will not have a serious or chronic illness, and most episodes of cough will subside spontaneously. The differentiation between wet and dry cough has not been shown to be predictive of etiology or response to empiric treatment. Since fewer than 5% of coughs persisting for longer than 8 weeks are postinfectious in etiology (an exception is pertussis), further investigation and treatment may be warranted in this population.

The boy in the vignette has symptoms that are most suggestive of a habitual cough. A habitual cough is often initiated by an identifiable infectious or inflammatory process, but the cough fails to resolve as expected when the inciting process resolves. The associated cough is typically loud, harsh, and brassy, and may be described as "honking." The hallmark is complete or near-complete resolution of cough with sleep; the cough may also be absent with distraction. Underlying psychopathology may be present, but is not required for the diagnosis.

Acute bronchitis may occur with mycoplasmal associated illness, however, bronchitis or an inflammation of the larger airways is much less common in children than in adults. Protracted bacterial bronchitis, characterized by a chronic wet cough, has recently been described in the pediatric population. Bronchoscopic analysis and lavage reveals an intense neutrophilic airway inflammation. Commonly isolated organisms on culture include: Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. Response to antibiotic therapy is typically excellent. This diagnosis should not be routinely entertained during a period of acute and viral symptoms.

Foreign body aspiration is most frequently encountered in children less than 3 to 5 years of age. Associated cough may arise from a foreign body located in the airway, esophagus, or external ear canal (Arnold nerve). Affected children may present acutely with cough and wheezing, but may also present later, after a "honeymoon period," with a chronic cough. A history of a witnessed choking or aspiration event is present in fewer than 40% of cases. Inspiratory and expiratory or lateral decubitus radiography is recommended when aspiration of a foreign body is suspected. However, because very few (6%-15%) aspirated materials are radio-opaque, this may not establish the diagnosis. A high index of suspicion and a low threshold for otolaryngologic evaluation of the airway are required.

Gastroesophageal reflux (GER) may provoke cough by various mechanisms. Refluxate in the esophagus may irritate the vagus nerve and stimulate cough. Alternatively, cough receptors at the larynx may be activated by laryngopharyngeal reflux events. Lastly, refluxate may enter the airway during microaspiration events and stimulate tracheobronchial cough receptors. A high percentage of children with respiratory symptoms have GER detectable with abnormal esophageal pH, but symptoms may be subtle or atypical, particularly in young children. A causal

association between GER and cough remains controversial. Cough may provoke reflux events through increased intrathoracic and intra-abdominal pressures and transient lower esophageal sphincter relaxations. A cough associated with GER is often worse with supine positioning and during sleep because of decreased motor tone and esophageal sphincter relaxation. An 11-year-old child with GER disease would be expected to report some symptoms of abdominal discomfort, dyspepsia, acid taste, nausea, or vomiting.

Sinusitis is a common cause of chronic cough in children and adolescents. Symptoms may include headache, nasal congestion, and foul breath. The cough is often worse in the supine position (thus, typically at night) because of postnasal drip. Young children, however, often do not report classic symptoms, and a chronic cough may be the only presenting feature. Risk for sinusitis may be increased by predisposing factors for sinus ostial obstruction or infection, such as nasal polyps, allergic rhinitis, ciliary dysfunction, cystic fibrosis, and immunodeficiency. Criteria that suggest acute bacterial rather than viral rhinosinusitis include persistent symptoms lasting 10 or more days without evidence of improvement, onset with severe symptoms/signs for at least 3 to 4 days, or worsening symptoms after a typical time course of upper respiratory symptoms. Because of the symptom overlap between viral and bacterial sinusitis, treatment with antibiotics is not generally recommended in the first 48 to 72 hours of illness.

The differential diagnosis of chronic cough in children also includes tracheo- and bronchomalacia, vascular malformations, airway neoplasm, infection (eg, pertussis or parapertussis), and neurologic disorders such as Tourette syndrome. A thorough history and physical examination should be performed to optimally direct diagnostic testing and therapeutic interventions.

PREP Pearls

- Cough is a protective airway reflex most commonly associated with uncomplicated viral illnesses of the upper respiratory tract
- Habitual cough is typically harsh in character, may occur several times per minute, and often is absent or quiets significantly during periods of sleep or distraction.

ABP Content Specifications(s)

- Plan appropriate management for cough of various etiologies

Suggested Readings

- Chang AB, Berkowitz RG. Cough in the pediatric population. Otolaryngol Clin North Am. 2010;43(1):181-198. doi: http://dx.doi.org/10.1016/j.otc.2009.11.010.
- Chow AW, Benninger MS, Brook I, et al. Executive summary: IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clin Infect Dis. 2012:54(8):1041-1045. doi: http://dx.doi.org/10.1093/cid/cir1043.
- Kantar A, Bernardini R, Paravati F, Minasi D, Sacco O. Chronic cough in preschool children. Early Hum Dev. 2013;89 Suppl 3:S19-S24. doi: http://dx.doi.org/10.1016/j.earlhumdev.2013.07.018.

Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. Chest. 2006;129(5):1132-1141. doi: http://dx.doi.org/10.1378/chest.129.5.1132.
Wagner JB, Pine HS. Chronic cough in children. Pediatr Clin North Am. 2013;60(4):951-967. doi: http://dx.doi.org/10.1016/j.pcl.2013.04.004.

Question 50

A 7-year-old boy is brought to your office for a health supervision visit. You saw the boy 1 year ago for a learning disorder. He had struggled in kindergarten. Prior to first grade, he underwent a comprehensive evaluation, which revealed a full-scale IQ of 67 and adaptive composite score of 67. You ordered fragile X testing that showed 250 CGG repeats. At the next visit, you told the family that he did not have fragile X syndrome. You diagnosed him with intellectual disability and recommended that he should receive special education resources in school. As you review your records today, you notice your error regarding the fragile X results and disclose your mistake to the mother.

Of the following, the BEST description of this type of error is

A. diagnostic error
B. medical negligence
C. near miss
D. sentinel event
E. systems error

Correct Answer: A

The term "medical error" refers to a mistake in action or judgment. In the case in the vignette, there was an error in diagnosis; the correct diagnosis was not made despite the fragile X test results showing 250 repeats (normal is 5-44 repeats, full mutation is more than 200 repeats).

There are many taxonomies and descriptions of various errors and adverse events. Brief descriptions are listed in this critique, but the reader is referred to the Suggested Readings for detailed definitions. Medical negligence is a legal term referring to a situation where there is an act or an omission that results in injury to the patient. In the case described in this vignette, there was no injury to the patient, so this is not a case of medical negligence. In healthcare, a "near miss" is an event that had the potential to cause harm but did not. An example of this is a patient being prescribed the wrong dose of a medication, but not having any adverse effects from taking that dose or the wrong dose being caught by the pharmacist prior to administration. The case in the vignette is an error, not a near miss. Sentinel events are unexpected events that result in death or significant injury, for example, amputating the wrong limb. There was no significant injury to this patient in the event, so this is not a sentinel event. A systems error is an error attributable to the healthcare delivery process, for example, the lack of sufficient nursing staff leading to delays in medication administration in the hospital. The case in the vignette is a diagnostic error on the part of the provider.

When errors occur, it is important to disclose the error to the patient (when appropriate) and family, as was done in this case. Offering an apology is also appropriate, regardless of whether there is injury to the patient. Barriers to disclosing errors should be recognized; these can include the belief that the family would not want to know about the error or that the family might not understand the error that was made. Overcoming barriers to disclosing medical errors is important in creating and maintaining a bond between providers and families and in fostering a culture of patient safety.

PREP Pearls

- Medical errors do not always cause adverse events or injury.
- Medical errors should be disclosed to patients (when appropriate) and families.

ABP Content Specifications(s)

- Differentiate the findings associated with dose-related adverse drug reactions from those of idiosyncratic reactions
- Recognize and apply ethical principles regarding medical errors
- Recognize and apply ethical principles regarding malpractice

Suggested Readings

- Garbutt J, Brownstein DR, Klein EJ, et al. Reporting and disclosing medical errors pediatricians' attitudes and behaviors. Arch Pediatr Adolesc Med. 2007;161(2):179-185. doi: http://dx.doi.org/10.1001/archpedi.161.2.179.
- Kohn KT, Corrigan JM, Donaldson MS. To Err Is Human: Building a Safer Health System. Washington, DC: National Academy Press; 2000:287 pp.
- Leonard MS. Patient safety and quality improvement: medical errors and adverse events. Pediatr Rev. 2010;31(4):151-158. doi: http://dx.doi.org/10.1542/pir.31-4-151.
- Neuspiel DR, Stubbs EH, Liggin L. Improving reporting of outpatient pediatric medical errors. Pediatrics. 2011;128(6):e1608-e1613. doi: http://dx.doi.org/10.1542/peds.2011-0477.
- US Centers for Disease Control and Prevention. Fragile X syndrome (FXS): how fragile X syndrome is inherited. US Centers for Disease Control and Prevention website. http://www.cdc.gov/ncbddd/fxs/inherited.html.

Question 51

A 6-year-old boy with acute lymphoblastic leukemia in consolidation therapy is admitted to the hospital because of fever and neutropenia associated with shock. He has an indwelling central venous catheter. Vital signs show a temperature of 39°C, heart rate of 160 beats/min, blood pressure of 70/40 mm Hg, and respiratory rate of 30 breaths/min. On initial physical examination, he is tired appearing and in moderate respiratory distress. Lungs are clear to auscultation bilaterally. His heart is regular with no murmurs, and capillary refill time is 4 seconds. His abdomen is soft, nontender, and non-distended. He is given three 20 mL/kg boluses of normal saline. Blood cultures are drawn, and vancomycin and cefepime are started. Ten minutes after the infusion of vancomycin is started, he develops itching, flushing, and an erythematous rash covering his trunk and upper extremities. There is no change in his breathing or hemodynamics.

Of the following, the MOST appropriate course of action is to

A. administer clindamycin, 10 mg/kg intravenously
B. administer diphenhydramine, 1 mg/kg intravenously
C. administer hydrocortisone, 2 mg/kg intravenously
D. decrease the rate of the vancomycin infusion
E. discontinue vancomycin

Correct Answer: D
The child in this vignette has fever, neutropenia, and septic shock. He receives fluid resuscitation and empiric antibiotics. He develops "red man syndrome" (RMS) with infusion of vancomycin. Since administration of appropriate antimicrobials impacts mortality, decreasing the rate of the vancomycin infusion is the best choice presented.

"Red man syndrome" is a common, adverse drug reaction that occurs in children and adults receiving vancomycin. The mild end of the spectrum of RMS includes mild flushing, urticaria, and pruritis. Severe manifestations include generalized erythema, intense pruritis, and distributive shock. The proposed mechanism for RMS is an anaphylactoid reaction from mast cell degranulation caused by vancomycin.

"Red man syndrome" can be avoided in many cases by infusing the medication over 60 minutes, and can be ameliorated by discontinuing or slowing the infusion. In this child with septic shock, fever, and neutropenia, empiric treatment for methicillin-resistant Staphylococcus aureus (MRSA) is necessary, so discontinuing vancomycin or changing antibiotics to less effective MRSA coverage would not be good options. Even though RMS may be caused by mast cell degranulation, treatment with antihistamines has not been found to protect patients from developing RMS, nor does it ameliorate rash or pruritis. Hydrocortisone can be helpful in anaphylactic reactions, but this clinical scenario does not fit anaphylaxis.

Drug reactions are either immunologic or nonimmunologic. Immunologic reactions include type I (immunoglobulin E-mediated), type II (cytotoxic), type III (immune complex), and type IV (delayed). Nonimmunologic drug reactions include pseudoallergenic reactions caused by direct mast cell degranulation, such as in RMS, and idiosyncratic reactions, which are rare, unpredictable events that cannot be explained by the known pharmacologic mechanism of the drug. Examples of idiosyncratic reactions include drug-induced hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency and aspirin sensitivity causing bronchospasm.

A serious adverse drug event is any undesirable consequence of a medical product in a patient that results in death, hospitalization, disability, birth defect, or a required intervention to prevent damage. Any of these should be reported to the US Food and Drug Administration (FDA) either by healthcare professionals or by consumers. The FDA Adverse Event Reporting System (FAERS) is a database containing information on the reports of serious adverse drug events and medication errors submitted to the FDA. This is an important system to evaluate safety concerns of medications and medical devices. Based on evaluation of safety concerns, the FDA may take regulatory action with the intent of improving safety, for example, restricting the usage of the drug or device, labeling changes, warning users, or removing the product from the market.

"Red man syndrome" is a common, adverse drug reaction caused by infusion of vancomycin. In patients who depend on this medication for survival (for example, the child in this vignette with fever, neutropenia, and septic shock), slowing the infusion is the most appropriate course of action.

PREP Pearls

- "Red man syndrome" is a common adverse drug reaction likely due to direct mast cell degranulation ranging from minor cutaneous signs to severe pruritis and shock.
- Adverse drug reactions may be immune-mediated, such as type I (immunoglobulin E-mediated), type II (cytotoxic), type III (immune complex), and type IV (delayed), and nonimmune-mediated.
- Diphenhydramine is not indicated in the treatment of Red Man syndrome.

ABP Content Specifications(s)

- Differentiate the findings associated with dose-related adverse drug reactions from those of idiosyncratic reactions
- Understand the circumstances for and process of reporting adverse drug reactions to the Food and Drug Administration

Suggested Readings

- Myers AL, Gaedigk A, Dai H, James LP, Jones BL, Neville KA. Defining risk factors for Red Man syndrome in children and adults. Pediatr Infect Dis J. 2012;31(5):464-468. doi: http://dx.doi.org/10.1097/INF.0b013e31824e10d7.
- Sivagnanam S, Deleu D. Red Man syndrome. Crit Care. 2003;7(2):119-120. doi: http://dx.doi.org/10.1186/cc1871.

Question 52

You are called to the newborn nursery to evaluate a 14-hour-old full-term male neonate born by vacuum-assisted vaginal delivery at 41 weeks of gestation after an uncomplicated pregnancy. He had a seizure lasting 3 minutes. A heel-stick blood glucose level is 24 mg/dL (1.3 mmol/L). An intravenous line is placed and his hypoglycemia is corrected with rapid infusion of 2 mL/kg of 10% dextrose in water followed by a continuous infusion of 10% dextrose in water. A serum sample obtained prior to correction of his hypoglycemia and run in the laboratory later returns at 20 mg/dL (1.1 mmol/L). His birth weight was 3.2 kg. Physical examination after correction of his hypoglycemia shows a rectal temperature of 37°C, heart rate of 120 beats/min, respiratory rate of 30 breaths/min, and blood pressure of 65/40 mm Hg. You note wandering nystagmus. Genital examination shows a stretched phallic length of 1.5 cm. The right testicle is not palpable and the left testicle is palpable high in the scrotum.

Of the following, the MOST likely diagnosis is

A. hypopituitarism
B. isolated growth hormone deficiency
C. Kallmann syndrome
D. partial androgen insensitivity syndrome
E. Prader-Willi syndrome

Correct Answer: A

The neonate described in the vignette has hypopituitarism evidenced by severe hypoglycemia and small penis size. The small penis and undescended testicle are due to gonadotropin deficiency and the hypoglycemia is due to other anterior pituitary hormone deficiencies. The wandering nystagmus suggests septo-optic dysplasia, which causes vision impairment and is associated with hypopituitarism. The post-date gestational age and need for assisted delivery are also consistent with hypopituitarism.

Micropenis is defined as a normally formed penis with a stretched phallic length that is more than 2.5 standard deviations below the mean for age. For a term infant, a stretched phallic length of less than 2 to 2.5 cm meets the definition for micropenis. A table of mean stretched phallic length and 2.5 standard deviations below the mean for various ages can be found in the Harriet Lane Handbook, 20th edition. Stretched phallic length is measured from the base of the symphysis pubis to the tip of the glans with gentle tension applied. For the term infant described in the vignette, the stretched phallic length of 1.5 cm clearly meets the definition of micropenis. The term microphallus refers to a small phallic structure in the setting of genital ambiguity.

Micropenis is due to a deficiency of fetal testosterone later in gestation when testosterone dependent phallic growth and testicular descent occur. Testosterone, with local conversion to dihydrotestosterone, is necessary for differentiation of the male genitalia during the first trimester. Fetal testosterone production during the first trimester, however, is controlled by placental human chorionic gonadotropin acting via the fetal testicular luteinizing hormone receptor. Therefore, when fetal gonadotropin (luteinizing hormone) deficiency is present, there is normal differentiation of the male genitalia during the first trimester, but testosterone deficiency later in gestation when fetal gonadotropins control testosterone production resulting in abnormal differentiation of the male genitala. Thus, micropenis, without other genital ambiguity, is often due to gonadotropin deficiency, which may be isolated or associated with other pituitary hormone deficiencies. Inadequate testosterone production near the end of gestation due to primary testicular dysfunction, such as with Klinefelter syndrome, can also result in micropenis.

Kallmann syndrome is isolated gonadotropin deficiency associated with anosmia or hyposmia. Micropenis with cryptorchidism is a common presentation of Kallmann syndrome, but hypoglycemia is not a feature due to the lack of other pituitary hormone deficiencies. Partial androgen insensitivity syndrome is due to mutations in the androgen receptor. In rare cases, it can present with an isolated micropenis, but generally, the genitalia are more ambiguous and hypoglycemia is not a feature. Hypogonadism is a prominent feature of Prader-Willi syndrome and cryptorchidism and micropenis are common. Hypoglycemia may occur due to poor intake, but other characteristics of the syndrome would be expected such as hypotonia, poor feeding, respiratory problems, and dysmorphic features. As growth hormone seems to play a role in phallic growth, isolated growth hormone deficiency could present with micropenis, but the severe hypoglycemia is not likely.

Babies born with micropenis should undergo evaluation in the immediate newborn period to detect and treat potentially life-threatening conditions. If genital ambiguity is present, the

neonate should be evaluated for disorders of sexual differentiation and monitored to prevent any potentially associated adrenal crisis. For neonates with micropenis without other genital ambiguity, monitoring for hypoglycemia and evaluation for other pituitary hormone deficiencies should occur.

PREP Pearls

- Criteria for micropenis is a stretched phallic length of less than 2.5 standard deviations below the mean, or less than 2 to 2.5 cm in a term infant.
- Gonadotropin deficiency is high on the differential diagnosis of micropenis and can be isolated or associated with other anterior pituitary hormone deficiencies.
- Babies with micropenis should be evaluated in the immediate newborn period to prevent potential adrenal crisis or other life-threatening consequences of hypopituitarism.
- Infants with micropenis and genital ambiguity should be evaluated for disorders of sexual differentiation.

ABP Content Specifications(s)

- Understand the clinical diagnosis of micropenis

Suggested Readings

- Mark T. Endocrinology. In: Engorn D, Flerlage J, eds. The Harriet Lane Handbook. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:214-245.
- Palmer JS, Palmer JS. Management of abnormalities of the external genitalia in boys. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. Campbell-Walsh Urology. 11th ed. Philadelphia, PA: Saunders Elsevier; 2015:3368-3398.
- Vogt KS, Bourgeois MJ. Microphallus. Medscape. http://emedicine.medscape.com/article/923178-overview#a5. Updated December 3, 2014.

Question 53

You perform a health supervision visit for an adolescent. She is planning a vacation trip to a sunny location. Her parents are concerned because she has a history of easily becoming sunburned, and they ask for guidance on the risks potentially associated with sun damage to the skin and methods to protect her from the hazards of ultraviolet radiation.

Of the following, the BEST advice to offer this patient is to

A. apply artificial sunless tanning products before travel
B. apply sunscreen products every 2 hours and after swimming when in the sun
C. use sun protection only for exposure between 10 AM and 2 PM
D. obtain a tan from a tanning salon before travel
E. wear light-colored clothing when in the sun

Correct Answer: B
The proper application of effective sunscreen products is the best method to decrease sun damage to the skin and minimize the associated risks. Sun protective factor (SPF) refers to the ability of a sunscreen to block ultraviolet B rays. It is recommended that sunscreen with SPF of 15 or greater be applied 15 to 30 min before sun exposure, and then reapplied every 2 hours and after swimming, sweating, or drying off. The 2011 American Academy of Pediatrics Council on Environmental Health and Section on Dermatology policy statement identifies the hazards of ultraviolet radiation (UVR) and recommends that pediatric healthcare providers incorporate counseling about UVR exposure routinely into health supervision visits.

The acute reaction to excessive UVR is sunburn. The degree of sunburn depends on several factors, including skin thickness, the amount of melanin in the epidermis, the intensity and duration of exposure to the sun, underlying medical conditions, and the use of photosensitizing medications. In addition, there are modifying factors such as elevation, atmospheric or cloud filter, and reflection off surfaces. Chronic exposure to UVR leads to skin aging, with resultant decreased elasticity, deeper wrinkles, and discoloration. Skin damage resulting from cumulative sun exposure over long periods is important in the pathogenesis of basal cell carcinoma, squamous cell carcinoma, and melanoma. Similar damage can occur to the eyes. Photokeratitis or focal retinal burns may occur with acute overexposure to UVR. Long-term eye exposure is associated with an increased risk of cataracts, pterygium, corneal degenerative changes, and cancer of the skin around the eye. Exposure to artificial sources of UVR (sunlamps, tanning beds) has similar acute and chronic effects on the skin and eyes.

Despite the awareness that UVR causes skin cancer, compliance with sun protection guidelines is inconsistent. To protect against the potential harmful effects of UVR to the skin and eyes, anticipatory guidance should include the following recommendations:

- Avoid suntanning and sunburning
- Wear protective clothing including a hat with brim
- Wear protective sunglasses
- Apply sunscreen with an SPF of 15 or higher every 2 hours and after swimming, sweating, or drying off with a towel
- Limit exposure to midday sun
- Play in the shade
- Do not use artificial tanning sources, such as sunlamps or tanning parlors

Commonly held misconceptions need to be addressed with patients and families. Most sunless tanning products do not offer any significant ultraviolet protection. Products that do contain sunscreen will provide UVR protection, but need to be reapplied, as does any sunscreen product. Although avoiding midday sun exposure when the sun is most intense is important, sun protection is needed throughout the day, even when cloudy. Evidence does not support a protective effect of the use of tanning salons before sun exposure. In fact, this practice may lead to a higher level of radiation exposure because of the combination of radiation from the tanning process followed by less sun precaution taken, in the mistaken belief that the tan is protective. Clothing can be an excellent UVR barrier. Although white clothing may keep one cooler, darker

colors and tightly woven fabrics have a higher protective value. The regular use of sunscreen can decrease actinic keratoses, the precursor to squamous cell carcinoma. However, there is no conclusive evidence that sunscreen use prevents melanoma or basal cell carcinoma.

PREP Pearls

- The best method to decrease sun damage is the proper application of sunscreen products every 2 hours and after swimming or sweating.
- The use of artificial sunless tanning products and pretravel salon tanning does not decrease the need for appropriate use of sunscreen.

ABP Content Specifications(s)

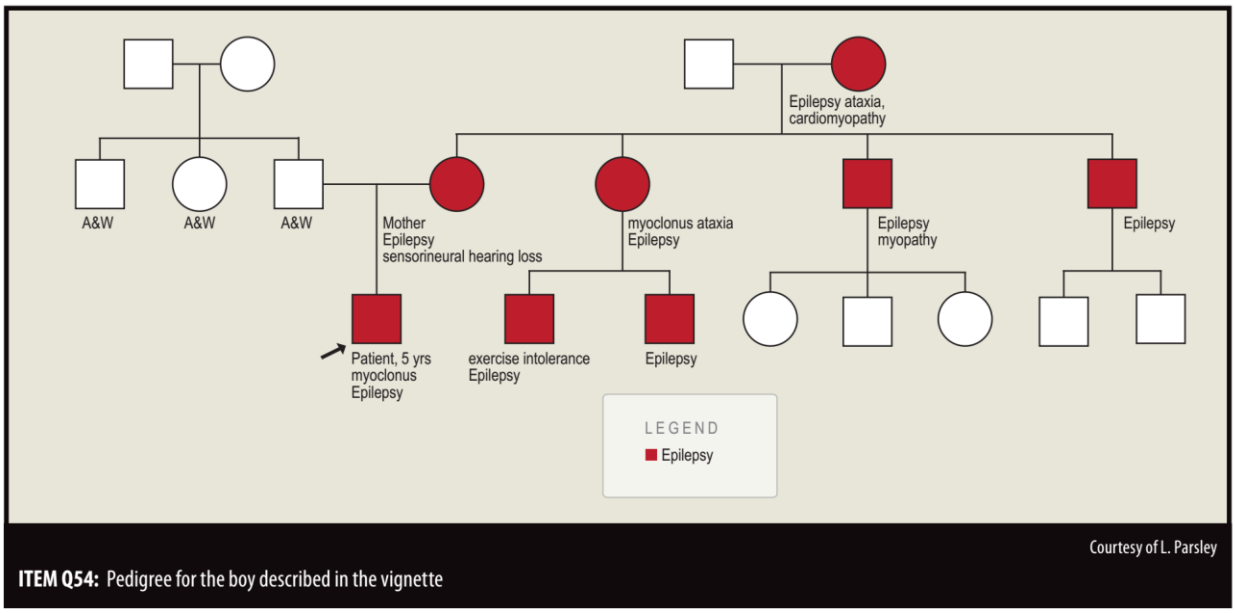
- Understand the clinical findings and risks associated with sun damage to the skin

Suggested Readings

- Council on Environmental Health, Section on Dermatology. Ultraviolet radiation: a hazard to children and adolescents. Pediatrics. 2011;127(3):588-597. doi: http://dx.doi.org/10.1542/peds.2010-3501.
- Guy GP Jr, Thomas CC, Thompson T, Watson M, Massetti GM, Richardson LC. Vital signs: melanoma incidence and mortality trends and projections: United States, 1982-2030. MMWR Morb Mortal Wkly Rep. 2015;64(21):591-596. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6421a6.htm.
- Leach J. Sunburn: effects and management. Pediatr Rev. 1983;5(1):13-17. doi: http://dx.doi.org/10.1542/pir.5-1-13.
- Paller AS, Hawk JLM, Honig P, et al. New insights about infant and toddler skin: implications for sun protection. Pediatrics. 2011;128(1):92-102. doi: http://dx.doi.org/10.1542/peds.2010-1079.

Question 54

You are evaluating a 5-year-old boy hospitalized with worsening seizures. History reveals that he had a period of normal development followed by the onset of myoclonus. His symptoms progressed to include seizures, muscle weakness, exercise intolerance, increased clumsiness, visual problems, and mild sensorineural hearing loss. The boy's growth has slowed. Notable laboratory findings include elevated serum and cerebrospinal fluid lactate, pyruvate, and protein levels. Several maternal relatives are similarly affected to varying degrees. The family pedigree is shown in Item Q54.



ITEM Q54: Pedigree for the boy described in the vignette

Of the following, the BEST next test to confirm the diagnosis is

A. brain magnetic resonance imaging
B. dilated eye examination
C. electrocardiogram
D. muscle biopsy
E. urine organic acids

Correct Answer: D
The boy in the vignette has a mitochondrial disorder called MERRF (myoclonic epilepsy with ragged red fibers). This is a multisystem disorder that begins with myoclonus, progressing to generalized epilepsy, weakness, ataxia, and eventually dementia. Onset typically occurs after normal early childhood development. Other findings can include sensorineural hearing loss, poor growth, optic atrophy, and cardiomyopathy. Ragged red fibers are present on skeletal muscle biopsy. MERRF is caused by a mitochondrial DNA (mtDNA) gene mutation, MT-TK (m.8344A>G), in 80% of cases. Heteroplasmy is a term used to describe the varying tissue distribution of mutated mtDNA among the organ systems in the human body. Skeletal muscle biopsy is the most reliable method to detect the pathogenic gene variant, given the heteroplasmy commonly demonstrated in mtDNA disorders. Sometimes the gene mutation can be found in leukocytes as well. For example, the brain may have more abnormal mtDNA than the eye. Thus, different organ systems can have differing effects of a mtDNA pathogenic gene change, depending on the amount of mutant mtDNA in that organ.

The mitochondrial genome is a 16.5 kilobase circular chromosome, found in the mitochondria rather than the nucleus. Most cells contain about 1,000 mtDNA molecules, distributed among hundreds of mitochondria. One exception is the mature oocyte, which contains more than 100,000 copies of mtDNA (both mutant and normal) because of the restriction and subsequent amplification of mtDNA that occurs during oogenesis. The fraction of mutant mtDNA in offspring can vary considerably within a family, depending on the number of mutant mtDNA in the mother and the random chance separation and distribution of mutant mtDNA known as the mitochondrial genetic bottleneck. Hundreds of rearrangements and point mutations have been discovered in mtDNA, which are associated with disease, often involving the musculoskeletal and nervous systems.

The pedigree shown in the vignette clearly demonstrates mitochondrial or maternal inheritance. Sperm mitochondria are eliminated from the embryo, therefore mtDNA is inherited completely from the mother. A man with an mtDNA pathogenic mutation cannot transmit the variant to any of his offspring. However, a woman will transmit her pathogenic variant to all of her offspring because her mitochondria are the only contributing component of mtDNA.

Electrocardiography, urine organic acids, or a dilated eye examination may show abnormalities in the boy in the vignette, but would not confirm a specific diagnosis. Brain magnetic resonance imaging might demonstrate brain atrophy and basal ganglia calcification in this case, but would also not be diagnostic. Multigene panels for MERRF are available to clinicians. This testing can be performed on leukocytes, skin fibroblasts, buccal mucosa, and, most reliably, skeletal muscle.

PREP Pearls

- MERRF (myoclonic epilepsy with ragged red fibers) is a multisystem disorder that begins with myoclonus, progressing to generalized epilepsy, weakness, ataxia, and eventually dementia, with onset typically occurring after a normal early childhood development.
- Skeletal muscle biopsy, with testing for respiratory chain enzyme analysis, pathogenic gene variants, and ragged red fibers, is the most reliable method to diagnose a patient with a mitochondrial disorder.
- Mitochondrial inheritance is maternally inherited. A man with a mitochondrial DNA (mtDNA) pathogenic mutation cannot transmit the variant to any of his offspring because of the elimination of the sperm mitochondria from the embryo. A woman will transmit her pathogenic variant to all of her offspring because her mitochondria are the only contributing component of mtDNA.

ABP Content Specifications(s)

- Recognize the inheritance pattern associated with mitochondrial inheritance

Suggested Readings

- Chinnery PF. Mitochondrial disorders overview. GeneReviews. http://www.ncbi.nlm.nih.gov/books/NBK1224/. Updated August 14, 2014.
- DiMauro S, Hirano M. MERRF. GeneReviews. http://www.ncbi.nlm.nih.gov/books/NBK1520/. Updated January 29, 2015.
- Rahman S. Mitochondrial disease and epilepsy. Dev Med Child Neurol. 2012;54(5):397-406. doi: http://dx.doi.org/10.1111/j.1469-8749.2011.04214.x.

Question 55

A 15-year-old adolescent girl who has not been to your office since she was 11 years of age presents today for a health supervision visit. Her mother expresses concern that the girl has not yet started having menstrual periods, although her breast development began at 10 years of age. A review of the adolescent's growth chart shows that her height has dropped from the 60th percentile to the 10th percentile over the last 4 years.

Of the following, the MOST appropriate next step in her evaluation and management would be to

A. obtain bone age radiograph
B. order thyroid function tests
C. perform a thorough history and physical examination
D. perform pelvic ultrasonography
E. perform screening tests for inflammatory bowel disease

Correct Answer: C
Although the exact age of the onset of puberty varies, development of secondary sexual characteristics typically begins between ages 8 and 13 years in girls and 9 and 14 years in boys. Puberty is considered delayed in girls with no breast development by age 13 years, failure to menstruate by age 16 years, or more than 5 years between the initiation of breast development and menarche. Delayed puberty is accompanied by a slowing of linear growth and results short stature.

The differential diagnosis for delayed puberty is quite broad and includes constitutional delay, hypothyroidism, gonadal failure (eg, Turner syndrome), inflammatory bowel disease, inadequate nutrition, and pituitary tumors. The most appropriate next step in the evaluation and management of the girl in the vignette is to narrow the differential diagnosis by performing a thorough history and physical examination. Inquiry about the past medical history should focus on any history of chronic disease, congenital anomalies, surgical history, medication or drug use, and family history. A review of the growth chart, with attention to the rate of linear growth and how growth compares with weight gain may be helpful in differentiating nutritional deficiencies from endocrinopathies.

Initial laboratory tests to consider for the evaluation of delayed puberty include a complete blood count, inflammatory markers such as erythrocyte sedimentation rate, electrolytes, blood urea nitrogen, creatinine, and liver enzymes. Screening for thyroid dysfunction should also be considered. Pelvic ultrasonography may be performed in girls with pubertal delays to determine the presence of normal anatomy.

Bone age radiography can be useful in evaluating an adolescent with delayed puberty and slow linear growth, because it compares the chronologic age and height age to skeletal maturation, which allows for assessment of the potential for further skeletal growth. A delayed bone age can be seen with chronic medical conditions, endocrinopathies, and constitutional delay. Comparison of the bone age, height age, and chronologic age can help differentiate among the potential causes of delayed puberty.

PREP Pearls

- Puberty is considered delayed in girls if there is a lack of breast development by age 13 years, failure to menstruate by age 16 years, or more than 5 years between the initiation of breast development and menarche.
- To narrow the broad differential diagnosis for causes of pubertal delay, the first step in evaluation should be a thorough history and physical examination.

ABP Content Specifications(s)

- Plan the appropriate evaluation of premature arrest of previously normal growth rate in an adolescent

Suggested Readings

- Bordini B, Rosenfield RL. Normal pubertal development: part II: clinical aspects of puberty. Pediatr Rev. 2011;32(7):281-292. doi: http://dx.doi.org/10.1542/pir.32-7-281.
- Mansfield MJ, Swartz JM. Abnormal growth and development. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. Neinstein's Adolescent and Young Adult Health Care: A Practical Guide. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:103-114.
- Rosen DS. Physiologic growth and development during adolescence. Pediatr Rev. 2004:25(6):194-200. doi: http://dx.doi.org/10.1542/pir.25-6-194.

Question 56

An 18-month-old boy is brought to your office by his mother who tells you she is concerned about his speech. He cooed and babbled until 9 months of age, but does not use or repeat any words. He does not turn his head when his name is called or make eye contact when spoken to. However, he makes good eye contact at other times and will point to draw the attention of his mother to things he finds interesting. He reacts when there are loud noises, such as when his mother vacuums the carpet. When given a crayon, he will scribble spontaneously. He can hold a cup. He enjoys running and throwing a ball to his parents. His favorite toys are cars and trains.

Of the following, the MOST likely evaluation to identify the cause of this patient's developmental problems is an evaluation of his

A. cognitive and adaptive skills
B. hearing
C. social-emotional development
D. speech and language development
E. vision

Correct Answer: B
The 18-month-old boy in this vignette has language delay and an audiology evaluation will identify his profound hearing loss. He has the characteristic lack of progression in expressive language after a period of cooing and babbling seen in children with profound hearing loss. He does not turn his head when called or make eye contact when spoken to, but responds appropriately when the individual is in his line of sight. While this child reacts to a loud vacuum, he is responding to its vibrations rather than to its sound. The remainder of his development appears normal for his age and he demonstrates appropriate social skills and joint attention.

The differential diagnosis for a child with language delay includes language impairment, autism spectrum disorder (ASD), global developmental delay (GDD) or intellectual disability, and hearing loss. Language delay can be seen in each of these 4 conditions. Language delay does not necessarily progress to language impairment. Young children may have a maturational or developmental delay in speech or language that resolves with time. However, language impairment exists when difficulties in learning language persist beyond this age and cause impairment. Autism spectrum disorder is suspected when language and social interactions are atypical and when unusual patterns of behaviors or interests are present. Global developmental delay (if younger than 5 years of age) or intellectual disability (if older than 5 years of age) is suspected when other delays in development (eg, motor, cognitive, adaptive) are present. Hearing loss, as the etiology of language delay, is suspected when there is difficulty understanding spoken language and difficulty producing speech sounds.

Autism spectrum disorder is characterized by deficits in social communication and interactions, along with restricted, repetitive patterns of behaviors, interests, or activities. Language can be atypical in tone, in inflections used, or in the repetition of words, phrases, or sentences (echolalia). Children with ASD often have difficulty with pragmatic (social) language, such as initiating, sustaining, and navigating conversations and social interactions. Nonverbal communication, including use of eye contact and gestures or understanding of another person's body language or facial expressions, can be impaired. One early clue to ASD is when there is a lack of pointing to request from another person (protoimperative point) and/or to alert another person to one's interest in an object, person, or event (protodeclarative point). The lack of shared attention in an activity with another person (joint attention) and the lack of ability to see things from another person's perspective (Theory of Mind) are key features of autism. In addition, children with ASD often demonstrate behavioral rigidity and can have significant difficulty with change. They may demonstrate repetitive or stereotypic motor movements such as hand flapping, rocking, or spinning. They may have hypo- or hypersensitivity to sensory stimuli such as loud noises (eg, blow dryers, public toilets, blenders, vacuums), sticky or rough substances, food textures (eg, soft, crunchy, mixed), or visual input (eg, lights, patterns, movement). Play may lack imagination, involve unusual objects, be ritualistic (eg, lining things up), or be sensory motor (eg, mouthing, banging, spinning).

Intellectual disability is a disorder that starts during the developmental period and includes both intellectual and adaptive functioning deficits. Global developmental delay may be a more appropriate term for children younger than 5 years of age, as measures of cognition are more

reliable and predictive after that time. Language delay, particularly receptive language delay, can be the first sign of intellectual disability in a young child. In addition to delayed language, delays are apparent in problem-solving skills and self-help skills Motor delays may also be present. When ASD and intellectual disability (or GDD) coexist, ASD is not diagnosed unless the deficits and patterns of behavior are inappropriate for the child's developmental level.

Hearing loss occurs in 6 in 1,000 at birth; 1 to 2 in 1,000 have severe or profound hearing loss. Universal newborn hearing screening via testing of otoacoustic emissions and auditory brainstem response has improved detection of early hearing loss. Otoacoustic emissions testing is normal when the cochlea is structurally intact. Auditory brainstem response testing, or brainstem auditory evoked response testing, is normal when the auditory nerve is normal. Normal hearing is assumed when these tests are normal. Children with speech/language delays or for whom there are concerns about hearing should receive a formal audiology evaluation. Newborn hearing screens may have been normal for children with mild-to-moderate, progressive, or acquired hearing loss. Children with severe-to-profound hearing loss will coo and babble until 6 to 9 months of age and then will stop progressing in their language development. They may appear to respond to loud sounds when they can feel the vibrations. Children with mild-to-moderate hearing loss have the most difficulty with soft sounds and high-frequency sounds.

Item C56 delineates some of the differences between these conditions (when not coexisting with other conditions).

Item C56. Findings Identified in Autism Spectrum Disorder, Intellectual Disability/Global Developmental Delay, and Hearing Loss.

	Autism Spectrum Disorder	Intellectual Disability/ Global Developmental Delay	Hearing Loss
Language	Delayed and/or atypical	Likely receptive language +/- expressive language delay	Delayed
Hearing	Normal	Normal	Abnormal
Cognition	Normal	Impaired	Normal
Social reciprocity, joint attention	Impaired	Present	Present
Orientation to name	Often deficient	Present	May be deficient, depending on degree of hearing loss
Stereotypies	Present	May be present with more severe levels of intellectual disability	May be present with severe sensory deficits

Courtesy of Y. Liu

A complete evaluation for a child with developmental delay would include all options provided in the vignette. An assessment of cognitive and adaptive skills would help identify possible GDD. This child's scribbling, cup holding, running, and ball throwing are age-appropriate and are not consistent with GDD. Evaluating the child's social-emotional development can help determine if this child has an ASD. However, this diagnosis is less likely given his good joint attention (eg, protodeclarative point). A speech and language evaluation is indicated for this child's delayed language development, but would not identify the etiology of his developmental problems. Importantly, hearing and vision should be assessed in any child for whom there is concern about development. Vision impairment would not account for this child's language delay and is unlikely to be substantial in this child who makes good eye contact, points, and throws a ball to his parents. Although evaluation of all options presented is helpful, this child's presentation is most consistent with hearing impairment, and a hearing evaluation would most likely identify the etiology of this child's language delay.

Irrespective of etiology, a referral to an early intervention program is indicated once significant developmental delay is detected in a child younger than 3 years of age. Early intervention programs are federally funded under Part C of the Individuals with Disabilities Education Act. Services are provided to children from birth to 3 years of age with delays in development or who are at high risk for developmental delays. Prompt treatment for these delays improves the outcomes of these children. This child should be referred to an early intervention program at the same time an audiology evaluation is being arranged.

PREP Pearls

- The differential diagnosis for a child with language delay includes language impairment, autism spectrum disorder, global developmental delay/intellectual disability, and hearing loss.
- Children with speech/language delays or for whom there are concerns about hearing should receive a formal audiology evaluation. Newborn hearing screens may have been normal for children with mild-to-moderate, progressive, or acquired hearing loss.
- Children with severe to profound hearing loss will coo and babble until 6 to 9 months of age and then will stop progressing in their language development. They may appear to respond to loud sounds when they can feel the vibrations.

ABP Content Specifications(s)

- Distinguish findings associated with autism spectrum disorder from those of an intellectual disability
- Distinguish findings associated with autism spectrum disorder from those of profound hearing loss

Suggested Readings

- Grindle CR. Pediatric hearing loss. Pediatr Rev. 2014;35(11):456-464. doi: http://dx.doi.org/10.1542/pir.35-11-456.
- Harrington JW, Allen K. The clinician's guide to autism. Pediatr Rev. 2014;35(2):62-78. doi: http://dx.doi.org/10.1542/pir.35-2-62.

Question 57

A 3-year-old girl is brought to your office for a health supervision visit by her father. The girl has been your patient since birth. You are aware that her parents divorced when she was 18 months of age, and that they share custody.

A review of the girl's chart indicates that she has been healthy and that she has had no recent visits for any acute concerns. She has expressed no somatic complaints to either parent. The father states that the girl is very active and seems to be developing appropriately. She recently started preschool and is adjusting well.

The girl's vital signs and growth parameters are all within normal ranges for her age. She is very interactive and cooperative with you throughout the visit. A complete physical examination, including inspection of her genitalia, reveals no abnormalities. You begin providing age-appropriate anticipatory guidance to the father while a nurse walks with the girl so that she can pick out some stickers.

When the girl leaves the room, the father asks whether you can tell based on your physical examination if his daughter could have been sexually abused. He is concerned about this because the girl's mother recently became engaged to her boyfriend, whom the father does not trust. When you ask him whether the child has made any statements related to being abused by the mother's boyfriend, he denies this but states: "You just never know." He is also concerned because he has noticed the girl intermittently "touching her own private parts" when she is playing in the bathtub over the past 2 to 3 months.

Of the following, the MOST accurate statement related to this father's concern is that

A. a forensic examination for sexual abuse is indicated
B. the girl's recent behaviors can be normal for her age
C. the mother's boyfriend should be reported to child protective services
D. sexual abuse is unlikely because the girl has a normal physical examination
E. sexual abuse should be suspected because of the girl's recent behaviors

Correct Answer: B
The father of the young girl in the vignette raises a question about whether his daughter could be a victim of sexual abuse, citing her recent behavior of touching her genitalia while bathing, as well as his distrust of another adult who is in contact with the girl. Of the answer options listed, the most accurate statement related to the father's concern is that the girl's recent behaviors can be normal for her age.

It is imperative that all pediatric providers recognize the history, signs, and symptoms of sexual abuse, as well as which patients require emergent evaluation for sexual abuse or assault. Sexual abuse is prevalent in society, and it is highly likely that all pediatricians will encounter sexually abused children during the course of their careers. Sexual abuse occurs when a child is engaged in or knowingly exposed to a sexual situation. Some cases of sexual abuse involve physical contact between the victim and perpetrator, with or without digital, oral, anal, or vaginal penetration. In other cases, there may be no physical contact, but the child is made to witness sexual acts or pornography. Some cases may even involve commercial exploitation of the victim through forced prostitution or participation in child pornography. In most cases of sexual abuse, perpetrators are known to the victim by virtue of being relatives, family friends, neighbors, or community members.

Child sexual abuse may present to the attention of pediatric providers in a number of ways. Children may be brought for evaluation after disclosure of sexual abuse to a relative, other nonprofessional, or to a professional such as a teacher, social worker, or counselor. While disclosure may occur soon after the child is exposed to abuse, disclosure of sexual abuse is often delayed for weeks, months, or even years, so that medical attention is sought outside of the acute period.

Concern for sexual abuse may arise when children demonstrate worrisome behaviors. Parents may sometimes become concerned about developmentally normal child sexual behaviors, which may include preschool-aged children undressing in front of others and touching their own genitals. Pediatricians can educate and reassure parents in cases of developmentally appropriate, transient behaviors such as the ones displayed by the 3-year-old girl in the vignette. On the other hand, highly sexualized behaviors such as coercing others to engage in sexual acts or explicitly imitating intercourse are uncommon and not developmentally normal in children, and therefore necessitate a comprehensive evaluation for sexual abuse.

Children who are victims of sexual abuse may also present with nonspecific physical or emotional complaints, including unexplained abdominal pain, genital pain, encopresis, change in school performance, abrupt behavioral changes, or difficulty sleeping. While these symptoms are nonspecific for sexual abuse, questioning about stressors, including abuse, should be incorporated into the evaluation of these complaints while simultaneously investigating for organic etiologies.

In cases that are much less common, specific physical findings, such as anogenital injuries or signs of sexually transmitted infection in a prepubertal child, will bring sexual abuse to the

attention of a provider. As with evaluations for other pediatric complaints, key components of the evaluation of child sexual abuse include a careful, thorough history, physical examination, indicated laboratory studies, and formation of an appropriate management plan. A 2013 clinical report from the American Academy of Pediatrics Committee on Child Abuse and Neglect, provides pediatricians with evidence-based guidance regarding the evaluation of children in the primary care setting when sexual abuse is suspected. Included in the guidelines is the most appropriate way to approach the medical history and physical examination, appropriate laboratory testing, reporting to child protective service agencies, and working with families to mitigate the adverse effects of sexual abuse.

For the young girl in the vignette who has disclosed no history of sexual abuse, who is displaying developmentally-appropriate behavior, and who has no findings concerning for sexual abuse on history or physical examination, a forensic examination for sexual abuse is not indicated. The timing and nature of the reported or suspected abuse are important factors to consider when determining whether forensic evidence collection is indicated. In most states, forensic evidence collection is required if sexual abuse involving the exchange of bodily fluids occurred within the past 72 hours. Studies have demonstrated that forensic evidence is rarely obtained from prepubertal children after 24 hours following the occurrence of abuse. As with physical examination findings, confirmatory forensic evidence is certainly not required to make a diagnosis of child sexual abuse.

Reporting sexual abuse by the mother's boyfriend to child protective services is not the most appropriate action at this time, given that there is not a high clinical suspicion that the girl in the vignette has been sexually abused. Whenever a reasonable suspicion for sexual abuse exists, all providers are obligated to report the suspicion to child protective services, in addition to local law enforcement agencies (if the identity of the perpetrator is known). In some cases, children may present for evaluation when one parent accuses another parent (or his/her contacts) of sexually abusing the child. These cases can be extremely challenging, especially if the pediatrician believes that allegations of sexual abuse may be related to a custody dispute or other parental conflict. All concerns must be taken seriously and evaluated in these situations. If the evaluation does not support a history of sexual abuse but a parent continues to express concern, the family may need referral to a mental health expert or to a pediatric child abuse specialist.

The statement that sexual abuse is unlikely because the girl has a normal physical examination is incorrect. A normal physical examination does not exclude the possibility of sexual abuse. In fact, most sexual abuse victims have normal anogenital examinations and multiple studies have found that definitive physical findings are not commonly present in sexual abuse victims. It is important for pediatricians to educate caregivers that a physical examination alone cannot determine whether their child has been sexually abused.

Finally, the girl's recent behavior of touching her genitals while bathing certainly falls into the range of developmentally normal behavior for a preschool-aged child. This particular behavior does not indicate that the girl has been a victim of sexual abuse.

PREP Pearls

- A normal physical examination does not exclude the possibility of sexual abuse.
- In most states, forensic evidence collection is required if sexual abuse involving the exchange of bodily fluids occurred within the past 72 hours. However, forensic evidence is rarely obtained from the bodies of prepubertal children after 24 hours following the occurrence of abuse. As with physical examination findings, confirmatory forensic evidence is certainly not required to make a diagnosis of child sexual abuse.
- Whenever a reasonable suspicion for sexual abuse exists, all providers are obligated to report the suspicion to child protective services and reporting to law enforcement may also be required.

ABP Content Specifications(s)

- Recognize which patients require emergent evaluation and physical examination for sexual abuse or assault
- Recognize that most children examined for sexual abuse will have normal examination findings
- Recognize the history, signs, and symptoms of sexual abuse

Suggested Readings

- Fortin K, Jenny C. Sexual abuse. Pediatr Rev. 2012;33(1):19-32. doi: http://dx.doi.org/10.1542/pir.33-1-19.
- Jenny C, Crawford-Jakubiak JE, Committee on Child Abuse and Neglect. The evaluation of children in the primary care setting when sexual abuse is suspected. Pediatrics. 2013;132(2):e558-e567. doi: http://dx.doi.org/10.1542/peds.2013-1741.
- Wood JN, Callahan JM, Christian CW. Child abuse/assault. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. Textbook of Pediatric Emergency Medicine. 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:657-670.

Question 58

A 10-year-old boy with spina bifida is brought to his pediatrician for evaluation of cloudy urine. He has a history of neurogenic bladder requiring catheterization. He has had multiple urinary tract infections in the past. Vital signs show a temperature of 38.1°C, respiratory rate of 20 breaths/min, heart rate of 88 beats/min, and blood pressure of 110/60 mm Hg. On physical examination, he has no motor function of his lower extremities. Laboratory data show:

Urinalysis, 3+ leukocytes, nitrite negative
Urine Gram stain, gram-positive cocci in pairs and chains

Of the following, the BEST therapy for this infection is

A. ampicillin
B. cefixime
C. cephalexin
D. nitrofurantoin
E. trimethoprim-sulfamethoxazole

Correct Answer: A

The best choice for the treatment of the urinary tract infection in the boy in this vignette is ampicillin. The Gram stain reveals gram-positive cocci in pairs and chains. The most likely pathogen in this vignette is Enterococcus, therefore ampicillin is the preferred choice.

Enterococci are normal flora of the gastrointestinal tract of humans and other animals. They are widely recognized as a cause of urinary tract infections, as well as bacteremia, endocarditis, and wound infections. Since they reside in the human gastrointestinal tract, they must be considered in the presence of intra-abdominal infections. Rarely, enterococci can cause meningitis. Enterococci are opportunists and their rise to prominence has been attributed to a growing population of patients that are immunocompromised or severely ill and necessitate medical devices such as central venous or urinary catheters. Enterococci should be considered in any child who requires chronic bladder catheterization and develops an urinary tract infection. In addition, enterococci frequently develop resistance to antibiotics.

Enterococci are intrinsically resistant to cephalosporins, therefore cefixime and cephalexin would not be correct choices. Cephalosporins are appropriate antimicrobials to use for urinary tract infections caused by gram-negative enteric bacteria. The vignette, however, reveals that the etiology of the infection is due to a gram-positive organism.

Nitrofurantoin can be used for the treatment of cystitis caused by a susceptible gram-negative or gram-positive organism or for prophylaxis of urinary tract infections. Nitrfurantoin has activity against susceptible enterococci, but either penicillin or ampicillin are preferred agents for uncomplicated urinary tract infections.

The use of trimethoprim-sulfamethoxazole for enterococcal urinary tract infections is controversial. While there are some in vitro data to suggest susceptibility, this may not correlate with clinical outcomes and thus is not the best treatment for this patient.

PREP Pearls

- Enterococci are widely recognized as a cause of urinary tract infections, as well as bacteremia, endocarditis, and wound infections, and must be considered in intra-abdominal infections.
- Enterococci are opportunists and their rise to prominence has been attributed to a growing population of patients that are immunocompromised or severely ill and necessitate medical devices such as central venous or urinary catheters.
- Enterococci are intrinsically resistant to cephalosporins.

ABP Content Specifications(s)

- Recognize the clinical syndromes associated with enterococcal infections

Suggested Readings

- American Academy of Pediatrics. Non-group A or B streptococcal and enterococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:750-753.
- Butler KM. Enterococcal infection in children. Semin Pediatr Infect Dis. 2011;17(3):128-139. doi: http://dx.doi.org/10.1053/j.spid.2006.06.006.

Question 59

A 9-month-old female infant born at 26 weeks of gestation has chronic diarrhea and worsening edema. There is no history of vomiting, fever, or other symptoms. Her history is remarkable for a long course of poor weight gain. On physical examination, the infant's temperature is 37.3°C, heart rate is 96 beats/min, respiratory rate is 25 breaths/min, and blood pressure is 80/34 mm Hg. She appears small and is in no distress.

She is currently on a cow milk–based formula and takes 4 to 6 ounces every 3 to 4 hours. She also eats pureed food twice daily and teething crackers several times per day. A recent calorie count calculated her intake to be 120 kcal/kg. The dietician reviewed the formula mixing instructions at the last visit and found that the mother was mixing correctly. Her physical examination is only remarkable for bilateral lower extremities with 2+ pitting edema.

The infant's evaluation for failure to thrive has been extensive, including normal cardiac echocardiography and liver ultrasonography. Laboratory results are shown:

Laboratory Test

Laboratory Test	**Result**
Complete blood cell count	Normal
Hepatic transaminases	Normal
Albumin	2.8 g/dL (28 g/L)
Immunoglobulin G	105 mg/dL (1.05 g/L) (normal = 246-904)
Immunoglobulin A	10 mg/dL (100 g/L) (normal = 36-80)
Immunoglobulin M	9 mg/dL (90 mg/L) (normal = 40-143)
C-reactive protein	0.6 mg/L (5.7 nmol/L)

Urinalysis is negative. Stool study results are pending.

Of the following, the infant's MOST likely diagnosis is

A. celiac disease
B. infantile inflammatory bowel disease
C. lymphangiectasia
D. portal hypertension
E. systemic lupus erythematous disease

Correct Answer: C
The infant in this vignette has protein-losing enteropathy (PLE) caused by lymphangiectasia, a dilation of the intestinal lymphatic vessels resulting in chronic diarrhea and protein loss. Her low serum protein including low immunoglobulins, poor weight gain, edema, and diarrhea support this diagnosis.

The presentation of protein or calorie malnutrition varies based on the underlying etiology. The differential diagnosis includes inadequate intake, increased demand because of a medical condition (ie, cardiac or liver disease), and malabsorption. The presentation and characteristic laboratory findings will vary depending on the underlying cause of the malnutrition (Item C59).

Item C59. Presentation and Laboratory Findings Associated With Malnutrition.

Cause of Malnutrition	Presentation	Characteristic Laboratory Finding(s)	Example of Disease Process
Caloric deficiency	• Bradycardia • Cachexia • FTT • Low temperature	• Acidosis • Iron-deficiency anemia	• Inadequate intake • Marasmus
Protein-calorie deficiency	• Alopecia • Abdominal distention • Dermatitis • Edema • Fatty liver • FTT	• Acidosis • Hypoalbuminemia • Hypoglycemia • Iron-deficiency anemia • Low serum potassium, magnesium, and phosphorus	• Inadequate intake • Kwashiorkor
Fat malabsorption	• FTT • Pale, bulky, malodorous stools	• Elevated prothrombin time • Low fat soluble vitamins (A, D, E, K) • Low triglycerides and cholesterol	• Chronic liver disease • Cystic fibrosis
Protein-losing enteropathy	• Diarrhea • Edema • FTT	• Edema • Elevated stool α-1 antitrypsin • Low serum proteins - Albumin - Immunoglobulins	• Bowel infections • Celiac disease • Congestive heart failure • Gastrointestinal malignancy • Inflammatory bowel disease • Lymphangiectasia • Small bowel bacterial overgrowth • Vasculitis
Increased caloric need	• FTT • Varies based upon underlying diagnosis	• Varies based on underlying diagnosis	• Chronic lung disease • Congenital cardiac disease

FTT, failure to thrive

Courtesy of C. Waasdorp Hurtado

Celiac disease may cause PLE, but is less likely in this case, given the age of the infant and symptoms that preceded the intake of gluten. Portal hypertension may also result in PLE, but is unlikely in this child with normal findings on abdominal examination (without hepatomegaly or splenomegaly) and normal liver function. Systemic lupus erythematosus may cause PLE, but there are no physical examination or laboratory findings that support this diagnosis. Finally, infantile inflammatory bowel disease typically presents with large volumes of bloody diarrhea, severe failure to thrive, anemia, and elevated serum inflammatory markers.

PREP Pearls

- Protein-losing enteropathy (PLE) presents with diarrhea, edema, and low serum protein levels.
- Stool a-1 antitrypsin level will be elevated in PLE.
- Edema is present in patients with protein-calorie malnutrition

ABP Content Specifications(s)

- Recognize the clinical features associated with protein or calorie deficiency, including edema and malnutrition
- Plan the diagnostic evaluation of a patient with suspected protein-losing enteropathy, while considering its causes

Suggested Readings

- Braamskamp MJ, Dolman KM, Tabbers MM. Clinical practice: protein-losing enteropathy in children. Eur J Pediatr. 2010;169(10):1179-1185. doi: http://dx.doi.org/10.1007/s00431-010-1235-2.
- Hartman C, Shamir R, Hecht C, Koletzko B. Malnutrition screening tools for hospitalized children. Curr Opin Clin Nutr Metab Care. 2012;15(3):303-309. doi: http://dx.doi.org/10.1097/MCO.0b013e328352dcd4.
- Jaffe A. Failure to thrive: current clinical concepts. Pediatr Rev. 2011;32(3):101-108. doi: http://dx.doi.org/10.1542/pir.32-3-100.
- Kerzner B, Milano K, MacLean WC Jr, Berall G, Stuart S, Chatoor I. A practical approach to classifying and managing feeding difficulties. Pediatrics. 2015;135(2):344-353. doi: http://dx.doi.org/10.1542/peds.2014-1630.

Question 60

During a visit for a sports physical examination, you discuss sports injury prevention with a 14-year-old adolescent and her family. She plays on the school soccer team. Her parents are concerned about her risk of knee injury because their 16-year-old son recently tore his anterior cruciate ligament (ACL) while playing basketball. The parents want to know more about their daughter's risk of an ACL injury.

Of the following, the MOST accurate statement regarding their daughter's risk of this injury is that

A. a neuromuscular training program would reduce her risk
B. her risk is lower than her brother's because of her age
C. her risk is lower than her brother's because of her sex
D. playing soccer in a support brace would reduce her risk
E. soccer is a low-risk sport for this injury

Correct Answer: A

Discussing sports injury prevention with children and families is an important part of the preparticipation physical evaluation (PPE). The adolescent in the vignette and her parents should be told that she could mitigate her risk of an anterior cruciate ligament (ACL) tear and other knee injuries by participating in a neuromuscular training program.

Once an athlete suffers an ACL tear, his or her risk of arthritis increases approximately 10-fold, regardless of how the injury is treated. Female adolescent athletes who participate in sports involving jumping and changing direction, such as basketball and soccer, have a particularly high rate of ACL injury. The most common mechanisms of this injury include landing from a jump, twisting with the foot planted, and sudden deceleration.

The main goal of the PPE is to screen young athletes for conditions that might make participation in athletic activities unsafe. Pediatricians can also use the PPE visit to promote injury prevention strategies. Healthcare providers should educate athletes at high risk for ACL tear about neuromuscular training programs that reduce the risk of injury. Neuromuscular training programs that emphasize control of knee position during sports have been shown to decrease the risk of knee injuries. Successful programs incorporate strengthening, balance, and plyometric (jump) training and cues for athletes that encourage proper technique.

Athletes who participate in sports with a high risk of ankle sprains, such as football and basketball, should be counseled about the protective effect of strengthening programs and ankle braces. Athletes should be asked about any prior history of injuries. Inadequate rehabilitation of prior injuries is a risk factor for future injuries.

The adolescent in the vignette has a risk for ACL injury that is higher than that of her brother because of her sex. Girls participating in soccer and basketball have higher rates of ACL tear than boys in those sports do. Support braces may prevent ankle sprains, but have not been shown to reduce the risk for ACL tears.

PREP Pearls

- Neuromuscular training programs that emphasize strengthening, balance, and good technique can reduce the risk of knee ligament injuries.
- Female adolescent athletes have a particularly high rate of anterior cruciate ligament injuries.

ABP Content Specifications(s)

- Understand the importance of skeletal maturity in determining the appropriate type of physical training
- Understand the role of conditioning in preventing injuries in athletes of various ages
- Recognize the importance of adequate rehabilitation of current injury in the prevention of future injury among athletes

Suggested Readings

- LaBella CR, Hennrikus W, Hewett TE. Anterior cruciate ligament injuries: diagnosis, treatment, and prevention. Pediatrics. 2014;133(5):e1437-1450. doi: http://dx.doi.org/10.1542/peds.2014-0623.
- McGuine TA, Hetzel S, Wilson J, Brooks A. The effect of lace-up ankle braces on injury rates in high school basketball players. Am J Sports Med. 2012;40(1):49-57. doi: http://dx.doi.org/10.1177/0363546511406242.

Question 61

A 9-year-old boy is brought to your office for "a pimple on his left eyelid." His mother reports that the lesion has been present for the past 4 weeks. The area has increased in size slightly over the past 4 weeks and is not tender. On physical examination, you find a 5 mm, painless, rubbery lesion located on the left lower eyelid. There is no erythema of the eyelid (Item Q61).

Of the following, the BEST approach for initial management of this patient is

A. incision and drainage
B. referral to an ophthalmologist
C. treatment with an oral cephalexin
D. treatment with a topical erythromycin
E. warm compresses 4 times a day

Correct Answer: E
The boy in this vignette has a chalazion of the left lower eyelid. A chalazion results from an inflammatory process involving the meibomian glands of the upper or lower eyelid. It typically presents as a firm, slow growing, nontender, rubbery nodule in the lower or upper eyelid, which varies between 3 to 10 mm. The skin overlying a chalazion has minimal, if any, changes. The lesion tends to be chronic, lasting for several weeks to months. As recommended for the boy in this vignette, the treatment for a chalazion consists of warm compresses to the eyelid multiple times a day. The chalazion is not the result of an infectious process, so antibiotics (either topical or oral) are not indicated unless there is also a secondary infection present. A secondary infection of a chalazion will typically present with the onset of pain and tenderness. Most chalazia will resolve on their own with the warm compresses; however, excision may be necessary if the chalazion distorts vision or leads to a cosmetic issue. A referral to an ophthalmologist is not indicated until routine treatment has been tried. Incision and drainage of the chalazion is not helpful, as there is no infection to drain.

In contrast to a chalazion, a hordoleum represents a more acute infectious process of the glands of the eyelid (the meibomian glands or the glands of Zeis or Moll). Staphylococcus aureus is the usual agent associated with these infections. An external hordoleum, also known as a common stye, involves an infection of the glands of Zeis or Moll that are associated with the hair follicles of the eyelid. The lid margin can be mildly red and swollen and the infection points to the lid margin. Treatment of choice for an external hordoleum consists of warm compresses to help relieve the obstruction and promote drainage. An internal hordoleum results from an infection of the meibomian gland, the large sebaceous gland that has its opening at the lid margin. The swelling tends to be more diffuse and the infection will point to either the lid margin or the conjunctival surface of the eye. Treatment for an internal hordoleum consists mainly of warm compresses. A topical antibiotic ointment is sometimes also applied to prevent spreading of the infection to adjacent hair follicles. Oral antibiotics or surgical excision and drainage may be required in extreme cases where the infection progresses

PREP Pearls

- A chalazion tends to be chronic in nature, lasting weeks to months, whereas a hordoleum (stye) tends to be more acute.
- The main treatment for both chalazion and hordoleum is warm compresses.
- Staphylococcus aureus is most commonly associated with styes.

ABP Content Specifications(s)

- Plan the appropriate management of a chalazion
- Plan the appropriate management of a stye
- Differentiate the clinical findings associated with a stye from those of a chalazion

Suggested Readings

- Otlisky SE, Hug D, Plummer LS, Stahl ED, Ariss MM, Lindquist TP. Abnormalities of the lids. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:3033-3034.
- Rosales T. Infections of the eye. In: Berkowitz, CD, ed. Berkowitz's Pediatrics: A Primary Care Approach. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:496-497.
- Wald ER. Periorbital and orbital infections. Pediatr Rev. 2004;25(9):312-320. doi: http://dx.doi.org/10.1542/pir.25-9-312.

Question 62

You are caring for a full-term male newborn in the neonatal intensive care unit. The pregnancy was complicated by maternal immune thrombocytopenic purpura, for which his mother received intravenous immunoglobulin, with the last dose given 3 weeks before delivery. His blood type is B–. At birth, he had a platelet count of 15 × 103/μL (15 × 109/L). On physical examination, he is well-appearing without any evidence of bleeding.

Of the following, the BEST next step in management for this neonate is to give

A. an infusion of anti-Rh antibody
B. an infusion of intravenous immunoglobulin
C. reassurance to the infant's mother that no further treatment is warranted
D. a transfusion of maternal platelets collected by pheresis
E. a transfusion of single donor leukodepleted and irradiated platelets

Correct Answer: B

Neonatal thrombocytopenia can result from decreased production or increased destruction of platelets. The maternal and family histories are critical to ascertaining the correct etiology. This neonate's mother has a known diagnosis of active idiopathic thrombocytopenic purpura (ITP), for which she received intravenous immunoglobulin (IVIG) 3 weeks before delivery. This strongly suggests that the neonate's thrombocytopenia is caused by platelet destruction because of passive transmission of antibodies through the placenta. The appropriate treatment for severe neonatal thrombocytopenia caused by maternal ITP is an infusion of IVIG.

Although anti-Rh therapy is appropriate treatment for ITP in children, its mechanism of action requires that it coat the patient's red blood cells. The antibody-coated red blood cells then occupy the Fc receptors in the spleen and prevent the destruction of antibody-coated platelets by competitive inhibition. The neonate in the vignette has a B-negative blood type, meaning that his red blood cells do not express the Rh antigen, so this treatment would not be effective.

Neonatal alloimmune thrombocytopenia (NAIT) is the platelet equivalent of neonatal Rh disease that affects the red blood cells. The fetal platelets express a paternally inherited antigen, most commonly PlA1, which is foreign to the mother. The mother produces antibodies to that antigen, which cross the placenta and cause neonatal thrombocytopenia, while having no effect on the maternal platelet count. The antibodies are maternal and not produced by the neonate, therefore their titer drops with time after birth. If the neonatal thrombocytopenia is severe, it should be treated with a transfusion of maternal platelets collected via apheresis. The maternal platelets will not express the offending antigen, and will therefore not be destroyed by the circulating antibody. In the vignette, the mother has a known diagnosis of ITP, which means that she is producing an antibody to her own platelets. It is likely that that same antibody is causing the neonate's thrombocytopenia. Transfusion of maternal platelets would therefore not help, because they would also be destroyed by the antibody.

If the child in the vignette were experiencing acute, life-threatening bleeding, then the immediate transfusion of the most available unit of platelets would be a reasonable course of action. In maternally transmitted ITP, however, the antibody is typically reactive with a common platelet antigen, so platelets transfused from an unrelated donor will likely also have an abbreviated lifespan. This would therefore not be the treatment of choice for a stable neonate with maternally transmitted ITP.

Neonates with severe thrombocytopenia are at a greater risk for intracranial hemorrhage than are older children. Although it would be reasonable to observe an older child with a platelet count of $15 \times 10^3/\mu L$ ($15 \times 10^9/L$), it would not be recommended for a neonate.

PREP Pearls

- Maternal immune thrombocytopenic purpura (ITP) can result in neonatal thrombocytopenia because of the maternal production of antibodies to her own platelets, which cross the placenta and cross-react with fetal platelets. If severe, it is treated with an infusion of intravenous immunoglobulin.
- The maternal and family histories are critical to determining the etiology of neonatal thrombocytopenia.
- A maternal history of ITP or other autoimmune disorder should raise concern for neonatal ITP, whereas a history of prior children with neonatal thrombocytopenia and no maternal history of autoimmunity should raise concern for neonatal alloimmune thrombocytopenia.
- Neonatal alloimmune thrombocytopenia results from maternal antibody production to an antigen expressed on fetal platelets, which is not expressed on maternal platelets. If severe, it is treated with a transfusion of maternal platelets, because these do not express the offending antigen.

ABP Content Specifications(s)

- Understand the role of medications in the development of thrombocytopenia
- Understand the role of medications in the development of thrombocytopenia
- Recognize the significance of thrombocytopenia in neonates and older children and manage appropriately

Suggested Readings

- Buchanan GR. Thrombocytopenia during childhood: what the pediatrician needs to know. Pediatr Rev. 2005;26(11):401-409.
- Roberts IAG, Murray NA. Neonatal thrombocytopenia: new insights into pathogenesis and implications for clinical management. Curr Opin Pediatr. 2001;13(1):16-21.
- Sillers L, van Slambrouck C, Lapping-Carr G. Neonatal thrombocytopenia: etiology and diagnosis. Pediatr Ann. 2015;44(7):e175-e180. doi: http://dx.doi.org/10.3928/00904481-20150710-11.

Question 63

A 2-week-old female newborn is brought to your office for a health supervision visit. The mother is concerned that, for the past 2 days, the baby has not been breastfeeding well. The newborn tires after feeding for only 5 minutes and had only 2 wet diapers today. She was delivered at 39 weeks of gestation to a 23-year-old gravida 1 para 0 woman. Her Apgar scores were 8 and 9 at birth and 5 minutes, respectively, and she had a birthweight of 3,500 g. The pregnancy was uncomplicated and the mother was group B Streptococcus negative.

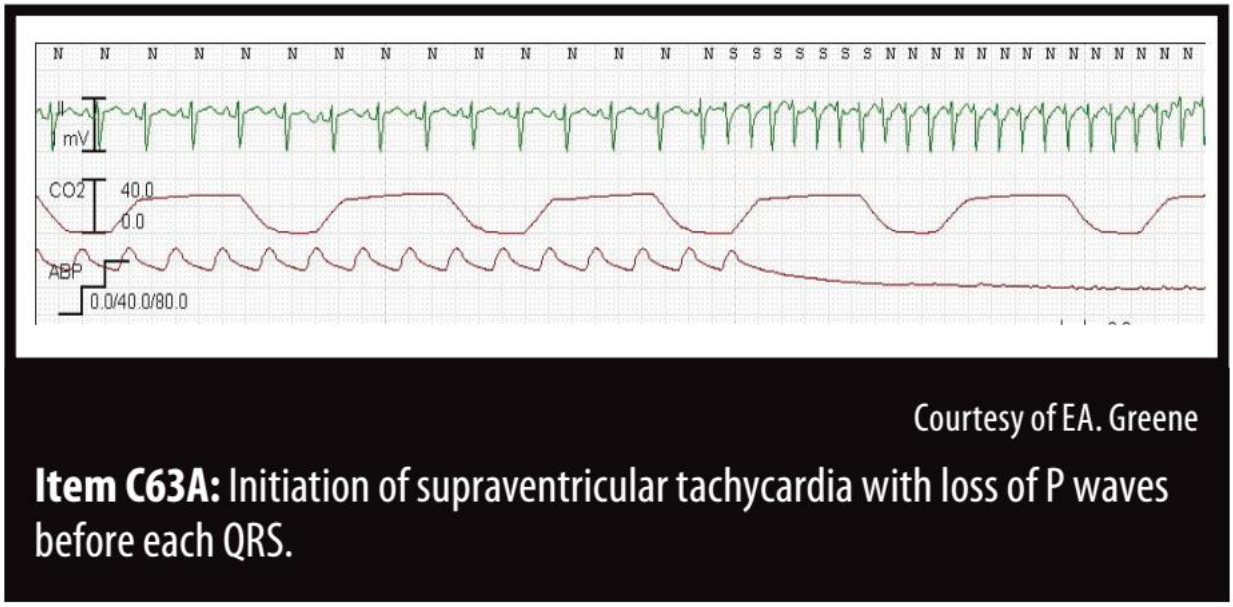
On physical examination, the newborn appears sleepy. Her heart rate is 270 beats/min, respiratory rate is 60 breaths/min, blood pressure is 82/40 mm Hg, and oxygen saturation is 95% in room air. She is warm and well perfused. Breath sounds are clear. A 2/6 systolic murmur can be heard at the left upper sternal border, with no gallop or rub. Her liver is palpable 2 cm below the right costal margin. Capillary refill time is 2 seconds. You refer the patient to the emergency department where they perform electrocardiography.

Of the following, the MOST likely finding on this test is

A. atrial fibrillation
B. junctional tachycardia
C. sinus tachycardia
D. supraventricular tachycardia
E. ventricular tachycardia

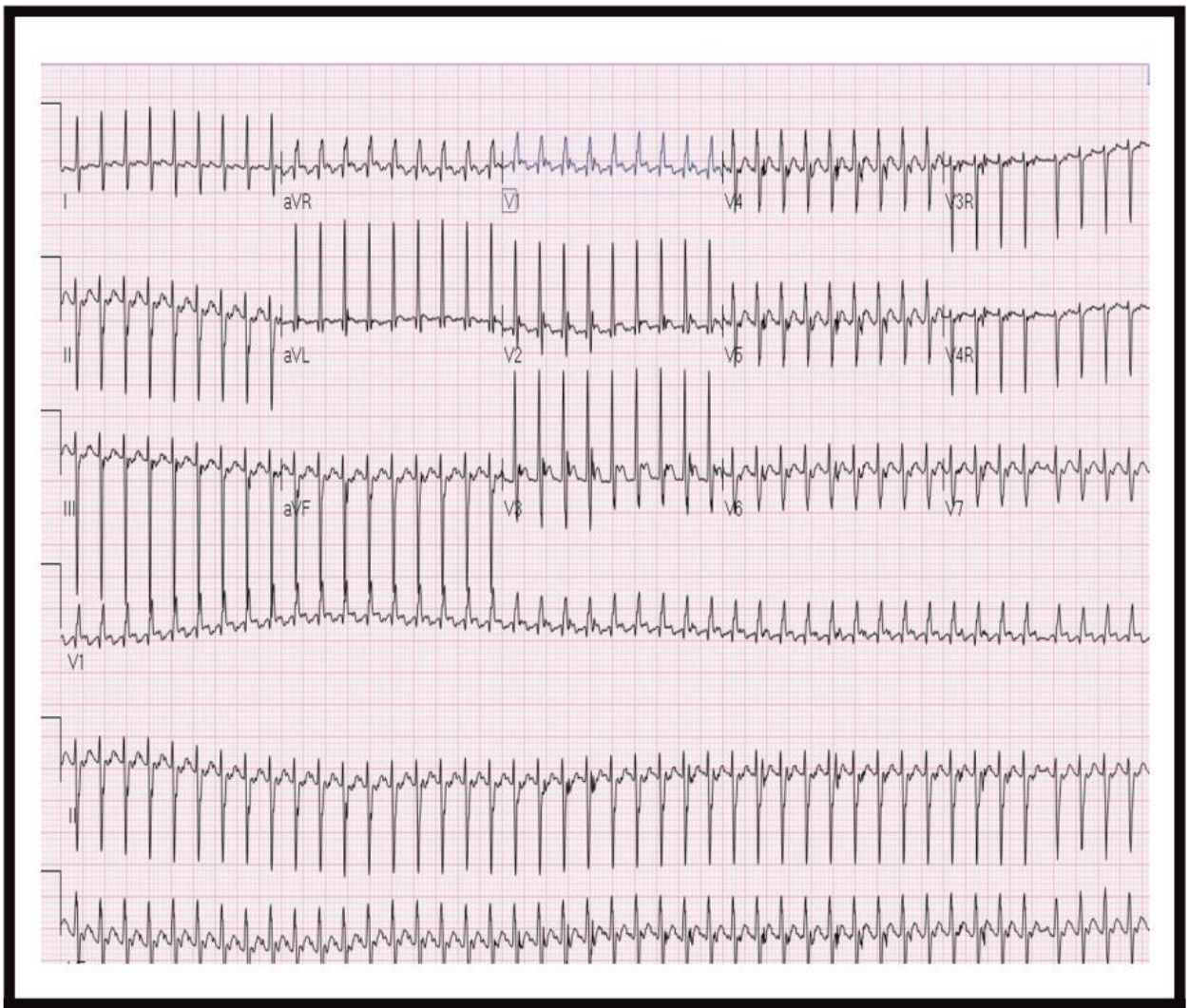
Correct Answer: D

The newborn in this vignette was previously well, with no history of a murmur at birth. Her oxygen saturation is minimally decreased, but is not suggestive of a mixing lesion or congenital heart disease with decreased pulmonary blood flow. The most common cause for a heart rate of 270 beats/min in this age group is an accessory pathway–mediated, reentrant supraventricular tachycardia (SVT). This may be associated with Wolff-Parkinson-White syndrome (WPW) or pre-excitation. Electrocardiography (ECG) in the usual form of reentrant SVT will be narrow complex and very regular. P waves will not be seen before the QRS complexes (Item C63A, Item C63B).



Courtesy of EA. Greene

Item C63A: Initiation of supraventricular tachycardia with loss of P waves before each QRS.



Courtesy of EA. Greene

ITEM C63B: Fifteen-lead electrocardiography in a supraventricular tachycardia case. The heart rate is 270 beats/min, there are no P waves before the QRS, but there is a suggestion of a P wave after the QRS in some leads such as V6 and V7. Note the single sinus beat seen in the fourth to last beat on the tracing. There is a normal P wave preceding that QRS complex.

Atrial fibrillation (AF) would be very unlikely in childhood. If present, it might suggest an ingestion. Other possible causes include congenital heart disease, mitral valve disease with a

large dilated left atrium, and alcohol binge drinking (also known as holiday heart). Atrial fibrillation is thought to be the cause of sudden death in patients with WPW, in whom the rapid atrial rate causes a very rapid ventricular rate and ultimately ventricular fibrillation. The ECG in AF is irregular, with small, difficult-to-identify P waves. If a patient with WPW has syncope, it must be presumed that there was AF with rapid conduction, which places the child at risk for sudden death.

Ectopic atrial tachycardia is a more common arrhythmia in infancy, would likely have a rate of 220 to 240 beats/min, and would be regular. Premature atrial contractions may occur when the patient is in sinus rhythm. A visible change may be noted in the P wave axis when the arrhythmia starts. Since P waves cannot always be seen on telemetry, a 12-lead ECG is needed to assess for a change in P wave morphology. This rhythm may create hemodynamic instability, but may also be a rate that the infant can tolerate for several hours. In that case, the infant may become fatigued over time.

Atrial flutter may be seen in newborns and often resolves spontaneously soon after birth. It is also seen in older children and adolescents with structural heart disease. The ECG will show large sawtooth P waves, especially in V1. Variable atrioventricular block may be seen with 2 to 4 P waves for each QRS. The P wave morphology may not be appreciated until the patient has been given adenosine, producing a transient atrioventricular block.

Patients with congenital heart disease, who have undergone extensive surgical procedures such as the Fontan, may have P waves that are very small and difficult to see. Sinus node dysfunction and a resting bradycardia may also be seen. In such patients, who may have a baseline heart rate of 50 beats/min, a heart rate of 120 beats/min should raise suspicion that they are actually experiencing an atrial flutter.

Congenital junctional ectopic tachycardia is very rare. The ECG will show a junctional rate that is more rapid than the sinus rate. Both the sinus and junctional rates will be regular, but different, causing a varying “P-R” interval due to atrioventricular dissociation.

The baby in the vignette has a heart rate that is too rapid for sinus tachycardia in a term newborn, and a history of fluid loss or fever would be expected. The ECG in sinus tachycardia will show P waves before each QRS and the axis will be normal, with upright P waves in II, III, and aVF.

Ventricular tachycardia (VT) may occur in a newborn, but a rate of 270 beats/min would likely cause more cardiovascular instability than is described in the vignette. In VT, the QRS would be wide for age, and dissociation is seen (the ventricular rate will be faster than the sinus rate, just as described for junctional rhythm). A benign form of ventricular ectopy can be seen in newborns, in which case, the ventricular and sinus rates are almost identical. When the sinus node accelerates, the ventricular rhythm becomes suppressed. This usually resolves spontaneously within a few months after birth. Children with occasional ventricular ectopy are often asymptomatic. Those with VT and some children with ventricular ectopy may present with syncope or palpitations, and often will have symptoms with exercise or high catecholamine

states. The family history is key in determining risk. Structural heart disease must be ruled out. The patient's history, surrounding circumstances, and symptoms help determine the degree of danger an arrhythmia poses.

The most common cause for SVT in infants is reentry due to an accessory pathway. The ECG will most commonly show a regular, narrow complex rhythm greater than 220 beats/min.

PREP Pearls

- Reentrant supraventricular tachycardia due to an accessory pathway is a common tachyarrhythmia in infants.
- The relationship of the P wave to the QRS, and P wave morphology are useful clues to the type and origin of a tachyarrhythmia.

ABP Content Specifications(s)

- Recognize the electrocardiographic characteristics of various cardiac dysrhythmias
- Recognize the clinical findings associated with various cardiac dysrhythmias

Suggested Readings

- Dubin AM, Cuneo BF, Strasburger JF, Wakai RT, Van Hare GF, Rosenthal DN. Congenital junctional ectopic tachycardia and congenital complete atrioventricular block: a shared etiology? Heart Rhythm. 2005;2(3):313-315. doi: http://dx.doi.org/10.1016/j.hrthm.2004.11.016.
- Greene EA, Van Hare G. Neonatal arrhythmias. In: Stevenson DK, Cohen RS, Sunshine P, eds. Neonatology: Clinical Practice and Procedures. New York, NY: McGraw-Hill; 2015:293-308.
- Ko JK, Deal BJ, Strasburger JF, Benson DW Jr. Supraventricular tachycardia mechanisms and their age distribution in pediatric patients. Am J Cardiol. 1992;69(12):1028-1032. doi: http://dx.doi.org/10.1016/0002-9149(92)90858-V.
- Pike JM, Greene EA. Fetal and neonatal supraventricular tachyarrhythmias. NeoReviews. 2012;13(10):e605-e614. doi: http://dx.doi.org/10.1542/neo.13-10-e605.
- Van Hare G. Disturbances of rate and rhythm of the heart. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:2250.

Question 64

A 2-month-old male infant is brought to your office for a health supervision visit. His mother reports that, despite her best efforts, she has been having a very difficult time breastfeeding over the past few weeks. She becomes tearful, admits to not sleeping well, and has felt overwhelmed for the past several days. She reports feeling ashamed of having to use formula for her son's nutrition and has dropped out of her "new parent" support group. She had read about infant attachment during her pregnancy and worries that her son will develop psychological problems if she decides to give up breastfeeding altogether.

Of the following, the BEST next step for this mother is to

A. change to an elemental formula
B. have other caregivers care for her son periodically to give her a break
C. reassure her that her worries will pass
D. refer her to a lactation consultant
E. screen and refer her for maternal depression

Correct Answer: E

This infant's mother is correct that infant-parent attachment is a predictor of a child's psychosocial health later in life. Infant-parent attachment is an infant's sense of having a secure source of reassurance and comfort when facing unanticipated, unfamiliar, or unsettling events. Infant-parent attachment is developed in the first 6 months of life. It is determined largely by the pattern in which the caregiver responds to the infant when the infant is distressed, frightened, or ill. Responses can be loving, sensitive, and consistent; responses can also be rejecting, insensitive, and inconsistent. If in times of distress, the caregiver responds consistently in a sensitive, loving way, the infant will likely develop a secure attachment, feel safe to express negative emotion, and expect reassurance. When the caregiver responds in a negative way, either by ignoring the infant, minimizing the infant's distress, or becoming frustrated, the infant may respond by displaying less negative emotion or by crying excessively. In this circumstance, infants learn that they cannot rely on caregivers for comfort. Caregivers who respond in a frightening or otherwise atypical way can lead to infants having disorganized, insecure attachment with caregivers, as occurs in cases of child maltreatment. Thus, the quality of the parent-infant interaction during times of distress is most associated with developing secure attachment.

Infant-parent attachment has been linked to a variety of long-term psychosocial outcomes. Insecure attachment has been linked to obesity. Disorganized attachment, such as seen with child maltreatment, is associated with later behavior problems and poor self-regulation.

In times of distress, several factors can affect the quality of the parent-child interaction. The mother in the vignette is displaying signs of post-partum depression, which is associated with impaired infant-parent attachment. Screening for maternal depression and facilitating treatment if needed is the best option for promoting secure attachment for the infant in the vignette. The father's mental health has also been linked to infant-parent attachment. Programs to support parents of infants, such as postnatal home visiting programs, have also had positive associations with infant-parent attachment. While studies show an association of breastfeeding with secure attachment, it is most likely explained by the quality of the dyadic feeding experience, rather than the modality itself.

The infant has not demonstrated problems tolerating breast milk or cow's milk formula (pain, excessive spitting, poor growth, bloody stools), so changing to elemental formula or referral to a lactation consultant, is not indicated. Reassurance may lead to a missed opportunity to treat this mother's depression. Encouraging the mother to engage in self-care activities by securing other caregivers' help may be a helpful adjunct to evidence-based care for maternal depression, but this is not the first-line treatment.

PREP Pearls

- Infant-parent attachment established during the first 6 months of life is associated with later psychosocial well-being.
- Infant-parent attachment develops through caregivers' responses to the child during times of distress.
- Infant-parent attachment is negatively affected by parental depression.

ABP Content Specifications(s)

- Understand the various factors that influence parent-infant attachment

Suggested Readings

- Frazier KF, Scharf RJ. Parent-infant attachment. Pediatr Rev. 2015;36(1):41-42. doi: http://dx.doi.org/10.1542/pir.36-1-41.
- Lind JN, Li R, Perrine CG, Schieve LA. Breastfeeding and later psychosocial development of children at 6 years of age. Pediatrics. 2014;134 Suppl 1:S36-S41. doi: http://dx.doi.org/10.1542/peds.2014-0646G.

Question 65

You are asked to evaluate a male neonate delivered earlier today to a 23-year-old woman who recently emigrated from Africa. The baby is full term, based on the mother's history, but appears very small. The mother did not receive regular prenatal care and has no documentation of any prenatal tests. She reports no major medical issues during her pregnancy other than a few minor viral illnesses. She reports only 2 sexual partners in her life and denies any unusual vaginal discharge or genitourinary symptoms.

Physical examination of the neonate shows a small slightly jaundiced infant with a birth weight of 2,600 g and length of 46 cm. Head circumference is 32.5 cm. Lung fields are clear. A 3/6 systolic murmur is heard at the left sternal border, with transmission into the lung fields. The murmur extends past S2, and no ejection click is appreciated. The liver can be palpated 2 cm below the right costal margin (CM), and the spleen is palpable 2.5 cm below the left CM. A diffuse dark erythematous maculopapular rash is present on the torso. An ophthalmology consult has been requested for absent red reflexes bilaterally.

Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	6,900/μL (6.9 x 10^9/L)
Lymphocytes	50%
Neutrophils	45%
Monocytes	5%
Hemoglobin	17 g/dL (170 g/L)
Hematocrit	51%
Platelet count	77 x 10^3/μL (77 x 10^9/L)
Alanine aminotransferase	93 U/L
Aspartate aminotransferase	69 U/L

Head ultrasonography is shown (Item Q65).

Item Q65: Head ultrasonography for the neonate described n the vignette. Courtesy of P Lee

Of the following, the MOST likely pathogen to be causing these findings in this neonate is

A. cytomegalovirus
B. herpes simplex virus
C. rubella virus
D. Toxoplasma gondii
E. Treponema pallidum

Correct Answer: C
The most likely pathogen causing the abnormal findings in the neonate in the vignette is rubella virus. This neonate has a congenitally acquired infection, resulting in congenital rubella syndrome. Rubella is 1 of the original 5 infections grouped together to create the TORCH (Toxoplasma, Other [syphilis], Rubella, Cytomegalovirus [CMV], and Herpes simplex) acronym for congenitally acquired infections. However, in addition to these 5 infections, numerous other infections such as varicella-zoster virus, enteroviruses, parvovirus B-19, Zika virus, hepatitis B, C, E, and HIV can be responsible for congenital infection, leading some to suggest the TORCH acronym be revised or replaced. All of these infections can present with an abnormal physical examination and laboratory values.

Congenital rubella syndrome (CRS) occurs when a susceptible pregnant woman contracts rubella and becomes viremic, with transmission to the fetus through the placenta. The rubella virus creates a chronic infection damaging the fetal blood vessels with subsequent ischemia to developing organ systems. This results in the commonly reported CRS manifestations. This infection can persist well after birth. The classic triad of CRS is sensorineural deafness, cataracts, and cardiac defects, but rubella can affect any organ system, causing intrauterine growth retardation, meningoencephalitis, interstitial pneumonia, hepatosplenomegaly, jaundice, hepatitis, long bone lucencies, lymphadenopathy, hemolytic anemia, thrombocytopenia, and a characteristic blueberry muffin rash from extramedullary hematopoiesis. Fetal demise or premature delivery can occur. The likelihood of defects and their severity depends on the timing of infection, with earlier infection leading to more severe damage, and little risk of congenital defects with infection after the 18th to 20th weeks of pregnancy. The majority of neonates with congenital rubella infection are asymptomatic at delivery, but develop subsequent abnormalities that may not present until school age or even later. Late findings include permanent bilateral sensorineural hearing loss, diabetes mellitus, and other endocrine disorders, eye disease (pigmentary retinopathy, glaucoma, and microphthalmos), learning disabilities from a progressive and ultimately fatal panencephalitis, and immune defects with antibody production and T-cell response.

Rubella is rare in the United States because of widespread measles, mumps, and rubella immunization, and in April 2015, the Pan American Health Organization declared rubella and CRS eradicated from the Americas. Congenital rubella syndrome continues to be seen in the United States, but occurs in infants of infected immigrants from countries without established rubella immunization programs. As rubella remains endemic and widespread in many developing countries, the rate of CRS can be as high as 90 per 100,000 live births.

Of the pathogens listed, only rubella virus causes cardiac defects and an absent red reflex indicating cataracts. Periventricular and diffuse intracerebral calcifications would be expected with congenital CMV and toxoplasma infections, respectively, not the normal head ultrasonography shown. This neonate's head circumference is small, but not consistent with microcephaly, which would also be expected with CMV and Zika virus. While toxoplasma causes a chorioretinitis, there would be white spots on the retina, rather than a complete absence of red reflex. Children with congenital syphilis are often asymptomatic, but rhinitis ("snuffles"),

pseudoparalysis, and skeletal abnormalities could be present, which are not described for the neonate in the vignette. The maculopapular rash of syphilis can be diffuse, but is notable on the palms, soles, and diaper area. Children with congenital herpes simplex virus infection are often asymptomatic and without vesicular lesions.

PREP Pearls

- Rubella and congenital rubella syndrome have been eradicated from the Americas as of 2015, but cases still occur in immigrants from countries without rubella immunization programs and their babies.
- Congenital rubella syndrome rates can be as high as 90 out of 100,000 live births in countries where rubella is endemic and uncontrolled
- Of all of the classic TORCH infections, only rubella causes congenital heart defects and cataracts.

ABP Content Specifications(s)

- Recognize the clinical features associated with congenital and postnatally acquired rubella virus infection
- Understand the epidemiology of the rubella virus

Suggested Readings

- American Academy of Pediatrics. Rubella. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:688-695.
- Berger BE, Navar-Boggan AM, Omer SB. Congenital rubella syndrome and autism spectrum disorder prevented by rubella vaccination—United States, 2001-2010. BMC Public Health. 2011;11:340. doi: http://dx.doi.org/10.1186/1471-2458-11-340.
- Grant GB, Reef SE, Dabbagh A, Gacic-Dobo M, Strebel PM. Global progress toward rubella and congenital rubella syndrome control and elimination – 2000-2014. MMWR Morb Mortal Wkly Rep. 2015;64(37):1052-1055. doi: http://dx.doi.org/10.15585/mmwr.mm6437a5.
- Pitts SI, Wallace GS, Montana B, et al. Congenital rubella syndrome in child of woman without known risk factors, New Jersey, USA. Emerg Infect Dis. 2014;20(2):307-309. doi: http://dx.doi.org/10.3201/eid2002.131233.
- US Centers for Disease Control and Prevention (CDC). Three cases of congenital rubella syndrome in the postelimination era--Maryland, Alabama, and Illinois, 2012. MMWR Morb Mortal Wkly Rep. 2013;62(12):226-229. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6212a3.htm.

Question 66

An 8-year-old boy presents to your office for a health supervision visit. The family recently moved to the state and the boy has had difficulty adjusting. A review of systems is significant for longtime daytime and nocturnal enuresis. His family history is significant for nocturnal enuresis in the dad until age 12 years. Physical examination reveals a pale and visibly anxious patient with a temperature of 37.8°C, heart rate of 110 beats/min, respiratory rate of 16 breaths/min, and blood pressure of 125/80 mm Hg. His weight is 22 kg (10th percentile) and height is 115 cm (< 5th percentile). The boy's physical examination is otherwise normal. His urinalysis demonstrates a specific gravity of 1.005, pH of 6.0, and 3+ protein, with no blood, leukocyte esterase, or nitrates.

Of the following, the MOST likely cause of this boy's enuresis is

A. chronic kidney disease
B. genetic
C. psychogenic polydipsia
D. stress
E. urinary tract infection

Correct Answer: A

Enuresis is diagnosed in children aged 5 years or older who void in bed or their clothes twice or more per week for 3 consecutive months. Primary enuresis occurs in children with no interval of sustained dryness. Secondary enuresis is diagnosed in children with sustained dryness for a period of 6 months (for nocturnal enuresis) or 3 months (for diurnal enuresis).

Polyuria is characterized by increased total urine volume resulting from an underlying defect in water balance. This presents with the excretion of large volumes of dilute urine, as seen in patients with chronic kidney disease, diabetes mellitus (osmotic diuresis), diabetes insipidus (antidiuretic hormone disorders), and psychogenic polydipsia. It is important to note that the symptoms of frequency, nocturia, or enuresis are often not associated with increased urinary volume.

The 8-year-old boy in the vignette has an abnormal voiding pattern of primary daytime and nocturnal enuresis, which needs further evaluation. His growth restriction (height < 5th percentile), pallor, and elevated blood pressure suggest an underlying chronic kidney disease (CKD). Furthermore, symptoms of enuresis and a specific gravity of 1.005 on urinalysis point to an underlying urine concentration defect associated with increased urine volume. Proteinuria (3+) on urine dipstick analysis is also an indicator of underlying kidney disease in this patient.

Congenital anomalies of the kidney and urinary tract (CAKUT) and cystic kidney diseases (nonglomerular CKD) account for nearly 60% of pediatric CKD. Tubulointerstitial injury associated with CAKUT leads to reduced urinary concentration (acquired nephrogenic diabetes insipidus) and these patients usually present with polyuria with or without enuresis. Proteinuria can be seen in patients with underlying glomerular disease or tubulointerstitial injury. Persistent proteinuria may be the only indicator of renal disease in asymptomatic patients. Persistent dipstick-positive proteinuria or a urine protein-creatinine ratio higher than 0.2, is considered abnormal. Children with CKD usually have poor growth. In the North American Pediatric Renal Trials and Collaborative Studies, the mean height and weight of children with CKD were 1.44 and 0.88 standard deviations below age- and sex-specific normal values. Reduced renal erythropoietin production with CKD also leads to a normocytic normochromic anemia, consistent with anemia of chronic inflammation. These children are also at increased risk for iron and vitamin B12 deficient anemia because of the poor nutritional status associated with advanced stages of CKD.

Further evaluation in children suspected of having CKD should include urinalysis, serum creatinine, serum electrolytes, complete blood count, iron profile, and lipid profile, as well as ultrasonography of the kidneys. Glomerular filtration rate (GFR) is estimated from serum creatinine using the Schwartz formula (GFR = 0.413 ´ height [in centimeters]/serum creatinine [enzymatic method]) and is then used for diagnosing and stratifying risk in CKD.

In the early stages of CKD (GFR > 60 mL/min per 1.73 m2), patients are often asymptomatic. Symptoms of abnormal voiding patterns (enuresis or polyuria), poor growth, and pallor can be

subtle and may be missed in the early stages of CKD. Patients with advanced stages of CKD associated with lower GFR are increasingly symptomatic.

Psychogenic polydipsia presents with increased water intake. Laboratory testing would demonstrate a low urine osmolality, consistent with water overload. Maximal urine concentration is usually impaired (500-600 mOsm/kg) compared with that in normal patients (≥ 800 mOsm/kg). A parental history of nocturnal enuresis is associated with an increased risk for nocturnal enuresis in children. One or both the parents with a history of prolonged nighttime wetting have been reported, respectively, in nearly 50% and 75% of the children with nocturnal enuresis. Recent-onset stress, such as moving to a new home and school, can sometimes lead to secondary nocturnal enuresis in children, but is unlikely for the boy in the vignette who has poor growth and abnormal findings. In this case, urinary tract infection is an unlikely diagnosis in the absence of fever; urinary symptoms such as dysuria, flank pain, or burning micturition; and the absence of pyuria, nitrates, and bacteria on urinalysis. None of the response choices, other than CKD, explains the additional findings of poor growth, pallor, increased blood pressure, and proteinuria seen in this patient.

PREP Pearls

- Congenital anomalies of the kidney and urinary tract (CAKUT) and cystic kidney diseases (nonglomerular chronic kidney disease [CKD]) account for nearly 60% of pediatric CKD.
- Tubulointerstitial injury associated with CAKUT leads to reduced urinary concentration (acquired nephrogenic diabetes insipidus) and usually presents with polyuria with or without enuresis.
- In the early stages of CKD (GFR >60 mL/min per 1.73 m2), patients are often asymptomatic.
- Symptoms of abnormal voiding patterns (enuresis or polyuria), poor growth, and pallor may be subtle and thereby missed in the early stages of CKD.

ABP Content Specifications(s)

- Recognize the clinical and laboratory findings associated with voiding dysfunction
- Identify the possible renal causes of nocturnal incontinence

Suggested Readings

- Kidney Disease Improving Global Outcomes, National Kidney Foundation. KDIGO 2012: Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-163. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf.
- Massengill SF, Ferris M. Chronic kidney disease in children and adolescents. Pediatr Rev. 2014;35(1):16-29. doi: http://dx.doi.org/10.1542/pir.35-1-16.

Question 67

You are called to talk about neonatal eye prophylaxis to a 32-year-old gravida 4, para 3 woman at 39 weeks of gestation with a history of alcohol use, anxiety, and depression. She is not taking any medications, but sees a mental health therapist regularly. The mother's prenatal laboratory test results are significant for blood type B positive and positive for group B Streptococcus. She was admitted in active labor and has requested her baby not receive the "eye medicine" after delivery.

Of the following, the statement that BEST supports your recommendation and rationale for prophylactic ophthalmic erythromycin is

A. conjunctivitis caused by Neisseria gonorrhoeae can result in corneal ulceration and visual impairment
B. conjunctivitis typically presents in the first 6 hours after birth
C. erythromycin ointment should be applied to the eyes within 6 hours of birth
D. prophylactic erythromycin eliminates the risk of conjunctivitis from bacteria and viruses
E. silver nitrate typically causes chemical conjunctivitis

Correct Answer: A

The best rationale for the use of prophylactic erythromycin ointment for the baby in the vignette is prevention of ophthalmia neonatorum. Ophthalmia neonatorum, or neonatal conjunctivitis, is most often caused by Neisseria gonorrhoeae or Chlamydia trachomatis. Risk factors for the development of ophthalmia neonatorum include untreated maternal infection and vaginal delivery. Prior to the introduction of ophthalmic prophylaxis, the incidence of ophthalmia neonatorum was as high as 10%. In the developing world, ophthalmia neonatorum continues to affect up to 12% of infants and is the leading cause of infant blindness.

In 1881, a German obstetrician and gynecologist named Dr. Carl Crede instituted prophylactic treatment for asymptomatic neonates with silver nitrate. Prophylaxis with silver nitrate decreases the risk of neonatal conjunctivitis, but may cause a self-limited chemical conjunctivitis in some patients. The onset of symptoms of ophthalmia neonatorum varies based on the etiology. N gonorrhoeae presents with thick purulent discharge and chemosis within 1 to 5 days of delivery. Left untreated, it may cause corneal ulceration and lead to blindness. Chlamydia trachomatis typically presents between 5 and 14 days after birth with copious watery discharge and eye lid edema with sparing of corneal involvement.

Use of erythromycin ointment is mandated in the majority of states. Rather than focus on the legal mandate, counseling should focus on the proposed benefit for the infant. Erythromycin prophylaxis has not been proven to decrease the risk of infection caused by viruses or bacteria other than N gonorrhoeae.

Given within 1 hour after birth, erythromycin prophylaxis is effective. Administration beyond the initial hour after delivery have not been adequately studied.

PREP Pearls

- Ophthalmia neonatorum, or neonatal conjunctivitis, is most often caused by Neisseria gonorrhoeae and Chlamydia trachomatis.
- Silver nitrate and erythromycin are effective prophylaxis against ophthalmia neonatorum.
- Silver nitrate may cause a chemical conjunctivitis in some infants.

ABP Content Specifications(s)

- Plan appropriate eye prophylaxis for a newborn infant

Suggested Readings

- American Academy of Pediatrics. Prevention on neonatal ophthalmia. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book; 2015 Report of the Committee on Infectious Diseases.30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:972-974.
- Bell TA, Grayston JT, Krohn MA, Kronmal RA. Randomized trial of silver nitrate, erythromycin, and no eye prophylaxis for the prevention of conjunctivitis among newborns not at risk for gonococcal ophthalmitis. Pediatrics. 1993;92(6):755-760. http://pediatrics.aappublications.org/content/92/6/755.full-text.pdf.
- Poland RL. Consultation with the specialist: eye prophylaxis in the newborn infant. Pediatr Rev. 1993;14(11):423.

Question 68

A 16-year-old adolescent boy visits the emergency department for evaluation of left knee pain and swelling, which began 1 day prior. He has no history of trauma and denies fever. On physical examination, he is well appearing with a temperature of 37.2°C. At rest, the patient holds his left knee slightly flexed. The knee is warm to touch, with a notable effusion. He is resistant to examination maneuvers that attempt to fully extend or flex the joint, and he walks with a limp. Other physical examination findings include mild bilateral conjunctival injection and tenderness to palpation at the Achilles tendon insertion sites bilaterally. The remainder of his physical examination is unremarkable. Synovial fluid obtained by joint aspiration shows a white blood cell count of 10,000/μL (10 × 109/L) and the Gram stain is negative for organisms.

Of the following, the MOST appropriate treatment for this patient is

A. intra-articular vancomycin
B. intravenous vancomycin
C. joint immobilization
D. oral corticosteroids
E. oral nonsteroidal anti-inflammatory drug

Correct Answer: E
The patient in the vignette has reactive arthritis, an inflammatory arthritis associated with a prior infection at a site other than the affected joint, often gastrointestinal or genitourinary. Although the pathogenesis of reactive arthritis is unclear, associated bacteria include Chlamydia trachomatis, Neisseria gonorrhoeae, Shigella, Salmonella, Yersinia, Campylobacter species, and Streptococcus pyogenes. Reactive arthritis is more common in adolescents and adults than in younger children and has a 3:1 male to female predominance. It is typically a mono- or oligoarthritis and is often accompanied by other signs of inflammation including enthesitis, dactylitis, uveitis, conjunctivitis, urethritis, or rash. Synovial fluid is typically sterile with signs of inflammation including elevated leukocyte counts.

Reactive arthritis is best treated with nonsteroidal anti-inflammatory medications, with the addition of intra-articular or systemic corticosteroids only in refractory cases. Intra-articular and systemic antibiotics are not indicated, though if a preceding or concurrent infection is identified, appropriate antibiotic treatment may be warranted. Joint immobilization does not have a role in the treatment of reactive arthritis.

Reactive arthritis must be distinguished from other causes of arthritis in children, including juvenile idiopathic arthritis, septic arthritis, lyme arthritis, systemic lupus erythematosus, and toxic synovitis. A detailed history and comprehensive physical examination is essential. If the diagnosis of septic arthritis is a serious consideration, synovial fluid analysis must be performed, because a delay in treatment can lead to joint damage. Ultrasonography, radiography, or magnetic resonance imaging can also aid in diagnosis.

PREP Pearls

- Reactive arthritis is typically a mono- or oligoarthritis often associated with other signs of inflammation, including enthesitis, dactylitis, uveitis, conjunctivitis, urethritis, or rash.
- Reactive arthritis is associated with a prior infection, often gastrointestinal or genitourinary.
- Reactive arthritis is best treated with nonsteroidal anti-inflammatory medications.
- Synovial fluid analysis must be performed to exclude septic arthritis if this diagnosis is considered strongly.

ABP Content Specifications(s)

- Recognize the clinical findings associated with reactive arthritis and manage appropriately
- Plan the appropriate diagnostic evaluation of synovitis

Suggested Readings

- Carter JD, Hudson AP. Reactive arthritis: clinical aspects and medical management. Rheum Dis Clin North Am. 2009;35(1):21-44. doi: http://dx.doi.org/10.1016/j.rdc.2009.03.010.
- John J, Chandran L. Arthritis in children and adolescents. Pediatr Rev. 2011;32(11):470-480. doi: http://dx.doi.org/10.1542/pir.32-11-470.

Question 69

You are seeing a 10-week-old infant for a health supervision visit. She was born at term to a primigravida mother via normal spontaneous vaginal delivery. Her birthweight was 4.0 kg. The infant's parents report that she has noisy breathing that is worse after eating, with crying, and in the supine position. The noise is inspiratory and high pitched in quality. There is no history of diaphoresis, apnea, cyanosis, or loss of consciousness; however, the infant appears dyspneic during feedings and takes 25 to 30 minutes to drink a 4-ounce bottle of formula. Often, after feedings, the infant has nonprojectile emesis. There have been no sick contacts and she has had no upper respiratory symptoms or fever.

On physical examination, the infant's weight is 4.5 kg. She is alert and in no acute distress, with mild agitation and crying during your examination. Her respiratory rate is 50 breaths/min. You note inspiratory stridor associated with suprasternal and substernal retractions. Her lungs are otherwise clear without wheezing or asymmetric aeration. Her cardiac examination reveals mild tachycardia but no murmur with a heart rate of 160 beats/min. The abdomen is soft and nontender, with a liver edge palpable at the right costal margin.

Of the following, this infant's MOST likely diagnosis is

A. laryngomalacia
B. laryngotracheobronchitis
C. tracheomalacia
D. vascular ring
E. ventricular septal defect

Correct Answer: A

The infant in the vignette is exhibiting classic symptoms of laryngomalacia, the most common cause of infantile inspiratory stridor. Laryngomalacia is a medial prolapse of the epiglottis, aryepiglottic folds, or arytenoid cartilages, which obstructs the airway, thereby creating airway noise and variable degrees of respiratory compromise (Item C69). Symptoms often worsen with supine positioning, crying, feeding, or agitation. Risk factors include hypotonia, redundant laryngeal tissue, and inadequate cartilaginous support.

Symptoms of laryngomalacia are usually noted within the first 1 to 4 weeks after birth. Symptoms may progress until approximately 6 months of age, with most cases then resolving spontaneously by age 12 to 18 months. Exacerbating factors include gastroesophageal reflux (GER), dysphagia, and aspiration. Severely affected infants may experience difficulty in feeding, failure to gain weight, cyanotic episodes, and/or obstructive sleep apnea. The diagnosis of laryngomalacia may be made clinically and confirmed with direct flexible fiberoptic laryngoscopy. Treatment of laryngomalacia is largely supportive. Infants may benefit from medical treatment of comorbid conditions, such as GER. In severe cases with significant obstruction or growth failure, surgical management with supraglottoplasty or tracheostomy may be considered to restore airway patency.

Tracheomalacia describes a collapsible tracheal wall. This may be congenital or acquired. Tracheomalacia often affects the distal one-third of the trachea, but full-segment malacia may also occur. Episodes of airway obstruction are more likely to occur during periods of increased airflow (crying, eating, coughing). In infants, the normally poorly supportive tracheal cartilage may contribute to collapse of the tracheal wall and narrowing of the tracheal lumen. Typical symptoms include expiratory stridor and/or monophonic wheezing. Congenital tracheomalacia generally improves by 6 to 12 months of age. Acquired narrowing and/or collapsibility of the trachea may also result from infection, mass effect, innominate artery compression, vascular ring formation, chronic pulmonary aspiration, or as sequelae to a tracheoesophageal fistula. Other comorbidities may include cardiac anomalies and GER disease.

Laryngotracheobronchitis is more commonly known as croup. Croup is typically preceded by a viral prodrome, and is often attributable to parainfluenza, though multiple other viral illnesses may be causative. The onset of croup is usually gradual and the progression is slow. Presenting symptoms include hoarseness, stridor, a barking “seal-like” cough, and low-grade fever. Airway symptoms may improve with exposure to cool air or mist. Anterior/posterior radiographs of the airway reveal a narrowing at the subglottis (“steeple sign”). Children with laryngomalacia or tracheomalacia may present with recurrent “croup,” and the diagnosis of an airway anomaly may be overlooked. Although vascular rings can present with symptoms similar to those seen in the infant described in the vignette, laryngomalacia is a more common cause on congenital stridor. It is important to consider these diagnoses in patients with recurrent symptomatology.

PREP Pearls

- Laryngomalacia is the most common cause of neonatal stridor.
- Both laryngomalacia and tracheomalacia may present with chronic cough, recurrent wheezing, and/or noisy breathing.
- A high index of suspicion is required to differentiate airway malformation from more common syndromes such as viral illness, croup, or asthma.

ABP Content Specifications(s)

- Understand the various etiologies of tracheomalacia
- Recognize the clinical findings associated with tracheomalacia and laryngomalacia

Suggested Readings

- Castilloux J, Noble AJ, Faure C. Risk factors for short- and long-term morbidity in children with esophageal atresia. J Pediatr. 2010;156(5):755-760. doi: http://dx.doi.org/10.1016/j.jpeds.2009.11.038.
- Greifer M, Santiago MT, Tsirilakis K, Cheng JC, Smith LP. Pediatric patients with chronic cough and recurrent croup: the case for a multidisciplinary approach. Int J Pediatr Otorhinolaryngol. 2015;79(5):749-752. doi: http://dx.doi.org/10.1016/j.ijporl.2015.03.007.
- Thompson DM. Laryngomalacia: factors that influence disease severity and outcomes of management. Curr Opin Otolaryngol Head Neck Surg. 2010;18(6):564-570. doi: http://dx.doi.org/10.1097/MOO.0b013e3283405e48.

Question 70

The mother of a 6-year-old girl brings her for evaluation because she is concerned about a “bald spot” on her daughter’s scalp that was first noted 3 weeks ago. Since that time, the area has gotten somewhat smaller. The girl has been in good health and takes no medications. Her temperature is 37°C and other vital signs are normal. The physical examination is normal, with the exception of a round patch of nearly complete hair loss on the parietal scalp. The scalp appears normal without erythema or scaling (Item Q70).

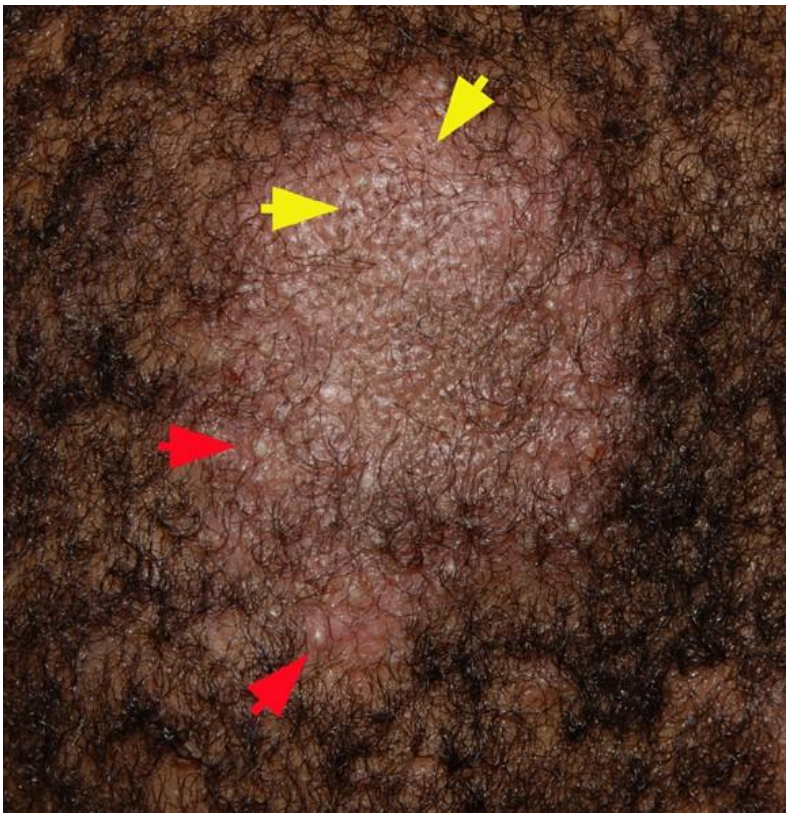
Item Q70: A patch of nearly complete alopecia. Courtesy of D Krowchuk

Of the following, the MOST appropriate treatment is

A. clotrimazole topically
B. griseofulvin orally
C. mupirocin topically
D. no intervention
E. referral for cognitive behavioral therapy

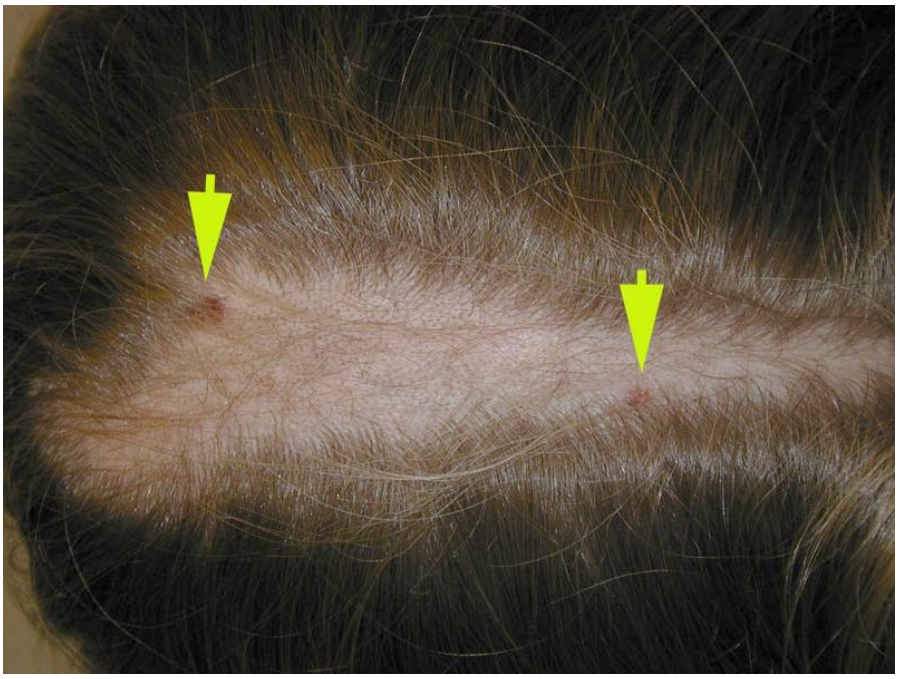
Correct Answer: D

The girl in the vignette has a round patch of nearly complete hair loss and a normal-appearing scalp. These findings suggest the diagnosis of alopecia areata. Since the patch is small and improving, no therapy is necessary. In the absence of scale, evidence of inflammation (erythema or pustule formation), or "black-dot" hairs (the remnants of broken hairs within follicles), tinea capitis is unlikely and antifungal therapy is not indicated (Item C70A). Traction on hairs, often the result of tight braiding, may result in alopecia. Some patients develop folliculitis (Item C70B) that occasionally is treated with a topical or oral antibiotic. Cognitive behavioral therapy may be used for those who have hair-pulling disorder (trichotillomania), characterized by a patch of incomplete alopecia within which hairs of differing lengths may be seen (Item C70C).



Item C70A: Tinea capitis: patches of hair loss within which one may see scale, "black-dot" hairs (yellow arrows), or pustules (red arrows). Courtesy of D Krowchuk

Item C70B: Traction on hairs may result in erythematous follicular papules or pustules (arrows). Continued traction may result in alopecia. Courtesy of D Krowchuk



Item C70C: Trichotillomania: an area of incomplete hair loss is seen within which hairs of differing lengths are present. Two areas hemorrhage (arrows) are present at sites where hairs were pulled. Courtesy of D Krowchuk

Alopecia areata is an autoimmune disease in which T lymphocytes target specific autoantigens expressed by hair follicles. Genetic susceptibility (approximately 15% of patients have an affected first-degree relative) and environmental insults (physical or emotional stress, hormones, infection) contribute to the disease process. Associated autoimmune diseases, particularly thyroiditis, occur rarely in affected children. The prevalence of alopecia areata is estimated to be 0.2% and the lifetime risk is 1% to 2%. Two-thirds of patients have onset of disease before 16 years of age.

The typical presentation of alopecia areata is the sudden appearance of one or a few round or oval well-defined patches of hair loss; the scalp is normal. At the periphery of patches of alopecia, one may observe short hairs that are broader distally than proximally (exclamation-point hairs). Some patients develop numerous areas of hair loss or a circumferential loss of hair involving the temporal, parietal, and occipital scalp (the ophiasis pattern). In a minority of patients (approximately 10%), the disease progresses to loss of all or nearly all scalp (alopecia totalis) or body (alopecia universalis) hair (Item C70D). Nail pitting occurs in about 20% of patients (Item C70E).

Item C70D: Alopecia totalis. Courtesy of D Krowchuk

Item C70E: Multiple small nail pits Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012

The prognosis for patients with alopecia areata is variable. For those with a few small patches of hair loss, most will regrow hair within 1 year. In such cases, observation may be appropriate. The prognosis is more guarded for those who have extensive hair loss, the ophiasis pattern, a coexisting autoimmune disorder, or a family history of alopecia areata.

Treating alopecia areata is challenging and those who have significant disease are best managed by a dermatologist. First-line therapy typically employs a potent topical corticosteroid (class I [eg, betamethasone dipropionate] or class II [eg, betamethasone valerate]), often in conjunction with topical minoxidil. Other options include intralesional or oral corticosteroids, excimer laser, topical anthralin, or topical immunotherapy using squaric acid dibutyl ester or diphenylcyclopropenone. Areas of hair loss can be masked by hairstyle changes, hats, or headbands. For those with extensive involvement, a wig may be helpful. Locks of Love (http://www.locksoflove.org/) is an organization that provides hairpieces to financially disadvantaged children younger than 21 years of age. The National Alopecia Areata Foundation (https://www.naaf.org/) provides information and support for patients and families.

PREP Pearls

- Alopecia areata presents as 1 or more round patches of hair loss; the scalp appears normal.
- For children who have 1 patch or a few patches of alopecia areata, the chance of spontaneous regrowth of hair is very good.
- The prognosis is guarded for those who have extensive hair loss, the ophiasis pattern, a coexisting autoimmune disorder, or a family history of alopecia areata.
- Initial therapy of alopecia areata most often includes a potent topical corticosteroid and topical minoxidil.

ABP Content Specifications(s)

- Recognize the clinical findings associated with alopecia areata and manage appropriately

Suggested Readings

- Castelo-Soccio L. Diagnosis and management of alopecia in children. Pediatr Clin North Am. 2014;61(2):427-442. doi: http://dx.doi.org/10.1016/j.pcl.2013.12.002.
- Hordinsky M, Donati A. Alopecia areata: an evidence-based treatment update. Am J Clin Dermatol. 2014;15(3):231-246. doi: http://dx.doi.org/10.1007/s40257-014-0086-4.
- Krowchuk DP, Mancini AJ. Alopecia areata. Pediatric Dermatology: A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012:471-478.

Question 71

An 8-month-old female infant is brought to your office 1 day following discharge from the hospital. She had been growing and developing well until she was hospitalized 3 days ago following 3 seizures at home without fever. She had no prior history of seizures. She was started on phenobarbital on the day of admission. During the hospital stay, her brain magnetic resonance imaging was normal, but her electroencephalogram showed epileptiform discharges and generalized slowing. She has not had any more seizures. Her phenobarbital level on the day of discharge was 10 μg/mL (43 μmol/L) (therapeutic range 15-40 μg/mL).

Today, she is sleepy but arousable. Her mother reports she is drinking her usual amount of formula. The physical examination is otherwise unremarkable.

Of the following, the BEST next step today for this infant is

A. add levetiracetam
B. check a serum ammonia level
C. increase the phenobarbital dose
D. provide reassurance
E. recheck the serum phenobarbital level

Correct Answer: D
The infant in the vignette has been started on phenobarbital for seizures and is not having any seizures or significant adverse effects from phenobarbital, so the best next step is to provide reassurance to the parents. Although her phenobarbital level was subtherapeutic 3 days after starting the medication, the long half-life of phenobarbital (20 to 133 hours in infants) makes it unlikely that the serum level had reached steady state when the test was drawn. Steady state serum drug levels are achieved in about 5 half-lives. If the dose is increased now, the eventual steady state level will probably be too high. Clinicians should be familiar with an anticonvulsant's pharmacological profile (half-life, drug-drug interactions, etc) in order to appropriately order and interpret anticonvulsant levels and results.

Adding levetiracetam is not necessary because the infant is not having seizures, and in general, it is preferable to maximize the dose of the first anticonvulsant before adding a second one. Although the infant in the vignette is sleepy, she continues to drink her usual amount of formula, so it is not necessary to recheck the serum phenobarbital level just 1 day after the most recent level was checked. The sleepiness is most likely a side effect of phenobarbital that will wear off. Since the most recent level was low, it is unlikely that it has risen over 1 day to a toxic level. However, if there is concern for medication dose error causing toxicity, checking a level may be appropriate. Phenobarbital does not typically cause hyperammonemia, so this is not the best next step.

PREP Pearls

- Steady state serum drug levels are achieved in about 5 half-lives.
- Somnolence can be a side effect of starting phenobarbital, even when the serum level is not toxic.

ABP Content Specifications(s)

- Plan the appropriate evaluation of serum anticonvulsant drug concentrations, including limitations and timing

Suggested Readings

- Major P, Thiele EA. Seizures in children: laboratory diagnosis and management. Pediatr Rev. 2007;28(11):405-414. doi: http://dx.doi.org/10.1542/pir.28-11-405.
- Schachter SC. Antiseizure drugs: mechanism of action, pharmacology, and adverse effects. UpToDate. Available online only with subscription.

Question 72

A 4-month-old infant with a history of neonatal hypoxic ischemic encephalopathy and seizure disorder is hospitalized for pertussis. Since being initially discharged from the hospital at 2 weeks of age, she has not had any seizures. She is on phenobarbital as prescribed by a neurologist, and her last level was 20 μg/mL (86.2 μmol/L) (therapeutic range, 15-40 μg/mL) 2 weeks prior to admission. For the current illness, she presented with rhinorrhea, paroxysmal cough, and perioral cyanosis. She has been treated with supportive care, oxygen as needed, and was started on erythromycin. Between the coughing episodes, she is otherwise at her baseline, taking feeds by mouth, and has continued to be seizure-free. On the fourth day of hospitalization, she becomes increasingly lethargic. She has not had seizure activity or fevers. Vital signs show a temperature of 37°C, heart rate of 110 beats/min, blood pressure of 65/30 mm Hg, and respiratory rate of 15 breaths/min. On physical examination, she is hypotonic and difficult to arouse. Pupils are 3 mm equal and reactive. Heart is regular rate and rhythm with no murmurs. Capillary refill time is 1 second. Breath sounds are clear and equal. Abdomen is soft, nontender, and non-distended with no organomegaly.

Of the following, the test MOST likely to reveal a cause of her lethargy is

A. ammonia level
B. electroencephalogram
C. lumbar puncture
D. magnetic resonance imaging of the brain
E. phenobarbital level

Correct Answer: E
The infant in the vignette has a seizure disorder that was well-controlled on phenobarbital with adequate levels. After she was started on erythromycin for suspected pertussis, she became increasingly lethargic, hypopneic, and hypotensive. These signs are consistent with barbiturate toxicity caused by elevated phenobarbital levels from inhibition of hepatic metabolism of phenobarbital by erythromycin.

Hepatic metabolism involves transforming hydrophobic compounds into hydrophilic metabolites that can be excreted in the bile or urine. Phase I hepatic metabolism adds a functional group to the parent compound by oxidation, reduction, or methylation. Phase II metabolism involves conjugation of these functional groups with hydrophilic substrates such as glutathione, glucuronides, sulfate groups, or acetyl groups. After phase II metabolism, the modified drug may be excreted in the bile or urine. Hepatic cytochrome P450 (CYP) mono-oxygenases are important in the metabolism of endogenous compounds such as steroid hormones, bile acids, and fatty acids, as well as a majority of the medications that are used clinically. Some drugs may affect the hepatic metabolism of other medications by either stimulating or inhibiting CYP enzymatic systems. Examples of commonly prescribed drugs that inhibit hepatic metabolism include erythromycin, ciprofloxacin, and omeprazole. Examples of medications that can induce hepatic metabolism include rifampin, phenytoin, and carbamazepine.

The infant in this vignette had therapeutic phenobarbital levels, but showed signs of barbiturate toxicity after starting erythromycin, a medication known to inhibit hepatic metabolism. Thus, obtaining a phenobarbital level is the answer choice most likely to reveal the cause of her lethargy. If nonconvulsive status epilepticus were suspected as a cause of lethargy, an electroencephalogram would be helpful. However, it is less likely because her seizures have been well-controlled up to this point. Lumbar puncture would be helpful if meningitis or encephalitis were suspected, but there was no fever or other prodrome of illness suggestive of meningitis. Magnetic resonance imaging of the brain would be helpful if an anatomic or cerebrovascular cause of lethargy was suspected, but it is not likely in this scenario. Lastly, an ammonia level would be helpful to diagnose inborn errors of metabolism, but there is no evidence to suspect these conditions.

PREP Pearls

- Hepatic metabolism of endogenous lipophilic substrates and most medications available for clinical use involve phase I metabolism to add a functional group to the parent drug and phase II metabolism that conjugates the functional group to a hydrophilic compound.
- Medications that either inhibit or stimulate the cytochrome P450 system may affect levels of other drugs that are metabolized in the liver.

ABP Content Specifications(s)

- Understand which drugs stimulate or inhibit hepatic metabolism

Suggested Readings

- Loebstein R, Koren G. Clinical pharmacology and therapeutic drug monitoring in neonates and children. Pediatr Rev. 1998;19(12):423-428.
- Tetelbaum M, Finkelstein Y, Nava-Ocampo AA, Koren G. Back to basics: understanding drugs in children: pharmacokinetic maturation. Pediatr Rev. 2005;26(9):321-328. doi: http://dx.doi.org/10.1542/pir.26-9-321.
- Wagner J, Abdel-Rahman SM. Pediatric pharmacokinetics. Pediatr Rev 2013;34(6):258-269. doi: http://dx.doi.org/10.1542/pir.34-6-258.

Question 73

According to data from the National Health and Nutrition Examination Survey (NHANES), the prevalence of obesity among children 2 to 19 years of age in the United States from 2011 to 2012 was 17%.

Of the following, the BEST direct use of this and similar earlier data has been

A. calculation of a lower life expectancy for children in this cohort
B. determination of future health effects of childhood obesity
C. determination of the causes of childhood obesity
D. identification of childhood obesity as a risk factor for adult obesity
E. identification of childhood obesity as a significant public health problem

Correct Answer: E
The National Health and Nutrition Examination Survey (NHANES) data described in this question are from cross-sectional prevalence studies of childhood obesity. Such prevalence studies identified childhood obesity as a significant public health problem. Prevalence studies can identify emerging health problems and provide important information that leads to the prioritization of public health issues, development of public health initiatives, and the development of future studies.

Causation can not be determined from cross-sectional prevalence studies, so determination of the causes of childhood obesity from the described studies is not possible. Furthermore, longitudinal information on the cohort is not provided, so calculation of a lower life expectancy for children in this cohort, determination of future health effects of childhood obesity, and identification of childhood obesity as a risk factor for adult obesity is not possible.

Causes of childhood obesity would be better studied as a case-control study. Case-control studies begin with the outcome (childhood obesity) and exposure history (potential causes of childhood obesity) is ascertained. Challenges of case-control studies include selecting appropriate controls and recall or information bias. Life expectancy, determination of future health effects of childhood obesity, and identification of childhood obesity as a risk factor for adult obesity would be best studied as a cohort study. Cohort studies are longitudinal studies, which can be either prospective or reconstructed retrospectively, that follow patients over time for development of outcomes. Prospective cohort studies are less susceptible to selection bias. They are time-consuming, expensive, and subject to loss of follow-up.

PREP Pearls

- Prevalence studies can identify emerging health problems, and provide important information that leads to the prioritization of public health issues, development of public health initiatives, and the development of future studies.
- Causation can not be determined from cross-sectional prevalence studies.
- Cohort study groups are defined by the exposure and followed over time for development of the outcome. Case-control study groups are defined by the outcome and exposures are ascertained retrospectively.

ABP Content Specifications(s)

- Understand the uses and limitations of descriptive epidemiologic studies

Suggested Readings

- Hartung DM, Touchette D. Overview of clinical research design. Am J Health Syst Pharm. 2009;66(4):398-408. doi: http://dx.doi.org/10.2146/ajhp080300.
- Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014;311(8):806-814. doi: http://dx.doi.org/10.1001/jama.2014.732.
- Pearce N. Classification of epidemiological study designs. Int J Epidemiol. 2012;41(2):393-397. doi: http://dx.doi.org/10.1093/ije/dys049.
- Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Epidemiology. 2007;18(6):805-835. doi: http://dx.doi.org/10.1097/EDE.0b013e3181577511.

Question 74

A male infant is brought to your office for a health supervision visit. He was born at term and has been healthy since birth. While performing the physical examination, you assess the developmental milestones he has achieved. The infant smiles responsively and vocalizes with vowel sounds, but does not squeal or laugh. He can track an object horizontally to midline and sometimes past midline. You note a mild head lag when you pull him to the sitting position from supine, and he makes an effort to hold his head midline when held upright. When placed in the prone position, he is able to lift his head up to 45 degrees. The infant's hands are open and relaxed much of the time, and he will hold an object placed in his hand. He is not yet reaching for objects, nor bringing his hands to the midline.

Of the following, the age that BEST matches this infant's developmental abilities is

A. 1 month
B. 2 months
C. 3 months
D. 4 months
E. 2 weeks

Correct Answer: B
The infant described in the vignette exhibits the cognitive/behavioral and motor milestones typically attained by 2 months of age: social smile, cooing, visually tracking an object past midline, diminishing head lag, and disappearance of the grasp reflex. Smiling responsively rather than smiling spontaneously is a key milestone to observe at 2 months of age.

Most infants can vocalize with vowels or coo by 2 months of age. Language then progresses with laughing beginning closer to 3 months of age and squealing at 4 months of age. The addition of consonant sounds, or babbling, is typical of a 6-month-old infant, followed by polysyllabic babbling at 9 months of age.

Visual receptive skills progress from the newborn's ability to fix on the mother's face to following objects to midline at 1 month of age, past midline at 2 months of age, and 180 degrees at 3 to 4 months of age.

The progression of head control is a clinical measure of early gross motor skills. A 2-week-old neonate will exhibit poor head control. Mild head lag when pulled to sitting position from supine, the ability to lift the head to 45 degrees when prone, and the attempt to hold the head erect when upright is typical of a 2-month-old infant. By 3 months of age, the head lag should be minimal when pulled to sitting and most infants will be able to lift the head up to 90 degrees when prone. A 4-month-old infant can lift both the head and chest when prone.

The attainment of fine motor skills is exhibited through the progression of hand skills. Newborns' hands are flexed and fisted most of the time. The involuntary grasp reflex disappears at 2 months of age, allowing the infant to hold an object placed in the hand. Reaching for and swiping at a toy occurs at 3 months of age and is followed by voluntary grasp at 4 months. Bringing hands together in the midline is noted at 3 to 4 months of age, with progression to transferring objects from hand to hand at 6 months of age.

The infant described in the vignette has more advanced milestones than would be expected at 2 weeks or 1 month of age. At 1 month of age, the infant would demonstrate the ability to lift his head only slightly, track visually to midline but not beyond, and smile spontaneously but not socially. At 3 months of age, the infant should have more advanced visual receptive skills with the ability to follow for a full 180 degrees and in a circular motion; plus, reaching for objects and stronger head control should be evident. By 4 months of age, an infant should be laughing, squealing, grasping objects voluntarily, and lifting both the chest and head when prone.

PREP Pearls

- Most 2-month-old infants will smile responsively, vocalize with vowels (cooing), visually track an object past midline, hold an object placed in their hand, lift their head to 45 degrees when prone, and attempt to hold their head erect when held upright.

ABP Content Specifications(s)

- Evaluate the cognitive and behavioral developmental progress/status of an infant at 2 months of age, including recognition of abnormalities
- Evaluate the motor developmental progress/status of an infant at 2 months of age, including recognition of abnormalities

Suggested Readings

- Bickley LS. Bates' Guide to Physical Examination and History Taking. 11th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2012:1024 pp.
- Feigelman S. The first year. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:65-69.
- Feigelman S. The second year. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:70-75.
- Schonhaut L, Armijo I, Pérez M. Gestational age and developmental risk in moderately and late preterm and early term infants. Pediatrics. 2015;135(4):e835-e841. doi: http://dx.doi.org/10.1542/peds.2014-1957.
- Stein REK. Are we on the right track? Examining the role of developmental behavioral pediatrics. Pediatrics. 2015;135(4):589-591. doi: http://dx.doi.org/10.1542/peds.2014-3274.
- Weitzman C, Wegner L, Section on Developmental and Behavioral Pediatrics, Committee on Psychosocial Aspects of Child and Family Health, Council on Early Childhood, Society for Developmental and Behavioral Pediatrics. Promoting optimal development: screening for behavioral and emotional problems. Pediatrics. 2015;135(2):384-395. doi: http://dx.doi.org/10.1542/peds.2014-3716.

Question 75

You are approached by the mother of an intellectually normal 10-year-old girl with a rare metabolic disorder who is interested in pursuing a pediatric clinical drug trial for her disorder. It is a phase 3 trial with blinding. In order to advise her, you review the current guidelines regarding ethical issues and pediatric clinical drug trials.

Of the following, the statement that BEST complies with these guidelines is that

A. assent should be obtained from an intellectually normal minor who is 5 years of age or older
B. financial incentives should be provided to healthcare providers who recruit patients
C. an independent data- and safety-monitoring committee should be in place
D. the informed consent document should be written at a high school level
E. parental/guardian consent can be waived under extenuating circumstances

Correct Answer: C
The performance of research studies in the pediatric population is paramount to achieving safe and effective treatments for children. Clinical drug research has, for the most part, relied on extrapolating information from adult drug studies and off-label use. This practice has placed children at increased risk for adverse effects and ignored the fact that growth and maturation alter the kinetics, toxicities, and end-organ responses of medications in children. In addition, some disorders predominantly affect children rather than adults. Therefore, it is extremely important that formal drug studies involve children and allow them access to older drugs or newer agents.

Pediatric clinical drug research must be performed in an ethically responsible manner, taking into account the wishes of the child and parents while minimizing harm. Ethical guidelines to protect human subjects during scientific investigation have been used for many years to avoid exploitation of human subjects and protect their individual rights. Federal regulations govern these protections. Regulations regarding children as subjects of scientific research were updated in 2005.

Pediatric research proposals must meet the following criteria:

Consideration must be made for the distinct physiology, anatomy, psychology, pharmacology, medical needs, and social consequences of the children and their families.
The study must possess meaningful and measurable outcomes, with adequate comparative data and adequate enrollment numbers, to answer the research question and be scientifically applicable and important for the pediatrics population and the individual subject.
A robust safety plan must be in place throughout the study. The study should maximize benefit while minimizing risk. An independent data- and safety-monitoring committee (DSMC) should be in place for all phase 3 drug trials and some phase 1 and 2 trials. When a DSMC is lacking, a robust data-monitoring plan must be implemented.
The study should take into consideration the sex, ethnic, racial, and socioeconomic status of the children and their families.
The study must be in congruence with all local, regional, and national regulatory guidelines and laws.
Parent(s) or guardian(s) must agree or give permission for the child's participation in the clinical research study. No drug research may occur without express informed consent from the parent/guardian and the subject if the child is old enough to give consent. Assent should be obtained from a child who has reached an intellectual age of 7 years or older. Many institutional review boards require assent from children older than 7 years of age, unless they have significant cognitive delays.
The parent(s) or the minor have the right to withdraw consent/assent and participation in the study at any time during the process.
Financial incentives to healthcare providers for recruiting children are prohibited because of the potential element of undue influence and coercion; however, compensation is quite common for children and adults involved in research studies.

The informed consent should be written in a language that can be easily understood. In general, this means it should be written in a sixth to eighth grade reading level for adult participants. If the consent is written in a secondary language for the individual, the information should be provided via an interpreter in the primary language. If obtaining assent from a child, he/she should be able to fully understand the research study, its purpose, its procedures, his/her participation, duration, and potential risk/discomfort.
The American Academy of Pediatrics firmly believes in providing appropriate access to clinical drug research for existing and new therapeutic agents to children while considering the immense responsibility of the pediatric community, pharmaceutical companies, and regulatory agencies to design and implement quality studies in children.

PREP Pearls

- A robust safety plan must be in place throughout any pediatric research study, that should include an independent data- and safety-monitoring committee (DSMC) for all phase 3 drug trials. In studies without a DSMC, a robust data-monitoring plan must be implemented.
- Financial incentives to healthcare providers for recruiting children to participate in clinical drug research are prohibited because of the potential element of undue influence and coercion.
- The informed consent should be written in a language that can be easily understood. In general, this means it should be written at a sixth to eighth grade reading level for adult participants.

ABP Content Specifications(s)

- Recognize and apply ethical principles regarding research involving children

Suggested Readings

- Committee on Pediatric Research. Policy statement: promoting education, mentorship, and support for pediatric research. Pediatrics. 2014;133(5):943-949. doi: http://dx.doi.org/10.1542/peds.2014-0448.
- Shaddy RE, Denne SC. Clinical report: guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations. Pediatrics. 2010;125(4):850-860. doi: http://dx.doi.org/10.1542/peds.2010-0082.

Question 76

You are seeing a 12-year-old transgender girl for a health supervision visit. The mother asks to speak with you privately. During the discussion, the mother expresses concern that her child has no friends because she is transgender. She asks you how she can best support her child.

Of the following, your BEST advice for the mother is that she should

A. be aware of the increased risk of depression in transgender children
B. encourage the child to delay gender expression until she is older
C. encourage gender conformation surgery as soon as possible
D. have the child treated for gender dysphoria with reparative therapy
E. recognize that the child's transgender identification is likely a fad

Correct Answer: A

Children who do not identify with any peers are at risk for psychological difficulty. Children may feel isolated for a multitude of reasons, including sexual orientation or gender identity. Sexual orientation refers to an individual's pattern of arousal by and attraction toward others, whereas gender identity refers to an individual's sense of being male, female, or neither. Since the existence of societal stigma resulting from homophobia and heterosexism, transgender youth have experienced higher rates of depression and suicidal ideation than their gender-conforming peers.

Many children will experiment with gender expression and roles at a young age, but a pervasive, consistent, persistent, and insistent sense of being another gender is characteristic of transgender youth. Gender dysphoria is defined as a marked difference between an individual's experienced gender and his or her natal sex. The difference must be present for at least 6 months and cause clinically significant distress. More detailed interviewing of the adolescent in this vignette would be required to appropriately assess for gender dysphoria (Item C76).

Item C76. Suggested Approaches to Obtaining a Gender Dysphoria History for the Primary Care Clinician.*

Examples of Gender Nonconforming Behavior and Preferences	Examples of Suggested Questions and Phrasing
Gender identity different from the sex assigned at birth	Some young people feel that they were born in the wrong body; have you ever felt like that?
Persistence of gender identity different from the sex assigned at birth	How long have you felt that you were a boy/girl?
Gender nonconforming behavior	What kind of toys would you like to play with? Do you prefer to wear girls' or boys' underwear? What do you (and what would you) like to wear when you swim? Who are your favorite fantasy characters? What do you (and what would you like to) dress up as at Halloween? What character from the TV shows or movies do you admire?
Evaluation of source of distress	What kind of thoughts make you feel sad? What do you think about your body?

*The purpose of obtaining a sensitive and thorough gender dysphoria-related history is not to diagnose gender dysphoria; rather it is designed to assess the necessity for referral and further evaluation by a mental health clinician.

Reprinted with permission from Lopez X, Stewart S, Jacobson-Dickman E. Approach to children and adolescents with gender dysphoria. *Pediatr Rev.* 2016:37: 89-98

Encouraging the child in the vignette to delay gender expression may be interpreted as rejection. Rejection has been associated with depressive symptoms, self-harm, and suicidality.

The Endocrine Society clinical practice guideline for the treatment of transsexual persons recommends that the suppression of pubertal hormones start when the child first exhibits physical changes of puberty, but no earlier than sexual maturity ratings of 2 to 3. Initiation of cross-sex steroids for pubertal development of the desired opposite sex should begin at approximately 16 years of age. The Endocrine Society recommends deferring surgery until the individual is at least 18 years of age.

Reparative therapy involves techniques designed to convert one's sexual orientation from homosexual to heterosexual. The American Psychological Association and the American Psychiatric Association oppose such treatment.

PREP Pearls

- Adolescents who do not identify with any peers are at risk for psychological difficulty.
- Gender dysphoria is defined as a marked difference between an individual's experienced gender and his or her natal sex. The difference must be present for at least 6 months and cause clinically significant distress.
- The Endocrine Society clinical practice guideline for the treatment of transsexual persons recommends that the suppression of pubertal hormones start when the adolescent first exhibits physical changes of puberty, followed by initiation of cross-sex steroids for pubertal development of the desired opposite sex at approximately 16 years of age.

ABP Content Specifications(s)

- Recognize the risks associated with adolescents who do not identify with any peers ("loners")

Suggested Readings

- American Academy of Pediatrics. Section on Lesbian, Gay, Bisexual, and Transgender Health and Wellness webinars. American Academy of Pediatrics website. https://www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/solgbt/Pages/Education.aspx.
- Committee on Adolescence. Policy statement: office-based care for lesbian, gay, bisexual, transgender, and questioning youth. Pediatrics. 2013;132(1):198-203. doi: http://dx.doi.org/10.1542/peds.2013-1282.
- Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al. Endocrine treatment of transsexual persons: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2009;94(9):3132-3154. doi: http://dx.doi.org/10.1210/jc.2009-0345.
- Lopez X, Stewart S, Jacobson-Dickman E. Approach to children and adolescents with gender dysphoria. Pediatr Rev. 2016;37(3):89-98. doi: http://dx.doi.org/10.1542/pir.2015-0032.

Question 77

A 3-year-old boy is brought to your office for a health supervision visit. During the visit, you observe him playing with his toys. He pretends that his action figures are talking to each other and you hear him use jargon, with an occasional word or two in Spanish and in English. When you ask him a question, he looks at you, smiles, and responds verbally and with gestures, but you have a difficult time understanding his speech. When asked, he can follow a multistep direction and can point to different actions in pictures. The boy's mother tells you that what you are observing is typical and states that she understands about half of what he says. She is not concerned, as his father and older brother had been "late talkers" and her son is growing up in a bilingual household. The boy's past medical history is unremarkable. He passed both hearing and vision screens in your office, and his physical examination is within normal limits.

Of the following, you are MOST likely to advise your patient's mother that her son

A. has a maturational lag in language and will catch up to his peers
B. is likely to have delays in cognitive-adaptive development
C. should have language skills similar to those of a monolingual child
D. will have problems with language-based learning
E. will have speech intelligible to strangers by 4 years of age

Correct Answer: C
A typical child exposed to 2 languages should not have a significant delay in their language development when compared to a child in a monolingual household. Adding up a child's words from both languages should result in a total vocabulary size similar to that of a child exposed to 1 language.

Language is a symbolic means of communication with several components. Receptive language is the understanding of another's language, whereas expressive language is the production of language. Pragmatics is the social use of language. Speech is the articulation of sounds to communicate.

Typical language development begins with the infant's preference for looking at faces, particularly the eyes and mouth, and for listening to voices. In early language development, receptive language is significantly ahead of expressive language. Infants start recognizing their name around 6 months of age and then additional single words around 8 to 10 months of age. The ability to understand simple commands begins in the second year after birth. Children are generally able to follow a 1-step direction by 1 year of age, 2-step direction by 2 years of age, and 3-step direction by 3 years of age. Expressive language begins with cooing (musical vowel sounds), followed by babbling (consonant-vowel sounds) around 3 to 6 months of age, and first words around 12 months of age. Jargoning also occurs around 12 months of age and consists of babbling with adult-like intonation and inflection. In immature jargoning, there are no understandable words, whereas in mature jargoning, occasional words are mixed in with the babbling. Expressive language is first gained slowly, but then "explodes," typically in the later part of the second year after birth, when the child has a vocabulary of about 50 words and begins to produce 2-word phrases. Children typically speak 1 word by 1 year of age, combine 2 words by 2 years of age, and combine 3 words by 3 years of age. Complete sentences with increasing complexity develop in the preschool years and children are able to have conversations. During the period of rapid language development (3-4 years of age), developmental dysfluency with repetition of words and phrases can occur, but typically self-resolves by 4 to 5 years of age. Children are approximately 50% intelligible to unfamiliar adults by 2 years of age, 75% by 3 years of age, and 100% by 4 years of age. Although children should be fully intelligible to strangers by 4 years of age, certain speech sounds may not be well articulated until 8 years of age. Major milestones of typical language development are shown in Item C77.

Item C77. Major Milestones of Typical Language Development.

	Expressive Language	Receptive Language	Speech
3 months of age	Cooing	Interest in human voices and faces	N/A
6 months of age	Babbling	Responds to name	N/A
9 months of age	Points; says "Mama-Dada"	Understands single words and "no"	N/A
1 year of age	Single words	Follows a 1-step direction	N/A
2 years of age	2-word combinations	Follows a 2-step direction	50% intelligible
3 years of age	3+ word sentences	Follows a 3-step direction	75% intelligible; developmental dysfluency may occur
4 years+ of age	Complex sentences; conversations	Able to listen to and answer questions about a short story	100% intelligible
8 years of age	Can tell a sequential story that is understood by others	Understands information heard when explained	Speech sounds articulated correctly

N/A, not applicable

Courtesy of Y Liu

Factors influencing language development include the richness of language in the child's environment, socioeconomic status, and family history of speech/language problems. Exposure to larger amounts of language with more varied and child-directed language interactions positively influences language development. Reading to young children promotes their language development. Language exposure and access to books tend to be limited in low socioeconomic

environments. A family history of speech/language problems or reading problems is associated with delayed expressive language. As previously discussed, bilingualism is not a factor in language delay. Similarly, delayed language cannot be attributed to sex; boys are not significantly behind girls in language development.

Language delay does not necessarily progress to language disorder. Young children may have a maturational or developmental delay in speech or language that resolves with time. However, a speech or language disorder exists when difficulties in learning language or developing speech skills persist and cause impairment. About half of "late talkers" continue to have language difficulties at 4 years of age. Language disorders are present in about 2% to 3% of school-age children and speech disorders are present in about 3% to 6%. Speech disorders include phonologic disorders (articulation problems) and stuttering. Stuttering occurs in 1% of children and is characterized by impaired speech fluency. Speech sounds are prolonged, parts of words are repeated, pauses are present, and facial tension can be apparent when the child attempts to speak.

The 3-year-old boy in the vignette demonstrates a significant delay in his expressive language and decreased intelligibility, even to his mother. His language is still at the mature jargoning stage, as compared to the expected 3-word utterance stage. While it is possible that his language and speech may improve, his delay in expressive language is not mild and a "wait and see" approach would be of disservice to this child. The boy's receptive language, play, and ability to point to actions in pictures are appropriate for his age, which lessens concern for cognitive-adaptive impairment. This child will not necessarily have problems with language-based learning, but as a child with language delay, he is at risk. Therefore, this child should be monitored for possible development of those issues in school. This child's speech should be 75% intelligible, but is only 50% intelligible to his mother. He may not develop speech intelligible to unfamiliar adults by 4 years of age as expected without further evaluation and intervention.

This child and any other child in whom a speech/language delay or disorder is considered should be referred for an audiology evaluation and speech/language evaluation. Evaluation of other developmental domains should be considered, as speech/language delay may be the presenting sign for other conditions such as global developmental delay, intellectual disability, or autism spectrum disorder. Evaluation and treatment may be accessed through Early Intervention programs if the child is younger than 3 years of age and through the school district if older than 3 years of age.

PREP Pearls

- A typical child exposed to 2 languages should not have a significant delay in their language development when compared to a child in a monolingual household.
- Delayed language cannot be attributed to sex; boys are not significantly behind girls in language development.
- Although children should be fully intelligible to strangers by 4 years of age, certain speech sounds may not be well articulated until 8 years of age.
- Children with language delay are at higher risk for problems with language-based learning.

ABP Content Specifications(s)

- Recognize age-related normal and abnormal variations in speech and language
- Understand factors that influence language development

Suggested Readings

- Coplan J. Language delays. In: Augustyn M, Zuckerman B, Caronna EB, eds. The Zuckerman Parker Handbook of Developmental and Behavioral Pediatrics for Primary Care. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2010:258-262.
- McQuiston S, Kloczko N. Speech and language development: monitoring process and problems. Pediatr Rev. 2011;32(6):230-239. doi: http://dx.doi.org/10.1542/pir.32-6-230.

Question 78

A 13-year-old previously healthy adolescent girl presents to the emergency department with a 2-hour history of a severe "cramping" sensation in her right lower abdomen that awoke her from sleep. The pain has been constant since its onset. She has felt nauseous and has had 8 episodes of nonbilious vomiting since the pain began. She had a cough and nasal congestion over the past 2 days, but denies any other associated symptoms, including fever and diarrhea. She denies any prior episodes of similar pain, as well as any history of trauma. She “felt fine” earlier in the evening when she went out to dinner with her mother and older sister.

The patient’s first menstrual cycle was at 11 years of age, and her last menstrual period was approximately 3 weeks ago. She denies any current vaginal discharge, bleeding, or any sexual activity.

In the emergency department, her vital signs are a temperature of 36.8°C, heart rate of 90 beats/min, blood pressure of 128/78 mm Hg, respiratory rate of 20 breaths/min, and pulse oximetry of 98% (room air). On physical examination, she appears to be in moderate distress due to pain, but her mental status is normal. The cardiac and respiratory examinations are normal. Her abdomen is tender to palpation over the right lower quadrant and suprapubic region, but she displays no peritoneal signs. Her extremities are warm and well-perfused. Physical examination is otherwise unremarkable.

As you are completing your physical examination, the adolescent reports increasing nausea and has another episode of nonbilious emesis. Her mother asks you what could be causing her symptoms.

Based on the patient's history and physical examination findings, the MOST likely diagnosis is

A. acute appendicitis with perforation
B. acute food poisoning
C. ovarian torsion
D. right lower lobe pneumonia
E. right ovarian cyst

Correct Answer: C
The adolescent girl in the vignette presents with acute onset of constant unilateral abdominal pain, nausea, and vomiting, without associated fever or diarrhea. Based on her history and physical examination findings, her most likely diagnosis is ovarian torsion.

It is important for all pediatric providers to recognize the clinical findings associated with ovarian torsion. Ovarian torsion had been estimated to account for nearly 3% of all cases involving acute abdominal pain in children. Pediatric patients account for an estimated 15% of all ovarian torsion cases, with major centers reporting between 0.3 and 3.5 pediatric cases annually. Ovarian torsion has been described in all ages, occurring at an average age of 10 years among children. While ovarian torsion is more common following menarche, it may affect children in the prepubertal period as well.

Ovarian torsion begins when an ovary twists on its pedicle, resulting in obstruction of venous outflow and lymphatic drainage, leading the ovary to become engorged and edematous. If not corrected, the persistent increase in ovarian parenchymal pressure may result in occlusion of arterial blood flow and infarction of the affected ovary.

Clinical findings of ovarian torsion include abrupt onset of severe, constant, unilateral pain located in the pelvis or lower abdomen. The right ovary tends to be affected more commonly than the left. Associated symptoms include nausea and vomiting, as well as urinary tract symptoms such as dysuria and frequency. On examination, a tender mass may be palpable. In patients presenting with suspected ovarian torsion, pelvic ultrasonography should be obtained. If ovarian torsion is highly suspected clinically, laparoscopy may be required to both diagnose and treat the condition.

Acute appendicitis with perforation is less likely to be the diagnosis for the patient in the vignette than ovarian torsion. While there can be considerable overlap in the clinical findings of ovarian torsion and acute appendicitis, patients with ovarian torsion (as noted in the girl in the vignette) are much less likely to have fever, migratory pain, or peritoneal signs such as rebound tenderness on examination. Furthermore, the onset of symptoms of acute appendicitis (especially acute appendicitis complicated by perforation) would typically be expected to be less abrupt than the sudden onset of symptoms that occurs with ovarian torsion.

Although acute food poisoning could certainly lead to acute onset of nausea and vomiting, patients with this diagnosis would not be expected to have localized abdominal tenderness on physical examination, as is noted in the adolescent in the vignette.

Children with lower lobe pneumonia may present with abdominal pain because of visceral innervation. However, associated symptoms including fever, cough, and tachypnea are typically present in these children, and these findings are not present in the adolescent in the vignette.

Although patients with ovarian cysts may present with lower abdominal or pelvic pain, many ovarian cysts are asymptomatic or cause only mild discomfort. Abdominal or pelvic pain due to ovarian cysts is much less likely to be associated with nausea and vomiting, which are prominent symptoms displayed by the patient in the vignette who is presenting with acute ovarian torsion.

PREP Pearls

- Clinical findings of ovarian torsion include abrupt onset of severe, constant, unilateral pain located in the pelvis or lower abdomen. Associated symptoms include nausea and vomiting, as well as urinary tract symptoms such as dysuria and frequency.
- While ovarian torsion is more common following menarche, it may affect children in the prepubertal period as well.
- Pelvic ultrasonography should be performed in patients presenting with suspected ovarian torsion. If ovarian torsion is highly suspected clinically, laparoscopy may be required to both diagnose and treat the condition.

ABP Content Specifications(s)

- Recognize the clinical findings associated with ovarian torsion

Suggested Readings

- Breech LL, Adams Hillard PJ. Adnexal torsion in pediatric and adolescent girls. Curr Opin Obstet Gynecol. 2005;17(5):483-489.
- Ross A, LeLeiko NS. Acute abdominal pain. Pediatr Rev. 2010;31(4):135-144. doi: http://dx.doi.org/10.1542/pir.31-4-135.
- Schmitt ER, Ngai SS, Gauche-Hill M, Renslo R. Twist and shout!: pediatric ovarian torsion clinical update and case discussion. Pediatr Emerg Care. 2013;29(4):518-526. doi: http://dx.doi.org/10.1097/PEC.0b013e31828a7822.

Question 79

A 6-year-old previously unvaccinated boy presents to the pediatric clinic for immunizations. He has a history of seizures and takes a daily antiepileptic medication. His last seizure occurred 1 month ago.

Of the following, the MOST appropriate vaccination for this child is

A. DTaP
B. DT
C. Td
D. Tdap
E. TT

Correct Answer: A

The child in the vignette should be vaccinated with DTaP. DTaP is licensed only for individuals though 6 years of age and should be administered as such. Since this patient's seizure disorder is long-standing and controlled, there is no contraindication to receiving pertussis vaccine. Of the available answer choices, DTaP would provide the most comprehensive vaccination in an age-appropriate fashion.

Diphtheria and tetanus toxoids, either in the form of DT (the pediatric formulation for those ≤ 6 years of age) or Td (formulation for those ≥ 7 years of age) can be used in settings were pertussis vaccination is contraindicated. Contraindications to pertussis vaccination include anaphylaxis after a previous dose of pertussis-containing vaccine and encephalopathy within 7 days of receipt of pertussis vaccine without another identifiable cause. In order to avoid ascribing symptoms to vaccine, it is recommended that vaccine be deferred in patients with an evolving neurologic condition. While not contraindicated, it should be used with caution in individuals who previously developed Guillain-Barré syndrome within 6 weeks after receiving a tetanus toxoid-containing vaccine. Individuals with stable neurologic conditions or a family history of seizures should receive DTaP. Additionally, a family history of a severe reaction to a pertussis-containing vaccine would not be considered a contraindication.

In comparison to DTaP, Tdap vaccines contain reduced quantities of diphtheria toxoid and pertussis components to reduce local reactions. Tdap is licensed only for a single dose. In pregnancy, there is off-label use and it is administered in each pregnancy. Other than in settings where pertussis vaccination is contraindicated, Td can be used for tetanus prophylaxis in wound management and for routine decennial booster when the individual has previously received Tdap. It can also be used for catch-up vaccinations in individuals 7 years of age or older after Tdap has been given.

Tetanus-toxoid containing vaccine, TT, is available in the United States for individuals 7 years of age or older. Combination vaccines are preferred over individual component vaccine.

PREP Pearls

- DTaP is the pediatric formulation for those 6 years of age or younger and Tdap is the formulation for those 7 years of age or older.
- Stable neurologic conditions or a family history of seizures are not contraindications for DTaP vaccine.
- Contraindications for DTaP include anaphylaxis after a previous dose or to a vaccine component, or development of an encephalopathy within 7 days of receipt of vaccine.

ABP Content Specifications(s)

- Know the differences in the composition of DT and dT
- Plan the administration of DT or dT based on the age of the patient

Suggested Readings

- American Academy of Pediatrics. Pertussis (whooping cough). In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:608-621.
- Snyder J, Fisher D. Pertussis in childhood. Pediatr Rev. 2012;33(9):412-421. doi: http://dx.doi.org/10.1542/pir.33-9-412.

Question 80

The mother of a 4-year-old girl calls poison control after finding the child playing with a bottle of eye drops. The girl told her mother she thought it looked like a little baby bottle when she was discovered holding it to her lips. The eye drops are a common over-the-counter brand used to treat allergy symptoms. The bottle is now empty, and the mother is unsure of the quantity of liquid it had contained. The girl is alert and well appearing. Her heart rate is 65 beats/min based on the mother's report.

Of the following, the BEST next step in the management of this possible ingestion is

A. activated charcoal administration within 2 hours
B. close observation by the parents at home
C. hemodynamic monitoring for 4 hours
D. naloxone administration urgently
E. vomiting induced immediately

Correct Answer: A

The child in this vignette has an uncommon, yet potentially serious adverse outcome related to accidental ingestion of a topical antihistamine-decongestant product. Activated charcoal should be administered within 1 to 2 hours of ingestion. Over-the-counter (OTC) preparations are widely marketed and commonly used by patients to help ease symptoms of the common cold or seasonal allergies. Since these preparations are readily available in most households, there are significant safety concerns about adverse drug effects and the risk of unintentional ingestions or overdoses.

Oral ingestion of topical ophthalmic preparations containing an α-2 adrenergic agent will lead to sympatholytic symptoms, including hypotension, bradycardia, miosis, hypothermia, hyporeflexia, as well as central nervous system (CNS) symptoms and respiratory depression. Imidazolines are found in many OTC topical ophthalmic and nasal decongestants, and when ingested, can lead to systemic toxicities similar to those seen with clonidine poisoning. A minimum toxic dose of the topical imidazolines has not been established, but ingestion of as little as 2.5 to 5 mL has been reported to cause serious symptoms. Onset of symptoms can be rapid and generally occurs within 4 to 6 hours after ingestion. Admission and close monitoring is warranted for all symptomatic children who have ingested topical imidazolines. Symptoms should be managed with supportive treatment and usually resolve within 24 hours. Those who are asymptomatic may be observed closely at home for 24 hours. Children who are asymptomatic 6 hours after ingestion may be discharged from the hospital if continued close supervision for 24 hours can be assured, as well as ready access to return for care if needed.

The girl in the vignette is already exhibiting bradycardia, so close observation at home is not appropriate. In addition, because the interval from ingestion is uncertain, she should be transported to an emergency center via ambulance with hemodynamic monitoring. Monitoring should be continued until she is asymptomatic for at least 6 hours. For gastrointestinal decontamination, activated charcoal must be administered within 1 to 2 hours of ingestion (< 1 hour for rapidly absorbed toxins). Naloxone use is controversial and is recommended only in cases of severe mental status depression and cardiorespiratory compromise. Inducing vomiting with ipecac is not recommended for treatment of toxic ingestions because CNS depression may develop rapidly from ipecac use and complicate patient management.

Knowledge of the current recommendations for the use of common OTC products, as well as their adverse effects and potential for toxicity, is important for all practitioners. Advice regarding appropriate use, including safe storage and handling, in addition to discussions on efficacy, must be a part of conversations with patients and families, especially those with young children. The OTC topical imidazoline preparations are tasteless and highly potent after ingestion, yet are not packaged in child-resistant containers and are often not kept out of reach of children. The OTC cold and cough preparations often contain antihistamines, antitussives, decongestants, or expectorants; some are combined with antipyretics.

In 2008, the US Food and Drug Administration formally recommended against the use of OTC cold and cough medicines in children younger than 2 years of age because of the risk of serious

adverse effects. The American Academy of Pediatrics advises against the use of OTC cold and cough medicines in children younger than 6 years of age stating the efficacy and risk of such medications require further study. Since the implementation of these labeling changes, US poison centers have received fewer reports of severe and fatal adverse effects of OTC cold and cough medications.

PREP Pearls

- Oral ingestion of topical ophthalmic preparations containing an α-2 adrenergic agent may lead to systemic sympatholytic symptoms.
- Admission and close monitoring are warranted for all symptomatic children who have ingested topical imidazolines.
- Asymptomatic children who have ingested imidazolines may be observed closely at home for 24 hours.
- Activated charcoal is most effective for gastrointestinal decontamination when administered within 2 hours of ingestion.

ABP Content Specifications(s)

- Know the components and the common adverse effects and toxicities of common over-the-counter preparations , and advise regarding their appropriate use

Suggested Readings

- Eddy O, Howell JM. Are one or two dangerous?: clonidine and topical imidazolines exposure in toddlers. J Emerg Med. 2003;25(3):297-302. doi: http://dx.doi.org/10.1016/S0736-4679(03)00206-3.
- Lowry JA, Leeder JS. Over-the-counter medications: update on cough and cold preparations. Pediatr Rev. 2015;36(7):286-298. doi: http://dx.doi.org/10.1542/pir.36-7-286.
- Pappas DE, Hendley JO. The common cold and decongestant therapy. Pediatr Rev. 2011;32(2):47-55. doi: http://dx.doi.org/10.1542/pir.32-2-47.
- Rangan C, Everson G, Cantrell FL. Central alpha-2 adrenergic eye drops: case series of 3 pediatric systemic poisonings. Pediatr Emerg Care. 2008;24(3):167-169. doi: http://dx.doi.org/10.1097/PEC.0b013e3181668aee.

Question 81

A full-term female neonate is delivered to a 45-year-old woman following a prenatal course complicated by minimal medical care, with no prenatal ultrasound or laboratory evaluation. The neonate initially appears well, demonstrating a vigorous cry with Apgar scores of 5and8. You are called to evaluate the neonate 10 hours later after an episode of bilious emesis.

Her vital signs on your arrival include a temperature of 37.8°C, heart rate of 139 beats/min, respiratory rate of 36 breaths/ min, and blood pressure of 70/40 mm Hg. The neonate is pale and ill appearing, with intermittent bilious emesis. Her abdomen is distended with high-pitched bowel sounds. She has no palpable mass. A nasogastric tube is placed without difficulty and 15 mL of bilious fluid is suctioned out.

Of the following, the BEST test to confirm diagnosis is

A. abdominal computed tomography
B. abdominal radiograph
C. abdominal ultrasonography
D. magnetic resonance imaging
E. upper gastrointestinal tract series

Correct Answer: E

The newborn in the vignette has a presentation that is consistent with gastrointestinal obstruction. An upper gastrointestinal tract (UGI) series will best evaluate the anatomy to identify an obstruction. An abdominal radiograph would show a dilated stomach suggestive of obstruction, but would not confirm or localize the obstruction. Abdominal computed tomography requires significant radiation exposure without significant benefit over the UGI series. Abdominal ultrasonography may not visualize the obstruction. Finally, magnetic resonance imaging would require oral contrast and possibly sedation, and takes significantly longer to perform without providing significant benefit over the UGI series.

The differential diagnosis of bilious emesis and/or projectile vomiting in a newborn includes:

- Duodenal atresia
- Jejunal atresia
- Malrotation with midgut volvulus
- Meconium ileus

Management and evaluation include gastric decompression, intravenous fluid management, maintenance of euglycemia, radiographic evaluation to identify the location of obstruction, and consultation with a pediatric surgeon.

PREP Pearls

- An upper gastrointestinal tract series will best evaluate the anatomy when looking for obstruction in a newborn with bilious emesis.
- Gastric decompression is a key step in the treatment of a newborn with bilious or projectile emesis.
- A pediatric surgeon should participate in the evaluation of a newborn with bilious or projectile emesis.

ABP Content Specifications(s)

- Plan the evaluation of projectile vomiting in a newborn infant, and manage appropriately
- Plan the appropriate management of bilious vomiting in a newborn infant

Suggested Readings

- Juang D, Snyder CL. Neonatal bowel obstruction. Surg Clin North Am. 2012;92(3):685-711. doi: http://dx.doi.org/10.1016/j.suc.2012.03.008 .
- Marine MB, Karmazyn B. Imaging of malrotation in the neonate. Semin Ultrasound CT MR. 2014;35(6):555-570. doi: http://dx.doi.org/10.1053/j.sult.2014.08.004 .
- Parashette KR, Croffie J. Vomiting. Pediatr Rev. 2013;34(7):307-319. doi: http://dx.doi.org/10.1542/pir.34-7-3 .

Question 82

A 10-year-old boy presents to your clinic for a preparticipation sports physical before the fall soccer season. He participates in 1-hour long practices twice weekly and has a 1-hour long game each Saturday. The boy's parents ask you what their son should drink to remain well hydrated during soccer practices and games. The boy is 55 inches tall and weighs 86 pounds, with a body mass index of 20 kg/m2 (88th percentile for age).

Of the following, the BEST beverage choice for this boy is

A. chocolate milk
B. an oral rehydration solution
C. a sports drink with electrolytes, dextrose, and sucrose
D. a sugar-free energy drink
E. water

Correct Answer: E

For sports activities lasting 1 hour or less, water is sufficient for hydration. Sports drinks or other beverages containing sugar and electrolytes are not necessary. Since the boy in the vignette is at risk for obesity, water is also the best beverage to offer before and after his soccer practices and games.

Many products are marketed to children and adolescents as substances that will enhance sports performance. There is evidence that replacement of electrolytes may be beneficial for activities lasting longer than 1 hour. Sports drinks generally contain both electrolytes and sugar, and because of the added sugar, they may be more palatable to children than plain water and may encourage better hydration with longer activity. However, healthy snacks can be offered, along with water, as an alternative to sports drinks.

An oral rehydration solution may be appropriate for an athlete with dehydration, but that is not the situation for the child in the vignette. Chocolate milk has recently been touted as containing the ideal ratio of carbohydrates to protein, promoting muscle recovery after exercise. However, this boy is at risk for obesity and participates in short practice sessions, so water is preferable to both a sports drink and chocolate milk. Energy drinks generally contain high amounts of caffeine, and are not recommended for young children or adolescents and may even be detrimental.

The preparticipation physical evaluation provides an opportunity for healthcare providers to ask young athletes about attempted weight loss or gain and the use of performance-enhancing supplements. Young athletes may be interested in dietary practices rumored to enhance sports performance. Participation in an athletic activity that favors a lean physique, such as dancing, wrestling, or gymnastics, is a risk factor for unhealthy calorie restriction. Children and adolescents participating in sports with an emphasis on a muscular physique, such as football and track and field, are more likely to take dietary supplements purported to promote weight gain or build muscle, such as a protein supplement. Since most adolescents consume adequate dietary protein, supplementation is unnecessary. In addition, many supplements can cause serious adverse effects and may contain ingredients not listed on the labels.

PREP Pearls

- For sports activities lasting 1 hour or less, water is sufficient for hydration.
- Sports drinks may be more palatable to children because of the added sugar and may encourage hydration with longer activity.
- Energy drinks generally contain high amounts of caffeine and are not recommended for young children or adolescents.
- Supplements are not regulated by the federal government and may contain ingredients not listed on the labels, raising concern about their safety.

ABP Content Specifications(s)

- Know the indications for and adverse effects when student athletes ingest sports energy drinks and protein supplements
- Identify the nutritional needs and complications associated with sports and recreational activities, including cheer leading and dancing

Suggested Readings

- Committee on Sports Medicine and Fitness. Promotion of healthy weight-control practices in young athletes. Pediatrics. 2005;116(6):1557-1564. doi: http://dx.doi.org/10.1542/peds.2005-2314.
- Council on Sports Medicine and Fitness, Council on School Health, Bergeron MF, Devore C, Rice SG. Policy statement: climatic heat stress and the exercising child and adolescent. Pediatrics. 2011;128(3):e741-e747. doi: http://dx.doi.org/10.1542/peds.2011-1664.
- De Souza MJ, Nattiv A, Joy E, et al. 2014 female athlete triad coalition consensus statement on treatment and return to play of the female athlete triad: 1st international conference held in San Francisco, CA, May 2012, and 2nd international conference held in Indianapolis, IN, May 2013. Clin J Sport Med. 2014;24(2):96-119. doi: http://dx.doi.org/10.1097/JSM.0000000000000085.

Question 83

You receive a call from an anxious father whose 6-year-old daughter was just diagnosed with head lice. The father has several questions regarding the etiology, treatment, and prevention of head lice.

Of the following, you are MOST likely to tell the father that

A. any person that shares a bed with his daughter should be treated, even if no live lice are found
B. no nit" policies for return to school have been effective in reducing the transmission of lice
C. routine lice screening at schools has been effective in reducing the transmission of lice
D. treatment with 1% permethrin should be repeated in 3 to 5 days if live lice are seen
E. untreated head lice has been associated with transmission of Lyme disease

Correct Answer: A

For the girl in the vignette found to have head lice, the most appropriate recommendation to the father is that any person that shares a bed with his daughter should be treated, even if no live lice are found. Despite the fact that head lice are not a health hazard and are not known to spread disease, lice continues to be a source of great anxiety for many parents, teachers, and children. The annual cost associated with lice and lice treatment (including remedies, lost wages, school system expenses) is estimated at $1 billion. Many of these expenses are due to a misunderstanding of the human lice life cycle and proper ways to screen and treat lice.

The adult head louse is typically 2 to 3 mm in length and is tan or gray in color. The female head louse can live up to 3 to 4 weeks and lays up to 10 eggs per day. These eggs firmly attach to the hair usually within 4 mm of the scalp. The eggs typically hatch after 7 to 12 days, releasing a nymph that will undergo 3 more nymph stages until becoming an adult louse 9 to 12 days later. Approximately 1.5 days after becoming an adult, the female adult louse begins to lay eggs. This cycle will repeat itself every 3 weeks unless treatment for the lice is initiated.

Lice can move only by crawling; transmission typically occurs through direct contact (head-to-head contact). Indirect transmission through objects such as hats and combs is a much less likely mode of transmission. Diagnosis of lice is made by the identification of an adult louse, nymph, or egg in the scalp.

Treatment for lice consists not only of topical treatment of the scalp, but preventive measures to help stop the spreading of lice. All household members should be checked for lice and treated if nits within 1 cm of the scalp or live lice are found. Additionally, all family members who share a bed with the patient should be treated as well, regardless of whether any lice or nits are found on examination. Despite the fact that indirect transmission is much less likely to occur than direct transmission, it is advised to wash hair care items and bedding of the patient. Additionally, items that have come into contact with the patient's head over the past 24 to 48 hours (clothing, headgear, furniture, carpeting, and rugs) should be cleaned as well. Items such as clothing and rugs should be washed and dried at a temperature greater than 54.4°C, and furniture and carpeting should simply be vacuumed.

There are multiple topical agents used to treat head lice, with 1% permethrin or pyrethrins being the first-line agents unless significant resistance to permethrin has been reported. If live lice are still seen 7 to 10 days after application of the 1% permethrin or pyrethrins, a repeat application is recommended. Many other topical agents (including malathion 0.5%, benzyl alcohol 5%, topical ivermectin, and spinosad) are available when first-line agents do not work or if resistance is high. The safety, efficacy, and price of these agents should be examined in order to determine the best treatment for the patient.

It is important to make sure that school personnel have been properly educated on lice transmission and treatment. The routine lice screening at schools has not been shown to be effective at reducing lice transmission rates at school and is also not cost effective. A child should not be restricted from school because of lice, not on the day of diagnosis or on any day

after. The “no-nit” policies, where patients are excluded from school until all nits have been removed, should not be enforced or tolerated.

PREP Pearls

- Pyrethrins and 1% permethrin are first-line treatment for head lice.
- Children with lice should not be excluded from schools.
- Lice screening in schools and “no nit” policies have not been shown to be effective in reducing the spread of lice in schools.

ABP Content Specifications(s)

- Understand the life cycle of human lice

Suggested Readings

- American Academy of Pediatrics. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Pediculosis capitis. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:597-601.
- Bloomfield D. Head lice. Pediatr Rev. 2002;23(1):34-35. doi: http://dx.doi.org/10.1542/pir. 23-1-34.
- Devore CD, Schutze GE, Council on School Health and Committee on Infectious Diseases. Head lice. Pediatrics. 2015;135(5):e1355-e1365. doi: http://dx.doi.org/10.1542/peds.2015-0746.

Question 84

A 2-year-old girl with hemoglobin SS presents to the emergency department with a temperature of 37.4°C and fussiness. On physical examination, her heart rate is 162 beats/min, her blood pressure is 78/52 mm Hg, and her oxygen saturation in room air is 96%. She appears pale and her spleen tip is palpable 3 cm below the left costal margin. Her examination is otherwise normal. A complete blood cell count is shown:

Laboratory Test

Laboratory Test	Patient Results
White blood cell	13,000/μL (13×10^9/L)
Hemoglobin	5.1 g/dL (51 g/L)
Mean corpuscular volume	88 fL
Platelets	95×10^3/μL (95×10^9/L)
Reticulocyte count	35%

Of the following, the BEST next step in management is to

A. administer intravenous (IV) ceftriaxone
B. administer IV morphine
C. initiate therapy with hydroxyurea
D. administer IV normal saline
E. transfuse packed red blood cells

Correct Answer: E

The girl in the vignette has splenic sequestration. It is critical to rapidly recognize this event, as it can quickly result in very severe anemia and death. This sickle cell–related crisis occurs when sickling in the vasculature of the spleen entraps red blood cells, resulting in rapid splenic engorgement and a severe, potentially life-threatening anemia. Splenic sequestration is most common in children younger than 5 years, but can occur at any age. It typically presents, as in the child in the vignette, with signs of severe anemia (tachycardia, pallor, and fussiness), thrombocytopenia, and a palpable spleen. Fever may be present. One of the most effective interventions for reducing mortality in young children with sickle cell disease has been teaching parents to palpate for a spleen in their child daily. Splenic sequestration associated with sickle cell disease should be treated with a transfusion of packed red blood cells. If the anemia is very severe, the transfusion should be given slowly, over several hours, and typically in aliquots of 5 to 7 mL/kg. This approach avoids further cardiac stress. In addition, the spleen will eventually "release" the entrapped red blood cells, leading to a rapid rise in hemoglobin; if too much blood was transfused when this occurs, the child can experience a hyperviscous state.

Hemoglobin SS disease occurs when both β-globin genes located on chromosome 11p15.5 contain a point mutation, resulting in the replacement of glutamic acid with valine at position 6. This results in a qualitatively defective hemoglobin molecule that is prone to polymerization with resultant deformation of the red blood cell membrane. This, in turn, leads to an abbreviated red blood cell lifespan, chronic hemolysis, and frequent small vessel occlusion with resultant end-organ damage. Although patients with hemoglobin SS experience myriad chronic illnesses, they also experience a number of acute and potentially rapidly fatal "crises" (Item C84).

Item C84. Acute Sickle Cell Crises.

Acute sickle cell crises	Common clinical manifestations
Acute chest syndrome	• Sickling of red blood cells in the pulmonary vasculature leads to pulmonary infarction, pain, poor inspiratory effort, atelectasis and hypoxia • Typically occurs with fever • Hypoxia can be life-threatening
Aplastic crisis	• Typically associated with viral suppression of erythropoiesis, most often parvovirus B-19 • Given the shortened lifespan of the SS red blood cell, even transient erythropoietic failure can lead to life-threatening anemia
Hyper-hemolytic crisis	• Typically triggered by a viral infection • Leads to an increased rate of hemolysis over baseline, often beyond the point of the marrow's ability to compensate • Can lead to life-threatening anemia from hemolysis
Splenic sequestration	• Sickling occurs in the spleen with occlusion of the splenic vasculature • Entrapment of the red blood cells in the spleen leads to splenic engorgement • Can result in life-threatening anemia
Vaso-occlusive crisis	• Pain is frequently severe, often requiring narcotics for management • May occur concomitantly with fever

Courtesy of J. Fish

Virtually all patients with hemoglobin SS are functionally hyposplenic or asplenic because of chronic sickling and vascular injury in the spleen, and thereby prone to bacteremia with encapsulated organisms. Every fever in a child with sickle cell disease should be treated as bacteremia until proven otherwise. A blood culture should be performed, with a complete blood cell count and reticulocyte count, and a broad-spectrum antibiotic (most typically, a third-generation cephalosporin) should be administered as quickly as possible. Although the girl in the vignette is clearly ill, she has not been febrile. Ceftriaxone may be administered, but it would not

address her underlying, acute, life-threatening problem. The girl in the vignette has fussiness, which could be a sign of pain. The administration of morphine would be the correct choice for pain management in a child with sickle cell disease, but would not address her underlying, acute, life-threatening problem.

Hydroxyurea increases the production of hemoglobin F, a fetal variant of hemoglobin that is not prone to polymerization. This decreases the concentration of hemoglobin S in the cell, thereby reducing polymerization, membrane deformation, and sickling. The use of hydroxyurea in the sickle cell population has greatly reduced morbidity, and should be considered in a child with sickle cell disease who has had frequent hospitalizations or life-threatening crises. Hydroxyurea does not work quickly, and would not be the appropriate treatment for an acute sickle cell–related crisis.

Dehydration magnifies the impact of sickled cells in the vasculature, and increases the frequency of crises in children with sickle cell disease. In the absence of heart failure, all children with sickle cell disease presenting with an acute illness should receive maintenance intravenous fluids. However, care should be taken because children presenting with severe anemia (< 4 g/dL) may already be in a state approaching high-output cardiac failure. Intravenous normal saline would be an appropriate therapy for the girl in the vignette, but would not address her underlying, acute, life-threatening problem.

PREP Pearls

- Splenic sequestration in sickle cell disease presents with severe anemia, thrombocytopenia, and a palpable spleen.
- Splenic sequestration in sickle cell disease is a medical emergency, and can be rapidly fatal because of very severe anemia.
- Splenic sequestration associated with sickle cell disease should be treated with packed red blood cell transfusions, always administered slowly and in small aliquots.

ABP Content Specifications(s)

- Plan the appropriate management of a sequestration crisis in a patient who has sickle cell disease
- Recognize the clinical and laboratory findings of an aplastic crisis in a patient who has sickle cell disease

Suggested Readings

- Brousse V, Buffet P, Rees D. The spleen and sickle cell disease: the sick(led) spleen. Br J Haematol. 2014;166(2):165-176. doi: http://dx.doi.org/10.1111/bjh.12950.
- Driscoll MC. Sickle cell disease. Pediatr Rev. 2007;28(7):259-268. doi: http://dx.doi.org/10.1542/pir.28-7-259.
- McCavit TL. Sickle cell disease. Pediatr Rev. 2012;33(5):195-206. doi: http://dx.doi.org/10.1542/pir.33-5-195.

Question 85

You are participating in your hospital's monthly patient safety meeting. Recently, a provider incorrectly ordered hepatitis B immunoglobulin on the wrong infant. The nurse did not recognize the error prior to administration of the medication. No adverse outcome was noted. The parents were informed of the medication error. After reviewing the case, you identify factors that may have contributed to the error: common surnames and a higher than average daily census on the date of the error.

Of the following, the BEST description of this medication error is

A. communication error
B. medical negligence
C. nonpreventable adverse event
D. preventable adverse event
E. sentinel event

Correct Answer: D

The medication error described in the vignette is best described as a preventable adverse event. In 1999, the Institute of Medicine published a report titled "To Err is Human" highlighting the epidemic of medical errors and their associated societal and monetary costs. In response, over the past 15 years, healthcare organizations have focused on classifying, analyzing, and reducing medical errors.

A preventable adverse event is an error that can be prevented when appropriate systems and human factors are addressed. In this vignette, both common surname and high patient census are factors that may have contributed to the adverse event. Possible solutions include alternative naming systems and surge staffing during times of high census.

A communication error is a human error where information is not properly conveyed between providers. For example, verbal orders given by a physician may be incorrectly interpreted by a nurse, resulting in a communication error. There is no evidence of communication error in this scenario.

Medical negligence results from improper diagnosis or treatment by a provider. If another comparable level provider would not reasonably choose the course of action, it may be considered medical negligence. In this vignette, because administration of hepatitis B immunoglobulin was indicated for the patient for whom it was intended, medical negligence did not occur.

Some adverse events cannot be prevented. For example, there is a risk of intravenous (IV) infiltration with placement of a peripheral IV catheter. Limiting flow rates and frequent examination of the IV site may minimize this risk.

Sentinel events are those resulting in death or serious injury. They may or may not be related to medical error. In this scenario, there was no harm to the patient, suggesting this was not a sentinel event.

PREP Pearls

- Medical errors are common, costly, and dangerous.
- Preventable adverse events often result from problems with systems of care.
- Despite the focus on decreasing medical error, there remain nonpreventable adverse events that cannot be completely addressed by altering systems of care.

ABP Content Specifications(s)

- Understand and apply the definition of a preventable adverse event
- Understand and apply the definition of a non-preventable adverse event

Suggested Readings

- Leonard MS. Patient safety and quality improvement: medical errors and adverse events. Pediatr Rev. 2010;31(4):151-158. doi: http://dx.doi.org/10.1542/pir.31-4-151.
- Pereira-Argenziano L, Levy FH. Patient safety and quality improvement: terminology. Pediatr Rev. 2015;36(9):403-413. doi: http://dx.doi.org/10.1542/pir.36-9-403.

Question 86

A 9-year-old boy with a history of a viral illness with fever 2 weeks ago presents to your office with a complaint of worsening midsternal chest pain. The pain began 2 days ago, and last night was so severe that he was unable to lie down or sleep. He states that it hurts to take a deep breath.

On physical examination, the boy's heart rate was 150 beats/min, respiratory rate was 30 breaths/min, blood pressure was 92/48 mm Hg, and oxygen saturation was 98% in room air. He has increased chest pain with movement. You examined him in a sitting position and heard normal breath sounds throughout, with no rhonchi, rales, or wheezing. His cardiac examination was significant for a loud intermittent friction rub heard best when he leaned forward.

You referred the boy to the emergency department, where you re-examine him 2 hours later. At that time, his heart rate is 150 beats/min, respiratory rate is 36 breaths/min, and blood pressure is 86/46 mm Hg. His lungs remain clear to auscultation. His heart sounds are now muffled.

Of the following, the MOST likely cause of this boy's signs and symptoms is

A. Kawasaki disease
B. myocardial ischemia
C. pericardial effusion
D. pneumonia
E. supraventricular tachycardia

Correct Answer: C

The boy in the vignette is complaining of positional chest pain that worsens with chest wall motion and breathing. He has tachycardia and a friction rub caused by pericardial inflammation; this finding changes with position or movement of the heart closer to the chest wall. This combination of signs and symptoms is therefore most likely a pericardial effusion.

The boy shows progression in his clinical course, with a decrease in blood pressure and muffled heart sounds. That combination of findings is suggestive of cardiac tamponade, the presence of enough pericardial fluid to cause the right atrium to collapse. This leads to decreased filling of the right atrium and right ventricle, with decreased return to the left atrium and ventricle. The systemic output and blood pressure will then plummet. In this vignette, the boy's progression is rapid. The presentation may differ in patients with serositis and autoimmune disease, who can develop very large effusions over a prolonged period, becoming unstable when their pericardium can no longer enlarge. Recognition of impending tamponade requires a high index of suspicion in either setting and can be lifesaving (Item C86).

Kawasaki syndrome may cause coronary artery dilation and aneurysms, as well as carditis and even shock, but would not usually cause positional chest pain. If the boy were having myocardial ischemia from a coronary anomaly, his pain would not be expected to worsen with rest or supine positioning. On physical examination, the boy has no focal lung findings to suggest pneumonia. It is possible to see pneumonia and pleural effusion in combination with a pericardial effusion, however, there is no decrease in his breath sounds to suggest that. The boy's heart rate of 150 beats/min is slower than would be expected for supraventricular tachycardia in a child this age.

PREP Pearls

- Pericardial effusions cause positional chest pain and may produce a friction rub.
- Pericardial tamponade can develop quickly; early diagnosis is crucial.

ABP Content Specifications(s)

- Recognize the clinical findings associated with pericardial tamponade

Suggested Readings

- Chang S, Maharaj S. Brief images: massive pericardial effusion. Images Paediatr Cardiol. 2014;16(3):1-3. http://europepmc.org/articles/PMC4521324;jsessionid=kPRwvBE1koPh1wwxMuVk.0.
- Durani Y, Giordano K, Goudie BW. Myocarditis and pericarditis in children. Pediatr Clin North Am. 2010;57(6):1281-1303. doi: http://dx.doi.org/10.1016/j.pcl.2010.09.012.
- Flores-González JC, Rubio-Quiñones F, Hernández-González A, et al. Pneumonia and purulent pericarditis caused by Streptococcus pneumoniae: an uncommon association in the antibiotic era. Pediatr Emerg Care. 2014;30(8):552-554. doi: http://dx.doi.org/10.1097/PEC.0000000000000186.
- Imazio M, Gaita F, LeWinter M. Evaluation and treatment of pericarditis: a systematic review. JAMA. 2015;314(14):1498-1506. doi: http://dx.doi.org/10.1001/jama.2015.12763.
- Van Hare G. Disturbances of rate and rhythm of the heart. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:2250.

Question 87

A 3-year-old girl is brought to your office for a health supervision visit. Her weight and height are at the third and 50th percentiles, respectively. Her mother is not concerned about her growth. A feeding history reveals that she "doesn't really ask for food and just gets what she wants." She typically "throws a tantrum" at meal times. Her favorite food is "chips." Her mother is employed as a food service worker with an erratic schedule, with a mix of day and night shifts and frequent last minute changes. When her mother is at work, she is cared by her great-grandmother, who complains that the child doesn't want to eat, or her father, who "doesn't cook and usually eats by himself." The mother acknowledges that fruits and vegetables are rarely purchased because "they go bad." There is no history of cough, vomiting, gagging, drooling, or diarrhea. A review of her medical chart reveals a visit 3 months ago for mild abdominal pain, thought to be caused by constipation. Polyethylene glycol was prescribed, but her mother did not fill the prescription because the girl's symptoms had improved.

Of the following, the MOST likely reason for this child's poor growth is

A. constipation
B. gastroesophageal reflux disease
C. malabsorption
D. feeding choices of caregivers
E. poor oral-motor skills

Correct Answer: D

The growth of the girl in the vignette is likely impacted by her chaotic caretaking structure and a range of neglectful caregiver feeding styles. In a neglectful caregiver feeding style, caregivers do not attend to a child's hunger cues and essentially leave the child to fend for herself. The child in this vignette is not being provided consistent mealtimes or a wide variety of healthy foods. Lack of distinct mealtimes reinforces "grazing," which does not allow for natural hunger-full cycles and lead to reduced energy intake. She may develop tantrums at meals if meals are stressful, not routine, and if she is not hungry. Multiple caregiver switches at the last minute are another source of stress and may make coordinating a mealtime routine, where a range of healthy foods are offered, difficult.

Other types of parent feeding styles can be problematic. Indulgent feeders cater to a child's demands, providing unhealthy foods at will. This can disrupt normal hunger signals and lead to overconsumption of high-calorie foods. Controlling feeders may use force, negative consequences, or rewards in order to get the child to eat specific foods. This counterproductive feeding style also ignores a child's natural hunger cues and can lead to poor self-regulation of food intake.

Questions about parent anxiety around eating, strategies for food refusal, and mealtime environment can help clarify different parent feeding styles. If not clear from questioning, a parent-provided video of feeding interactions may be helpful. Neglectful feeding style can reflect social or mental health problems among caregivers and can be a signal that the child is being neglected in other ways. Parental education around appropriate nutrition, responding to a child's hunger cues, setting limits around grazing and food choice, and using mealtimes for socio-emotional development can help. Recommending enrollment in the Supplemental Nutrition Assistance Program and Head Start or other early childhood education programs can reinforce office-based nutrition education and offer more stability to families.

Lack of a history of choking and gagging makes oral-motor problems less likely. The child has no signs of gastroesophageal reflux disease, which include postprandial gagging and pain. While severe constipation can affect appetite, mild constipation is less likely to do so. Malabsorption is unlikely, given a lack of diarrhea and current abdominal pain.

PREP Pearls

- Obtaining details around caregiver feeding patterns can illuminate psychosocial reasons behind low weight in the setting of preserved height.
- Inconsistent and chaotic mealtimes, food offerings, and social eating experiences can negatively impact hunger cues, nutritional intake, and growth.

ABP Content Specifications(s)

- Differentiate normal variations in feeding patterns from those that reflect poor parenting

Suggested Readings

- Kerzner B, Milano K, MacLean WC, Berall G, Stuart S, Chatoor I. A practical approach to classifying and managing feeding difficulties. Pediatrics. 2015;135(2):344-353. doi: http://dx.doi.org/10.1542/peds.2014-1630.
- Phalen JA. Managing feeding problems and feeding disorders. Pediatr Rev. 2013;34(12):549-557. doi: http://dx.doi.org/10.1542/pir.34-12-549.

Question 88

A 15-year-old ill-appearing adolescent is referred to the emergency department by her pediatrician. She had been seen by the pediatrician 1 week ago for a sore throat. She was found to have a positive rapid streptococcal test, and treated with erythromycin for 10 days. She has been compliant with the antibiotic and was improving until 2 nights ago, when the sore throat abruptly worsened. She has been feeling cold, with left-sided neck and ear pain, and refusing to eat or drink because of the pain. Her past medical history is remarkable only for a penicillin allergy and parental refusal of immunizations. Further history reveals that she is sexually active and uses condoms most of the time.

Physical examination shows an uncomfortable, tired, ill-appearing female adolescent with a temperature of 39.3°C, heart rate of 110 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 125/70 mm Hg. Her voice is muffled and somewhat difficult to understand.

The nares are clear without rhinorrhea or drainage, the lung fields are clear to auscultation, heart sounds are regular but rapid, and the abdomen is benign. She is unable to fully open her mouth for you to examine her pharynx, but your limited examination shows dry mucous membranes with pooled saliva in the mouth, a 2+ tonsil on the right, and a 4+ tonsil on the left. There is marked erythema and swelling of the left anterior tonsillar pillar and soft palate without exudate.

Of the following, the MOST likely cause of these findings is

A. Corynebacterium diphtheria
B. Epstein-Barr virus
C. Haemophilus influenzae
D. Neisseria gonorrhoeae
E. Streptococcus pyogenes

Correct Answer: E

The most likely cause of the findings in the adolescent in the vignette is Streptococcus pyogenes, which has caused a peritonsillar abscess (PTA or quinsy). Over half of deep neck infections are PTA, making it the most common type of deep neck infection in pediatrics. Peritonsillar abscess occurs more frequently in adolescents and young adults than in younger children. Peritonsillar abscess usually begins as a tonsillitis or pharyngitis that develops into a cellulitis of the tissue between the palatine tonsil capsule and the superior pharyngeal constrictor, palatopharyngeus, and palatoglossal muscles. If this inflammatory reaction leads to the collection of pus, a PTA occurs. The growing abscess can create progressive airway obstruction and compromise, or spread into adjoining muscles and the carotid sheath.

The typical findings of a patient with PTA are fever, severe throat pain (usually unilateral, reflecting the affected tonsil), a muffled "hot potato" voice, and dysphagia, leading to drooling or pooling of saliva in the mouth. On examination, one tonsil is usually erythematous and enlarged, with exudates and associated swelling of the nearby posterior soft palate. The tonsil may be inferomedially, and the uvula contralaterally, displaced. Trismus from irritation and spasm of the lateral pterygoid muscle occurs in over two-thirds of PTA, distinguishing it from pharyngitis or tonsillitis. Trismus may make it difficult to do a good examination to confirm the presence or absence of pharyngeal findings. Trismus and uvular deviation are frequently absent in children. Peritonsillar abscess is typically polymicrobial with the predominant species being Streptococcus pyogenes, Staphylococcus aureus (both methicillin-sensitive S aureus and methicillin-resistant S aureus), and respiratory anaerobes.

The patient in the vignette has a history of a Streptococcus pyogenes infection with fever, unilateral neck and ear pain, dysphagia, and odynophagia. On examination, she has the "hot potato" voice, trismus, pooling of saliva, and a unilaterally enlarged erythematous tonsil, indicating PTA.

Patients with Corynebacterium diphtheriae infection would also have fever, dysphagia, and throat pain, but would have marked edema of the throat and neck, creating the characteristic "bull neck" with loss of the angle of the jaw, sternocleidomastoid borders, and medial border of the clavicles. After 2 to 5 days, the pathognomonic gray pseudomembrane (which is not a true membrane, but a layer of dead cells, fibrin, leukocytes, erythrocytes, and bacteria adhering to bleeding, swollen mucosa) forms over the tonsils, uvula, pharyngeal walls, and soft palate. The erythromycin she had taken would be the treatment of choice for diphtheria.

Epstein-Barr virus presents with fever, dysphagia, throat pain, and fatigue, but the associated tonsillar hypertrophy would be bilateral. The trismus and muffled voice would not be expected.

Although fever, dysphagia, muffled voice, and pooling of saliva would be expected with epiglottitis, Haemophilus influenzae type b is not the most common cause of this in adolescents and adults, even in those who have not been immunized, as in the patient in the vignette. Furthermore, the throat examination in epiglottitis is normal.

Most cases of Neisseria gonorrhoeae pharyngitis are asymptomatic, but would present as a straightforward pharyngitis with sore throat, pharyngeal exudate, and cervical lymphadenopathy, not with the findings seen in the adolescent in the vignette.

Although this penicillin-allergic adolescent was treated with erythromycin for her initial Streptococcus pyogenes pharyngitis, the US Centers for Disease Control and Prevention has reported a growing concern for S pyogenes resistant to erythromycin. While the numbers remain low in the United States, they are high in countries like Finland and Japan, and are slowly rising. Resistance could explain how the adolescent in the vignette developed a PTA while on seemingly appropriate antibiotic therapy.

PREP Pearls

- Peritonsillar abscess (PTA) is the most common deep neck infection in pediatrics, especially in adolescents and young adults, and the associated upper airway obstruction is potentially life-threatening.
- Trismus and contralateral uvular deviation are helpful to differentiate PTA from pharyngitis and tonsillitis, but may be absent in children.
- Streptococcus pyogenes is an important cause of PTA. Penicillin remains the treatment of choice. Erythromycin is appropriate for penicillin-allergic patients, but there is low, steadily increasing resistance in the United States.

ABP Content Specifications(s)

- Recognize the complications associated with invasive and non-invasive Streptococcus pyogenes infection

Suggested Readings

- American Academy of Pediatrics. Group A streptococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:732-744.
- Gereige R, Cunill-De Sautu B. Throat infections. Pediatr Rev. 2011;32(11):459-469. doi: http://dx.doi.org/10.1542/pir.32-11-459.
- Langlois DM, Andreae M. Group A streptococcal infections. Pediatr Rev. 2011;32(10):423-430. doi: http://dx.doi.org/10.1542/pir.32-10-423.
- May R, Bordley C. Index of suspicion: case 3: fever and dysphagia in a 4-year-old girl. Pediatr Rev. 2012;33(6):279-284. doi: http://dx.doi.org/10.1542/pir.33-6-279.

Question 89

You are supervising a resident who is seeing a 3-year-old boy for a health supervision visit. The boy's history is significant for chronic kidney disease associated with bilateral dysplastic kidneys. His temperature is 37.8°C, heart rate is 70 beats/min, respiratory rate is 16 breaths/min, and blood pressure is 115/74 mm Hg. His weight is 8 kg (< 5th percentile) and height is 85 cm (< 5th percentile). Other than pallor, the remainder of the boy's physical examination is normal. The resident asks you about associated growth issues and the management of nutrition in children with chronic kidney disease.

Of the following, the MOST accurate statement about children with this condition is that

A. growth failure should be treated with recombinant human growth hormone
B. malnutrition is an uncommon cause of growth failure
C. they require more than the recommended dietary protein intake for age and sex
D. they require restriction of fat and water soluble vitamins to less than the recommended intake for age and sex
E. they require restriction of protein to less than the recommended intake for age and sex

Correct Answer: C

In children with chronic kidney disease (CKD), poor appetite, decreased intestinal absorption of nutrients, and metabolic acidosis lead to malnutrition. Adequate nutrition is essential for optimum growth and neurocognitive development in children. A dietician with expertise in both pediatrics and renal nutrition should collaborate with the treating physician to address the energy, protein, vitamin, mineral, and electrolyte needs of each individual patient.

Restriction of protein intake is not recommended in children, in view of their unique needs for growth and neurocognitive development. Also, protein restriction has not been linked with improved outcomes in CKD. Protein intake between 100% and 140% of the dietary reference intake (DRI), based on age and sex, is recommended for children with CKD and a glomerular filtration rate (GFR) of 30 to 60 mL/min per 1.73 m2. In children with a GFR less than 30 mL/min per 1.73 m2, the recommended protein intake is between 100% and 120% of the DRI for age and sex.

Poor growth is a major complication of children with CKD and a marker for disease severity. Inadequate nutrition and fluid and electrolyte abnormalities, including metabolic acidosis, osteodystrophy, and disturbances of the growth hormone/insulin-like growth factor I axis, contribute to growth impairment in children with CKD. Before initiating therapy with recombinant growth hormone, other factors contributing to growth impairment should be adequately treated. Supplemental enteral feeding via gastrostomy and nasogastric tubes is indicated in children with CKD who have inadequate spontaneous intake to meet growth requirements. Other supportive measures include treatment of (1) electrolyte and fluid losses, (2) metabolic acidosis, (3) anemia, and (4) renal osteodystrophy. Management of renal osteodystrophy includes routine measurement of calcium, phosphorus, parathyroid hormone, and vitamin D levels. Interventions for renal osteodystrophy include dietary phosphorus restriction, vitamin D supplementation, and oral phosphate binders.

Children with CKD should receive 100% of the DRI for their age and sex for both fat and water-soluble vitamins. In children with a GFR less than 15 mL/min per 1.73 m2, water-soluble vitamin supplementation is indicated. However, vitamin A supplementation is not routinely recommended because of an increased risk for hypervitaminosis A secondary to accumulation of vitamin A metabolites.

PREP Pearls

- Restriction of protein intake is not recommended in children with chronic kidney disease (CKD), in view of their unique needs for growth and neurocognitive development.
- Protein restriction has not been linked with improved outcomes in CKD. Protein intake between 100% and 140% of the dietary reference intake (DRI), based on age and sex, is recommended for children with CKD and a glomerular filtration rate (GFR) of 30 to 60 mL/min per 1.73 m2.
- In children with a GFR less than 30 mL/min per 1.73 m2, the recommended protein intake is between 100% and 120% of the DRI for age and sex. Children with CKD should receive 100% of the DRI for their age and sex for both fat and water-soluble vitamins.
- Poor growth is a major complication of children with CKD, and a marker for disease severity.

ABP Content Specifications(s)

- Plan the dietary management of renal insufficiency in patients of various ages
- Recognize the nutritional deficiencies associated with renal disease

Suggested Readings

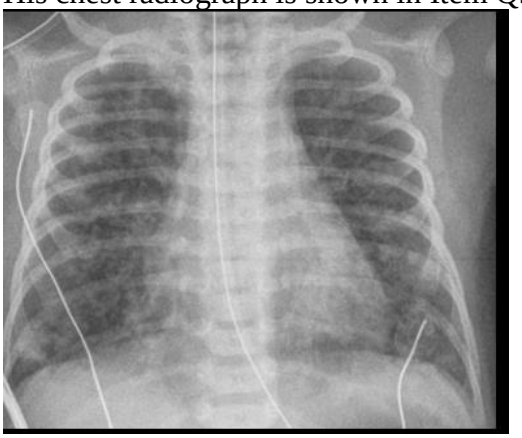
- KDOQI Work Group. KDOQI clinical practice guidelines for nutrition in chronic renal failure: 2008 update. Am J Kidney Dis. 2009;53(suppl 2):S1. doi: http://dx.doi.org/10.1053/j.ajkd.2008.11.017.
- Massengill SF, Ferris M. Chronic kidney disease in children and adolescents. Pediatr Rev. 2014;35(1):16-29. doi: http://dx.doi.org/10.1542/pir.35-1-16.
- Whyte DA, Fine RN. Chronic kidney disease in children. Pediatr Rev. 2008;29(10):335-341. doi: http://dx.doi.org/10.1542/pir.29-10-335.

Question 90

You are called to the newborn nursery to evaluate a neonate with respiratory distress. The mother is a 32-year-old gravida 4, para 3 woman with a history of obesity and type A1 gestational diabetes mellitus admitted in active labor at 38 weeks of gestation. Prenatal laboratory test results were significant for positive group B Streptococcus. Rupture of membranes was less than 4 hours and meconium-stained amniotic fluid was noted. A male neonate was born vaginally without assistance. Apgar scores were 8 and 8 and 1 and 5 min, respectively. In the nursery, his vital signs show a temperature of 37°C, heart rate of 155 beats/min, respiratory rate of 72 breaths/min, and blood pressure of 84/57 mm Hg. Pulse oximetry on the right hand reads 70% in room air. Mild respiratory distress with nasal flaring and intermittent grunting is noted on physical examination. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	24,700/μL (24.7×10^9/L)
Hemoglobin	13.7 g/dL (137 g/L)
Platelet count	267×10^3/μL (267×10^9/L)

His chest radiograph is shown in Item Q90.



Of the following, the MOST likely diagnosis is

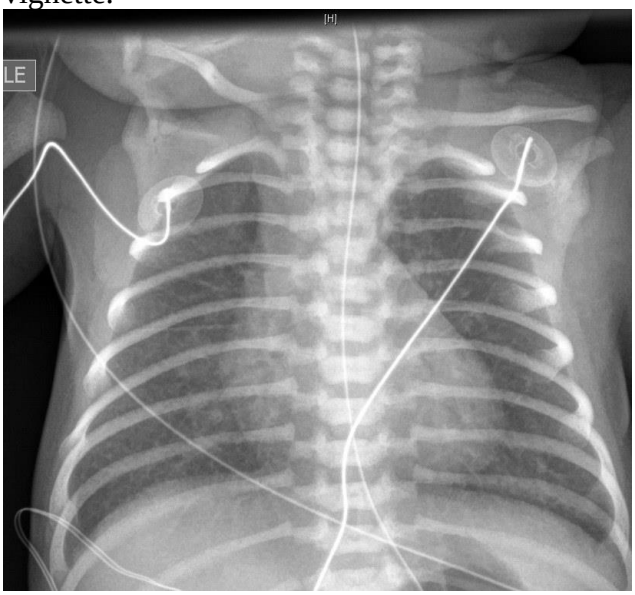
A. meconium aspiration syndrome
B. pleural effusion
C. pneumonia
D. respiratory distress syndrome
E. transient tachypnea of the newborn

Correct Answer: A

Given the clinical presentation and appearance on chest radiograph, meconium aspiration syndrome (MAS) is the most likely diagnosis for the neonate in this vignette. Meconium aspiration syndrome is caused by aspiration of meconium-stained amniotic fluid either before birth or during delivery. Most neonates with MAS are late term with gestational age greater than 41 weeks. The incidence of MAS has decreased due to changes in obstetric practice, with fewer mothers delivering infants after 41 weeks. Clinically, neonates with MAS will present with severe respiratory distress, grunting, and cyanosis, and will require respiratory support. On examination, there may be meconium staining of the umbilical cord, skin, and nails.

Meconium aspiration syndrome causes a characteristic chest radiograph with asymmetric patchy infiltration. Meconium in the lungs inactivates surfactant. Thus, neonates with MAS may require high pressure and oxygen to maintain ventilation and oxygenation. This increases their risk of pneumothorax with positive pressure. They are also at risk of pulmonary hypertension. The diagnosis of MAS is made with clinical history and chest radiograph. While the mortality associated with MAS has decreased, infants with MAS continue to be at increased risk for reactive airway disease, which may persist into childhood.

In comparison, neonates with transient tachypnea of the newborn (TTN) also present with respiratory distress and an oxygen requirement. On examination, they classically have a hyperexpanded barrel chest. However, on chest radiograph, TTN shows increased perihilar markings and fluid in the fissure (Item C90). These findings are not seen in the neonate in this vignette.



Item C90: Chest radiograph for a newborn with transient tachypnea. 2017_PREP_SA_Q_Data 2017_PREP_SA_Content_Spec_Assign Media Table Permission and Media Tracking Question Trends Writer Trends Keys Perm Keys Courtesy of M LaTuga

Transient tachypnea of the newborn results from delayed activation of efflux of water out of the lung by Na-K channels. Normally, these channels are activated during delivery, and possibly induced by stress hormones. There are a number of risk factors for TTN including cesarean delivery, infection, maternal diabetes, and male sex.

Pleural effusion may be caused by infection, congestive heart failure, or MAS. Since neonates are supine, small pleural effusions rarely cause significant respiratory distress on examination. On chest radiograph, there may be blunting of the costophrenic angle or a diffuse haziness caused by layering of pleural fluid.

Respiratory distress syndrome is a disease of premature neonates born less than 37 weeks of gestation. It is characterized by inadequate surfactant production. As a consequence of poor compliance, on chest radiograph, there is poor lung expansion. Microatelectasis appears as a homogenous ground glass appearance.

Pneumonia in a neonate is most commonly caused by group B Streptococcus (GBS). Presentation includes respiratory distress and perinatal risk factors for infection, including prolonged rupture of membranes, chorioamnionitis, and positive maternal GBS status. On chest radiograph, neonates exhibit a bilateral diffuse infiltrate.

PREP Pearls

- Meconium aspiration syndrome is a disease of late term infants with gestational age greater than 41 weeks.
- Meconium aspiration syndrome has a characteristic chest radiograph appearance of patchy infiltrates.
- Transient tachypnea of the newborn on chest radiograph shows increased perihilar markings and fluid in the right horizontal fissure.

ABP Content Specifications(s)

- Identify the signs and symptoms of transient tachypnea of the newborn, and manage appropriately
- Recognize the characteristic clinical and radiographic appearance of meconium aspiration syndrome in a newborn infant, and manage appropriately

Suggested Readings

- Dargaville PA, Copnell B. The epidemiology of meconium aspiration syndrome: incidence, risk factors, therapies, and outcome. Pediatrics. 2006;117(5):1712-1721. doi: http://dx.doi.org/10.1542/peds.2005-2215.
- Yeh TF. Core concepts: meconium aspiration syndrome: pathogenesis and current management. NeoReviews. 2010;11(9):e503-e512. doi: http://dx.doi.org/10.1542/neo.11-9-e503.

Question 91

A 4-year-old girl presents to your office for evaluation of left ear pain and drainage. She has had at least 5 episodes of acute otitis media in her lifetime, the most recent of which was 3 months ago. The girl has been complaining of ear pain since this morning. She has not had a fever. This morning, her parents noted yellow crusting at the edge of her ear canal and on her pillow. The family returned yesterday from a weeklong camping trip during which the girl swam daily in a lake. On physical examination, the girl is well appearing with a temperature of 37.4°C. She cries when you touch the pinna or tragus of her left ear. Her left tympanic membrane cannot be visualized because of purulent material that fills the canal. The portion of the left ear canal that is visible is erythematous.

Of the following, the MOST helpful factor for making the diagnosis in this patient is

A. absence of fever
B. history of recurrent acute otitis media
C. history of recent swimming
D. pain with manipulation of the ear
E. presence of purulent debris in the ear canal

Correct Answer: D

The girl in this vignette has otitis externa (OE). Otitis externa typically presents with the rapid onset of symptoms of ear canal inflammation, including otalgia and otorrhea. Physical examination reveals tenderness of the tragus or pinna, diffuse ear canal edema, and/or erythema. Otitis externa must be distinguished from other causes of otorrhea and otalgia, the most common of which is acute otitis media (AOM) with rupture of the tympanic membrane. The diagnosis of AOM requires the acute onset of a purulent middle-ear effusion and inflammation. Other possible causes of otorrhea include the following:

- cerebrospinal fluid leakage with basilar skull fracture.
- cholesteatoma
- chronic suppurative otitis media
- eczematous otitis externa
- foreign body
- furunculitis of the ear canal
- Langerhans cell histiocytosis
- necrotizing otitis externa
- otomycosis

The most helpful factor in distinguishing between OE and a ruptured AOM is the finding of tenderness with manipulation of the ear. Although fever is more likely with AOM than OE, it can be present with either diagnosis. A child with recurrent AOM is not predisposed to having OE. Although swimming can increase a child's risk of developing OE, this historical feature is not specific to a diagnosis of OE. Both OE and ruptured AOM will lead to purulent discharge in the ear canal.

Disruption of the epithelial lining of the external auditory canal from microtrauma (eg, aggressive cleaning or insertion of earplugs or hearing aids), prolonged exposure to moisture, or dermatologic conditions like eczema or seborrhea can lead to OE. Cerumen typically creates a slightly acidic pH, which inhibits bacterial growth; removal of cerumen can alter this pH and increase the risk of developing infection.

Treatment of OE should include appropriate pain management as well as topical treatment with antiseptics, antimicrobials, corticosteroids, or combination medications. Oral treatment is not indicated in uncomplicated OE.

PREP Pearls

- Tenderness of the tragus or pinna is a hallmark sign of otitis externa (OE).
- OE occurs when the epithelial lining of the external ear canal is disrupted and bacterial overgrowth occurs.

ABP Content Specifications(s)

- Formulate a differential diagnosis of otitis externa
- Understand the natural history of otitis externa

Suggested Readings

- Kaushik V, Malik T, Saeed SR. Interventions for acute otitis externa. Cochrane Database Syst Rev. 2010;1:CD004740. doi: http://dx.doi.org/10.1002/14651858.CD004740.pub2.
- Long M. Otitis externa. Pediatr Rev. 2013;34(3):143-144. doi: http://dx.doi.org/10.1542/pir.34-3-143.
- Rosenfeld RM, Schwartz SR, Cannon CR, et al. Clinical practice guideline: acute otitis externa. Otolaryngol Head Neck Surg. 2014;150(1 suppl):S1-S24. doi: http://dx.doi.org/10.1177/0194599813517083.

Question 92

You are seeing a 3-year-old girl for a new patient health supervision visit. She was born at term and her birth history was unremarkable. The girl began attending daycare at 8 months of age, and since then, has had 7 documented episodes of pneumonia. On 4 occasions, a chest radiograph was obtained, which demonstrated consolidation in the left lower lobe. Each event was treated with a 10-day course of oral antibiotics, with good response. Between episodes, the girl is well, active, and playful. Her parents deny symptoms of dyspnea and she tolerates exertion well. There is no history of chronic cough, wheezing, or stridor. Review of systems is negative for recurrent or chronic otitis media, organ abscesses, or skin infections.

On physical examination, the girl is well appearing. Her respiratory rate is 20 breaths/min. An examination of the head, eyes, ears, nose, and throat is normal, with no nasal drainage and normal tympanic membranes without evidence of effusion. Her lungs are clear bilaterally, with a mild decrease in aeration at the left lung base. Her abdomen is soft and nontender without organomegaly. The girl's extremities are well perfused with no cyanosis, clubbing, or edema. You obtain a chest radiograph, which reveals a wedge-shaped consolidation in the posterior aspect of the left lower lobe.

Of the following, the girl's presentation is MOST consistent with a diagnosis of

A. chronic pulmonary aspiration
B. foreign body aspiration
C. primary ciliary dyskinesia
D. pulmonary sequestration
E. severe combined immunodeficiency

Correct Answer: D

The girl in the vignette has a presentation that is most consistent with a pulmonary sequestration. Various congenital lesions may occur in the lung, and further evaluation is warranted when children present with recurrent radiographic abnormalities.

A child with recurrent pneumonia should undergo a radiographic examination of the chest 4 to 8 weeks after antibiotic treatment, during an asymptomatic period, to determine resolution of inflammatory disease. For a child with recurrent clinical chest signs and symptoms, diagnoses such as immunodeficiency and suppurative lung disease should be explored. Persistence of an abnormal radiographic finding in an asymptomatic individual suggests a congenital lung lesion, and merits further evaluation.

Pulmonary sequestration accounts for approximately 6% of congenital lung lesions. Sequestration occurs when a segment of lung tissue has no communication with the normal tracheobronchial tree and receives its vascular supply from an aberrant systemic artery. This arterial supply may not be clearly visualized on computed tomography (CT) because of the small caliber. Three-dimensional Doppler ultrasound, CT angiography, and magnetic resonance imaging will more clearly delineate the vascular supply. The ideal imaging option is best chosen in consultation with pediatric radiology, taking into consideration the risks of radiation exposure and/or sedation.

Pulmonary sequestration may be intralobar or extralobar. Intralobar sequestrations, accounting for approximately 75% of cases, are contained within a normal lobe of lung tissue and are covered by the same visceral pleura as the remainder of the lung. The predominant location is the posterior basal segment of the lower lobes, with the left lung more commonly affected than the right. Intralobar sequestrations are most commonly diagnosed in later childhood or during adolescence. Typically, a history of recurrent pneumonia is found. In contrast, extralobar sequestrations are separated from the remainder of the lung by a distinct pleural covering. Most are found in the thorax, but rarely, may be found below or within the diaphragm. Extralobar sequestrations generally present during infancy. Sixty percent of those affected will have another congenital abnormality, the most common of which is congenital diaphragmatic hernia.

Although abnormal chest radiographs may be associated with all the other conditions listed, they would not be expected in an otherwise asymptomatic child. The child with chronic pulmonary aspiration typically has a history of recurrent pneumonia or pneumonitis that is variable in location. In between episodes of aspiration, clinical and radiographic resolution is expected. The child with a chronically retained foreign body in the tracheobronchial tree may present late with pneumonia, abscess formation, or bronchiectasis. Associated symptoms are likely. The child with primary ciliary dyskinesia may have recurrent bronchitis and/or pneumonia, but would also have chronic cough, chronic purulent rhinitis, and recurrent ear and sinus infections. A child with severe immunodeficiency who has pneumonia would not be be asymptomatic or expected to have a lobar preference.

Congenital pulmonary airway malformation or CPAM (previously designated as congenital cystic adenomatoid malformation or CCAM) may affect 1 or more lung lobes, and may occur unilaterally or bilaterally. These intrapulmonary lesions are generally cystic in appearance. In utero and/or in the setting of infection, the cysts may be filled with fluid and the radiographic appearance may be confused with sequestration. In CPAM, communication between the lesion and the normal tracheobronchial tree is intact, with a normal vascular supply. Nearly 100% of CPAMs can be detected on antenatal ultrasound by a gestational age of 20 weeks.

Congenital lobar hyperinflation (CLH; previously designated as congenital lobar emphysema) is a congenital lung lesion with a unique appearance. In CLH, hyperinflation of 1 or more pulmonary lobes occurs with symptoms resulting from compression of surrounding structures; mediastinal shift may be seen. The left upper and right middle lobes are most commonly affected.

The management of congenital lesions of the lung is controversial. Pulmonary sequestrations may become infected repeatedly, which may be an indication for surgical removal. Removal of large lesions may be necessary because of compression of surrounding vital structures. Small, nonprogressive, and asymptomatic lesions may be observed, but there is a small associated risk of malignant transformation to pleuropulmonary blastoma or rhabdomyosarcoma for some individuals with CPAM.

PREP Pearls

- A pulmonary sequestration is a segment of lung tissue that has no communication with the tracheobronchial tree, receiving its blood supply from an aberrant systemic artery.
- Pulmonary sequestrations are commonly diagnosed in late childhood or adolescence, with a history of recurrent pneumonia.
- Individuals with recurrent pneumonia should undergo follow-up radiography during a period of wellness, to help differentiate between recurrent and persistent disease.
- Plain radiographs may lack the sensitivity required to differentiate pulmonary sequestration from congenital pulmonary airway malformation; consultation with radiology is recommended to optimize the approach to further imaging.

ABP Content Specifications(s)

- Recognize the clinical findings associated with congenital malformations of the lower airway

Suggested Readings

- Durell J, Lakhoo K. Congenital cystic lesions of the lung. Early Hum Dev. 2014;90(12):935-939. doi: http://dx.doi.org/10.1016/j.earlhumdev.2014.09.014.
- Stanton M, Njere I, Ade-Ajayi N, Patel S, Davenport M. Systematic review and meta-analysis of the postnatal management of congenital cystic lung lesions. J Pediatr Surg. 2009;44(5):1027-1033. doi: http://dx.doi.org/10.1016/j.jpedsurg.2008.10.118.

Question 93

A 17-year-old adolescent is brought to your office for follow-up after her first sports-related concussion. She is a competitive soccer player, and last week, she and another player collided, their heads hit together, and the adolescent sustained a concussion. She was evaluated in the emergency department and discharged home. Her father, who has multiple sclerosis, is her coach and has kept her out of practice and games since the concussion. She reports that not being able to play soccer is making her "depressed and irritable." She has been an A student, but is having difficulty concentrating at school. You recommend graded return to academic and physical activity, and mandate complete recovery before returning to play. Her father asks you about long-term cognitive consequences of this concussion.

Of the following, the MOST accurate statement about the long-term consequences from this concussion is

A. her baseline academic achievement decreases her risk of neurocognitive deficits
B. her family history increases her risk of long-term neurocognitive deficits
C. it is unlikely that she will have detectable neurocognitive deficits
D. neurocognitive deficits are more likely if she keeps heading the ball
E. wearing protective headgear during contact sports will decrease her risk of permanent neurocognitive deficits

Correct Answer: C

The adolescent in the vignette has had her first sport-related concussion and is having symptoms of postconcussive syndrome. If she does not get a second concussion during recovery, it is most likely that she will have no detectable neurocognitive sequelae from this concussion. There are no specific treatment recommendations aside from achieving complete recovery before returning to play and avoiding further concussions. Specific helmet types and protective head gear have not been shown to prevent concussions in soccer players.

Repetitive concussion is probably a risk factor for long-term neurocognitive deficits, although the number or severity of concussions needed to cause long-term deficits is unknown. Personal characteristics such as apolipoprotein E4 genotype and history of learning disability or migraines (but not multiple sclerosis) may increase susceptibility for chronic deficits after a concussion. Heading the ball in soccer, however, has not been shown to increase the risk of deficits.

Repetitive concussions are linked to the development of chronic traumatic encephalopathy. This is a neurodegenerative disorder that progresses after the person has stopped sustaining concussions. Diagnosis can only be made on autopsy, and there is active research to find biomarkers to enable earlier diagnosis. Research to determine risk factors for long-term neurocognitive deficits after head trauma is also ongoing, and return-to-play guidelines are changing in response to new information. Clinicians should keep themselves updated on the newest return-to-play guidelines. The US Centers for Disease Control and Prevention Heads Up website, listed in the Suggested Readings, is an excellent resource.

PREP Pearls

- Prevention of concussion and recurrent concussion are the best known ways to prevent long-term neurocognitive sequelae from concussions.
- Specific helmet types have not been shown to prevent sport-related concussions.

ABP Content Specifications(s)

- Understand the long-term neurologic and behavior consequences of head trauma

Suggested Readings

- Giza CC, Kutcher JS, Ashwal S, et al. Summary of evidence-based guideline update: evaluation and management of concussion in sports. Neurology. 2013;80(24):2250–2257. doi: http://dx.doi.org/10.1212/WNL.0b013e31828d57dd.
- Meehan WP III, Bachur RG. Sport-related concussion. Pediatrics. 2009;123(1):114-123. doi: http://dx.doi.org/10.1542/peds.2008-0309.
- US Centers for Disease Control and Prevention. Heads up to youth sports. US Centers for Disease Control and Prevention website. http://www.cdc.gov/headsup/youthsports/. Updated August 19, 2015..

Question 94

A 16-year-old adolescent presents to the emergency department after sustaining chest trauma when his all-terrain vehicle flipped over. He is currently awake and alert, but is complaining of difficulty breathing and has severe pain on the lower anterior aspect of his right chest. Vital signs show a temperature of 37°C, respiratory rate of 24 breaths/min, heart rate of 120 beats/min, blood pressure of 110/70 mm Hg, and oxygen saturation of 92% on room air. His breathing is rapid and shallow. On auscultation, there is good air entry in all segments of the left lung. The inferior aspect of the right chest moves inward upon inspiration and outward upon expiration. The right lung has decreased breath sounds at the base.

Of the following, the BEST next step is to

A. administer morphine sulfate, 5 mg intravenously
B. obtain computed tomography of the chest
C. perform endotracheal intubation
D. perform internal fixation of anterior ribs
E. place a chest tube

Correct Answer: A

The patient in this vignette has suffered chest trauma causing difficulty breathing and severe rib pain. In addition, he has paradoxical chest wall movement in which the affected segment moves inward during inspiration and outward during exhalation. This clinical condition is known as flail chest, and the mainstay of treatment is pain control with morphine sulfate.

Chest trauma is very common in the United States. There are numerous causes, including motor vehicle accidents, assaults, and sports-related injuries. Blunt chest injury is the most common form and the force of the compression often causes rib fracture. Flail chest is caused by rib fracture in at least 4 consecutive ribs in 2 places. During normal breathing with an intact rib cage, negative intrapleural pressure draws air into the alveoli and the chest expands as the alveoli fill. During inspiration in flail chest, the negative intrapleural pressure pulls the affected segment against the underlying lung, causing collapse of that segment and that region of lung. Conversely, during exhalation, positive intrapleural pressure pushes the flail segment outward.

Evaluation and management of flail chest begins with a standard trauma assessment of airway, breathing, and circulation. Decreased breath sounds and impaired oxygenation or ventilation may indicate pneumothorax, hemothorax, or lung contusion. Hemodynamic compromise may indicate a more significant hemothorax or tension pneumothorax. If flail chest is determined to be the primary lesion, management depends on the severity of impairment of oxygenation and ventilation. The adolescent in the vignette is slightly hypoxic on room air, but has difficulty breathing and severe pain. Patients with rib fractures and flail chest can have pain upon breathing with chest expansion, leading to splinting, which then causes impaired ventilation and atelectasis. Management includes pain control, encouragement of mobility, and pulmonary toileting. Thus, administration of morphine sulfate is the best step in management for the patient in this vignette.

Intubation and mechanical ventilation can allow the flail segment to move along with the rest of the unaffected rib cage, but it is not necessary because this child is maintaining adequate oxygenation and ventilation. Chest computed tomography is not necessary because the diagnosis can be made with clinical findings. Internal fixation of the anterior ribs is indicated for patients with more extensive flail chest who require thoracic surgery for other injuries, those who cannot be weaned from mechanical ventilation, and more severe chest wall instability. Lastly, a chest tube would be indicated if the patient had a concomitant hemothorax or pneumothorax.

PREP Pearls

- Flail chest is caused by blunt chest trauma with rib fractures in at least 4 adjacent ribs and at least 2 places.
- Flail chest can be diagnosed clinically by paradoxical movement inward of the flail segment during inspiration and movement outward upon exhalation.
- Management of flail chest includes pain control and pulmonary toilet. If oxygenation and ventilation are severely impaired, positive pressure ventilation (and in some cases, surgical fixation) may be indicated.

ABP Content Specifications(s)

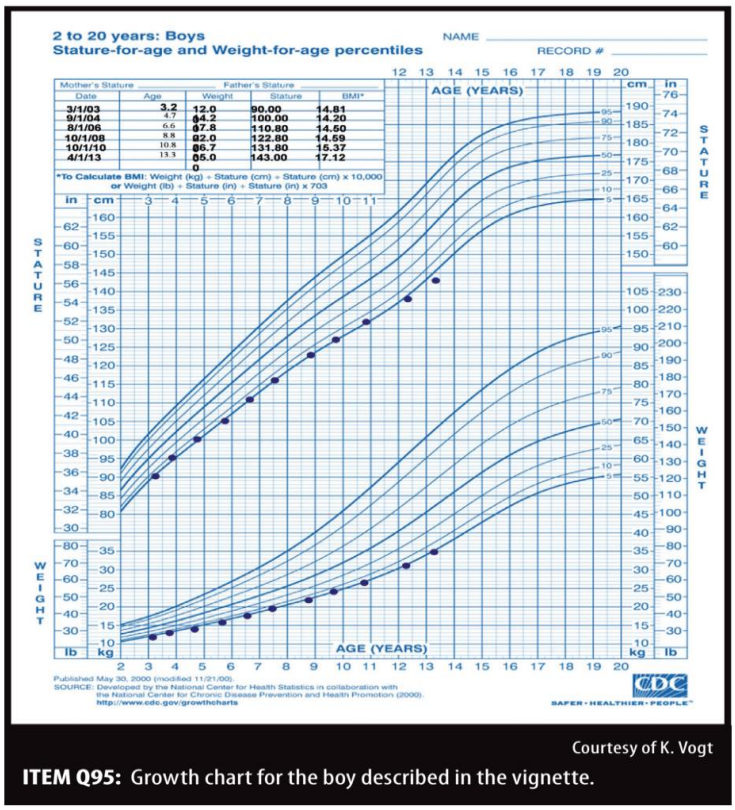
- Recognize the clinical findings associated with a hemothorax or flail chest

Suggested Readings

- Cataneo A, Cataneo DC, de Oliveira FHS, Arruda KA, El Dib R, de Oliveira Carvalho P. Surgical versus nonsurgical interventions for flail chest. Cochrane Database Syst Rev. 2015;7:CD009919. doi: http://dx.doi.org/10.1002/14651858.CD009919.pub2.
- Pettiford BL, Luketich JD, Landreneau RJ. The management of flail chest. Thorac Surg Clin. 2007;17(1):25-33. doi: http://dx.doi.org/10.1016/j.thorsurg.2007.02.005.
- Yasuda R, Okada H, Shirai K, et al. Comparison of two pediatric flail chest cases. Scand J Trauma Resusc Emerg Med. 2015;23(1):73. doi: http://dx.doi.org/10.1186/s13049-015-0156-5.

Question 95

You are seeing a 13-year-old adolescent for a preparticipation examination to play soccer. He is generally healthy and does not take any medication. He and his mother state that he is the smallest player on his soccer team. His growth curves are shown (Item Q95). He has no other concerns and denies headaches, vision problems, fatigue, abdominal pain, joint pain, polyuria, and polydipsia. His mother is 165 cm tall and had menarche at 12 years of age. His father is 175 cm tall and continued to grow in height during college. Physical examination shows a temperature of 37°C, blood pressure of 106/52 mm Hg, heart rate of 68 beats/min, respiratory rate of 16 breaths/min, weight of 35 kg (fifth percentile), height of 143 cm (third percentile), and body mass index of 17 kg/m2 (24th percentile). He has a sexual maturity rating of 2 for pubic hair and genital development. The remainder of his physical examination is unremarkable. A bone age radiograph is read as 11 years.



ITEM Q95: Growth chart for the boy described in the vignette.

Of the following, the BEST next step in the management of this patient is to

A. counsel him on ways to increase calories in his diet
B. provide reassurance regarding his final adult height
C. recommend follow-up in 2 to 3 months for re-evaluation
D. refer for consideration of growth hormone therapy
E. refer for gastrointestinal evaluation

Correct Answer: B
The patient described in the vignette has constitutional delay of growth and puberty. He has no evidence by history or physical examination of an underlying growth disorder or systemic disease, and he is in early puberty, making permanent hypogonadism unlikely. Providing reassurance regarding final height with follow-up in 6 to 12 months to follow growth and pubertal progression is appropriate.

Evaluation of constitutional delay includes ruling out underlying disorders. The history should focus on known medical problems, review of systems, and family history to include parents' heights and pubertal timing. A family history of constitutional delay is common. Genetic potential can be estimated using the formulas:

For boys: [mother's height + father's height + 5 inches (13 cm)]/2

For girls: [mother's height + father's height - 5 inches (13 cm)]/2

Target height range is this number +/- 2 inches (5 cm)

A bone age radiograph is delayed in constitutional delay and consistent with pubertal development. If height is plotted for bone age, it falls within the target height range percentiles, as noted for the boy in this vignette. Any laboratory work done to screen for underlying systemic disease, such as complete blood cell count, serum chemistries, erythrocyte sedimentation rate, celiac screen, urinalysis, and thyroid function is normal. Gonadotropins and testosterone show normal pre-pubertal levels.

Constitutional delay is the most common cause of short stature and delayed puberty in children, especially in boys, but remains a diagnosis of exclusion. The boy in this vignette is healthy and growing at just below the fifth percentile for height until recently. His body mass index is normal, making caloric deficiency and gastrointestinal or other systemic disease unlikely. His recent height velocity appears to have decreased because his peers are starting their pubertal growth spurts, while his growth velocity remains at a normal pre-pubertal level. Because of the increasingly apparent height discrepancy as compared to their typically developing peers, children with constitutional delay often come to medical attention around this age. There is a family history of constitutional delay in the boy's father, given his continued growth during college. The boy's bone age is 2 years delayed and consistent with his height age and pubertal stage, both about 11 years. His delayed bone age predicts future catch-up growth. Predicted adult height in this boy based on current height and bone age is 174 cm (68.5 inches), which is consistent with his target height range of 176.6 cm (69.5 inches) +/- 5 cm (2 inches).

Management of constitutional delay consists of reassurance regarding future pubertal development and height, in addition to clinical observation. Constitutional delay, however, can cause significant psychosocial distress. Referral to a pediatric endocrinologist for a short course of testosterone once a boy is 14 years of age and has no or minimal puberty on examination is a treatment option. One regimen is a testosterone ester 100 mg intramuscularly monthly for 3

months. The goal of testosterone therapy is to facilitate pubertal progression and promote earlier initiation of the pubertal growth spurt. There is no significant effect on final height. Girls with constitutional delay can be offered low-dose estrogen to promote pubertal development and progression, but there is greater concern about estrogen's effect on premature closure of the growth plates.

Counseling the boy on ways to increase calories in his diet is not the best answer because his body mass index is normal. Referral for gastrointestinal evaluation is not preferred due to lack of evidence of an underlying disorder. Growth hormone therapy is not indicated, so referral for consideration of growth hormone therapy is not appropriate. Although follow-up is indicated, 2 to 3 months will likely be too short of a time frame and providing reassurance is the better answer.

PREP Pearls

- Constitutional delay is the most common cause of short stature and delayed puberty in children and is considered a normal variant.
- Constitutional delay is a diagnosis of exclusion and most often occurs in otherwise healthy children with a family history of constitutional delay.
- Treatment of constitutional delay consists of reassurance regarding final adult height with the option of a short course of sex steroid therapy for those who have significant distress regarding their short stature and delayed puberty.

ABP Content Specifications(s)

- Plan the appropriate management of constitutional delay of puberty
- Plan the appropriate diagnostic evaluation of constitutional delay of puberty

Suggested Readings

- Kaplowitz PB. Delayed puberty. Pediatr Rev. 2010;31(5):189-195. doi: http://dx.doi.org/10.1542/pir.31-5-189.
- Palmert MR, Dunkel L. Clinical practice. Delayed puberty. N Engl J Med. 2012;366(5):443-453. doi: http://dx.doi.org/10.1056/NEJMcp1109290.
- Rogol AD, Hayden GF. Etiologies and early diagnosis of short stature and growth failure in children and adolescents. J Pediatr. 2014;164(5 Suppl):S1-S14. doi: http://dx.doi.org/10.1016/j.jpeds.2014.02.027.

Question 96

A previously healthy 3-year-old girl is brought to your office for evaluation of a possible vitamin overdose. While cleaning the child's room, an empty bottle of chewable multivitamins was found. The girl's mother reports she purchased this bottle 1 or 2 weeks ago. She is not aware of the bottle's initial quantity, but states that it is a large bottle purchased at the bulk store. She is certain this product does not contain iron. For the past 2 days, the girl has had a decreased appetite and has vomited twice. The mother reports that the girl seems clumsier when walking. The girl's physical examination is remarkable for hepatomegaly and blurred optic disks.

Of the following, the vitamin MOST likely to be associated with these signs and symptoms is

A. A
B. B12
C. C
D. D
E. E

Correct Answer: A
The girl in the vignette presents with the subtle findings associated with hypervitaminosis A. Acute or long-term vitamin A excess may cause hepatotoxicity and increased intracranial pressure (pseudotumor cerebri). Clinical signs and symptoms include:

- Headache
- Fatigue
- Malaise
- Irritability
- Anorexia
- Vomiting
- Bulging fontanelle
- Diplopia
- Papilledema
- Pruritic desquamating skin
- Angular cheilitis
- Hepatomegaly

Painful bone abnormalities caused by hyperostosis (especially in the midshaft of the long bones)
Alopecia or coarsening of the hair and ataxia
Vitamin A toxicity may also occur in adults. A single dose of more than 200 mg (> 660,000 units) will cause symptoms of acute toxicity. Most cases of vitamin A toxicity are caused by long-term ingestion of more than 10 times the recommended daily dietary allowance.

Daily vitamin supplements are readily available for purchase over-the-counter. Many of the preparations for children are tasty and chewable in fun shapes that are attractive to children. The packaging is often not childproof. There is a significant risk for overdosage and toxicity if young children ingest large quantities of vitamins acutely or have long-term overuse. Parents need to be cautioned to handle these products with extreme care.

There is no known toxicity associated with excess vitamin B12 ingestion. Hypervitaminosis C can be followed by a “rebound” deficiency. Symptoms of acute vitamin D intoxication are the result of hypercalcemia, which may lead to emesis, anorexia, pancreatitis, hypertension, arrhythmias, nephrolithiasis, renal failure, and central nervous system effects. Acute vitamin E toxicity is rare. Long-term intake of excess vitamin E supplementation has been associated with an increased risk for sepsis in premature infants and increased risk for hemorrhage and mortality in others.

PREP Pearls

- Acute or long-term vitamin A excess may cause hepatotoxicity and increased intracranial pressure (pseudotumor cerebri).
- The packaging of chewable vitamins poses a risk for accidental overdosage and toxicity from hypervitaminosis in children.

ABP Content Specifications(s)

- Recognize the signs and symptoms of hypervitaminosis

Suggested Readings

- James MB, Leonard JC, Fraser JJ Jr, Stuemky JH. Hypervitaminosis A: a case report. Pediatrics. 1982;69(1):112-115. http://pediatrics.aappublications.org/content/69/1/112.
- Kleinman RE, Greer FR. Pediatric Nutrition. 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2013:1477 pp.
- Lam HS, Chow CM, Poon WT, et al. Risk of vitamin A toxicity from candy-like chewable vitamin supplements for children. Pediatrics. 2006;118(2):820-824. doi: http://dx.doi.org/10.1542/peds.2006-0167.

Question 97

As a clinical researcher involved in the development of drugs to treat pediatric metabolic disorders, you must design a study to investigate a new drug intended to reduce hyperammonemia in patients with urea cycle disorders. You seek a study design that will best evaluate the risks and benefits of treatment.

Of the following, the study design that would BEST meet your aim is

A. active study registry
B. case-control
C. cross-sectional
D. population-based cohort
E. randomized controlled trial

Correct Answer: E

The best study design to evaluate the risks and benefits of the proposed new drug treatment is a randomized controlled trial (RCT). This is the ideal study design for establishing causal relationships between outcomes and treatments. In a RCT, subjects are randomized into groups whose characteristics are closely matched to focus on the variable being studied. This type of study reduces the effect of confounding variables and their influence on outcomes. These studies are always conducted in a prospective manner and ideally are double-blinded. Some RCTs are limited by small sample size and brief duration, which can affect the ability to detect rare adverse effects and quantify treatment-related harms.

An active study registry uses observational study methods for the collection and maintenance of uniform data on a population of specific interest. This method is used to assess long-term outcomes, uncommon complications, or adverse effects. In this type of registry, the study population will be routinely contacted over time for updates on outcomes, causes of death, or other complications.

A case control study is a retrospective study that uses subjects who are similar and divides them into groups based on the absence or presence of the outcome of interest. The study then compares the presence of specific risk factors in each group. For example, one could study whether drinking sweet tea causes type 2 diabetes. A case control study would examine how many sweet tea drinkers versus non-sweet tea drinkers were diagnosed with type 2 diabetes. Cause and effect may be suggested in this type of study, but not definitively determined. This type of study is relatively weak because of the presence of many uncontrollable factors that could likewise affect outcome.

A cross-sectional study is a good method to ascertain the efficacy of a diagnostic test. It compares the results of a new diagnostic or screening test with a known gold standard in the same population group. This allows the investigator to assess the new test's accuracy, sensitivity, and specificity. This would be an appropriate method to evaluate a new autism screening test by comparison to a known autism screening test with good results, such as the Modified Checklist for Autism in Toddlers (M-CHAT).

A population-based cohort study is a prospective study that divides subjects into groups based on the presence or absence of a proposed risk factor, and then follows the subjects prospectively over time. Cohort studies may follow a population of patients with a disease, for example, and monitor the subjects for events as they occur over time. At the conclusion of the study, the frequency of the outcome(s) is calculated and compared across the groups. This type of study is best for obtaining valid information about the prognosis of a condition over time. This type of study can have many confounders, is expensive to perform, and takes a long time to achieve results.

PREP Pearls

- The best study design to evaluate the risks and benefits of a proposed new treatment is a randomized controlled trial (RCT), which establishes causal relationships between treatments and outcomes.
- A cross-sectional study is the best method to ascertain the efficacy of a diagnostic test by comparing a new diagnostic or screening test with a known gold standard test in the same population group.
- A population-based cohort study is best for obtaining valid information about the prognosis of a condition over time. It is a prospective study that divides subjects into groups based on the presence or absence of a proposed risk factor and then follows the subjects prospectively.

ABP Content Specifications(s)

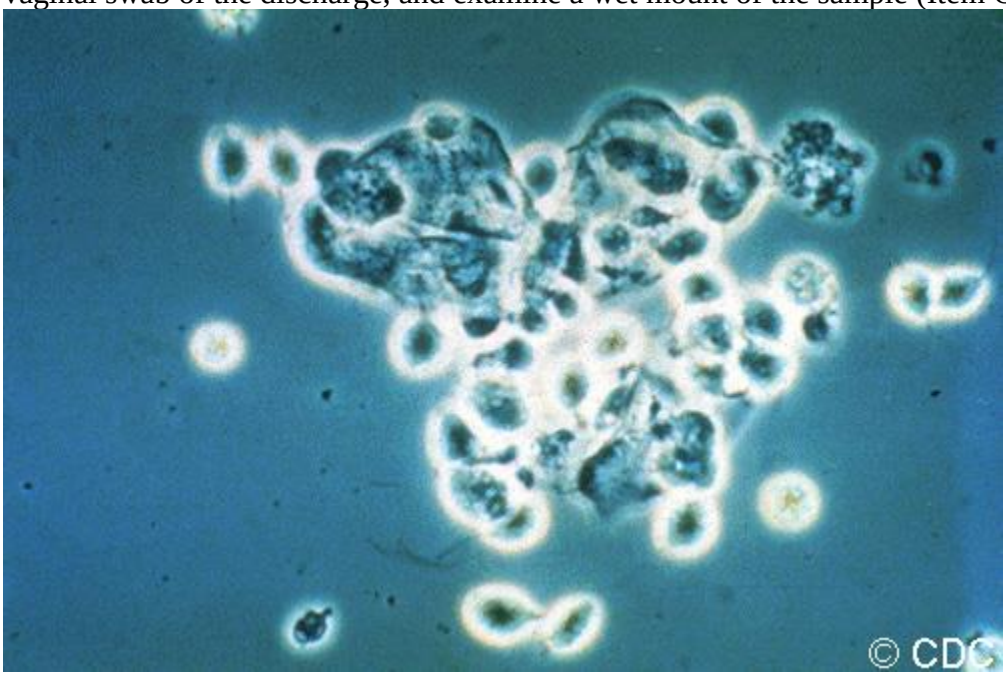
- Identify the study design most likely to yield valid information about the accuracy of a diagnostic test
- Identify the study design most likely to yield valid information about the prognosis of a condition
- Identify the study design most likely to yield valid information about the benefits and/or harms of an intervention

Suggested Readings

- Palaia A. Research and statistics: study design and data sources. Pediatr Rev. 2013;34(8):371-372. doi: http://dx.doi.org/10.1542/pir.34-8-371.
- Perry-Parrish C, Dodge R. Research and statistics: validity hierarchy for study design and study type. Pediatr Rev. 2010;31(1):27-29. doi: http://dx.doi.org/10.1542/pir.31-1-27.

Question 98

A 16-year-old adolescent girl presents to your office for evaluation of a vaginal discharge that began 4 days ago. She denies fever, nausea, vomiting, abdominal pain, or dysuria. She is sexually active and reports inconsistent condom use. Her last menstrual period was 2 weeks ago. Her physical examination is remarkable only for a purulent vaginal discharge. You obtain a vaginal swab of the discharge, and examine a wet mount of the sample (Item Q98A, Item Q98B).



Item Q98A: Wet mount sample from patient described in the vignette. Courtesy of the CDC, Joe Miller and the Public Health Information Library.

Of the following, the BEST next step in the management of this patient would be to prescribe

A. azithromycin 2 g orally as a single dose
B. ceftriaxone 250 mg intramuscularly as a single dose
C. doxycycline 100 mg orally twice a day for 7 days
D. metronidazole 2 g orally as a single dose
E. metronidazole 500 mg orally daily for 7 days

Correct Answer: D
The wet mount examination of the vaginal discharge demonstrates that the patient in the vignette has trichomoniasis. Trichomoniasis is a common sexually transmitted infection worldwide. It is caused by the protozoan, Trichomonas vaginalis. The estimated prevalence of T vaginalis infection among women of reproductive age in the United States is 2.3 million (3.1%). Risk factors for T vaginalis infection include having multiple sexual partners, a greater number of lifetime sexual partners, and other sexually transmitted diseases. Symptoms of T vaginalis infection in girls include purulent vaginal discharge, vulvovaginal pruritus and irritation, abdominal pain, dysuria, and dyspareunia.

Visualization of the motile organism on a vaginal wet mount is commonly used for diagnosis of T vaginalis because this technique is easy and quick. However, this method of diagnosis is relatively insensitive. Culture is considered the gold standard for diagnosis of trichomoniasis because its specificity approaches 100%, but this test is not widely available and its sensitivity can be as low as 75%. Nucleic acid amplification testing provides both the most sensitive and most specific means of diagnosing T vaginalis.

According to the 2015 Sexually Transmitted Diseases Treatment Guidelines published by the US Centers for Disease Control and Prevention, the recommended treatment regimen for T vaginalis is metronidazole 2 g orally in a single dose or tinidazole 2 g orally in a single dose. Abstinence from alcohol is recommended during treatment with nitroimidazoles because concurrent use can result in a disulfuram-like reaction. Alcohol should be avoided for an additional 24 hours after completion of metronidazole and 72 hours after completion of tinidazole.

Antibiotics other than the nitroimidazoles would not appropriately treat the infection in this patient. Due to compliance concerns, a single dose of metronidazole is recommended as opposed to twice daily dosing for seven days. Concurrent treatment for all sexual partners is recommended for microbiologic cure and prevention of transmission and reinfections. Regardless of the partner’s treatment status, all women should be retested within 3 months after initial treatment of T vaginalis.

PREP Pearls

- Trichomoniasis is a common sexually transmitted infection worldwide, caused by the protozoan Trichomonas vaginalis.
- Symptoms of T vaginalis infection in girls include purulent vaginal discharge, vulvovaginal pruritus and irritation, abdominal pain, dysuria and dyspareunia.
- The recommended treatment regimen for T vaginalis is metronidazole 2 g orally in a single dose or tinidazole 2 g orally in a single dose. Abstinence from alcohol is recommended during treatment with nitroimidazoles.

ABP Content Specifications(s)

- Recognize the clinical features associated with Trichomonas vaginalis infestation, and manage appropriately, including management of sexual partners
- Plan the appropriate diagnostic evaluation when Trichomonas vaginalis infestation is suspected
- Understand the epidemiology of Trichomonas vaginalis

Suggested Readings

- Helms DJ, Mosure DJ, Metcalf CA, et al. Risk factors for prevalent and incident Trichomonas vaginalis among women attending three sexually transmitted disease clinics. Sex Transm Dis. 2008;35(5):484-488. doi: http://dx.doi.org/10.1097/OLQ.0b013e3181644b9c.
- Kaskowitz A, Quint E. A practical overview of managing adolescent gynecologic conditions in the pediatric office. Pediatr Rev. 2014;35(9):371-381. doi: http://dx.doi.org/10.1542/pir.35-9-371.
- Sutton M, Sternberg M, Koumans EH, McQuillan G, Berman S, Markowitz L. The prevalence of Trichomonas vaginalis infection among reproductive-age women in the United States, 2001-2004. Clin Infect Dis. 2007;45(10):1319-1326. doi: http://dx.doi.org/10.1086/522532.
- Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015;64(RR03):1-137. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6403a1.htm.

Question 99

A 9-year-old boy is brought to your office by his mother for concerns about poor grades. As a preschooler, he received speech therapy for language delay, causing her to worry about possible struggles when starting school. Her worries increased when the start of kindergarten coincided with her separation from his father. She was relieved when he kept up with his classmates. However, this year, her son has been getting into trouble at school for disruptive behaviors. While her son enjoys working with numbers, he protests and delays working on classroom reading and writing assignments. Homework time at both his mother's and father's home has been ending in tears and tantrums. It is a struggle to get her son to school in the morning. He tells you that he does not want to go to school because "it's boring." The child's mother reports that she needed extra help in school as a child and that her brother had been in a special class at school. She feels that her son needs extra help and wants to get as much assistance for him as possible. Her ex-husband disagrees and thinks that he just needs to work harder.

Of the following, the BEST next step is to recommend

A. completion of behavioral rating scales by the child's parents and teacher
B. evaluation of the child's learning profile
C. family therapy to address the dynamics between the child and his parents
D. meeting with the child's teacher to discuss modifying his homework
E. placement of the child in a special education class

Correct Answer: B

There are several clues that the 9-year-old-boy in this vignette's academic underachievement is primarily due to a learning disability. He has specific difficulties with language-based learning (eg, reading, writing), but no problems with math. There is increased risk for such due to his previous language delay, as well as the presence of learning problems in his mother and learning disability in his uncle. The timing of this child's difficulties is typical; students with weakness or disability in reading may struggle in the fourth grade when academic demands increase and there is a switch from "learning to read" to "reading to learn." Evaluation of this child's learning profile through his school district is the best next step to help identify any learning disabilities and determine eligibility for special education services.

A variety of factors can contribute to academic underachievement. Often, more than one of these factors affect an individual child. Conditions such as learning disabilities, attention-deficit/hyperactivity disorder, developmental disorders, and brain injury can interfere with a child's ability to learn and to demonstrate what has been learned. Mental health conditions, such as anxiety, depression, or oppositional defiant disorder, can negatively impact learning and performance in school. Physical health problems such as acute or chronic illness (with corresponding school absences), sensory impairments in vision or hearing, pain, and adverse effects of medications (eg, sedation, cognitive slowing) can contribute to challenges with learning and academic achievement. Substance use and sleep problems can impact alertness, memory, and cognition. Furthermore, a child's temperament can make a difference. A slow-to-warm child may not participate fully in class activities, whereas a difficult child may become frustrated and give up quickly on new or challenging material. Any of these conditions are particularly troublesome when not recognized, diagnosed, or adequately addressed.

In addition to child-specific factors, aspects of the child's environment can contribute to poor school performance. The child's academic environment (eg, fit with teachers, quality of instruction, expectations) influences learning and school performance. The attitudes of others (eg, family, peers) towards education can impact the child's own perceptions and motivation to learn. Additional priorities such as work, sports, and extracurricular activities can compete for the child's time and energy. Important family issues to consider include parental discord, separation, or divorce; family mental health or physical health problems; and poverty or homelessness. Safety issues at home (eg, abuse), the neighborhood (eg, violence) and school (eg, bullying), should also be considered.

Psychoeducational evaluation is indicated when academic underachievement is present and parents should submit their request for this assessment to their school in writing. Areas that may be examined include cognitive ability, achievement relative to peers, information processing, and social-emotional functioning. Academic strengths and weaknesses are identified as part of this assessment. The information gathered can be helpful in identifying the causes of the child's underachievement, determining next steps to address those causes, and determining eligibility for special education services.

About 13% of children in the United States receive special education services. The Individuals with Disabilities Education Act (IDEA) is a federal law enacted in 1975 and most recently reauthorized in 2004 to ensure that children with disabilities receive a free and appropriate public education. The child is first evaluated to determine if they meet eligibility criteria under a special education disability category (eg, specific learning disability, speech or language impairment, other health impaired, emotional disturbance, intellectual disability, autistic-like behaviors, hearing impairment, visual impairment, traumatic brain injury). The evaluation must occur in a timely manner, according to federal law. If the child qualifies for special education services, an Individualized Education Program (IEP) will be developed for the child, outlining the services and accommodations that will be provided to the child to meet his educational needs. According to IDEA, these services should be provided in the least restrictive environment (LRE), meaning that the child should be educated in typical educational settings with children without disabilities as much as possible. Although some children will require intensive services in a separate special education classroom or school, if feasible, a child should receive support in a regular classroom with his typical peers.

The 9-year-old boy in this vignette has academic underachievement and is presenting with disruptive behaviors in class, tantrums around homework, and school refusal. There are conflicts within the child's family in interactions around homework, getting to school, and parental views of the child's needs. Completion of behavioral rating scales by the child's parents and teacher would be useful for outlining his specific disruptive behaviors and screening for conditions such as attention-deficit/hyperactivity disorder. Family therapy may help the parents understand the child's struggles and increase their ability to support him. Modifying the child's homework may help decrease frustration. However, as the behavioral difficulties and conflicts center around reading and writing in class and at home, all of these measures would not address the underlying reason for the child's problems. The best next step would be to focus on the probable cause of these difficulties, a learning disability. An evaluation of this child's learning profile is necessary to determine if a learning disability is present. If IEP eligibility under learning disability is confirmed, placement in the LRE means that this child would most likely receive services within his regular classroom or that he may be pulled out of class to receive more intensive assistance for part of his day rather than be placed in a special education class for his entire school day.

It is essential for the primary care provider to understand the various factors that may affect a child's academic achievement and the parameters under which special education services are rendered. Guiding the child's family in navigating the educational process and advocating on the behalf of a struggling patient for assessment and assistance can improve that child's access to appropriate instruction and services to support his learning and academic success.

PREP Pearls

- Psycho-educational evaluation is indicated when academic underachievement is present and parents should submit their request for this assessment in writing to their school.
- According to the Individuals with Disabilities Education Act, these services should be provided in the least restrictive environment: the child should be educated in typical educational settings with children without disabilities as much as possible.
- Students with weakness or disability in reading may struggle in the fourth grade when academic demands increase and there is a switch from "learning to read" to "reading to learn."

ABP Content Specifications(s)

- Recognize that factors such as temperament, family environment, illness, medications, and mental disorders contribute to academic underachievement
- Understand the educational criteria required for placement in special classrooms and the factors affecting those decisions

Suggested Readings

- Byrd RS. School failure: assessment, intervention, and prevention in primary pediatric care. Pediatr Rev. 2005;26(7):233-243. doi: http://dx.doi.org/10.1542/pir.26-7-233.
- Dworkin PH. School failure. In: Augustyn M, Zuckerman B, Caronna EB, eds. The Zuckerman Parker Handbook of Developmental and Behavioral Pediatrics for Primary Care. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011:317-321.

Question 100

A 13-year-old adolescent presents to the emergency department with pain in his upper abdomen that began when he was struck by his bicycle handlebar while trying to perform a jump. The pain began immediately following the injury, but has been worsening since the injury occurred about 6 hours ago. He was not able to fall asleep because of the severity of his pain and has had 3 episodes of vomiting over the past 2 hours. He has no significant past medical or surgical history, takes no medications, and has no allergies.

In the emergency department, he appears very uncomfortable and is lying on his right side with his legs drawn up toward his chest. His vital signs show a temperature of 36.5°C, heart rate of 98 beats/min, blood pressure of 102/70 mm Hg, respiratory rate of 16 breaths/min, and pulse oximetry of 100% (room air).

On physical examination, there is a 2 x 3 centimeter area of bruising over his left upper quadrant (LUQ). Bowel sounds are present on auscultation. His abdomen is soft with marked tenderness to palpation over the LUQ and voluntary guarding. There is no other involuntary guarding or rebound tenderness. His extremities are warm and well-perfused, and his pulses are normal. There are no signs of head or spine trauma and no abnormalities on neurologic examination. The adolescent has another episode of vomiting in the emergency department following your physical examination.

You obtain blood samples for laboratory studies, establish intravenous access, and order a dose of intravenous fentanyl to help alleviate the patient's pain. You advise him and his parents that further investigation is needed to pinpoint the source of his abdominal pain.

Of the following, the MOST appropriate next step in this patient's evaluation is

A. computed tomography of the abdomen
B. diagnostic peritoneal lavage
C. endoscopic retrograde cholangiopancreatography
D. exploratory laparotomy of the abdomen
E. plain radiography of the abdomen

Correct Answer: A

The 13-year-old adolescent in the vignette presents with abdominal pain and vomiting, along with focal tenderness and guarding over the left upper quadrant of his abdomen after sustaining blunt abdominal trauma. Given his history and physical examination findings, splenic injury should be highly suspected. The most appropriate next step in his evaluation is computed tomography (CT) of the abdomen.

All pediatric providers should be able to plan the initial evaluation of a patient with a suspected splenic injury. The spleen is the most commonly injured solid abdominal organ. Most splenic injuries arise from automobile-pedestrian trauma, though falls and bicycle accidents are also common mechanisms. Due to the highly vascular nature of the spleen, there is potential for significant morbidity and mortality from splenic injuries due to blood loss into the peritoneal cavity.

Children with splenic injuries may present with either diffuse or localized abdominal pain. Patients typically have tenderness to palpation over the left upper quadrant of the abdomen. Referred left shoulder pain (Kehr sign) due to the presence of subphrenic blood may be an associated presenting symptom.

For hemodynamically stable children with suspected splenic injuries, CT of the abdomen is considered the most sensitive diagnostic tool and best method for evaluating solid organ injury, allowing definition of both the site and extent of the injury. Focused abdominal sonography for trauma (FAST) may also play a useful role in the evaluation of children following blunt abdominal trauma as a means of rapidly identifying free fluid. Its use in the pediatric population is still under study.

Prior to the advent of CT and FAST, diagnostic peritoneal lavage (DPL) was a more widely used tool for evaluation following abdominal trauma. Its use has decreased significantly in recent years. While DPL is quite sensitive for the detection of intraabdominal bleeding and hollow visceral injuries, it is both nonspecific and invasive with associated morbidity. Computed tomography of the abdomen is the preferred study over DPL in a hemodynamically stable child such as the adolescent in the vignette.

Endoscopic retrograde cholangiopancreatography is a specialized diagnostic technique used to evaluate the bile ducts, pancreatic duct, and gallbladder. This diagnostic study would not play a useful role in the evaluation of the patient in the vignette with suspected splenic injury.

Diagnostic laparotomy would not be indicated in the hemodynamically stable patient in the vignette who has findings concerning for splenic injury, which is most commonly managed nonoperatively. Indications for immediate diagnostic laparotomy are limited in children following blunt abdominal trauma. In most cases, emergent laparotomy is not required and further diagnostic studies will guide either elective operative management or clinical observation. Indications for immediate diagnostic laparotomy include significant persistent

hemodynamic instability in patients with evidence of abdominal injury (and the absence of extra-abdominal injury), significant abdominal distention with associated hypotension, and pneumoperitoneum.

Abdominal radiographs would not be highly useful in the evaluation of the patient in the vignette. Although abdominal radiography could help to detect the presence of pneumoperitoneum, it would not be useful in identifying and assessing the grade of a splenic injury (or any other solid organ injuries). Computed tomography of the abdomen would be more useful in this patient's evaluation.

PREP Pearls

- For hemodynamically stable children with suspected splenic injuries, computed tomography of the abdomen is considered the most sensitive diagnostic tool and best method for evaluating solid organ injury, allowing definition of both the site and extent of the injury.
- Children with splenic injuries may present with either diffuse or localized abdominal pain. Patients typically have tenderness to palpation over the left upper quadrant of the abdomen. Referred left shoulder pain (Kehr sign) due to the presence of subphrenic blood may be an associated finding.

ABP Content Specifications(s)

- Plan the appropriate initial evaluation in a patient with a suspected ruptured spleen

Suggested Readings

- Saladino RA, Lund DP. Abdominal trauma. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. Textbook of Pediatric Emergency Medicine. 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:1115-1125.
- Saxena AK. Pediatric abdominal trauma workup. Medscape. http://emedicine.medscape.com/article/1984811-workup#showall. Updated August 14, 2015..

Question 101

A 5-month-old male infant presents to the infectious diseases clinic for follow-up. He has a history of herpes encephalitis treated with a 3-week course of parenteral acyclovir as a neonate. He has been receiving oral acyclovir for herpes suppression since that time.

Of the following, the adverse effect that is most likely to require monitoring in this infant is

A. arthritis
B. dermatitis
C. myelosuppression
D. nephropathy
E. transaminitis

Correct Answer: C

Of the listed choices, the adverse effect that is most likely to require monitoring for the infant in this vignette is myelosuppression. Infants receiving 6 months of acyclovir suppressive therapy after neonatal herpes simplex infection should have absolute neutrophil counts assessed at 2 and 4 weeks after starting treatment and then monthly.

A study conducted through the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group found improved developmental outcomes for neonates with herpes encephalitis who received 6 months of viral suppression with oral acyclovir compared to placebo. Suppressive therapy also reduces recurrence of cutaneous disease. As a result of these data, it is now standard of care to treat infants who have had neonatal herpes simplex virus infection with 6 months of acyclovir following parenteral therapy. In the study described, a trend for increased neutropenia in the infants who were treated with acyclovir was identified. For infants with a history of central nervous system encephalitis, 25% of those treated with acyclovir developed an absolute neutrophil count of less than or equal to 500 cells/μL, compared to 5% of those on placebo. Therefore, monitoring of absolute neutrophil counts is recommended.

Nephropathy as a result of tubular precipitation of acyclovir can occur with intravenous administration, not oral therapy. Nephropathy is more common with rapid infusion and in patients with dehydration. Changes in renal function are thought to occur in 5% to 10% of patients receiving parenteral acyclovir. Dermatitis and transaminitis are thought to occur in 1% to 2% of patients receiving parenteral acyclovir therapy. Arthritis has not been associated with acyclovir therapy in postmarketing surveillance or case reports.

Antivirals directed against other Herpesviridae have similar adverse effects. Myelosuppression is also the most common adverse effect of ganciclovir and valganciclovir, drugs used for the treatment and prevention, respectively, of cytomegalovirus infection in immunocompromised patients. Rash, gastrointestinal symptoms, and increased serum creatinine and liver enzymes can occur with ganciclovir and valganciclovir.

The adverse effect profile for neuraminidase inhibitors (oseltamivir, zanamivir) used for influenza infections differs. Like most medications, gastrointestinal symptoms are common, as are insomnia and vertigo. Neuropsychiatric events such as delirium and hallucinations have also been reported.

PREP Pearls

- Infants receiving 6 months of acyclovir suppressive therapy after neonatal herpes simplex infection are at risk for developing drug-associated neutropenia.
- Nephropathy as a result of tubular precipitation of acyclovir can occur with intravenous administration, not oral therapy.
- Neuropsychiatric events such as delirium and hallucinations have been reported with neuraminidase inhibitors.

ABP Content Specifications(s)

- Recognize the adverse effects associated with the use of various antiviral drugs

Suggested Readings

- American Academy of Pediatrics. Herpes simplex. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:432-445. .
- Kimberlin DW, Whitley RJ, Wan W, et al. Oral acyclovir suppression and neurodevelopment after neonatal herpes. N Engl J Med. 2011;365(14):1284-1292. doi: http://dx.doi.org/10.1056/NEJMoa1003509.
- Razonable RR. Antiviral drugs for viruses other than human immunodeficiency virus. Mayo Clin Proc. 2011;86(10):1009-1026. doi: http://dx.doi.org/10.4065/mcp.2011.0309.

Question 102

A 15-year-old adolescent girl presents to your office with her mother. She has been experiencing intermittent crampy abdominal pain that is generalized and lasts for several hours. There is no association with eating, voiding, or defecation. The adolescent denied nausea, vomiting, and diarrhea. She passes stools daily without difficulty, with intermittent bright and dark red blood. Her mother reported no family history of food allergy, celiac disease, or constipation. Her father has been diagnosed with a polyposis syndrome.

On physical examination, the adolescent's temperature is 37.5°C, heart rate is 90 beats/min, respiratory rate is 17 breaths/min, and blood pressure is 105/75 mm Hg. She is alert and well nourished. Her abdomen is soft, flat, and nontender, with no palpable mass and normal bowel sounds. Her rectal examination is normal, without hemorrhoid or fissures. You note brown macules on her lips, tongue, and hands. The remainder of her physical examination is unremarkable.

Laboratory results are shown:

Laboratory test	**Result**
Hemoglobin	10 g/dL (100 g/L)
Platelet count	$220 \times 10^3/\mu L$ ($220 \times 10^9/L$)
Stool guiac test	Positive

Of the following, the MOST likely diagnosis is

A. Cowden syndrome

B. familial polyposis coli

C. Gardner syndrome

D. juvenile polyposis syndrome

E. Peutz-Jeghers syndrome

Correct Answer: E

The adolescent in the vignette has Peutz-Jeghers syndrome identified by her hematochezia, freckling, and family history of polyposis. Many inherited polyposis syndromes carry an increased risk of cancer (Item C102). Because of the elevated cancer risk, these patients should receive routine oncology and gastroenterology evaluations. Many centers have multidisciplinary polyposis clinics that include genetic counselors to aid in the diagnosis and assist with planning cancer screening.

Item C102. Inherited Polyposis Syndromes.

Inherited polyposis syndrome	Hamartomatous or Adenomatous	Mode of Inheritance	Clinical Features	Cancer Risk (%)	Gene
Juvenile polyposis	Hamartomatous	AD	>5 juvenile polyps	• Colorectal (39) • Stomach, pancreas small bowel (21)	• *SMAD4/DPC4* • *BMPR1A* • *STK11/LKB1*
Peutz-Jeghers	Hamartomatous	AD	• Mucocutaneous • Hyperpigmentation • Freckling of hands and feet	• Uterus/cervix (10) • Breast (54) • Colorectal (39) • Gastric (29) • Ovary (21) • Lung (15) • Small bowel (13) • Pancreas (11-36) • Testicle (1)	*STK11/LKB1A*
Cowden	Hamartomatous	AD	• Macrocephaly • Papillomatous papules • Acral keratosis	• Breast (85) • Thyroid (35) • Kidney (33) • Endometrial (29) • Colorectal (9) • Melanoma (6)	• *PTEN* • *SDH* • *KLLN*
Bannayan-Riley-Ruvalcaba	Hamartomatous	AD	• Macrocephaly • Developmental delay • Lipomas • Hemangiomas	• Breast (85) • Thyroid (35) • Endometrial (28)	*PTEN*
Familial adenomatous polyposis	Adenomatous	AD	• Osteomas • Desmoid tumors • Hypertrophy of retinal pigment epithelium • Dental abnormalities	• Colon (100) • Small bowel, thyroid, hepatoblastoma, pancreas (1-12)-	*APC*
Attenuated familial adenomatous polyposis	Adenomatous	AD	• Osteomas • Desmoid tumors • Hypertrophy of retinal pigment epithelium • Dental abnormalities	• Colorectal (70) • Duodenal (4-12) • Thyroid (1-2)	*APC*
Gardner	Adenomatous	AD	• Osteoma • Epidermal inclusion cysts • Desmoid tumors • Dental abnormalities	• Colorectal (100) • Duodenal (4-12) • Pancreas, thyroid (2)	*APC*

AD, autosomal dominant

Courtesy of C. Waasdorp Hurtado

PREP Pearls

- Hematochezia, mucocutaneous freckling, and a family history of polyposis suggest a diagnosis of Peutz-Jeghers syndrome.
- Many polyposis syndromes have increased colorectal and other cancer risks.
- Familial adenomatous polyposis has a 100% lifetime risk of colon cancer.

ABP Content Specifications(s)

- Recognize the clinical features associated with inherited polyposis syndromes that are associated with a risk of colon cancer

Suggested Readings

- Brosens LA, Offerhaus GJ, Giardiello FM. Hereditary colorectal cancer: genetics and screening. *Surg Clin North Am*. 2015;95(5):1067-1080. doi: http://dx.doi.org/10.1016/j.suc.2015.05.004.
- Campos FG, Figueiredo MN, Martinez CA. Colorectal cancer risk in hamartomatous polyposis syndromes. *World J Gastrointest Surg.* 2015;7(3):25-32. doi: http://dx.doi.org/10.4240/wjgs.v7.i3.25.
- Leoz ML, Carballal S, Moreira L, Ocaña T, Balaguer F. The genetic basis of familial adenomatous polyposis and its implications for clinical practice and risk management. *Appl Clin Genet.* 2015;8:95-107. doi: http://dx.doi.org/10.2147/TACG.S51484.
- Syngal S, Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW. ACG clinical guideline: genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015;110(2):223-262. doi: http://dx.doi.org/10.1038/ajg.2014.435.
- Thakkar K, Fishman DS, Gilger MA. Colorectal polyps in childhood. *Curr Opin Pediatr.* 2012;24(5):632-637. doi: http://dx.doi.org/10.1097/MOP.0b013e328357419f.

Question 103

A 2-year-old girl is brought to your office because she refuses to move her right arm. Her father reports that, several hours earlier, he was walking with her and holding her hand. The girl pulled away from him and then cried out in pain. On physical examination, the girl holds her right elbow in a slightly flexed position with the forearm pronated. She does not appear to have tenderness with palpation of the upper arm, elbow, forearm, or wrist. There is no redness or bruising.

Of the following, the MOST accurate statement regarding this girl's injury is that it

A. can result from a fall on an outstretched hand
B. generally results in swelling around the elbow
C. involves dislocation of the proximal radius
D. more commonly occurs in boys
E. occurs only in children younger than 5 years of age

Correct Answer: A

The girl in the vignette has experienced an annular ligament displacement, or nursemaid's elbow. This condition has also been referred to as radial head subluxation. However, annular ligament displacement is now the preferred term because it describes the anatomic injury most accurately. The most common mechanism of injury involves traction on the forearm that allows the annular ligament to slip between the radial head and the capitellum. In about one-third of cases, annular ligament displacement occurs as a result of a fall or other nontraction mechanism.

Annular ligament displacement typically occurs in children between 1 and 5 years of age, though infants and older children can be affected as well. Most families describe a traction or traumatic mechanism of injury, though in about 20% of cases, there is no clear precipitating injury. About half of affected children present with the arm held in the classic position, with the elbow somewhat flexed and the forearm pronated. The presence of swelling, bruising, or point tenderness around the elbow should prompt evaluation for upper extremity fracture. In the absence of signs suggesting fracture, reduction maneuvers can be safely tried. There are 2 standard reduction techniques. The provider can fully extend the elbow with supination and traction on the forearm, followed by flexion (supination/flexion method). Alternatively, the provider can fully extend the elbow, followed by full pronation of the forearm (hyperpronation method). When the reduction maneuver is successful, a child will typically begin using the affected extremity within a few minutes. Approximately 15% of children will experience recurrent displacement. A short trial of cast immobilization may be helpful for children with frequent annular ligament displacement.

Swelling around the elbow is uncommon in children with nursemaid's elbow and should prompt evaluation for more serious injuries. Although the term radial head subluxation has been used to describe this injury, the annular ligament is the structure that is displaced with this injury, rather than the proximal radius. Girls appear to have a slightly higher rate of annular ligament displacement. Though much less commonly seen, this injury has been described in young infants and middle school-aged children.

PREP Pearls

- Annular ligament displacement is the preferred term for nursemaid's elbow because this term most accurately describes the anatomy of the injury.
- Approximately two-thirds of children with annular ligament displacement have a traction mechanism.
- The presence of swelling, bruising, or point tenderness around the elbow should prompt evaluation for upper extremity fracture.

ABP Content Specifications(s)

- Recognize the clinical findings associated with subluxation of the radial head, and manage appropriately

Suggested Readings

- Browner EA. Nursemaid's elbow (annular ligament displacement). *Pediatr Rev.* 2013;34(8):366-367. doi: http://dx.doi.org/10.1542/pir.34-8-366.
- Rudloe TF, Schutzman S, Lee LK, Kimia AA. No longer a "nursemaid's" elbow: mechanisms, caregivers, and prevention. *Pediatr Emerg Care.* 2012;28(8):771-774. doi: http://dx.doi.org/10.1097/PEC.0b013e3182624906.
- Sarwark JF, LaBella CR. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014: 650 pp.

Question 104

You are examining a full term 4-day-old male newborn and are unable to palpate the right testis. The remainder of the physical examination is unremarkable.

Of the following, the BEST approach for management of this patient is

A. initiate a trial of low-dose gonadotropin-releasing hormone
B. referral to a surgeon if the testis remains undescended at 6 months
C. obtain a karyotype if the testis has not descended by 2 months
D. perform ultrasonography on the scrotum
E. referral to a surgeon if the testis remains undescended at 1 year

Correct Answer: B
The newborn in this vignette should be observed until 6 months of age and then referred to a surgeon if the testis has not descended by that time. Approximately 4.5% of male infants will be born with an undescended testicle, making cryptorchidism the most common genital disorder identified at birth. The majority of undescended testicles will descend by 3 months of age, and by 6 months of age, only 0.8% of male infants will still have an undescended testicle. A testis that has not descended by 6 months of age is unlikely to descend. Infants should therefore be referred to pediatric surgery or urology by 6 months of age, not later.

The primary care provider should palpate the testes at each health supervision visit. Observation of an undescended testis is appropriate until 6 months of age, at which point the patient should be referred to a surgical specialist for further evaluation and management. Providers should not perform ultrasonography or any other imaging prior to referral, as the results add very little to management decisions. Furthermore, hormonal therapy should not be initiated because studies have shown a lack of efficacy.

An undescended testicle should be treated surgically with an orchidopexy between 6 to 18 months of age. The consequences of an unrepaired, undescended testicle include testicular malignancy, decreased fertility, associated hernia, and possible torsion of the undescended testis. It is important to distinguish between undescended testicles and retractile testicles. A retractile testis is a testis that has descended into the scrotum, but can move in and out of the scrotum. It is typically associated with a brisk cremasteric reflex and can often be misdiagnosed as an undescended testicle. However, unlike an undescended testis, a retractile testis can be brought down into the scrotum. Retractile testes do not need to be surgically corrected, but need to be monitored at least annually at health supervision visits, as up to one-third of boys with retractile testes can develop an acquired undescended testis.

A karyotype or further workup is not necessary for the patient in this vignette who has a normal phallus and one palpable testis present. An infant with a male phallus and bilateral nonpalpable testes requires a workup for a disorder of sexual development that would include a karyotype and hormone profile.

PREP Pearls

- A male with an undescended testicle should be referred to a surgical specialist at 6 months of age.
- Scrotal ultrasonography and hormonal therapies are not useful for the diagnosis and management of undescended testicles.

ABP Content Specifications(s)

- Understand the natural history of cryptorchidism
- Differentiate the findings associated with undescended testes from those of retractile testes

Suggested Readings

- Elder JS. Disorder and anomalies of the scrotal contents. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:2592-2597.
- Kolon TF, Herndon CD, Baker LA, et al. Evaluation and treatment of cryptorchidism: AUA guideline. *J Urol*. 2014;192(2):337-345. doi: http://dx.doi.org/10.1016/j.juro.2014.05.005.

Question 105

You are the senior resident caring for a hospitalized 11-year-old girl with poorly controlled systemic lupus erythematosus. The appropriate dose found in your hospital's formulary for immunosuppressant "X" is 10 mg/kg per day divided twice daily. The rheumatologist asks you to prescribe drug X at 30 mg/kg per day divided twice daily, based on several published case reports, as well as her personal experience.

You enter a computerized order for the medication at the dose requested by the attending physician. The computer indicates that the dose requested is out of the acceptable range. You override the computer and enter the dose as 30 mg/kg as requested by the rheumatologist. One hour later, a hospital pharmacist calls you to discuss the dose of the drug ordered. When you confirm the dose, the pharmacist says that given the significant adverse-effect profile of the drug, she cannot accept the order from a resident.

Of the following, the BEST response to the pharmacist is to

A. ask to speak with her supervisor; she should have accepted your confirmation of the prescription
B. cancel the order and discuss with the rheumatologist on rounds the next day
C. change the dose of the drug to 10 mg/kg divided twice per day
D. order an alternative immunosuppressant at the dosage the pharmacist recommends
E. provide the pharmacist with the contact information for the rheumatologist

Correct Answer: E

The interactions detailed in the vignette likely occur many times per day in every healthcare settings. The pace of healthcare advances is very fast, and it is challenging for physicians, pharmacists, and formularies to keep up with the latest medications and their recommended doses, especially for uncommon disorders. Modern medical advances have led to a cure for many more illnesses, but the resulting complexity has also led to unintended consequences. More than 7,000 patients die annually in the United States from medication errors, and between 5% and 27% of all pediatric medication orders result in a medication error. Safety protocols are essential to protect children from such errors.

Successful medication delivery to hospitalized children in the United States depends on a team that includes at least 1 practitioner to order the drug, 1 pharmacist to prepare the drug, and 1 nurse to administer the drug. Often, the team is far larger than that. Every member of that team is responsible for the safe administration of the drug, and as such, every team member needs to have the ability and confidence to "hard-stop" the administration of a drug if they perceive that some aspect of the medication order may be an error. In the vignette, the resident has ordered a high-risk nonformulary drug at a dose unfamiliar to the pharmacist. Given that this may represent a medication error, the pharmacist correctly prevented the administration of the drug until her concerns have been satisfactorily addressed. Since this drug is being prescribed based on the medical opinion and experience of the attending physician, the most appropriate course of action in this case is to have the pharmacist discuss the issue directly with the attending physician.

It is incumbent upon the team as a whole to ensure that all members are comfortable that an order does not represent a medication error. It would be inappropriate for the pharmacist to simply accept the resident's reassurance that the correct dose of the drug had been ordered and ignore her own discomfort. While canceling the order may prevent a potential medication error, a delay in treatment may not be in the patient's best interest. Simply changing the attending physician's suggested management of the patient without discussing it with her would not be appropriate.

PREP Pearls

- Medication errors are common in pediatrics and often lead to harm.
- Interdisciplinary interactions and teamwork are key components of safety systems that can reduce the rate of medication errors.

ABP Content Specifications(s)

- Understand the role of computerized order entry and dose-range checking in reducing medication errors
- Understand the role of ancillary services such as the pharmacy in the prevention of medication errors

Suggested Readings

- Leonard MS. Patient safety and quality improvement: reducing risk of harm. *Pediatr Rev.* 2015;36(10):448-458. doi: http://dx.doi.org/10.1542/pir.36-10-448.
- Rinke ML, Bundy DG, Velasquez CA, et al. Interventions to reduce pediatric medication errors: a systematic review. *Pediatrics*. 2014;134(2):338-360. doi: http://dx.doi.org/10.1542/peds.2013-3531.
- Schriefer J, Leonard MS. Patient safety and quality improvement: an overview of QI. *Pediatr Rev.* 2012;33(8):353-360. doi: http://dx.doi.org/10.1542/pir.33-8-353.

Question 106

A 2-month-old male infant born with tetralogy of Fallot is brought to your office for a health supervision visit. The infant has been doing well, without any symptoms of his cardiac abnormality. His oxygen saturation before receiving immunizations today was 88% on room air. When vaccinations are administered, the infant has a prolonged crying episode and appears cyanotic. Upon recheck, his oxygen saturation is 70% and continues to drop into the 50% range, with visible worsening of his cyanosis and an increase in his respiratory rate from a baseline of 40 breaths/min to 70 breaths/min.

Of the following, the BEST initial management for this infant is

A. bag-mask ventilation

B. intravenous furosemide

C. knee chest position

D. oral midazolam

E. oral propranolol

Correct Answer: C
Infants with tetralogy of Fallot (TOF) are at risk for hypercyanotic spells or episodes. Placement in the knee chest position is the best first intervention if a hypercyanotic spell is suspected. The 4 components of TOF are perimembranous ventricular septal defect (VSD), pulmonic stenosis, overriding aorta, and right ventricular hypertrophy.

When an infant with TOF is in a normal resting state, the shunt across the VSD will be from the left ventricle (LV) to the right ventricle (RV). The degree of cyanosis in this state will depend on the degree of pulmonic stenosis and right ventricular outflow tract (RVOT) obstruction, or more specifically, the adequacy of the pulmonary blood flow. As this worsens, the oxygen saturation may decrease slowly over time and the pulmonic stenosis murmur will increase in intensity.
In the case of a hypercyanotic spell, the systemic vascular resistance (SVR) drops in response to fever or other cause of vasodilation. This decreased resistance changes the intracardiac hemodynamics. If resistance through the RVOT is much greater than the SVR, the VSD shunt will then reverse and flow from the RV to the LV. With aortic override, the aorta straddles the ventricular septum at the VSD and is displaced to the right. This further potentiates the ability, in the case of a sudden decrease in SVR, for blood to flow from the RV into the aorta rather than the pulmonary artery. As a result, the blood arriving at the peripheral circulation will be acidotic and hypoxemic. Acidosis will cause hyperventilation, which increases return of blood to the right ventricle. A greater and greater percentage of the blood sent to the peripheral circulation will be desaturated as the spell progresses, and will manifest as lower and lower systemic saturations seen on pulse oximetry. The pulmonic stenosis murmur during a hypercyanotic spell will become softer, as evidence of the decrease in pulmonary flow. The reason that the knee chest position is the best first intervention for a suspected hypercyanotic spell is that it will instantly increase the SVR.

Bag-mask ventilation would help to decrease the carbon dioxide level and increase the systemic pH, but would not address the underlying pathophysiology. Providing 100% oxygen would be helpful, ensuring that the circulating blood volume is as well saturated as possible.
Intravenous furosemide would worsen the situation, decreasing the blood volume reaching the lungs as well as the systemic circulation. This infant is not in congestive heart failure with excess pulmonary flow. In this case, there is too little pulmonary flow, and a fluid bolus would be a good intervention after performing a knee-chest maneuver.

Oral midazolam would not be the best first intervention, because it would not address the underlying pathophysiology of low SVR. If sedation is indicated to calm the infant and decrease hyperventilation, morphine would be the drug of choice (after performing the knee-chest maneuver, providing oxygen and a fluid bolus). Early reports suggest that intranasal fentanyl may be effective as well because of its rapid absorption.

Oral propranolol would not be effective for initial management of a rapidly progressing hypercyanotic spell. Propranolol is thought to help relax the infundibulum or subpulmonic muscle bundles. Oral propranolol has been successfully used to help prevent hypercyanotic spells in situations in which surgical treatment of TOF is not immediately available. The

intravenous form of the drug has also been used in difficult to control hypercyanotic spells, after the interventions noted earlier have been instituted. Propranolol may cause or worsen hypotension in a volume-depleted patient, thereby decreasing pulmonary blood flow, so it would not be a good first intervention.

Management of a hypercyanotic spell should proceed with the following steps:
1. Placement in the knee-chest position.
2. Administration of oxygen, with calming measures.
3. Placement of an intravenous line to give a fluid bolus.
4. Administration of morphine, either intramuscularly or subcutaneously.

If these measures are unsuccessful, sodium bicarbonate should be considered to reverse the metabolic acidosis and decrease the secondary hyperventilation. Intravenous propranolol may be given, but may cause hypotension. α-agonists, including phenylephrine, can be given to raise the SVR, but can also cause unwanted vasoconstriction in other vascular beds such as the kidney.

PREP Pearls

- A hypercyanotic spell is usually precipitated by crying, fever, or other causes of decreased systemic vascular resistance.
- The knee-chest maneuver raises the systemic vascular resistance, decreasing the right-to-left shunt across the ventricular septal defect.
- Management of a hypercyanotic spell should proceed with the following steps:
    1. Placement in the knee-chest position.
    2. Administration of oxygen, with calming measures.
    3. Placement of an intravenous line to give a fluid bolus.
    4. Administration of morphine, either intramuscularly or subcutaneously.

ABP Content Specifications(s)

- Plan immediate management of a hypoxic episode in a child who has cyanotic congenital disease

Suggested Readings

- Bernstein D. Tetralogy of Fallot. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:2211-2215..
- Roche SL, Greenway SC, Redington AN. Tetralogy of Fallot with pulmonary stenosis, pulmonary atresia, and absent pulmonary valve. In: Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents.* 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:1029-1052..
- Tsze DS, Vitberg YM, Berezow J, Starc TJ, Dayan PS. Treatment of TOF hypoxic spell with intranasal fentanyl. *Pediatrics*. 2014;134(1):e266-e269. doi: http://dx.doi.org/10.1542/peds.2013-3183.

Question 107

A 2-year-old boy is brought to your office for a health supervision visit. He has developmental delay and microcephaly. He is cruising but not independently walking, and his parents report that he is difficult to feed, spits out his food, and seems to have difficulty swallowing. At times, they have to hold him down during meals. He has lost 1 kg since his most recent visit 6 months ago, and his weight is now less than the third percentile. You have referred them to an early intervention program, but his father refused to let the early intervention providers in their home. You have referred them to a gastroenterologist, a feeding specialist, and a neurologist, but they missed these appointments and have not rescheduled. Cab vouchers have been provided to the family for travel to their specialty appointments. The parents state they understand that you are recommending specialty care, but his father says they will not go to that hospital "because they hurt children there."

Of the following, the MOST appropriate next step in management is to

A. ask the family to consider your recommendations again and follow-up in 3 months
B. give the family handouts on feeding and developmental delay
C. offer to arrange a multidisciplinary evaluation at a different hospital
D. offer to connect the family to the parents of another child with similar problems
E. report the family to the state child welfare agency for suspected medical neglect

Correct Answer: E

Neglect is a form of child maltreatment and typically takes 1 of 5 forms:

1. Medical neglect—failing to provide adequate medical care for a child
2. Physical neglect—failing to provide basic needs (nutrition, shelter, clothes) or child abandonment
3. Educational neglect—failing to enroll the child in school or providing homeschooling, allowing frequent absenteeism, or ignoring special education needs
4. Emotional neglect—isolating the child, withholding emotional support, exposing the child to interpersonal violence or substance abuse
5. Supervisional neglect—leaving the child alone or improperly supervised, failing to keep the child from safety hazards

This vignette represents a patient with medical neglect and should be reported to the state, county, or regional child welfare agency. Medical neglect stems from caregivers either failing to seek healthcare when signs of illness appear or caregivers who fail to carry out recommendations from healthcare professionals. However, not all of these instances constitute medical neglect.

The American Academy of Pediatrics policy statement on medical neglect indicates the following criteria:

- A child is harmed or at risk of harm due to a lack of recommended care
- Such care would likely benefit the child in significant ways
- The expected benefit exceeds its morbidity (such that reasonable caregivers would choose treatment)
- It is clear that the caregivers could access care but do not
- The caregiver understands the recommendations for care

Nearly all states have mandated reporting laws requiring physicians to report cases of suspected child abuse and neglect to a child welfare agency.

Neglect is approximately 3 times as common as abuse; approximately 770,000 neglect cases are reported each year. In longitudinal studies of children who were neglected, neglect was associated with poorer social, emotional, cognitive, behavior, and growth outcomes. Several child, family, and community factors can put a child at risk for neglect: poverty, unemployment, caregiver mental health, and substance use problems. Children who have developmental delays are also at higher risk. Social connectedness, caregiver resilience, and parenting skills are protective factors. By reporting suspected cases of child neglect to child welfare agencies, caregivers can be evaluated for additional support, resources, and interventions that may address the neglect and its underlying reasons.

Failing to carry through with recommendations due to poor caregiver health literacy, cultural beliefs, or inadequate medical coverage is not medical neglect. In addition, if the recommended care has uncertain benefits or significant adverse effects, it may be reasonable that the caregiver declines treatment. In this vignette, the child is exhibiting poor growth likely due to inadequate caloric intake, with his developmental delays contributing. His condition will likely improve

with treatment. His father expresses an understanding of your recommendations, so addressing gaps in knowledge with handouts or connection to another family would likely be ineffective. Arranging an evaluation at another hospital may delay treatment further and is not a reasonable alternative.

PREP Pearls

- Child neglect is 3 times more common than abuse.
- Child neglect can take a variety of forms: medical, physical, educational, emotional, and supervisional.
- Caregiver health illiteracy, cultural practices, and inadequate medical coverage can mimic medical neglect.

ABP Content Specifications(s)

- Know the different subtypes of neglect: medical, supervisional, physical and educational
- Understand the epidemiology of and the psychosocial and environmental risk factors for neglect

Suggested Readings

- Child Welfare Information Gateway, US Department of Health and Human Services. Act of omission: an overview of child neglect. Child Welfare Information Gateway website. http://www.childwelfare.gov/pubs/focus/acts/index.cfm.
- Jenny C. Recognizing and responding to medical neglect. *Pediatrics*. 2007;120(6):1385-1389. doi: http://dx.doi.org/10.1542/peds.2007-2903.

Question 108

You are called to see a postpartum 24-year-old woman in labor and delivery. She emigrated from El Salvador 1 year ago, and was found to be HIV-positive during her prenatal care here in the United States. She just delivered a 3,000 g full term female newborn and has a 3-year-old son who was born in El Salvador and emigrated with her. The 3-year-old boy is stated to be very small for his age and is frequently sick, but has only been seen once in the emergency department during the past year. She is requesting HIV testing for both of her children.

Of the following, the BEST recommendations to evaluate these 2 children are

A. HIV-1/HIV-2/p24 Ag immunoassay for both
B. HIV-1/HIV-2/p24 Ag immunoassay for the 3-year-old boy, and a HIV nucleic acid test for the newborn
C. HIV nucleic acid test for both
D. HIV nucleic acid test for the 3-year-old boy, and a HIV antibody with Western blot confirmation for the newborn
E. HIV RNA viral loads for both

Correct Answer: B
The best recommendation to evaluate the 3-year-old boy and female newborn for HIV infection is a HIV antibody with Western blot confirmation for the 3-year-old boy and a HIV nucleic acid test for the newborn.

HIV infection in young children (younger than 13 years of age, as defined by the US Centers for Disease Control and Prevention) who are presexual and have not been exposed to infected blood products or injectable drugs occurs through transmission from an HIV-infected mother to her child during pregnancy, labor, delivery, or breastfeeding. In contrast, adolescents and adults acquire the virus mostly through sexual and parenteral (injection drug use) transmission. More than 80% of the world's HIV infections are through heterosexual transmission, with women representing over half of the 35 million people living with HIV/AIDS. About 3.2 million, or about 9%, of the total are children younger than 15 years of age, with an estimated 240,000 new global pediatric cases in 2013.

HIV continues to be a major global problem, with only 1.2 million individuals, or less than 5% of the world's HIV-positive population, living in the United States. Aggressive prevention of mother-to-child transmission programs through early identification of HIV infection during pregnancy via prenatal screening, reduction of maternal HIV viral loads to undetectable levels with antiretroviral drugs, neonatal antiretroviral prophylaxis, and avoidance of breastfeeding by HIV infected mothers have dropped the number of neonates born with HIV in the United States from 1,650 in 1991 to 107 in 2013. Therefore, pediatric HIV has become quite rare, with most pediatricians' experience limited to assessment for HIV infection in neonates born to a HIV-positive mother.

HIV may be difficult to diagnose in early childhood because symptoms of HIV, such as lymphadenopathy, hepatosplenomegaly, oral candidiasis, failure to thrive, and developmental delays, are not specific to HIV. However, certain infections are AIDS-defining conditions, including Pneumocystis jirovecii pneumonia, esophageal candidiasis, and cytomegaloviral pneumonia, colitis, encephalitis, or retinitis, and should raise concern for HIV or other immune deficiencies.

HIV testing in children older than 18 months of age is the same as screening and diagnostic testing for adults and would begin with a laboratory-based fourth-generation HIV-1 antibody/HIV-2 antibody/p24 antigen immunoassay. While endemic in West Africa, HIV-2 is still rare in the United States, with only 166 confirmed cases from 1988 to 2010. Including the HIV p24 structural capsid protein antigen helps identify early infection during the 20- to 30-day window after infection has occurred until HIV antibody is present.

HIV testing in children younger than 18 months of age is more complicated because maternal HIV antibodies, which have crossed the placenta into the baby, can be detected far longer than the 2 to 6 months that is typical of other maternal antibodies. Thus, the HIV-1/2 immunoassay will be positive regardless of the infant's true status. Nucleic acid testing of unique viral genetic material, such as HIV DNA polymerase chain reaction or HIV RNA assays, is required to

correctly identify a true HIV infection in children younger than 18 months of age. HIV p24 antigen assays are not recommended for HIV testing in children younger than 18 months of age in the United States, as they are less sensitive than the aforementioned nucleic acid tests.

For individuals older than 18 months of age, nucleic acid testing is an alternative method of testing for HIV infection, but is not as sensitive as the current HIV-1/2 immunoassays. However, it currently assesses only for HIV-1 infection and should typically be used to clarify or confirm negative or indeterminate immunoassay results.

PREP Pearls

- Only 1.2 million people or less than 4% of the world's total HIV-positive population live in the United States. Only 107 infants infected with HIV were born in the United States in 2013.
- The recommended initial screening for individuals 18 months of age or older would be a fourth-generation HIV-1 Ab/HIV-2 Ab/p24 Ag immunoassay.
- The recommended initial screening for individuals younger than 18 months of age requires nucleic acid testing of unique viral genetic material, such as HIV DNA polymerase chain reaction or HIV RNA assays.

ABP Content Specifications(s)

- Plan appropriate screening for human immunodeficiency virus infection in at-risk infants and children older than 18 months of age
- Understand the epidemiology of human immunodeficiency virus, including the modes of transmission and how to minimize transmission risk
- Identify the clinical features associated with AIDS in patients of various ages

Suggested Readings

- American Academy of Pediatrics. Addendum: evaluation and management of the infant exposed to HIV-1 in the United States. Pediatrics. 2012;130(6):1183-1184. doi: http://dx.doi.org/10.1542/peds.2012-2965.
- American Academy of Pediatrics. Human immunodeficiency virus infection. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:453-476.
- Branson BM, Owen SM, Wesolowski LG, et al. Laboratory testing for the diagnosis of HIV infection: updated recommendations. US Centers of Disease Control and Prevention website. http://stacks.cdc.gov/view/cdc/23447.
- Havens PL, Mofenson LM. Clinical report: evaluation and management of the infant exposed to HIV-1 in the United States. Pediatrics. 2009;123(1):175-187. doi: http://dx.doi.org/10.1542/peds.2008-3076.

Question 109

A 3-month-old female infant presents to the emergency department with vomiting, decreased activity, and poor weight gain. She was born to a 36-year-old gravida 2, para 1 woman at 34 weeks of gestation via cesarean delivery because of a breech presentation. The pregnancy was complicated by gestational diabetes and maternal seizure disorder. On physical examination, the infant is fussy. Her weight is 4.1 kg (birthweight of 2.9 kg), temperature is 37.3°C, heart rate is 130 beats/min, and respiratory rate is 30 breaths/min. She has decreased skin turgor and dry mucous membranes. Her examination is otherwise unremarkable. Laboratory tests are shown:

Laboratory Test	**Patient Result**
Serum Results	
Sodium	129 mEq/L (129 mmol/L)
Potassium	3.2 mEq/L (3.2 mmol/L)
Chloride	82 mEq/L (82 mmol/L)
Bicarbonate	41 mEq/L (41 mmol/L)
Blood urea nitrogen	27 mg/dL (9.6 mmol/L)
Creatinine	0.4 mg/dL (35 μmol/L)
Glucose	98 mg/dL (5.4 mmol/L)
Calcium	9.6 mg/ dL (2.4 mmol/L)
Phosphorus	5.2 mg/dL (1.68 mmol/L)
Urine Results	
Sodium	41 mEq/L (41 mmol/L)
Potassium	114 mEq/L (114 mmol/L)
Chloride	80 mEq/L (80 mmol/L)

Of the following, the MOST likely diagnosis in the patient is

A. Bartter syndrome
B. cystic fibrosis
C. distal renal tubular acidosis (RTA)
D. proximal RTA
E. pyloric stenosis

Correct Answer: A

The infant in the vignette presents with inadequate weight gain, metabolic alkalosis, hypokalemia, hyponatremia, and hypochloremia. Among the response choices, her most likely diagnosis is Bartter syndrome.

Hypochloremia in clinical settings is usually associated with metabolic alkalosis resulting from chloride loss associated with gastrointestinal or renal losses. In patients with hypochloremia and metabolic alkalosis, chloride depletion contributes to persistent alkalosis. Evaluation and treatment for the underlying metabolic alkalosis is the preferred approach for patients with hypochloremia.

The underlying cause of metabolic alkalosis is not usually apparent based on a patient's presenting history and physical examination. Urine chloride measurement is helpful in identifying intravascular volume status and thereby the underlying etiology of metabolic alkalosis. The renal response to decreased effective circulating volume (dehydration) is to increase reabsorption of salt (sodium chloride) and water, thereby increasing effective circulatory volume. This leads to low urinary sodium and chloride (< 20 mEq/L [20 mmol/L]) concentrations. Urinary chloride is a better indicator of volume status than urinary sodium in metabolic alkalosis because sodium is the cation binding to the increased bicarbonate filtered into the tubular fluid. Thus, urinary chloride is appropriately low (< 20 mEq/L) in patients with volume contraction compared with urinary sodium, which may be increased in response to increased tubular bicarbonate. Identification of hypovolemia (low urinary chloride) versus volume repletion (urinary chloride > 40 mEq/L [40 mmol/L]) helps in identifying the underlying etiology of metabolic alkalosis.

Renal tubular disorders with sodium chloride wasting present with metabolic alkalosis in association with high urinary chloride levels (> 20–40 mEq/L). Both Bartter syndrome and Gitelman syndrome are characterized by hypokalemia and metabolic alkalosis. Bartter syndrome results from a primary defect in sodium chloride reabsorption in the medullary thick ascending limb of the loop of Henle, similar to the effect of chronic furosemide therapy. Bartter syndrome often presents in childhood with growth restriction, hypokalemia, metabolic alkalosis, and polyuria or polydipsia. Gitelman syndrome results from mutations in the gene coding for the thiazide-sensitive sodium chloride transporter in the distal tubule. Gitelman syndrome generally presents in late childhood or adulthood with muscle cramps (hypokalemia), polyuria, and/or polydipsia. In contrast to Bartter syndrome, patients with Gitelman syndrome have reduced urinary calcium and hypomagnesemia (more common). Children with either Bartter or Gitelman syndrome will be volume depleted because of excessive salt and water losses secondary to the underlying renal tubular defects. This volume depletion accounts for the compensatory hyperreninemia and hyperaldosteronism seen in these patients.

Patients with mineralocorticoid excess, such as primary aldosteronism, Liddle syndrome, apparent mineralocorticoid excess syndrome, or licorice ingestion (glycyrrhizic acid) typically present with hypertension, hypokalemia, and metabolic alkalosis (with high urinary chloride). Chronic therapy with loop or thiazide diuretics leads to volume depletion (contraction) and metabolic alkalosis associated with a high urinary chloride level. In patients with diuretic abuse, the urinary chloride may vary from low to high depending on diuretic use.

Excessive loss of gastric secretions leading to loss of hydrochloric acid, as seen with vomiting, pyloric stenosis, or continuous nasogastric suctioning may present with metabolic alkalosis, volume depletion, and a low urinary chloride level (<20 mEq/L). Metabolic alkalosis with low urinary chloride level (< 20 mEq/L) is also seen in patients with laxative abuse, cystic fibrosis with loss of chloride-rich sweat, and congenital chloride diarrhea.

The diagnosis of renal tubular acidosis (RTA) should be considered in a young infant with failure to thrive, recurrent vomiting, rickets, episodes of dehydration, recurrent nephrolithiasis, and persistent metabolic acidosis and hypokalemia. Renal tubular acidosis is an inherited or acquired defect in the ability of the kidneys to either absorb filtered bicarbonate or excrete ammonia, and is characterized by a normal anion gap metabolic acidosis. There are 4 forms of RTA: distal or type 1, proximal or type 2, mixed or type 3 (with features of both type 1 and 2), and hypoaldosteronism or type 4. distal RTA is associated with failure to thrive, polyuria, hypokalemia, and medullary nephrocalcinosis (due to hypercalciuria and hypocitraturia). Generalized proximal tubular dysfunction is seen in patients with Fanconi syndrome. In addition to metabolic acidosis and hypokalemia, Fanconi syndrome is associated with rickets (phosphaturia leading to hypophosphatemic rickets), dipstick-positive glucosuria with normal plasma glucose concentration, and aminoaciduria/tubular proteinuria (urine dipstick-negative for protein and quantitative urine tests positive for amino acids and protein).

PREP Pearls

- Hypochloremia is usually seen in association with metabolic alkalosis.
- Urine chloride measurement is helpful in assessing intravascular volume status, and thereby the underlying etiology of metabolic alkalosis.
- Mineralocorticoid excess, or renal tubular disorders with sodium chloride wasting (Bartter and Gitelman syndrome), present with metabolic alkalosis in association with high urinary chloride levels (> 20–40 mEq/L [20–40 mmol/L]).
- Bartter syndrome is caused by a primary defect in sodium chloride reabsorption in the medullary thick ascending limb of the loop of Henle, as seen in chronic furosemide therapy.
- Metabolic alkalosis with low urinary chloride (< 20 mEq/L) is seen in patients with gastrointestinal losses, laxative abuse, cystic fibrosis with loss of chloride-rich sweat, and congenital chloride diarrhea.

ABP Content Specifications(s)

- Recognize the various etiologies of hypochloremia

Suggested Readings

- Jaffe AC. Failure to thrive: current clinical concepts. *Pediatr Rev*. 2011;32(3):100-108. doi: http://dx.doi.org/10.1542/pir.32-3-100.
- Kallen RJ. Renal tubular acidosis. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DM, eds, *American Academy of Pediatrics Textbook of Pediatric Care*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:2554-2571..
- Schwaderer AL, Schwartz GJ. Back to basics: acidosis and alkalosis. *Pediatr Rev*. 2004;25(10):350-357. http://pedsinreview.aappublications.org/content/25/10/350.extract.

Question 110

A 16-year-old adolescent boy presents to your clinic for evaluation of nose pain and swelling after he was hit in the face while playing basketball. His nose bled immediately after the incident, but this was controlled quickly with pressure to his nasal bridge. He complains of swelling, difficulty breathing through his nose, and pain when his nose is touched. On physical examination, the distal portion of the patient's nasal bone is deviated to the right. He has dried blood at the edge of each naris. Inspection of his intranasal cavity reveals a tense red mass on each side of his nasal septum (Item Q110).

Item Q110: Nasal septum from the patient described in the vignette.
Reprinted with permission from Reprinted with permission from Ginsburg CM, Leach JM. Infected nasal

Of the following, the BEST next step in management of this patient's condition is

A. closed reduction of the fracture

B. drainage of the mass

C. follow-up visit in 2 weeks

D. intranasal phenylephrine

E. oral clindamycin

Correct Answer: B
This patient in the vignette has a nasal septal hematoma that must be drained. Hematomas form when blood accumulates between the septal cartilage and the overlying mucosal layer, typically after nasal trauma. Patients experience nasal obstruction, pain, and rhinorrhea. On physical examination, a red or blue fluctuant mass arising from the septum obstructs the nasal cavity. The mass is most often bilateral, but can be unilateral. Septal hematomas are fluctuant and boggy, whereas a deviated nasal septum is firm to palpation. Untreated, septal hematomas exert pressure on the adjacent cartilage, causing ischemia and necrosis. Irreversible necrosis can occur within 72 to 96 hours and leads to deformity. Therefore, prompt drainage is imperative.

Neither management of an associated fracture without drainage of the hematoma nor follow-up in 2 weeks would be appropriate in the presence of a septal hematoma. Intranasal phenylephrine and other decongestants would not be effective in alleviating pressure on the nasal cartilage or preventing ischemia in this case. Although antibiotics are typically used in the postdrainage treatment of nasal septal hematoma, antibiotic administration would not be the best next step in management.

PREP Pearls

- Nasal septal hematomas present with nasal obstruction, pain, and rhinorrhea after trauma.
- Physical examination findings of nasal septal hematomas include a fluctuant red or bluish mass arising from the septum.
- Prompt drainage of a nasal septal hematoma is imperative to prevent nasal cartilage ischemia, necrosis, and deformity.

ABP Content Specifications(s)

- Recognize the physical findings associated with a hematoma of the nasal septum, and manage appropriately

Suggested Readings

- Ginsburg C. Consultation with the specialist: nasal septal hematoma. *Pediatr Rev.* 1998;19(4):142-143. doi: http://dx.doi.org/10.1542/pir.19-4-142.
- Sanyaolu LN, Farmer SE, Cuddihy PJ. Nasal septal hematoma. *BMJ*. 2014;349:g6075-g6079. doi: http://dx.doi.org/10.1136/bmj.g6075.
- Sayim I, Yazici ZM, Bokurt E, Kayham F. Nasal septal hematoma and abscess in children. *J Craniofac Surg*. 2011;22(6):e17-e19. doi: http://dx.doi.org/10.1097/SCS.0b013e31822ec801.

Question 111

You are seeing a 12-year-old boy with Duchenne muscular dystrophy for a health supervision visit. He has had 2 episodes of pneumonia in the last year, involving the right upper and left lower lobe, respectively. He is confined to a wheelchair because of moderate to severe diffuse muscle weakness and atrophy. He has moderate scoliosis with a thoracolumbar curvature of 40 degrees. The boy continues to eat and drink by mouth, and there is no reported choking, gagging, or coughing with oral intake. He is unable to perform pulmonary function testing with acceptable or reproducible technique. A videofluoroscopic swallow study, obtained 2 years ago, demonstrated laryngeal penetration with thin liquids and nectar thick liquids. During a recent hospitalization, polysomnography confirmed normal oxygenation and ventilation during sleep. Bronchoscopy revealed diffuse airway mucosal inflammation with a significantly elevated lipid-laden macrophage count.

The boy is seated in a motorized wheelchair. On physical examination, his vital signs are normal. He is diffusely weak. An examination of his head, eyes, ears, nose, and throat is normal. The boy's lungs are clear throughout, with fair to moderate aeration. There are no retractions. His cardiac rhythm is normal with a 2/6 systolic ejection murmur heard at the left sternal border. His abdomen is soft and nontender. His extremities are warm and well perfused.

Of the following, the management option MOST likely to prevent pneumonia in this patient is

A. high-frequency chest wall oscillation therapy
B. modification of his feeding regimen
C. nocturnal bilevel positive airway pressure
D. posterior spinal fusion
E. treatment with sildenafil

Correct Answer: B
For the boy in the vignette, given the time elapsed since his most recent swallowing study, the management option most likely to prevent pneumonia would be modification of his feeding regimen. Reassessment of his aspiration risk would be recommended. In the setting of neuromuscular weakness, such as in Duchenne muscular dystrophy, chronic pulmonary aspiration is the most likely cause of recurrent pneumonia. Feeding by mouth is an activity that typically provides great pleasure to both the affected child and his family, therefore, the risk of aspiration-related pulmonary disease must be assessed with consideration of the child's quality of life. Decisions regarding modification of feeding regimens will vary widely, based on individual and family wishes, and these conversations should begin at an early point in disease management.

Normally, swallowing is a complex process of coordination involving skeletal and smooth musculature, cranial and spinal innervation, and the autonomic nervous system, as well as volitional and reflexive control mechanisms. In patients with profound muscular weakness, the normal protective laryngeal reflexes are frequently compromised or absent, and direct aspiration may occur with eating, drinking, or oral secretions. Furthermore, the lower esophageal sphincter may lack tone, allowing gastroesophageal refluxate to reach the thoracic inlet with aspiration into the tracheobronchial tree. The gastric acid may further compromise laryngeal sensation and function. The long-term effects of pulmonary aspiration can be devastating. Related inflammatory changes may cause scarring and/or bronchiectasis, and may contribute to chronic respiratory failure. Aspiration is the primary cause of death in neurologically impaired children. A high index of suspicion is required to diagnose chronic pulmonary aspiration, particularly in patients with neuromuscular dysfunction. Although aspiration into the tracheobronchial tree is typically associated with cough, choking, or gagging, patients with neuromuscular weakness often lack the muscle tone and strength needed to demonstrate these symptoms. Cough, even when present, may be ineffective. The child with neuromuscular disease is therefore at risk for silent aspiration; food or liquid may pass through and below the level of the true vocal cords without reflexive cough or other obvious symptoms. Normal chest radiography in a child with suggestive symptoms does not exclude the diagnosis of aspiration.

Various methods are available to evaluate a child for pulmonary aspiration. A videoflouroscopic swallow study (VFSS) is the only assessment method that provides visualization of the oral, pharyngeal, laryngeal, and upper esophageal phases of swallowing. In an attempt to limit the child's exposure to ionizing radiation, the study often does not evaluate the late portion of feedings, and will not assess for "fatigue aspiration" unless this component is specifically requested. Although adult studies have demonstrated high sensitivity with moderate specificity, data on the sensitivity and specificity of the VFSS in children are limited.

A fiberoptic endoscopic evaluation of swallowing is generally performed collaboratively with both otolaryngology and speech and language pathology. A laryngoscope is inserted through the nose, and the patient eats and drinks while the larynx is under direct visual inspection, allowing observation of any salivary, liquid, or solid aspiration.

Bronchoscopic examination of a child with chronic pulmonary aspiration will often demonstrate diffuse inflammation. A lipid-laden macrophage index (LLMI) may be obtained with bronchoalveolar lavage, but is technique dependent. Recent data demonstrated that an LLMI of more than 165 had 98.6% sensitivity, 78% specificity, and 87.8% overall accuracy as a diagnostic test of aspiration (112 children). An elevated LLMI may also be found in other conditions such as cystic fibrosis, pulmonary fat embolism, and in those receiving total parenteral nutrition with intralipids.

Radionuclear testing for aspiration involves the placement of a small aliquot of a radioactive tracer into the buccal pouch, followed by serial imaging to determine if tracer activity is later detectible in the trachea or lower airway. This method has generally fallen out of favor because of low sensitivity and specificity.

If oral feeding or drinking appears to be unsafe, modification of the feeding regimen should be pursued. Thickening of liquids taken by mouth may allow more functional laryngeal sensation in children with mild compromise. In more severe cases of laryngeal and/or muscular dysfunction, an alternate feeding route may be necessary, such as a nasogastric tube. This would require the education of caregivers regarding proper placement and maintenance. Alternatively, a gastrostomy or jejunostomy tube may be placed using either a traditional or minimally invasive technique. For those with chronic salivary aspiration, salivary gland ligation and/or excision may be considered in consultation with an otolaryngologist. Medications such as glycopyrrolate or scopalomine may be prescribed to decrease salivation, but their side effect profiles must be considered.

High-frequency chest wall oscillation would provide improved airway clearance. However, without an effective cough, clearance will still be compromised and airway damage will continue from unaddressed pulmonary aspiration events. A recent polysomnogram suggested effective nocturnal ventilation, therefore, nocturnal bilevel positive airway pressure would not prevent the boy's recurrent pneumonias. Of note, children with neuromuscular weakness and even mild degrees of sleep-disordered breathing are at risk for loss of functional residual capacity and recurrent atelectasis, which may mimic recurrent pneumonia. Therefore, regular evaluations of sleep efficiency and sleep-related ventilation are recommended for affected children. Although the boy's scoliosis may contribute to restrictive lung disease and compromised spinal and chest wall muscular activity, a posterior spinal fusion would not resolve the muscular weakness and laryngeal sensation defects that contribute to chronic aspiration. Finally, children with chronic pulmonary aspiration and/or chronic sleep-disordered breathing are at risk for pulmonary hypertension and cor pulmonale. This boy's systolic murmur merits further evaluation, but treatment with sildenafil would not prevent episodes of pneumonia, and therefore would not be the initial step in management.

PREP Pearls

- Children with neuromuscular weakness may experience silent pulmonary aspiration, and a high index of suspicion is required to prevent associated morbidity and mortality.
- Chronic pulmonary aspiration may occur directly with oral secretions, oral intake, or during reflux events.
- A multidisciplinary approach to patients with chronic pulmonary aspiration, including primary care, pulmonary medicine, otolaryngology, speech and language pathology, and nutrition, among others, is beneficial.
- Chronic pulmonary aspiration is a leading cause of morbidity and mortality in patients with neuromuscular weakness.

ABP Content Specifications(s)

- Recognize the significance of pneumonia in a child with a neuromuscular disease, and manage appropriately

Suggested Readings

- Boesch RP, Daines C, Willging JP, et al. Advances in the diagnosis and management of chronic pulmonary aspiration in children. *Eur Resp J.* 2006;28(4):847-861. doi: http://dx.doi.org/10.1183/09031936.06.00138305.
- Furuya ME. Cutoff value of lipid laden alveolar macrophages for diagnosing aspiration in infants and children. *Pediatr Pulmonol.* 2007;42(5):452-457. doi: http://dx.doi.org/10.1002/ppul.20593.
- Tutor JD, Gosa MM. Dysphagia and aspiration in children. *Pediatr Pulmonol.* 2012;47(4):321-337. doi: http://dx.doi.org/10.1002/ppul.21576.

Question 112

A 22-month-old boy is brought to your clinic for persistent vomiting. His mother reports that for the past 2 weeks he has woken up most mornings, complained of a headache, and vomited once or twice, but after that, he is able to eat and drink normally for the rest of the day. He has not had a fever, abdominal pain, diarrhea, constipation, or sick contacts. On physical examination, his growth parameters are normal, and his heart, pulmonary, and abdominal examinations are unremarkable. His neurological examination shows equal use of all extremities, normal reflexes, and a stiff-legged, wobbly gait.

Of the following, the additional finding MOST likely to be seen in this child is

A. clinodactyly
B. head tilt
C. periorbital edema
D. petechiae
E. sacral hair tuft

Correct Answer: B
Early morning vomiting, headache, and gait imbalance is the clinical triad that suggests increased intracranial pressure due to a posterior fossa brain tumor. New head tilt or torticollis can also be seen when there is a tumor in this location, and of the choices, would be the additional finding most likely to be seen in the child in this vignette. Other presenting signs and symptoms of a posterior fossa brain tumor can come from involvement of the cerebellum (ataxia, dysmetria, nystagmus) or brainstem (dysconjugate gaze, hemifacial weakness, hemiparesis, or Horner syndrome [ipsilateral miosis, ptosis, and anhidrosis]). Signs of increased intracranial pressure include headache, nausea, vomiting, and encephalopathy. It is important for clinicians to know that early morning headaches are common in children and can have a variety of causes, including migraine and sleep apnea. As in the case in the vignette, it is the prominent early-morning vomiting that is most suggestive of a posterior fossa brain tumor. Primary brain tumors in children younger than 4 years of age often occur in the posterior fossa. Common posterior fossa brain tumors in children include medulloblastomas, ependymomas, pilocytic astrocytomas, atypical teratoid rhabdoid tumors, and brainstem gliomas. Medulloblastoma is the most common malignant primary brain tumor in childhood, with an incidence of 0.51 per 100,000 person-years; the incidence peaks from ages 5 to 9 years. Early clinical symptoms and presentation do not differ based on tumor type, so diagnosis is based on imaging characteristics and pathology. If a brain tumor or increased intracranial pressure is suspected, urgent brain imaging with either computed tomography or magnetic resonance is needed.

Clinodactyly, an incurving of the digits of the hands, can be seen in isolation or in association with one of many genetic syndromes, but not brain tumors. Sacral hair tuft is associated with spinal cord malformations, not with brain tumors. Periorbital edema and petechiae are possible sequelae or complications of brain tumors and their treatment, but they are not typical presenting signs of brain tumors in children.

PREP Pearls

- Early morning vomiting, not just headache, is suggestive of a posterior fossa brain tumor.
- New head tilt or torticollis can be a presenting sign of a brain tumor.

ABP Content Specifications(s)

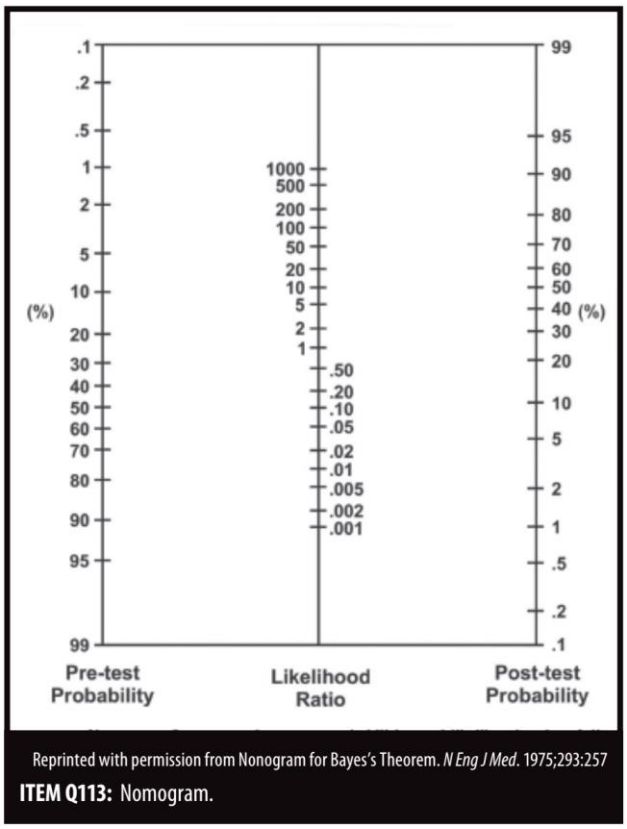
- Recognize the clinical findings associated with a brain tumor, including craniopharyngioma

Suggested Readings

- Crawford J. Childhood brain tumors. *Pediatr Rev*. 2013;34(2):63-78. doi: http://dx.doi.org/10.1542/pir.34-2-63.
- Medina LS, Kuntz JM, Pomeroy S. Children with headache suspected of having a brain tumor: a cost-effectiveness analysis of diagnostic strategies. *Pediatrics*. 2001;108(2):255-263. doi: http://dx.doi.org/10.1542/peds.108.2.255.

Question 113

A 2-month-old male infant presents to the emergency department in late winter with a 2-day history of cough, rhinorrhea, decreased feeding, and progressive difficulty breathing. Based on the infant's clinical picture and the case mix you have seen recently, you estimate an approximately 50% chance that he is infected with respiratory syncytial virus (RSV). You send a rapid RSV antigen test, which is positive. It is known that patients who have RSV are 5 times more likely to have a positive test than are patients who do not have the disease.



Reprinted with permission from Nonogram for Bayes's Theorem. *N Eng J Med*. 1975;293:257

ITEM Q113: Nomogram.

Applying the nomogram shown in Item Q113, the post-test probability that he has RSV is

A. 1%

B. 20%

C. 50%

D. 80%

E. 99%

Correct Answer: D
The infant in the vignette has symptoms of bronchiolitis. The pre-test probability that he has a respiratory syncytial virus (RSV) infection is approximately 50%, based on your estimate of the prevalence of RSV and taking into account the entire clinical picture, including demographics, presentation, location, and season.

To best determine the post-test probability of whether he has RSV infection, the clinician should take into account:

1. The probability that he has the disease prior to sending the test, which is known as the pre-test probability
2. The degree to which the results of the test changes the probability, which is known as the likelihood ratio (LR)
3. The result of the test

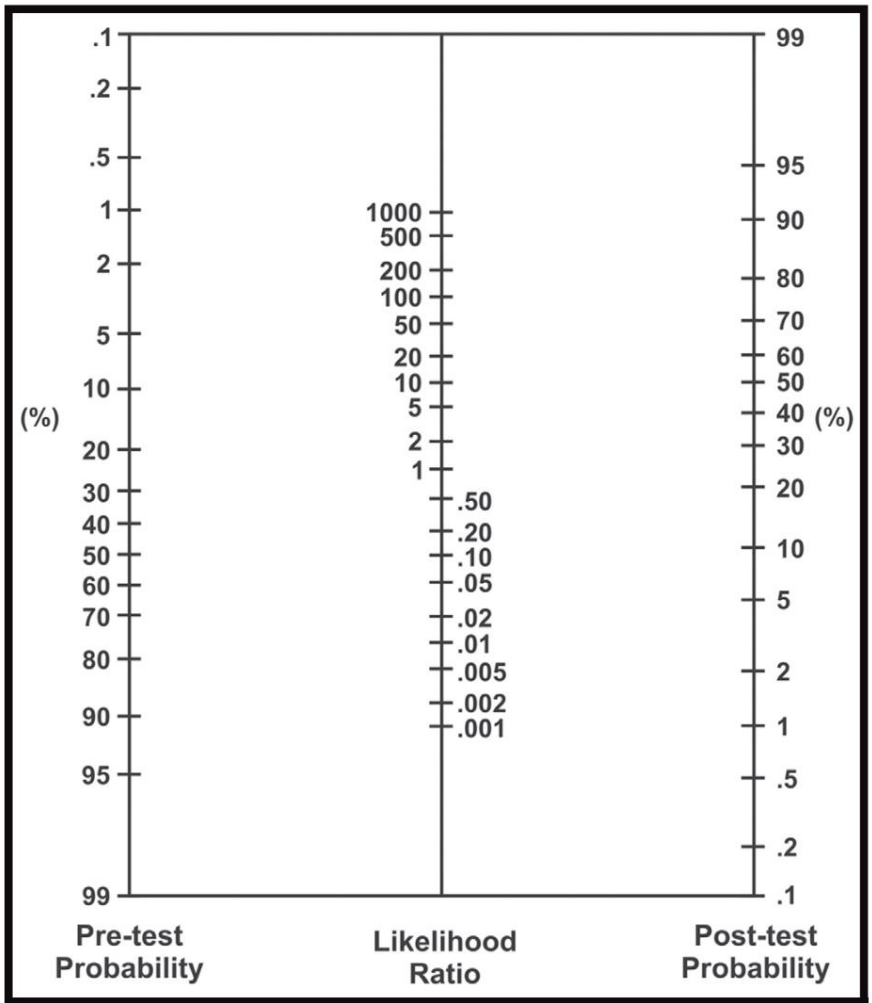
The likelihood ratio (LR) is the percentage of people with an illness with a given test result divided by the percentage of people without the illness with the same test result. Sensitivity, specificity, LR for a positive test, and LR for a negative test can all be calculated with a 2 x 2 table as shown in Item C113A. The Fagan nomogram (Item C113B) can be used to determine how a test with a known LR can predict the post-test probability if the pretest probability is known. This is done by drawing a straight line starting from the pretest probability through the likelihood ratio and recording the result of the post-test probability.

C113A. Calculation of the Sensitivity, Specificity, and Likelihood Ratio (LR).

	Disease	
Positive Test Result	Present a	Absent b
Negative Test Result	c	d
	a+c	b+d

Sensitivity = a/(a+c)
Specificity = d/(b+d)
LR for a positive test = [a/(a+c) ÷ b/(b+d)] or sensitivity ÷ (1-specificity)
LR for a negative test = [c/(a+c) ÷ d/(b+d)] or (1-sensitivity) ÷ specificity

Reprinted with permission form Crewe S and Rowe PC. "Research and Statistics: Likelihood Ratio in Diagnosis." *Pediatr Rev.* 2011;32;296.



Reprinted with permission from Nomogram for Bayes's Theorem, *N Engl J Med.* 1975; 293:257

ITEM C113B: Fagan nomogram.

Incidence is the rate of disease occurrence and prevalence is the number of cases of disease existing in a given population. Incidence and prevalence are directly proportional to pretest probability and therefore impact post-test probability when a test with a given LR is applied. For example, if one is considering whether a patient with fever and toxic appearance has Ebola in the United States, post-test probability with a positive test will still be very low, even if the test were relatively sensitive and specific,because the prevalence of Ebola is almost zero. Conversely, if one is clinically certain that a patient has a disease, the post-test probability would still be high even after a negative test. In both scenarios, the clinician should consider not testing because the result would not likely change management.

For the infant in the vignette, you have assigned a pretest probability of 50%, so a positive test must lead to a post-test probability of greater than 50%. Since patients with RSV are 5 times more likely to have a positive RSV test than patients without RSV, the LR is 5. To conclude an approximate post-test probability of 80%, a line is drawn starting from 50% through the LR of 5.

PREP Pearls

- The Fagan nomogram can be used to ascertain post-test probability when a likelihood ratio is applied to a given pretest probability.
- The pretest probability takes into account the clinical picture and incidence and prevalence of a disease in the selected population.

ABP Content Specifications(s)

- Understand pre-test and post-test probability
- Understand prevalence and incidence

Suggested Readings

- Carvajal DN, Rowe PC. Research and statistics: sensitivity, specificity, predictive values, and likelihood ratios. *Pediatr Rev.* 2010;31(12):511-513. doi: http://dx.doi.org/10.1542/pir.31-12-511.
- Crewe S, Rowe PC. Research and statistics: likelihood ratio in diagnosis. *Pediatr Rev.* 2011;32(7):296-298. doi: http://dx.doi.org/10.1542/pir.32-7-296.

Question 114

A 15-year-old Hispanic female adolescent is seen for follow-up in your clinic 1 month after receiving a diagnosis of type 2 diabetes. Her diagnosis followed an evaluation for recurrent vaginal candidiasis and was based on a fasting plasma glucose of 130 mg/dL (7.2 mmol/L) and a hemoglobin $A1_C$ of 7.8%. Low-density lipoprotein cholesterol was 120 mg/dL (3.1 mmol/L). Metformin was started and she was seen by a nutritionist and a diabetes educator. She has made healthy changes in her diet and is now walking 1 hour per day. Her blood sugars have gradually decreased into the 90 to 120 mg/dL (5-6.7 mmol/L) range. On physical examination today, her temperature is 37°C, blood pressure is 125/82 mm Hg, heart rate is 89 beats/min, weight is 80 kg, height is 158 cm, and body mass index is 32 kg/m^2 (> 95th percentile). She has acanthosis nigricans over the nape of her neck. Cardiovascular, respiratory, and abdominal examinations are normal.

Of the following, the BEST test to obtain today is

A. electrolytes
B. hemoglobin A1C
C. spot urine albumin-to-creatinine ratio
D. thyroid-stimulating hormone
E. tissue transglutaminase antibody

Correct Answer: C
As hyperglycemia is present for an undetermined amount of time prior to the diagnosis of type 2 diabetes mellitus (DM), screening for comorbidities and long-term complications should begin at diagnosis. These screening tests include a blood pressure and lipid panel as cardiovascular disease risk factors, dilated eye examination for retinopathy, foot examination for neuropathy, and spot urine albumin-to-creatinine ratio for albuminuria/nephropathy. The patient described in the vignette has not yet had a urine albumin-to-creatinine ratio, so it is indicated at this time. Although not given as answer choices, she should also have a dilated retinal examination and baseline foot examination.

In type 2 DM, the timing of some screening tests is different than for type 1 DM. For type 1 DM, given the prolonged exposure to hyperglycemia required for development of complications, recommendations for screening for retinopathy are at least 10 years of age and at least 3 to 5 years of diabetes; for albuminuria, at least 5 years of diabetes. Thyroid-stimulating hormone and tissue transglutaminase antibody, a screening test for celiac disease, are recommended screening tests for type 1 DM given the autoimmune etiology, but not for type 2 DM. It is too soon to check a hemoglobin A1c. The hemoglobin A1c correlates with the last 2 to 3 months of blood sugars and would still reflect prediagnosis values. The 3-month follow-up visit would be a more appropriate time to recheck the hemoglobin A1c. Electrolytes would not add additional information.

The patient described in the vignette meets diagnostic criteria for diabetes with a fasting plasma glucose greater than or equal to 125 mg/dL (6.9 mmol/L) and a hemoglobin A1c greater than or equal to 6.5%. Her presenting symptom of recurrent vaginal candidiasis is common in females with type 2 DM. Her age, Hispanic ethnicity, and obesity are risk factors for type 2 DM. Her acanthosis nigricans is a sign of insulin resistance and her elevated blood pressure is a feature of the metabolic syndrome, also associated with insulin resistance.

Short-term complications of type 2 DM include hyperglycemic hyperosmolar state and, less frequently, diabetic ketoacidosis. Features of the hyperglycemic hyperosmolar state include altered mental status and significant hyperglycemia without significant acidosis or ketosis.
A 2013 American Academy of Pediatrics clinical practice guideline outlines the management of newly diagnosed type 2 DM in children and adolescents. Insulin and metformin are the only pharmacologic agents currently US Food and Drug Administration-approved for treatment of type 2 DM in youth. Insulin should be initiated when ketosis is present, when the plasma glucose is greater than or equal to 250 mg/dL or hemoglobin A1c is greater than 9%, or when the diagnosis of type 1 DM versus type 2 DM is not clear. Transition to oral metformin may be possible once glycemic control is achieved. As for the patient described in the vignette, metformin is the first-line pharmacologic therapy for those who do not meet criteria for insulin and should be started at diagnosis. For all patients with type 2 DM, healthy lifestyle changes in diet and physical activity are very important. Optimally, care is provided by a diabetes team, including a diabetes educator, nutritionist, and behavioral therapist. Self-monitoring of blood glucose should occur for those on insulin, when treatment regimen is initiated or changed, for

those not meeting treatment goals, and during acute illnesses. Hemoglobin A1c should be measured every 3 months, with a goal of less than 7% in most cases.

PREP Pearls

- Screening for comorbidities and long-term complications of type 2 diabetes mellitus should begin at diagnosis.
- In the absence of ketosis and significant hyperglycemia, metformin is the first-line pharmacologic therapy for type 2 diabetes and should be initiated at diagnosis.
- Lifestyle modifications regarding nutrition and physical activity should be a part of the management plan for all children and adolescents with type 2 diabetes.

ABP Content Specifications(s)

- Recognize the short- and long-term complications associated with type 2 diabetes
- Plan the appropriate management of type 2 diabetes

Suggested Readings

- American Diabetes Association. Standards of medical care in diabetes: (11) Children and adolescents. *Diabetes Care*. 2015;38(Suppl):S70-S76. doi: http://dx.doi.org/10.2337/dc15-S014.
- Copeland KC, Silverstein J, Moore KR, et al. Management of newly diagnosed type 2 diabetes mellitus (T2DM) in children and adolescents. *Pediatrics*. 2013;131(2):364-382. doi: http://dx.doi.org/10.1542/peds.2012-3494.
- Dileepan K, Feldt MM. Type 2 diabetes mellitus in children and adolescents. *Pediatr Rev*. 2013;34(12):541-548. doi: http://dx.doi.org/10.1542/pir.34-12-541.
- Springer SC, Silverstein J, Copeland K, et al. Management of type 2 diabetes mellitus in children and adolescents. *Pediatrics*. 2013;131(2):e648-e664. doi: http://dx.doi.org/10.1542/peds.2012-3496.

Question 115

You are seeing a 12-year-old girl in your clinic for a health supervision visit. She is concerned about the new appearance of "dirt" in her ears, which she is unable to remove. On physical examination, her vital signs, growth velocity, and body mass index are all within normal range for age. Her sexual maturity rating is 2 for breast and 3 for pubic hair development. The remainder of her examination is unremarkable, except for the skin findings on both ears (Item Q115).

Item Q115: Findings for the girl described in the vignette. Pediatrics in Review July 1, 2005 vol. 26 no. 7 250-261 doi: 10.1542/pir.26-7-250 Reprinted with permission of Hanley & Belfus, from Lucky AW. Managing adolescent acne. Adolesc Med. 2002;12:355-374 Krowchuk DP, Lucky AW. Managing adolescent acne. Adolesc Med. 2002;12:355–374 - Hanley & Belfus publisher Duryea

Of the following, the BEST description of this girl's acne is

A. closed comedonal
B. nodular
C. open comedonal
D. popular
E. pustular

Correct Answer: C
The girl in the vignette has open comedonal acne, which is characterized by small dome-shaped papules with an open orifice that appears blackened. The black color is speculated to be secondary to oxidation of keratinous lipoid material at the opening, deposition of melanin, or interference of light transmission.

Acne vulgaris is a very common skin disorder that can occur at any age, but primarily affects adolescents and young adults. It is important for pediatric healthcare providers to recognize the clinical findings of the different types and degrees of acne to educate patients and prescribe appropriate therapy.

Acne vulgaris is a chronic inflammatory process of the pilosebaceous unit. Increased sebum production, obstruction of the follicular ostium, proliferation of *Propionibacterium acnes*, and secondary inflammation all contribute to the development of acne. Acne can be classified as comedonal (closed or open), inflammatory (papules, pustules, nodules, cysts), or mixed. Closed comedones are tiny yellowish-white or flesh-colored papules without surrounding erythema, commonly known as whiteheads. They are caused by obstructed follicles leading to trapped epithelial cells and sebum. Open comedones have a dilated follicular orifice that gives the blackhead appearance. As comedones rupture and become inflamed, erythematous papules or pustules are created. Pustules larger than 5 mm in diameter are termed nodules. As these lesions grow deeper and larger, sinus tracts and cysts can develop. The degree of inflammation is key to potential scar formation.

Acne is often classified as mild, moderate, or severe. The number and type of lesions, distribution, and the presence or absence of scarring are typically considered in grading severity (Item C115A).

Item C115A. Acne Severity.

Grading	Predominant Lesion Type	Distribution	Scarring	Other Factors
Mild	Few to several comedones, few scattered papules	Less than one-fourth of face, mostly T zone	None	None
Moderate	Many papules and pustules, variable comedones, 1 to 2 nodules	Roughly one-half of face	Few, shallow	Involvement of the chest and back
Severe	Numerous papules and pustules and nodules; variable comedones; sinus tracts and/or cysts	Face, back, and/or chest	Moderate to extensive, hypertrophic and/or deep	Drainage, hemorrhage, pain

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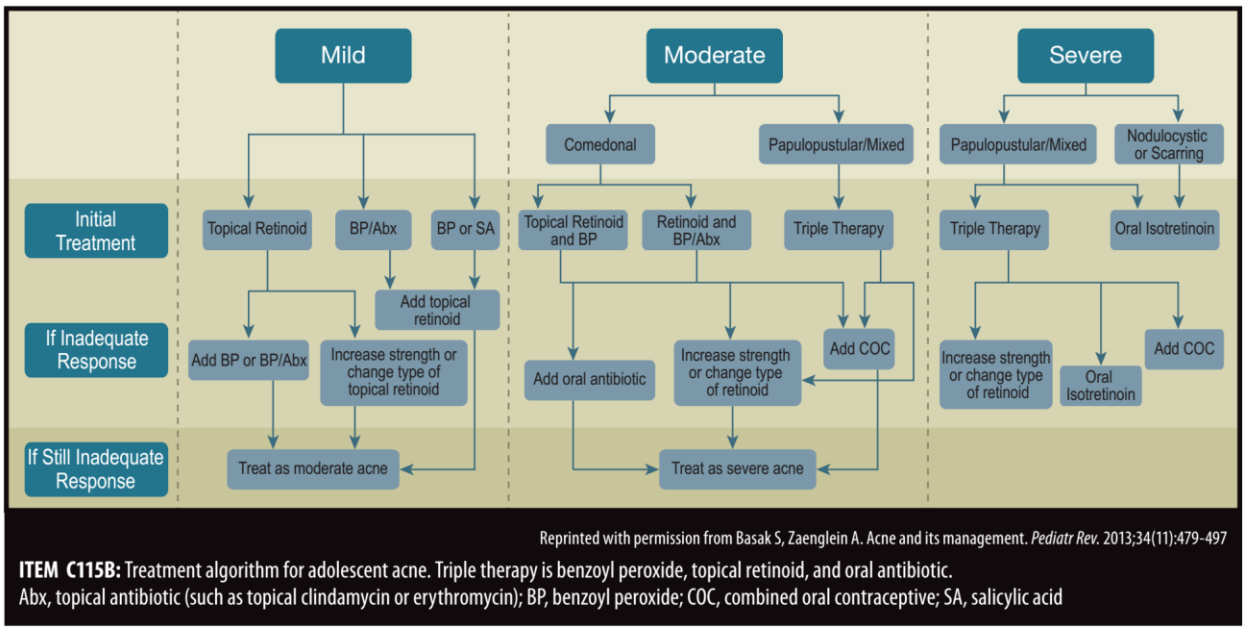
Evidence-based guidelines from the American Acne and Rosacea Society, and endorsed by the American Academy of Pediatrics, were published in 2013. Effective treatment (Item C115B) must be individualized, based on the type and severity of acne, while considering the response to previously attempted therapies (both over-the-counter and prescription), cost, the likelihood of compliance, and the psychosocial impact of disease. Patient education is vital to a successful outcome.



Reprinted with permission from Basak S, Zaenglein A. Acne and its management. *Pediatr Rev.* 2013;34(11):479-497

ITEM C115B: Treatment algorithm for adolescent acne. Triple therapy is benzoyl peroxide, topical retinoid, and oral antibiotic.
Abx, topical antibiotic (such as topical clindamycin or erythromycin); BP, benzoyl peroxide; COC, combined oral contraceptive; SA, salicylic acid

PREP Pearls

- Acne is categorized as comedonal (closed or open), inflammatory (papules, pustules, nodules, cysts), or mixed.
- Acne severity is classified as mild, moderate, or severe, based on the number, type, and distribution of lesions or scarring.
- Treatment must be individualized based on the type and severity of acne, while considering cost effectiveness and likelihood of compliance

ABP Content Specifications(s)

- Recognize the clinical findings associated with acne

Suggested Readings

- Basak S, Zaenglein A. Acne and its management. *Pediatr Rev*. 2013;34(11):479-497. doi: http://dx.doi.org/10.1542/pir.34-11-479.
- Eichenfield LF, Krakowski AC, Piggott C, et al. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. *Pediatrics*. 2013;131(S3):S165-S187. https://www.ncbi.nlm.nih.gov/pubmed/23637225.
- Krowchuk DP. Managing adolescent acne: a guide for pediatricians. *Pediatr Rev*. 2005;26(7):250-261. doi: http://dx.doi.org/10.1542/pir.26-7-250.

Question 116

A mother brings her 6-year-old son to your office for evaluation of increasingly abnormal behavior, sleep disturbance, and developmental regression. Her pregnancy was uncomplicated. The boy's birth history and infancy were unremarkable, and his newborn screen was normal. His medical history is notable for recurrent ear, nose, and throat infections. When he was younger, the boy's speech was delayed and he began to demonstrate mild behavior problems. He has become increasingly anxious, aggressive, destructive, and restless since that time. The boy used to know his letters, shapes and colors, but no longer recognizes them consistently. On physical examination, he has macrocephaly, slightly coarse facial features, a mildly enlarged liver, and a small umbilical hernia. He has normal muscle tone, no skin findings, and no unusual odor. Screening in the office demonstrates that he has mild hearing loss bilaterally and normal vision. Family history is unremarkable. You suspect an inborn error of metabolism.

Of the following, the MOST likely diagnosis is

A. biotinidase deficiency
B. maple syrup urine disease
C. peroxisomal disorder
D. phenylketonuria
E. Sanfilippo syndrome

Correct Answer: E
The boy in the vignette has mucopolysaccharidosis type III, known as Sanfilippo syndrome. Sanfilippo syndrome is an autosomal recessive disorder caused by a deficiency in 1 of 4 lysosomal enzymes involved in the degradation of a glycosaminoglycan called heparan sulfate. The clinical course of Sanfilippo syndrome has 3 stages. The first stage occurs between the ages of 1 and 4 years, when the child begins to show developmental delay after developing normally. Stage 2 occurs around 3 to 4 years of age, with developmental regression, severe behavioral problems, and progressive mental deterioration. During this time, facial dysmorphology becomes more obvious, with coarsening of facial features, synophrys (hair between the eyebrows), thick lips, and macrocephaly. Hearing loss develops that is mainly conductive. In the third and final stage, the behavioral problems disappear as the child becomes more mentally incapacitated with severe dementia. Swallowing difficulties and spasticity emerge, with these children ultimately becoming gastrostomy tube-dependent and unable to walk. There may be mild hepatosplenomegaly, as well as frequent otitis media, sinus infections, and respiratory problems. Most affected children die at the end of the second or the beginning of the third decade of life. No effective therapy is available at this time.

Developmental regression is a serious red flag that suggests the presence of an inborn error of metabolism associated with neurologic deterioration and intellectual disability. Any patient presenting with developmental regression warrants a genetic and neurologic evaluation with a subsequent thorough investigation for metabolic disorders and brain magnetic resonance imaging. Hundreds of metabolic disorders can present with progressive neurologic deterioration. The differential diagnosis depends on the constellation of symptoms, which may include epilepsy, dystonia, ataxia, organomegaly, visual loss, hearing loss, myoclonus, paraplegia, spasticity, unusual odors, and others. There are specific treatments that, if begun very early in life, can lead to a normal or near-normal outcome. Examples of treatable metabolic disorders that are otherwise associated with intellectual disability include biotinidase deficiency, maple syrup urine disease, and phenylketonuria. These 3 disorders are currently included in newborn screening.

Biotinidase deficiency presents in young children with progressive seizures, hypotonia, ataxia, developmental delay, vision problems, hearing loss, and skin rashes with alopecia. Children treated from early infancy with oral biotin (5-10 mg) daily can live a normal life. Once developmental delay and other neurologic problems have occurred, they are generally irreversible. This disorder highlights the importance of newborn screening for early diagnosis and treatment.

Patients with maple syrup urine disease present with a “maple syrup” odor, elevated branched-chain amino acids (isoleucine, leucine, valine), ketonuria, irritability, and poor feeding in the first few days after birth. By 4 to 5 days of age, they will rapidly decompensate, developing lethargy, intermittent apnea, opisthotonus, and encephalopathy. Treatment consists of dietary leucine restriction, specially manufactured branched chain amino acid-free foods, isoleucine and valine supplementation, and frequent clinical and biochemical screening.

Peroxisomal disorders commonly present with hypotonia, poor feeding, distinctive facies, seizures, retinal dystrophy, sensorineural hearing loss, developmental delay, and liver cysts with hepatic dysfunction. These patients do not have coarse facial features. Bone stippling may be noted on skeletal survey. Laboratory evaluation will demonstrate elevation of the very-long-chain fatty acid levels.

Phenylketonuria presents with a mousy or musty odor, microcephaly, epilepsy, decreased skin and hair pigmentation, eczema, and progressive intellectual disability. Biochemical screening reveals an elevated plasma phenylalanine level. No hepatosplenomegaly is noted. This disorder is treatable with dietary management, which should begin in early infancy to minimize deficit.

PREP Pearls

- Sanfilippo syndrome is a mucopolysaccharide disorder caused by the inability to degrade heparan sulfate, leading to progressive mental deterioration, coarse facial features, joint stiffness, mild hepatosplenomegaly, and eventually, death.
- Developmental regression is a serious red flag warranting deeper investigation for inborn errors of metabolism associated with neurologic deterioration and intellectual disability.

ABP Content Specifications(s)

- Identify common metabolic causes of intellectual disabilities

Suggested Readings

- Andrade F, Aldámiz-Echevarría L, Llarena M, Couce ML. Sanfilippo syndrome: overall review. *Pediatr Int.*2015;57(3):331-338. doi: http://dx.doi.org/10.1111/ped.12636.
- Moeschler JB, Shevell M, Committee on Genetics. Comprehensive evaluation of the child with intellectual disability or global developmental delays. *Pediatrics*. 2014;134(3):e903-e918. doi: http://dx.doi.org/10.1542/peds.2014-1839.

Question 117

A 16-year-old adolescent girl presents to your clinic to discuss birth control options. She reports that she is sexually active and has had 2 male partners. She had a pregnancy scare approximately 3 months ago and wants to know if she needs parental consent to start birth control pills. You live in a state that allows minor consent for contraceptive services.

Of the following, based on the information you have, you advise the patient that she can receive

A. birth control pills without parental consent at her current age
B. birth control pills without parental consent only after the age of 17 years
C. birth control pills without parental consent only from a clinic receiving Title X funding
D. emergency contraception only by prescription without parental consent
E. over-the-counter emergency contraception without parental consent only after the age of 17 years

Correct Answer: A

Laws related to minor consent for medical care vary by state. In many states, consent may be further differentiated to specify consent for screening for sexually transmitted infections, consent for contraceptive services, and consent for general medical care. It is the responsibility of providers to become familiar with relevant laws in the states in which they practice. Laws governing minor consent for contraceptive services do not specify where these services may be rendered (eg, Title X-funded clinics).

In 2006, progestin-only emergency contraceptive pills became available over the counter in all states for women age 17 years and older. In 2013, federal courts removed the point-of-sale age restrictions for these products.

PREP Pearls

- Laws related to minor consent for medical care vary by state.
- It is the responsibility of healthcare providers to become familiar with relevant laws in the states in which they practice.

ABP Content Specifications(s)

- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding minors as decision-makers
- Understand when it is appropriate to have a minor involved in making decisions about his or her medical care

Suggested Readings

- Guttmacher Institute. Home page. Guttmacher Institute website. http://www.guttmacher.org.
- US Food and Drug Administration. FDA approves plan B one-step emergency contraceptive for use without a prescription for all women of child-bearing potential. US Food and Drug Administration website. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm358082.htm. Updated June 21, 2013.

Question 118

You are meeting with the parents of a 15-year-old adolescent boy and 8-year-old boy for a parents-only visit. They inform you that they are getting a divorce. They are planning on selling their current home and will both find new homes within a reasonable travel distance. The children will continue to attend the same schools. They have been careful to refrain from arguing in front of the children, but state that they are having a difficult time agreeing on custody arrangements.

Of the following, the BEST recommendation is to have

A. the children decide with whom they wish to live

B. custody decisions determined by the courts

C. joint custody with equal division between parents

D. a regular schedule with flexibility for change

E. weekdays at one home and weekends at the other home

Correct Answer: D
Children of divorced families do best with a regular schedule with flexibility for change. These children are already going through many changes and losses; as much stability in routines and schedules as is possible is best for the children. However, there must also be flexibility to change these schedules as needed to accommodate for the changing needs of the children (eg, extracurricular activities, special events).

Approximately half of first marriages end in divorce. While 85% of divorced adults remarry, 40% of these new marriages also end in divorce. Divorce affects over 1 million children per year, causing multiple changes in these children's lives. Not only does the family structure change, but the child's living circumstances also change. The child's home environment, school placement, childcare arrangements, extracurricular activities, community, routines, peer groups, and available supports may all be affected. The child's lifestyle may change due to decreased income and resources.

Regardless of the developmental stage of the child, consistency in routine is key in helping the child adjust to the changes around divorce. Infants may cry more and have problems with sleep. Young children can exhibit separation anxiety, fearfulness, and aggression. Preschoolers, who are engaged in magical thinking, may believe that they caused the breakup and may attempt to control their surroundings. They may have nightmares, become clingier, or act out. Young children require consistent routines and caregivers to develop secure attachment and to address and prevent fear of abandonment. School-age children and adolescents may have academic underachievement, may become moody, and test boundaries. Adolescents may also exhibit externalizing and internalizing problems such as substance abuse, delinquency, depression, and anxiety. Consistent behavioral expectations and routines with limit setting are helpful for older children. No matter the age, these children are dealing with changes that are outside of their control, including the loss of their family unit and may respond with anger and grief. They may withdraw socially or exhibit somatic symptoms. Consistency with structure and routine provides stability and helps with both short- and long-term adjustment and leads to better outcomes. Inconsistent schedules are associated with poorer social and mental health outcomes.

Custodial issues are important in how children adapt to divorce. Previously, mothers were the primary custodians with periodic visits from the fathers. However, children do better when both biological parents are available to provide care to their children and when they can continue their relationships with each parent. It is important for the child's father to have a consistent presence. Joint physical custody is common with half-time or one-thirds to two-thirds time as typical examples of how time is divided between parents. The specifics vary according to logistical considerations such as age of child, distance between homes, location of work and school, and living arrangements. Joint custody arrangements are complex and work best when both parents are able to communicate effectively with each other, work cooperatively, assist with transitions between households, and are respectful of each other and the child's wishes. When parents cannot agree on a parenting plan, mediation is preferred over using the courts as this avoids costs and conflict. The courts are generally involved in more acrimonious situations. It is also

important to keep in mind that custody arrangements may need adjustment as the children mature.

Whatever the custody arrangement, parental conflict is a major determinant of how children do with the divorce of their parents. Cooperative co-parenting is most helpful in children's adjustment to the divorce. Children of married or divorced parents do better if their parents do not fight in front of them. If exposed to conflict, the children are more likely to have externalizing behavioral problems and academic underachievement.

In the vignette, the children's wishes should be respected and considered, but should not be the ultimate determinant of custody arrangements, as they may not be aware of additional considerations or logistics. When parents are respectful of each other as parents and when they have their children's interests at heart, custody decisions are best made without going through the courts to avoid cost and conflict. While joint custody with equal division between parents appears fair, this may not be logistically reasonable and may be disruptive to a child who thrives on routine and who has difficulties with transitions. While weekdays at one home and weekends at the other home may assist with some of the difficulties in transitions, this may not be the ideal circumstance for all families. A regular schedule with flexibility for change is the best recommendation for families.

Pediatricians can assist parents in planning for their children's needs through the events before and after the divorce. They can encourage families to maintain routines, activities, contacts, discipline, and responsibilities in as normal a fashion as possible. They can guide parents in keeping the children's best interests in mind as the family adjusts to the changes in their lives.

PREP Pearls

- Children of divorced families do best with a regular schedule with flexibility for change.
- No matter the developmental stage of the child, consistency with structure and routine provides stability, helps with both short- and long-term adjustment, and leads to better outcomes.
- Whatever the custody arrangement, parental conflict is a major determinant of how children do with the divorce of their parents. Cooperative co-parenting is most helpful in children's adjustment to the divorce.

ABP Content Specifications(s)

- Understand the custodial issues associated with divorce and the effect of those issues on patients of various ages

Suggested Readings

- Cohen GJ, American Academy of Pediatrics, Committee on Psychosocial Aspects of Child and Family Health. Helping children and families deal with divorce and separation. *Pediatrics*. 2002;110(5):1019-1023. http://pediatrics.aappublications.org/content/110/5/1019.
- Kaplan-Sanoff M. Divorce. In: Augustyn M, Zuckerman B, Caronna EB, eds. *The Zuckerman Parker Handbook of Developmental and Behavioral Pediatrics for Primary Care.* 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011:446-449.
- Kleinsorge C, Covitz LM. Impact of divorce on children: developmental considerations. *Pediatr Rev.* 2012;33(4):147-155. doi: http://dx.doi.org/10.1542/pir.33-4-147.

Question 119

The mother of a 3-year-old boy calls your office for guidance after her son ingested a small amount of windshield wiper fluid. About 30 minutes ago, the boy was playing in the garage while his father was working on the family car. He drank from a jar in which the father had poured about 4 oz of windshield wiper fluid. The boy spit out much of the fluid and told his parents that he drank "bad juice." However, the mother still thinks he may have swallowed as much as a tablespoon.

The mother tells you that her son is currently displaying no symptoms of illness and is acting normally. He has no significant past medical or surgical history, and he takes no medications. The mother asks for your recommendation about the best course of action at this time.

Of the following, the recommendation you are MOST likely to give is

A. he should be given activated charcoal as soon as possible
B. he should have a follow-up appointment with you within the next week
C. he will need further evaluation only if symptoms develop over the next 2 hours
D. he will need further laboratory tests in the emergency department
E. no further evaluation or treatment is needed

Correct Answer: D
The 3-year-old boy in the vignette inadvertently ingested approximately 1 tablespoon of windshield wiper fluid, which contains methanol as its primary ingredient. He is currently asymptomatic. The best recommendation to give his mother is that he will need further laboratory testing in the emergency department.

All providers of pediatric care must recognize the signs and symptoms of methanol ingestion, and understand the management of children who have ingested methanol. Methanol is an alcohol that can be highly toxic in small quantities: as little as a sip may lead to toxicity in small children. Methanol is found in a number of common household products, including windshield washer fluid, perfumes, portable cooking fuels, and printing solutions. In the United States, most cases of methanol toxicity are attributed to ingestion of windshield wiper fluid.

Methanol's toxicity arises primarily from its metabolites. The alcohol is converted by alcohol dehydrogenase to formaldehyde, which is then metabolized to formic acid. Formic acid, the main toxic metabolite, results in a profound anion gap metabolic acidosis and inhibits oxidative phosphorylation. In addition to its metabolic effects, methanol ingestion may result in toxicity to the central nervous, gastrointestinal, and visual systems. Initial central nervous system manifestations last only several hours and may include disinhibition and drowsiness, similar to ethanol toxicity. More severe central nervous system sequelae, which are a result of accumulation of formic acid, include seizures, coma, Parkinsonian-like symptoms, and cerebral edema, and can develop within 12 to 24 hours after ingestion. Gastrointestinal complications include abdominal pain, nausea, and vomiting. Visual disturbances are the hallmark of methanol poisoning, as the optic nerve and pigmented retinal cells are particularly susceptible to formic acid's direct toxic effects. Potential visual sequelae may include color changes, photophobia, blurred vision, "snowfield vision," and complete blindness. In these cases, physical examination may reveal hyperemia or pallor of the optic discs, loss of pupillary response, and optic atrophy with permanent vision loss in the most severe cases. Ingestions of very large quantities of methanol may result in cardiac arrhythmias, pulmonary edema, and circulatory collapse. Pancreatitis and acute kidney failure are additionally rare but potentially serious sequelae.

Methanol's potential to cause significant toxicity, even in small quantities, warrants further evaluation in children presenting after known or suspected ingestion of methanol, including laboratory testing to assess for the development of toxicity. Methanol is an osmotically-active substance, so elevation of the serum osmol gap is expected following ingestion, although this finding is neither completely sensitive nor specific for methanol ingestion. Serum electrolytes (along with measurement of blood urea nitrogen, creatinine, and glucose) and an arterial blood gas measurement are also indicated in evaluating children with methanol poisoning. Results of these studies can aid in identifying the presence of metabolic acidosis and an osmol gap. As methanol is metabolized to formic acid, the serum osmol gap will fall, while an elevated anion gap metabolic acidosis eventually develops. Serum methanol and formate levels may help to guide the management of patients following methanol ingestion, although these measurements are not rapidly available in many centers. Serum methanol concentrations of 20 mg/dL or higher are associated with toxicity if untreated, so clinical intervention is indicated at this threshold. A

patient's serum methanol concentration in mg/dL can be approximated by multiplying the osmolar gap by 3.

Methanol (along with other toxic alcohols) are poorly adsorbed by activated charcoal. Therefore, activated charcoal would not be useful in the management of the boy in the vignette.

Directing the boy to follow up within 1 week would not be appropriate, given that he is at risk for developing significant toxicity from conversion of methanol to its toxic metabolite over the next several hours. This patient is in need of prompt evaluation to determine his need for further management.

Advising the boy's mother that no further evaluation is needed orthat further evaluation should be pursued only if symptoms develop over the next 2 hours would both be incorrect recommendations that could result in significant adverse consequences. Since methanol is metabolized slowly, clinical effects may not become apparent until 8 to 24 hours after ingestion. This delay in the accumulation of formic acid provides an opportunity for clinical intervention to prevent the development of significant toxicity from methanol ingestion.

Fomepizole, a competitive antagonist of alcohol dehydrogenase, minimizes the conversion of methanol to its toxic metabolite and is the antidote of choice for patients at significant risk for methanol poisoning. Although expensive, fomepizole has few adverse effects and has replaced ethanol as the treatment of choice for methanol toxicity in recent years. Hemodialysis may be indicated for children with extremely high serum methanol concentrations.

PREP Pearls

- Visual disturbances are the hallmark of methanol poisoning, as the optic nerve and pigmented retinal cells are particularly susceptible to formic acid's direct toxic effects.
- Since methanol is metabolized slowly, its clinical effects may not become apparent until 8 to 24 hours after ingestion. This delay in the accumulation of methanol's toxic metabolite (formic acid) provides clinicians with a critical opportunity to prevent the development of significant toxicity from methanol ingestion through appropriate clinical intervention.
- Methanol's potential to cause significant toxicity, even in small quantities, warrants further evaluation in children presenting after known or suspected ingestion of methanol, including laboratory testing to assess for the development of toxicity.
- Serum electrolytes, blood urea nitrogen, creatinine, glucose, and an arterial blood gas measurement should be obtained in children presenting after a known or suspected methanol ingestion, along with a serum methanol level in centers where this is available.
- Fomepizole is the antidote of choice for patients at significant risk for methanol poisoning.

ABP Content Specifications(s)

- Recognize the signs and symptoms of methanol ingestion, and manage appropriately

Suggested Readings

- Fein DM, Sue Y. Methanol ingestion. *Pediatr Rev*. 2011;32(12):549-550. doi: http://dx.doi.org/10.1542/pir.32-12-549.
- Kerns W II, Brent J. Methanol toxicity. STAT!Ref: ACP Smart Medicine with AHFS application. http://online.statref.com/publictitleinfo/titleinfo.aspx?fxid=539.
- O'Donnell KA, Osterhoudt KC, Burns MM, Caiello, Henretig FM. Toxicologic emergencies. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. *Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:1061-1114.

Question 120

An 8-year-old boy with asthma is brought to the emergency department for evaluation of respiratory distress. He has had 2 days of fever and cough, and recently developed labored breathing. His best friend was recently diagnosed with influenza. Vital signs show a temperature of 39.2°C, respiratory rate of 35 breaths/min, heart rate of 130 beats/min, and blood pressure of 110/70 mm Hg. On physical examination, he is wheezing and has marked intercostal retractions.

Of the following, the antiviral with influenza activity that is MOST likely to cause bronchospasm in this patient is

A. amantadine
B. oseltamivir
C. ribavirin
D. rimantadine
E. zanamivir

Correct Answer: E
The medication that is most likely to cause bronchospasm is zanamivir. Zanamivir is a neuraminidase inhibitor that is administered by inhalation of a powder. This mechanism has been linked to bronchospasm in patients with asthma, as well as in individuals without airway disease. While reactive airway disease is not a contraindication to the use of zanamivir, it is not recommended in this population.

Patients with asthma, along with individuals with other underlying pulmonary conditions, are considered to be at high risk of developing severe influenza. In the 2014 to 2015 season, 26% of children hospitalized for influenza in the United States had asthma or underlying reactive airways disease. Other high-risk groups include children with diabetes mellitus, hemodynamically significant cardiac disease, immunosuppression, and neurologic disorders. Amantadine and rimantadine are adamantanes, antiviral agents that are thought to prevent release of viral nucleic acid into the host cell by blocking the M2 protein. The adamantanes are no longer recommended for the treatment of influenza infections, as there are high levels of resistance against the adamantanes in influenza A viruses and they have no activity against influenza B viruses. Adverse effects most commonly ascribed to the adamantanes include central nervous system and gastrointestinal symptomatology.

There are 3 licensed neuraminidase inhibitors: oseltamivir, zanamivir, and peramivir. Peramivir was licensed in December of 2014 and has not been studied fully in children. Oseltamivir and zanamivir are the only antivirals currently recommended for prophylaxis and treatment of influenza infections in children. Currently, most influenza viruses are susceptible to the neuraminidase inhibitors. If there is concern for osteltamivir or peramivir resistance, use of intravenous zanamivir (which is investigational) is recommended. Adverse events ascribed to the neuraminidase inhibitors in general include gastrointestinal symptoms. Neuropsychiatric events have been reported, but are rare.

Ribavirin is an antiviral that inhibits viral replication. It is US Food and Drug Administration-labeled for treatment of respiratory syncytial virus infections in certain compromised populations. It is also used off-label for the treatment of hepatitis C. Due to toxicity concerns, including hemolytic anemia, teratogenicity, and the availability of influenza-specific therapies, ribavirin is not recommended for treatment of influenza infections.

PREP Pearls

- Oseltamivir and zanamivir are the only antivirals currently recommended for prophylaxis and treatment of influenza infections in children.
- Zanamivir has been linked to bronchospasm in patients with asthma and in individuals without airway disease.
- Most influenza viruses are susceptible to the neuraminidase inhibitors.

ABP Content Specifications(s)

- Plan appropriate antiviral therapy for the treatment of influenza, while considering drug-resistant strains
- Recognize the risk factors for complications associated with influenza virus infection, including those that lead to hospitalization

Suggested Readings

- American Academy of Pediatrics. Influenza. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:476-493.
- Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2015-2016. *Pediatrics*. 2015;134(4):1-17. doi: http://dx.doi.org/10.1542/peds.2015-2920.

Question 121

You are seeing a 16-year-old adolescent girl in your office for recurrent abdominal pain. She reports periumbilical pain that occurs 5 to 6 times weekly and is described as a twisting feeling that ranges from 4 to 7 on a scale of 10. She denies associated fever, weight loss, nausea, or vomiting. She does note an improvement in her symptoms after defecation in approximately 50% of her episodes. She was seen in the emergency department 2 weeks ago for an episode of pain, at which time laboratory studies were ordered. These laboratory results are shown:

Laboratory Test	**Result**
Hemoglobin	13 g/dL (13 g/L)
Platelets	$300 \times 10^3/\mu L$ ($300 \times 10^9/L$)
C-reactive protein	0.9 mg/L (8.6 nmol/L)
Tissue transglutaminase	14 mg/L
Immunoglobulin A	45 mg/dL (450 mg/L)
Complete metabolic panel	Within normal limits

You believe the patient meets the criteria for a diagnosis of irritable bowel syndrome.
Of the following, the BEST treatment for her symptoms is

A. digestive enzymes

B. gluten-free diet

C. peppermint oil

D. promotility medication

E. proton pump inhibitor therapy

Correct Answer: C
Peppermint oil has been shown to be effective in patients with irritable bowel syndrome (IBS). Peppermint oil's active ingredient, menthol, causes relaxation and reduction of spasms of the gastrointestinal smooth muscle by blocking Ca2+ channels.

Irritable bowel syndrome is a functional gastrointestinal disorder that is not an organic disease, but a set of symptoms that occur together. The most common symptoms are abdominal pain with diarrhea, constipation, or both. According to the ROME III diagnostic criteria, symptoms must occur at least 3 days a month n the past 3 months without other identified organic etiology. Studies show that 10% to 20% of high school students and 6% to 10% of middle school students have IBS. The pain may change with stooling pattern and may be relieved by defecation.
The etiology of IBS is not well understood. Several pathophysiologic causes have been identified, including brain-gut signaling problems; dysmotility; hypersensitivity; bacterial gastroenteritis; small intestinal bacterial overgrowth; mental health issues, including anxiety and depression; and genetic causes. It is likely that for some patients there are several factors at play.

Irritable bowel syndrome can present in various ways. The management of IBS varies greatly, depending on the subtype and severity of symptoms (Item C121). Treatment options include medications, diet, and behavioral modification. Increasing numbers of medications are available to treat IBS, but none are approved for use in patients younger than 18 years.
Since IBS is a functional gastrointestinal disorder, there is no role for digestive enzymes, promotility agents, or proton pump inhibitors in its treatment. Although some patients experience improvement in symptoms with a gluten-free diet, no studies currently support this as a therapy for IBS.

Item C121. Irritable Bowel Syndrome (IBS) Review.

IBS type	Symptoms	Treatment Options
IBS	Abdominal pain or discomfort at least 3 days/month in the past 3 months, associated with ≥2 of the following: • Improvement with defecation • Onset associated with change in stool frequency • Onset associated with change in stool form	• Peppermint oil • Diet modification - Increased water - Increased fiber, both soluble and nonsoluble • Cognitive behavioral therapy • Hypnosis
IBS-C (constipation)	Abdominal pain or discomfort at least 3 days/month in the past 3 months, associated with ≥2 of the following: • Improvement with defecation • Onset associated with change in stool frequency • Onset associated with change in stool form ≥1 of the following symptoms on at least 25% of occasions: • Abnormal stool frequency (<3/week) • Abnormal stool form (bumpy/hard) • Abnormal stool passage • Bloating • Passage of mucus	• Peppermint oil • Diet modification - Increased water - Increased fiber, both soluble and nonsoluble • Constipation medications - Polyethylene glycol - Stimulant laxatives - Linaclotide - Lubiprostone • Cognitive behavioral therapy • Hypnosis
IBS-D (diarrhea)	Abdominal pain or discomfort at least 3 days/month in the past 3 months, associated with ≥2 or more of the following: • Improvement with defecation • Onset associated with change in stool frequency • Onset associated with change in stool form • Diarrhea > 25% of the time	• Peppermint oil • Diet modification - Reduce sorbitol and fructose - Reduce fried and fatty foods - Increase soluble fiber - Increase water • Antidiarrheal medications • Cognitive behavioral therapy • Hypnosis • Treat small intestinal bacterial overgrowth
IBS-M (mixed)	Above criteria with alternating diarrhea and constipation	See above

Courtesy of C. Waasdorp Hurtado

PREP Pearls

- Peppermint oil has been shown to be effective for the treatment of abdominal pain associated with irritable bowel syndrome (IBS).
- Diet modification can play a significant role in the treatment of IBS.
- IBS is not an organic disease. It is a group of symptoms that occur together.
- The most common symptoms of IBS are abdominal pain with diarrhea, constipation, or both.

ABP Content Specifications(s)

- Recognize the clinical features associated with irritable bowel syndrome, and manage appropriately

Suggested Readings

- Chiou E, Nurko S. Management of functional abdominal pain and irritable bowel syndrome in children and adolescents. *Expert Rev Gastroenterol Hepatol.* 2010;4(3):293-304. doi: http://dx.doi.org/10.1586/egh.10.28.
- Hyams JS. Irritable bowel syndrome, functional dyspepsia, and functional abdominal pain syndrome. *Adolesc Med Clin.*2004;15(1):1-15. doi: http://dx.doi.org/10.1586/egh.10.28.
- Rutten JM, Benninga MA, Vlieger AM. IBS and FAPS in children: a comparison of psychological and clinical characteristics. *J Pediatr Gastroenterol Nutr.* 2014;59(4):493-499. doi: http://dx.doi.org/10.1097/MPG.0000000000000452.
- Wall GC, Bryant GA, Bottenberg MM, Maki ED, Miesner AR. Irritable bowel syndrome: a concise review of current treatment concepts. *World J Gastroenterol.* 2014;20(27):8796-8806. .

Question 122

A 16-year-old female cross-country runner presents to your office for follow-up of a right hip injury. The team physician at her high school recently diagnosed her with a stress fracture of the right femoral neck and recommended that she follow-up with you for ongoing management. She has been using crutches to ambulate and reports occasional mild hip pain. The patient and her family ask your advice on management of her current symptoms.

Of the following, the BEST medication regimen for this patient is

A. acetaminophen orally as needed

B. hydrocodone and ibuprofen orally every 6 hours as needed

C. ibuprofen orally every 6 hours for 1 week

D. naproxen orally every 12 hours as needed

E. topical diclofenac gel applied to the anterior hip every 6 hours

Correct Answer: A

The patient in the vignette has occasional mild hip pain and should try acetaminophen to manage her pain. This adolescent has a femoral neck stress fracture. These particular fractures are concerning because complete fracture of the femoral neck can disrupt blood supply to the femoral head and result in avascular necrosis with permanent damage to the hip joint.
Since she has only occasional mild pain, treatment with hydrocodone or other opioids is not indicated.

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the production of prostaglandins necessary for bone healing and have been shown to delay bone healing in animal studies and in several clinical studies; however, no large-scale randomized trials have demonstrated this effect. There is a concern that these medications may affect bone healing, therefore their use should be avoided in fractures with a high risk of complication or nonunion, particularly if other options exist.

Nonsteroidal anti-inflammatory drugs are effective analgesic, antipyretic, and anti-inflammatory medications, and are used commonly in infants, children, and adolescents. Since they are inexpensive and easily obtainable without a prescription, they carry a potential for overuse and abuse. Aspirin and other NSAIDs are not without adverse effects. The most common adverse effect is gastrointestinal (GI) tract irritation with associated nausea, heartburn, and epigastric abdominal pain. Serious GI tract complications such as bleeding and ulceration can also occur. One class of NSAIDs, cyclooxygenase-2 (COX-2) inhibitors, was developed with the goal of reducing GI tract side effects; however, the GI benefit of these medications over traditional NSAIDs is unclear.

Long-term use of NSAIDs can impair renal function, with elevated creatinine, hyperkalemia, and proteinuria seen in up to 5% of patients. Generally, renal function returns to baseline when NSAIDs are discontinued, but some children exhibit permanent renal damage even in the absence of underlying kidney disease. Elevation of serum hepatic enzymes has rarely been associated with prolonged use of NSAIDs, particularly aspirin and other salicylates. Use of COX-2 inhibitors appears to increase the risk of cardiac events in adults, however, healthy children and adolescents are unlikely to experience cardiovascular adverse effects with NSAIDs. The use of aspirin and other salicylates is contraindicated for infants, children, and adolescents because of the risk of Reye syndrome; disease-specific exceptions exist (eg, Kawasaki disease). Reye syndrome is an acute hepatitis and encephalopathy linked to aspirin use in children with viral infections, such as influenza and varicella.

PREP Pearls

- Nonsteroidal anti-inflammatory medications (NSAIDs) may impair bone healing and should not be used by individuals with fractures that have a high risk of nonunion or other complication.
- The most common adverse effect of NSAID use is gastrointestinal tract irritation.
- Reye syndrome is an acute hepatitis and encephalopathy linked to aspirin use in children with viral infections, such as influenza and varicella.

ABP Content Specifications(s)

- Recognize the risks associated with the use of aspirin
- Recognize the risks associated with the use of nonsteroidal anti-inflammatory drugs

Suggested Readings

- Feucht CL, Patel DR. Analgesics and anti-inflammatory medications in sports: use and abuse. *Pediatr Clin North Am*. 2010;57(3):751-774. doi: http://dx.doi.org/10.1016/j.pcl.2010.02.004.
- Geusens P, Emans PJ, de Jong JJ, van den Bergh J. NSAIDs and fracture healing. *Curr Opin Rheumatol*. 2013;25(4):524-531. doi: http://dx.doi.org/10.1097/BOR.0b013e32836200b8.

Question 123

You are working in the emergency department when a cyanotic 4-month-old infant arrives by ambulance. She has no significant medical history, and on her physical examination, she looks well other than cyanosis of her mucous membranes. She is not tachypneic and her pulse oximetry is 96% on room air. The cyanosis does not improve with administration of oxygen and you suspect methemoglobinemia. In talking with her mother, you learn that the patient lives in a farmhouse built in 1920, which the parents have been renovating. The baby drinks formula prepared using well water from the farm.

Of the following, the MOST likely contaminant leading to this patient's cyanotic episode is

A. arsenic
B. lead
C. mercury
D. nitrates
E. trichloroethylene

Correct Answer: D
The infant in this vignette has methemoglobinemia caused by exposure to high levels of nitrates, a chemical often found in well water. Nitrate contamination often results from sewage or use of fertilizer. The nitrates are converted to nitrites in the infant's stomach. Nitrites oxidize the iron in hemoglobin to the ferric (Fe^{+++}) state, forming methemoglobin that binds oxygen poorly. Methemoglobinemia typically presents only with cyanosis. This may first be noted as the percentage of methemoglobin reaches 3%, but symptoms become more obvious as the methemoglobin level reaches 20%. The cyanosis is typically the only symptom, but as the percentage of methemoglobin increases, other symptoms including irritability, tachypnea, and changes in mental status may be noted. In the presence of methemoglobinemia, the pulse oximeter does not give accurate readings, especially at methemoglobin levels above 30%. Poison control or a toxicologist should be consulted if methemoglobinemia is suspected. No treatment is typically required for patients with a percentage of methemoglobin less than 20%, other than identification and removal of the source of nitrates.

Approximately 15% to 20% of homes in the United States obtain their drinking water from wells. Well water is not regulated by the US Environmental Protection Agency and wells are minimally regulated by states. Well water may contain chemical, microbiologic, and radioactive contaminants. The most common contaminants include *Cryptosporidium*, *Escherichia coli*, lead, arsenic, nitrates/nitrites, and trichloroethylene/perchloroethylene. Of the contaminants listed, only nitrates are associated with the cyanosis described for the infant in the vignette.
It is also important to be aware of toxic substances that may contaminate food sources. The most common food contaminants are microbes, especially *Salmonella*, *Campylobacter jejuni*, *Toxoplasma gondii*, Norovirus, *Listeria monocytogenes*, and *E coli* 0157:H7. Other contaminants that may be found in food sources include pesticide residues and chemicals that may be found in some fish (including mercury and chlorinated hydrocarbons). High levels of pesticides raise concern for effects on the immune system, endocrine system, and neurodevelopment.

Recently, bisphenol A (BPA) has been noted to be a contaminant of both water and food due to storage in plastic bottles and containers. The BPA contaminant has been associated with early puberty, neurotoxicity, and increased weight gain.

PREP Pearls

- Well water contains many contaminants including lead, arsenic, nitrates, trichloroethylene/perchloroethylene, *Cryptosporidium*, and *Escherichia coli*.
- The most common food contaminants are microbes, especially *Salmonella*, *Campylobacter jejuni*, *Toxoplasma gondii*, Norovirus, *Listeria monocytogenes*, and *E coli* 0157:H7.
- Bisphenol A is an emerging contaminant of food and water due to storage in plastic containers.

ABP Content Specifications(s)

- Know the toxic substances that may contaminate food sources (eg, mercury, Escherichia coli)
- Know the contaminants potentially found in drinking water (eg, mercury, Escherichia coli)

Suggested Readings

- Greer FR, Shannon M, Committee on Nutrition, Committee on Environmental Health. Infant methemoglobinemia: the role of dietary nitrate in food and water. *Pediatrics*. 2005;116(3):784-786. doi: http://dx.doi.org/10.1542/peds.2005-1497.
- Karr C. Addressing environmental contaminants in pediatric practice. *Pediatr Rev*. 2011;32(5):190-200. doi: http://dx.doi.org/10.1542/pir.32-5-190.
- Rogan WJ, Brady MT, Committee on Environmental Health, Committee on Infectious Diseases. Drinking water from private wells and risks to children. *Pediatrics*. 2009;123(6):e1123-e1137. doi: http://dx.doi.org/10.1542/peds.2009-0752.

Question 124

An 18-year-old young man with hemoglobin SS disease presents to the emergency department with a 24-hour history of tactile fever and new-onset shaking chills. He had been previously well. His history is remarkable for 1 admission per year for sickle cell pain crises since he started hydroxyurea 5 years ago. On physical examination, the patient appears somewhat uncomfortable. His temperature is 39.9°C, heart rate is 96 beats/min, respiratory rate is 30 breaths/min, and blood pressure is 90/70 mm Hg. His examination is remarkable for a flow murmur on cardiac examination, but is otherwise normal.

Of the following, based on his presentation, the patient's MOST likely diagnosis is

A. acute chest syndrome

B. Escherichia coli sepsis

C. hydroxyurea toxicity

D. splenic sequestration crisis

E. Streptococcus pneumoniae sepsis

Correct Answer: E
Hemoglobin SS disease occurs when both β-globin genes located on chromosome 11p15.5 contain a point mutation, resulting in the replacement of glutamic acid with valine at position 6. This results in a qualitatively defective hemoglobin molecule that is prone to polymerization, with resultant deformation of the red blood cell membrane (sickling). This, in turn, leads to an abbreviated red blood cell lifespan, chronic hemolysis, and frequent small vessel occlusion with resultant end-organ damage. Virtually all patients with hemoglobin SS are functionally hyposplenic or asplenic because of chronic sickling and vascular injury in the spleen, and they are prone to bacteremia with encapsulated bacteria.

The patient in the vignette has presented with signs and symptoms of sepsis, including fever, tachycardia, hypotension, and rigors. It is critical to rapidly recognize sepsis because it can quickly result in disseminated intravascular coagulation and death. Every fever in a child with sickle cell disease should be considered an emergency and treated as bacteremia until proven otherwise. A blood culture should be performed with a complete blood cell count and reticulocyte count, and a broad-spectrum antibiotic (typically a third-generation cephalosporin) should be administered as quickly as possible. *Streptococcus pneumoniae* is the most frequent causative agent of sepsis in patients with sickle cell disease. Prophylactic daily penicillin in children up to 5 years of age and the use of pneumococcal vaccines have been two of the most significant medical advances for reducing the morbidity and mortality of sickle cell disease. It is important to recognize that even patients who have been taking prophylactic penicillin and have received pneumococcal vaccines can still experience pneumococcal sepsis.

Acute chest syndrome includes a triad of respiratory distress, hypoxemia, and an infiltrate on chest radiography or a clinical lung examination consistent with a focal pneumonia. Although the patient in the vignette is clearly quite ill, he did not present with the stigmata of acute chest syndrome.

Hydroxyurea increases the production of hemoglobin F, a fetal variant of hemoglobin that is not prone to polymerization. This decreases the concentration of hemoglobin S in the cell, thereby reducing polymerization, membrane deformation, and sickling. The expanding use of hydroxyurea in the sickle cell population has greatly reduced morbidity, and should be considered in a child with sickle cell disease who has had frequent hospitalizations or life-threatening crises. Hydroxyurea does not cause fever or shaking chills.

Splenic sequestration occurs when sickling in the vasculature of the spleen entraps red blood cells, resulting in rapid splenic engorgement and a severe, potentially life-threatening anemia. Splenic sequestration is most common in children younger than 5 years, but can occur at any age. Affected children typically present with signs of severe anemia (tachycardia, pallor, and fatigue), thrombocytopenia, and a palpable spleen. Fever may or may not be present. Given the patient's age and rigors, splenic sequestration is unlikely.

PREP Pearls

- Patients with sickle cell disease are functionally asplenic, and thus at risk for sepsis with encapsulated organisms.
- *Streptococcus pneumoniae* is the most common cause of sepsis in patients with sickle cell disease.

ABP Content Specifications(s)

- Plan appropriate prophylaxis in children of various ages who have sickle cell disease
- Recognize complications that increase the risk of death in patients who have sickle cell disease, and manage appropriately
- Recognize the increased risk of infection with encapsulated organisms in children with asplenia

Suggested Readings

- Baskin MN, Goh XL, Heeney MM, Harper MB. Bacteremia risk and outpatient management of febrile patients with sickle cell disease. *Pediatrics*. 2013;131(6):1035-1041. doi: http://dx.doi.org/10.1542/peds.2012-2139.
- Brousse V, Buffet P, Rees D. The spleen and sickle cell disease: the sick(led) spleen. *Br J Haematol*. 2014;166(2):165-176. doi: http://dx.doi.org/10.1111/bjh.12950.
- Driscoll MC. Sickle cell disease. *Pediatr Rev*. 2007;28(7):259-268. doi: http://dx.doi.org/10.1542/pir.28-7-259.
- McCavit TL. Sickle cell disease. *Pediatr Rev*. 2012;33(5):195-206. doi: http://dx.doi.org/10.1542/pir.33-5-195.

Question 125

A 9-year-old girl was seen in the emergency department (ED) with a 10-day history of fever. She had a rash on her trunk 1 week earlier, and at the time of presentation, was having trouble walking because of left knee pain. She was admitted to the hospital for intravenous antibiotics for presumptive septic arthritis. Her physical examination on admission was remarkable only for mild left knee swelling with overlying erythema. She had no murmur or hepatosplenomegaly. Results of laboratory studies performed in the ED are shown:

Laboratory Test	**Patient Result**
Erythrocyte sedimentation rate	52 mm/h
C-reactive protein level	5.4 mg/L (51.4 nmol/L)
White blood cell count	11,500/μL (11.5×10^9/L)
Neutrophils	60%
Lymphocytes	37%
Eosinophils	3%
Hemoglobin	12 g/dL (120 g/L)
Hematocrit	37%
Platelets	375 x 10^3/μL (375×10^9/L)

Blood culture specimens were obtained. The next day her right elbow became erythematous and painful, and her knee swelling was resolved. Her elbow improved over the next 48 hours and she was discharged home after 7 days of antibiotics with negative blood cultures.

One month later, the girl was brought to your office by her parents, who requested a referral to a developmental psychologist. Her mother stated that the girl had become very distractible, or at the very least, she could not seem to sit still in class. They were wondering if she needed medication for attention-deficit/hyperactivity disorder.

Of the following, the cardiac diagnosis for which this girl is MOST at risk is

A. coronary artery aneurysms secondary to Kawasaki disease
B. dilated cardiomyopathy secondary to viral myocarditis
C. endocarditis secondary to septic arthritis
D. heart disease secondary to rheumatic fever
E. pericardial effusion secondary to systemic lupus erythematous

Correct Answer: D
The girl in the vignette is most at risk for heart disease secondary to rheumatic fever, based on her history of polyarthritis, rash, fever, and elevated levels of acute phase reactants. The diagnosis of acute rheumatic fever (ARF) is made using the 5 major and 5 minor Jones criteria (Item C125A). Two major criteria or 1 major and 2 minor criteria, along with evidence of a preceding group A *Streptococcus* (GAS) infection, are required to make the diagnosis. The same criteria are used for recurrent rheumatic fever. However, recurrent rheumatic fever in a patient with rheumatic heart disease (RHD) requires only 2 minor criteria, with evidence of a previous GAS infection. The finding of Sydenham chorea alone is adequate to make the diagnosis, without any supporting evidence or elevation of acute phase reactants, because it may occur much longer after the initial GAS infection (2 weeks to 2 years).

Item C125A. Classic Jones Criteria for the Diagnosis of Acute Rheumatic Fever.

Major	Minor
Polyarthritis	Arthralgia
Carditis	Prolonged PR interval
Chorea	Fever
Subcutaneous nodules	Elevated acute phase reactants
Erythema marginatum	History of rheumatic fever

Courtesy of A. Brown

In 2015, for regions in which ARF is a major public health problem, the World Heart Foundation modified the Jones criteria to allow polyarthralgia or monoarthritis to be considered a major criterion, especially if the patient has received anti-inflammatory medication. Subclinical carditis was also added as a major criterion for ARF in endemic areas, as was subclinical carditis seen on echocardiography without abnormal findings on cardiac examination.

The diagnosis of ARF could not have been made on the initial encounter for the girl in the vignette because no laboratory studies were conducted to document GAS infection. A positive throat culture or anti-streptolysin (ASO) titer would be supporting evidence for an acute infection, and an anti-DNase B antibody would be helpful later on in the illness.

The girl's rash was not documented because it had already disappeared by the time she was seen in the hospital. The rash associated with rheumatic fever, erythema marginatum, is distinctive and evanescent (Item C125B). Subcutaneous nodules are a rare finding appearing on the extensor surfaces of the extremities (Item C125C)**.**Sydenham chorea is described as involuntary purposeless motions, muscular weakness, and discoordination, which may be associated with emotional lability. Sydenham chorea may present weeks to months after an attack of ARF.

This child now has symptoms of hyperactivity, which presented after her acute febrile illness. Hyperactivity can be associated with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS).

Item C125B: *Evanescent rash associated with rheumatic fever. Courtesy of G Nankervis. Reprinted with permission from Kimberlin DW, Brady, MT, Jackson, MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL American Academy of Pediatrics; 2015.*

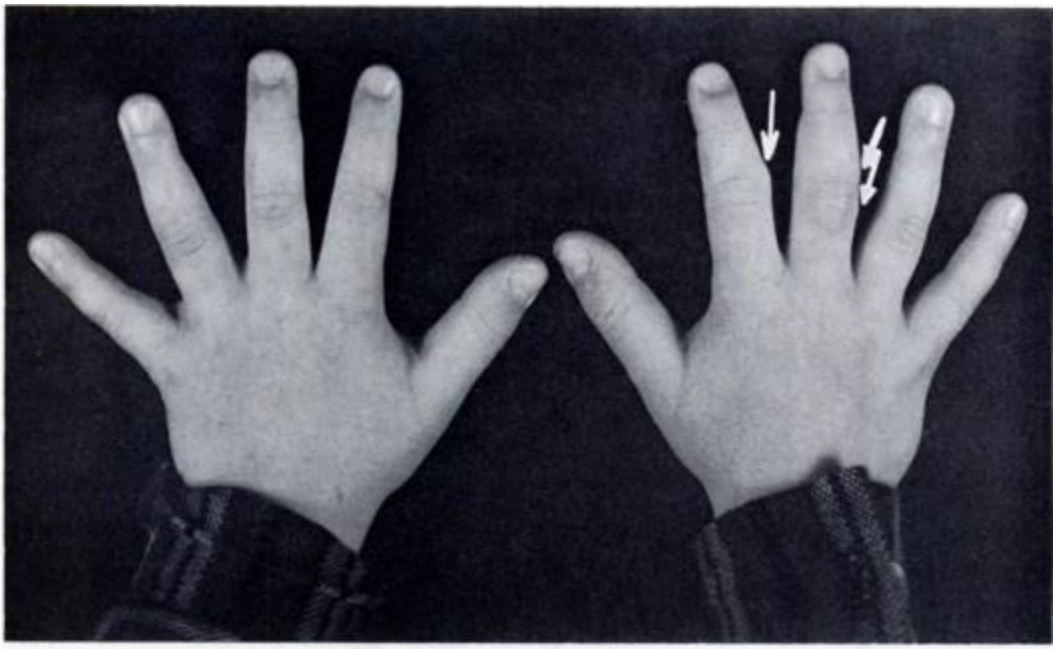


FIG. 1. Photograph of the hands of the reported case. Photograph taken 18 months after biopsy.

Item C125C: *Subcutaneous nodules can be associated with rheumatic fever. Reprinted with permission from Altman and P. R. Caffrey. Subcutaneous rheumatic nodules. Pediatrics. 1964;34:869-872.*

Treatment of GAS infection is crucial for preventing ARF. This requires timely diagnosis and treatment with a full course of antibiotics. Secondary prevention, after a first episode of rheumatic fever, is essential to prevent RHD or to stabilize the disease process in patients already affected. This requires penicillin injections every 3 or 4 weeks, and will involve an interdisciplinary care team that includes primary care, infectious diseases, and cardiology practitioners.

The recommended duration of subacute bacterial endocarditis prophylaxis in a patient who has had ARF depends on whether the patient had carditis or had RHD See Gerber MA, Baltimore RS, Eaton CB, et al (Suggested reading number 1, for more information).

PREP Pearls

- The diagnosis of acute rheumatic fever (ARF) is made with the modified Jones criteria.
- Secondary prevention with penicillin prophylaxis, for patients who had ARF, is important in the prevention of rheumatic heart disease.

ABP Content Specifications(s)

- Plan the appropriate initial management of rheumatic fever
- Plan appropriate diagnostic evaluation of rheumatic fever

Suggested Readings

- Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. *Circulation*. 2009;119(11):1541-1551. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.109.191959.
- Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015;131(20):1806-1818. doi: http://dx.doi.org/10.1161/CIR.0000000000000205.

Question 126

A 2-year-old girl is brought to your office for a health supervision visit. The mother has brought her 4-year-old sibling, and the 2 children are playing in the corner of your examination room. You confirm that the patient has approximately 50 words, is using 2-word phrases, and half of her speech is understandable. As you are talking with her mother, you hear the 2-year-old girl cry "No!," followed by the 4-year-old sibling saying "Ow! She bit me!" Her mother cries "Stop biting!" and then turns to you to ask why her child bites.

Of the following, the MOST likely reason for this child's behavior is

A. autism spectrum disorder

B. emerging behavioral disorder

C. exposure to violence at home

D. inability to adequately verbalize her frustration

E. speech/language delay

Correct Answer: D
Biting another child or adult, as seen in this vignette, is very common in older infants and young children, and probably represents a young child's inability to express herself when experiencing frustration, such as having to share a toy when she does not want to.

Biting occurs frequently in childcare settings, typically starts around 9 to 13 months of age, peaks at 22 to 24 months of age, and declines after 2.5 years of age as language and emotional regulation develop. Bites from young children rarely break the skin of the victim. Recommended caregiver response to biting includes showing empathy toward the bitten, a firm and timely negative statement (eg, "No biting! Biting hurts!"), positive encouragement when the child is behaving well when frustrated, and avoiding those frustrating situations where a child is likely to bite.

If it is part of a larger pattern of ongoing aggression toward others and rule-breaking that is disruptive and not responsive to techniques, biting beyond a developmental age of 3 years may signify a behavioral disorder. Self-biting can be a symptom of autism spectrum disorder or obsessive-compulsive disorder.

The child's mother reports language development typical for a 2-year-old child, so she does not have a speech delay. Speech-language and social-emotional developmental delays, as well as conduct disorder, have been shown to be associated with exposure to intimate partner violence, but there is no evidence suggesting an association with biting behaviors of normal childhood.

PREP Pearls
- Biting others is a normal part of childhood development.
- Biting incidents decrease after 2.5 years of age.
- Biting can be part of a constellation of ongoing aggressive behaviors in older children with conduct disorder.

ABP Content Specifications(s)
- Recognize factors related to biting at various developmental stages

Suggested Readings

- Garrard J, Leland N, Smith DK. Epidemiology of human bites to children in a day-care center. *Am J Dis Child*. 1988;142(6):643-650.
- Zahrt DM, Melzer-Lange MD. Aggressive behavior in children and adolescents. *Pediatr Rev*. 2013;32(8):325-332. doi: http://dx.doi.org/10.1542/pir.32-8-325.

Question 127

A 15-year-old adolescent who recently emigrated from rural Brazil presents to the emergency department with a 3-week history of epigastric pain and weakness. The abdominal pain is 7 out of 10 and most often occurs with meals and at bedtime. He reports anorexia, with a 10 lb unplanned weight loss; occasional vomiting, typically of food but with possible blood; and blood in his stool. He denies any significant past medical or family history. He admits to taking his aunt's celecoxib, several times a week for the pain.

Physical examination reveals a pale adolescent in no acute distress. He is alert and oriented. His temperature is 37.2°C, heart rate is 100 beats/min, respiratory rate is 16 breaths/min, and blood pressure is 95/65 mm Hg. On physical examination, you observe pallor of the conjunctivae, face, palms, and nail beds. He has equal breath sounds bilaterally with normal air flow, normal cardiac examination, and mild-moderate epigastric tenderness to palpation. Stool is very dark and grossly bloody. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	14,200/μL (14.2 x 10^9/L)
Neutrophils	60%
Lymphocytes	35%
Monocytes	5%
Hemoglobin	6.9 g/dL (69 g/L)
Hematocrit	22%
Platelet count	210 x 10^3/μL (210 x 10^9/L)
Erythrocyte sedimentation rate	25 mm/h

The prothrombin time, partial thromboplastin time, and international normalized ratio are all normal.

He is admitted to the hospital, and after stabilization, undergoes an upper gastrointestinal endoscopy, which finds several oval, punched-out lesions with smooth, white bases and surrounding erythematous and edematous mucosa at the duodenal bulb. Biopsies are performed and the results are pending.

Of the following, the test MOST likely to confirm his diagnosis is

A. abdominal computed tomography
B. colonoscopy
C. Helicobacter pylori stool antigen
D. serum celecoxib level
E. stool for ova and parasites

Correct Answer: C
The test most likely to confirm the diagnosis in this 15-year-old adolescent with gastrointestinal bleeding is *Helicobacter pylori* stool antigen. *H pylori* is the most common chronic bacterial infection in humans and has been found in all age groups and populations; at least 50% of the world's population has been infected. Epidemiologic evidence suggests that most infections are acquired in childhood, even in developed countries, and persist. Only 10% to 15% of *H pylori* infections result in peptic ulcer disease (PUD). Risk factors for *H pylori* infection include lower socioeconomic status, living in a developing country, and crowded living conditions early in life. Consumption of salted food and being Hispanic or African-American also increases risk, independent of socioeconomic status.

Peptic ulcer disease is primarily caused by *H pylori* infection or nonsteroidal anti-inflammatory drug (NSAID) usage. The primary presentation of *H pylori* infection is dyspepsia manifesting as epigastric pain, which worsens with eating. Other "alarm features" for PUD are anorexia, unexplained weight loss, recurrent vomiting, and reported gastrointestinal bleeding. On physical examination, tachycardia, pallor, and guaiac-positive stools with or without frank blood can be found.

The diagnosis of PUD caused by *H pylori* can be made with noninvasive tests such as the urea breath test or *H pylori*stool antigen in patients without alarm symptoms. The patient in this vignette has multiple alarm symptoms, therefore upper endoscopy with biopsies of any ulcers is the most appropriate initial diagnostic step. It would also be reasonable to obtain the *H pylori* stool antigen for more rapid diagnosis while awaiting biopsy results. *H pylori* immunoglobulin G serologic tests are very sensitive, less specific, cannot distinguish past from current infection, and have a low positive predictive value in low prevalence countries like the United States. Therefore, use of the widely available and more accurate stool antigen is recommended over serologies in the United States for the primary diagnosis of *H pylori*. Other rarer causes of PUD include other infections such as herpes simplex virus type 1 and cytomegalovirus; drugs including clopidogrel, sirolimus, spironolactone, corticosteroids; selective serotonin reuptake inhibitors; disorders such as gastrinoma, systemic mastocytosis, carcinoid, sarcoidosis, and Crohn disease; and radiation therapy.

Abdominal computed tomography would not help diagnose PUD from NSAID usage or *H pylori.* While anemia and grossly bloody stools could be consistent with inflammatory bowel disease, evidence of colitis would be expected over ulcers; therefore, colonoscopy is not indicated in this patient. Gastrointestinal parasites are not associated with PUD and *H pylori* would not be identified by evaluating stool for ova and parasites. Celecoxib is a cyclooxygenase-2 selective inhibitor, with reduced risk for PUD compared to traditional NSAIDs. The patient in the vignette is taking this less frequently than the recommended daily dosage. Serum for celecoxib level is not indicated, even if the test were commercially available.

PREP Pearls

- *Helicobacter pylori* is the most common chronic bacterial infection in humans, with over half of the world's population affected.
- "Alarm features" for peptic ulcer disease are epigastric pain, anorexia, unexplained weight loss, recurrent vomiting, pallor, and reported gastrointestinal bleeding or guaiac-positive stools.
- Use of the widely available and more accurate stool antigen test is recommended for the primary diagnosis of *H pylori* over immunoglobulin G serologies in the United States.

ABP Content Specifications(s)

- Identify risk factors for Helicobacter pylori infection
- Recognize the major clinical features associated with Helicobacter pylori infection
- Plan appropriate management for a patient with Helicobacter pylori infection
- Plan the diagnostic evaluation of Helicobacter pylori infection

Suggested Readings

- American Academy of Pediatrics. Helicobacter pylori infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds.*Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:379-381.
- Koletzko S, Jones NL, Goodman KJ, et al. Evidence-based guidelines from ESPGHAN and NASPGHAN for Helicobacter pylori infection in children. *J Pediatr Gastroenterol Nutr.* 2011;53(2):230-243. .
- Lopes AI, Vale FF, Oleastro M. Helicobacter pylori infection – recent developments in diagnosis. *World J Gastroenterol*. 2014;20(28):9299-9313..
- Yucei O. Prevention of Helicobacter pylori infections in childhood. *World J Gastroenterol.* 2014;20(30):10348-10354. doi: http://dx.doi.org/10.3748/wjg.v20.i30.10348.

Question 128

A 10-year-old boy presents to the emergency department with a 4-day history of diarrhea. There has been no vomiting, but he has had decreased fluid intake. On physical examination, his temperature is 37.3°C, heart rate is 120 beats/min, respiratory rate is 22 breaths/min, and blood pressure is 94/60 mm Hg. There is decreased skin turgor and dry mucous membranes. His examination is otherwise normal. Laboratory results are shown:

Laboratory Test	**Patient Result**
Sodium	139 mEq/L (139 mmol/L)
Potassium	2.5 mmol/L (2.5 mmol/L)
Chloride	89 mEq/L (89 mmol/L)
Bicarbonate	18 mEq/L (18 mmol/L)
Calcium	9.6 mg/ dL (2.4 mmol/L)
Phosphorus	4.9 mg/dL (1.58 mmol/L)
Blood urea nitrogen	27 mg/dL (9.6 mmol/L)
Creatinine	0.6 mg/dL (53 μmol/L)

Of the following, the BEST next step in the management of this boy's condition is

A. enteral potassium chloride
B. enteral potassium phosphate
C. increased intake of potassium-rich foods
D. intravenous potassium chloride
E. intravenous sodium bicarbonate

Correct Answer: A

The boy in the vignette presents with clinical features consistent with dehydration, and does not have muscular or cardiac manifestations of acute and severe hypokalemia. However, in view of the severity of his hypokalemia (potassium < 2.5 mEq/L [2.5 mmol/L]) and its acute onset, pharmacologic correction is indicated.

Potassium chloride is preferred over potassium phosphate, potassium citrate, or potassium bicarbonate for supplementation. Potassium chloride results in quicker potassium repletion per dose than other forms. Also, as seen in the child in the vignette, hypokalemia is commonly associated with hypochloremia; potassium chloride would then ameliorate both the hypochloremia and hypokalemia.

In patients with no contraindication to oral intake, enteral administration (2–4 mEq/kg per day, up to 120–240 mEq per day) is the preferred route for potassium replacement. The risk for hyperkalemia is higher when intravenous (IV) potassium is administered because of the potential for errors in administration. Cautious IV dosing of potassium is recommended (0.5–1 mEq/kg of IV potassium over 1 hour). Intravenous administration at a concentration of less than 20 mEq/L (< 20 mmol/L) decreases the risk for phlebitis. Central venous access is required if a potassium concentration of more than 40 mEq/L (> 40 mmol/L) is prescribed. Potassium citrate or potassium bicarbonate is generally used in children with hypokalemia associated with renal tubular acidosis.

Asymptomatic hypokalemic patients with serum potassium ranging from 3 mEq/L (3 mmol/L) to 3.5 mEq/L (3.5 mmol/L) can be treated with increased intake of dietary potassium, along with correction of the underlying cause of hypokalemia.

Potassium is the most abundant intracellular cation and plays an important role in body homeostasis. Hypokalemia is defined as a serum potassium level of less than 3.5 mEq/L (laboratories usually set the lower limit of reference between 3.0 and 3.5 mEq/L). In newborns (preterm and term) and infants, due to the immaturity of renal tubular function, this range is higher (3.7–4.1 mEq/L [3.7–4.1 mmol/L]), depending on the local laboratory assay technique.

The clinical features of hypokalemia include muscle weakness or paralysis, cardiac arrhythmias, and impaired urinary concentrating ability. The presence of these features is dependent on the rapidity of onset and the duration of hypokalemia. Decreased urinary concentrating ability and chronic kidney injury usually result from prolonged and persistent hypokalemia, whereas the muscular and cardiac manifestations are seen with a rapid and acute decline in potassium levels. Mild potassium deficits usually present with muscle cramps and weakness. Severe potassium depletion (potassium <2 .5 mEq/L) leads to muscle weakness beginning in the lower extremities and progressing to the trunk and upper extremities; it may even progress to respiratory difficulty secondary to paralysis of the diaphragm and respiratory muscles. Severe hypokalemia can also result in rhabdomyolysis and myoglobinuria. It is important to recognize that the release of intracellular potassium associated with muscle breakdown may elevate serum potassium levels, complicating the identification of an underlying hypokalemia in these patients. Ileus from

decreased activity of the intestinal muscle and distension may lead to anorexia, nausea, and vomiting in patients with hypokalemia.

Premature atrial and ventricular beats, sinus bradycardia, paroxysmal atrial or junctional tachycardia, atrioventricular block, and ventricular tachycardia or fibrillation are reported in association with hypokalemia. The electrocardiogram changes characteristic of hypokalemia include PR prolongation, flattening of T waves, and ST depression. U waves, seen after the T waves on the precordial leads, may be seen in patients with profound hypokalemia

PREP Pearls

- For potassium replacement or supplementation, potassium chloride is generally preferred over potassium phosphate, potassium citrate, or potassium bicarbonate.
- The enteral route is preferred over intravenous administration for potassium supplementation.
- Hypokalemia, with a serum potassium level ranging from 3 to 3.5 mEq/L (3–3.5 mmol/L), can be treated with increased intake of dietary potassium.
- Severe potassium depletion (potassium < 2.5 mEq/L) leads to muscle weakness beginning in the lower extremities, progressing to the trunk and upper extremities. Prompt potassium supplementation is indicated in these patients.

ABP Content Specifications(s)

- Recognize the clinical and laboratory features associated with hypokalemia, and manage appropriately, including during an emergency situation

Suggested Readings

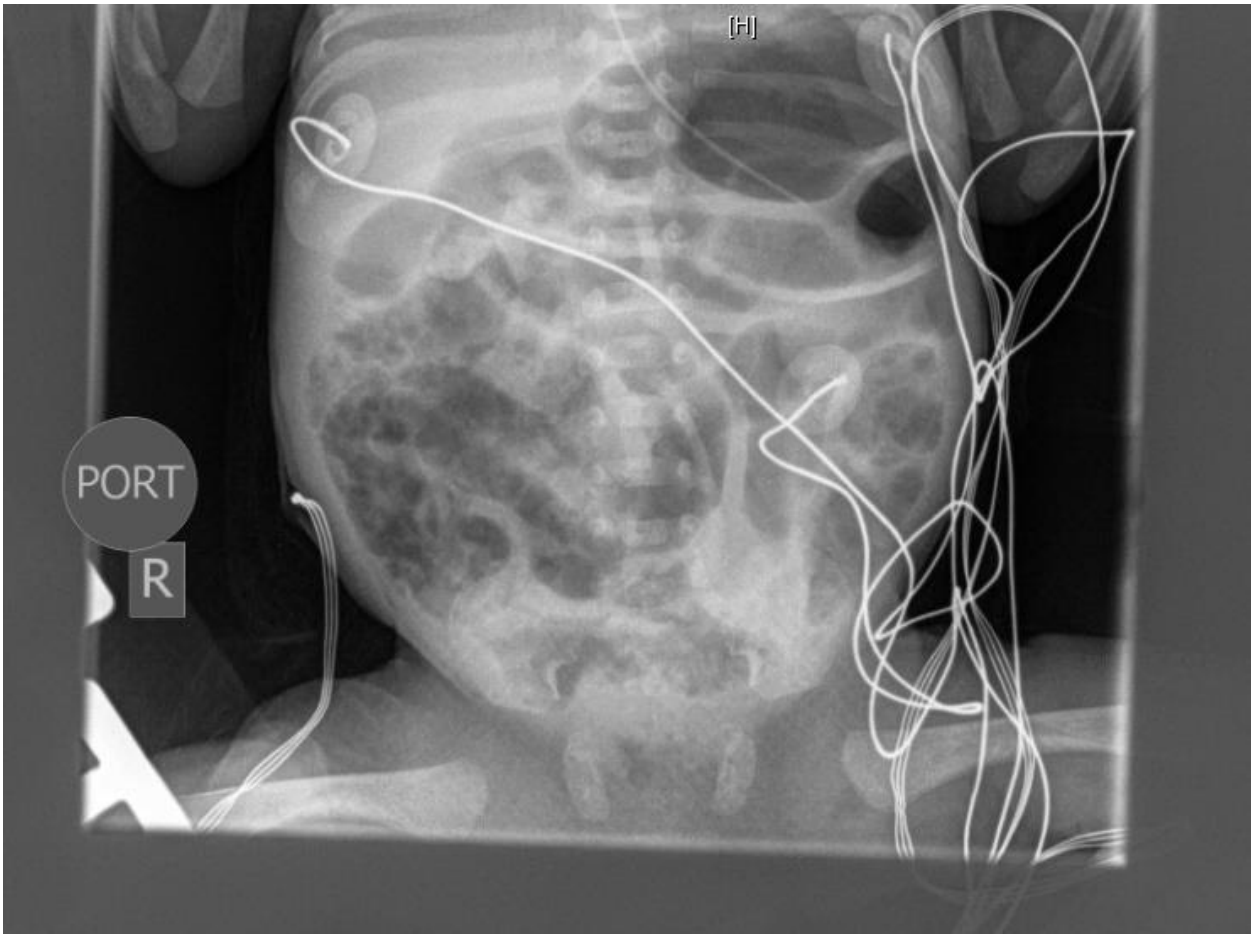
- Mahajan PV. Fluids and electrolytes in clinical practice. In: Kleigman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:471-480.
- Somers MJ, Traum AZ. Hypokalemia in children. *UpToDate*. Available online only with subscription..

Question 129

You are called to the bedside of a premature infant in the neonatal intensive care unit. He is a former 28-week-gestation infant with a birthweight of 874 g, now with a postconceptional age of 32 and 1/7 weeks. His active medical problems include bronchopulmonary dysplasia, requiring nasal continuous positive airway pressure with FiO_2 of 21%, apnea of prematurity being treated with caffeine, and anemia of prematurity. He had been on enteral feeds with maternal breast milk until 5 days ago and now is on premature formula feeds. His bedside nurse reports increased episodes of apnea over the past 4 hours. On physical examination, his vital signs show a temperature of 36.7°C, heart rate of 156 beats/min, respiratory rate of 45 breaths/min, and a blood pressure of 75/43 mm Hg. The infant is breathing comfortably with mild abdominal distension. Mild abdominal tenderness is noted on palpation. His extremities are well perfused. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	6,500/μL (6.5×10^9/L)
Hemoglobin	11.6 g/dL (116 g/L)
Platelet count	123×10^3/μL (123×10^9/L)
Sodium	132 mEq/L (132 mmol/L)
Potassium	4.5 mEq/L (4.5 mmol/L)

The infant's radiograph is shown in Item Q129**.**



Item Q129: *Abdominal radiograph for the infant described in the vignette. Courtesy of M LaTuga*

Of the following, the MOST likely diagnosis is
A. apnea of prematurity
B. bronchopulmonary dysplasia
C. cow's milk protein allergy
D. feeding intolerance
E. necrotizing enterocolitis

Correct Answer: E
Based on the clinical presentation, radiographic findings, and laboratory results, the most likely diagnosis for the infant in this vignette is necrotizing enterocolitis (NEC). Necrotizing enterocolitis is an inflammatory disease of the intestine that affects approximately 10% of extremely low birthweight infants weighing less than 1,000 g at birth. Infants with NEC have disruption of the intestinal mucosal barrier, allowing bacterial translocation into the intestinal wall. A subset of infants with NEC will have transmural necrosis, bowel perforation, and require surgical intervention. Though the pathogenesis remains unclear, NEC has been associated with prematurity, formula feedings, and treatment with broad spectrum antibiotics in the absence of culture-proven infection. Clinically, infants may present with subtle nonspecific findings such as abdominal distension, increased episodes of apnea and bradycardia, and temperature instability.

Abdominal radiography may show pneumatosis intestinalis with air noted in the intestinal wall, portal venous gas, or free air after bowel perforation. Laboratory findings include mild hyponatremia, leukopenia, and thrombocytopenia. Treatment for NEC remains supportive with antibiotic administration, bowel decompression, and bowel rest. Surgical intervention for bowel perforation from NEC may involve placement of an ostomy and mucous fistula or peritoneal drain placement. Mortality from NEC ranges from 30% to 50%, depending on other comorbid conditions. Infants who survive an episode of NEC have an increased risk of long-term neurocognitive impairment.

Apnea of prematurity and bronchopulmonary dysplasia are not associated with abdominal distension or abdominal tenderness, as was found in the infant in this vignette. Cow milk protein allergy has not been well documented in premature infants. Feeding intolerance is defined by the presence of milk or partially digested milk in the stomach prior to the next feeding with or without abdominal distension. Unlike the infant in this vignette, abdominal radiography should be normal with feeding intolerance.

PREP Pearls

- Necrotizing enterocolitis (NEC) is an inflammatory disease of the intestine with high mortality and morbidity.
- Infants with NEC may present with subtle findings such as hypothermia or feeding intolerance.
- In an infant with NEC, abdominal radiography will show pneumatosis intestinalis, portal venous gas, or free air.

ABP Content Specifications(s)

- Recognize the clinical and laboratory features associated with necrotizing enterocolitis in a newborn infant

Suggested Readings

- Maheshwari A, Carlo WA. Digestive system disorders. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:867-879.
- Morowitz MJ, Poroyko V, Caplan M, Alverdy J, Liu DC. Redefining the role of intestinal microbes in the pathogenesis of necrotizing enterocolitis. *Pediatrics*. 2010;125(4):777-785. doi: http://dx.doi.org/10.1542/peds.2009-3149.

Question 130

You are called to the nursery to see a male neonate born at 38 weeks of gestation to a 24-year-old gravida 1 para 0 woman who received routine prenatal care. Ultrasonography performed at 30 weeks of gestation because of poor fetal growth revealed hyperechogenic bowel and periventricular intracranial calcifications. At delivery, the small-for–gestational age neonate was noted to have a diffuse petechial rash and hepatosplenomegaly.

Of the following, the condition MOST commonly associated with this neonate's condition is

A. cerebral palsy

B. learning disability

C. seizures

D. sensorineural hearing loss

E. vision impairment

Correct Answer: D
The newborn in the vignette has congenital cytomegalovirus (CMV) infection. Congenital CMV is the most common cause of nonhereditary sensorineural hearing loss. In utero manifestations of congenital CMV disease include the following:

- Growth restriction
- Hepatosplenomegaly
- Hydrops
- Hyperechogenic fetal bowel
- Microcephaly
- Oligo- or polyhydramnios
- Periventricular intracranial calcifications

Many neonates are asymptomatic. In those with symptoms, frequent findings include the following:

- Hemolytic anemia
- Hepatosplenomegaly
- Hypotonia
- Jaundice
- Microcephaly
- Petechiae
- Seizures

Although children with a history of congenital CMV infection can have cerebral palsy, intellectual disability, learning disability, or seizures, sensorineural hearing loss is the most common clinical sequela of congenital CMV infection. Hearing loss is identified in one-third to one-half of infants with symptomatic disease.

Hearing loss is a common pediatric condition. One in 1,000 newborns and 2 in 1,000 young children experience hearing loss; by age 18 years, 17 in 1,000 will have some degree of permanent hearing loss. Hearing loss in early childhood can lead to delays in speech, language, social, and cognitive development. Some children with hearing loss also experience delays in gross motor development. Untreated hearing loss can have dramatic effects on educational attainment and mental health. Although young infants with profound hearing loss will develop prelingual language skills at a normal pace, after age 6 to 9 months, they will lose these skills and will not progress. Parents may note that children with hearing loss do not make eye contact or turn to sound, although even those with profound hearing loss may react to shouts or other loud sounds because they can feel vibrations. Once hearing loss is identified, treatment aims to minimize the duration or degree of hearing loss, maximize remaining hearing, and provide appropriate strategies to optimize communication and development.

Hearing loss is classified as conductive, sensorineural, mixed, or central (Item C130).

Item C130. Classification of Hearing Loss.

Type of Hearing Loss	Definition	Examples
Conductive	Disruption of sound waves traveling through outer or middle ear	• Blockage of external auditory canal (eg, cerumen) • Cholesteatoma • Malformation of auditory ossicles • Microtia/atresia of outer ear • Otitis media • Otosclerosis • Tympanic membrane perforation
Sensorineural	Pathology at the level of the cochlea, inner ear, or auditory nerve	• Anatomic malformations • Barotrauma • Hereditary hearing loss (syndromic or isolated) • Infection, including congenital cytomegalovirus infection • Meningitis • Neurologic conditions (eg, stroke, multiple sclerosis) • Noise exposure • Ototoxic drug exposure • Penetrating trauma • Premature birth
Mixed	Combination of conductive and sensorineural hearing loss	
Central	Hearing loss that results from damage to the auditory processing centers of the brain	• Brain injury • Stroke

Courtesy of I. Larson

PREP Pearls

- Conductive hearing loss includes disruption of sound traveling to the cochlea or middle ear. Etiologies include congenital anomalies, blockages in the external canal, and conditions that affect the integrity and function of the tympanic membrane and ossicles.
- Sensorineural hearing loss occurs at the cochlea, inner ear, or auditory nerve and includes hereditary hearing loss, congenital and postnatal infections, trauma, and exposure to drugs and noise.
- Unrecognized and untreated hearing loss can lead to developmental delays and learning problems.

ABP Content Specifications(s)

- Recognize conditions that contribute to hearing loss/impairment in patients of various ages, and the effects of that hearing loss on language development and learning
- Understand the natural history and etiologies of conductive hearing loss
- Understand the etiologies (eg, infectious, genetic, traumatic) of sensorineural hearing loss
- Recognize age-related clinical findings associated with hearing loss of various etiologies

Suggested Readings

- Boppana SB, Ross SA, Fowler KB. Congenital cytomegalovirus infection: clinical outcome. *Clin Infect Dis*. 2013;57(suppl 4):S178-S181. doi: http://dx.doi.org/10.1093/cid/cit629.
- Grindle C. Pediatric hearing loss. *Pediatr Rev*. 2014;35(11):456-464. doi: http://dx.doi.org/10.1542/pir.35-11-456.
- Kral A, O'Donoghue GM. Profound deafness in childhood. *N Engl J Med.* 2010;363(15):1438-1450. doi: http://dx.doi.org/10.1056/NEJMra0911225.

Question 131

A 5-year-old previously healthy and fully immunized boy is seen in your office with malaise, myalgias, upper respiratory symptoms, and fever for 3 days. Influenza A virus is confirmed with a rapid antigen test, and you recommend supportive care. Four days later, he is brought to the emergency department (ED) by ambulance with coarse inspiratory stridor and acute respiratory distress. For 2 to 3 days before the rapid progression of his symptoms, the boy had exhibited a croupy cough. His parents report that in the 6 to 8 hours before his presentation to the ED, the boy complained of throat pain and was refusing to eat or drink.

On arrival at the ED, the boy has a temperature of 40°C. His oxygen saturation is 76% in room air. On physical examination, he appears anxious and has a respiratory rate of 45 breaths/min. Poor aeration is noted on auscultation. The boy quickly becomes combative and requires intubation with signs of respiratory failure. During intubation, the anesthesiologist notes a normal-appearing posterior oropharynx and copious purulent secretions in the airway. Chest radiography reveals a dense left lingular infiltrate.

Of the following, the MOST likely cause for this boy's respiratory compromise is

A. bacterial tracheitis

B. epiglottitis

C. influenza pneumonitis

D. lobar pneumonia

E. peritonsillar abscess

Correct Answer: A

The boy in the vignette is exhibiting signs and symptoms highly suggestive of bacterial tracheitis.

Bacterial tracheitis is also known as bacterial laryngotracheobronchitis or membranous croup. This condition causes upper airway obstruction, and should be suspected in any child who presents with cough, stridor, and respiratory distress. Affected patients typically present with high fever and a toxic appearance. Recently, the spectrum of disease has been expanded to include a less severe clinical presentation, designated as *exudative tracheitis*. Bacterial tracheitis may be life threatening, and a high index of suspicion is essential to prevent a delay in diagnosis. It is critical to differentiate these children from those with the more common viral laryngotracheobronchitis or croup, and from those with epiglottitis.

Bacterial tracheitis usually presents as a complication of an initial acute respiratory viral infection; case reports have consistently found an association with influenza A. It is more commonly seen during the fall and winter months. The most common pathogens isolated on cultures of tracheal aspirates include *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis.* Methicillin-resistant *S aureus* is relatively uncommon. Whereas croup typically affects children between the ages of 6 months and 3 years, bacterial tracheitis is usually seen in children from 6 months to 14 years of age, with a peak in incidence between 3 and 8 years. Younger patients are more likely to progress to respiratory failure, requiring mechanical ventilatory support. The most common symptoms at presentation include cough, stridor, hoarseness, fever, and tachypnea. Stridor may be biphasic. The cough is typically dry, despite the associated airway inflammation and tracheal secretions. Drooling and odynophagia are generally not seen.

Children with bacterial tracheitis are often initially treated for croup, because of overlaps in the clinical presentation. Therefore, acute worsening of clinical status or failure to improve with treatment for croup should elicit concern for bacterial tracheitis.

Chest radiographs are often nonspecific in cases of bacterial tracheitis, but approximately 50% will also have pneumonia. Lateral views of the airway and chest may reveal an irregular "shaggy" tracheal contour because of exudative prominence and inflammatory change. Flexible bronchoscopy will reveal intense inflammation and subglottic exudative material. Treatment includes respiratory support and broad-spectrum antibiotics, which may be narrowed once culture results are available. Bronchoscopic intervention may be required to remove tracheal membranes from the airway. Otolaryngology consultation is recommended because membranes may be fibrinous, hemorrhagic, and adherent in nature. Corticosteroids may be used to treat airway edema, however, the balance of risk versus benefit must be considered, particularly in the setting of a patient with toxic effects and potentially sepsis. Complications of bacterial tracheitis may include toxic shock syndrome, acute respiratory distress syndrome, and septic shock.
The boy in the vignette is fully immunized, thus epiglottitis is unlikely. In the past, *Haemophilus influenzae* type B (HIB) was a leading cause of epiglottitis, however, this has become uncommon since the implementation of routine immunization with the HIB vaccine. Epiglottitis does still

occur, and may be caused by staphylococci, streptococci, or nontypeable *H influenzae*. In contrast to viral and bacterial tracheitis, epiglottitis is typically not preceded by a viral prodrome. On laryngoscopy, the otolaryngologist will visualize a cherry red and markedly enlarged epiglottis. If epiglottitis is clinically suspected, a care team consisting of otolaryngology and anesthesiology should be gathered before examining the child's throat or otherwise causing any agitation. This is because acute laryngospasm and complete obstruction of the airway may occur and is associated with a high level of morbidity and mortality.

A child with influenza pneumonitis may present with a toxic appearance, but wheezing and fine crackles, rather than stridor, would be expected on auscultation. In addition, chest radiography would likely reveal a diffuse interstitial or alveolar pattern, rather than a focal infiltrate. It is unlikely that a child with an isolated lingular infiltrate would experience respiratory failure.
A peritonsillar abscess may cause stridor and airway obstruction. However, examination of the posterior oropharynx typically reveals asymmetry and deviation of the uvula.

PREP Pearls

- Bacterial tracheitis should be considered in any child who presents with stridor and respiratory compromise.
- Bacterial tracheitis should be considered in a child who has acute worsening of symptoms or fails to improve with treatment for acute laryngotracheobronchitis or croup.
- Bacterial tracheitis is often preceded by a viral illness.

ABP Content Specifications(s)

- Recognize the clinical findings, including disease course, associated with tracheitis
- Plan the appropriate management of tracheitis
- Identify the pathogens most likely associated with tracheitis

Suggested Readings

- Hopkins A, Lahiri T, Salerno R, Heath B. Changing epidemiology of life-threatening airway infections: the reemergence of bacterial tracheitis. *Pediatrics*. 2006;118(4):1418-1421. doi: http://dx.doi.org/10.1542/peds.2006-0692.
- Hopkins BS, Johnson KE, Ksiazek JM, et al. H1N1 influenza A presenting as bacterial tracheitis. *Otolaryngol Head Neck Surg*. 2010;142(4):612-614. doi: http://dx.doi.org/10.1016/j.otohns.2010.01.005.
- Miranda AD, Valdez TA, Pereira KD. Bacterial tracheitis: a varied entity. *Pediatr Emerg Care.* 2011;27(10):950-953. doi: http://dx.doi.org/10.1097/PEC.0b013e3182309d45.

Question 132

A 24-month-old girl is brought to your clinic for her 2-year health supervision visit. Her father reports she has stopped saying words she used to know, and she twirls her hands a lot. Her occipital frontal circumference growth curve shows a plateau. Her height and weight have increased as expected for age. The remainder of the physical and neurological examination is unremarkable. The father asks if she has autism.

Of the following, the MOST likely diagnosis is

A. Angelman syndrome
B. autism spectrum disorder
C. inborn error of metabolism
D. Landau-Kleffner syndrome
E. Rett syndrome

Correct Answer: E
The girl in the vignette has Rett syndrome. Rett syndrome is characterized by a predictable progression of clinical findings. The earliest finding is a decline in head growth. Head circumference is typically normal at birth, but a deceleration in growth velocity is noticeable as early as 2 to 3 months of age. Early language acquisition occurs on time, but between 1 and 2 years of age, receptive and expressive language are lost. At the same time, the child's ability to purposefully use the hands is lost and "hand-wringing" starts. Seizures may start around this time as well. Rett syndrome is due to a mutation in the *MECP2* gene on the X chromosome. It is an X-linked dominant disorder, so most patients are girls. There are rare cases of boys with *MECP2* mutation who have a diagnosis of Rett syndrome. Patients with Rett syndrome have autistic features, but this is due to their underlying diagnosis.

The term "neurodegenerative disorders" covers a broad range of genetic, metabolic, and neurological syndromes that affect the brain. The child can be symptomatic from birth or can acquire symptoms later in life. By definition, neurodegenerative disorders include a progressive decline in functioning, although as in the case in the vignette, there can be a plateau or even transient improvements during the clinical course. Clinicians should be alert to the loss of previously acquired abilities or skills, such as vision, language, hearing, hand use, ambulation, or mood regulation.

Angelman syndrome is a neurogenetic syndrome characterized by near absence of expressive language, intellectual disability, gait ataxia, and a characteristic, happy personality. Often, there is microcephaly. Symptoms become apparent around 6 months of age. Key features distinguishing Angelman syndrome from Rett syndrome are the absence of language development (in Rett syndrome, language develops, but then regresses) and lifelong microcephaly (in Rett syndrome, the head growth is initially normal, but then there is a plateau). Autism spectrum disorder is a neurodevelopmental disorder with characteristic patterns of behavior, interaction, and communication. Many children with a neurogenetic syndrome have features of autism. Thus, it is important for clinicians to consider whether there are symptoms of another underlying condition when evaluating a child for autism. The girl in the vignette has several clinical features seen in children with autism, however, the deceleration in head growth and language regression suggest that she has Rett syndrome.

Inborn errors of metabolism (IEMs) cause a wide variety of neurodevelopmental symptoms, including developmental regression and autistic features, such as described for the girl in the vignette. Her presentation is very characteristic of Rett syndrome and therefore this is the most likely diagnosis. If genetic testing does not confirm Rett syndrome, however, IEMs such as cerebral creatine deficiency should be considered. Creatine deficiency presents in young children with developmental delay, seizures, autistic features, and sometimes movement disorders or self-mutilation. There is overlap between this presentation and that of Rett syndrome, Angelman syndrome, and autistic spectrum disorder. It is important to consider IEMs because disease progression can be slowed by dietary modifications, as in the case of creatine deficiency.

Landau-Kleffner syndrome is an epileptic syndrome characterized by language regression as early as 3 years of age; there are often autistic features. Head size is unaffected and convulsive seizures are rare. Diagnosis is made on electroencephalogram, which shows electrical status epilepticus during sleep. Landau-Kleffner syndrome should be considered in a child aged 3 to 7 years when there is either language regression or consideration for a diagnosis of autism.

PREP Pearls

- Language regression, deceleration of head growth, and loss of purposeful hand use in a girl suggests a diagnosis of Rett syndrome.
- Near-absence of language development, lifelong microcephaly, and ataxic gait in a boy or a girl suggests a diagnosis of Angelman syndrome.

ABP Content Specifications(s)

- Recognize the clinical findings associated with a degenerative disorder of the central nervous system

Suggested Readings

- Chistodoulou J. MECP2-related disorders. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1497/.
- Dagli AI, Mueller J, Williams CA. Angelman syndrome. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1144/.
- Mercimek-Mahmutoglu S, Salomons GS. Creatine deficiency syndromes. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK3794/.

Question 133

An 18-month-old previously healthy boy presents to the emergency department with 3 days of fever, poor feeding, vomiting, and foul-smelling diarrhea. He has been vomiting about 15 times per day and has had about 10 watery stools per day. There are several other children in his daycare that have similar symptoms. His mother says he has not been able to keep down sips of water or juice without vomiting. He has been increasingly lethargic and has developed difficulty breathing in the last 12 hours. Vital signs show a temperature of 38.2°C, heart rate of 160 beats/min, respiratory rate of 32 breaths/min, blood pressure of 80/60 mm Hg, and oxygen saturation of 100% on room air. On physical examination, the child is awake but minimally interactive. Mucous membranes are dry, eyes are sunken, and extremities are cool with capillary refill time of 4 seconds. He is breathing comfortably and his lungs are clear to auscultation and equal bilaterally. Heart is hyperdynamic, with no rubs, murmurs, or gallops.

Of the following physiologic derangements, the MOST likely to be present in this child is

A. decreased intravascular volume
B. decreased pulmonary vascular resistance
C. decreased systemic vascular resistance
D. increased arteriolar capacitance
E. increased central venous pressure

Correct Answer: A

The boy in this vignette has hypovolemic shock from gastroenteritis and dehydration. He is tachycardic and has a capillary refill time of 4 seconds. Of the choices listed, the most likely physiologic derangement is decreased intravascular volume.

Shock is a life-threatening condition characterized by inadequate oxygen or substrate delivery to meet metabolic demands of end organs. The most common form of shock worldwide is hypovolemic shock because of the high incidence of life-threatening diarrheal illness. Other causes of hypovolemic shock include bleeding, burn injury, and excessive diuretic use. Oxygen delivery is equal to the product of cardiac output and oxygen content. Cardiac output is the product of stroke volume and heart rate. Stroke volume is dependent on preload, afterload, and contractility. Preload is the volume of blood filling the ventricles at the end of diastole. In hypovolemic shock, stroke volume is low because of inadequate preload from decreased intravascular volume. In compensated hypovolemic shock, elevated circulating catecholamines cause tachycardia, increased inotropy, and arteriolar vasoconstriction. Signs of hypovolemic shock include delayed capillary refill time, cool skin, dry mucous membranes, skin tenting, and diminished peripheral pulses.

Capillary refill time is tested by compressing a capillary bed briefly so that the skin blanches and recording the time required for the skin to become pink. It is a simple, objective, noninvasive clinical indicator. Determinants of capillary refill time include stroke volume and arteriolar capacitance. Accordingly, cardiogenic shock with decreased stroke volume and other conditions associated with systemic vasoconstriction, such as some instances of sepsis, toxic ingestions, and cool ambient temperatures, can also cause delayed capillary refill time. The American Heart Association's Pediatric Advanced Life Support curriculum recommends using capillary refill time as an early marker of compensated shock and that interventions such as aggressive fluid resuscitation can restore perfusion and reverse shock. Decreased capillary refill time, or "flash" (rapid) capillary refill, is seen in conditions of vasodilation, such as "warm" sepsis and some toxic ingestions. A patient can have shock with either normal or decreased capillary refill time. Indeed, conditions causing vasodilation may be associated with pooling of blood in the arterioles and venules, causing low preload. Also, diastolic hypotension may occur in these conditions because blood continues to "run off" into dilated arteriolar beds during diastole. Since ambient temperatures may also affect capillary refill time, the entire clinical picture should be considered before making a judgment of intravascular volume.

Pulmonary vascular resistance is not affected in hypovolemic shock. Systemic vascular resistance is usually elevated in hypovolemic shock because of elevated circulating catecholamines and diversion of blood away from the skin and splanchnic circulation. This causes a decrease in arteriolar capacitance, as opposed to increased arteriolar capacitance, which can be seen with conditions of systemic vasodilation such as early septic shock. Increased central venous pressure is not correct because intravascular depletion decreases blood volume and venous pressure.

PREP Pearls

- Capillary refill time of 3 seconds or greater can be a marker of compensated shock, and may require therapies to increase cardiac output depending on the etiology.
- Capillary refill time of less than 1 second, also known as "flash" capillary refill, indicates vasodilation and increased arteriolar capacitance, and in selected cases, can also be associated with shock.

ABP Content Specifications(s)

- Understand the factors that affect capillary refilling time

Suggested Readings

- Raimer PL, Han YY, Weber MS, Annich GM, Custer JR. A normal capillary refill time of = 2 seconds is associated with superior vena cava oxygen saturations of = 70%. *J Pediatr*. 2011;158(6):968-972. doi: http://dx.doi.org/10.1016/j.jpeds.2010.11.062.
- Yager P, Noviski N. Shock. *Pediatr Rev*. 2010;31(8):311-319. doi: http://dx.doi.org/10.1542/pir.31-8-311.

Question 134

You receive a call from your state newborn screening laboratory regarding an abnormal thyroid-stimulating hormone (TSH) level of 250 mIU/L (normal, < 30 mIU/L) for a male neonate drawn on the second day of life. You call the family and see the neonate in your office the same day. He is currently 7 days old and was born at 40 weeks of gestation by spontaneous vaginal delivery after an uncomplicated pregnancy. His parents have no concerns, except that the newborn screen results are abnormal. He is breastfeeding on demand every 2 to 3 hours without difficulty and having soft, yellow, seedy stools after almost every feed. His birth weight was 3.4 kg and today's weight is 3.3 kg. Physical examination is unremarkable.

Of the following, the BEST next step is

A. obtain confirmatory TSH and free thyroxine, and await the results

B. obtain confirmatory TSH and free thyroxine, and start levothyroxine today

C. refer to pediatric endocrinology

D. repeat the newborn screen and see back in 1 week

E. start levothyroxine today and see back in 1 week

Correct Answer: B
The neonate described in the vignette has congenital hypothyroidism with a significantly elevated thyroid-stimulating hormone (TSH) level on newborn screening. Confirmatory venous TSH and free thyroxine should be drawn and, given the filter paper TSH level of greater than 40 mIU/L, levothyroxine should be started immediately, without waiting for the confirmatory test results. Referral to pediatric endocrinology is appropriate, but obtaining the confirmatory venous sample and treatment for the elevated TSH level should not be delayed.

Timely treatment of congenital hypothyroidism is essential to prevent cognitive impairment. Levothyroxine should be initiated by 2 weeks of age at a recommended starting dose of 10 to 15 μg/kg per day. Levothyroxine is not available as a liquid preparation and should not be compounded due to dosing inaccuracies. Rather, the tablet should be crushed and given orally to the infant in a small amount of breast milk, formula, or water. Alternatively, the infant may suck the crushed tablet fragments from a moistened finger placed directly into the infant's mouth. Thyroid function tests are monitored every 1 to 2 months in the first 6 months of life with a goal free thyroxine level in the upper half of the normal range and TSH in the normal range.

Most infants with congenital hypothyroidism are asymptomatic shortly after birth, as there is some placental transfer of maternal thyroxine. If signs and symptoms are present, prolonged jaundice, large anterior fontanelle, open posterior fontanelle, and umbilical hernia are the most common. When diagnosis is delayed or when both mother and fetus are hypothyroid, as occurs in areas of endemic iodine deficiency, more severe clinical features of congenital hypothyroidism are present. These additional features may include weak cry, low activity level, poor feeding, constipation, dry skin, developmental delay, and poor growth. The infant in Item C134 displays typical characteristics of coarse facial features, eyelid myxedema, large tongue, and broad, flattened nasal bridge. Depending on the etiology, a goiter may be present.

Item C134: *Infant with coarse facial features, eyelid myxedema, large tongue, and broad, flattened nasal bridge. Beltroy E, Umpaichitra V, Gordon S, Castells S. Visual diagnosis. Pediatr Rev. 2003;24(1):116-122.*

Abnormal thyroid gland development (dysgenesis), which includes ectopic thyroid tissue, is the most common etiology of congenital hypothyroidism. Defects in thyroid hormone synthesis, known as dyshormonogenesis, are the next most common. In the absence of goiter, which suggests dyshormonogenesis, the etiology can generally be determined by workup with ultrasonography to detect thyroid tissue in the neck and nuclear medicine scan for functional thyroid tissue. However, treatment should not be delayed to allow for performance of these tests.

Acquired hypothyroidism is most often due to autoimmune destruction of thyroid tissue and usually presents in older children and adolescents. Females in adolescence are more often affected than males. Common symptoms include fatigue, constipation, dry skin, and in females, menstrual irregularities. Common examination findings include poor growth, relative bradycardia, dry skin and hair, and delayed return of deep tendon reflexes. The thyroid gland may be enlarged and have a firm, heterogeneous texture. The diagnosis of hypothyroidism is made with an elevated TSH and low free thyroxine. Thyroid peroxidase and anti-thyroglobulin antibodies are often detectable in autoimmune hypothyroidism. Treatment is with levothyroxine replacement.

PREP Pearls

- When thyroid stimulating hormone (TSH) is greater than 40 mIU/L on filter paper newborn screening, confirmatory venous TSH and free thyroxine should be drawn and levothyroxine started immediately without waiting for the confirmatory test results.
- Timely treatment of congenital hypothyroidism is essential to prevent cognitive impairment. Levothyroxine should be initiated by 2 weeks of age at a starting dose of 10 to 15 μg/kg per day.
- Most infants with congenital hypothyroidism are asymptomatic.

ABP Content Specifications(s)

- Recognize the signs and symptoms of congenital and acquired hypothyroidism
- Plan the appropriate management of congenital and acquired hypothyroidism
- Plan the appropriate diagnostic evaluation of hypothyroidism

Suggested Readings

- Diaz A, Lipman Diaz EG. Hypothyroidism. *Pediatr Rev.* 2014;35(8):336-347. doi: http://dx.doi.org/10.1542/pir.35-8-336.
- Léger J, Olivieri A, Donaldson M, et al. European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. *J Clin Endocrinol Metab.* 2014;99(2):363-384. doi: http://dx.doi.org/10.1210/jc.2013-1891.
- Rose SR, Brown RS, Lawson Wilkins Pediatric Endocrine Society. Update of newborn screening and therapy for congenital hypothyroidism. *Pediatrics*. 2006;117(6):2290-2303. doi: http://dx.doi.org/10.1542/peds.2006-0915.

Question 135

A 13-year-old adolescent presents to your office for evaluation of worsening right thigh pain. Two weeks ago, while playing soccer, she sustained a "bad bruise" when another player kneed her in the middle of her right thigh. Initially, the injured area was very tender to touch, felt firm, and appeared swollen. The adolescent applied ice, took a nonsteroidal anti-inflammatory medication, and rested. After a few days, she felt able to slowly return to exercise. However, over the past 2 days, her thigh pain has progressed to the point that it is painful to bear weight. Her temperature is 38°C, heart rate is 100 beats/min, respiratory rate is 20 breaths/min, and blood pressure is 115/70 mm Hg. Her physical examination is remarkable only for pain on palpation of the mid to distal right thigh, with limited range of motion of the knee, and a limp favoring the right leg. The tender area feels firm, but there is no appreciable swelling, overlying erythema, or warmth. Her complete blood cell count results are shown:

Laboratory test	**Result**
White blood cell count	18,000/μL (18×10^9/L)
Neutrophils	75%
Lymphocytes	20%
Eosinophils	3%
Monocytes	2%
Hemoglobin	13.5 g/dL (135 g/L)
Platelet count	460 $\times 10^3$/μL (460×10^9/L)

Of the following, the test MOST likely to determine the patient's diagnosis is

A. blood culture
B. computed tomography of the right femur and knee
C. erythrocyte sedimentation rate
D. magnetic resonance imaging of the right femur and knee
E. plain radiography of the right femur and knee

Correct Answer: D
The adolescent in the vignette presents with a history of worsening thigh pain after partial recovery from trauma that occurred 2 weeks earlier. This illness course and the physical examination findings of low-grade fever, tachycardia, localized pain, and limp should raise concerns for acute hematogenous osteomyelitis (AHO). To make a definitive diagnosis of AHO, the best next step would be magnetic resonance imaging (MRI) of the femur and knee.

Initially, the signs and symptoms of AHO can be subtle and nonspecific, so a high index of suspicion is essential to making a timely diagnosis. Magnetic resonance imaging is the preferred imaging modality to make this diagnosis because of its high sensitivity and ability to provide relatively precise anatomic information, especially early in the disease. Isolation of bacteria from bone or adjacent structures confirms the diagnosis, but is positive in only about one-third of cases. Blood cultures will yield a pathogen in approximately 50% of cases of AHO. Computed tomography (CT) can be useful and may be necessary when metallic orthotic prosthetic devices are present or when MRI is not a feasible option. However, MRI is superior to CT in identifying the presence of bone marrow edema and swelling, or pus in the soft tissues adjacent to infected bone early in the course of the illness. Ancillary studies, such as erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP), are helpful in the evaluation of suspected osteomyelitis. Although elevation of these acute-phase reactants is not specific, they may be useful for monitoring response to therapy.

Plain radiography usually reveals soft tissue edema 3 days after the onset of infection, muscle swelling at 3 to 7 days, and evidence of periosteal reaction by 10 to 21 days, followed later by bony destruction. With the duration of the illness in this case, plain radiography might show findings consistent with AHO, but MRI would be more definitive.

This case highlights the common clinical presentation of bony infection. Acute hematogenous osteomyelitis may be preceded by trauma. The metaphysis of long bones, especially the femur and tibia, is the most common location. Typically, signs and symptoms gradually progress, becoming localized to the area of infection. On physical examination, focal pain and tenderness at the site of infection, mild swelling, and limited range of motion or decreased function of the involved limb may be evident. Most patients are febrile, though fever may be low grade. At presentation, laboratory findings often include a modest peripheral leukocytosis with or without an increase in immature polymorphonuclear leukocyte count, ESR, and serum CRP. Erythrocyte sedimentation rate may not rise appreciably until the infection has been present for about 1 week. C-reactive protein tends to become elevated sooner and returns to normal more rapidly than the ESR. When there is associated septicemia, AHO may present more acutely and the patient will appear more ill. Infants may present with pseudoparalysis because of pain with movement of the affected extremity.

PREP Pearls

- Magnetic resonance imaging is the preferred diagnostic test early in the course of suspected acute hematogenous osteomyelitis (AHO) because of its sensitivity and ability to precisely detail the anatomic findings.
- Localized pain and tenderness with limited range of motion or decreased function of the involved extremity are the clinical hallmarks of AHO.

ABP Content Specifications(s)

- Recognize the clinical findings associated with osteomyelitis in various anatomic locations

Suggested Readings

- Conrad DA. Acute hematogenous osteomyelitis. *Pediatr Rev.* 2010;31(11):464-471. doi: http://dx.doi.org/10.1542/pir.31-11-464.
- Kaplan SL. Osteomyelitis. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:3322-3326.

Question 136

You are called to the newborn nursery to evaluate a 3-day-old female newborn with worsening neurologic status. The full-term newborn was delivered via repeat cesarean delivery after an unremarkable pregnancy. She was initially doing well after birth. At approximately 12 to 24 hours of age, the mother noted a sweet, caramel-like odor. At 2 days of age, the newborn was feeding poorly, becoming irritable, and then developed drowsiness that progressed to lethargy, intermittent apnea, opisthotonus, and hypertonia. On day 3 after birth, the newborn developed "bicycling" movements of the legs. On physical examination, the newborn appears mildly dehydrated, lethargic, and hypertonic. Initial laboratory workup shows mild metabolic acidosis (pH = 7.3) and a blood ammonia level of 280 μg/dL (200 μmol/L). A complete blood cell count, lactate, calcium, and glucose are normal. A sepsis workup is initiated with cultures pending. You suspect an inborn error of metabolism.

Of the following, the BEST next test to confirm your suspected diagnosis is

A. biotinidase level
B. ceruloplasmin level
C. lysosomal enzyme screen
D. serum amino acids
E. very-long-chain fatty acids

Correct Answer: D
The newborn in the vignette has maple syrup urine disease (MSUD). By 12 to 24 hours of age, neonates with classic MSUD will have a maple syrup odor that is evident, especially in the cerumen. Plasma concentrations of branched-chain amino acids (isoleucine, leucine, and valine) and alloleucine will be elevated on serum amino acid analysis. Branched-chain hydroxyacids and ketoacids are evident on urine organic acid analysis. By 2 to 3 days of age, affected infants experience ketonuria, fussiness, and poor feeding. By 4 to 7 days of age, encephalopathy ensues, with opisthotonus, intermittent apnea, and lethargy progressing to respiratory failure and coma.

Maple syrup urine disease is an inborn error of metabolism belonging to the subtype known as organic acidemias. Organic acidemias are characterized by the excretion of non-amino organic acids in the urine, caused by an enzymatic deficiency in specific steps involved in amino acid catabolism. Other organic acidemias include:

- Glutaric acidemia type I
- Isovaleric acidemia, homocystinuria
- Methylmalonic acidemia
- Propionic acidemia
- 3-hydroxy-3-methylglutaryl-Coenzyme A (HMG-CoA) lyase deficiency

All are inherited in an autosomal recessive manner. Typically, newborns with these disorders appear well during the first few days after birth, with rapid decompensation to an encephalopathic state if not quickly identified. Common laboratory abnormalities include:

- Acidosis
- Elevated liver function tests
- Hyperammonemia
- Ketosis
- Low blood glucose
- Neutropenia

Recommended laboratory tests in the setting of a suspected organic acidemia include serum amino acids, urine organic acids, ammonia level, and a plasma acylcarnitine profile. Patients have improved outcomes if the disorder is identified in the first 10 days after birth and appropriate treatment and dietary restrictions are implemented.

With the advent of newborn screening programs using tandem mass spectrometry, MSUD is commonly identified shortly after birth, thus allowing for life-saving early treatment. Management includes dietary leucine restriction, specially manufactured branched chain amino acid-free foods, supplementation with isoleucine and valine, and intermittent biochemical monitoring. Care also includes clinical evaluations by a team specializing in metabolic disorders, including a biochemical geneticist, genetic counselor, and a metabolic dietitian. These patients are at increased risk for metabolic decompensation during periods of catabolic stress, such as intercurrent illness, and may require frequent hospitalization to manage the metabolic disorder appropriately and prevent the serious complication of brain edema.

Biotinidase levels screen for biotinidase deficiency. This disorder presents in young children with the slow evolution of neurologic abnormalities, including seizures, hypotonia, ataxia, developmental delays, vision problems, hearing loss, alopecia, and a skin rash.

Ceruloplasmin levels, in conjunction with copper levels, screen for Menkes disease. This disorder presents with a period of normal development in early infancy, followed by developmental regression, coarse, kinky hair (pili torti), and tortuosity of the carotid arteries and vasculature of the brain.

Mucopolysaccharidoses are identified through lysosomal enzyme screening and urine glycosaminoglycans. These disorders typically present with a slowly progressive coarsening of facial features, joint stiffness, and developmental regression.

Very-long-chain fatty acids screen for peroxisomal disorders, which present with a slow progression of hypotonia, poor feeding, dysmorphic facies, seizures, hepatic dysfunction, retinal dystrophy, and sensorineural hearing loss.

PREP Pearls

- Neonates with maple syrup urine disease (MSUD) appear well for the first 1 to 2 days after birth, and then experience a rapid progression to an encephalopathic state. Symptoms typically start with ketonuria, a maple syrup odor, poor feeding, and opisthotonus.
- Neonates with classic MSUD will have elevated plasma concentrations of branched-chain amino acids (isoleucine, leucine, and valine) and alloleucine on plasma amino acid analysis.
- Organic acidemias are caused by enzymatic deficiencies in specific steps of amino acid catabolism.
- Organic acidemias are inherited in an autosomal recessive pattern.

ABP Content Specifications(s)

- Plan the appropriate immediate and long-term management of organic acidemias, while considering the long-term prognosis
- Recognize the clinical features associated with organic acidemias

Suggested Readings

- Häberle J. Clinical and biochemical aspects of primary and secondary hyperammonemic disorders. *Arch Biochem Biophys.* 2013;536(2):101-108. doi: http://dx.doi.org/10.1016/j.abb.2013.04.009.
- Seashore MR. The organic acidemias: an overview. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1134/. Updated December 22, 2009. .
- Strauss KA, Puffenberger EG, Morton DH. Maple syrup urine disease. *GeneReviews*.

- van Karnebeek CD, Shevell M, Zschocke J, Moeschler JB, Stockler S. The metabolic evaluation of the child with an intellectual developmental disorder: diagnostic algorithm for identification of treatable causes and new digital resource. *Mol Genet Metab.* 2014;111(4):428-438. doi: http://dx.doi.org/10.1016/j.ymgme.2014.01.011.

Question 137

You are seeing a 16-year-old adolescent boy who recently transferred to your practice for evaluation of fatigue. His parents report that he has had debilitating fatigue for 9 months, causing him to miss approximately 3 days of school per week. The patient denies any other symptoms. Since the onset of his symptoms, multiple physicians, including several primary care providers, an endocrinologist, cardiologist, pulmonologist, and rheumatologist, have evaluated the patient. His evaluation thus far has included complete blood cell counts, inflammatory markers, thyroid studies, metabolic panels, an echocardiogram, polysomnography, and an adrenocorticotropic hormone stimulation test, all of which have been unremarkable. The fatigue has not improved during this period.

Of the following, the MOST appropriate next step in the evaluation and management of this patient would be to

A. administer a trial of modafinil
B. obtain Epstein-Barr virus serologies
C. order computed tomography of the sinuses
D. order magnetic resonance imaging of the brain
E. perform a thorough psychosocial assessment

Correct Answer: E
The adolescent boy in the vignette has already had an extensive and unremarkable evaluation for the more common organic causes of fatigue. The most appropriate next step would be to conduct a thorough psychosocial assessment to determine if there are any stressors. Fatigue is a common complaint among adolescents, and represents a major reason for prolonged school absenteeism. Organic causes of fatigue include endocrinopathies, infections, malignancy, and systemic illnesses. Psychological causes include depression and anxiety. Insufficient or inadequate sleep, whether related to an underlying sleep disorder or poor sleep hygiene, can also cause fatigue. The HEEADSSS tool can be used to guide the psychosocial assessment of an adolescent. A HEEADSSS interview should include questions about the **h**ome environment, **e**ducation and employment, **e**ating, **a**ctivities, **d**rugs, **s**exuality, **s**uicide/depression, and **s**afety from injury. The adolescent should be interviewed privately, without a parent present.

Modafinil is used for the management of narcolepsy, which is typically diagnosed by polysomnography in conjunction with a multiple sleep latency test. Effective treatment plans for narcolepsy include both medications as well as behavioral interventions.
For the adolescent in the vignette, a thorough psychosocial assessment should be performed before any additional testing, such as Epstein-Barr virus serologies, computed tomography of the sinuses, or magnetic resonance imaging of the brain.

PREP Pearls

- The HEEADSSS tool can be used to guide the psychosocial assessment of an adolescent.
- A HEEADSSS interview should include questions about the **h**ome environment, **e**ducation and employment, **e**ating, **a**ctivities, **d**rugs, **s**exuality, **s**uicide/depression, and **s**afety from injury.

ABP Content Specifications(s)

- Understand the importance of evaluating family dynamics in adolescent patients, including stressors and methods of coping with stress

Suggested Readings

- Fowler T, Duthie P, Thapar A, Farmer A. The definition of disabling fatigue in children and adolescents. *BMC Fam Pract*. 2005;6:33. doi: http://dx.doi.org/10.1186/1471-2296-6-33.
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- Jasik CB, Ozer EM. Preventive health care for adolescents and young adults. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. *Neinstein's Adolescent and Young Adult Health Care: A Practical Guide*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:50-69.
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- Wolbeek MT, van Doornen LJP, Kavelaars A, Heijnen CJ. Severe fatigue in adolescents: a common phenomenon? *Pediatrics*. 2006;117(6):e1078-e1086. doi: http://dx.doi.org/10.1542/peds.2005-2575.

Question 138

An 8-year-old boy is brought to your office for a health supervision visit. When you enter the examination room, you notice that he is playing on a tablet. When you ask what he is playing, he tells you excitedly about his favorite game, which involves gathering weapons and materials to fight against other players. He talks about how his friends and cousins play the same game and how they communicate through the game with each other. His 5-year-old and 2-year-old brothers are standing next to him, watching what is happening on the tablet.

Of the following, the MOST appropriate recommendation is to

A. allow all but the 2-year-old brother to use the tablet
B. eliminate all portable media use in the household
C. install software on their home computer to monitor internet use
D. remove the game before the children start to exhibit aggressive behaviors
E. supervise the communications that their son makes through the tablet

Correct Answer: E

It is important for the parents of the 8-year-old boy in the vignette to supervise the communications that he is making through the tablet. Safety is important when children engage in technology, particularly when they interact with others online. Children may not have appropriate judgment and understanding of what type of information is safe or suitable to share with others, particularly with those who they do not know. Children expose themselves to manipulation and may also share inappropriate information, pictures, or videos that could then be disseminated to unintended recipients. This can result in damage to a child's reputation, friendships, and self-esteem.

Media includes television, computers, video games, cell phones, tablets, and other digital devices. Children spend more time on media than in school or in any other activity besides sleep. The mobility of media via laptops and handheld devices (eg, cell phones, video players, tablets) increase access. Older children and adolescents spend more than 7 hours a day on media. Many children have televisions in their bedrooms and most children and adolescents have access to the Internet. Computer time is spent on social networking, playing games, and watching videos. The majority of adolescents own cell phones and most use text messaging. More than half of adolescents connect to a social media site (eg, social networking site, gaming site, video site, blog) at least once a day. Media's influence on children and adolescents can be both positive and negative.

Media use has been associated with problems such as aggressive behaviors, inattention, obesity, substance use, and sleep problems. Media can be problematic in content and time spent in its use. Media violence (eg, television, video games) results in desensitization of children to violence and has been associated with aggressive behaviors. Children may be exposed to inappropriate content, such as sexually explicit messages or images. Advertisements of unhealthy foods (eg, sugary snacks, fast food) and alcoholic beverages can also influence children. Those engaged in social media can be subject to cyberbullying, where digital media is used to threaten or intimidate. Sexting, or sending of sexually explicit images or messages, can result in disciplinary actions and emotional distress. Privacy concerns are also present, as children and adolescents may share too much information or post inappropriate material.

Children and adolescents have a difficult time limiting their use of media. The time spent on media displaces time that could have been spent on activities such as family time, schoolwork, physical activity or play, and creative endeavors. When used at night (particularly after bedtime), media may interfere with sleep and subsequently interfere with school performance and daytime behaviors. When adolescents engage in cell phone use while driving, they may endanger themselves and others. Even background media use (eg, television), particularly around young children, distracts the child, distracts the parent, and reduces their interactions with each other. On the other hand, media can be beneficial in enhancing learning, health, and connection with others. High-quality programs such as "Sesame Street" may teach young children language, numbers, geography, cooperative play, and tolerance for people of other backgrounds. Media use can enhance knowledge and collaborative learning of older children around school assignments and projects. For adolescents, websites and text messaging can be used to promote knowledge,

healthy behaviors, compliance with medication, and attendance at health appointments. Video games that include physical activity ("exergaming") may promote health. Media can convey prosocial messages such as inclusion and altruism. For older children and adolescents, social media is an important mechanism for communicating with friends and family and for making connections with others who share their interests. Social media can be a vital venue for developing and sharing creativity, talent, and skills (eg, music).

As children may learn and imitate both positive and negative behaviors from media, it is essential that pediatricians counsel patients and their families on its proper use. First, pediatricians should routinely ask about media use at health maintenance visits. It is important to ask about the amount of recreational screen time and the presence of a television or Internet connected device in the child's bedroom. Most children report that their parents have no rules about content or time limits on media use, except for computer use. Those with media in their bedroom are at higher risk for the aforementioned adverse effects. As recommended by the American Academy of Pediatrics (AAP), pediatricians should discourage screen media use (except video-chatting) for children younger than 18 months of age, as well as discourage the presence of screen media in the child's bedroom before bed, at mealtimes, and at parent-child playtimes. Children 2 to 5 years of age should be limited to under 1 hour a day of high-quality educational programming. Parents should monitor their children's use of media, particularly their online use. They should co-view media with their children, discuss the content with them, and reinforce any prosocial messages. They should ensure that websites are reliable and are appropriate for their child to view. They should check privacy settings and online profiles, consider using parental controls, and assist their children with interpreting information found online. Parents should establish a family plan for media use (healthychildren.org/mediauseplan) and model appropriate media use. A family plan may include rules about time spent on media and use of social media, text messaging, and cell phones. Rules may also include technology-free times (eg, mealtime, bedtime). Children should be advised not to give out personal information online and not to watch shows or play games inappropriate for themselves or for friends and family (eg, siblings, young relatives) watching or playing with them. Reading, physical activity, creative activities, and adequate sleep should be emphasized.

In this vignette, there are 3 children: ages 8 years, 5 years, and 2 years. The AAP discourages media exposure (except video-chatting) for children younger than 18 months of age. Use of the tablet does not need to be restricted from the 2-year-old child if parents are co-viewing high-quality programming with their child. Moreover, it would be unrealistic to eliminate all portable media use in the household. While installing internet monitoring software on the home computer can be helpful, it does not address the issues related to portable digital devices, online communication with others through other means, or exposure of the younger brothers to content that may not be appropriate for their age (eg, media violence). Appropriate supervision of what each child views, plays, and uses, as well as limits on use, should be placed. The most appropriate recommendation would be to supervise the communications that are made through the tablet.

Pediatricians can influence how families address media use in their children by providing age-appropriate counseling. A helpful resource from the AAP is safetynet.aap.org.

PREP Pearls

- Media use has been associated with problems such as aggressive behaviors, inattention, obesity, substance use, and sleep problems.
- Media can be beneficial in enhancing learning, health, and connection with others.
- Pediatricians should routinely ask about the amount of recreational screen time. The presence of a television or Internet-connected device in the child's bedroom identifies children at increased risk of adverse effects from media.

ABP Content Specifications(s)

- Understand the potential effects of various media on child and adolescent behavior
- Counsel patients regarding the proper use of the internet and social networking sites

Suggested Readings

- American Academy of Pediatrics. Policy statement: Media and Young Minds. *Pediatrics*. 2016;138(5): 2013;132(5):e20162591. doi: http://dx.doi.org/10.1542/peds.2016-2591.
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- Hogan MJ. Prosocial effects of media. *Pediatric Clin North Am*. 2012;56(3):635-645. doi: http://dx.doi.org/10.1016/j.pcl.2012.03.020.
- Yolanda RC, Radesky J, Christakis D, Moreno MA, Cross C, Council on Communications and Media. Children and Adolescents and Digital Media. Pediatrics. 2016;138(5): doi: http://dx.doi.org/10.1542/peds.2016-2593.

Question 139

A 9-year-old previously healthy boy is brought to the emergency department (ED) by paramedics after he was injured when the car he was riding in, travelling 40 miles per hour, struck a tree. The boy was restrained only with a lap belt. He was not ejected from the car, but his upper body was thrown forward and he bumped his left forehead on the driver's seat headrest. He was alert and oriented when the paramedics arrived at the scene of the accident.
The paramedics immobilized his entire spine using a pediatric backboard and cervical spine collar prior to transport.

In the ED, he is anxious but fully oriented. He reports pain in his head, abdomen, and back. His vital signs include a temperature of 37.1°C, heart rate of 100 beats/min, respiratory rate of 18 breaths/min, blood pressure of 100/72 mm Hg, and pulse oximetry of 98% (room air).
On physical examination, the boy's airway is clear, he is breathing spontaneously with normal respiratory effort, and his pulses and perfusion are normal. A superficial abrasion over his left forehead is noted. He has bruising over his lower abdomen. His abdomen is soft and non-distended, but it is tender to palpation in the periumbilical area and both lower quadrants. He displays no peritoneal signs. You note no bruising or step-offs on palpation of the boy's spine, but he has tenderness to palpation over the mid-lumbar spine at the level of L2-L3. A rectal examination reveals normal rectal tone with guaiac-negative stool. You note no abnormalities in the boy's extremity strength, sensation, or reflexes on neurologic examination.

As you proceed with your evaluation, the boy continues to complain of pain in his back, despite administration of an intravenous analgesic.

Of the following, the MOST likely etiology of his back pain is

A. acute herniation of the intervertebral disc between L2-L3
B. acute spasm of the lumbar paraspinal musculature
C. anterior spinal cord syndrome
D. referred pain from a retroperitoneal hematoma
E. a transverse fracture involving a mid-lumbar vertebral body

Correct Answer: E
The 9-year-old boy in the vignette presents with tenderness over his mid-lumbar spine, along with lower abdominal bruising and tenderness, following a motor vehicle collision in which he was restrained with only a lap belt. His neurologic examination reveals no deficits.

The most likely cause of his back pain is a transverse fracture involving a mid-lumbar vertebral body, otherwise known as a Chance fracture. Chance fractures are transverse fractures through the vertebral body that arise most often following motor vehicle collisions in which the affected individual was restrained by only a lap belt. Inappropriate or improperly positioned seat belts are commonly implicated in the occurrence of Chance fractures in children. While the boy in the vignette displays no neurologic deficits, Chance fractures can be associated with injury to the spinal cord and can lead to permanent neurological injury. Associated intraabdominal injuries are frequent, occurring in up to two-thirds of affected patients. Intra-abdominal injuries should be highly suspected, especially when a "seat belt sign" (bruising across the abdomen in the pattern of the seat belt) is present.

Spine fractures and spinal cord injuries are fortunately relatively rare in children. Only 5% of all spinal cord injuries occur in the pediatric age group. Despite this, spinal injuries are associated with significant morbidity and mortality when they do affect children. The consequences of missing early signs of spinal cord injury can be devastating. Therefore, it is imperative for all pediatric providers to recognize signs of spinal injury.

The 2 leading mechanisms for spinal injuries in pediatric patients involve motor vehicle collisions (usually involving younger children) and sports-related injuries (most commonly affecting adolescents). Falls from significant heights and child abuse can be additional causative mechanisms. Children with injuries to the spine often have other injuries involving multiple organ systems. Spine injuries should be highly suspected in children with an abnormal spine or neurologic examination, a high-risk injury mechanism, or a distracting injury, even in the absence of findings on plain radiographs. A distracting injury could include any painful injury, such as a displaced long bone fracture, that might lead a child to underestimate or neglect discomfort in other anatomic sites such as the spine.

It is important that full cervical and thoracolumbar spine immobilization is maintained until spine injury can be excluded in all children following trauma. Patients with injury to the spinal column are at risk for spinal cord injury, even if no such injury is apparent at the time of evaluation. Children presenting with pain, tenderness, decreased range of motion, deformity, or other symptoms localizing to the neck or back following trauma must be managed with the highest level of caution.

Intervertebral disc herniation is much less common in children than in adults. While intervertebral disc herniation may occur acutely as a result of trauma, presentation of this entity in young children is very rare. Clinical findings associated with intervertebral disc herniation may include back pain, sciatica (sharp pain radiating below the knees), limitation of spinal flexibility and passive straight-leg raising, and even decreased strength or reflexes in severe

cases. Neither sciatica nor neurologic deficits are found in the boy in the vignette and a fracture involving the lumbar vertebrae would be a more likely diagnosis.

Although the boy in the vignette could be experiencing some pain due to strain or spasm of his paraspinal musculature, midline pain with palpation over the bony spine would not be an expected finding with paraspinal muscle spasm. Fracture to the spinal column must be ruled out before attributing this boy's back pain to the etiology of muscle spasm or strain. Given the fact that the boy has point tenderness with palpation of the lumbar spine, a fracture involving his lumbar vertebrae is the more likely cause of his back pain.

Anterior spinal cord syndrome is a characteristic pattern of spinal cord injury resulting from infarction of the spinal cord in the territory supplied by the anterior spinal artery. This syndrome is characterized by paraplegia and a loss of pain and temperature sensation (with preservation of position, vibration, and deep pressure sensation). The boy in the vignette displays no neurologic deficits whatsoever. Although a lumbar vertebral fracture could lead to spinal cord injury in this boy, he currently has no clinical findings suggesting anterior spinal cord syndrome.

Chance fractures may certainly be associated with retroperitoneal and other intra-abdominal injuries. The boy in the vignette has bruising across his lower abdomen ("seat belt sign"), as well as abdominal tenderness on examination. He should undergo a thorough evaluation for intra-abdominal injury with close monitoring for signs of intraperitoneal blood loss. However, a retroperitoneal hematoma is not likely to be the cause of his back pain, which is localized to the midline directly over his lumbar vertebrae.

Spine injuries, with or without neurologic abnormalities, must always be considered in children with multiple injuries or following a high-risk mechanism of injury. Consultation with a spine surgeon should be obtained emergently for any child found to have a spine injury, or whenever a high clinical suspicion for spine injury is present (even without confirmatory radiologic findings).

PREP Pearls

- Though rare in children, spinal injuries are associated with significant morbidity and mortality. The consequences of missing early signs of spinal cord injury can be devastating.
- Chance fractures are transverse fractures through the vertebral body that arise most often following motor vehicle collisions in which the affected individual was restrained by only a lap belt. Inappropriate or improperly positioned seat belts are commonly implicated in the occurrence of Chance fractures in children.
- It is essential that full cervical and thoracolumbar spine immobilization be maintained in all children following trauma until spine injury can be excluded. Spinal cord injury may be present, even if no such injury is apparent at the time of evaluation.
- Children presenting with pain, tenderness, decreased range of motion, deformity, or other symptoms localizing to the neck or back following trauma should be suspected to have a spine injury and must be managed with the highest level of caution.

ABP Content Specifications(s)

- Recognize the clinical findings associated with spinal trauma

Suggested Readings

- American College of Surgeons. Pediatric trauma. *Advanced Trauma Life Support Student Course Manual.* 9th ed. Chicago, IL: American College of Surgeons; 2012: 366 pp.
- American College of Surgeons. Spine and spinal cord trauma. *Advanced Trauma Life Support Student Course Manual*. 9th ed. Chicago, IL: American College of Surgeons; 2012: 366 pp.
- Le TV, Baaj AA, Deukmedjian A, Uribe JS, Vale FL. Chance fractures in the pediatric population: a review. *J Neurosurg Pediatr.* 2011;8(2):189-197. doi: http://dx.doi.org/10.3171/2011.5.PEDS10538.
- Parent S, Mac-Thiong JM, Roy-Beuadry M, Sosa JF, Labelle H. Spinal cord injury in the pediatric population: a systematic review of the literature. *J Neurotrauma.* 2011;28(8):1515-1524. doi: https://www.ncbi.nlm.nih.gov/pubmed/21501096 .

Question 140

A 12-year-old boy with moderate persistent asthma presents to the pediatric clinic for wheezing in September. He has had 3 days of rhinorrhea and cough. This morning, he developed shortness of breath and has had increased use of his rescue inhaler. Vital signs show a temperature of 37.7°C, respiratory rate of 30 breaths/min, heart rate of 110 beats/min, and blood pressure of 100/55 mm Hg. On physical examination, he is in mild distress, and auscultation reveals diffuse wheezing and a prolonged expiratory phase.

Of the following, the MOST likely etiology for the illness in this patient is

A. adenovirus

B. coronavirus

C. parainfluenza

D. respiratory syncytial virus

E. rhinovirus

Correct Answer: E
The most likely etiology for the illness in the patient in this vignette is rhinovirus. Rhinoviruses are associated with approximately two-thirds of all asthma exacerbations. While the other viruses listed can be associated with an asthma exacerbation, rhinovirus is the most likely cause.

Rhinoviruses are the principal cause of the common cold, accounting for one-half to two-thirds of all colds. Peak rhinovirus activity occurs in spring and fall. Typical symptoms include rhinorrhea, congestion, sore throat, cough, and malaise. The common cold has a major economic burden related to lost productivity and treatment-related costs. Compared to adults, young children have more episodes of the common cold annually, have longer duration of symptoms, and shed the virus longer. While in general the common cold has a mild course of illness, it has been associated with other respiratory tract infections including pneumonia. Groups at greater risk of lower respiratory tract infections due to rhinoviruses include patients with asthma, infants, elderly individuals, and immunocompromised hosts.

Coronaviruses are the second leading cause of the common cold, accounting for 10% to 15% of cases. The common cold caused by rhinoviruses and coronaviruses are indistinguishable with regard to symptom severity and duration. Less frequently, coronaviruses are associated with lower respiratory tract infections. However, there are 2 coronaviruses that are distinguished by severe respiratory clinical illness: severe acute respiratory syndrome (SARS)-coronavirus and Middle East respiratory syndrome (MERS)-coronavirus. First recognized in 2003 in Asia, SARS led to an outbreak that sickened more than 8,000 people. Middle East respiratory syndrome was first reported in 2012 and is believed to have 30% to 40% mortality. All cases of MERS have been linked to the Arabian Peninsula.

Adenoviruses, parainfluenza viruses, and respiratory syncytial viruses can all cause the common cold, each accounting for 5% or less of cases, though traditionally, other clinical syndromes are ascribed to these infections. Adenoviruses are an infrequent cause of the common cold, but can cause a variety of infections, including pharyngitis, conjunctivitis, pneumonia, gastroenteritis, hepatitis, and meningoencephalitis. Parainfluenza viruses are the most common cause of croup, but can cause infection of the entire respiratory tract. While respiratory syncytial virus is a commonly recognized cause of bronchiolitis, it more commonly causes an upper respiratory tract infection.

PREP Pearls

- Rhinoviruses are the principal cause of the common cold, accounting for one-half to two-thirds of all colds.
- Compared to adults, young children have more episodes of the common cold annually, have longer duration of symptoms, and shed the virus longer.
- Rhinoviruses are associated with approximately two-thirds of all asthma exacerbations.

ABP Content Specifications(s)

- Recognize the clinical features associated with rhinovirus infection
- Recognize the epidemiology of rhinovirus infection

Suggested Readings

- American Academy of Pediatrics. Rhinovirus infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:676-677.
- Jacobs SE, Lamson DM, St George K, Walsh TJ. Human rhinoviruses. *Clin Microbiol Rev*. 2013;26(1):135-162. doi: http://dx.doi.org/10.1128/CMR.00077-12.

Question 141

You are seeing a 10-day-old breastfed male neonate in your office for follow-up of jaundice. He was delivered at term by spontaneous vaginal delivery after an uncomplicated prenatal course. There was no ABO incompatibility. His postnatal course has been complicated by jaundice, with an initial total bilirubin of 10 mg/dL (171 μmol/L) 36 hours after birth. His bilirubin level has continued to increase. He has been feeding well and has no other symptoms of illness.
On physical examination, the neonate has a temperature of 37°C, a heart rate of 130 beats/min, and a respiratory rate of 27 breaths/min. His weight is 5% below birthweight. He is sleepy, but arouses easily. His anterior fontanelle is open, soft, and flat. On cardiovascular examination, there is a regular rate and rhythm, without murmur. His abdomen is soft and nontender with no palpable hepatosplenomegaly. His sclerae are icteric and his skin is jaundiced, including his lower extremities. There is no rash.

Of the following, the BEST next laboratory test to help identify this neonate's diagnosis is:

A. alanine aminotransferase

B. aspartate aminotransferase

C. complete blood count

D. direct bilirubin

E. gamma-glutamyltransferase

Correct Answer: D
The direct bilirubin test is the best method to determine the presence of cholestasis that may be the result of biliary atresia or other obstructive etiology. Neonatal physiologic jaundice is common and typically benign, with resolution occurring by 2 weeks after birth. Neonatal cholestasis, identified by elevated conjugated (direct) hyperbilirubinemia, occurs because of a defect in production, defect with transport, metabolic disorder, or mechanical obstruction. The differential diagnosis of cholestasis in a newborn is reviewed in Item C141.

Item C141. Differential Diagnosis of Neonatal Cholestasis.

Obstructive	• Allagille syndrome • Biliary atresia • Choledochal cyst • Congenital hepatic fibrosis • Cystic fibrosis • Gallstones • Inspissated bile • Sclerosing cholangitis
Defect in production	Bile acid synthesis defect
Alterations in transport	Progressive familal intrahepatic cholestasis (PFIC)
Metabolic	• Alpha-1 antitrypsin deficiency • Congenital disorders of glycosolation • Cystic fibrosis • Galactosemia • Inborn errors of metabolism • Mitochondrial disease • Niemann-Pick disease • Tyrosinemia • Wolman disease
Endocrine	• Hypothyroidism • Panhypopituitarism
Other	• Congestive heart failure • Infection • Immunologic - Neonatal lupus • Vascular malformations

Courtesy of C. Waasdorp Hurtado

The clinical presentation of neonatal obstructive cholestasis includes jaundice with scleral icterus, pale stools, poor weight gain, and at times, hepatomegaly. The evaluation should include a thorough history and physical examination along with liver function tests, direct bilirubin, g-glutamyltransferase, and coagulation studies. Additional studies may include acute infectious hepatitis titers, a-1 antitrypsin phenotype, TORCH (**t**oxoplasmosis, **o**ther agents, **r**ubella, **c**ytomegalovirus, and **h**erpes simplex) titers, urine cytomegalovirus, urine culture, newborn screening, and serum bile acids. Abdominal ultrasonography and magnetic resonance cholangiopancreatography (MRCP) can be used to evaluate for anatomic etiologies such as a choledochal cyst. If there is concern for biliary atresia, surgical cholangiography should be completed to evaluate patency of the bile duct.

Cholestasis is managed by correction of the underlying etiology when possible, such as treatment of urinary tract infection or sepsis. If cholangiography confirms biliary atresia, a Kasai portoenterostomy should be completed urgently to allow for bile drainage. The outcome is best when this surgery is completed within the first 60 days after birth.
Fat malabsorption is a complication of cholestasis. Children with cholestasis should be given a formula high in medium-chain triglycerides to improve absorption and thereby maximize nutrition. Fat-soluble vitamins should be supplemented and levels followed by means of serologic testing. Ursodeoxycholic acid is used to increase bile formation and antagonize the hydrophobic bile acids on the gastrointestinal membranes, thereby reducing conjugated bilirubin levels.

Since there is a high morbidity and mortality risk and a need for early diagnosis, the greatest priority would be to diagnose a child who has cholestasis related to biliary atresia. The literature clearly shows that direct bilirubin screening is the best initial method to evaluate for biliary atresia in infants with elevated bilirubin. Measurement of alanine aminotransferase and aspartate aminotransferase would be used to diagnose hepatitis. A complete blood cell count is helpful to identify infants with elevated bilirubin caused by hemolysis. gamma-glutamyltransferase is used to identify obstructive processes such as stones or anatomic abnormalities.

PREP Pearls

- Direct bilirubin is the best serum screening test for biliary atresia.
- The differential diagnosis for neonatal cholestasis includes obstruction, production defects, transport alterations, endocrine abnormalities, and a few miscellaneous etiologies.
- Fat malabsorption is a complication of cholestasis, and should be addressed by increasing medium-chain triglycerides and fat-soluble vitamins in the diet.

ABP Content Specifications(s)

- Recognize the clinical features associated with biliary atresia, and manage appropriately
- Plan the initial management of obstructive jaundice
- Recognize the clinical features associated with a choledochal cyst
- Plan the appropriate diagnostic evaluation for a patient in whom biliary atresia is suspected

Suggested Readings

- Brumbaugh D, Mack C. Conjugated hyperbilirubinemia in children. *Pediatr Rev.* 2012;33(7):291-302. doi: http://dx.doi.org/10.1542/pir.33-7-291.
- De Bruyne R, Van Biervliet S, Vande Velde S, Van Winckel M. Clinical practice: neonatal cholestasis. *Eur J Pediatr*.2011;170(3):279-284. doi: http://dx.doi.org/10.1007/s00431-010-1363-8.
- Feldman AG, Sokol RJ. Neonatal cholestasis. *NeoReviews*. 2013;14(2):e63-e73. doi: http://dx.doi.org/10.1542/neo.14-2-e63.
- Hartley JL, Gissen P, Kelly DA. Alagille syndrome and other hereditary causes of cholestasis. *Clin Liver Dis.*2013;17(2):279-300. doi: http://dx.doi.org/10.1016/j.cld.2012.12.004.

Question 142

A 15-year-old adolescent presents to your office for evaluation of left shoulder pain after a fall directly onto the lateral aspect of the left shoulder. On physical examination, you note mild swelling and tenderness at the distal end of the clavicle. He reports pain when he adducts his shoulder. He does not have any weakness with upper extremity muscle testing. Anteroposterior, axillary, and scapular Y radiographs of the shoulder are normal.

Of the following, the MOST likely diagnosis is

A. acromioclavicular joint sprain

B. occult clavicle fracture

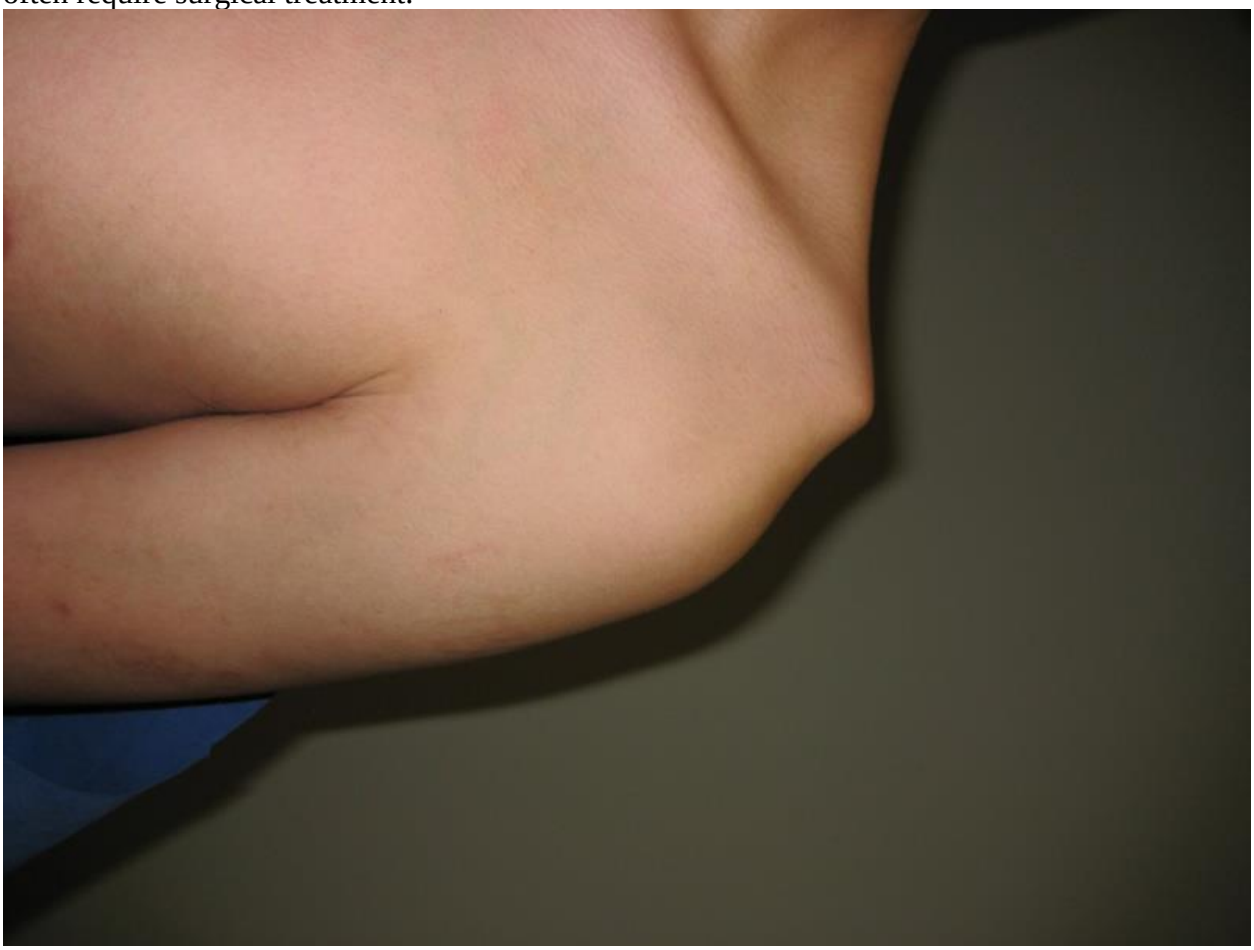
C. rotator cuff tear

D. shoulder dislocation with spontaneous reduction

E. sternoclavicular dislocation

Correct Answer: A

The patient in the vignette has sustained an acromioclavicular (AC) joint sprain, often referred to as a shoulder separation. The most common mechanisms of injury are a blow to the AC joint or a fall onto the lateral aspect of the shoulder. The AC joint sprains typically occur in adolescents or adults who participate in collision sports such as football, rugby, and hockey. Injured athletes typically have tenderness at the AC joint and pain with adduction of the arm across the chest. Clavicle displacement is often visible with higher-grade injuries (Item C142). The distal clavicle is held in position by the AC ligament and 2 coracoclavicular (CC) ligaments. The Rockwood classification stratifies AC joint injuries into 6 types, based on whether the injury involves only the AC ligament or both the AC and CC ligaments, and the direction and degree of clavicular displacement. Lower-grade injuries are generally treated with conservative measures such as rest, a sling for comfort, and range-of-motion exercises once pain has abated. Type I injuries often heal within 1 to 2 weeks. Type II and type III injuries may take 1 to 3 months to heal. Higher -grade injuries with a large degree of clavicular displacement (eg, type IV, V, and VI) often require surgical treatment.



Item C142: Clavicle displacement as seen in higher-grade injury. Courtesy of R Carl

An occult distal clavicle fracture is unlikely in this patient's case. His shoulder radiographs were normal and these films would include the distal clavicle. In addition, distal clavicle fractures are uncommon in children. The patient's history is not consistent with a shoulder joint dislocation. Rotator cuff tears are uncommon in children and cause weakness of the affected muscles. The adolescent in the vignette does not have the pain or deformity at the sternoclavicular joint that would be associated with a sternoclavicular joint dislocation.

PREP Pearls

- The most common mechanisms of acromioclavicular (AC) joint injuries are a blow to the AC joint or a fall onto the lateral aspect of the shoulder.
- Injuries to the AC joint typically present with tenderness at the AC joint and pain with adduction of the arm across the chest.

ABP Content Specifications(s)

- Recognize the clinical and radiographic findings associated with acromioclavicular separation

Suggested Readings

- Sarwark JF, LaBella CR. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014: 650 pp..
- Stucken C, Cohen SB. Management of acromioclavicular joint injuries. *Orthop Clin North Am.* 2015;46(1):57-66. doi: http://dx.doi.org/10.1016/j.ocl.2014.09.003.

Question 143

A girl is brought to your office for a health supervision visit. When you enter the room, the patient is walking around, stoops to pick up an object on the floor, and hands it to her father. She has 2 to 3 words and points to objects that she wants her father to notice. Her father reports that she is unable to climb steps and cannot point to any body parts when asked.

Of the following, the MOST likely age of the child is

A. 12 months

B. 15 months

C. 18 months

D. 21 months

E. 24 months

Correct Answer: B
The girl in this vignette is displaying the developmental and behavioral characteristics of a typically developing 15-month-old child. From a gross motor perspective, a 15-month-old child is typically walking, running stiff-legged, and can climb on furniture. She has the ability to stoop in order to pick up an object off of the floor and hand the object to someone else. From a fine motor standpoint, a 15-month-old child can build a tower of 3 to 4 cubes, place 10 cubes in a cup, release a pellet into a bottle, turn pages in a book, and point at objects. In regard to language, a 15-month-old child typically has 3 to 5 words, demonstrates mature jargoning, and can imitate environmental sounds. The girl in the vignette may be able to point to 1 body part when asked. In regards to emotional development, a 15-month-old child has also started to show empathy and is starting to hug.

A 12-month-old child typically is not yet running and typically cannot stoop to pick objects off of the floor. Children at 18, 21, and 24 months of age typically have more than 2 to 3 words (10 to 15 words, 25 to 50 words, and greater than 50 words, respectively). At 18 months of age, a child can point to 3 body parts, while a 21-month-old child can point to 5 body parts. A child begins to independently climb the stairs holding a rail and placing both feet on the same step at 22 months of age.

PREP Pearls
- A 15-month-old child can walk well and stoop to pick up objects off of the floor.
- A 15-month-old child typically has 3 to 5 words and can imitate environmental sounds.

ABP Content Specifications(s)
- Evaluate the motor developmental progress/status of a child at 15 months of age
- Evaluate the cognitive and behavioral developmental progress/status of a child at 15 months of age

Suggested Readings

- Gerber RJ, Wilks T, Erdie-Lalena C. Developmental milestones: motor development. *Pediatr Rev.* 2010;31(7):267-277. doi: http://dx.doi.org/10.1542/pir.31-7-267.
- Wilks T, Gerber RJ, Erdie-Lalena C. Developmental milestones: cognitive development. *Pediatr Rev.* 2010;31(9):364-367. doi: http://dx.doi.org/10.1542/pir.31-9-364.

Question 144

A 2-year-old girl presents to the emergency department with a severe nosebleed that has lasted 2 hours despite pressure applied appropriately to the nose. Her medical history is remarkable for "easy bruising," frequent nosebleeds, and gum bleeding when brushing her teeth. Her physical examination is remarkable for a steady trickle of blood coming from her right nostril; multiple palpable ecchymoses on her shins bilaterally; and petechiae on the bridge of her nose, under her eyes, and on her arm where a tourniquet had been applied for placement of an intravenous catheter.

Her laboratory results are shown:

Laboratory Test	Patient Result
Prothrombin time	12.2 seconds
Partial thromboplastin time	32 seconds
Platelet count	$203 \times 10^3/\mu L$ ($203 \times 10^9/L$)
Blood type	A positive
von Willebrand antigen	95% (normal range 50%–150%)
von Willebrand activity	98% (normal range 50%–150%)

Of the following, the diagnosis MOST consistent with this girl's presentation is

A. Glanzmann thrombasthenia
B. factor VIII deficiency
C. immune thrombocytopenia purpura
D. type I von Willebrand disease
E. type IIB von Willebrand disease

Correct Answer: A

The clinical findings seen in the girl in the vignette suggest a congenital bleeding disorder. Of note, she has had unusual bleeding since birth, repeated mucosal bleeding (such as gum bleeding while tooth brushing), palpable bruising, and petechiae. The normal prothrombin time (PT), partial thromboplastin time (PTT), and platelet number effectively rule out disorders of the coagulation cascade or platelet number. It is therefore likely that this girl has a disorder of platelet function. In platelet function disorders, platelets are present, but cannot activate to effectively form a clot. The most common congenital platelet function disorders are Bernard-Soulier syndrome (a disorder of platelet adhesion) and Glanzmann thrombasthenia (a disorder of platelet aggregation). The most appropriate management for life-threatening bleeding in a child with a known or suspected platelet function disorder is to transfuse functional platelets.

The formation of a functional clot requires 2 components, fibrin and platelets. Fibrin is the end product of the coagulation cascade. The absence of any coagulation cascade factors can result in failure to form a clot, and would be associated with a prolonged PT or PTT. Prothrombin time and PTT are effective measures of the functionality and presence of the components of the coagulation cascade, except for the conversion of fibrinogen to fibrin. Therefore, a normal PT and PTT rule out a deficiency of factor VIII. The girl in the vignette does not have idiopathic thrombocytopenic purpura because of the normal platelet number.

Von Willebrand disease (vWD) is the most common congenital bleeding disorder. Von Willebrand factor is a linking factor that allows functional platelets to bind to fibrin to form a clot. Von Willebrand disease is the result of decreased function or absence of von Willebrand factor; vWD has multiple phenotypes, ranging from mild to severe bleeding disorders that mirror the degree of dysfunction or absence of von Willebrand factor. The different types of vWD include types 1, 2A, 2B, 2M, 2N, and 3. Although the girl's presentation is consistent with severe vWD, her normal measured von Willebrand factor levels rule out this diagnosis.

PREP Pearls

- Two of the most common congenital platelet function disorders are Glazmann thrombasthenia and Bernard-Soulier syndrome.
- The formation of a clot requires normal platelet numbers and function, as well as the ability to form fibrin.
- The treatment for bleeding in a patient with a platelet function disorder is the infusion of platelets with normal function.

ABP Content Specifications(s)

- Formulate a differential diagnosis of a purpuric rash that is not associated with sepsis
- Recognize clinical findings associated with qualitative platelet disorders

Suggested Readings

- Carpenter SL, Abshire TC, Anderst JD, Section on Hematology/Oncology, Committee on Child Abuse and Neglect. Evaluating for suspected child abuse: conditions that predispose to bleeding. *Pediatrics*. 2013;131(4):1357-1373. doi: http://dx.doi.org/10.1542/peds.2013-0196.
- Journeycake JM, Buchanan GR. Coagulation disorders. *Pediatr Rev*. 2003;24(3):83-91. doi: http://dx.doi.org/10.1542/pir.24-3-83.
- Sharathkumar AA, Pipe SW. Bleeding disorders. *Pediatr Rev*. 2008;29(4):121-130. doi: http://dx.doi.org/10.1542/pir.29-4-121.

Question 145

A 1-month-old infant is brought to your office for a health supervision visit. He is noted to have a respiratory rate of 80 breaths/min, blood pressure of 90/60 mm Hg, heart rate of 170 beats/min, and an oxygen saturation of 90% on room air. His weight is 3.2 kg (birthweight, 2.9 kg). On physical examination, the infant has no stridor, wheezing, or other adventitious sounds. Mild intercostal retractions are noted. His cardiac examination reveals a regular rate and rhythm, with a 3/6 holosystolic murmur heard best at the left midsternal border and throughout the precordium. The liver edge is palpable 4 cm below the right costal margin. The medical student shadowing you asks whether oxygen therapy should be started. You explain that oxygen might make the infant's condition worse, and that this situation requires a different therapeutic approach.

Of the following, the BEST next step in the management of this infant's condition is

A. furosemide to treat pulmonary edema

B. lorazepam to sedate the infant

C. morphine to decrease hyperventilation

D. normal saline bolus to increase cardiac output

E. propranolol to decrease outflow tract obstruction

Correct Answer: A

The best next step in the treatment of the infant in the vignette would be administration of furosemide. The infant is exhibiting symptoms of pulmonary edema, with respiratory distress and an oxygen saturation of only 90%. A holosystolic murmur is heard on physical examination, and his liver edge is palpable 4 cm below the right costal margin. This clinical picture suggests cardiac failure with increased pulmonary blood flow.

This infant's history and physical examination are consistent with a ventricular septal defect (VSD). He has a holosystolic murmur, which will obscure S1, beginning before any flow is expected in the cardiac cycle when all the valves are closed. If this infant had tetralogy of Fallot (TOF), we would expect a pulmonary ejection murmur. There is also no history of the saturation plummeting as would be expected with a hypercyanotic spell.

At approximately 4 weeks of age, the pulmonary vascular resistance falls. In the case of a VSD, flow increases from the left ventricle to the right ventricle, causing increased pulmonary blood flow and resulting pulmonary edema. The heart rate increases in response to the increased blood volume returning to the left ventricle.

Furosemide, at a dose of 1 mg/kg given intravenously, would be the recommended treatment for this boy's pulmonary edema. Since this infant's pulmonary flow is high, oxygen would not be helpful and might make the left-to-right shunt through the VSD worse.

Neither sedation nor morphine would be appropriate in this case, as they might cause respiratory depression. This infant's hyperventilation is a compensatory mechanism needed to enhance oxygenation and ventilation, with the abnormal lung physiology caused by pulmonary overcirculation; it is not the worsening of a right-to-left shunt, as happens in a hypercyanotic spell in TOF.

A normal saline bolus would not be helpful in this situation, because the blood flow to the lungs is already excessive. Propranolol would not be helpful in the case of pulmonary edema. There is no evidence of right ventricular outflow tract obstruction on clinical examination.

PREP Pearls

- Infants with a ventricular septal defect (VSD) will often present with volume overload and congestive failure at 4 weeks of age when their pulmonary vascular resistance decreases
- Diuresis to treat the resulting pulmonary edema is needed.
- Oxygen may increase the left-to-right shunt through a VSD, worsening pulmonary edema.

ABP Content Specifications(s)

- Plan the appropriate initial management of congestive heart failure in children of various ages
- Plan the appropriate initial diagnostic evaluation of congestive heart failure in children of various ages

Suggested Readings

- Hsu DT, Pearson GD. Heart failure in children: part I—history, etiology, and pathophysiology. *Circ Heart Fail*. 2009;2(1):63-70. doi: http://dx.doi.org/10.1161/CIRCHEARTFAILURE.108.820217.
- Hsu DT, Pearson GD. Heart failure in children: part II—diagnosis, treatment, and future directions. *Circ Heart Fail.*2009;2(5):490-498. doi: http://dx.doi.org/10.1161/CIRCHEARTFAILURE.109.856229.
- Pacifici GM. Clinical pharmacology of furosemide in neonates: a review. *Pharmaceuticals*. 2013;6(9):1094-1129. doi: http://dx.doi.org/10.3390/ph6091094.

Question 146

A 15-year-old adolescent is brought to the office for vomiting. He describes effortless postprandial regurgitation after at least 1 meal daily for 1 month. He occasionally reswallows food. He complains of frequent abdominal pain and nausea, but no diarrhea or bloating. He has lost 2 kg over the last month. He has taken an over-the-counter H2 blocker without improvement.

Of the following, the MOST likely diagnosis is

A. cyclic vomiting

B. eating disorder

C. functional abdominal pain

D. Helicobacter pylori infection

E. rumination disorder

Correct Answer: E
The adolescent in this vignette has rumination syndrome, characterized by repeated episodes of effortless regurgitation of recently ingested food. Typically, regurgitated food is kept in the mouth and is rechewed, reswallowed, or spit out.

Rumination syndrome can be associated with weight loss or malnutrition, and is often disruptive to a child's daily life, especially in school. Regurgitation is effortless and occurs, on average, about 20 minutes after meals. Nighttime episodes are rare. It can be treated with a behavioral technique whereby patients engage in diaphragmatic breathing during the rumination episodes. Patients with rumination disorder are often misdiagnosed and undergo extensive testing prior to diagnosis. In 1 review, patients had symptoms, on average, 2.2 years prior to diagnosis, with 46% of patients having been hospitalized to work up symptoms, while 53% had undergone upper endoscopy. One-third of these patients had abdominal ultrasonography performed.

Cyclic vomiting is characterized by intermittent periods of severe vomiting over several hours to a few days, following by several days to weeks of not vomiting. Rumination syndrome is frequently misdiagnosed as bulimia. The adolescent in the vignette does not have a preoccupation with weight or appearance. The adolescent in the scenario is unlikely to have functional abdominal pain given the associated regurgitation. While *Helicobacter pylori* is a possible cause of this adolescent's symptoms, it is less likely due to the effortlessness of the regurgitation and lack of bloating.

PREP Pearls

- Rumination disorder should be considered in effortless, daily vomiting.
- Rumination disorder can be treated with behavioral therapy.
- Rumination disorder is frequently misdiagnosed and the diagnosis is commonly delayed.

ABP Content Specifications(s)

- Recognize the clinical manifestations of rumination, and manage appropriately

Suggested Readings

- Chial HJ, Camilleri M, Williams DE, Litzinger K, Perrault J. Rumination syndrome in children and adolescents: diagnosis, treatment and prognosis. *Pediatrics*. 2003;111(1):158-162. doi: http://dx.doi.org/10.1542/peds.111.1.158.
- International Foundation for Functional Gastrointestinal Disorders. Rumination syndrome in children and adolescents. International Foundation for Functional Gastrointestinal Disorders website. http://www.aboutkidsgi.org/site/upper-gi-disorders/rumination-syndrome. Updated September 12, 2014.

Question 147

An 8-month-old female infant presents to the office with a 2-day history of fever, irritability, crying, vomiting, and blood-streaked diarrhea. She was a full term infant and has no significant past medical history. The parents report no recent travel other than to visit the maternal aunt for Thanksgiving 12 days ago. The aunt had prepared chitterlings (hog intestines), but the infant did not eat any and only took formula and boiled rice the aunt had made specifically for her. No one at dinner reported any subsequent illnesses. After returning home, she developed fever, was diagnosed with otitis media, and started on a course of amoxicillin, which is nearing completion. Her immunizations are up to date.

Physical examination shows an irritable, crying female infant with a temperature of 39°C, heart rate of 120 beats/min, and respiratory rate of 30 breaths/min. Her anterior fontanelle is slightly sunken and her lips and mucosa are dry. She is making tears. Her lungs are clear to auscultation bilaterally and her heart sounds are normal. Her abdomen is soft, with no guarding or rebound tenderness. There is a large amount of urine, as well as blood-tinged diarrhea in her diaper. The baby is admitted to the local hospital for intravenous hydration and continued on amoxicillin. A routine stool culture is sent. She improves and is discharged after 48 hours. Three days later, the infant returns to your office and appears stable and well-hydrated. Her stool culture is noted to be negative for *Salmonella*, *Shigella*, and *Campylobacter* species. The mother reports that the patient is improving, but that the vomiting, fever, and bloody diarrhea are still present.

Of the following, the MOST likely infectious etiology for this infant is

A. Bacillus cereus

B. Clostridium difficile

C. Rotavirus

D. Trichinella

E. Yersinia enterocolitica

Correct Answer: E
The most likely infectious etiology in the infant in the vignette with bloody diarrhea is *Yersinia enterocolitica*. *Yersinia* species are gram-negative rods and 3 of the species are human pathogens: *Yersinia pestis* (spread by infected fleas infesting rats), *Yersinia pseudotuberculosis*, and *Yersinia enterocolitica*. The latter 2 species cause yersiniosis, a febrile diarrheal illness. *Yersinia* species are primarily zoonoses, causing disease in domestic and wild animals. Humans are not part of the natural bacterial life cycle and are inadvertent hosts. The principal reservoir of *Y enterocolitica* is swine, particularly domesticated pigs. *Y pseudotuberculosis* is rare in the United States and is found in rodents, birds, cattle, goats, sheep, deer, and other mammals. Yersiniosis primarily occurs through ingestion of contaminated food or water, especially undercooked or raw pork, and contact with animals. It has been associated with the preparation of chitterlings (also known as chitlins), which are prepared from pig intestines that must be carefully cleaned and rinsed before being boiled and stewed to prevent transmission. In 1988, an outbreak occurred in Georgia in 14 bottle-fed infants with a median age of 3 months. None of the infants had contact with the chitterlings, but the infection most likely occurred due to cross-contamination of the bottles or formula by those preparing the chitterlings.

After an incubation period of 1 day to 2 weeks (typically 4 to 6 days), patients develop fever and diarrhea (often bloody in children), with abdominal pain, nausea, and vomiting that is indistinguishable from other acute diarrheal illnesses. Up to 20% of patients report pharyngitis (possibly from the affinity *Yersinia* species have for lymphoid tissue). The pharyngitis may provide an important diagnostic clue for the diarrhea's etiology, as this is not associated with other acute bacterial diarrheas. The course of illness may be more insidious than other bacterial diarrheas, with patients in one study not seeking medical attention for over 1 week, and stool cultures not requested by providers for almost 2 weeks from onset. The duration of diarrhea is typically longer than the usual acute gastroenteritis, sometimes persisting up to 3 weeks. Older children and adults may develop pseudoappendicitis, with right lower quadrant pain and elevated white blood cell counts. Abdominal pain from ileocecal mesenteric adenitis and terminal ileitis can occur. Younger children, immunocompromised patients, and individuals with iron overload syndromes are at risk of *Yersinia* bacteremia or sepsis. Postinfectious complications include reactive arthritis (particularly those with HLA-B27 antigen) and erythema nodosum. *Y enterocolitica* grows more slowly than other enterobacterial pathogens on routine laboratory media. If yersiniosis is suspected, the microbiology laboratory should be notified so that additional special media can be used to isolate the *Yersinia* and prevent false-negative results.

There is no good evidence that antibiotics are of any benefit in the treatment of acute uncomplicated yersiniosis. Treatment for *Yersinia* sepsis may be necessary for patients with severe disease or significant underlying conditions. A fluoroquinolone (ie, ciprofloxacin), doxycycline (if older than 8 years of age), and trimethoprim-sulfamethoxazole (especially for pediatric patients) would be the oral drugs of choice. Intravenous therapy would include a third-generation cephalosporin, such as ceftriaxone or a fluoroquinolone, plus gentamicin.

Bloody diarrhea, exposure to chitterlings, failure to respond to amoxicillin, and protracted illness in the infant in the vignette are all expected with a diagnosis of yersiniosis. While *Bacillus cereus* can cause severe nausea, vomiting, and diarrhea, the diarrhea is usually nonbloody, and *B cereus* arises from fried rice that has been sitting at room temperature for hours, not boiled rice. Rotavirus could cause prolonged fever, vomiting, and diarrhea, but the diarrhea would not be bloody, and this patient's immunizations, which would include the rotavirus vaccine series, are up to date. While *Trichinella* roundworms are commonly found in swine, it would come from the meat, not the intestines. Most trichinosis is subclinical, but acute trichinosis can present with diarrhea, nausea, vomiting, and abdominal pain, followed by fever, periorbital edema, and myalgias as the larvae migrate through the muscles. *Clostridium difficile* should be a consideration in a patient on antibiotics, who develops fever, abdominal pain, and bloody diarrhea, but pseudomembranous colitis rarely occurs before the first 12 to 24 months of life. *C difficile* toxin may be present with positive laboratory findings, but neonates and infants appear to lack the ability to bind and process the clostridial toxin, creating asymptomatic carriage and preventing colitis from occurring.

PREP Pearls

- *Yersinia enterocolitica* is associated with fever and diarrhea (often bloody in children), abdominal pain, nausea, and vomiting that is frequently indistinguishable from other acute diarrheal illnesses. Yersiniosis is associated with a slow subclinical onset and protracted duration of up to 3 weeks.
- Pharyngitis may provide an important diagnostic clue for *Yersinia* as the causative pathogen because pharyngitis is not associated with other acute bacterial diarrheas.
- Antibiotics are not beneficial in the treatment of acute uncomplicated yersiniosis.

ABP Content Specifications(s)

- Recognize the clinical features associated with Yersinia enterocolitica infection
- Plan appropriate management for a patient with Yersinia enterocolitica infection

Suggested Readings

- American Academy of Pediatrics. Yersinia enterocolitica and Yersinia pseudotuberculosis infections (enteritis and other illnesses). In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:868-870.
- Ong KL, Gould LH, Chen DL, et al. Changing epidemiology of Yersinia enterocolitica infections: markedly decreased rates in young black children, Foodborne Diseases Active Surveillance Network (FoodNet), 1996-2009. *Clin Infect Dis*. 2012;54 Suppl 5:S385-S390. doi: http://dx.doi.org/10.1093/cid/cis053.

Question 148

A 6-week-old male infant is brought to your office for follow-up after a visit to the emergency department (ED) for fussiness. He was born at full term to a 20-year-old gravida 1 para 0 woman via normal vaginal delivery. In the ED, he was diagnosed with dehydration, given intravenous fluid resuscitation, and then discharged. The infant is exclusively formula fed. According to his mother, he feeds well and has several wet diapers a day. There is a history of similar episodes in several men on the maternal side of the family. On physical examination, the infant is fussy. His weight is 3.1 kg (birthweight was 3.9 kg), his temperature is 37.3°C, heart rate is 177 beats/min, and respiratory rate is 41 breaths/min. His physical examination is significant for decreased skin turgor, a flat anterior fontanelle, dry mucous membranes, and prolonged capillary refill.

Of the following, this infant is MOST likely to be diagnosed with

A. hypernatremia due to renal dysplasia
B. hypernatremia due to renal failure
C. hypernatremia due to a urinary concentrating defect
D. hyponatremia due to proximal tubular defect
E. hyponatremia due to renal dysplasia

Correct Answer: C
Episodes of recurrent dehydration, a positive family history of similar episodes in men, and the infant's age support a diagnosis of nephrogenic diabetes insipidus (DI). He had a recent emergency department (ED) visit for dehydration and he still displays the clinical features of dehydration (decreased skin turgor, a flat anterior fontanelle, dry mucous membranes, and prolonged capillary refill along with tachycardia and weight loss). Dehydration with the absence of a preceding illness and adequate feeding and urination suggests a urine-concentrating defect.

The balance of the compensatory responses of thirst and antidiuretic hormone (ADH) secretion influences the development of hyponatremia or hypernatremia in children with dehydration. Hyponatremia in patients with dehydration secondary to gastrointestinal fluid loss occurs because of the replacement of lost fluids with free water. Hypernatremic dehydration with gastrointestinal losses is usually associated with increased free water loss or decreased water intake, as seen in patients with altered sensorium (eg, developmental delay) or infants dependent on caregivers for fluid intake. In patients with recurrent episodes of dehydration, disorders associated with increased free water loss should be suspected, such as diabetes mellitus (osmotic diuresis), DI (ADH disorders), and psychogenic polydipsia.

Diabetes insipidus occurs secondary to either decreased secretion of ADH, known as central DI, or renal resistance to ADH effects, known as nephrogenic DI. The clinical presentation of DI includes polyuria, polydipsia, and increased thirst. Although patients with DI may present with varying degrees of dehydration, laboratory evaluation will consistently demonstrate hypernatremia in association with dilute urine (urine osmolality < plasma osmolality). Fluid management in patients with hypernatremia includes replacement of the free water deficit along with any ongoing losses and maintenance fluids. Free water deficit is calculated using the following formula:

0.6 x weight (in kilograms) ([serum sodium/140] – 1)

The free water deficit should be replaced over 48 to 72 hours to avoid rapid decrease in serum osmolality. As a guide, a safe rate at which the serum sodium concentration should be lowered is 10 to 12 mEq/L (10–12 mmol/L) per day. Rapid decrease in serum osmolality and sodium is associated with increased risk for cerebral edema because of fluid shift from the extracellular fluid (lower osmolality after correction) to the brain cells (intracellular). Cerebral edema associated with rapid correction may lead to altered sensorium and seizures

Nephrogenic DI in children occurs secondary to a mutation in either the ADH-receptor (*AVPR2*) or the aquaporin 2 channels. *AVPR2* mutations, accounting for 90% of cases, have an X-linked inheritance, with males more severely affected than females. Neonates and infants with nephrogenic DI present with irritability, failure to thrive, dehydration, and a strong preference for water. There is often a history of recurrent emergency department visits for hypernatremic dehydration. Central DI may be idiopathic (most common) or secondary to central nervous system tumors, infiltrative lesions (eg, histiocytosis), or trauma (surgical or nonsurgical). Older patients with DI usually present with polyuria and increased water intake. Polyuria may or may

not be associated with nocturia and/or an increased frequency of micturition. Older patients with central DI may present with headaches, vomiting, or neurologic symptoms related to central nervous system lesions. Water restriction is often used to differentiate nephrogenic DI from central DI, but is not indicated in neonates and infants.

Renal dysplasia associated with congenital anomalies of the kidney and urinary tract (CAKUT) and cystic kidney diseases (nonglomerular) accounts for nearly 60% of pediatric chronic kidney disease (CKD). Tubulointerstitial injury associated with CKD leads to reduced urine-concentrating ability (acquired nephrogenic DI). These patients typically present with polyuria with or without enuresis. Growth restriction (height < 5th percentile), pallor, and elevated blood pressure in a patient with an abnormal voiding pattern (primary daytime and nocturnal enuresis) are suggestive of CKD. Proteinuria may be seen in patients with underlying glomerular disease and/or tubulointerstitial injury. It is important to note that persistent proteinuria may be the only indication of renal disease in asymptomatic patients. Persistent dipstick-positive proteinuria or a urine protein-creatinine ratio higher than 0.2 is abnormal.

In most cases, renal dysplasia/CAKUT is identified on prenatal ultrasonography. Abnormalities noted on renal ultrasonography such as hydronephrosis (unilateral versus bilateral), increased echogenicity of renal parenchyma, renal size (small or enlarged), cysts, and bladder abnormalities help determine the diagnosis and management in children with CKD associated with renal dysplasia/CAKUT. Patients with poor prenatal care are likely to present later, with clinical features of CKD or associated urinary tract (more common) or respiratory (less common) symptoms. Postnatally, male newborns or infants with posterior urethral valves usually present with urinary tract infection, failure to thrive, abdominal distension (from an enlarged bladder), poor urinary stream, or voiding difficulty.

Respiratory problems associated with renal dysplasia are most commonly seen in the neonatal period. Neonates with severe renal dysplasia may have oligohydramnios because of decreased fetal urinary excretion associated with severe bladder outlet obstruction. This leads to pulmonary hypoplasia, because normal amniotic fluid levels are required for normal lung development (between 16 and 28 weeks of gestation). Expected outcomes for neonates with lung hypoplasia caused by severe renal dysplasia are poor.

Proximal tubular defects usually present with clinical features associated with renal tubular acidosis. The diagnosis of renal tubular acidosis should be considered in a young infant with failure to thrive, recurrent vomiting, rickets, episodes of dehydration, recurrent nephrolithiasis, and persistent metabolic acidosis and/or hypokalemia. Fanconi syndrome is a disorder with generalized proximal tubular dysfunction. In addition to metabolic acidosis and hypokalemia, patients with Fanconi syndrome may present with rickets (phosphaturia leading to hypophosphatemic rickets), glucosuria (dipstick-positive glucosuria with normal plasma glucose concentration), and aminoaciduria/tubular proteinuria (urine dipstick negative for protein and quantitative urine tests positive for amino acids and protein).

Improper formula preparation should be considered in all infants with a history of inadequate weight gain. Serum chemistry results in such patients usually demonstrate hyponatremia secondary to dilution of formula with excess free water.

PREP Pearls

- In patients with recurrent episodes of dehydration, disorders associated with increased free water loss should be suspected.
- Increased free water loss is seen in diabetes mellitus (osmotic diuresis), diabetes insipidus (DI; antidiuretic hormone disorders), and psychogenic polydipsia
- Tubulointerstitial injury associated with chronic kidney disease leads to reduced urinary concentration (acquired nephrogenic DI). These patients usually present with polyuria with or without enuresis.
- The presence of hyponatremia or hypernatremia in patients with dehydration is influenced by the balance of the compensatory responses of thirst and antidiuretic hormone secretion.
- Patients with DI present with polyuria, polydipsia, and increased thirst. Although they may present with varying degrees of dehydration, laboratory evaluation is consistent with hypernatremia in association with dilute urine (urine osmolality < plasma osmolality).

ABP Content Specifications(s)

- Identify symptoms associated with hypernatremia, including those associated with rapid rehydration

Suggested Readings

- Jain A. Body fluid composition. *Pediatr Rev.* 2015;36(4):141-152. doi: http://dx.doi.org/10.1542/pir.36-4-141.
- Linshaw MA. Back to basics: congenital nephrogenic diabetes insipidus. *Pediatr Rev*. 2007;28(10):372-380. doi: http://dx.doi.org/10.1542/pir.28-10-372.
- Massengill SF, Ferris M. Chronic kidney disease in children and adolescents. *Pediatr Rev.* 2014;35(1):16-29. doi: http://dx.doi.org/10.1542/pir.35-1-16.
- Saborio P, Tipton GA, Chan JCM. Diabetes insipidus. *Pediatr Rev*. 2000;21(4):122-129. doi: http://dx.doi.org/10.1542/pir.21-4-122.

Question 149

You are reviewing the list of infants to be screened by the pediatric ophthalmologist for retinopathy of prematurity (ROP). It includes an infant born at 34 weeks of gestation that is now 4 weeks of age. He was born to a 32-year-old woman with a history of substance abuse who presented with placental abruption. He weighed 1.6 kg at birth, required surfactant administration for respiratory distress syndrome, and remained intubated for the first 3 weeks of life. He received antibiotics until blood cultures were negative for 72 hours and a red blood cell transfusion. A nurse in your neonatal intensive care unit questions his inclusion for screening.

Of the following, the clinical factor that MOST qualifies this infant for ROP screening is

A. duration of intubation
B. gestational age
C. maternal history of substance abuse
D. placental abruption
E. red blood cell transfusion

Correct Answer: A

The infant in this vignette should be screened for retinopathy of prematurity (ROP) because he remained intubated for 3 weeks. Retinopathy of prematurity is a disorder of abnormal retinal vascular growth seen in premature infants. Compared to the in utero environment, the retina of infants born prematurely is exposed to a relative hyperoxia, which contributes to the development of ROP. Infection, necrotizing enterocolitis, and bronchopulmonary dysplasia are associated with an increased risk of ROP. Based on recent data, the pathogenesis of ROP may be due to a relative increase in vascular endothelial growth factor compared to insulin-like growth factor 1.

In the United States, screening for ROP is recommended for infants born at less than 30 weeks gestation or weighing less than 1,500 g at birth. Infants with a gestational age greater than 30 weeks or weighing more than 1,500 g at birth should be screened if they have a complicated clinical course. Screening should be performed on dilated pupils by an experienced ophthalmologist. For infants who need ROP screening, the initial examination should occur at a postconceptional age of 31 to 32 weeks or a chronologic age of 4 weeks, whichever comes first. Gestational age is a criterion for ROP screening when gestational age is less than 30 weeks. The infant in this vignette does not qualify for screening based on gestational age.

There is no association between maternal substance use and ROP. Therefore, screening for ROP would not be indicated based on maternal substance use.

While there are preliminary data showing a relationship between placental pathology and increased risk of ROP, it has not consistently been associated with an increased risk of ROP. Thus, placental abruption would not qualify this infant for ROP screening.
There is no association between red blood cell transfusion and rates of ROP.

PREP Pearls

- Infants born at less than 30 weeks gestation or with a birth weight less than 1,500 g require screening for retinopathy of prematurity (ROP).
- Infants with gestational age greater than 30 weeks or birthweight greater than 1,500 g only need screening for ROP if they had a complicated clinical course.
- Screening for ROP should occur at postconceptional age of 31 to 32 weeks or chronologic age of 4 weeks, depending on which comes first.

ABP Content Specifications(s)

- Plan the appropriate screening and clinical evaluation of retinopathy of prematurity

Suggested Readings

- American Academy of Pediatrics Section on Ophthalmology, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*. 2013;131(1):189-195. doi: http://dx.doi.org/10.1542/peds.2012-2996.
- Olitsky SE, Hug D, Plummer LS, Stahl ED, Ariss MM, Lindquist TP. Disorders of the retina and vitreous. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:3049-3056.

Question 150

A 5-year-old boy presents to your office for evaluation of a rash on his forearm. The rash began yesterday as a small red bump that spread (Item Q150). The rash is intensely pruritic. After you discuss your diagnosis and treatment recommendations with the patient's mother, she asks if there is anything they can do to prevent recurrence of this rash.

Item Q150: Rash on patient's forearm. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology: A Quick Reference Quide. 2nd ed. Elk Grove Village, IL: American Acacdemy of Pediatrics; 2012.

Of the following, the MOST accurate recommendation is

A. allergen immunotherapy
B. avoidance of the inciting agent
C. immunization against the causative organism
D. routine use of a topical emollient
E. there is no known method to reduce recurrence

Correct Answer: B

The rash in this photograph is Rhus dermatitis, an allergic contact dermatitis caused by exposure to a plant in the *Rhus* or *Toxicodendron* genus of plants. Plants in this group include poison ivy, poison oak, and poison sumac, all of which produce a highly allergenic oil called urushiol. Rhus dermatitis is an erythematous, pruritic, papulovesicular rash that is often linear. In sensitized individuals, the rash appears 8 to 48 hours after contact with urushiol, and new lesions can continue to appear up to 3 weeks after exposure. The timing of symptom development helps differentiate this rash from a primary irritant contact dermatitis, which appears immediately after exposure.

Rhus dermatitis is a classic delayed type IV hypersensitivity reaction that acts via cell-mediated immunity. Urushiol binds to antigen-presenting cells (APCs) in the skin. The APCs then travel to a regional lymph node where antigens are processed and presented to CD4+ T lymphocytes. These lymphocytes become activated and release cytokines. Fifty percent to 70% of the general population is sensitized and clinically susceptible; peak frequency for sensitization occurs between the ages of 8 and 14 years.

Avoidance is the only method to prevent recurrence. Desensitization is a lengthy process with many bothersome side effects (generalized pruritus, urticaria, etc), and any benefit is temporary, with effects waning within months. Immunization is not the correct response as Rhus dermatitis is not an infectious disease. Although fabric and some creams and sprays can provide a barrier to keep urushiol off the skin, avoidance continues to be most effective for preventing recurrence of Rhus dermatitis.

PREP Pearls

- Rhus dermatitis occurs in sensitized individuals after exposure to urushiol, an oil found in poison oak, poison ivy, and poison sumac.
- Rhus dermatitis is a delayed type IV hypersensitivity reaction, with symptoms appearing 8 to 48 hours after exposure.

ABP Content Specifications(s)

- Understand the pathophysiology of rhus dermatitis

Suggested Readings

- Spiewak R. Immunotherapy of allergic contact dermatitis. *Immunotherapy*. 2011;3(8):979-996. doi: http://dx.doi.org/10.2217/imt.11.89.
- Tanner TL. Rhus (toxicodendron) dermatitis. *Prim Care*. 2000;27(2):493-502.

Question 151

You are seeing a 2-year-old girl with trisomy 18 and severe neurologic compromise for a health supervision visit. She has had 12 documented episodes of pneumonia, 6 of which have been associated with respiratory failure. Chest radiography has not demonstrated any specific lobar recurrence pattern. A prior necrotizing pneumonia involving the right lower lobe resulted in pneumatocele formation.

The girl's nutrition consists of oral feedings of milk, juice, and pureed baby foods from a bottle and spoon. You suspect that she is suffering from complications of chronic pulmonary aspiration and order a fiberoptic endoscopic evaluation of swallowing. The study reveals direct aspiration with saliva and all food consistencies without an associated cough response.

On physical examination, the girl is hypotonic and in no acute distress. Her respiratory rate is 26 breaths/min. There is copious saliva in the oral cavity and posterior oropharynx. The girl frequently gags and chokes on her secretions. Auscultation of her lungs reveals coarse breath sounds and transmitted upper airway noise. Her extremities are well perfused, without cyanosis or edema. Examination of the heart and abdomen is within normal limits.

You discuss the girl's care plan with her parents, including advance directives. They request that all potential care options be continued for their daughter.

Of the following, the management option MOST likely to prevent pulmonary aspiration in this girl is

A. feeding via gastrostomy tube
B. glycopyrrolate 3 times daily
C. laryngotracheal separation
D. salivary gland ligation/excision
E. tracheostomy

Correct Answer: C
The girl in the vignette has had multiple episodes of pneumonia complicated by respiratory failure, necrotizing pneumonia, and pneumatocele. In children with neurodevelopmental compromise and muscular weakness or discoordination, silent aspiration is common and injury may occur in the absence of overt symptoms. The risk of scarring, bronchiectasis, and loss of pulmonary function in children affected with chronic pulmonary aspiration is significant. In conversations with caregivers, the risk of continued aspiration events should be reviewed and care directives discussed.

Aspiration may occur directly with oral feedings, in a retrograde manner during episodes of gastroesophageal reflux, or from an inability to manage salivary secretions. A patient with aspiration may be evaluated using various methods. The study chosen in the vignette, a fiberoptic endoscopic evaluation of swallowing, uniquely allows the otolaryngologist and speech and language pathologist to directly visualize the path of oral secretions and/or feedings. During the period of inspection, pooling of material in the valleculae, effectiveness of clearance with swallowing, and any aspiration events can be documented, as well as the presence or absence of associated cough.

The most definitive preventive treatment for chronic pulmonary aspiration is a laryngotracheal separation (LTS) procedure. In appropriate cases, an LTS can prevent aspiration pneumonia, improve respiratory stability, and thereby allow a child to be cared for at home. In LTS, the digestive and respiratory tracts are separated. A tracheoesophageal diversion connects the upper trachea to the cervical segment of the esophagus, while the proximal trachea is closed with formation of a blind tracheal pouch. A tracheostomy is required, providing a connection to the mid/distal trachea. Largely dependent on the degree of antecedent airway and pulmonary injury, surgically treated patients may or may not require respiratory support in the form of supplemental oxygen or chronic mechanical ventilation. It is important to inform caregivers that children with LTS will no longer be able to phonate. Education related to tracheostomy care will also be required.

Several alternate management options are available for patients with chronic aspiration, but none are as effective as LTS in preventing all aspiration events. If the aspiration events occur primarily with direct aspiration of oral feedings, an alternate route of feeding, such as a gastrostomy tube, may be pursued. However, this will not prevent aspiration and pulmonary damage resulting from reflux events or salivary aspiration.

Glycopyrrolate or scopolamine may be effective in reducing the burden of salivary aspiration through their anticholinergic effects, but their side effect profiles must be considered and tolerance must be closely monitored. This treatment will not affect the risk of oral feeding aspiration or retrograde reflux aspiration. A complication of Nissen fundoplication may be pooling of secretions from the oral cavity in the distal esophagus, causing gagging and secondary salivary aspiration.

Salivary gland ligation and excision procedures are effective in preventing episodes of pneumonia caused by aspiration of oral secretions. Injection of the submandibular or parotid glands with botulinum toxin may also be considered. With this approach, as many as 88% of patients may see a decrease in saliva production, but side effects include parotitis and viscous secretions, which may be difficult to clear from the airway. Neither treatment will prevent retrograde aspiration events.

A tracheostomy allows direct access to the airway for suctioning and pulmonary toileting. However, a tracheostomy may contribute to aspiration events and can be expected to prevent a functional swallow as a result of decreased laryngeal sensation, decreased elevation of the larynx, and an inability to elevate subglottic pressure as normally occurs during swallowing and before effective coughing.

PREP Pearls

- Although multiple options exist for the management of chronic pulmonary aspiration, a laryngotracheal separation is the most definitive approach.
- Salivary aspiration may continue to cause pulmonary disease after direct and retrograde aspiration have been optimally addressed.
- A fiberoptic endoscopic evaluation of swallowing offers direct visualization of the airway with regard to salivary and other aspiration events.

ABP Content Specifications(s)

- Understand the effect of a tracheostomy on aspiration

Suggested Readings

- Chida I, Tamura K, Nakagawa S, Ando M, et al. Clinical outcomes of tracheoesophageal diversion and laryngotracheal separation in neurologically impaired children. *Auris Nasus Larynx*. 2013;40(4):383-387. doi: http://dx.doi.org/10.1016/j.anl.2012.11.001.
- Cook SP. Laryngotracheal separation in neurologically impaired children: long-term results. *Laryngoscope*. 2009;119(2):390-395. doi: http://dx.doi.org/10.1002/lary.20044.
- El-Hakim H, Richards S,Thevasagayam MS. Major salivary duct clipping for control problems in developmentally challenged children. *Arch Otolaryngol Head Neck Surg*. 2008;134(5):470-474. doi: http://dx.doi.org/10.1001/archotol.134.5.470.
- Hara H, Hori T, Sugahara K, Ikeda T, Kajimoto M, Yamashita H. Effectiveness of laryngotracheal separation in neurologically impaired pediatric patients. *Acta Otolaryngol.* 2014;134(6):626-630. doi: http://dx.doi.org/10.3109/00016489.2014.885119.

Question 152

A 10-year-old girl is brought to the emergency department by her parents because she cannot walk. Her symptoms started 2 days ago with tripping on stairs and curbs. Yesterday, she could not stand up from a sitting position, and this morning she could not get out of her bed. Her physical examination shows an anxious-appearing girl with a soft voice, lying on a stretcher. She can wiggle her legs, but cannot lift them off the stretcher. Her hands have a weak grip, but she can raise her arms off the stretcher, her pupils are reactive, and her facial movements are strong. You cannot elicit any deep tendon reflexes.

Of the following, the BEST next step in evaluation is

A. computed tomography of the head
B. magnetic resonance imaging of the spine
C. negative inspiratory force measurement
D. serum botulism toxin assay
E. serum lead level

Correct Answer: C
The girl in the vignette has Guillain-Barré syndrome. Her weakness has progressed rapidly and she may have respiratory muscle involvement. Of the choices, the best next step in evaluation is a negative inspiratory force measurement. If this is abnormal, she may require immediate respiratory support. Once she is stable, diagnostic testing can proceed.

Guillain-Barré syndrome is an inflammatory disorder affecting the peripheral nerves. Low back pain and numbness in the toes and feet are common, but the most significant symptom is ascending weakness. This starts with weakness in the feet and ankles. Patients report tripping, especially on stairs or curbs, when weak foot dorsiflexion makes them unable to pick up their foot over the obstacle. When weakness affects the proximal lower extremities, patients report difficulty rising out of a chair. They may need to use their arms to pull themselves up. Weakness in the hands presents with inability to grasp objects tightly, such as when trying to unscrew a jar lid. Respiratory muscle weakness presents initially with increased respiratory rate without increased work of breathing. A patient with respiratory muscle weakness can look paradoxically at ease, even when they have significant hypoventilation. It is critical for clinicians to recognize the presentation of ascending weakness and assess respiratory status promptly.

The girl in the vignette has weakness and areflexia, which suggests a peripheral nervous system disorder. Brain imaging is not helpful in this clinical situation. Botulism affects the neuromuscular junction and causes a descending paralysis, often with mydriasis. Severe facial weakness and eyelid weakness can be mistaken for unconsciousness, but limb movements are usually preserved or less affected. The girl in the vignette has preserved facial muscle strength, making botulism very unlikely. Acute lead toxicity causes a motor neuropathy, classically resulting in bilateral wrist drop. Ascending weakness is not a presentation of lead toxicity. The diagnosis of Guillain-Barré syndrome is made based on the clinical presentation. Supportive evidence includes magnetic resonance imaging of the spine showing nerve root enhancement, especially in the cauda equina, but this is not always present. Cerebrospinal fluid studies often show high protein with normal white blood cell count (cytoalbuminological dissociation), but cerebrospinal fluid studies can be normal early in the course.

PREP Pearls

- Ascending weakness with areflexia suggests a diagnosis of Guillain-Barré syndrome.
- Descending weakness with mydriasis suggests a diagnosis of botulism.

ABP Content Specifications(s)

- Recognize the clinical findings associated with Guillain-Barre syndrome and the progression of disease

Suggested Readings

- Francisco AMO, Arnon SS. Clinical mimics of infant botulism. *Pediatrics*. 2007;119(4):826-828. doi: http://dx.doi.org/10.1542/peds.2006-0645.
- Rosen BA. Guillain-Barré syndrome. *Pediatr Rev.* 2012;33(4):164-171. doi: http://dx.doi.org/10.1542/pir.33-4-164.

Question 153

You are caring for a 12-year-old boy who has been in the intensive care unit for 5 days after sustaining a severe head injury in a car accident. He has an intracranial pressure monitor in place and has received osmotherapy with hypertonic saline, mechanical ventilation, and deep sedation. Despite these therapies, his intracranial pressures have been elevated. His current laboratory studies compared to 12 hours previously are shown in Item Q153 .

	12 hours previously	Current
Sodium	145 mEq/L (145 mmol/L)	165 mEq/L (145 mmol/L)
Chloride	110 mEq/L (110 mmol/L)	131 mEq/L (131 mmol/L)
Potassium	4 mEq/L (4 mmol/L)	4.2 mEq/L (4.2 mmol/L)
Bicarbonate	22 mEq/L (22 mmol/L)	19 mEq/L (19 mmol/L)

His medications have remained the same, and include 3% saline 0.1 mL/kg per hour, morphine infusion, phenytoin every 12 hours enterally, cefazolin every 8 hours intravenously, and ranitidine every 12 hours enterally. His urine output is now 10 mL/kg per hour and his urinalysis shows a specific gravity of 1.005.

Of the following, the MOST likely cause of his hypernatremia is

A. dehydration
B. diabetes insipidus
C. excess intravenous sodium load
D. hyperaldosteronism
E. syndrome of inappropriate antidiuretic hormone

Correct Answer: B
The boy in this vignette has suffered a severe traumatic brain injury several days prior. Over a period of several hours, his serum sodium level has risen by 20 mEq/L (20 mmol/L) and he is producing a very large amount of dilute urine. This clinical picture is consistent with diabetes insipidus (DI).

Diabetes insipidus is caused by decreased secretion or decreased action of antidiuretic hormone arginine vasopressin (AVP). Arginine vasopressin is produced by the hypothalamus and stored in the posterior pituitary gland. Secretion of AVP into the bloodstream is tightly regulated by increased plasma osmolality or by decreased arterial blood pressure. In the kidney, AVP facilitates the insertion of aquaporin channels to the apical surface of collecting duct cells, which allows water to be reabsorbed from the lumen of the nephron into the bloodstream. Derangement of these processes leads to diabetes insipidus, characterized by excessive water secretion. Injury to the hypothalamus and posterior pituitary gland, which can be caused by traumatic brain injury, hypoxic-ischemic injury, tumors, and postoperative changes, can cause central DI. Nephrogenic DI is caused by resistance to AVP at the level of the collecting duct from a vasopressin receptor defect, medications, or toxins that interfere with the transport of water through aquaporin channels.

The prevalence of post-traumatic DI varies, ranging from 2.9% to 51%. Risk factors for developing post-traumatic DI include low Glasgow coma scale score, cerebral edema, and high injury severity. The clinical hallmarks of DI are polyuria with dilute urine, hypernatremia, and dehydration. Urine output usually exceeds 5 mL/kg per hour, urine-specific gravity is usually less than 1.010 g/cm^3, and serum sodium concentration is usually greater than 145 mEq/L (145 mmol/L). This constellation of findings in the setting of trauma or neurological surgery usually indicates DI. Post-traumatic DI usually occurs in the first few days following trauma. It can be a transient condition if the head injury itself is survivable. Recovery from DI can occur with resolution of edema and vessel regeneration of the affected area. Isotonic maintenance fluid is usually used to prevent a rapid drop in serum sodium and cerebral edema. In the acute setting of severe traumatic brain injury, a continuous infusion of AVP is preferred because it is readily titratable. Serum sodium levels should be monitored frequently. Management of chronic central DI generally involves replacing free water to prevent dehydration and administration of AVP. In the chronic setting, oral desmopressin can be given to replace the missing hormone. Patients who have an intact thirst mechanism can often regulate their own free water intake.

Excessive sodium administration, usually in the form of hypertonic saline treatment, can be distinguished from DI as a cause of hypernatremia by a higher specific gravity, higher urine sodium, and lower urine output seen in this condition. Dehydration as a primary cause of hypernatremia is not likely in this case because of the high urine output. Hyperaldosteronism can cause hypernatremia, but it is rare in trauma, and does not cause high urine output. Syndrome of inappropriate antidiuretic hormone is a condition of low urine output and hyponatremia caused by increased amount or action of AVP.

PREP Pearls

- Diabetes insipidus is caused by inadequate amount (central) or inadequate action (nephrogenic) of arginine vasopressin hormone.
- Central diabetes insipidus is caused by injury to the hypothalamus or posterior pituitary gland by traumatic brain injury, hypoxic-ischemic injury, tumors, or postsurgical injury.

ABP Content Specifications(s)

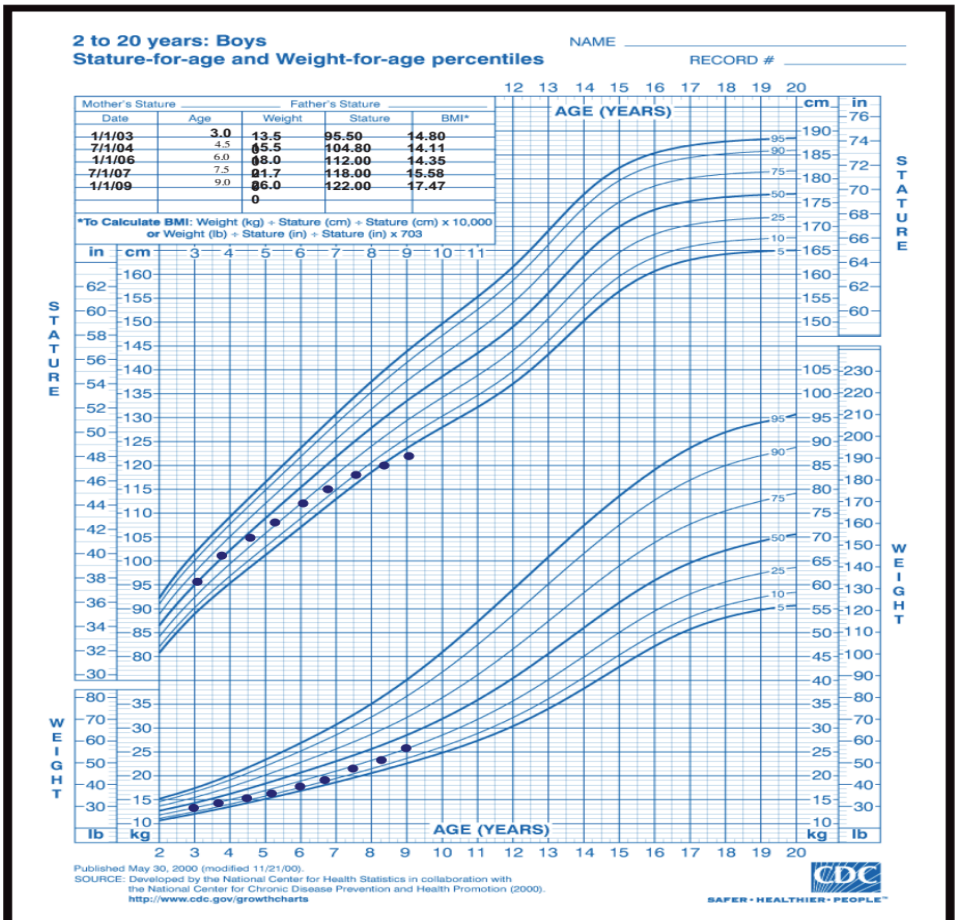
- Recognize the association between cranial injury/surgery and diabetes insipidus

Suggested Readings

- Capatina C, Paluzzi A, Mitchell R, Karavitaki N. Diabetes insipidus after traumatic brain injury. *J Clin Med*. 2015;4(7):1448-1462. doi: http://dx.doi.org/10.3390/jcm4071448.
- Saborio P, Tipton GA, Chan JCM. Diabetes insipidus. *Pediatr Rev* 2000;21(4):122-129. doi: http://dx.doi.org/10.1542/pir.21-4-122.

Question 154

A 9-year-old boy is brought to your office for a health supervision visit. He has a history of moderate-persistent asthma, allergic rhinitis, and eczema. His medications include fluticasone 110 µg 2 puffs inhaled twice daily, montelukast 5 mg daily, cetirizine 10 mg daily, fluticasone 2 squirts each nostril daily, albuterol 4 puffs inhaled as needed, and skin emollients twice daily. He requires albuterol about twice each month and has been treated with 2 short courses of oral steroids in the past 6 months for exacerbations associated with upper respiratory infections. He is doing well in school and is active in his community soccer league. He and his mother have no concerns today. Vital signs show a temperature of 37°C, blood pressure of 106/65 mm Hg, heart rate of 70 beats/min, respiratory rate of 20 breaths/min, oxygen saturation of 98%, weight of 26 kg (26th percentile), height of 122 cm (third percentile), and body mass index of 17.5 kg/m^2 (73rd percentile). His growth curves are shown in Item Q154 . Physical examination is significant for dry skin patches over both antecubital fossae.



Courtesy of K. Vogt

ITEM Q154: Growth chart for the boy described in the vignette.

Of the following, the MOST likely etiology of his abnormal growth pattern is

A. cystic fibrosis
B. exogenous steroid exposure
C. growth hormone deficiency
D. hypothyroidism
E. uncontrolled asthma

Correct Answer: B
The patient described in the vignette has growth failure due to exogenous corticosteroid exposure from chronic inhaled and nasal steroids. Corticosteroids have a growth suppressive effect while causing weight gain. This patient continues to follow his weight percentile while his height percentiles decreased, so his body mass index percentile increased. Growth failure due to systemic absorption of inhaled corticosteroids is an increasingly recognized complication.

Weight rather than height is usually primarily affected in cystic fibrosis, gastrointestinal disease, and malnutrition. Uncontrolled asthma could cause poor growth, but similarly, weight would be primarily affected and the vignette describes relatively well-controlled asthma. Hypothyroidism and growth hormone deficiency can present with similar growth patterns. However, there are no other symptoms suggestive of hypothyroidism or potential causes for growth hormone deficiency for the patient in this vignette.

The most common cause of Cushing syndrome in children is exogenous steroid exposure, including that from inhaled and topical steroids. The most common signs and symptoms of Cushing syndrome include weight gain with linear growth failure, round face, facial plethora, violaceous abdominal striae, hypertension, easy bruising, and proximal muscle weakness. Endogenous Cushing syndrome is very rare in children and can be due to an adrenocorticotropic-secreting pituitary adenoma or adrenal cortical overactivity. Laboratory investigation may show hypokalemia. In the case of exogenous steroid exposure, serum cortisol levels are low as endogenous corticosteroid production is suppressed. Once exogenous steroids are withdrawn, adrenal crisis can occur during an acute illness if endogenous adrenal function has not yet recovered from suppression. Until endogenous adrenal function has recovered, stress dose steroids are indicated during illness. Screening tests for endogenous Cushing syndrome include 24-hour urine free cortisol, midnight salivary cortisol, or 1-mg overnight dexamethasone suppression test. A morning cortisol level that does not suppress after dexamethasone is consistent with endogenous Cushing syndrome.

PREP Pearls

- Excess corticosteroid exposure commonly causes linear growth failure with relative weight gain.
- Other signs and symptoms of Cushing syndrome include round face, facial plethora, violaceous abdominal striae, hypertension, easy bruising, and proximal muscle weakness.
- The most common cause of Cushing syndrome in children is exogenous steroid exposure. Endogenous Cushing syndrome is very rare in children

ABP Content Specifications(s)

- Identify the clinical features associated with Cushing syndrome, including that associated with exogenous corticosteroid therapy

Suggested Readings

- Klein J, Vuguin P, Hyman S. Cushing syndrome. *Pediatr Rev.* 2014;35(9):405-407. doi: http://dx.doi.org/10.1542/pir.35-9-405.
- Stratakis CA. Cushing syndrome in pediatrics. *Endocrinol Metab Clin North Am*. 2012;41(4):793-803. doi: http://dx.doi.org/10.1016/j.ecl.2012.08.002.

Question 155

The parents of a 2-year-old girl bring her to your office for evaluation of a bulge in her groin they noticed while bathing her. They reported noticing an intermittent fullness in this area over the past few weeks when she was standing, but because they did not notice it when they lay her down to change her diaper, they were not concerned. However, today the fullness has persisted and it seems to be tender to touch. There has never been any erythema and the girl has been otherwise well.

On physical examination, the girl's vital signs are normal for age and she is afebrile. The right inguinal area appears fuller than the left (Item Q155). A 2 × 3 cm tender mass is palpable. The remainder of the physical examination is unremarkable.

Item Q155: Inguinal area of the girl described in this vignette Reprinted with permission form Palmer LS. Hernias and Hydorceles. Pediatr Rev. 2013;34 (10) 457-464

Of the following, the BEST next step in management is to

A. attempt gentle manual reduction
B. initiate treatment with trimethoprim-sulfamethoxazole
C. obtain Bartonella henselae titers
D. obtain a complete blood cell count with differential
E. refer to pediatric surgery for a nonurgent evaluation

Correct Answer: A

The girl in the vignette has an indirect inguinal hernia. She exhibits tenderness on palpation, raising concern that the hernia may be incarcerated or strangulated. Gentle manual reduction is the best next step in management. Inguinal masses are common in pediatric patients of varying ages and the history and physical examination findings are key to differentiating between these abnormalities.

Inguinal hernias frequently present as an intermittent bulge in the groin that tends to be more evident when the patient is standing. The mass may be present constantly or recur during periods of increased abdominal pressure (crying, coughing, or straining with stooling or voiding). Often, the mass is undetectable when the patient is supine, as during diaper changes, because the hernia contents spontaneously reduce and return to the abdomen. Failure of the processus vaginalis in boys or the canal of Nuck in girls to obliterate completely will leave varying degrees of patency. This accounts for the variable clinical picture of hernias and hydroceles seen. The physical examination finding of a bulge that originates above the inguinal ligament and extends into the vulva in girls, or into the hemiscrotum in boys, is characteristic of an indirect hernia.

In girls, the hernia often contains the ovary and fallopian tube. When there is pain or tenderness on palpation of the hernia mass, gentle reduction should be immediately attempted by applying upward and slightly lateral pressure. After successful manual reduction, a nonurgent but timely referral to a pediatric surgeon is warranted. If reduction is not successful, the hernia is defined as incarcerated. The practitioner may opt to obtain ultrasonography to evaluate the contents of the hernia sac or refer immediately to a surgeon. However, vascular compromise of an incarcerated hernia will develop and progress because of edema from venous and lymphatic obstruction (ie, strangulation), and the mass will become painful. A strangulated hernia is a surgical emergency.

Other causes of inguinal masses include retractile or undescended testes in boys, lymph nodes, or rarely, tumors. Lymph nodes are located below or lateral to the inguinal ligament, so the position of the mass helps to distinguish lymphadenopathy from an inguinal hernia. Lymphadenopathy is characterized by enlarged nontender lymph nodes. Inguinal lymphadenopathy can occur in conditions that cause generalized lymphadenopathy: infectious, metabolic, inflammatory, lymphoproliferative, or malignant. Localized lymphadenopathy is usually reactive and associated with skin and soft tissue infections or inflammation. Lymphadenitis should be suspected when the lymph nodes are tender or accompanied by overlying erythema, warmth, or fluctuance. In such cases, it would be appropriate to evaluate further with a complete blood cell count, test for *Bartonella henselae* titers to rule out cat scratch disease, or consider initiating treatment with trimethoprim-sulfamethoxazole.

PREP Pearls

- Manual reduction of an inguinal hernia should be attempted at the time of diagnosis by gently applying upward and lateral pressure.
- Immediate surgical referral or ultrasonography to determine the contents of the hernia sac is the next step if reduction is not successful.
- A strangulated hernia is a surgical emergency.
- In girls, a significant number of hernias contain the ovary and fallopian tube, so timely evaluation is critical.

ABP Content Specifications(s)

- Plan the appropriate diagnostic evaluation of an inguinal mass in patients of various ages
- Understand the causes of an inguinal mass in patients of various ages

Suggested Readings

- Blair RJ. Testicular and scrotal masses. *Pediatr Rev.* 2014;35(10):450-451. doi: http://dx.doi.org/10.1542/pir.35-10-450.
- Palmer LS. Hernias and hydroceles. *Pediatr Rev.* 2013;34(10):457-464. doi: http://dx.doi.org/10.1542/pir.34-10-457.
- Ziegler MM. Consultation with the specialist: diagnosis of inguinal hernia and hydrocele. *Pediatr Rev.* 1994;15(7):286-288. doi: http://dx.doi.org/10.1542/pir.15-7-286.

Question 156

A 2-week-old neonate presents to your office after his recent discharge from the neonatal intensive care unit (NICU). He is the third child delivered full-term to a 26-year-old mother via elective cesarean delivery secondary to breech position. Maternal prenatal laboratory results were unremarkable. His mother states that she felt less fetal movement with his pregnancy than with her other children. Shortly after delivery, he was transferred to the NICU because of profound hypotonia and discordant suck and swallow, eventually requiring enteral tube feeding that has continued at home. On physical examination, the neonate is small for gestational age with severe hypotonia, bilateral cryptorchidism, and a small penis. Facial features include bitemporal narrowing, a thin upper lip, and almond-shaped eyes. His newborn screen results are normal.

Of the following, the disorder that BEST fits this neonate's clinical presentation is

A. congenital myotonic dystrophy

B. fragile X syndrome

C. Prader-Willi syndrome

D. Rett syndrome

E. spinal muscular atrophy

Correct Answer: C
The neonate in the vignette has Prader-Willi syndrome (PWS), which is characterized by profound hypotonia and feeding problems in infancy. Prader-Willi syndrome typically presents with facial dysmorphology, including bitemporal narrowing, thin upper lip, and almond-shaped eyes, and hypogonadism, often manifested as cryptorchidism in boys. In infancy, failure to thrive is not unusual because of feeding difficulties and may require special nipples or enteral tube feedings. As affected children age, the feeding pattern transitions to excessive eating. This results in morbid obesity if they are not strictly supervised to monitor food intake, weight, height, and body mass index. Patients with PWS typically have mild-to-moderate intellectual disability, short stature, and behavioral difficulties.

Humans inherit 2 complete sets of chromosomes, one from each parent. In most cases, autosomal genes are expressed from both parent alleles. There is a subset of genes, known as imprinted genes, which show expression from only 1 parent in the gene pair. In many cases, this is a normal phenomenon; however, when expressed abnormally, these result in various genetic disorders. Genomic imprints are erased in both germ lines and reset in the gamete (sperm or egg) stage, resulting in reversibility depending on the parent of origin. Common disorders associated with imprinting defects include PWS, Angelman syndrome, Beckwith-Wiedemann syndrome, Russell-Silver syndrome, uniparental disomy 14, and Albright hereditary osteodystrophy.

Prader-Willi syndrome is caused by an abnormal parent-specific imprinting problem within the Prader-Willi-specific critical region on chromosome 15q11.1-q13. DNA methylation is used to determine whether the region is lacking the paternally contributed region and will confirm the diagnosis in 99% of affected individuals. Three genetic mechanisms can result in the absence of expression of the imprinted gene on the paternally derived PWS region: paternal deletion, maternal uniparental disomy 15, and an imprinting defect. The recurrence risk for PWS to siblings depends on the genetic mechanism involved. Typically, the risk is less than 1% if the affected patient has a deletion or uniparental disomy; however, it could be up to 50% if the patient has PWS because of an imprinting defect. Thus, confirmation of the genetic mechanism is critical for counseling parents about future pregnancies.

Congenital myotonic dystrophy presents with profound hypotonia, myopathic facies, intellectual disability, and commonly, respiratory insufficiency. This disorder does not manifest with hypogonadism.

Fragile X syndrome, an X-linked disorder, is characterized by moderate intellectual disability in boys and mild intellectual disability or learning disability in girls. As they age, a classic dysmorphology becomes evident in males, which includes macrocephaly, long face, protruding ears, joint laxity, and macro-orchidism. Fragile X syndrome does not usually present with hypotonia in infancy.

Rett syndrome presents only in girls. Their psychomotor development is normal in the first 6 to 18 months after birth, followed by developmental regression in language and motor skills. Girls with this disorder have classic repetitive, stereotypic hand movements.

Spinal muscular atrophy (SMA) presents with progressive muscle weakness caused by degeneration and loss of the anterior horn cells in the spinal cord and brain stem. Depending on the subtype, it can present from birth to young adulthood. Type 0 SMA and type 1 SMA manifest in infancy with profound hypotonia, joint contractures, tongue fasciculations, absent deep tendon reflexes, and minimal facial weakness with alert facies. Cognition is preserved while respiratory failure eventually ensues. Patients with SMA are not dysmorphic.

PREP Pearls

- Prader-Willi syndrome (PWS) is characterized by profound hypotonia, feeding problems, failure to thrive, hypogonadism, and a typical facial dysmorphology in infancy, which transitions with age to excessive appetite, mild-to-moderate intellectual disability, and potentially morbid obesity if the caloric consumption is not strictly supervised.
- Prader-Willi syndrome is caused by an abnormal parent-specific imprinting problem within the Prader-Willi–specific critical region on chromosome 15q11.1-q13, and is detected by DNA methylation of the critical region.
- Common disorders associated with imprinting defects include PWS, Angelman syndrome, Beckwith-Wiedemann syndrome, Russell-Silver syndrome, uniparental disomy 14, and Albright hereditary osteodystrophy.

ABP Content Specifications(s)

- Understand the role of imprinting in genetic disorders

Suggested Readings

- Butler MG. Genomic imprinting disorders in humans: a mini-review. *J Assist Reprod Genet.* 2009;26(9-10):477-486. doi: http://dx.doi.org/10.1007/s10815-009-9353-3.
- Cassidy SB, Schwartz S, Miller JL, Driscoll DJ. Prader-Willi syndrome. *Genet Med.* 2012;14(1):10-26. doi: http://dx.doi.org/10.1038/gim.0b013e31822bead0.
- Driscoll DJ, Miller JL, Schwartz S, Cassidy SB. Prader-Willi syndrome. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1330/. Updated February 4, 2016.
- McCandless SE, Committee on Genetics. Clinical report: health supervision for children with Prader-Willi syndrome. *Pediatrics*. 2011;127(1):195-204. doi: http://dx.doi.org/10.1542/peds.2010-2820.
- Ramsden SC, Clayton-Smith J, Birch R, Buiting K. Practice guidelines for the molecular analysis of Prader-Willi and Angelman syndromes. *BMC Med Genet.* 2010;11:70. doi: http://dx.doi.org/10.1186/1471-2350-11-70.

Question 157

You are evaluating a 17-year-old adolescent girl with a complaint of irregular menstrual periods. She reports that her menarche occurred at age 12 years. Her menstrual cycles have always been irregular, and for the last year, she has experienced menses every 3 to 4 months. Her last menstrual period was 6 weeks ago. She denies having ever had sexual activity. On physical examination, the patient is obese with a body mass index at the 97th percentile. She has moderate acne, acanthosis nigricans, and a Ferriman-Gallwey hirsutism score of 10. You suspect that she has polycystic ovary syndrome and send her for laboratory testing.

Of the following, the laboratory result MOST suggestive of this diagnosis is a(n)

A. decreased luteinizing hormone to follicle-stimulating hormone ratio

B. decreased thyroxine level

C. elevated fasting insulin level

D. elevated free testosterone level

E. elevated prolactin level

Correct Answer: D
The adolescent girl in the vignette has polycystic ovary syndrome (PCOS) a common reproductive endocrinopathy characterized by ovulatory dysfunction and hyperandrogenism. It affects 5% to 10% of women of reproductive age. The ovulatory dysfunction can manifest as amenorrhea/oligomenorrhea; anovulation/oligo-ovulation; or dysfunctional uterine bleeding. Hyperandrogenism presents as hirsutism, acne, or male pattern baldness/alopecia.

Laboratory findings in patients with PCOS include 1 or more elevated androgens: testosterone, free testosterone, dehydroepiandrosterone, or androstenedione. Although increased luteinizing hormone (LH) relative to follicle-stimulating hormone was the first laboratory abnormality identified in classic PCOS, elevated LH levels occur in only half of PCOS patients.

Diagnostic criteria for PCOS have been separately defined by the National Institutes of Health, Rotterdam European Society of Human Reproduction and Embryology/American Society of Reproductive Medicine consensus workshop group, and the Androgen Excess Society (Item C157).

Item C157. Criteria for the Diagnosis of Polycystic Ovary Syndrome.

Finding	NIH	Androgen Excess Society, 2009	Rotterdam, 2003
Androgen excess	Required	Required	2 of 3 required
Menstrual abnormality	Required	1 of 2 required	
Polycystic ovaries on ultrasound [at least 12 follicles measuring 2-9 mm or increased ovarian volume (>10cc)]	N/A		

N/A, not applicable

Courtesy of M. Trent

While insulin resistance is associated with PCOS and should be assessed in a patient with PCOS, an elevated fasting insulin level is not required for the diagnosis. Similarly, screening for prolactinomas and thyroid disorders is recommended as a part of the evaluation for suspected PCOS, but is not required for the diagnosis.

PREP Pearls

- Polycystic ovary syndrome (PCOS) is characterized by ovulatory dysfunction and hyperandrogenism.
- The ovulatory dysfunction in PCOS can manifest as amenorrhea/ oligomenorrhea, anovulation/oligo-ovulation or dysfunctional uterine bleeding.
- Hyperandrogenism in PCOS presents as hirsutism, acne, or male pattern baldness/alopecia.
- Laboratory findings in PCOS include 1 or more elevated androgens: testosterone, free testosterone, dehydroepiandrosterone, or androstenedione.

ABP Content Specifications(s)

- Identify the clinical findings associated with polycystic ovary syndrome

Suggested Readings

- Fleishman A, Gordon CM. Amenorrhea, hirsutism, and the polycystic ovary syndrome. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. Neinstein's Adolescent and Young Adult *Health Care: A Practical Guide*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:415-427.
- Gray SH. Menstrual disorders. *Pediatr Rev*. 2013:34(1):6-18. doi: http://dx.doi.org/10.1542/pir.34-1-6.

Question 158

A 9-year-old boy is brought to your office for problems with learning. He had been keeping up with his peers until this year when he began to have increasing difficulty with classwork. He has particularly struggled with longer assignments and projects. Concerned about his increasing frustration and poor academic performance, his parents have requested an evaluation through his school. His parents have a meeting at his school next week to review the results of his recent evaluation and to discuss what help their son might need. They have brought a copy of his assessment to their appointment and would like your help in understanding the results.

Academic achievement scores are:

- reading - 75
- math - 80
- writing - 74

Adaptive skills scores are:

- communication - 83
- daily living skills - 85
- motor skills - 94
- socialization - 88

Aptitude test scores are:

- verbal IQ - 93
- performance IQ - 85
- full scale IQ – 89

Of the following, the MOST likely diagnosis is

A. a learning disability in math
B. a learning disability in reading and writing
C. a learning disability in reading, writing, and math
D. mild intellectual disability
E. no learning disability

Correct Answer: B

Most measures of achievement, adaptive skills, and cognitive skills have standard scores with a mean of 100 and a standard deviation (SD) of 15. Scores at least 2 SDs below the mean (< 70 points) in both cognitive (aptitude) and adaptive measures are in the intellectually disabled range. The patient in this vignette has cognitive and adaptive scores that are within 1 SD of the mean on both measures of intelligence and adaptive functioning, and therefore does not have intellectual disability (ID). Achievement scores are generally within 1 SD (15 points) of cognitive scores. Verbal IQ scores correspond to language-based cognition and performance IQ scores correspond to non-language-based cognition. This child's achievement scores in reading (75) and writing (74) are more than 1 SD below his verbal IQ (93), raising concern for a learning disability in reading and writing. As his math score (80) is within 1 SD of his performance IQ (85), a learning disability in math is less likely. Therefore, this child is most likely to have a learning disability in reading and writing by the discrepancy definition of learning disability. By the low achievement definition of learning disability, this child has low academic achievement (more than 1.5 SD below the mean) in the setting of at least average cognition (IQ scores are within a SD of the mean) for both reading and writing. The timing of this child's difficulties is typical. Students with disability in reading may struggle around 9 to 10 years of age when academic demands increase and there is a switch from "learning to read" to "reading to learn."

Learning disabilities are present in 5% to 13% of children and are the most common category under which children receive special education services. Learning disabilities are persistent learning problems resulting in academic achievement below expectations for a child's intellectual potential. There are 2 main ways in which learning disabilities are defined. The traditional definition is a meaningful discrepancy between intelligence and achievement, as measured by standardized intelligence (aptitude or IQ) tests, and achievement tests as seen for the boy in this vignette. The level of significance is typically defined as a difference of 1 to 2 SDs. The second approach to defining a learning disability is by identifying low achievement in a child with at least low-average cognition. Children can qualify for special education services under either of these 2 definitions. In addition, the most recent reauthorization of the Individuals with Disabilities Education Act allows learning disability to be defined and identified by the student's failure to respond to increasing levels of research-based intervention (response to intervention).

Learning disabilities may occur in different areas of academic learning, such as reading, written expression, or mathematics. Learning disabilities in reading (dyslexia) are the most common. Dyslexia is caused by impairment in phonologic processing. These difficulties may be apparent early. Delays in speech and language development indicate risk for language-based learning problems. For children who initially compensate with bypass strategies or by expending more effort, their learning struggles become more apparent when reading comprehension becomes important around the fourth grade. Learning disabilities in writing (dysgraphia) may be related to problems with visual-spatial perception. These children have difficulty expressing ideas in writing. Learning disabilities in mathematics (dyscalculia) involve difficulties with understanding what numbers mean, their relationships to other numbers, and retrieval of basic math facts. When children have a learning disability, they typically avoid academic activities in

those areas of learning that are challenging to them. Children often have problems in more than 1 area, such as learning disabilities in both reading and writing.

Unlike children with learning disabilities who typically have problems with specific academic subjects, children with intellectual disability have general learning problems. Intellectual disability, previously known as mental retardation, is a chronic condition that starts during the developmental period and includes both intellectual and adaptive functioning deficits. IQ scores at least 2 SDs below the mean (< 70) in both cognitive and adaptive measures are in the intellectually disabled range. Similar to learning disabilities, reliance on test scores has now been de-emphasized. In the latest version of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, IQ test scores have been removed from the criterion, but are still considered important approximations of cognitive functioning. Cognitive abilities include the ability to reason, plan, solve problems, think abstractly, learn, and use appropriate judgment. Adaptive skills are those that allow a person to self-manage and perform everyday tasks for independent living in the areas of communication, interpersonal relationships, self-care, home and community living, health, safety, recreation, work, and functional academics (eg, money management). The prevalence of ID is approximately 1% to 2%. The majority (85%) of those with ID have mild ID. Children with mild ID are typically identified when they are unable to keep up academically in school.

Evaluation of a student's learning profile through his school district helps identify any learning disabilities and determine eligibility for special education services. The assessment should include psycho-educational evaluation in conjunction with a review of the child's educational history and classroom observations. Academic strengths and weaknesses are identified as part of this assessment. The information gathered can be helpful in identifying the causes of the child's underachievement, determining next steps to address those causes, and determining eligibility for special education services.

By reviewing the results of testing for the patient in this vignette, you are able to determine that this child requires educational intervention via direct instruction to address his weaknesses in reading and writing. You are able to guide his parents in advocating for appropriate educational services and support for their child. Addressing learning or intellectual disabilities early improves educational outcomes and minimizes harm to the child's self-esteem.

PREP Pearls

- There are 2 main ways in which learning disabilities are defined: 1) significant discrepancy between intelligence and achievement as measured by standardized intelligence (aptitude or IQ) tests and achievement tests; 2) low achievement in a child with at least low-average cognition.
- The most recent reauthorization of the Individuals with Disabilities Education Act allows learning disability to be defined by the student's failure to respond to increasing levels of research-based intervention to address the student's areas of weakness in learning (response to intervention).
- Significant impairment in both cognitive abilities and adaptive functioning are required for diagnosis of intellectual disability.

ABP Content Specifications(s)

- Distinguish the findings associated with learning disabilities from those of intellectual disabilities

Suggested Readings

- Rimrodt SL, Lipkin PH. Learning disabilities and school failure. *Pediatr Rev.* 2011;32(8):315-324. doi: http://dx.doi.org/10.1542/pir.32-8-315.
- Shea SE. Intellectual disability (mental retardation). *Pediatr Rev*. 2012;33(3):110-121. doi: http://dx.doi.org/10.1542/pir.33-3-110.

Question 159

A 16-year-old healthy adolescent girl is brought to your office for a follow-up visit, accompanied by her mother. She was seen and treated at a local emergency department yesterday after having multiple episodes of vomiting with inability to tolerate oral fluids. Her mother tells you that the adolescent was diagnosed with "a stomach flu" and dehydration, received 2 bags of intravenous fluids, and was discharged home after she drank a few ounces of ginger ale. Her urine pregnancy test was negative.

The mother brought her daughter to your office for re-evaluation this morning because "she still seems really run down," and has been complaining of worsening abdominal pain. She has had no vomiting since last evening. She has had no fever, diarrhea, cough, or congestion. The mother tells you that her daughter has also seemed very "stressed out" over the past 5 days since her boyfriend ended their relationship. The adolescent denies any vaginal discharge or bleeding; her last menstrual period was 2 weeks ago.

The patient's vital signs include a temperature of 37.1°C, heart rate of 100 beats/min, blood pressure of 118/70 mm Hg, respiratory rate of 16 breaths/min, and pulse oximetry of 100% on room air. On physical examination, she is tearful and seems to be in moderate distress due to pain. Her abdomen is soft with tenderness over her right upper quadrant. Her liver edge is palpable about 3 cm below her right costal margin. She has active bowel sounds and no peritoneal signs. A complete neurologic examination reveals no focal abnormalities. Genitourinary examination reveals no vaginal discharge or bleeding, and a bimanual examination reveals no adnexal or cervical motion tenderness.

Following the physical examination, you ask the patient's mother to give you an opportunity to talk with her daughter alone. When you ask the patient why she is tearful, she discloses to you that, over a 2-day period that ended approximately 36 hours ago, she took more than fifty 500 mg acetaminophen tablets because she was "in so much pain" after her boyfriend ended their relationship. She denies suicidal ideation and states that she took the medicine because "I just wanted something to take away my pain." She did not share this information with her mother or any staff in the emergency department yesterday because she felt embarrassed about taking the medication.

Of the following, the BEST next step in the management of this patient is to

A. arrange to see her again in your office within 24 hours for re-evaluation
B. obtain a serum acetaminophen level to determine her need for further therapy
C. obtain urgent child psychiatric consultation due to concern for suicidality
D. transfer her to the emergency department for activated charcoal
E. transfer her to the emergency department for N-acetylcysteine therapy

Correct Answer: E
The adolescent girl in the vignette presents with fatigue and right upper quadrant tenderness, which have developed since she intentionally ingested more than 25 g of acetaminophen over a 48-hour period. Her abdominal pain was preceded by multiple episodes of vomiting, which have now resolved. This patient's symptoms and clinical findings are highly suggestive of the development of hepatotoxicity as a result of acetaminophen poisoning. The best next step in her management is to transfer her to the emergency department for N-acetylcysteine (NAC) therapy.

Acetaminophen is the most commonly used analgesic and antipyretic in the United States. It is one of the most common pharmaceutical products ingested by young children, and is one of the top drugs taken by adolescents and adults in intentional drug overdoses. Clinical outcomes for children and adolescents presenting with acetaminophen poisoning are nearly always positive if appropriate management, including prompt (within 8 to 10 hours following ingestion) administration of NAC, is instituted. All pediatric providers should be able to recognize the signs and symptoms of acetaminophen toxicity and to manage them appropriately.

The risk for toxicity from acetaminophen ingestion in children and adolescents depends largely upon the situation surrounding exposure. Among adolescents, intentional ingestion due to suicidal intent is more prevalent. These ingestions tend to involve higher doses of acetaminophen, often taken as a single overdose. Intentional ingestion of other substances, in addition to acetaminophen, is not uncommon in these situations. Adolescents who ingest acetaminophen in an attempt to self-harm often underestimate its toxicity and develop hepatocellular injury more frequently than younger children with lower-dose, exploratory ingestions. These ingestions may be disclosed by the adolescent to friends, family members, and healthcare providers following ingestion, or they may be discovered only as a result of toxicological screening.

Unintentional ingestions of acetaminophen, often due to developmentally-normal exploratory behaviors, are more commonly observed among young children. Most of these ingestions involve small doses, and can often be managed in the primary care setting or even at home with appropriate anticipatory guidance.

Cases of significant acetaminophen toxicity due to unintentional repeated administration of supratherapeutic doses to children by well-meaning caregivers have been reported. Diagnosis of

these cases may be delayed because symptoms and signs are nonspecific and may be mistaken for symptoms of the illness for which acetaminophen was being given in the first place. Deliberate poisoning of infants with acetaminophen as a form of child abuse has also been reported.

The primary toxicity of acetaminophen is severe hepatic injury. Acetaminophen is metabolized in the liver to a highly reactive metabolite by the cytochrome P450 pathway. Its toxic intermediate is normally inactivated by conjugation with hepatic glutathione. In massive acetaminophen overdoses (or in situations of chronic acetaminophen ingestion), glutathione becomes depleted, allowing the toxic intermediate to bind to liver cells and cause cellular injury. This injury can lead to elevation of liver enzymes, hepatic dysfunction, and even hepatic failure and death.

An acute acetaminophen ingestion of greater than 150 to 200 mg/kg in children or greater than 7.5 g total in adults is potentially hepatotoxic. Patients who have taken supratherapeutic doses over the course of consecutive days are also at risk for hepatocellular injury.

Early signs and symptoms of acute acetaminophen poisoning in children are nonspecific and can often be mild. The expected clinical course of acute acetaminophen toxicity is often divided into 4 characteristic stages:

- Stage 1 (up to 24 hours post-ingestion): Patients may be entirely asymptomatic, or display nonspecific symptoms such as nausea, vomiting, malaise, and fatigue/lethargy
- Stage 2 (24 to 72 hours post-ingestion): Findings may include right upper quadrant pain, elevated hepatic enzymes, elevated prothrombin time (PT) and international normalized ratio of PT, and hepatic enlargement. In severe cases, evidence of nephrotoxicity (elevated blood urea nitrogen, creatinine, decreased urine output) and pancreatitis may be apparent.
- Stage 3 (72 to 96 hours post-ingestion): Progression to hepatic failure, and even renal failure and multisystem organ failure in severe cases. Death from acetaminophen poisoning occurs most commonly in this clinical stage.
- Stage 4 (4 to 14 days post-ingestion): Recovery

Clinical findings for the adolescent girl in the vignette indicate that she has progressed to "Stage 2" of acetaminophen toxicity. Transfer to an emergency department for immediate treatment with NAC and further management to help prevent progression to hepatic failure is crucial to her management.

Initial management of acute acetaminophen exposures in children should involve aggressive supportive care, decontamination with activated charcoal in those children presenting within 4 hours of ingestion, and administration of NAC when indicated. N-acetylcysteine is most beneficial if administered within 8 hours of an acute acetaminophen ingestion. When acute acetaminophen toxicity is suspected, a serum acetaminophen level should be obtained (ideally at 4 hours post-ingestion) and plotted on the Rumack-Matthew nomogram, which can be found in

many standard references on acetaminophen toxicity. Given the serum acetaminophen level and the number of hours post-ingestion, this nomogram can be used to classify the patent as at no risk, possible risk, or probable risk of hepatotoxicity. If the serum acetaminophen level falls above the possible risk threshold, treatment with NAC should be initiated. Hepatic enzyme levels, a coagulation profile, serum electrolytes, and a complete blood cell count should be obtained before initiating treatment, as well as following treatment.

Recommending that the adolescent follow up in the office within 24 hours would be an inappropriate choice related to her management. Her clinical findings indicate that she has progressed to "Stage 2" of acetaminophen toxicity (hepatocellular injury), and she is at high risk for progressing to complete hepatic failure and even death without immediate clinical intervention, including institution of NAC therapy.

Delaying referral to the emergency department in order to obtain a serum acetaminophen level would not be appropriate in the management of this patient. While obtaining a serum acetaminophen level (ideally 4 hours post-ingestion) to help determine the need for further therapy would be recommended for children presenting acutely after a known or suspected acetaminophen ingestion, this patient's presentation is delayed (approximately 72 hours after ingestion) and she is presenting with current findings that indicate hepatotoxicity arising after excessive acetaminophen ingestion. Immediate institution of NAC therapy would be indicated in her situation, regardless of her serum acetaminophen level.

Although assessment by a child psychiatric specialist is certainly indicated for the adolescent in the vignette due to her recent depressive symptoms and concern for suicidality, the more immediate priority in her management should involve emergent clinical interventions to prevent her from developing hepatic failure and failure of other organ systems. Child psychiatric consultation may be obtained after she has been medically stabilized.

While the administration of activated charcoal for gastrointestinal decontamination is recommended for children and adolescents presenting very soon after an acute acetaminophen overdose (provided that the airway is protected), the patient in the vignette is presenting days(not hours) after ingestion of a large amount of acetaminophen. She has unfortunately already had complete gastrointestinal absorption of the acetaminophen she ingested and is now displaying signs of hepatic toxicity. Activated charcoal would not have a clinical benefit at this point in her clinical course. For children presenting within 4 hours of a significant known or suspected acetaminophen ingestion, treatment with activated charcoal (1 g/kg) is recommended, provided that there are no contraindications to its administration, such as a concern that the child's airway is not adequately protected or gastrointestinal obstruction.

PREP Pearls

- Among adolescents, intentional ingestions of acetaminophen due to suicidal intent tend to involve high doses of acetaminophen, taken as a single overdose.
- An acute acetaminophen ingestion of greater than 150 to 200 mg/kg in children, or greater than 7.5 g total in adults is potentially hepatotoxic.
- Initial management of acute acetaminophen exposures in children should involve aggressive supportive care, decontamination with activated charcoal in those children presenting within 4 hours of ingestion, and administration of N-acetylcysteine when indicated.

ABP Content Specifications(s)

- Recognize the signs and symptoms of acetaminophen toxicity, and manage appropriately

Suggested Readings

- Argentieri J, Morrone K, Pollack Y. Acetaminophen and ibuprofen overdosage. *Pediatr Rev*. 2012;33(4):188-189. doi: http://dx.doi.org/10.1542/pir.33-4-188.
- Feng S-Y, Goto CS. Toxic ingestions and exposures. In: Stone CK, Humphries RL, Drigalla D, Stephan M, eds. Current Diagnosis and Treatment: Pediatric Emergency Medicine. New York, NY: McGraw-Hill; 2015:631-662.
- O'Donnell KA, Osterhoudt KC, Burns MM, Caiello, Henretig FM. Toxicologic emergencies. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. *Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:1061-1114.

Question 160

A 2-week-old neonate born at 34 weeks of gestation with gastroschisis develops fever. He is currently receiving parenteral nutrition through a peripherally inserted central catheter (PICC). Vital signs show a temperature of 38.1°C, respiratory rate of 60 breaths/min, heart rate of 165 beats/min, and blood pressure of 70/45 mm Hg. On physical examination, he is well perfused, has a defect of the abdominal wall, and a PICC line in the right femoral region. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	12,550/µL (12.6×10^9/L)
Segmented neutrophils	50%
Bands	15%
Lymphocytes	35%
Hemoglobin	9.3 g/dL (93 g/L)
Platelet count	430×10^3/µL (430×10^9/L)
Blood culture	Coagulase-negative staphylococci

Of the following, the BEST justification for prompt removal of the central line in this patient is

A. characteristics of pathogen
B. clinical status
C. multiple positive cultures
D. pathogen drug susceptibility
E. underlying condition

Correct Answer: C
The best justification for removal of the central line in the neonate described in this vignette is multiple positive cultures. For any intravascular infection in which there are multiple positive cultures while on appropriate therapy, the likelihood of successfully eradicating the pathogen with antimicrobial therapy alone is low. Therefore, removal of the source of infection is the best next step in management.

There are certain pathogens for which prompt line removal is indicated, even in the absence of multiple positive cultures. These include gram-negative bacteria and yeast. In addition, certain gram-positive pathogens that can cause severe infections, such as *Staphylococcus aureus*, would necessitate line removal. Growth of coagulase-negative staphylococci (CoNS) alone is not an absolute indication for line removal, as CoNS tend to behave in an indolent fashion and there is potential for clearing of the infection with antimicrobial therapy.

While CoNS can represent skin contamination in specimens from healthy children, in a child with an indwelling medical device, such as a peripherally inserted central catheter line, this organism is potentially and likely pathogenic. Many CoNS produce a biofilm that allow them to adhere to medical devices and simultaneously protect them from host defenses and antimicrobials. In addition to intravascular catheters, CoNS infections can occur with other devices, including cerebrospinal fluid shunts, urinary tract catheters, peritoneal shunts, and any foreign material such as prosthesis and grafts.

Clinical instability and sepsis are absolute indications for removal of infected intravascular catheters. Since the neonate in the vignette does not demonstrate these features, clinical status is not the preferred response.

In general, drug susceptibility is not utilized in the decision process for central line removal, unless there are no reasonable therapeutic options. Coagulase-negative staphylococci tend to be methicillin-resistant and resistant to most cephalosporins, which is why vancomycin is often the treatment of choice.

Underlying condition is often used in distinguishing contaminant from pathogenic organisms and used to determine the host's ability to combat infections. However, currently there are no specific recommendations for line removal based solely on a patient's underlying condition.

PREP Pearls

- For any intravascular infection in which there are multiple positive cultures while on appropriate therapy, removal of the source of infection is the best step in management.
- Prompt line removal is indicated for certain pathogens (gram-negative bacteria, yeast, and *Staphylococcus aureus*) and in the setting of clinical deterioration or sepsis.
- Many coagulase-negative staphylococci produce a biofilm that allow them to adhere to medical devices and simultaneously protect them from host defenses and antimicrobials.

ABP Content Specifications(s)

- Plan the appropriate treatment of a patient with an intravenous catheter-associated infection
- Understand the association of coagulase-negative staphylococcal infections with the presence of central venous catheters or other foreign bodies

Suggested Readings

- American Academy of Pediatrics. Staphylococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:715-732.
- Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;49(1):1-45. doi: http://dx.doi.org/10.1086/599376.

Question 161

You are seeing a 14-year-old adolescent girl in your office for her health supervision visit. On review of systems, she reports that she has frequent episodes of abdominal pain. The periumbilical episodes of pain come on quickly, with a pain level of 7 to 10 out of 10. She usually has associated symptoms of nausea, vomiting, and headache. She denies fevers, joint pain, rash, diarrhea, and weight loss. In between episodes, she feels well.
On physical examination, the patient's weight is 52 kg, heart rate is 92 beats/min, respiratory rate is 15 breaths/min, and blood pressure is 103/78 mm Hg.

Of the following, the diagnosis MOST consistent with this patient's presentation is

A. abdominal migraine
B. chronic constipation
C. cyclic vomiting syndrome
D. hereditary pancreatitis
E. inflammatory bowel disease

Correct Answer: A

The adolescent girl in the vignette most likely has abdominal migraines. Abdominal migraine is a functional gastrointestinal disorder defined by the ROME III criteria.

Diagnostic criteria include all of the following:

- Paroxysmal episodes of intense, acute periumbilical pain lasting for 1 hour or more that has occurred at least 2 times in a 12-month period
- Pain that interferes with normal function
- Pain-free periods lasting weeks to months
- Pain associated with 2 of the following: anorexia, nausea, vomiting, headache, photophobia, or pallor
- No evidence of organic etiology

The adolescent girl in this vignette is not ill enough during these episodes to raise concern for hereditary pancreatitis or inflammatory bowel disease. Cyclic vomiting syndrome may present in a similar way, but is associated with retching and vomiting that lasts hours to days. In addition, children with cyclic vomiting syndrome often do not have headaches or report pain as the primary complaint. Children with chronic constipation may have abdominal pain, but typically lack other associated symptoms.

An interdisciplinary team, including the child's pediatrician, a gastroenterologist, and a neurologist should be involved in the evaluation and management of abdominal migraine.

PREP Pearls

- Abdominal migraine is defined as paroxysmal episodes of abdominal pain that interfere with normal daily function and are associated with anorexia, nausea, vomiting, headache, photophobia, or pallor.
- Between episodes, children with abdominal migraine are pain free.
- Abdominal migraines are not associated with a change in stooling pattern.

ABP Content Specifications(s)

- Recognize the clinical features associated with abdominal migraine

Suggested Readings

- Carson L, Lewis D, Tsou M, et al. Abdominal migraine: an under-diagnosed cause of recurrent abdominal pain in children. *Headache*. 2011;51(5):707-712. doi: http://dx.doi.org/10.1111/j.1526-4610.2011.01855.x.
- Evans RW, Whyte C. Cyclic vomiting syndrome and abdominal migraine in adults and children. *Headache*. 2013;53(6):984-993. doi: http://dx.doi.org/10.1111/head.12124.
- Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology*. 2006;130(5):1527-1537. doi: http://dx.doi.org/10.1053/j.gastro.2005.08.063.

Question 162

A 10-year-old girl presents to your office for evaluation of left knee pain. She began having mild pain about 2 months ago during soccer season. Two weeks ago, she fell onto her knee and the pain became more severe. She had mild knee swelling at the time of her fall. The girl denies bruising, locking of the knee joint, a sense of knee instability, or limp. Physical examination is remarkable for tenderness over the inferior pole of the patella. Her radiographs are shown in Item Q162A and Item Q162B .

Item Q162A: Radiograph for the girl described in the vignette. Courtesy of R Carl

Item Q162B: Radiograph for the girl described in the vignette. Courtesy of R Carl

Of the following, the MOST likely diagnosis for this girl is
A. apophysitis of the inferior pole of the patella
B. patellar fracture
C. patellar dislocation
D. prepatellar bursitis
E. symptomatic bipartite patella

Correct Answer: A

The girl in the vignette has a history of insidious-onset knee pain with an aggravating injury and tenderness over the inferior pole of the patella. Her presentation is most consistent with apophysitis of the inferior pole of the patella, also known as Sinding-Larsen and Johansson syndrome. A physis is a growth plate that contributes to linear bone growth. An apophysis is a minor growth plate at a site where a tendon attaches to bone. Apophysitis refers to irritation of an apophysis because of traction or direct pressure. In most cases, apophysitis occurs without inciting injury. Sinding-Larsen and Johansson syndrome typically occurs in girls between the ages of 8 and 11 years and in boys between the ages of 10 and 13 years. Affected children often report activity-related pain at the inferior pole of the patella. The diagnosis is based on history and physical examination. Radiographs may be useful to rule out other conditions and may show sclerosis, bony fragmentation, or a small lucency at the apophysis. Children with Sinding-Larsen and Johansson syndrome may have recurrent symptoms over 1 to 2 years. The symptoms can typically be managed with the use of a patellar strap and rest from activities on days when the pain is particularly severe.

This girl's radiographs do not show a patellar fracture. In addition, a child with a patellar fracture would have difficulty bearing weight. Individuals with patellar dislocation often report feeling a "pop" or the sensation of something shifting out of place. Acute patellar dislocation usually presents with a large amount of swelling, difficulty bearing weight, and tenderness over the medial patellar facet or medial femoral epicondyle. Prepatellar bursitis, also referred to as housemaid's knee, nun's knee, and carpet-layer's knee, is unusual in children and adolescents. Frequent kneeling, or less commonly, a blow to the knee, leads to irritation and swelling of the bursa overlying the patella. This girl's radiographs do not show a bipartite patella, which is present in approximately 1% of the population. Bipartite patella does not usually cause symptoms, but can be aggravated by a fall or frequent kneeling.

PREP Pearls

- Individuals with apophysitis involving the inferior pole of the patella (Sinding-Larsen and Johansson syndrome) typically have a history of insidious-onset knee pain and tenderness over the inferior pole of the patella.
- About 1% of the population has a bipartite patella, which does not usually cause symptoms, but can be aggravated by a fall or frequent kneeling.

ABP Content Specifications(s)

- Recognize the clinical findings associated with sports-related prepatellar bursitis, and manage appropriately

Suggested Readings

- Sarwark JF, LaBella CR. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014: 650 pp.
- Wolf M. Knee pain in children: part 1: evaluation. *Pediatr Rev.* 2016;37(1):18-24. doi: 10.1542/pir.2015-0040.

Question 163

A 20-month-old girl is brought to your office with complaints of fever and right ear pain. On physical examination, her temperature is 38.5°C. The right ear shows a bright red tympanic membrane, which is bulging with a purulent effusion. The left ear is normal. You note that this is her fourth episode of otitis media in the last 7 months. Her last ear infection was 3 weeks ago and she was treated with amoxicillin.

Of the following, the BEST approach for management of this patient is to initiate a

A. 5-day course of amoxicillin and refer for insertion of tympanostomy tubes
B. 5-day course of amoxicillin and refer to audiology for a hearing screen
C. 5-day course of amoxicillin-clavulanate and follow-up in 3 weeks
D. 10-day course of amoxicillin-clavulanate and refer for insertion of tympanostomy tubes
E. 10-day course of amoxicillin-clavulanate followed by a daily prophylactic low dose of amoxicillin for 3 months

Correct Answer: D
The child in this vignette has recurrent otitis media and should be treated with a 10-day course of amoxicillin-clavulanate and referred for insertion of tympanostomy tubes. Recurrent otitis media (OM) is defined as 3 episodes of acute otitis media (AOM) in the previous 6 months or 4 episodes of AOM in the past 12 months, with at least 1 episode being in the preceding 6 months. There is complete resolution between each episode. It is appropriate to refer a child who meets criteria for recurrent AOM for insertion of tympanostomy tubes. The medical therapy for this patient would consist of a 10-day course of amoxicillin-clavulanate. Amoxicillin remains the treatment of choice for AOM, but the clinician should consider using an antibiotic with additional β-lactamase activity (such as amoxicillin-clavulanate) when the patient has been treated with amoxicillin in the past 30 days or has a history of AOM treatment failure with amoxicillin in the past. A standard 10-day antibiotic course is the recommended duration of treatment. A 7-day treatment course is recommended for children 2 to 5 years of age, and a 5-day course is appropriate for children 6 years of age and older. Prophylactic antibiotics for children with recurrent OM are not recommended given the questionable benefit, contribution to growing antibiotic resistance, and the associated risks, including gastrointestinal and allergic adverse effects. There is little evidence to support 10- to 14-day routine follow-up for OM; however, some providers may opt to see children with recurrent OM for a follow-up visit to monitor for resolution.

Children with recurrent OM typically have their first ear infection at younger than 1 year of age. Risk factors associated with frequent ear infections include lower socioeconomic status, siblings in the household, and daycare attendance. Children with allergies, immune deficiencies, chronic sinusitis, and craniofacial abnormalities such as a cleft palate are also at higher risk to develop ear infections. Other medical conditions associated with recurrent OM include Down syndrome, Goldenhar syndrome, Treacher Collins syndrome, Turner syndrome, and diseases associated with ciliary dysfunction.

Given the patient's age in the vignette, a 5-day course of antibiotics is not appropriate. Amoxicillin is not an appropriate antibiotic choice given that the patient has a history of recurrent OM and was treated with amoxicillin less than 30 days prior to the current infection. Prophylactic antibiotics are not recommended for children with recurrent OM.

PREP Pearls

- Recurrent otitis media (OM) is defined as 3 episodes of acute otitis media (AOM) in the past 6 months or 4 episodes of AOM in the past 12 months, with at least 1 episode being in the past 6 months.
- Prophylactic antibiotics are not recommended for children with recurrent AOM.
- Conditions associated with recurrent OM include Down syndrome, Goldenhar syndrome, Treacher Collins syndrome, Turner syndrome, and diseases associated with ciliary dysfunction.

ABP Content Specifications(s)

- Plan the appropriate management of recurrent otitis media, including follow-up evaluation and when an exacerbation has occurred
- Recognize conditions associated with recurrent otitis media

Suggested Readings

- Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media. *Pediatrics*. 2013;131(3):e964-e999. doi: http://dx.doi.org/10.1542/peds.2012-3488.
- Redjal N. Otitis media. In: Berkowitz CD, ed. *Berkowitz's Pediatrics: A Primary Care Approach*. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:459-464.
- Rosa-Olivares J, Porro A, Rodriguez-Varela M, Riefkohl G, Niroomand-Rad I. Otitis media: to treat, to refer, to do nothing: a review for the practitioner. *Pediatr Rev.* 2015;36(11):480-488. doi: http://dx.doi.org/10.1542/pir.36-11-480.

Question 164

A 12-year-old girl presents to your office for evaluation of fever and persistently enlarged lymph nodes. She reports a 6-week history of swollen glands in her neck and a 2-week history of intermittent fever. On reviewing her chart, you note that this is her third visit to the office with similar symptoms. During her previous 2 visits, she was prescribed an antibiotic for presumed lymphadenitis, with minimal response. She was initially treated with amoxicillin, followed by a course of high-dose amoxicillin/clavulanate.

At this visit, the girl complains of poor appetite, with a 2-kg weight loss over the last 2 weeks. She was born in the United States, has never traveled abroad, lives at home with her parents and a younger brother, and has no known sick contacts. She has no pets. On physical examination, the girl is awake and alert, but appears uncomfortable. Her temperature is 38.8°C, heart rate is 86 beats/min, respiratory rate is 22 breaths/min, and blood pressure is 96/74 mm Hg. There are 3 nontender, nonerythematous left posterior cervical lymph nodes, each measuring 1.5 to 2 cm. There is no axillary or inguinal adenopathy. The remainder of her physical examination is unremarkable. A complete blood cell count is normal for age.

Of the following, the MOST appropriate next management step for the girl in the vignette is to

A. prescribe azithromycin for Bartonella henselae
B. prescribe oral clindamycin
C. reassure the parents that adenopathy is common in this age group
D. refer to a pediatric oncologist
E. treat with isoniazid after performing a purified protein derivative test

Correct Answer: D

Lymphadenopathy is a common reason for visits to the pediatrician. The vast majority of the time, the lymphadenopathy represents nonpathologic reactive adenopathy or infectious lymphadenitis. The general pediatrician should be able to identify adenopathy for which the clinical course is out of the ordinary. The girl in the vignette has 3 "red flags" suggesting that the practitioner should have a high index of suspicion that this adenopathy is behaving atypically:

- The girl has presented 3 times for the same concern of adenopathy, each time receiving appropriate therapy for bacterial lymphadenitis, but with little change.
- At this visit, she complains of "B" (fever, weight loss > 5% of body weight, night sweats) symptoms, including fevers and weight loss.
- The adenopathy is persistently more than 1 cm.

Although this presentation may still represent reactive adenopathy, or an atypical infectious lymphadenitis, an oncological process is a serious consideration that warrants referral to an oncologist. A biopsy is likely indicated in this case, and generally, an oncologist should assess the patient and the adenopathy before obtaining a biopsy. There are 3 approaches to performing a lymph node biopsy and which one is selected depends on the suspected diagnosis. The 3 approaches are (1) open surgical biopsy (incisional or excisional), (2) core needle biopsy, and (3) fine needle aspiration.

An open surgical biopsy provides the most tissue for analysis, but it requires a surgical incision and typically the administration of general anesthesia. A core needle biopsy yields far less tissue than an open biopsy, but often enough to make the diagnosis. This procedure does not require an incision and can often be performed with local analgesia or with sedation rather than general anesthesia. Fine needle aspiration provides only minimal tissue and is often nondiagnostic; it can be easily performed at the bedside with local analgesia.

The girl in the vignette has no risk factors for tuberculosis or cat scratch disease, so empiric treatment for tuberculosis or *Bartonella henselae* is not appropriate.

Although the lymphadenopathy presented in the vignette may reflect adenitis with an atypical organism that would respond to clindamycin, the history along with the physical examination findings of nontender and nonerythematous lymph nodes are inconsistent with refractory lymphadenitis.

PREP Pearls

- Persistent lymphadenopathy more than 1 cm in diameter, despite appropriate antimicrobial therapy for bacterial adenitis, should warrant an evaluation by a pediatric oncologist.
- The presence of "B" symptoms (fever, weight loss > 5% body weight, night sweats) in the context of adenopathy should trigger a referral to a pediatric oncologist.
- Evaluation by an oncologist should occur before a biopsy of enlarged lymph nodes.

ABP Content Specifications(s)

- Plan the appropriate diagnostic evaluation of unexplained lymphadenopathy

Suggested Readings

- Friedmann A. Evaluation and management of lymphadenopathy in children. *Pediatr Rev*. 2008;29(2)53-60. doi: http://dx.doi.org/10.1542/pir.29-2-53.
- Geddes G, Butterly MM, Patel SM, Marra S. Pediatric neck masses. *Pediatr Rev.* 2013;34(3):115-125. doi: http://dx.doi.org/10.1542/pir.34-3-115.
- Sahai S. Lymphadenopathy. *Pediatr Rev.* 2013;34(5):216-227. doi: http://dx.doi.org/10.1542/pir.34-5-216.

Question 165

A 16-year-old adolescent collapses while playing basketball. He had been running down the court when it happened and injured his right hand when he fell. He is now awake and reports that he felt short of breath and had chest pain before the event. The adolescent denies any history of palpitations, but he has felt short of breath in the past with exercise and was prescribed an albuterol inhaler, which he did not use today. His father passed away, reportedly from a severe asthma attack, when the adolescent was 6 years of age. Other family members had died at a young age. There is no family history of seizures or congenital deafness. The adolescent is taken to the emergency department.

Of the following, the adolescent's presentation and family history are MOST suggestive of

A. anomalous coronary artery

B. hypertrophic cardiomyopathy

C. long QT syndrome

D. vasovagal syncope

E. Wolff-Parkinson-White syndrome

Correct Answer: B
The adolescent athlete in this vignette had a syncopal episode with exercise and felt symptoms of decreased cardiac output before his collapse. In retrospect, he remembers previous milder symptoms of shortness of breath with exercise, for which he was treated with albuterol. He also has a suspicious family history of early sudden death in his father and potentially in other relatives. This history is consistent with hypertrophic cardiomyopathy (HCM).

The most common cause of sudden death on the athletic field in the United States is hypertrophic cardiomyopathy. This condition has an autosomal dominant inheritance pattern. Basketball is the most common sport in which sudden cardiac death occurs. Patients with HCM may have syncopal events before sudden death.

The second most common cause for sudden death on the athletic field is an anomalous coronary artery. The preceding symptoms may be similar to those seen with HCM, but there is no pattern of inheritance with this disease. These patients may also have syncope.

Long QT syndrome (LQTS) can present with sudden cardiac arrest (SCA) or syncope with exercise, but it is not as common a cause of SCA as HCM. This syndrome also has an autosomal dominant inheritance. Patients with LQTS may have seizure-like events when ventricular arrhythmias, such as polymorphic ventricular tachycardia or torsades de pointes, occur. Long QT syndrome is associated with congenital deafness in some patients.

Vasovagal syncope is common in adolescents and in athletes. The event history and physical examination are the most important components of evaluation and diagnosis. Syncope may occur when a relatively hypovolemic athlete experiences overheating and vasodilation. Immediately after exercise, the athlete's catecholamines decrease, and the heart rate is no longer elevated to compensate for the relative hypovolemia. This may result in inadequate cardiac output and syncope. This syncopal event may be preceded by dizziness, but would not cause chest pain in a child with a normal heart. Vasovagal syncope may be seen in other family members, but would not be expected to cause early cardiac death.

Wolff-Parkinson-White syndrome (WPW) may cause syncope or sudden death. The most common arrhythmia associated with WPW is supraventricular tachycardia (SVT). This is a reentrant arrhythmia that uses the atrioventricular node for one arm of the circuit and the accessory pathway connection between the atrium and the ventricle as the other.

Supraventricular tachycardia can at times be very rapid and cause dizziness. If a patient with WPW has a syncopal event, however, the occurrence of a more dangerous rhythm must be presumed. If atrial fibrillation develops in patients with a very rapidly conducting accessory pathway, the rhythm may conduct to the ventricle and cause ventricular fibrillation. It would be likely that syncopal patients with WPW have a history of palpitations and may have felt their heart racing, but this may not always be the case. Chest pain and shortness of breath alone would be unlikely. Wolff-Parkinson-White syndrome is also very rarely inherited, and a family history of multiple members dying at a young age would be unlikely.

Any patient who has syncope with exercise requires a cardiac evaluation. A detailed personal and family history should be obtained, and a physical examination performed. Echocardiography will determine whether there is hypertrophic cardiomyopathy or an abnormal coronary artery origin. Orthostatic blood pressures are helpful to assess the patient's hydration status. Electrocardiography will assess for a prolonged QT interval or WPW, and may find signs of ischemia. If the initial evaluation does not reveal the diagnosis, the next step would be an exercise test to evaluate for catecholamine-sensitive arrhythmias including other forms of SVT and ventricular tachycardia. A 24-hour Holter monitor to screen for occult arrhythmias may be obtained. If there is any question about the coronary artery origins, a computed tomography angiogram can be performed.

The patient described in the vignette has several symptoms that would likely prompt inpatient observation. He was running down the court when the event occurred and he injured himself when he collapsed. He had chest pain just before the event and has a worrying family history of sudden death. Given that combination of factors, he would need a cardiac evaluation before leaving the hospital or clinic.

PREP Pearls

- Syncope occurring with exercise may be associated with an increased risk of sudden death and requires cardiac evaluation.
- Vasovagal syncope can usually be diagnosed with a careful history and physical examination.

ABP Content Specifications(s)

- Plan the appropriate evaluation of a syncopal or pre-syncopal episode, including episodes associated with exercise

Suggested Readings

- Harmon KG, Drezner JA, Wilson MG, Sharma S. Incidence of sudden cardiac death in athletes: a state-of-the-art review. *Heart*. 2014;100(16):1227-1234. doi: http://dx.doi.org/10.1136/heartjnl-2014-093872.rep.
- Liberthson RR. Sudden death from cardiac causes in children and young adults. *N Engl J Med.* 1996;334(16):1039-1044. doi: http://dx.doi.org/10.1056/NEJM199604183341607.
- Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. *Circulation*. 2009;119(8):1085-1092. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.108.804617.
- Strickberger SA, Benson DW, Biaggioni I, et al. AHA/ACCF Scientific Statement on the evaluation of syncope: from the American Heart Association Councils on Clinical Cardiology, Cardiovascular Nursing, Cardiovascular Disease in the Young, and Stroke, and the Quality of Care and Outcomes Research Interdisciplinary Working Group; and the American College of Cardiology Foundation: in collaboration with the Heart Rhythm Society: endorsed by the American Autonomic Society. *Circulation*. 2006;113(2):316-327. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.105.170274.

Question 166

A 3-month-old female infant is brought to your office for "excessive crying." Her mother reports that she cries consistently for 3 or 4 hours most evenings. She sometimes improves when being held and carried, but still "seems upset." Her mother reports that her belly feels "gassy" and that she has tried simethicone drops in the evening, but this has not helped. The infant is breastfeeding, and her mother has tried eliminating milk and soy from her diet. You diagnose infant colic.

Of the following, the MOST appropriate step in the management of this infant's symptoms is to recommend

A. an herbal tea mixture

B. infant massage therapy

C. simethicone drops 3 times daily

D. a soy-based formula

E. swaddling, gentle rocking, and decreased stimulation

Correct Answer: E

Infant colic, as defined by an infant crying more than 3 hours per day, more than 3 days per week, for more than 3 weeks at a time, is common, occurring in up to one-quarter of all infants. It peaks around 6 weeks of age and typically resolves by 4 months of age. Periods of crying typically occur in the late afternoon or evening. In between periods of crying, colicky infants feed and act normally. The growth trajectory and the examination of infants with colic are typically normal. No laboratory or imaging evaluation is needed for the diagnosis, but a detailed history and examination should rule out other causes of excessive crying: gastroesophageal reflux disease, constipation, occult fracture, infection, and feeding disorders.

Since it is so common, as well as disruptive and troubling to parents, many interventions have been tested in an attempt to find an easy, scalable, effective way to quiet excessive infant crying. These efforts have been largely unsuccessful, and the prevailing advice to parents of colicky infants is to be assured that this is a self-limited problem and is best handled by swaddling the infant and maintaining a quiet, soothing environment. Encouraging parents to recruit other trusted caregivers to swaddle and rock the crying infant may also be helpful in order to decrease the stress from caring for a colicky infant.

No other superior medical treatment for colic is available, but some interventions may help for select patients. There is some evidence to suggest that probiotics are helpful in exclusively breastfed infants. Maternal elimination diets or soy-based formula also appear to be helpful for some infants, but if a maternal elimination diet is ineffective, as in this vignette, a soy-based formula will likely not reduce symptoms. A recent systematic review suggests some nutritional supplements may hold promise (eg, fennel extract), but the evidence is too preliminary to recommend as a treatment. Infant massage therapy in this same systematic review did not appear to be effective. Studies of other therapies, such as reflexology, were too methodologically flawed to offer definitive conclusions. Simethicone is the most widely used medication for colic and has been shown in randomized trials to be no better than placebo. However, it is safe. Many parents may still want to try these interventions and suggesting that parents stop them after several weeks if there is no improvement may reduce unnecessary prolonged use.

PREP Pearls

- Colic is common, self-limited, and can be diagnosed with careful history and physical examination.
- Swaddling and gentle rocking in a low-stimulation environment is the recommended intervention.
- Probiotics and nutritional supplements have shown promise in early trials, but studies are too preliminary for them to be recommended in the treatment of infant colic.

ABP Content Specifications(s)

- Recognize the frequency of crying in infants of various ages
- Plan the appropriate evaluation of colic
- Plan the appropriate management of colic, while recognizing inappropriate therapy

Suggested Readings

- Cohen GM, Albertini LW. Colic. *Pediatr Rev*. 2012;33(7):332-333. doi: http://dx.doi.org/10.1542/pir.33-7-332.
- Perry R, Hunt K, Ernst E. Nutritional supplements and other complementary medicines for infantile colic: a systematic review. *Pediatrics*. 2011;127(4):720-733. doi: http://dx.doi.org/10.1542/peds.2010-2098.

Question 167

A family in your practice is referred to you by the local department of health after the father developed fever, fatigue, abdominal pain, nausea, vomiting, and jaundice. His evaluation confirms that he has hepatitis A. The mother has received prophylaxis from her internist and is requesting appropriate prophylaxis for her 3 children. The children include a 10-month-old female infant who is healthy and doing well, a 2-year-old boy with asthma managed on an albuterol inhaler, and a 9-year-old boy with Crohn disease who is stable on methylprednisolone and azathioprine. Review of the children's immunization records reveals none of them have ever been vaccinated for hepatitis A.

Of the following, the BEST recommendation regarding immune globulin (IG) for these children is

A. all should receive IG
B. none should receive IG
C. only the 10-month-old and 2-year-old should receive IG
D. only the 10-month-old and 9-year-old should receive IG
E. only the 10-month-old should receive IG

Correct Answer: D
The best recommendation for the 3 unvaccinated children in the vignette, exposed to a household contact with hepatitis A, is immune globulin for the healthy 10-month-old and 9-year-old children with severe Crohn disease on immunosuppressive therapy. The 2-year-old with asthma is not immunocompromised and should receive HAV vaccine.

Hepatitis A virus (HAV) is an RNA virus that is spread through contaminated food and water, and causes an acute hepatitis. It occurs worldwide, especially in lower socioeconomic global areas. Hepatitis A virus hepatitis is usually self-limited and rarely leads to fulminant hepatic failure, except in those with underlying liver disease. Seventy percent of children younger than 6 years of age with HAV infection are asymptomatic, while the majority of older children and adults with HAV infection have jaundice and hepatomegaly that can last for several weeks, HAV is one of the most common preventable infections contracted by travelers. Humans are the only known reservoir. HAV infections in the US have decreased by 95% since HAV vaccine became available in 1995.

Individuals with recent HAV exposure who have not been vaccinated for hepatitis A previously require postexposure prophylaxis as soon as possible because it can be easily spread through the fecal-oral route. For healthy persons aged 12 months to 40 years, single-antigen hepatitis A vaccine is preferred to IG for postexposure prophylaxis because the vaccine has the advantage of long-term protection, widespread availability, and ease of administration, and is as efficacious as IG. Immune globulin should be used for children younger than 12 months of age, immunocompromised individuals, patients with chronic liver disease, and those allergic to the vaccine or a vaccine component. Immune globulin, and perhaps the hepatitis A vaccine, are not indicated if exposure occurred more than 2 weeks prior because no information exists regarding their efficacy if administered more than 2 weeks after exposure.

For these 3 children, the 10-month-old infant should receive IG. The 2-year-old with asthma is not immunocompromised and should receive HAV vaccine. The 9-year-old would normally receive HAV vaccine as well, but is on the immunosuppressive drug azathioprine and on steroids, and should receive IG instead.

PREP Pearls

- For healthy persons aged 12 months to 40 years, single-antigen hepatitis A vaccine is preferred to immune globulin (IG) for post exposure prophylaxis because the vaccine has the advantage of long-term protection, widespread availability, and ease of administration, and is as efficacious as IG.
- Immune globulin should be used for children younger than 12 months of age, immunocompromised individuals, patients with chronic liver disease, and those allergic to the vaccine or a vaccine component. Immune globulin is not indicated for unvaccinated persons with recent hepatitis A virus (HAV) exposure if exposure occurred more than 2 weeks prior.
- Seventy percent of children younger than 6 years of age with HAV infection are asymptomatic.

ABP Content Specifications(s)

- Initiate appropriate post-exposure prophylaxis for hepatitis A virus infection

Suggested Readings

- Advisory Committee on Immunization Practices (ACIP), US Centers for Disease Control and Prevention (CDC). Update: prevention of hepatitis A after exposure to hepatitis A virus and in international travelers-updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 2007;56(41):1080-1084. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5641a3.htm.
- American Academy of Pediatrics. Hepatitis A. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:391-399.

Question 168

A previously healthy 10-year-old boy is brought to the emergency department (ED) for evaluation. He has had diarrhea for 5 days and bloody diarrhea for the past 2 days. The boy has become increasingly listless over the past several hours and his parents are very concerned. His temperature is 38.4°C, heart rate is 120 beats/min, respiratory rate is 28 breaths /min, and blood pressure is 90/50 mm Hg. He has normal growth parameters. Physical examination reveals an ill-appearing child with marked pallor and periorbital edema. A peripheral intravenous catheter is placed and a blood sample is sent to the laboratory for evaluation, which is shown:

Laboratory Test	**Patient Result**
Sodium	139 mEq/L (139 mmol/L)
Potassium	7.7 mEq/L (7.7 mmol/L)
Chloride	105 mEq/L (105 mmol/L)
Bicarbonate	13 mEq/L (13 mmol/L)
Blood urea nitrogen	83 mg/dL (29.6 mmol/L)
Creatinine	6.4 mg/dL (566 μmol/L)
Glucose	98 mg/dL (5.4 mmol/L)
Calcium	8.6 mg/dL (2.15 mmol/L)
Phosphorus	9.0 mg/dL (2.91 mmol/L)

You discuss the treatment of this boy with the ED resident. She asks whether any of the therapies available for the management of hyperkalemia share a similar mechanism of action.

Of the following, the MOST accurate response to the resident's question is

A. β-adrenergic agonists and calcium gluconate

B. β-adrenergic agonists and diuretics

C. calcium gluconate and dialysis

D. calcium gluconate and sodium bicarbonate

E. cation exchange resins and dialysis

Correct Answer: E

Diuretics, cation exchange resins, and hemodialysis promote excretion of potassium from the body, thereby sharing a similar mechanism of action for the treatment of hyperkalemia. A serum potassium concentration higher than the upper limit of normal (usually ranges from 5.0-5.5 mEq/L [5.0-5.5 mmol/L]) is characterized as hyperkalemia. Serum potassium concentrations higher than 7.0 mEq/L (7.0 mmol/L) are considered severe hyperkalemia and require urgent treatment.

Pseudohyperkalemia, or falsely-elevated serum potassium, is the most frequent cause of elevated potassium concentrations in the pediatric setting. This occurs because of red blood cell hemolysis associated with difficult blood draws. Clinical symptoms of hyperkalemia, such as muscle weakness or paralysis, are not seen until serum potassium concentrations are higher than 8.0 to 8.5 mEq/L (8.0-8.5 mmol/L). Therefore, in patients in whom hyperkalemia is associated with acute renal failure (elevated serum creatinine), true hyperkalemia is assumed and clinical management implemented urgently in view of the potential for life-threatening complications. In such cases, management includes serial electrocardiograms (EKGs), stabilization of the cardiac membrane, and decreasing the serum potassium concentration. Tall, peaked T waves are the earliest EKG abnormality seen, when serum potassium concentrations range from 5.5 to 6.5 mEq/L (5.5-6.5 mmol/L). As the serum potassium concentration rises, cardiac conduction is further impaired. Widening of QRS complexes and an increased PR interval are observed when serum potassium concentrations are between 6.5 and 7.5 mEq/L (6.5-7.5 mmol/L). Higher potassium concentrations are associated with broad and low amplitude P waves, a prolonged QT interval, and ST segment changes (elevation or depression). At serum potassium concentrations higher than 8 mEq/L (8 mmol/L), gradually widening QRS complexes progress to a sine wave configuration and P waves disappear. These patients are at high risk for ventricular fibrillation or asystole.

Given the inconsistent and limited benefit of agents that move potassium from the extracellular to the intracellular compartment, therapies aimed at removing potassium from the body should be started in a timely manner, depending on the severity of hyperkalemia and EKG changes. Diuretics (loop and thiazide) increase urinary potassium excretion and are most effective in lowering serum potassium concentrations in patients with normal or mild-to-moderate deterioration of renal function. Loop diuretics (furosemide 1 mg/kg; maximum dose 40 mg in patients with normal renal function) are preferred in the management of acute hyperkalemia. Higher doses (2-5 mg/kg per dose; up to 80 mg) can be given in patients with severe renal failure. Cation exchange resins (sodium polystyrene sulfonate) bind potassium and release a similar amount of sodium as the counter-ion. Sodium polystyrene sulfonate (1 g/kg) will exchange 1 mEq of potassium for each gram of resin, and can be repeated every 4 to 6 hours (maximum dose 30 g). The resin is dissolved in water and given enterally or as a retention enema. The onset of exchange is approximately 1 to 2 hours after administration and the potassium bound to the resin is excreted in the feces. Cation exchange resins should be avoided in neonates and children with underlying bowel disease. Dialysis (hemodialysis or peritoneal dialysis) removes potassium from the serum and is indicated if medical management fails to lower serum potassium, especially in patients with acute renal failure.

In addition to decreasing the serum potassium concentration, management of hyperkalemia is aimed at preventing life-threatening arrhythmias. Hyperkalemia leads to depolarization of the cardiac membrane. Intravenous (IV) calcium stabilizes the cardiac membrane by decreasing membrane excitability, thereby reducing the risk of cardiac conduction abnormalities and arrhythmias. Intravenous calcium gluconate (10%) is indicated for patients with severe hyperkalemia (>7.0 mEq/L), widening of the QRS complex or absent P waves, or arrhythmias assumed to be secondary to hyperkalemia. Intravenous calcium gluconate (0.5–1.0 mL/kg; elemental calcium 5 mg/kg) has a rapid onset of action. Cardiac stabilization effect with calcium gluconate administration is short lived and may need to be repeated. Calcium gluconate is not indicated in patients with hyperkalemia and isolated T wave changes alone.

As mentioned previously, the benefit of agents that move potassium from the extracellular to the intracellular compartment, such as the insulin-glucose IV infusion, inhaled b-adrenergic agonists, or sodium bicarbonate infusion, is inconsistent and limited. Insulin administration enhances the activity of the sodium potassium adenosine trisphosphatase pump in skeletal muscles. Since insulin infusion will lead to hypoglycemia, a simultaneous dextrose infusion must be started. Regular insulin (0.1 U/kg IV per hour along with D25 at 2 mL/kg per hour) as a continuous infusion, with frequent serum glucose monitoring.

Inhaled b-adrenergic agonists (eg, albuterol) lower potassium by 1 mEq/L (1 mmol/L). In adult studies, the effective dose of inhaled b-adrenergic agonists required for lowering potassium is nearly 4 times higher than the dose typically used for bronchodilation (a dose associated with an increased risk for tachycardia and arrhythmias). A study in neonates (weighing < 2,000 g) demonstrated that albuterol inhalation (0.4 mg) effectively lowered serum potassium compared with the control group receiving normal saline. b-adrenergic agonists may be started at doses used for managing bronchospasm, and increased in patients with persistent hyperkalemia (if needed) under close EKG monitoring. b-adrenergic agonists should be avoided in children known to be at risk for arrhythmias. Alkalosis induced with IV sodium bicarbonate (1-2 mEq/kg over 5-10 minutes) may be used to treat hypokalemia, even in the absence of acidosis. Since neither b-adrenergic agonists nor sodium bicarbonate have a predictable effect in lowering potassium, it should be used as an adjuvant; neither should be used as a single agent for treating urgent and severe hyperkalemia. Calcium gluconate and sodium bicarbonate are not compatible for simultaneous infusion, and if both are used, the IV lines need to be flushed between each administration.

Clinical management of hyperkalemia should include simultaneous identification of the underlying etiology and its correction. Special consideration should be given to correction of hypovolemia, discontinuation of medications associated with hyperkalemia (spironolactone, amiloride, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers), discontinuation of parenteral fluids containing potassium, and hormonal therapy in patients with adrenal insufficiency.

PREP Pearls

- Diuretics, cation exchange resins, and dialysis remove excess potassium from the body.
- Patients with hyperkalemia develop serial electrocardiogram changes with increasing hyperkalemia.
- Intravenous calcium gluconate (10%) is indicated for patients with severe hyperkalemia (> 7.0 mEq/L), widening of the QRS complex or absent P waves, and arrhythmias assumed to be secondary to hyperkalemia.
- Inhaled β-adrenergic agonists, insulin-glucose infusion, and sodium bicarbonate move serum potassium from the extracellular to the intracellular compartment.

ABP Content Specifications(s)

- Recognize the clinical and laboratory features associated with hyperkalemia, and manage appropriately, including during an emergency situation

Suggested Readings

- Mahajan PV. Fluids and electrolytes in clinical practice. In: Kleigman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:471-480.
- Selewski DT, Symons JM. Acute kidney injury. *Pediatr Rev.* 2014;35(1):30-41. doi: http://dx.doi.org/10.1542/pir.35-1-30.
- Weisberg LS. Management of severe hyperkalemia. *Crit Care Med.* 2008;36(12):3246-3251. doi: http://dx.doi.org/10.1097/CCM.0b013e31818f222b.

Question 169

You are evaluating a 1-week-old neonate who has developed a rash on the arms and legs. She was the product of an uncomplicated pregnancy, labor, and delivery. She has been well since birth, gaining weight normally. Her temperature is 37°C and other vital signs are normal. The physical examination is normal except for the vesicles and papules in a linear arrangement on the neonate's legs and arms (Item Q169A , Item Q169B).

Item Q169A: Papules and vesicles on the leg as described for the infant in the vignette. Courtesy of D Krowchuk

Item Q169B: Papules (some crusted) on the arm as described for the infant in the vignette. Courtesy of D Krowchuk

Of the following, the MOST likely diagnosis is

A. herpes simplex virus infection
B. herpes zoster
C. incontinentia pigmenti
D. Staphylococcus aureus infection
E. varicella

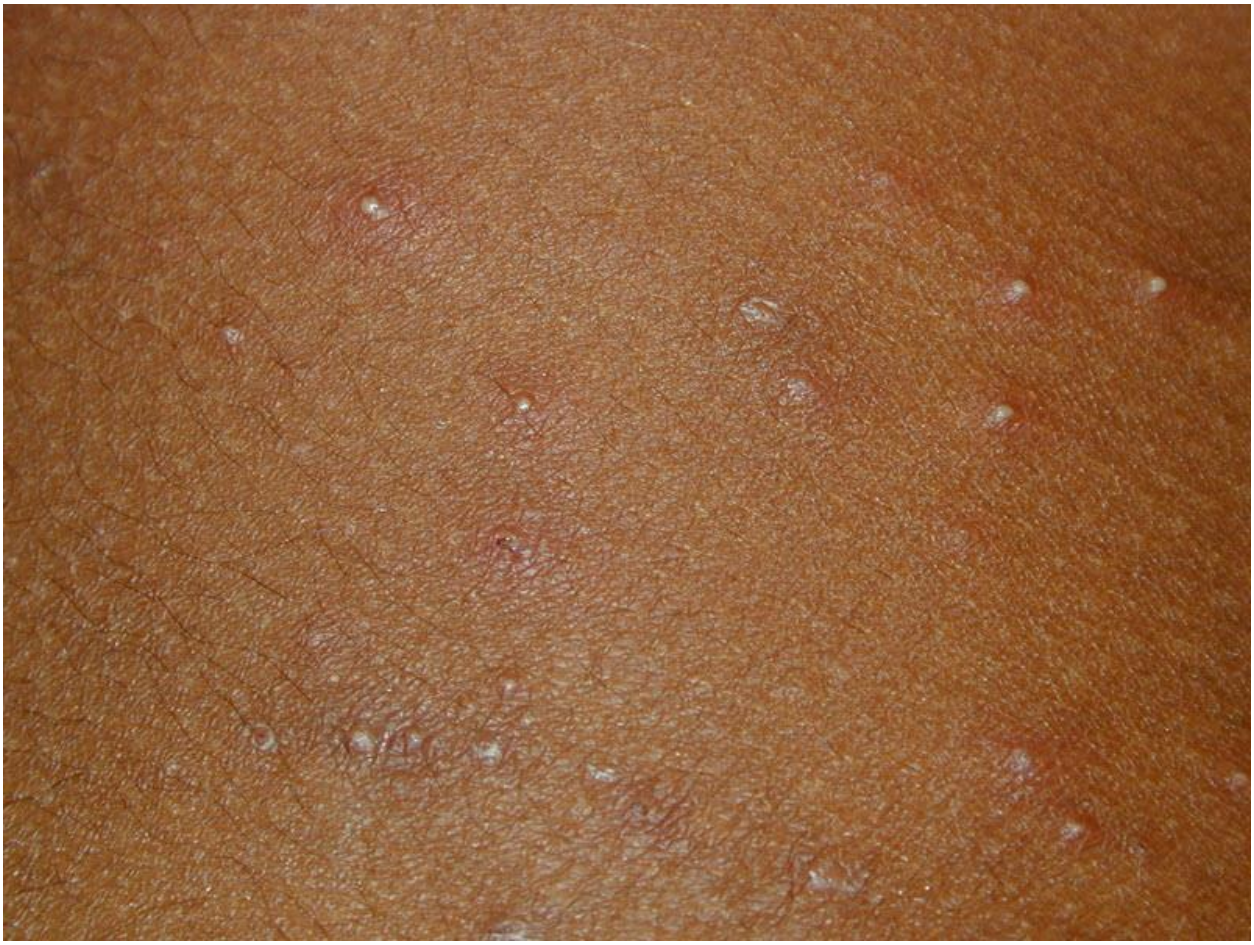
Correct Answer: C

The neonate in the vignette has a rash composed of vesicles and papules in a linear arrangement on the extremities. These findings are most consistent with a diagnosis of incontinentia pigmenti, an X-linked disorder that affects the skin, teeth, eyes, and central nervous system. The presence of vesicles at birth or in the first weeks of life should raise concern for possible herpes simplex virus (HSV) infection. However, HSV lesions are typically clustered vesicles on an erythematous base (Item C169A) and are not in a linear distribution. Herpes zoster has rarely been reported in neonates. As in cutaneous HSV infection, zoster lesions are grouped vesicles on an erythematous base; however, the groups are arranged along a dermatome (Item C169B). The classic lesion of varicella is a solitary vesicle on an erythematous base (a dew drop on a rose petal) (Item C169C). Folliculitis caused by *Staphylococcus aureus* produces pustules with surrounding erythema; a linear arrangement of lesions is not present (Item C169D).

Item C169A: Herpes simplex virus lesions. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012

Item C169B: Herpes zoster: clustered vesicles on an erythematous base in a dermatomal distribution. Courtesy of D Krowchuk

Item C169C: Varicella: Solitary vesicles on erythematous bases are present. However, other lesion stages are also present (ie, erythematous macules and papules) in varying stages of development. Courtesy of D Krowchuk



Item C169D: Folliculitis is characterized by pustules with surrounding erythema. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012

Incontinentia pigmenti (IP) is the result of mutations in the *IKBKG* (formerly *NEMO*) gene. In about 65% of cases, IP is the result of a de novo mutation. Incontinentia pigmenti is inherited in an X-linked manner; the majority of cases occur in girls, suggesting that it is a lethal mutation in most boys. Characteristic findings involve the skin, nails, and teeth. Skin lesions evolve through 4 stages, each of which serves a major diagnostic criterion (the presence of one or more major criteria is sufficient for diagnosis). The stages may overlap and not all of those affected exhibit all stages. Lesions follow the lines of Blaschko (the paths of embryonic cell migration), explaining the linear arrangement of lesions on the extremities and the swirled pattern on the trunk. The criteria for the 4 stages include:

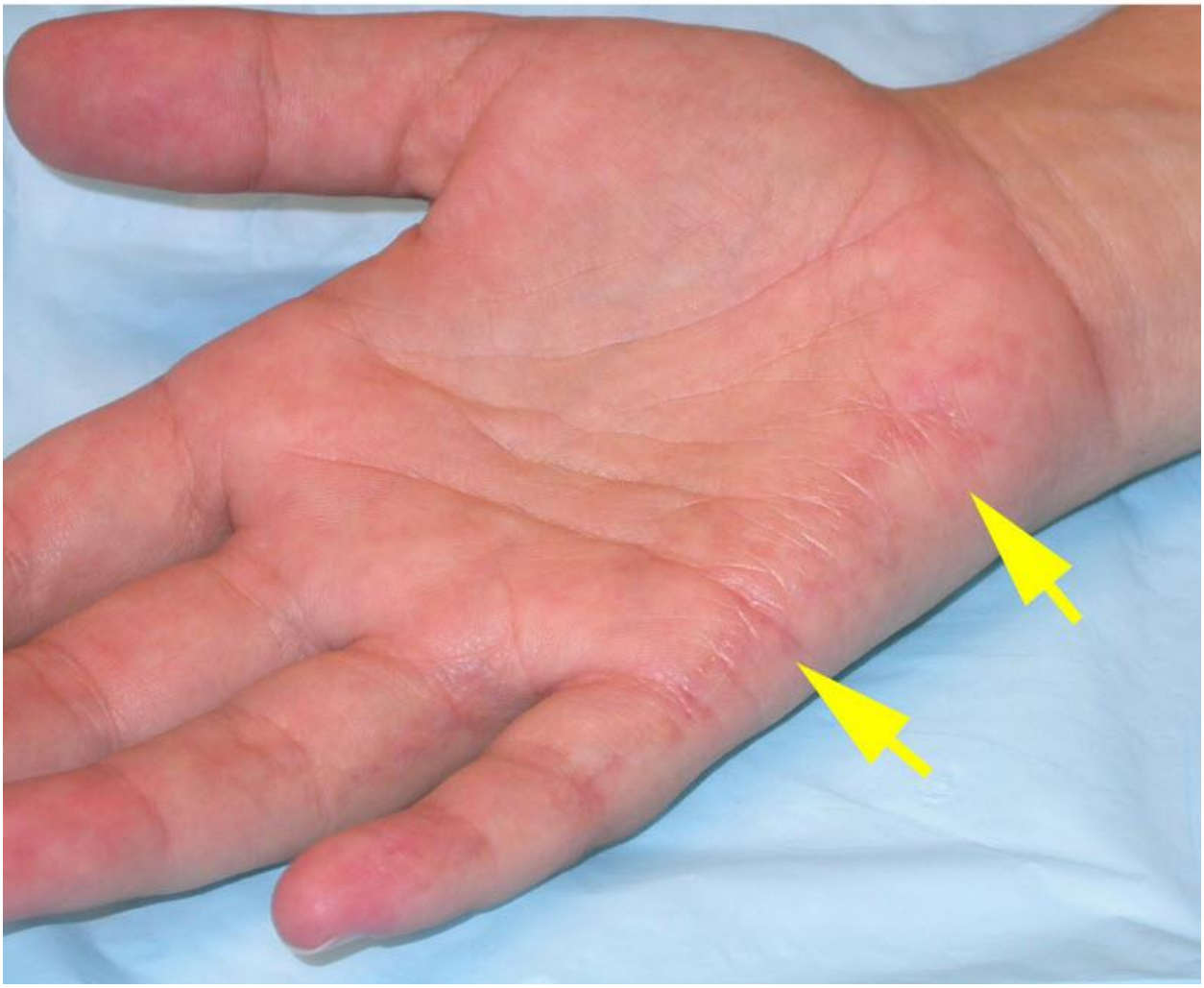
- Stage I: Vesicles are present at birth or within the first 6 to 8 weeks. Crops of vesicles come and go; this stage resolves by 18 months of age.
- Stage II: In approximately 70% of patients, as the vesicular phase is waning, wart-like papules appear (Item C169E). Typically, this stage lasts several months. This is also the

stage when dystrophic nails and abnormal dentition (absent, small, or conical) may be observed.

- Stage III: Hyperpigmentation (brown or slate gray) occurs in 80% of patients with IP; it is the most characteristic cutaneous finding (Item C169F). This stage begins at about 6 months of age and begins to fade during adolescence or early adulthood.
- Stage IV: Characterized by hypopigmented atrophic streaks (Item C169G) and alopecia.

Item C169E: Warty papules and vesicles are observed in this patient who has overlapping features of the first and second stages of incontinentia pigmenti Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012

Item C169F: Swirled hyperpigmentation on the trunk observed in Stage III incontinentia pigmenti. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012



Item C169G: Stage IV I with linear, atrophic, hypopigmented streaks (arrows). Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012

Incontinentia pigmenti may also involve the central nervous system (seizures or developmental delay) and eyes (neovascularization, cataracts, strabismus). As many as 65% of patients have leukocytosis with eosinophilia, particularly during stages I and II.
There is no treatment for IP. Genetic consultation is essential. Parents may have clinical evidence of IP (at times quite subtle) or appear normal but have germline mosaicism. If the mother is affected, there is a 50% chance of having another affected daughter and a 50% chance of losing a male embryo. Preimplantation genetic diagnosis may be an option for families in which the *IKBKG* variant has been identified. Since neovascularization can lead to retinal detachment, early ophthalmologic evaluation is indicated. Neurologic and dental consultations may be needed. The Incontinentia Pigmenti International Foundation provides information and support for families (http://www.ipif.org/).

PREP Pearls

- Incontinentia pigmenti (IP) presents with vesicles in a linear arrangement at birth or within the first weeks of life.
- In older children, linear and swirled hyperpigmentation, not present at birth, is characteristic of IP.
- Incontinentia pigmenti is the result of mutations in the IKBKG (formerly NEMO) gene. In about 65% of cases, IP is the result of a de novo mutation. Incontinentia pigmenti is inherited in an X-linked manner; the majority of cases occur in girls, suggesting that it is a lethal mutation in most boys.

ABP Content Specifications(s)

- Recognize the clinical findings associated with incontinentia pigmenti

Suggested Readings

- Krowchuk DP, Mancini AJ. Incontinentia pigmenti. *Pediatric Dermatology: A Quick Reference Guide.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012:449-454.
- Scheuerle AE, Ursini MV. Incontinentia pigmenti. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1472/.

Question 170

The mother of a 10-year-old boy calls your office for advice. The family is on vacation and she has just found a tick attached to her son's thigh. She asks you how she should remove the tick.

Of the following, the BEST method of removal is to

A. burn it with a match

B. cover it with nail polish

C. cover it with petroleum jelly

D. crush it with tweezers

E. use tweezers to pull it from the skin

Correct Answer: E

Ticks should be removed by using forceps or tweezers to pull steadily upwards from their point of attachment (Item C170). Care must be taken to avoid twisting or crushing the tick, because this may break the tick, leaving the head embedded in the skin. If this occurs, the head will be spontaneously expelled over time (as with any foreign body). Several methods of tick removal have been shown to be ineffective. Petroleum jelly, nail polish, and other occlusive substances have been proposed to induce detachment by suffocating the tick. These methods are not successful because ticks have a very low respiratory rate and it is difficult to create a completely occlusive barrier. Ticks should not be burnt with a match. This method of tick removal carries a high risk of injury, especially in uncooperative children, and has not been shown to induce detachment. The risk of contracting Lyme disease is low if a tick is attached for less than 24 to 36 hours; ticks should therefore be removed promptly.

PREP Pearls

- When removing a tick, grasp the tick close to the skin with forceps or tweezers and pull upwards with steady pressure.
- Ticks attached for less than 24 to 36 hours are unlikely to transmit Lyme disease.

ABP Content Specifications(s)

- Advise parents regarding the appropriate method to remove an attached tick

Suggested Readings

- Due C, Fox W, Medlock JM, Pietzsch M, Logan JG. Tick bite prevention and tick removal. *BMJ*. 2013;347:f7123. doi: http://dx.doi.org/10.1136/bmj.f7123.
- Needham GR. Evaluation of five popular methods for tick removal. *Pediatrics*. 1985;75(6):997-1002. http://pediatrics.aappublications.org/content/75/6/997.
- US Centers for Disease Control and Prevention. Tick removal and testing. US Centers for Disease Control and Prevention website. http://www.cdc.gov/lyme/removal/index.html. 2015.

Question 171

You are seeing a 10-month-old infant for follow-up after treatment for pneumonia. She has had 4 documented episodes of pneumonia, all confirmed with chest radiography. Involved lung segments have included the right middle lobe, right upper lobe, and left lower lobe. Six weeks after resolution of the third episode, a chest radiograph was obtained and read as normal. A recent computed tomography of the chest revealed bronchial wall thickening without bronchiectasis in the right upper and middle lobes. The infant was born at full term after an uncomplicated pregnancy. Her 2 older siblings are healthy. She is developing and growing normally. Her parents report that the infant has a chronic dry cough. There is no history of wheezing or respiratory failure. She does not exhibit symptoms of dysphagia; there is no cough or choking with oral intake. There are no identifiable symptoms of gastroesophageal reflux. There is no history of chronic rhinitis, recurrent otitis, sinusitis, abscess formation, or sepsis. A videofluoroscopic swallow study, sweat test, neutrophil oxidative burst testing, quantitative immunoglobulins, and B- and T-cell flow cytometry are all normal.

Of the following, the MOST likely cause of this infant's recurrent pneumonia is

A. chronic granulomatous disease

B. congenital pulmonary airway malformation (CPAM)

C. cystic fibrosis

D. primary ciliary dyskinesia

E. tracheoesophageal fistula

Correct Answer: E
The girl in this vignette has a history that is suggestive of an H-type tracheoesophageal fistula (TEF).

Recurrent pneumonia is defined as 2 or more episodes in a year or 3 or more lifetime episodes with radiographic clearance of densities in between occurrences. In a child with recurrent pneumonia, the differential diagnosis is broad but may be organized to allow an efficient clinical approach. The evaluation of recurrent pneumonia can be divided into subsets of persistent versus recurrent disease. Further clarity may be gained by determining whether the same or different lung segments are involved.

In this 10-month-old girl who is neurologically intact, without overt symptoms or radiographic evidence of direct aspiration or pathologic gastroesophageal reflux (GER), direct and retrograde aspiration is less likely. However, an H-type TEF may escape detection for prolonged periods because it is the only type of TEF that is unassociated with esophageal atresia.
A TEF allows gastric reflux secretions to enter the lung, causing chronic respiratory symptoms that may include wheezing, chronic cough, and recurrent pneumonia. In the setting of TEF, air enters from the trachea into gastrointestinal tract, contributing to abdominal distention and exacerbating GER and aspiration-related disease. An H-type TEF is diagnosed using bronchoscopy. Without pressurized contrast material directed at the area of the fistulous tract, a barium esophagram may fail to demonstrate small connections; radiologists should be informed of clinical suspicions accordingly.

A patient with radiographic and clinical pneumonia who fails to clinically improve with appropriate antibiotic therapy may require bronchoscopic evaluation for resistant organisms, atypical organisms (tuberculosis, fungal pathogens), or abscess formation.
Structural airway anomalies such as tracheomalacia, bronchomalacia, bronchiectasis, or stenosis may result in ineffective clearance and stasis of secretions, and contribute to recurrent or persistent infection. Both malacia and stenosis can be visualized using a bronchoscopic approach. Plain chest radiography is poorly sensitive for mild degrees of bronchiectasis, and further imaging with computed tomography may be required. Similar adverse effects on airway clearance may be seen when an airway is externally compressed; compression may be exerted through neoplasia (cystic lesions, lymphadenopathy, or malignancy) or from vascular malformations (vascular ring or sling). Intraluminal airway obstruction may be encountered with tumors (eg, carcinoid) or with a chronically retained foreign body. Finally, lobar atelectasis may be encountered in the setting of asthma and is frequently mistaken for recurrent pneumonia.
When the same lung segment is repeatedly affected, a radiograph is recommended 4 to 8 weeks after clinical recovery from pneumonia, when the child is asymptomatic, to allow for the lag seen between radiographic and clinical resolution. If the abnormality persists, the child must be further evaluated for the presence of a congenital lung lesion.

When a child presents with pneumonia affecting multiple or variable pulmonic lobes, an evaluation for suppurative lung disease (eg, cystic fibrosis), ineffective mucociliary clearance (eg, primary ciliary dyskinesia), immune dysfunction, and/or chronic aspiration is recommended.

Chronic granulomatous disease of childhood can present with recurrent infections and pneumonia but is X–linked in most cases, and therefore is more common in boys. It is associated with an abnormal neutrophil oxidative burst testing, which was normal in this patient.
In this infant with a normal interval chest radiograph and nonfocal findings consistent with chronic inflammation on computed tomography, a congenital lung lesion is unlikely. Cystic fibrosis (CF) should be considered in any child with chronic cough, even in the setting of a normal newborn screen. Although somewhat reassuring, symptoms of malabsorption may be absent in a subset of patients with CF who have pancreatic sufficiency. However, the classic pulmonary infection in patients with CF is endobronchial and lobar pneumonia is relatively uncommon. Bronchiectasis is the pathognomonic lung lesion of CF, and is related to chronic infection and inflammation. In this patient, the gold standard test for CF, a sweat test by pilocarpine iontophoresis, has been performed appropriately and reported as normal.
Patients with primary ciliary dyskinesia typically demonstrate a daily mucousy cough and chronic purulent rhinitis with recurrent middle ear and sinopulmonary infections. Although immunodeficiency should be considered in any child with a history of recurrent infection, infections of nonpulmonary sites (ears, skin, sinus) would also be expected.

PREP Pearls

- A high index of suspicion is required to make the diagnosis of an H-type tracheoesophageal fistula.
- In children with recurrent pneumonia of the same lung segment, radiography is recommended 4 to 8 weeks after clinical recovery, to ensure radiographic resolution.

ABP Content Specifications(s)

- Formulate a differential diagnosis of recurrent pneumonia

Suggested Readings

- Brand PL, Hoving MF, deGroot EP. Evaluating the child with recurrent lower respiratory tract infections. *Paediatr Respir Rev.* 2012;13(3):135-138. doi: http://dx.doi.org/10.1016/j.prrv.2011.02.005.
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- Panitch HB. Evaluation of recurrent pneumonia. *Pediatr Infect Dis J*. 2005;24(3):265-266.
- Patria MF, Esposito S. Recurrent lower respiratory tract infections in children: a practical approach to diagnosis. *Paediatr Respir Rev*. 2013;14(1):53-60. doi: http://dx.doi.org/10.1016/j.prrv.2011.11.001.

Question 172

A 4-year-old boy is brought to your clinic for follow-up after a recent hospitalization 1 week ago. Discharge summary shows that he presented with cough and tachypnea and a temperature of 35.8°C. His chest radiograph showed a lobar pneumonia. He received intravenous antibiotics and required oxygen in the hospital for 2 days, but he never had fever. In clinic, his mother says he is improved. On physical examination, his temperature is 35°C, heart rate is 98 beats/min, respiratory rate is 20 breaths/min, and body mass index is 18 kg/m^2 (93rd percentile). He is well-appearing and has no respiratory distress.

Of the following, the test MOST likely to reveal the cause of the hypothermia is

A. blood pressure
B. magnetic resonance imaging of the head
C. repeat chest radiograph
D. serum glucose
E. serum immunoglobulins

Correct Answer: B
The boy in the vignette has persistently low temperature, even during a lobar pneumonia. This implies a disorder of the thermoregulatory system, which is controlled in the hypothalamus. The hypothalamus interacts closely with the endocrine system and the autonomic nervous system to maintain thermostasis. Of the answers, the best test to diagnose a disorder of the thermoregulatory system is magnetic resonance imaging of the head. Lesions of the hypothalamus can include tumors such as gliomas or craniopharyngiomas, cysts, and granulomas as in Langerhans cell histiocytosis. Other symptoms of hypothalamic dysfunction include polyphagia and obesity (as seen in the boy in the vignette), hypersomnolence, precocious puberty, short stature, polydipsia, polyuria, and symptoms of adrenal insufficiency. Hypothalamic dysfunction is increasingly recognized in children, for example, as **R**apid-Onset **O**besity With **H**ypothalamic Dysfunction, **H**ypoventilation, and **A**utonomic **D**ysregulation (ROHHAD syndrome).

Hypothermia can have many causes. Imbalance between the ability to produce heat and the ability to prevent heat loss is more common than an abnormal thermoregulatory control system (due to a hypothalamic tumor or injury, for instance). In neonates, the inability to prevent heat loss contributes more to hypothermia than an immature thermoregulatory control system. Inability to produce heat, as in severe malnutrition, can contribute to the development of hypothermia. Other causes of hypothermia include sepsis, hypothyroidism, and hypoglycemia. Although no blood pressure is reported, hypertension or hypotension are unlikely to cause persistent hypothermia in this child. Chest radiograph is not indicated because the boy's respiratory symptoms have improved. Serum glucose and serum immunoglobulins are not indicated for this boy's current clinical presentation and would not be helpful in finding a cause of his hypothermia.

PREP Pearls
- Persistent hypothermia can be a sign of hypothalamic dysfunction.
- Hypothalamic tumors can impair temperature regulation.

ABP Content Specifications(s)
- Understand the effects of the immature/abnormal hypothalamic thermoregulatory system on the development of fever in infants and children who have diseases of the central nervous system

Suggested Readings

- Farooq O, Memon Z, Saikali N, Langan TJ. A 4-year-old male who has a persistent, severe headache. *Pediatr Rev*. 2012;33(4):175-177. doi: http://dx.doi.org/10.1542/pir.33-4-175.
- Ize-Ludlow D, Gray JA, Sperling MA, et al. Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation presenting in childhood. *Pediatrics*. 2007;120(1):e179-e188. doi: http://dx.doi.org/10.1542/peds.2006-3324.
- Ringer SA. Core concepts: thermoregulation in the newborn part i: basic mechanisms. *NeoReviews*. 2013;14(4):e161-e167. . doi: http://dx.doi.org/10.1542/neo.14-4-3161.

Question 173

A 2-year-old girl suffered partial and full-thickness burns 7 days ago that involved approximately 50% of her total body surface area. She is currently in the intensive care unit, intubated on mechanical ventilation, and sedated. Enteral feeding with a standard pediatric formula was initiated at day 2 following her injury to provide full calories based on estimated resting energy expenditure. She has not had fevers and blood cultures have been negative. No changes have been made to her sedatives. Over the past 24 hours, her hemodynamic status has worsened. Vital signs show a temperature of 37°C, heart rate of 150 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 70/50 mm Hg. Central venous pressure has increased from 10 to 15 cm H_2O. Physical examination reveals an intubated and sedated child. Burn dressings cover large areas of her trunk and extremities. Lungs are clear and equal bilaterally. Heart is regular, with no rubs, murmurs, or gallops. Abdomen is soft, nontender, and non-distended, with liver margin 3 cm below the right costal margin. Extremities are cool with capillary refill time of 4 seconds.

Of the following, the MOST likely cause of the child's hemodynamic worsening is

A. hyperkalemia

B. hyperlipidemia

C. hypermagnesemia

D. hypocalcemia

E. hypophosphatemia

Correct Answer: D
The child in this vignette has suffered an extensive burn injury and now has shock and heart failure. Of the choices, the nutritional deficiency most likely to cause heart failure is hypocalcemia.

Burn injuries cause a hypermetabolic state that can last up to 12 months after injury due to chronic inflammation, stress hormones, and elevated circulating catecholamines. As a result, children who suffer burns involving high percentage of total body surface area (%TBSA) have an increased energy expenditure and protein catabolism that can be up to 2 times normal. Aggressive nutritional support is important to optimize wound healing, to prevent a negative caloric and nitrogen balance, and to mitigate the pro-inflammatory response caused by a hypermetabolic state. The gold standard to estimate resting energy expenditure (REE) and caloric requirement is indirect calorimetry. Since indirect calorimetry requires a metabolic cart and specialized equipment and software, it is not always readily available. Caloric requirement can also be estimated by the Mayes equation, which takes into account weight and %TBSA:

Daily caloric requirement = 818 + 37.4*(weight in kg) + 9.3*%TBSA

Carbohydrates should account for 60% of energy requirement, 20% should be from fats, and 2.5 to 4 g/kg per day of protein should provide the remaining 20%. Overfeeding and excessive carbohydrate administration can also be harmful, leading to hyperglycemia, impaired wound healing, increased fat stores, and increased CO_2 production leading to delayed ventilator weaning. The preferred route of nutritional support is enteral because of its role in maintaining intestinal integrity. If enteral feeds are not tolerated, parenteral nutrition can be provided.

Severe burn injury can lead to additional requirements of vitamins, minerals, and trace elements. Hypocalcemia and hypomagnesemia can occur even when calcium and magnesium supplementation is administered, possibly from an upregulation of the parathyroid gland calcium-sensing receptor. Calcium released from the myocardial sarcoplasmic reticulum binds to troponin C, which leads to a series of conformational changes, resulting in interactions between actin and myosin and eventual sarcomere contraction. Calcium can thus be referred to as "nature's inotrope." Since myocardial contraction requires both calcium release from the sarcoplasmic reticulum as well as availability from the serum, hypocalcemia can cause congestive heart failure. It can be reversed by intravenous or enteral administration of calcium.

Hyperkalemia can occur in burn injury from cell lysis and can cause arrhythmia, but cannot cause congestive heart failure. Hypermagnesemia generally does not occur in burn injury. Hyperlipidemia can occur because of lipolysis in a catabolic state, but does not cause acute heart failure. Hypophosphatemia can be seen as a nutritional deficiency in burn injury, but does not usually cause heart failure.

PREP Pearls

- Burn injuries cause a hypermetabolic state that can last up to 12 months after injury due to chronic inflammation, stress hormones, and elevated circulating catecholamines.
- Caloric requirements in burn patients can be estimated by measuring resting energy expenditure or using equations taking into account total body surface area affected and weight.

ABP Content Specifications(s)

- Recognize the specific nutritional problems in children with burns

Suggested Readings

- Klein GL, Herndon DN. Burns. *Pediatr Rev.* 2004;25(12):411-417. doi: http://dx.doi.org/10.1542/pir.25-12-411.
- Yilmaz O, Kilic O, Ciftel M, Hakan N. Rapid response to treatment of heart failure resulting from hypocalcemic cardiomyopathy. *Pediatr Emerg Care*. 2014;30(11):822-823. doi: http://dx.doi.org/10.1097/PEC.0000000000000269.

Question 174

A 2-month-old female infant who is undergoing evaluation for prolonged jaundice is seen in your office for a health supervision visit. She was born at 41 weeks of gestation by cesarean delivery due to breech presentation with a birth weight of 3,500 g. The pregnancy was otherwise uncomplicated. Her neonatal course was significant for several episodes of hypoglycemia that resolved with feeding. She is currently bottle feeding with standard infant formula and will only feed for 5 minutes before falling asleep. She has 1 soft, yellow stool and 4 wet diapers daily. Vital signs today show a temperature of 36°C, heart rate of 132 beats/min, weight of 4 kg (third percentile), and length of 55 cm (25th percentile). Physical examination is significant for jaundice, scleral icterus, mild generalized hypotonia, and hepatomegaly with the liver edge palpable 2 cm below the right costal margin. Laboratory results are shown:

Laboratory test	Result
Total bilirubin	11.5 mg/dL (196.7 μmol/L)
Direct bilirubin	6.9 mg/dL (118.2 μmol/L)
Alanine aminotransferase	148 U/L
Aspartate aminotransferase	181 U/L
Alkaline phosphatase	721 U/L
Glucose	36 mg/dL (2.0 mmol/L)
Thyroid-stimulating hormone	2.5 mIU/L (reference range 0.4-4.2 mIU/L)
Free thyroxine	0.6 ng/dL (8 pmol/L) (reference range 1-1.9 ng/dL)

Of the following, the MOST likely diagnosis is

A. biliary atresia

B. cystic fibrosis

C. galactosemia

D. hypopituitarism

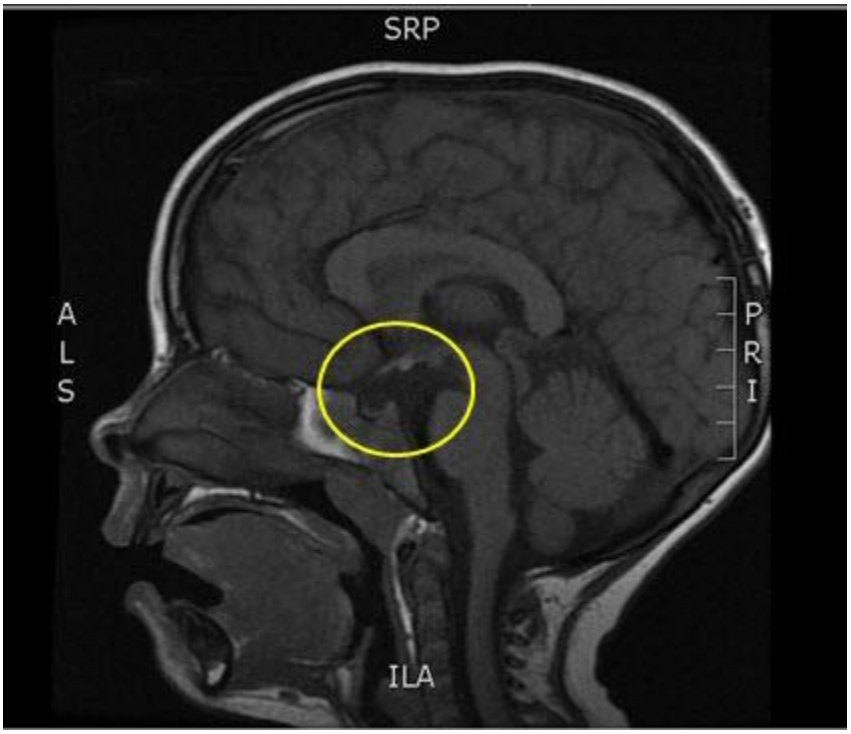
E. idiopathic neonatal hepatitis

Correct Answer: D
The infant described in the vignette has hypopituitarism with cholestatic jaundice and prolonged direct hyperbilirubinemia as the major presenting features. Although the differential diagnosis of direct hyperbilirubinemia is broad, evidence of hypopituitarism includes the history of hypoglycemia and the low free thyroxine with inappropriately normal thyroid-stimulating hormone (TSH) level. The post-date gestation, breech presentation, poor feeding, low weight percentile, and hypotonia are also features of hypopituitarism due to effects of anterior pituitary hormone deficiencies. The mechanism of hypopituitarism causing neonatal cholestasis is unknown, but the histologic finding is giant cell hepatitis. Biliary atresia, cystic fibrosis, galactosemia, and idiopathic neonatal hepatitis can all present with neonatal cholestasis, but are not associated with the other features of hypopituitarism. The diagnosis of hypopituitarism in infants who present with prolonged direct hyperbilirubinemia or hepatitis is often delayed due to the broad differential diagnosis.

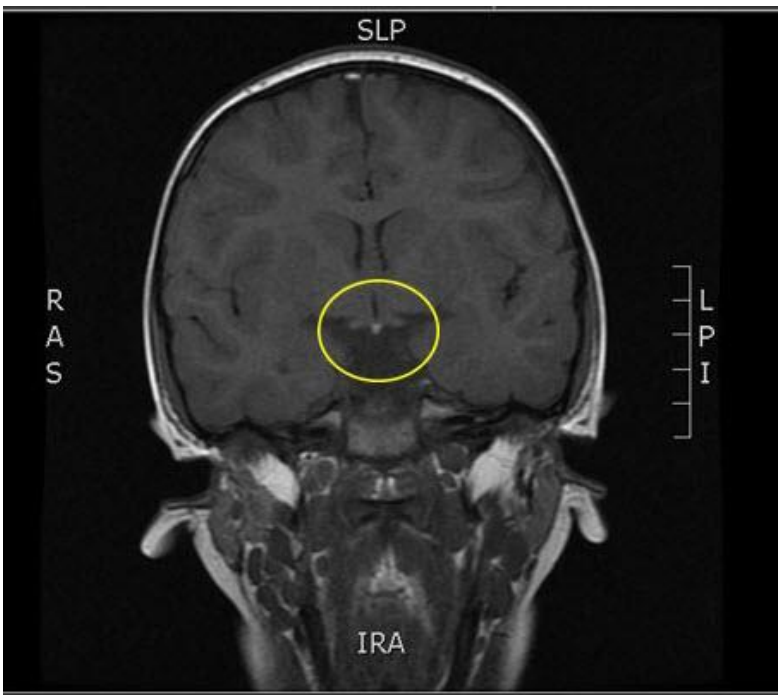
The predominant presenting symptom of congenital hypopituitarism is hypoglycemia. Due to gonadotropin deficiency, males may have a small penis and/or cryptorchidism. Depending on the etiology, nystagmus and midline defects may also be present. If the posterior pituitary hormone vasopressin is deficient, diabetes insipidus results.

In addition to hypoglycemia, laboratory evaluation may reveal hyponatremia due to central adrenal insufficiency, or hypernatremia if diabetes insipidus is present. Central adrenal insufficiency also results in a low serum cortisol level. Relative TSH deficiency results in a low free thyroxine level with a low or inappropriately normal TSH level. A random growth hormone level is a useful measure of growth hormone status in the first week of life. After this time period, insulin-like growth factor-1 and insulin-like growth factor binding protein-3 are more appropriate measures of growth hormone status and will be low in hypopituitarism.

Magnetic resonance imaging of the brain is indicated for those with hypopituitarism. An anatomic abnormality is likely in those with congenital hypopituitarism. The patient described in the vignette has pituitary stalk interruption syndrome: the triad of hypoplastic anterior pituitary, absent pituitary stalk (Item C174A), and ectopic posterior pituitary (Item C174B). Other potential findings on neuroimaging include evidence of septo-optic dysplasia with optic nerve hypoplasia and absent septum pellucidum or corpus callosum.



Item C174A: Hypoplastic anterior pituitary and absent pituitary stalk. Courtesy of K Vgt



Item C174B: Ectopic posterior pituitary (bright spot). Courtesy of K Vogt

PREP Pearls

- Hypoglycemia is the most prominent presenting feature of congenital hypopituitarism.
- Consider hypopituitarism in infants with prolonged direct hyperbilirubinemia, cholestatic jaundice, and neonatal hepatitis.
- Consider hypopituitarism in male infants with micropenis.

ABP Content Specifications(s)

- Recognize the clinical and laboratory features associated with hypopituitarism

Suggested Readings

- Geffner ME. Hypopituitarism in childhood. *Cancer Control*. 2002;9(3):212-222. https://www.moffitt.org/File%20Library/Main%20Nav/Research%20and%20Clinical%20Trials/Cancer%20Control%20Journal/v9n3/212.pdf.
- Götze T, Blessing H, Grillhösl C, et al. Neonatal cholestasis - differential diagnoses, current diagnostic procedures, and treatment. *Front Pediatr.* 2015;3:43. doi: http://dx.doi.org/10.3389/fped.2015.00043.
- Romesh K. Pediatric hypopituitarism. *Medscape*. 2015. http://emedicine.medscape.com/article/922410-overview. Updated November 2, 2015.

Question 175

The parents of a female adolescent bring her in for her annual health maintenance visit. She is a long-term survivor of cancer and the parents would like to discuss their concerns about potential future effects of radiation. She received chest irradiation, 20 Gy, as a part of her initial treatment plan at 10 years of age, so the oncologist recommends annual screening for breast cancer with mammogram or breast magnetic resonance imaging, beginning at 25 years of age.

Of the following, the primary childhood cancer that is associated with the GREATEST increased risk of breast cancer in this patient is

A. Hodgkin lymphoma

B. leukemia

C. neuroblastoma

D. non-Hodgkin lymphoma

E. Wilms tumor

Correct Answer: A

Young women who are survivors of childhood, adolescent, and young adult cancer and were treated with chest irradiation to fields that include breast tissue have an elevated risk of breast cancer. The highest risk group includes survivors of Hodgkin lymphoma; of these, historically, those treated with high doses of radiation to an extended mantel field were at greatest risk. Recent evidence has demonstrated that women treated with lower doses of radiation (10–19 Gy) to a large volume (whole lung field) also have an elevated risk of breast cancer. Those treated for other childhood cancers with chest irradiation that includes breast tissue also have an increased risk of breast cancer compared with the general population. This risk is lower than that for survivors of Hodgkin lymphoma and varies with respect to the radiation treatment received.

The mortality associated with breast cancer after childhood cancer is high. Therefore, recommendations for breast cancer surveillance for female survivors of childhood, adolescent, and young adult cancer have been issued. There are some differences between the details of the recommendations from various international groups. A recommendation of the International Late Effects of Childhood Cancer Guideline Harmonization Group, and discussed by Moskowitz, et al, is that evaluation for breast cancer with annual mammogram or breast magnetic resonance imaging should be done starting at age 25 or 8 years (whichever occurs later) after completing radiation therapy to the chest in women treated with greater than or equal to 20 Gy of irradiation to the chest received prior to age 30 years.

There are some general statements that apply to outcomes secondary to radiation exposure. Radiation sensitivity is:

- directly related to the rate of cell proliferation, that is, more rapidly dividing cells are more affected.
- directly related to the number of future cell divisions, that is, gonadal cells and hematopoietic stem cells are more affected.
- indirectly related to the degree of cell morphologic differentiation, that is, cells at the physeal growth plate that have not yet developed into bone or cartilage are more sensitive than those in the diaphysis.
- directly related to the age of the individual; children are more sensitive, have increased cell turnover, higher surface area-to-mass ratio, and smaller reserve.
- variable with the tissue; different tissues vary in their sensitivity to the effects of ionizing radiation (ie, lung is very sensitive, which is more sensitive than the liver, which itself is more sensitive than skeletal muscle, which is then more sensitive than skin).

PREP Pearls

- Among childhood cancer survivors, female patients with a history of Hodgkin lymphoma who were treated with chest irradiation are at greatest risk for developing breast cancer later in life.
- The risk of breast cancer is high and the mortality is substantial in women treated with radiation of 20 Gy or more to chest fields, including breast tissue.
- Annual screening with mammogram, breast magnetic resonance imaging, or both is recommended.

ABP Content Specifications(s)

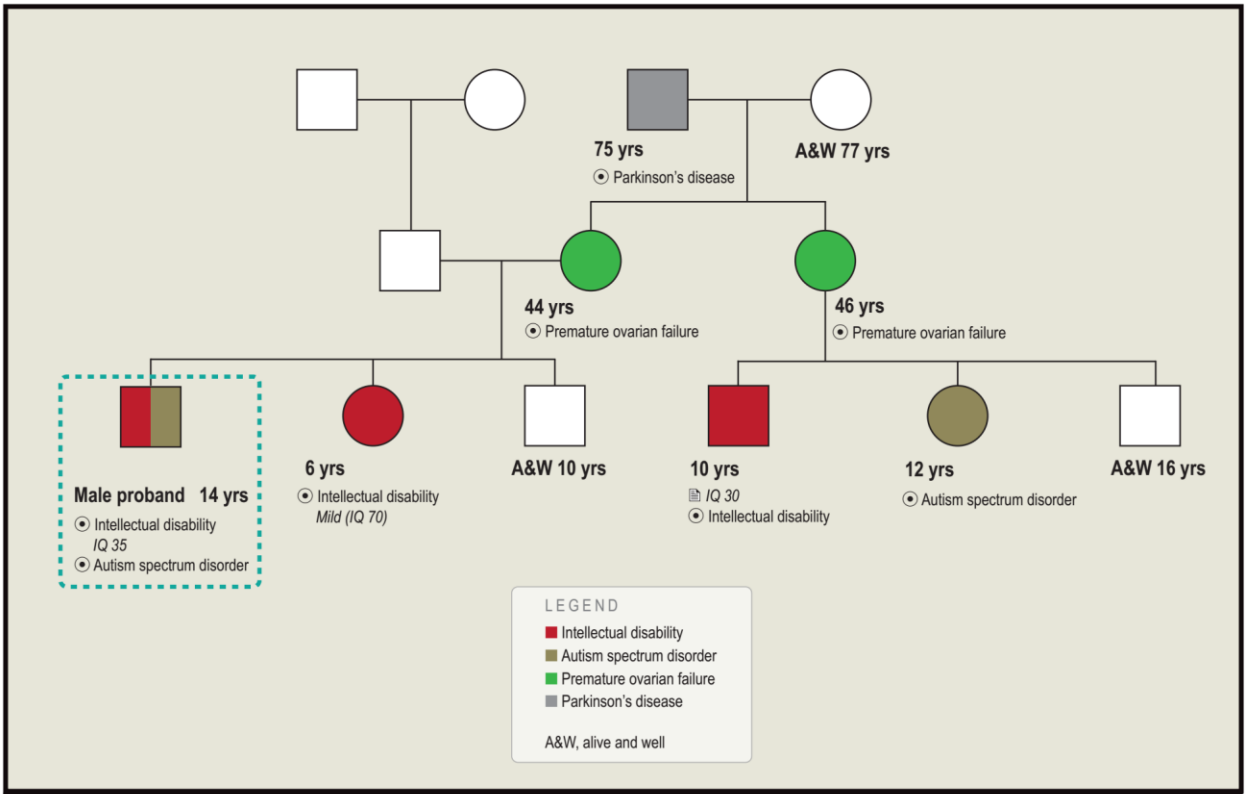
- Recognize the clinical presentation of radiation exposure and the risk factors (including medical imaging) for such exposure

Suggested Readings

- Brody AS, Frush DP, Huda W, Brent RL. Radiation risk to children from computed tomography. *Pediatrics*. 2007;120(3):677-682. doi: http://dx.doi.org/10.1542/peds.2007-1910.
- Moskowitz CS, Chou JF, Wolden SL, et al. Breast cancer after chest radiation therapy for childhood cancer. *J Clin Oncol*.2014;32(21):2217-2223. doi: http://dx.doi.org/10.1200/JCO.2013.54.4601.
- Mulder RL, Kremer LC, Hudson MM, et al. Recommendations for breast cancer surveillance for female survivors of childhood, adolescent, and young adult cancer given chest radiation: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. *Lancet Oncol.* 2013;14(13):e621-e629. doi: http://dx.doi.org/10.1016/S1470-2045(13)70303-6.
- Puch-Kapst K, Juran R, Stoever B, Wauer RR. Radiation exposure in 212 very low and extremely low birth weight infants. *Pediatrics*. 2009;124(6):1556-1564. doi: http://dx.doi.org/10.1542/peds.2008-1028.

Question 176

A 14-year-old adolescent boy with moderate intellectual disability and autism presents to your office for a health supervision visit. On physical examination, you note macrocephaly, long face, prognathism, and large testes. His family history is significant for a younger sister with mild intellectual disability and a maternal male first cousin with moderate intellectual disability. No genetic testing has been performed. The patient's mother, who is cognitively normal, experienced premature ovarian failure. The family pedigree is shown in Item Q176 .



Courtesy of L. Parsley

ITEM Q176: Pedigree for the adolescent described in the vignette.

Of the following, the BEST next test to confirm the diagnosis would be

A. FMR1 molecular analysis
B. genomic microarray
C. MECP2 molecular analysis
D. plasma phenylalanine concentration
E. Prader-Willi methylation testing

Correct Answer: A

The patient in the vignette has fragile X syndrome, one of the most common forms of inherited intellectual disability. Fragile X syndrome results from an abnormality in a gene on the X chromosome. More than 99% of affected individuals have a loss-of-function mutation in *FMR1*because of an increased number of CGG trinucleotide repeats (> 200) and abnormal methylation of the *FMR1* gene. Diagnosis is confirmed on *FMR1* molecular analysis. Fragile X syndrome is an X-linked autosomal-dominant, trinucleotide repeat disorder characterized by a phenomenon in genetics known as anticipation.

With anticipation, a condition tends to become more severe and manifests at an earlier age as it is passed down from one generation to the next. This is due to expansion of an unstable trinucleotide repeat that is prone to errors during cell division. In fragile X syndrome, anticipation occurs when an intellectually normal premutation carrier, an individual with 55 to 200 repeats, transmits an unstable FMR1 allele to their child. This unstable allele allows the parent's premutation to expand into a full mutation, with more than 200 CGG repeats, thus yielding an affected child. The premutation usually expands through the mother; it tends to be stable if passed down by the father. Other disorders with anticipation include myotonic dystrophy and Huntington disease.

Boys with a full fragile X mutation (> 200 CGG repeats) will have moderate-to-severe intellectual disability, whereas affected girls will have only mild intellectual disability or learning disabilities and can be intellectually normal in 50% of cases. Twenty-five percent of patients will also have autism spectrum disorder. Affected boys have a characteristic dysmorphology that includes a long face, large protruding ears, prominent forehead, prognathism, macrocephaly, and postpubertal macro-orchidism. In full-mutation individuals, the dysmorphology becomes more evident as the child ages, whereas premutation carriers have normal intellect and appearance. Male premutation (55-200 CGG repeats) carriers have an increased incidence of fragile X-associated tremor/ataxia syndrome (FXTAS), which resembles a Parkinson-like disorder with intention tremor, gait ataxia, and eventually dementia. Female premutation carriers are at risk for primary ovarian insufficiency, with cessation of menses before age 40 years. The pedigree in the vignette is consistent with an X-linked dominant disorder, with both males and females affected, but the males are affected to a much greater degree.

The American Academy of Pediatrics and the American College of Medical Genetics recommend chromosomal microarray and fragile X testing on all children with intellectual disability. A chromosomal microarray would be recommended for the patient in the vignette; however, the diagnosis based on his pedigree, history, and classic dysmorphology is most consistent with fragile X syndrome. *FMR1* molecular analysis would be the best test to confirm this diagnosis.

MECP2 molecular analysis is used to diagnose Rett syndrome. This disorder affects girls almost exclusively and is characterized by normal early growth and development, followed by a gradual

decline in developmental skills, loss of purposeful hand movement, classic hand wringing, acquired microcephaly, and intellectual disability.

Plasma phenylalanine concentration is used to identify elevated serum phenylalanine levels found in patients with phenylketonuria (PKU). Phenylketonuria presents with a mousy body odor, developmental regression, light skin and hair, eczema, seizures, and intellectual disability. This test is included on newborn screening because PKU is a treatable condition with the possibility of improving outcomes if treated in infancy and throughout the lifetime of the affected individual.

Prader-Willi methylation testing is used to confirm suspected cases of Prader-Willi syndrome (PWS). Prader-Willi syndrome presents in neonates with hypotonia, hypogonadism, and poor feeding. As affected children age, the signs and symptoms of PWS transition to hyperphagia, obesity, and intellectual disability.

Incontinentia pigmenti is another X-linked dominant condition, which that is lethal in males in utero; therefore, typically only affected females are seen.

PREP Pearls

- Fragile X syndrome is an X-linked dominant condition that results in moderate-to-severe intellectual disability in males along with a classic dysmorphology. In females, full mutation carriers can have normal intellect, mild intellectual disability, or learning disability.
- Fragile X syndrome is one of the most common inherited forms of intellectual disability. Diagnosis is confirmed with *FMR1* molecular analysis.
- X-linked dominant disorders can affect both males and females, but males are affected to a much greater degree because they have only one X chromosome. Affected men will pass the abnormal X to all of their daughters and none of their sons. Affected women will pass the affected X to 50% of their offspring of either sex.

ABP Content Specifications(s)

- Recognize the inheritance pattern associated with X-linked dominant disorders

Suggested Readings

- Chonchaiya W, Schneider A, Hagerman RJ. Fragile X: a family of disorders. *Adv Pediatr*. 2009;56:165-186. doi: http://dx.doi.org/10.1016/j.yapd.2009.08.008.
- Kronquist KE, Sherman SL, Spector EB. Clinical significance of tri-nucleotide repeats in Fragile X testing: a clarification of American College of Medical Genetics guidelines. *Genet Med.* 2008;10(11):845-887. doi: http://dx.doi.org/10.1097/GIM.0b013e31818b0c8a.
- Saul RA, Tarleton JC. FMR1-related disorders. *GeneReviews*. 2012. http://www.ncbi.nlm.nih.gov/books/NBK1384/. Updated April 26, 2012.

Question 177

A 5-year-old girl is brought to your office for evaluation of a malodorous vaginal discharge. Her mother reports that the girl has had a vaginal discharge intermittently over the last 6 months. During that time, she has had neither fever nor abdominal pain. The girl and her mother deny any history of sexual abuse or trauma. On physical examination, she has a vaginal discharge visible at the introitus. You are unable to perform any additional examination because of the girl's level of anxiety.

Of the following, based on her history and physical examination, the MOST likely cause for this girl's symptoms is

A. estrogen withdrawal
B. foreign body
C. rectovaginal fistula
D. sexual abuse
E. vaginal malignancy

Correct Answer: B
The most likely cause for the symptoms of the girl in the vignette is a retained foreign body in the vagina. Her presentation is consistent with vulvovaginitis, which typically presents with vaginal discharge, pruritus, vulvar irritation, or burning upon urination. The first step in the evaluation of a child with suspected vulvovaginitis is to obtain a thorough history from both the parent and child. All adolescents should be interviewed alone. Important elements of the history include the presence and characteristics of vaginal discharge, dysuria, pruritus, vaginal/vulvar irritation or lesions, hygiene practices, use of feminine hygiene products, and sexual activity/abuse.

Vulvovaginitis in a young child is commonly nonspecific and occurs most often because of poor hygiene or contact with irritants. In these cases, the discharge is typically nonpurulent, mucoid, and nonodorous. Treatment of nonspecific vaginitis focuses on improved hygiene and elimination of tight-fitting clothes and chemical irritants.

A retained foreign body is the most common cause of malodorous vaginal discharge in a young child, as seen in the girl in this vignette. In the case of suspected foreign body, an examination under anesthesia is often necessary for adequate visualization and removal.
Candidal vulvovaginitis is more common among adolescent girls than prepubescent girls. It may be associated with recent use of systemic antibiotics, diabetes mellitus, or immunosuppression. Symptoms and signs include nonodorous white discharge, pruritus, dysuria, vulvar and vaginal erythema, and edema. The diagnosis is typically made with a microscopic examination of a vaginal discharge wet-mount with 10% potassium hydroxide, illustrating pseudohyphae or budding yeast. Treatment consists of topical or oral antifungal medications.

Vaginal discharge secondary to estrogen withdrawal can be seen in the newborn period, associated with the loss of maternal estrogen. Rectovaginal fistulas are rare malformations. Although symptoms may include a malodorous vaginal discharge, affected individuals also typically have recurrent urinary tract infections and passage of feces through the vagina as well. For the girl in the vignette, there is no indication to suspect sexual abuse. However, among sexually active or sexually abused girls, screening for sexually transmitted organisms must be considered. *Trichomonas vaginalis* can cause vulvovaginitis among sexually active girls, with symptoms including *malodorous*, *yellow-green* vaginal discharge, dysuria, and vulvar pruritus. The diagnosis is typically made by microscopic examination of a vaginal discharge wet-mount demonstrating motile, flagellated organisms. *Trichomonas* vaginitis is treated with oral metronidazole.

Vaginal malignancy is rare in the pediatric population, and the girl's presentation makes this an unlikely diagnosis.

PREP Pearls

- The etiology of vulvovaginitis differs by age. A retained foreign body is the most common cause in a young child with malodorous vaginal discharge.
- For sexually active or sexually abused girls, screening for sexually transmitted organisms must be considered.

ABP Content Specifications(s)

- Recognize the etiology of a vaginal discharge in patients of various ages and manage appropriately

Suggested Readings

- Kokotos F, Adam HM. Vulvovaginitis. *Pediatr Rev*. 2006;27(3):116-117. doi: http://dx.doi.org/10.1542/pir.27-3-116.
- Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*.2015;64(RR03):1-137. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6403a1.htm.

Question 178

A 3-year-old girl is brought to your office for behavioral problems. When you enter the room, the girl quickly hides behind her mother. Her mother is concerned because each time the family attempts to leave their home, the girl cries and has a tantrum. This behavior began about 9 months ago when their neighbor acquired a pet dog. The girl has seen the dog several times and was frightened by its enthusiastic jumping and tail wagging. The dog barks loudly whenever the garage door opens. When the family goes to their neighborhood park, she does not want to leave the car, as people sometimes bring their pets to the park. She ran away when her aunt offered her a gift of a stuffed toy dog.

Of the following, the BEST next step is to

A. avoid taking the child to places where dogs might be present

B. begin a trial of a selective serotonin reuptake inhibitor

C. buy headphones for the child to wear

D. look at pictures of dogs in books

E. provide reassurance that the child will outgrow her fear of dogs

Correct Answer: D
The girl in this vignette has a specific phobia of dogs. Behavioral management strategies are first-line therapy for phobias, particularly in young children. Gradual desensitization is the indicated treatment strategy for specific phobias. This process starts with learning to tolerate the least frightening form of the stimulus (eg, pictures) and then learning to tolerate progressively more intense stimuli (eg, videos, objects, real-life situations).

Anxiety disorders affect 5% to 16% of children and adolescents. Anxiety is the anticipation of danger, whereas fear is the emotional response to an impending threat. Normal anxiety and fears are developmentally appropriate for the situation and can be protective. An anxiety disorder occurs when fears or worries are inappropriate for the developmental level of the child, are excessive for the situation, are significantly distressing, are persistent, or result in impairment in functioning. Types of anxiety disorders include separation anxiety, specific phobia, social anxiety, obsessive-compulsive disorder, generalized anxiety, and post-traumatic stress disorder.

A variety of different factors contribute to the development of anxiety disorders. Children with a behaviorally inhibited temperament tend to avoid new or unfamiliar situations and are more likely to develop anxiety. Anxiety disorders are more common in girls. In addition to a genetic predisposition towards anxiety disorders, parents who are anxious may reinforce their children's fears by modeling fearfulness, endorsing the danger of a situation, or by being overprotective. Traumatic experiences or learning information through media about frightening events may lead to persistent fears of similar situations. Stressors such as family dysfunction, peer problems, and academic struggles can also contribute to the development of an anxiety disorder.

Certain fears are common at various stages of development. Young children may be fearful of strangers or the dark, while preschoolers may fear animals or monsters. School-age children may fear natural disasters or injury. Adolescents may fear war, illness, or school failure. Many of these fears are temporary; however, these typical fears may become the subject of a specific phobia when these fears are excessive, unrealistic, prolonged (greater than 6 months), and impairing. Types of phobias can include fear of animals, the natural environment (eg, heights, water), blood-injection-injury (eg, needles), situations (eg, airplanes), or other (eg, loud sounds). In children with specific phobias, their fear and distress is beyond that warranted by the situation or object. These children become anxious when they anticipate encountering the fearful stimulus. Their anxiety may manifest as sweating, shaking, difficulty breathing, and tachycardia. The child will actively avoid the fear-provoking situation and become immediately and overly anxious when encountering the stimulus. They may also avoid pictures, sounds, or other reminders of the feared object or situation. Younger children may cling, tantrum, or cry. Older children may have somatic symptoms (headaches, stomachaches).

Typical fears can usually be addressed effectively through reassurance from the parents. This might include assurances that the parent will protect the child as needed. When the fears are at the level of a phobia, the primary method used to reduce symptoms is systematic desensitization through gradual and progressive exposure to the specific feared situation or object. Children who are developmentally ready can be taught how their body responds to their anxiety, can learn to

use relaxation techniques such as progressive muscle relaxation and visual imagery to calm themselves, or can learn to reframe the negative, anxious thoughts into a realistic view of the situation. Positive, helpful thoughts can support the child through their anxiety. Parents can support their children as they learn to manage their fears by respecting the child's feelings, but refraining from overprotection or allowance of avoidant behaviors.

Medication may be considered when behavioral therapy is not sufficient to address the child's fears or when other types of anxiety disorders coexist. Although not approved by the US Food and Drug Administration for treatment of anxiety disorders in children, selective serotonin reuptake inhibitors (SSRIs) have the best evidence, including randomized, controlled studies, for safe and effective treatment of anxiety disorders in children. Appropriate counseling about and monitoring for the risk of suicidal ideation with SSRIs should be done. Medication is used to stabilize the child's anxiety responses and allows the child to learn and benefit from behavioral strategies. The child is then better equipped to manage their anxiety when the medication is discontinued, typically after a year of clinical stability.

For the child in the vignette, avoidance of places where dogs might be present would not only be challenging, but will reinforce the child's fear and will sustain the child's anxiety. Headphones may aid the child in blocking the sound of barking, but does not address the underlying fear and would not prevent her excessive anxiety. Although a common childhood fear, this child's fear of dogs is significant in the degree of distress, avoidant behaviors, persistence, and impairment in functioning. Intervention is warranted to address the child's phobia. Behavioral management strategies are first-line in treatment of phobias and a trial of an SSRI is not indicated at this time. Systematic desensitization is indicated and exposure could start with looking at pictures of dogs in books.

Pediatricians can help guide parents in managing normal fears of childhood, identifying when those fears have become phobias, providing education on anxiety treatment, and connecting families with mental health professionals when impairment is present.

PREP Pearls

- An anxiety disorder occurs when fears or worries are inappropriate for the developmental level of the child, are excessive for the situation, are significantly distressing, are persistent, or result in impairment in functioning.
- In addition to a genetic predisposition towards anxiety disorders, parents who are anxious may reinforce their children's fears by modeling fearfulness, endorsing the danger of a situation, or by being overprotective.
- Gradual desensitization is the indicated treatment strategy for specific phobias. This process starts with learning to tolerate the least frightening form of the stimulus (eg, pictures) and then learning to tolerate progressively more intense stimuli (eg, videos, objects, real-life situations).

ABP Content Specifications(s)

- Recognize the clinical findings associated with phobias in patients of various ages, and manage appropriately
- Recognize the various environmental and biological contributors to the development of phobias and anxiety disorders

Suggested Readings

- Augustyn M. Overview of fears and phobias in children and adolescents. *UpToDate*. Available online only with subscription.
- Bagnell AL. Anxiety and separation disorders. *Pediatr Rev*. 2011;32(10):440-446. doi: http://dx.doi.org/10.1542/pir.32-10-440.

Question 179

An 8-year-old boy is brought by his mother to your office for evaluation of fatigue and headache over the past week. His mother states that the boy has seemed much more "moody" and has been sleeping more than usual since yesterday. He has been out of school for winter break over the past 8 days and he has not seemed interested in playing a new video game that he just received for Christmas, saying: "I just don't feel like it." The boy has had no cough or chest pain, but he mentioned to his mother that he felt like he was having trouble breathing after walking up the steps to his room last night.

The boy's mother denies that he has had any fevers, cough, rhinorrhea, vomiting, or diarrhea over the past week. His past medical history is significant only for attention-deficit/hyperactivity disorder. He takes methylphenidate daily during the school year, but has not been taking this medication over the past 8 days while he has been home.

The boy has had no recent travel. He was exposed to 2 cousins who had gastroenteritis last week, but he has had no gastrointestinal symptoms. The boy's father also complained of headache last week, but he is now away on a business trip and is feeling just fine. The mother tells you that she feels like she could also use a rest, as she has been feeling "really worn out" over the past several days as well.

In your office, the boy is afebrile and his vital signs are all within normal limits for his age. He appears slightly pale and somewhat tired, but answers all of your questions appropriately. The physical examination is otherwise unremarkable.

Of the following, the diagnostic test that would be MOST useful to obtain in this patient is

A. complete blood cell count with differential
B. computed tomography of the brain
C. influenza polymerase chain reaction assay
D. serum carboxyhemoglobin level
E. urine toxicology screen

Correct Answer: D
The 8-year-old boy in the vignette presents with headache, irritability, dyspnea, and progressive fatigue over the past week, in the absence of fever. These symptoms have developed since he has been home from school for winter break. His parents have experienced fatigue and headache during the same timeframe and no one in his household has displayed cough, congestion, or gastrointestinal symptoms. The diagnosis of carbon monoxide poisoning should be suspected given these elements of the boy's history. A serum carboxyhemoglobin level would be the most useful diagnostic test to obtain.

It is vital for all pediatric providers to recognize the signs and symptoms of carbon monoxide poisoning and to be able to manage children with carbon monoxide poisoning appropriately. Carbon monoxide is a colorless, tasteless, odorless, nonirritating gas that is produced as a byproduct of combustion by furnaces, heaters, and other fuel-powered devices used in the home, such as gas-powered generators. Carbon monoxide is also an important cause of early death related to house fires. Carbon monoxide poisoning poses a significant risk for morbidity and mortality in both children and adults.

Inhaled carbon monoxide results in significantly decreased oxygen delivery to the body tissues and vital organs, including the brain, via 2 important mechanisms: (1) it binds to hemoglobin with an affinity that is 240 times greater than that of oxygen, and (2) it shifts the oxyhemoglobin dissociation curve to the left and changes its shape. Through these mechanisms, carbon monoxide decreases blood oxygen content and impairs oxygen release to body tissues. It may also impair cellular respiration at the mitochondrial level.

Symptoms of carbon monoxide poisoning are generally nonspecific and range from headache, fatigue, shortness of breath, dizziness, nausea, vomiting, weakness, and behavioral changes to syncope, seizures, coma, and arrhythmias. Severe cases can result in hypoxic end-organ injury and death. Carbon monoxide poisoning may also be associated with delayed neurologic complications, including chronic headaches, difficulties with memory, and a decline in school performance, in those patients who survive. Patients with carbon monoxide poisoning may or may not have the classically described “cherry red” skin color, so the presence or absence of this cannot be relied upon to make the diagnosis. In addition, pulse oximetry measurements are typically normal in affected patients, as conventional pulse oximeters cannot distinguish between oxyhemoglobin and carboxyhemoglobin.

Since symptoms of carbon monoxide poisoning are very nonspecific, they can easily be attributed to more common illnesses including influenza, food poisoning, or overexertion. The peak incidence of carbon monoxide poisoning occurs during the winter months when outbreaks of influenza are also common. Carbon monoxide poisoning should be suspected when multiple patients from the same environment are presenting with similar symptoms that are not completely "classic" for influenza or other alternative diagnoses. Thorough inquiry regarding exposure to heating systems and other fuel-burning devices is essential to make this diagnosis. Carbon monoxide poisoning should be suspected in all fire victims.

Serum carboxyhemoglobin levels are useful in diagnosing carbon monoxide poisoning, and may help to guide management and determine prognosis. All patients with suspected carbon monoxide poisoning should be removed from the contaminated environment immediately and given 100% oxygen until serum carboxyhemoglobin levels normalize. High-flow oxygen decreases the half-life of carbon monoxide and enhances oxygen delivery. Children with severe toxicity from carbon monoxide exposure, including those with syncope, seizures, coma, metabolic acidosis, and signs of cardiac ischemia, may require hyperbaric oxygen therapy. Consultation with a toxicologist with experience in treating children with carbon monoxide poisoning is recommended in these cases. In the United States, guidance from a medical toxicologist may be obtained by calling the regional Poison Control Center at 1-800-222-1222.

While a complete blood cell count with differential could help in ruling out anemia as an underlying etiology for this boy's fatigue and aid in screening for an infectious etiology, it would not be useful in making the diagnosis of carbon monoxide poisoning in this patient. Computed tomography of the brain could help rule out intracranial pathology in this patient, but would not be helpful in identifying carbon monoxide poisoning as the cause of his symptoms.

Although infection with the influenza virus could cause the nonspecific symptoms of headache and fatigue in this boy, he lacks other typical symptoms, including fever, chills, cough, rhinorrhea, sore throat, and myalgias. An influenza polymerase chain reaction assay would not be useful in revealing this boy's diagnosis.

Urine toxicology screening would not provide useful information leading to the correct diagnosis in this boy. The slow progression of symptoms, along with a lack of any abnormalities related to his vital signs or physical examination, make drug intoxication an unlikely explanation for his clinical picture.

PREP Pearls

- Suspect carbon monoxide poisoning when multiple individuals from the same setting report nonspecific flu-like symptoms such as headache, weakness, fatigue, nausea, or vomiting. Carbon monoxide poisoning should also be suspected in all house fire victims.
- A serum carboxyhemoglobin level is used to confirm the diagnosis of carbon monoxide poisoning and can aid in guiding management and determining prognosis.
- All patients with suspected carbon monoxide poisoning should be removed from the contaminated environment immediately, and given 100% oxygen to decrease the half-life of carbon monoxide. Children with severe toxicity may require hyperbaric oxygen therapy, and consultation with a toxicologist is recommended in these situations.

ABP Content Specifications(s)

- Recognize the signs and symptoms of carbon monoxide poisoning, and manage appropriately

Suggested Readings

- Dubrey SW, Chehab O, Ghonim S. Carbon monoxide poisoning: an ancient and frequent cause of accidental death. *Br J Hosp Med (Lond)*. 2015;76(3):159-162. doi: http://dx.doi.org/10.12968/hmed.2015.76.3.159.
- Seeyave DM, Brown KM. Environmental emergencies, radiological emergencies, bites and stings. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. *Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:718-760.
- US Centers for Disease Control and Prevention. Carbon monoxide poisoning: frequently asked questions. US Centers for Disease Control and Prevention website. http://www.cdc.gov/co/faqs.htm. 2015.

Question 180

An 18-year-old young woman presents to the pediatric clinic for evaluation of a rash. She was initially ill with upper respiratory symptoms, and then 5 days later, developed pruritic lesions over her extremities. Vital signs show a temperature of 37.9°C, respiratory rate of 18 breaths/min, heart rate of 90 beats/min, and blood pressure of 105/65 mm Hg. On physical examination, she is uncomfortable, but nontoxic in appearance. There is a rash concentrated on her hands and legs (Item Q180).

Item Q180: Rash as described for the patient in the vignette. Reprinted with permission from Eng S, Moon A, Leander C, Del Vecchio M. Fever and petechial rash in a 9-year-old boy. Pediatr Rev. 2012;33(10):e69-e71.

Of the following, the MOST likely etiology for the illness is

A. coxsackievirus
B. Henoch-Schönlein purpura
C. immune thrombocytopenia
D. meningococcemia
E. parvovirus B19

Correct Answer: E

The most likely etiology of the illness for the young woman in this vignette is parvovirus. The young woman has petechial papulopurpuric gloves-and-socks syndrome (PPGSS) (Item C180A), which is most frequently caused by parvovirus B19. Petechial papulopurpuric gloves-and-socks syndrome is an infrequent manifestation of parvovirus B19 infection, but warrants attention given that it may be confused with other concerning systemic illnesses. Typically, PPGSS is preceded by a viral prodrome followed by development of a rash that tends to be restricted to the extremities. The rash can be pruritic and painful and can be associated with edema.

Item C180A: *Petechial papulopurpuric gloves-and-socks syndrome is most frequently caused byparvovirus B19. Reprinted with permission from Eng S, Moon A, Leander C, Del Vecchio M. Fever and petechial rash in a 9-year-old boy. Pediatr Rev. 2012;33(10):e69-e71.*

Parvovirus B19 infections are better known for the classic childhood exanthem, erythema infectiosum, or fifth disease. Erythema infectiosum is characterized by an intense red appearance of the cheeks. Additionally, parvovirus can cause a reticular rash that appears first over the trunk and can move to the arms, thighs, and buttocks (Item C180B). This rash can vary in intensity with heat. Infection can also cause arthralgias and arthritis, more commonly in adult women. Complications of parvovirus B19 infections include chronic erythroid hypoplasia in immunocompromised hosts, transient aplastic crises in patients with hemolytic anemia, and catastrophic effects on the fetus including spontaneous abortion and hydrops fetalis.

Item C180B: Reticular rash seen in parvovirus infection. Reprinted with permission from Kimberlin DW, Brady, MT, Jackson, MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL American Academy of Pediatrics; 2015.

Coxsackie viruses are a cause of hand-foot-and-mouth disease. The exanthem seen in this syndrome is typically described as maculopapular or papulovesciular. Vesicles tend to have a rim of redness (Item C180C). The rash can occur without oral lesions and is rarely associated with petechiae.

Item C180C: Vesicles seen in hand-foot-and-mouth disease. Reprinted with permission from Kimberlin DW, Brady, MT, Jackson, MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL American Academy of Pediatrics; 2015.

Henoch-Schönlein purpura (HSP) is the most common systemic vasculitis of childhood and is characterized by palpable purpura (Item C180D). There is symptom overlap between PPGSS and HSP, including purpura and edema. The exanthem of HSP tends to concentrate in gravity-

dependent areas, such as the lower extremities. Since HSP can involve the renal system, distinguishing the 2 illnesses has important prognostic implications.

Item C180D: Findings seen in Henoch-Schönlein purpura. Reprinted with permission from McInerny TK, Adam HM, Campbell DE, Kamat DM, DeWitt TG, Kelleher KJ, eds. American Academy of Pediatrics Textbook of Pediatric Care. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009:

Immune thrombocytopenia (ITP) is characterized by cutaneous and mucous membrane bleeding. In general, though patients can report a recent infection, there is not typically a prodrome prior to the onset of skin manifestations. Parvovirus infections can cause mild thrombocytopenia, but platelet values would not be expected to be as low as that seen in ITP.
New-onset purpuric lesions in a child should always raise concern for meningococcemia given the potential for a fulminant course with this illness (Item C180E). Meningococcemia is typically abrupt in onset. Initially, the rash can be maculopapular or petechial. In severe cases, death can ensue in hours. For the patient in this vignette, the evolution of symptoms and nontoxic appearance on examination would not be consistent with a diagnosis of meningococcemia.

Item C180E: Purpuric lesions seen in meningococcal disease. Reprinted with permission from Kimberlin DW, Brady, MT, Jackson, MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL American Academy of Pediatrics; 2015.

PREP Pearls

- Parvovirus B19 infection is the etiology of the classic childhood exanthem erythema infectiosum or fifth disease.
- Petechial papulopurpuric gloves-and-socks syndrome is an infrequent manifestation of parvovirus B19 infection characterized by a rash usually restricted to the extremities.
- Complications of parvovirus infections include chronic erythroid hypoplasia in immunocompromised hosts, transient aplastic crises in patients with hemolytic anemia, and catastrophic effects on the fetus including spontaneous abortion and hydrops fetalis.

ABP Content Specifications(s)

- Recognize the clinical features associated with erythema infectiosum
- Recognize the complications of parvovirus B19 infection

Suggested Readings

- American Academy of Pediatrics. Parvovirus B19. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:593-596.
- Eng S, Moon A, Leander C, Del Vecchio M. Fever and petechial rash in a 9-year-old boy. *Pediatr Rev.* 2012;33(10):e69-e71. doi: http://dx.doi.org/10.1542/pir.33-10-e69.

Question 181

You are making rounds in the newborn nursery with a group of medical students. The students ask you to educate them about newborn nutrition. You begin the presentation with a discussion about normal newborn nutritional needs and end with a discussion about neonates with increased nutritional needs. You ask the students to determine the caloric need for a 3-day-old neonate born at 29 weeks of gestation with complex congenital heart disease.

Of the following, the BEST estimate of this neonate's caloric need is

A. 90 kcal/kg per day
B. 100 kcal/kg per day
C. 110 kcal/kg per day
D. 120 kcal/kg per day
E. 140 kcal/kg per day

Correct Answer: E
The preferred response is 140 kcal/kg per day, which includes the additional caloric needs of a preterm infant with congenital cardiac disease. Item C181 reviews caloric needs by age. Caloric needs are increased in many chronic diseases, particularly cardiovascular disease. Increased calories are also required in cases of malabsorption, such as cholestasis or celiac disease.

Item C181. Caloric Needs by Age.

Age	Daily Caloric Needs (kcal/kg per day)	Anticipated Weight Gain/Day (g)
Preterm infant	90-120	20-30
Preterm infant with chronic disease	120-140	20-30
Term infant	100-110	20-30
6 months	80	10-15
1-3 years	80-100	5-10
4-6 years	80-90	3-5
7-10 years	70-90	3-5

Courtesy of C. Waasdorp Hurtado

PREP Pearls
- Preterm infants with chronic medical conditions have increased caloric needs.
- Caloric needs decrease with age.
- Malabsorption results in increased caloric requirements.

ABP Content Specifications(s)
- Understand the caloric requirements for patients of various ages, including those born prematurely, and the circumstances in which those requirements may change

Suggested Readings

- Cherry R, Thomas DW. Infant feeding in special circumstance. *Pediatr Rev.* 2008;29(8):274-280. doi: http://dx.doi.org/10.1542/pir.29-8-274.
- Ehrenkranz RA. Nutrition, growth and clinical outcomes. *World Rev Nutr Diet.* 2014;110:11-26. doi: http://dx.doi.org/10.1159/000358455.
- Griffin IJ, Cooke RJ. Nutrition of preterm infants after hospital discharge. *J Pediatr Gastroenterol Nutr.* 2007;45(suppl 3):S195-S203. doi: http://dx.doi.org/10.1097/01.mpg.0000302972.13739.64.

Question 182

A 14-year-old adolescent presents to your office for evaluation of bilateral knee pain. He describes a gradual onset of anterior knee pain beginning about 4 months ago. The pain is worse with prolonged sitting and when he runs during gym class. He does not recall an acute injury. He reports occasional mild swelling and the feeling that his knees may collapse under him while running. He denies locking or catching of the knee joint. On physical examination, there is bilateral tenderness along the medial facet of the patella and pain with compression of the patella onto the femoral trochlea.

Of the following, the condition MOST likely to be responsible for this patient's pain is

A. discoid lateral meniscus
B. iliotibial band syndrome
C. inflammatory arthritis
D. Osgood-Schlatter disease
E. patellofemoral pain syndrome

Correct Answer: E
The adolescent boy in the vignette has classic history and physical examination findings for patellofemoral pain syndrome (PFPS). He has chronic anterior knee pain without an inciting injury, pain with prolonged sitting, a feeling of instability with running, and no reported mechanical symptoms. Patellofemoral pain syndrome is one of the most common causes of knee pain in adolescents. Many affected individuals report pain with prolonged sitting, activity, and climbing or descending stairs. The feeling of instability is likely related to quadriceps inhibition and weakness. The classic physical examination findings for PFPS are tenderness over the medial patellar facet, pain with patellar compression, and mild swelling. Risk factors for PFPS include core and hip muscle weakness, genu valgum ("knocked knees"), pes planovalgus, patellar hypermobility, and a shallow femoral trochlear groove.

A physical therapy program emphasizing core and hip strengthening improves symptoms in most patients. Some athletes benefit from the use of a brace that holds the patella in place during physical activity.

Patellofemoral instability refers to either subluxation (partial displacement) or dislocation of the patella at the patellofemoral joint. There is considerable overlap in symptoms and anatomic risk factors of patellofemoral pain syndrome and patellar instability. After an initial patellar dislocation episode, swelling and loss of motion are common signs and may indicate osteochondral injury. Between one-third and one-half of affected individuals experience recurrent dislocation episodes.

Discoid lateral meniscus is a congenital anomaly with an abnormally shaped, thick meniscus. Although often asymptomatic, these individuals have an increased risk of meniscal tear. When symptomatic, a discoid lateral meniscus would likely cause pain over the lateral joint line and mechanical symptoms such as catching or locking. Iliotibial band syndrome presents with pain over the lateral aspect of the hip and knee. Inflammatory arthritis is less likely in this case than PFPS because the patient in the vignette has only mild swelling and does not have pain in other joints or constitutional symptoms. Osgood-Schlatter disease is a common cause of knee pain in adolescents, but would lead to pain over the tibial tubercle rather than pain around the patella.

PREP Pearls

- Individuals with patellofemoral pain syndrome often report pain with activity, prolonged sitting, and with climbing or descending stairs.
- Patellofemoral pain syndrome can lead to a feeling of knee instability when knee pain leads to inhibition of the quadriceps muscles

ABP Content Specifications(s)

- Recognize the historical and clinical findings associated with subluxation of the patella
- Identify risk factors associated with sports-related patellofemoral dysfunction

Suggested Readings

- Lankhorst NE, Bierma-Zeinstra SM, van Middelkoop M. Factors associated with patellofemoral pain syndrome: a systematic review. *Br J Sports Med*. 2013;47(4):193-206. doi: http://dx.doi.org/10.1136/bjsports-2011-090369.
- Sarwark JF, LaBella CR. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014: 650 pp.
- Wolf M. Knee pain in children: part 1: evaluation. *Pediatr Rev*. 2016;37(1):18-24. doi: http://dx.doi.org/10.1542/pir.2015-0040.

Question 183

The mother of a 4-year-old boy with a severe peanut allergy informs you that she is pregnant. The mother is worried about the potential for allergies in the new child, and she asks for advice on how to prevent food allergies. The mother plans to feed formula to the baby.

Of the following, the BEST advice for this mother is

A. delay the introduction of any solid foods until at least 7 to 8 months of age
B. delay the introduction of peanuts and other allergenic foods until 2 years of age
C. eat large amounts of peanuts and tree nuts during the pregnancy
D. feed the baby a hydrolyzed formula
E. feed the baby a soy-based formula

Correct Answer: D
To reduce the risk of developing food allergies, the baby in this vignette should be fed a hydrolyzed formula. Given that this future child will have a first-degree relative with a significant food allergy, the use of a hydrolyzed formula during the first 4 months of life may help prevent the development of both atopic disease and cow milk protein allergy. An extensively hydrolyzed formula may offer more benefits than a partially hydrolyzed formula, but the data are inconclusive. No advantage has been found with using soy formulas to prevent food allergies and more studies are needed to evaluate the effects of using an amino acid-based formula.

Exclusive breastfeeding for the first 4 to 6 months of age is recommended and is associated with decreased atopic dermatitis during the first 2 years of life and a decreased rate of wheezing in children prior to the age of 4 years. Exclusive breastfeeding has also been associated with decreased rates of cow milk protein allergy, but not food allergies in general. There is no evidence to support maternal avoidance of eggs and cow milk (during pregnancy and lactation) to help prevent the development of food allergies, but more research is necessary to determine the results of peanut avoidance during pregnancy and lactation. The research on the effects of early maternal exposure to peanuts or the maternal avoidance of peanuts has been inconclusive. The introduction of solid foods should occur between 4 to 6 months of age. Delaying the introduction of solid foods or specifically delaying the introduction of highly allergenic foods (cow milk protein, egg, fish, shellfish, peanuts, tree nuts, soy, and wheat) does not decrease the risk of developing food allergies. The early introduction of these highly allergenic foods may actually reduce the risk of food allergy.

PREP Pearls

- Hydrolyzed formulas may prevent the development of atopic disease and the cow milk protein allergy.
- Early introduction of highly allergenic food foods may reduce the risk of food allergy

ABP Content Specifications(s)

- Understand and apply current recommendations for feeding infants who are at risk for the development of food allergy

Suggested Readings

- Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015;372(9):803-813. doi: http://dx.doi.org/10.1056/NEJMoa1414850.
- Fleischer DM, Spergel JM, Assa'ad AH, Pongracic JA. Primary prevention of allergic disease through nutritional interventions. *J Allergy Clin Immunol Pract.* 2013;1(1):29-36. doi: http://dx.doi.org/10.1016/j.jaip.2012.09.003.
- Greer FR, Sicherer SH, Burks AW, Committee on Nutrition, Section on Allergy and Immunology. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*. 2008;121(1):183-191. doi: http://dx.doi.org/10.1542/peds.2007-3022.
- Thompson RL, Miles LM, Lunn J, et al. Peanut sensitisation and allergy: influence of early life exposure to peanuts. *Br J Nutr*. 2010;103(9):1278-1286. doi: http://dx.doi.org/10.1017/S000711450999376X.
- von Berg A, Filipiak-Pittroff B, Krämer U, et al. Allergies in high-risk school children after early intervention with cow's milk protein hydrolysates: 10-year results from the German Infant Nutritional Intervention (GINI) study. *J Allergy Clin Immunol*. 2013;131(6):1565-1573. doi: http://dx.doi.org/10.1016/j.jaci.2013.01.006.

Question 184

A 9-day-old Jewish newborn is brought to your office for evaluation of bleeding at his circumcision site. He was born at term via a cesarean delivery for failure to progress after an uncomplicated pregnancy. He was discharged from the hospital on the second day after birth. On the eighth day after birth, a ritual circumcision was performed by a certified mohel (expert in the Jewish rite of circumcision). Since that time, there has been continuous and significant bleeding at the circumcision site, requiring a change of blood-soaked bandages every 2 hours. There is no family history of bleeding disorders. The newborn's physical examination is remarkable only for mild pallor and a continuously oozing, circumferential circumcision wound around the glans of the penis. A complete blood cell count is normal. His prothrombin time is 12 seconds and partial thromboplastin time is 85 seconds. His von Willebrand antigen is 90% (normal range, 50%–150%) and von Willebrand activity is 95% (normal range, 50%–150%).

Of the following, the MOST likely diagnosis for the newborn in the vignette is

A. factor XIII deficiency
B. Glanzmann thrombasthenia
C. hemophilia A
D. protein C deficiency
E. type III von Willebrand disease

Correct Answer: C

The prolonged bleeding after circumcision in the newborn in the vignette suggests a congenital bleeding disorder. The formation of a functional clot requires 2 components, fibrin and platelets. Fibrin is the end-product of the coagulation cascade. The absence of any of the coagulation cascade factors can result in failure to form a clot and is associated with a prolonged prothrombin time (PT) or partial thromboplastin time (PTT). Prothrombin time and PTT are effective measures of the functionality and presence of the components of coagulation cascade, except for the conversion of fibrinogen to fibrin. The patient's prolonged PTT suggests an absence or dysfunction of a factor in the coagulation cascade. The gene for factor VIII is found on the X chromosome and is the subject of frequent spontaneous mutations. The deficiency of factor VIII is known as hemophilia A. Given that the child is male and therefore subject to X-linked disorders, factor VIII deficiency is the most likely diagnosis.

Factor XIII is responsible for clot stabilization. Since it plays a role after the formation of a clot, an absence of factor XIII would not prolong the PT or PTT; those are measures of the time to clot formation, not clot stabilization.

The most common congenital platelet function disorders are Bernard-Soulier syndrome (a disorder of platelet adhesion) and Glanzmann thrombasthenia (a disorder of platelet aggregation). Although both these disorders result in a bleeding phenotype, neither affects the clotting factor cascade, and therefore neither would result in a prolonged PTT.
Protein C is an anticoagulant protein. A deficiency of protein C would result in an increased risk of thrombosis, not an increased risk of bleeding.

Von Willebrand disease (vWD) is the most common congenital bleeding disorder. Von Willebrand factor is a linking factor that allows functional platelets to bind to fibrin to form a clot. Von Willebrand disease is the result of decreased function or absence of von Willebrand factor. Von Willebrand disease has multiple phenotypes ranging from mild to severe bleeding disorders that mirror the degree of dysfunction or absence of von Willebrand factor. There are several different types of vWD, including types 1, 2A, 2B, 2M, 2N, and 3. Although severe vWD could explain the neonate's presentation, his normal von Willebrand levels rule that out as the cause of his bleeding.

PREP Pearls

- Factor VIII deficiency, or hemophilia A, should be suspected in a male infant who presents with prolonged bleeding and a prolonged partial thromboplastin time.
- Hemophilia A is an X-linked disorder.

ABP Content Specifications(s)

- Recognize clinical findings associated with congenital coagulation factor deficiency

Suggested Readings

- Zimmerman B, Valentino LA. Hemophilia: in review. *Pediatr Rev.* 2013;34(7):289-295. doi: http://dx.doi.org/10.1542/pir.34-7-289

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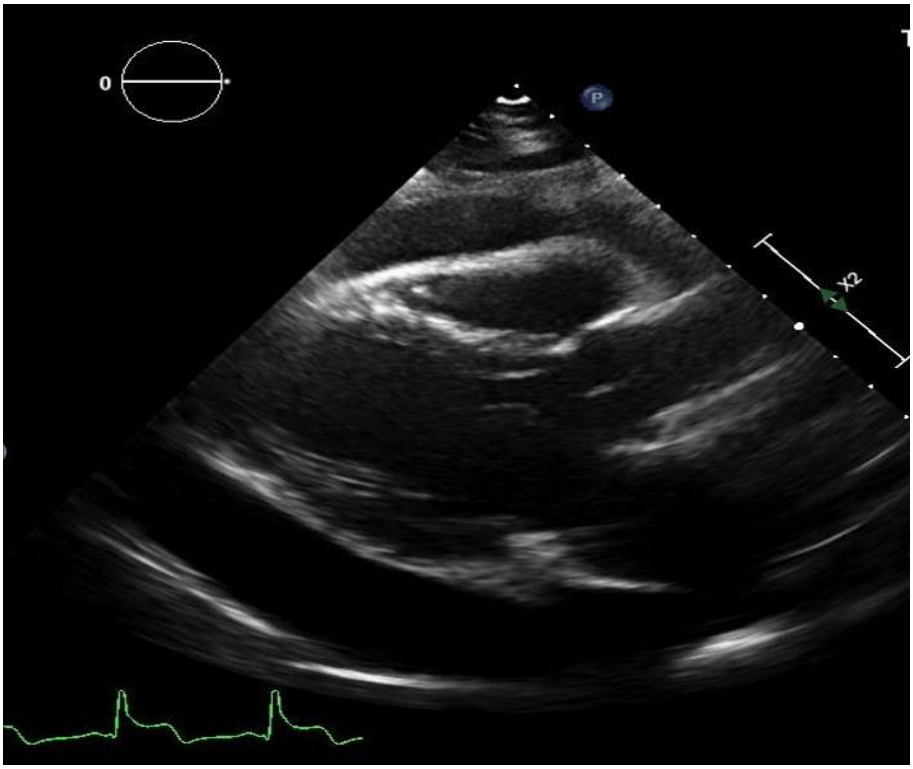
- Doering CB, Spencer HT. Replacing bad (F)actors: hemophilia. *Hematol Am Soc Hematol Educ Program.*2014;2014(1):461-467. doi: http://dx.doi.org/10.1182/asheducation-2014.1.461.
- Journeycake JM, Buchanan GR. Coagulation disorders. *Pediatr Rev*. 2003;24(3):83-91. doi: http://dx.doi.org/10.1542/pir.24-3-83.
- Sharathkumar AA, Pipe SW. Bleeding disorders. *Pediatr Rev.* 2008;29(4):121-130. doi: http://dx.doi.org/10.1542/pir.29-4-121.

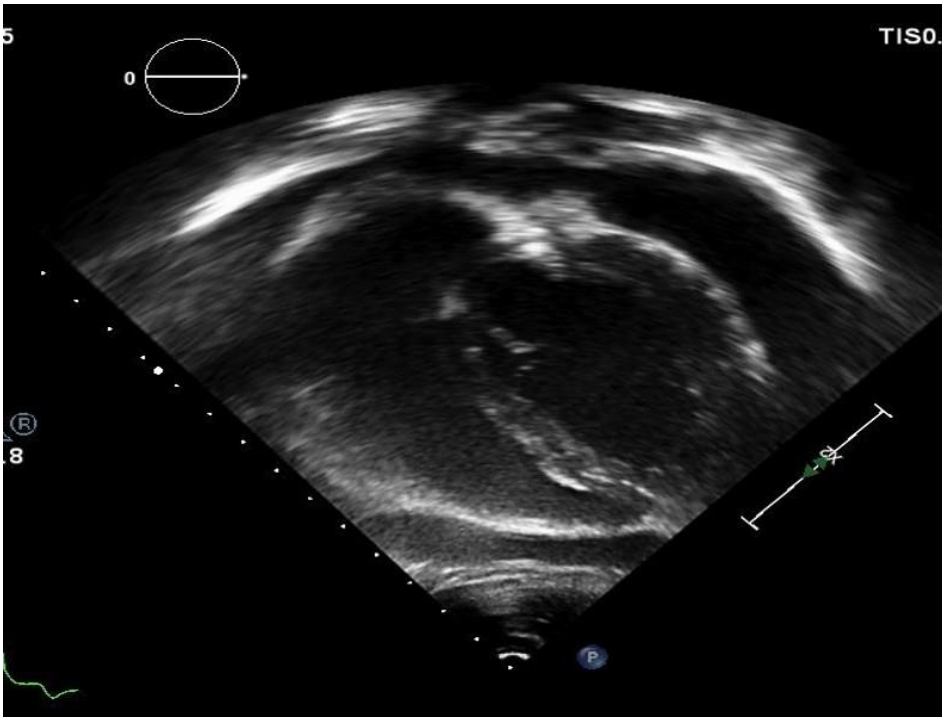
Question 185

A 12-year-old girl presents to the emergency department (ED) with chest pain, shortness of breath, and inability to sleep for 24 hours. She cannot lie flat on the stretcher as her chest pain becomes unbearable. She states that these symptoms have been present intermittently for approximately 2 months, but have worsened over the last 48 hours. One month ago, she had several days of right knee and left wrist swelling. She had been able to manage her pain with ibuprofen.

On physical examination, the girl's temperature is 37.5°C, heart rate is 130 beats/minute, respiratory rate is 28 breaths/minute, blood pressure is 120/70 mm Hg, and oxygen saturation is 98% in room air. Her breath sounds are diminished at the left base. Her cardiac examination is significant for muffled heart sounds and a soft friction rub, with no murmur or gallop. Her liver is palpable 1 cm below the right costal margin. The remainder of her examination is unremarkable. On chest radiography, there is an enlarged cardiac shadow, which obscures the left lung base. An echocardiogram shows a large pericardial effusion (Item Q185A , Item Q185B). Results of laboratory studies are shown:



Item Q185A: Echocardiogram for the girl described n the vignette. Courtesy of EA Greene



Item Q185B: Echocardiogram for the girl described n the vignette. Courtesy of EA Greene

Laboratory Test	**Patient Result**
White blood cells	3,000/mL (3 x 10^9/L)
Hemoglobin	9 g/dL (90 g/L)
Hematocrit	27%
Platelets	390 x 10^3/mL (390 ´ 10^9/L)
Sodium	141 mEq/L (141 mmol/L)
Potassium	4.2 mEq/L (4.2 mmol/L)
Chloride	104 mEq/L (104 mmol/L)
Bicarbonate	23 mEq/L (23 mmol/L)
Blood urea nitrogen	22 mg/dL (7.8 mmol/L)
Creatinine	1.4 mg/dL (124 mmol/L)
Erythrocyte sedimentation rate	85 mm/h

The only remarkable finding on urine dipstick test was 3+ protein.
Of the following, the MOST likely cause of this girl's pericardial effusion is

A. adenovirus infection
B. ibuprofen toxicity
C. lymphoma
D. occult trauma
E. systemic lupus erythematosus

Correct Answer: E
The clinical picture for the girl in the vignette is consistent with systemic lupus erythematosus (SLE). She presents with symptoms of positional chest pain and arthritis, which improved with ibuprofen. On physical examination, she is afebrile and has signs of a left pulmonary process, as well as a friction rub, suggesting a pericardial effusion that is confirmed on echocardiography. Her laboratory tests show protein in her urine, an elevated creatinine, and evidence of an inflammatory process as well as chronic disease, such as would be seen in SLE. The first presentation for SLE may be with a pericardial effusion. Nonsteroidal anti-inflammatory medication, such as ibuprofen or aspirin, is the usual initial medical intervention. Patients with hemodynamically significant effusions will require pericardiocentesis.

The girl has no current or preceding evidence of viral illness to suggest adenoviral infection. Lymphoma is unlikely because her chest radiographs showed no evidence of hilar adenopathy. A history of arthritis that responded to ibuprofen would be not be expected with lymphoma. Pericardial effusion from trauma would not be expected to cause symptoms over the course of 2 months, and would not be associated with elevated erythrocyte sedimentation rate or proteinuria. Evidence of trauma associated with this girl's symptoms might include rib fractures and possibly hematuria. Ibuprofen toxicity could present with an increased creatinine level and evidence of nephrotic syndrome or interstitial nephritis, just as SLE may. However, it would not be as likely to cause an elevated erythrocyte sedimentation rate or a pericardial effusion.

PREP Pearls
- Pericardial effusion can be acute or chronic.
- Systemic lupus erythematosus may present with a pericardial effusion.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of pericarditis

Suggested Readings

- Imazio M, Adler Y. Management of pericardial effusion. *Eur Heart J*. 2013;34(16):1186-1197. doi: http://dx.doi.org/10.1093/eurheartj/ehs372.
- Maharaj SS, Chang SM. Cardiac tamponade as the initial presentation of systemic lupus erythematosus: a case report and review of the literature. *Pediatr Rheumatol Online J*. 2015;13:9. doi: http://dx.doi.org/10.1186/s12969-015-0005-0.
- Ratnapalan S, Brown K, Benson L. Children presenting with acute pericarditis to the emergency department. *Pediatr Emerg Care*. 2011;27(7):581-585. doi: http://dx.doi.org/10.1097/PEC.0b013e31822251ba.
- Shakti D, Hehn R, Gauvreau K, Sundel RP, Newburger JW. Idiopathic pericarditis and pericardial effusion in children: contemporary epidemiology and management. *J Am Heart Assoc.* 2014;3(6):e001483. doi: http://dx.doi.org/10.1161/JAHA.114.001483.

Question 186

A 12-month-old girl is brought to your office for a health supervision visit. Her father asks you when she can start facing forward in her car seat.

Of the following, the MOST appropriate recommendation for this father is to switch to a front-facing position when

A. she is 15 months old
B. she is 18 months old
C. she is 24 months old
D. she is able to express her preference to sit front-facing
E. she weighs 20 pounds

Correct Answer: C

Motor vehicle-related crashes are the leading cause of death for US children and adolescents and nearly 400,000 each year are seen in the emergency department for injuries sustained in motor vehicle crashes. Child safety seats (CSSs) are an important mechanism to reduce the mortality and morbidity related to such crashes.

In 2011, the American Academy of Pediatrics issued updated recommendations to protect child passengers:

1. Infants and young children should ride rear-facing in an appropriate CSS until at least 2 years of age or when they outgrow their CSS by weight or height.
2. Once children are 2 years of age or they have outgrown their convertible car seat, they should ride forward facing in a CSS with a harness.
3. Once children have outgrown their CSS with a harness by weight or height, they should use a belt-positioning booster seat until they have grown to properly fit into a seat belt. This typically does not occur until the child has reached a height of 4 ft, 9 in (145 cm) and is 8 to 12 years of age.
4. Children who can use a seat belt should use one with both lap and shoulder restraints.
5. All children younger than 13 years of age should ride in the back seat.

In general, as children advance up to a different type of car seat, there is a decrease in the degree of protection the CCS provides. Child safety seats in the United States are highly regulated and standardized, and higher-priced CSSs do not necessarily confer greater protection. Weight and height limits for CSSs vary by manufacturer. For low birthweight and premature infants, caregivers should make note of the lower weight limits when selecting a CSS. Preterm infants are at risk for hypoxia and apnea when in car seats, so they should undergo a “car seat challenge” before discharge, whereby the infant’s cardiopulmonary status is measured while in the car seat for 90 min. For infants with cardiopulmonary compromise in a standard CSS, car beds can be used.

Motor vehicle-related crashes account for one-third of all deaths among US adolescents. Younger age while driving is associated with higher mortality, and one-quarter of adolescent drivers killed in motor vehicle-related crashes were intoxicated. Graduated driver licensing laws, whereby adolescent drivers are restricted to daytime driving and driving with fewer passengers, have been associated with reduced mortality in this age group. Discussions between parents and adolescents about driving while intoxicated, including strategies and alternatives to driving after an adolescent has become intoxicated, may help as well.

PREP Pearls

- Infants and young children should remain in a rear-facing child safety seat (CSS) until 2 years of age, or until the maximum height or weight for the child's CSS has been reached.
- With each "graduation" to a less restrictive CSS (ie, transitioning from a convertible CSS to a belt-positioning booster seat), a degree of protection is lost.
- Graduated driver licensing laws are an effective public health mechanism to reduce mortality related to motor vehicle crashes.

ABP Content Specifications(s)

- Recognize the major causes of automotive fatalities among young drivers (eg, drunk driving)
- Recommend appropriate car restraint systems, including car seats, based on the age and weight of the child, including those appropriate for premature infants

Suggested Readings

- Durbin DR. Child passenger safety. *Pediatrics*. 2011;127(4):e1050-e1066. doi: http://dx.doi.org/10.1542/peds.2011-0215.
- Hodges NL, Smith GA. Car safety. *Pediatr Rev.* 2014;35(4):155-160. doi: http://dx.doi.org/10.1542/pir.35-4-155.

Question 187

A 4-year-old girl is brought to your office for cold symptoms for the past 10 days. Her chief complaint is a mild sore throat, malaise, and fever to 38.3°C. The parents were not concerned because her symptoms were improving, but today the girl is complaining of chest pain and is refusing to eat or play. The pain is in the center of her chest and is worsened with deep breaths. She has no recent travel, and the only ill contact was a family friend from Eastern Europe who visited 2 weeks ago and had an upper respiratory infection. The girl has no significant past medical history, but she has an older sibling with autism and has not received vaccinations. Physical examination shows a female child in mild-moderate distress with a temperature of 38°C, heart rate of 150 beats/min, respiratory rate of 30 breaths/min, and blood pressure of 80/50 mm Hg. Her examination is significant for 2+ tonsils bilaterally with a thick gray exudate, shotty bilateral cervical adenopathy, intercostal retractions with occasional rales, distant S_1 and S_2, with an S_3 gallop. Her extremities are warm, with 2+ pulses bilaterally.

The electrocardiogram shows first degree A-V block with QTc prolongation and nonspecific ST-T wave changes.

Of the following, the BEST explanation for this clinical presentation is

A. Corynebacterium diphtheria
B. Haemophilus influenzae type B
C. methicillin-resistant Staphylococcus aureus
D. Streptococcus pneumoniae
E. Streptococcus pyogenes

Correct Answer: A

The 4-year-old girl in the vignette has clinical findings consistent with infection with *Corynebacterium diphtheriae*, causing respiratory diphtheria. Diphtheria takes its name from the Greek word diphthera, meaning leather, for the leathery appearance of the characteristic respiratory tract pseudomembrane. There are 4 biotypes of *C diphtheriae*: *gravis*, *intermedius*, *mitis*, and *belfanti*, and infection can cause respiratory disease, cutaneous disease, or asymptomatic carriage. With widespread availability of vaccines containing tetanus and diphtheria toxoid, respiratory diphtheria has remained rare in developed countries, but continues to be a serious health problem throughout sub-Saharan Africa, much of Asia, the Middle East, all countries of the former Soviet Union, in parts of South and Central America, and some Caribbean islands. Humans are the only known reservoir for *C diphtheriae*.

C diphtheriae produces a potent exotoxin that creates both local and systemic effects by entering cells and causing cell death. Not all strains of *C diphtheriae* are toxin-producing. In the skin, toxin can create chronic, indolent, nonhealing ulcers covered with a gray membrane, which may become coinfected with skin pathogens like *Staphylococcus aureus*and *Streptococcus pyogenes*. In the respiratory tract, the toxin causes local tissue destruction, which creates the pseudomembrane that is pathognomonic for diphtheria. This pseudomembrane is a tough layer of dead respiratory epithelial cells, fibrin, white and red blood cells, and bacteria firmly attached to the underlying respiratory mucosa.

After an incubation of 1 to 10 days (typically 2 to 5 days), patients present with an insidious onset of sore throat, malaise, anorexia, and low-grade fever less than 38.3°C. Diphtheria can infect any mucous membrane, but most commonly occurs in the pharynx and tonsils. After 2 to 3 days, the blue-white pseudomembrane forms and can then spread over the uvula, pharyngeal walls, and soft palate. In patients with severe disease, mucosal inflammation and reactive cervical lymphadenopathy lead to marked edema of the throat and neck, creating the characteristic "bull neck" with loss of the angle of the jaw, sternocleidomastoid borders, and medial border of the clavicles. Diphtheria patients often appear quite toxic, but rarely have fevers greater than 39.4°C because most of their symptoms are caused by the toxin, not the infection. Diphtheria toxin can be readily absorbed and cause complications in distant organ systems. Up to two-thirds of diphtheria cases develop ST-T wave changes, QTc prolongation, and/or first-degree heart block, usually as the respiratory symptoms begin to improve. Up to 25% of diphtheria patients have diminished heart sounds and a gallop. Myocarditis can develop 7 to 14 days after the onset of respiratory symptoms, but sometimes develops weeks later, and is a strong predictor for mortality. Neuritis is uncommon but much more likely in diphtheria patients with severe disease, which reflects the amount of toxin present. Paralysis of the soft palate and posterior pharyngeal wall are then followed by cranial neuropathies (usually III, VI, VII, and X). Peripheral neuritis develops weeks to months later, ranging from mild weakness to complete paralysis, without sensory involvement; this usually resolves completely.

Haemophilus influenzae type b, *Staphylococcus aureus*, and *Streptococcus pneumoniae* would not be expected to cause bacterial tonsillitis. While *Staphylococcus aureus* might cause myocarditis, and *Staphylococcus aureus* and *Streptococcus pneumoniae* might cause pericarditis

(with PR segment depression, ST segment elevation, and inverted T waves), these are not typical presentations or findings for these infections. *Streptococcus pyogenes* can cause tonsillitis, and first-degree heart block is a minor Jones criteria for diagnosing rheumatic fever. However, the onset of rheumatic fever is usually a few weeks after the tonsillitis, and other symptoms of rheumatic fever should be present. The most likely pathogen causing concomitant tonsillitis and electrocardiogram changes, especially in an unvaccinated child with an ill foreign contact, is *C diphtheriae.*

PREP Pearls

- Humans are the only known reservoir for Corynebacterium diphtheriae, and infection can cause respiratory disease, cutaneous disease, or asymptomatic carriage.
- Diphtheria patients often appear quite toxic, but usually have low-grade fevers less than 39.4°C because most of their symptoms are caused by the toxin, not the infection.
- Up to two-thirds of diphtheria patients develop myocarditis, with ST-T wave changes, QTc prolongation, and/or first-degree heart block, usually as the respiratory symptoms begin to improve, and up to 25% have diminished heart sounds and a gallop.

ABP Content Specifications(s)

- Recognize the clinical features associated with diphtheria

Suggested Readings

- American Academy of Pediatrics. Diphtheria. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed.* Elk Grove Village, IL: American Academy of Pediatrics; 2015:325-329.
- Wagner KS, White JM, Lucenko I, et al. Diphtheria in the postepidemic period, Europe, 2000-2009. *Emerg Infect Dis.*2012;18(2):217-225. doi: http://dx.doi.org/10.3201/eid1802.110987.
- Washington CH, Issaranggoon na ayuthaya S, Makonkawkeyoon K, Oberdorfer P. A 9-year-old boy with severe diphtherial infection and cardiac complications. *BMJ Case Rep.* 2014. doi: http://dx.doi.org/10.1136/bcr-2014-206085.

Question 188

A 10-year-old boy presents to your office for evaluation of recurrent episodes of gross hematuria over the last 6 months. His most recent episode started yesterday, along with symptoms of an upper respiratory tract infection. He denies dysuria, frequency, urgency, flank pain, or trauma. The boy's temperature is 37.7°C, heart rate is 76 beats/min, respiratory rate is 20 breaths/min, and blood pressure is 110/70 mm Hg. His physical examination findings are only significant for nasal congestion and a mildly inflamed oropharynx. A urine sample reveals cola-colored urine without visible blood clots.

Of the following, the boy's MOST likely diagnosis is

A. cystitis
B. immunoglobulin A nephritis
C. myoglobinuria
D. nephrolithiasis
E. systemic lupus erythematosus

Correct Answer: B

The differential diagnosis for red urine is quite extensive (Item C188A). An underlying etiology is more frequently identified in patients with gross hematuria than in those presenting with asymptomatic microscopic hematuria. On review of the history, physical examination, and urinalysis results for the boy in the vignette, the most likely diagnosis is immunoglobulin A (IgA) nephritis.

Item C188A. Differential Diagnoses of Gross Hematuria

Appearance	Source of Bleeding	Clinical Findings	Differential Diagnoses	Urinalysis findings
Cola, iced tea, or fruit punch colored	Glomerular or upper urinary tract	Usually painless hematuria, Symptoms related to underlying etiology	Glomerulonephritis	Positive hematuria finding on urine dipstick test; RBCs and RBC Casts on microscopy
			1) Hemoglobinuria: RBC hemolysis; 2) Myoglobinuria: Rhabdomyolysis	Positive hematuria finding on urine dipstick test, no RBCs on microscpy
Bright Red	Lower urinary tract	All have dipstick positive hematuria and RBC on microscopy		
		Flank pain radiating to groin;	Nephrolithiasis	Gravel/ dust/small stone in urine
		Dysuria; pain on micturition Fever may or may not be present	Urinary tract infection	Clots in urine, Urine dipstick also positive for nitrites, WBC's, and urine microscopy for WBC's, and bacteria
		History of renal trauma	Urinary tract trauma	
		No significant history;	Hypercalciuria*	Elevated urine calcium/creatinine ratio
			Renal cyst or mass Bladder cyst or mass Sickle cell disease	

*Hypercalciuria may present with pain or dysuria; RBC, red blood cells; WBC, white blood cells
Courtesy of G. Kapur

The presence of blood clots, with or without dysuria, is consistent with urinary tract bleeding. Bright red hematuria is usually indicative of lower urinary tract bleeding, whereas glomerular hematuria (as in nephritis) is described as cola-colored, tea-colored, or brown. Glomerulonephritis (GN) refers to an immune-mediated (noninfectious) inflammation of the renal parenchyma. Serum chemistries in GN show azotemia and dyselectrolytemias, depending on the severity of renal failure. In addition to standard renal function analysis, measurement of complement levels will further categorize patients as having hypocomplementemic GN (associated with a low C3) or normocomplementemic GN (associated with a normal C3) (Item C188B).

Item C188B. Complement Levels Associated with Different Causes of Acute Nephritis

Low C3 GN	Normal C3 GN
Postinfectious/Poststreptococcal GN	Immunoglobulin A GN
Membranoproliferative GN (more common)	Henoch-Schönlein purpura nephritis
Lupus nephritis	ANCA-associated GN
Shunt nephritis	Alport syndrome
Subacute bacterial endocarditis	Membranoproliferative GN (1/3 of cases)

ANCA, Antineutrophil cytoplasmic antibodies; GN, glomerulonephritis

Courtesy of G. Kapur

The timeframe for presentation of acute nephritis after infectious illness can provide clues to the cause. In patients with postinfectious GN, the infectious illness and acute nephritis are usually separated by 7 to 21 days. In contrast, the onset of acute GN within a few days of a viral infection is seen in IgA GN, Alport syndrome, and membranoproliferative GN (MPGN).
It can be difficult to differentiate MPGN from postinfectious GN, especially in patients with no history of preceding infection or in patients with a short interval between infection and the onset of nephritis. Since postinfectious GN is more common, patients should be presumptively treated for this and followed for resolution of hypocomplementemia and improvement in renal function. Hypocomplementemia resolves by 6 to 8 weeks in most cases of postinfectious GN, whereas persistently decreased C3 levels are suggestive of MPGN. In addition, nephrotic syndrome is more frequently seen in patients with MPGN than in postinfectious GN.

Recurrent gross hematuria is common with IgA nephritis and may occur with Alport syndrome, idiopathic hypercalciuria, Henoch Schönlein purpura, and nephrolithiasis, whereas recurrences are rare in postinfectious GN.

Pigmenturias (hemoglobinuria and myoglobinuria) can result in a positive dipstick test for blood, but lack the presence of red blood cells (RBCs) on microscopy. The urine will have clear sediment (lack of RBCs) with a red supernatant because of heme or myoglobin pigment. In patients with glomerular or lower urinary tract bleeding, the sediment is red (presence of RBCs) and the supernatant is clear. Signs and symptoms of myoglobinuria include myalgia, muscle weakness, and dark urine secondary to muscle breakdown. In children, this most often occurs with viral myositis, trauma associated with extensive muscle injury, excessive exertion, drug overdose, seizures, and metabolic disorders (hypokalemia increases the risk for muscle breakdown).

Flank pain radiating to the groin, hematuria (gross or microscopic), and passage of tiny particles in the urine are indicative of kidney stones. Without these signs and symptoms, nephrolithiasis is unlikely in this patient.

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease with multisystem involvement that may include skin, joints, kidneys, lungs, nervous system, serosal membranes, or other organs. Children with SLE may present with renal involvement alone, with hematuria and proteinuria on routine urine examination, nephrotic syndrome (proteinuria, edema, and hypoalbuminemia) or acute nephritis (acute renal failure, hematuria, and hypertension). Recurrent episodes of gross hematuria, as seen for the patient in the vignette, are not usually seen in SLE nephritis.

PREP Pearls

- Acute glomerulonephritis (GN) is characterized by the triad of cola-colored urine, hypertension, and azotemia.
- Patients with immunoglobulin A (IgA) nephropathy, Alport syndrome, idiopathic hypercalciuria, Henoch–Schönlein purpura, and nephrolithiasis may present with a history of recurrent episodes of gross hematuria.
- Immunoglobulin A nephropathy and postinfectious GN often present after an upper respiratory infection. With IgA nephropathy, the interval between the antecedent illness and nephritis is shorter.

ABP Content Specifications(s)

- Recognize the clinical findings associated with IgA nephropathy

Suggested Readings

- Azzarone G, Liewehr S, O'Connor K. Cystitis. *Pediatr Rev*. 2007;28(12):474-476. doi: http://dx.doi.org/10.1542/pir.28-12-474.
- Massengill SF. Hematuria. *Pediatr Rev.* 2008;29(10):342-348. doi: http://dx.doi.org/10.1542/pir.29-10-342.
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- VanDeVoorde RG III. Acute poststreptococcal glomerulonephritis: the most common acute glomerulonephritis. *Pediatr Rev.* 2015;36(1):3-13. doi: http://dx.doi.org/10.1542/pir.36-1-3.
- Varade WS. Nephritis. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DM, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:2358-2368.

Question 189

You are called to the full-term nursery to evaluate a 38-week-gestation neonate with hypoglycemia. The mother is a 34-year-old gravida 2, para 0 woman with type A1 gestational diabetes (hemoglobin $A1_C$ of 6.2%) and hypertension. The baby was delivered by cesarean delivery with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. In the delivery room, the baby's extremities were cool and her test strip glucose was 65 mg/dL (3.6 mmol/L). At 3 hours of life, she was brought to the nursery, where her test strip glucose was 30 mg/dL (1.7 mmol/L). The nurse is feeding the baby 10 mL of formula by mouth. You recommend repeating the test strip in 30 minutes and sending a plasma glucose test to the laboratory. The nurse asks why a plasma glucose sample needs to be checked.

Of the following, the BEST explanation for this baby is

A. a plasma glucose sample would most accurately diagnose hypoglycemia
B. poor circulation caused the test strip glucose to read falsely-high in the delivery room
C. the test strip glucose values are inaccurate because of maternal history
D. test strip glucoses are slow and usually inaccurate
E. test strip glucose read falsely-high due to inadequate blood sample volume

Correct Answer: A

For the neonate in this vignette, the best reason for obtaining a plasma glucose test is the limited accuracy of glucose oxidase test strips in diagnosing hypoglycemia in a neonate at low glucose levels. All neonates experience a physiologic drop in serum glucose levels in the first hour of life. Most neonates have sufficient glycogen stores, gluconeogenesis capacity, and appropriate glucose utilization such that glucose levels return to normal from the physiologic nadir within 4 hours. In comparison, neonatal hypoglycemia is characterized by persistently low glucose levels with or without clinical manifestations. A neonate who is symptomatic with jitteriness, irritability, or hypothermia should be treated with intravenous dextrose. Asymptomatic neonates should be treated if their plasma glucose levels are less than 40 mg/dL (2.2 mmol/L). Unfortunately, plasma glucose levels are not readily available at the bedside. Instead, point-of-care testing using glucose oxidase test strips is generally the test of choice. They are fast and generally reliable. However, at low glucose values, glucose oxidase test strips may vary by 10 to 20 mg/dL (0.6-1.1 mmol/L). Therefore, a plasma glucose test must be sent to confirm the diagnosis of neonatal hypoglycemia.

Poor perfusion in the delivery room would cause a falsely low glucose oxidase test strip.
In general, test strips are rapid and accurate in the normal range of glucose values. There is variability at high and low glucose values.

The maternal history of gestational diabetes does not alter the reliability of the test strips. A low blood volume would result in a falsely-low reading on a test strip, not a falsely high glucose value.

PREP Pearls

- Neonatal hypoglycemia diagnosed with glucose oxidase test strips must be confirmed with a plasma glucose test.
- Physiologic neonatal hypoglycemia should resolve by 4 hours of life.
- Neonates with symptomatic hypoglycemia should be treated with intravenous dextrose.
-

ABP Content Specifications(s)

- Understand the limitations associated with the rapid assessment of whole blood glucose concentrations utilizing glucose oxidase test strips in newborn infants

Suggested Readings

- Adamkin DH, Committee on Fetus and Newborn. Clinical report-postnatal glucose homeostasis in late-preterm and term infants. *Pediatrics*. 2011;127(3):575-579. doi: http://dx.doi.org/10.1542/peds.2010-3851.
- Sperling MA. Hypoglycemia. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:773-788.

Question 190

The parents of a 6-month-old infant are concerned about a bump on their son's penis that has been present for several weeks and does not appear to be painful. He has been afebrile and otherwise well. On physical examination, there is a 2 mm nontender, white, mobile mass just distal to the corona of the boy's penis. He is uncircumcised and you cannot fully retract his foreskin. His urethral meatus appears normal.

Of the following, the BEST next step in management of the infant's condition is

A. application of topical antibiotics
B. application of topical corticosteroids
C. daily stretching of the infant's prepuce
D. reassurance that no intervention is needed
E. referral to surgery for circumcision

Correct Answer: D
The mass described on the infant's penis in the vignette is smegma, an accumulation of desquamated epithelial cells and sebum trapped under the prepuce or foreskin. Smegma is benign and will disappear when the foreskin becomes retractile. It is normal for this 6-month-old infant to have a physiologic phimosis. In neonates, the foreskin is normally nonretractile and becomes increasingly retractable over time as the inner epithelium keratinizes. Physiologic phimosis is quite common up to the age of 5 or 6 years and is often present in older children as well. This is rare by adolescence, with only 1% of uncircumcised teenage boys having a nonretractile foreskin. Pathologic phimosis is the inability to retract the foreskin because of distal scarring. Until a boy's foreskin is retractile, there is no need to clean under the prepuce. Once the foreskin can be easily retracted, hygiene can be maintained by teaching children to gently retract their foreskin while bathing.

Topical antibiotics are not indicated because smegma is noninfectious. Topical corticosteroids can be used for the treatment of pathologic phimosis, but are not needed in this case. There is no reason to suggest stretching of the prepuce; in fact, aggressive retraction can lead to swelling that causes the foreskin to become trapped behind the glans, known as paraphimosis. Circumcision is not indicated for physiologic phimosis or smegma, but is recommended in some cases of pathologic phimosis.

PREP Pearls

- Smegma is a normal accumulation of epithelial cells and sebum under an infant's prepuce.
- Physiologic phimosis is quite common up to the age of 5 or 6, and can be normal at older ages as well. Most physiologic phimosis resolves spontaneously before puberty.

ABP Content Specifications(s)

- Recognize the significance of smegma accumulation beneath an infant's prepuce

Suggested Readings

- McGregor TB, Pike JG, Leonard MP. Pathologic and physiologic phimosis: approach to the phimotic foreskin. *Can Fam Physician.* 2007;53(3):445-448. http://www.cfp.ca/content/53/3/445.full.pdf+html.
- Wan S, Wang Y, Gu S. Epidemiology of male genital abnormalities: a population study. *Pediatrics*. 2014;133(3):e624-e627. doi: http://dx.doi.org/10.1542/peds.2013-2285.

Question 191

You are seeing a 16-year-old adolescent boy with cystic fibrosis in your office. Over the last 5 years, he has had poor adherence to medical recommendations, with frequent hospital admissions and marked losses in weight and lung function. In addition, he smokes cigarettes, frequently drinks beer, and has dropped out of school. His parents recently divorced. His weight and body mass index are at the fifth percentile. His forced expiratory volume in 1 second is 45% of predicted. His sputum cultures are growing a pan-resistant, mucoid *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. Computed tomography of the chest reveals bilateral bronchiectasis, most notably at the upper lobes. The adolescent and his parents have repeatedly declined gastrostomy tube placement for supplemental nutrition. On multiple occasions, you and the cystic fibrosis team have counseled the adolescent regarding the importance of managing his chronic disease. He has told at least 1 team member: "everything will be fine once I qualify for lung transplantation."

Of the following, the MOST appropriate next step in management of this patient is to

A. refer him for lung transplantation
B. refer him for palliative care
C. refer him for psychological/psychiatric support services
D. seek a court order for directly observed therapies
E. transfer his care to an adult cystic fibrosis center

Correct Answer: C
The most appropriate next step in management of this adolescent is referral for psychological/psychiatric support services. The 16-year-old patient in the vignette is experiencing many of the complications of late-stage cystic fibrosis (CF). A comprehensive approach to care across the life spectrum is advocated for patients with CF and many other chronic diseases in which increased survival has led to a concomitant increase in complications and comorbidities. The complex care regimen required in CF includes multiple medications, nutritional support, and airway clearance therapies. Difficulties families experience with managing care and nonadherence with various treatments may reflect the chronic stress of coping with a life-threatening illness; these patients often present with depression and/or anxiety.

Cystic fibrosis care has evolved over the years. Newborn screening for CF, now implemented in all 50 US states, has facilitated optimization of nutrition and respiratory health in affected children from infancy. Increasingly effective management with nutritional advancements, airway clearance options, inhaled antibiotics, and the newest CF transmembrane regulator modification agents has led to increased disease survival. The median age of survival for a child born and diagnosed with CF in 2010 is now estimated at 39 years.

Increased survivability allows patients to pursue life goals that were previously less available such as higher education, marriage, and parenthood. Accompanying the increased lifespan, however, has been an increase in disease and treatment-associated complications and comorbidities. These include, but are not limited to, an increased prevalence of CF-related liver disease, CF-related diabetes with attendant microvascular and renal complications, as well as vestibular and renal sequelae from years of aminoglycoside treatment for chronic pseudomonal infection. Lung transplantation may be indicated for end-stage pulmonary disease and frequent infections, giving further hope for disease survival. However, availability of organs is limited and patients may succumb to disease while awaiting transplantation. As children become adolescents and young adults, transition of care may be an additional stressor for the patient and their family; care providers may change and the primary responsibility for disease management shifts from the parent to the affected individual.

Adherence to CF treatment has historically been greater with respiratory and gastrointestinal medications compared with nutritional supplementation and chest physiotherapy. Treatment adherence worsens with age and disease severity. Quality of life may suffer with the burden of chronic disease management.

Reported rates of depression in patients with CF range from 9% to 29% in children and from 13% to 33% in adults. Similarly, rates of anxiety range from 30% to 33%. Parents and caregivers also demonstrate increased rates of depression and anxiety. High levels of depression have been associated with less positive beliefs regarding medications, which may then affect treatment adherence. Furthermore, depressed patients with CF require hospitalization at a rate more than 3 times that of their nondepressed counterparts. As seen with any patient with depression, those affected with CF are at increased risk for substance abuse and school failure.

For the patient in the vignette, a court order for directly observed therapies (DOTs) is not likely to afford a feasible or long-term option for chronic disease management. The DOTs are generally considered for treatment regimens of defined lengths, such as in the treatment of tuberculosis. Transfer of care to an adult center is not likely to result in improved adherence. Although the age recommended for transition to adult care is highly variable across centers, the boy in the vignette is somewhat young for this change. Most patients will transition to adult care between 17 and 23 years of age. Patients often have difficulty with care transitions, and every attempt should be made, ideally before implementation, to engage the patient in his or her own disease management.

Lung transplantation referral is recommended when the forced expiratory volume in 1 second (FEV_1) is 30% or less of that predicted. Referral is also appropriate when the FEV_1 is greater than 30%, but is demonstrating rapid and progressive decline. Psychosocial problems that cannot be resolved are a relative contraindication for transplantation. Candidates for a lung transplant must be free of substance addiction for at least 6 months. Nutritional concerns are also critically important, and have been identified as a negative predictor for surgical outcome.

In general, patients with CF and their caregivers should be engaged in care directive and end-of-life discussions. Palliative care focuses on the management of symptoms and improving quality of life, regardless of prognosis. In a survey of adults with CF, nearly 80% reported feeling comfortable talking to their care provider about advance directives. Therefore, palliation may be viewed as an option in those patients who wish to forego life-extending options such as transplantation. Patient age, disease severity, and mental health concerns should be considered and addressed; a unilateral referral to palliative care without addressing reasons for nonadherence is not advocated.

PREP Pearls

- Individuals with cystic fibrosis and other chronic diseases often have a significant burden of disease management.
- Depression and anxiety are frequently overlooked comorbid conditions in chronic disease.
- Depression and anxiety may adversely affect medication adherence and may be modifiable factors in disease progression.

ABP Content Specifications(s)

- Recognize the importance of planning for survival into adulthood for patients with cystic fibrosis

Suggested Readings

- Arias Llorente RP, Bousoño García C, Díaz Martín JJ. Treatment compliance in children and adults with cystic fibrosis. *J Cyst Fibros.* 2008;7(5):359-367. doi: http://dx.doi.org/10.1016/j.jcf.2008.01.003.
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Question 192

A 5-year-old boy is brought to your office with several months of back pain. The pain is diffuse across his lower back, worsens with activity, and resolves with rest. The pain does not radiate down his legs. On physical examination, he has a lordotic posture, and there is no scoliosis, sacral hair, or skin abnormalities. His lower extremities are thin and weak. He uses the Gowers maneuver to rise from the floor. His patellar deep tendon reflexes are normal; on plantar stroking, his toes go downward.

Of the following, the MOST likely diagnosis is

A. Becker muscular dystrophy
B. spinal muscular atrophy
C. tethered spinal cord
D. transverse myelitis
E. vitamin B12 deficiency

Correct Answer: C
The boy in the vignette has chronic back pain and lower extremity weakness. This suggests a disorder of the spinal cord (a myelopathy) with involvement of exiting nerve roots. Of the choices, the most likely diagnosis is a tethered cord. Tethered cord syndrome occurs when the caudal end of the spinal cord adheres to adjacent structures. This can occur as an isolated abnormality or in association with myelomeningocele, tumors, fatty filum etc. As the child grows, the spinal cord is stretched. This results in dysfunction of the conus and exiting nerve roots. Signs and symptoms of tethered cord include leg length discrepancy, foot deformities, scoliosis, neurogenic bladder, and recurrent urinary tract infections. Cutaneous signs are not always present, but there can be lumbar hypertrichosis, capillary hemangioma, dermal sinus tract, or a skin appendage.

Vitamin B_{12} deficiency causes a myelopathy that affects the posterior columns of the spinal cord. This results in decreased proprioception (resulting in falls), leg weakness, and spasticity, but not back pain. Transverse myelitis is an inflammatory myelopathy that presents acutely with pain and signs of spinal cord dysfunction; however, this boy's symptoms have been chronic. Other causes of myelopathy include mass lesions like hematomas or spinal cord tumors, spinal cord syrinx, trauma, genetic disorders such as hereditary spastic paraparesis, and infections including meningitis, myelitis, and abscesses. The clinical presentation should direct the initial diagnostic evaluation.

Becker muscular dystrophy and spinal muscular atrophy are disorders of the muscle and motor neuron, respectively; they are not typically associated with back pain. Becker muscular dystrophy causes muscle weakness with hyporeflexia or areflexia; spinal muscular atrophy causes weakness with areflexia in both arms and legs. These are not the correct diagnoses for the boy in the vignette.

PREP Pearls

- Chronic back pain with lower extremity weakness can be a sign of spinal cord disease
- Scoliosis, leg length discrepancy, and foot deformities can be a sign of tethered cord syndrome.
-

ABP Content Specifications(s)

- Understand the various etiologies of spinal cord disease

Suggested Readings

- Bui CJ. Tethered cord syndrome in children: a review. *Neurosurg Focus*. 2007;23(2):E2. http://thejns.org/doi/pdf/10.3171/FOC-07/08/E2.
- Liptak GS, Dosa NP. Myelomeningocele. *Pediatr Rev.* 2010;31(11):443-450. doi: http://dx.doi.org/10.1542/pir.31-11-443.

Question 193

A 3-year-old boy with severe obstructive sleep apnea underwent a tonsillectomy and adenoidectomy. There were no reported complications in the operating room and there was minimal bleeding. Postoperatively, he is admitted to the hospital for observation. Within 6 hours after the procedure, he develops a progressive oxygen requirement and respiratory distress. Vital signs show a temperature of 37°C, pulse of 120 beats/min, respiratory rate of 40 breaths/min, and blood pressure of 100/60 mm Hg. Pulse oximetry is 85% on 100% non-rebreather facemask. Physical examination reveals a tired-appearing child in severe respiratory distress. Tonsillectomy surgical sites appear clean and intact, with minimal bleeding. He has moist mucous membranes. Heart is regular. He is breathing shallowly, with subcostal and intercostal retractions. Air entry is adequate and equal bilaterally, with scattered crackles throughout. Abdomen is soft, nontender, and non-distended with no organomegaly. Arterial blood gas analysis reveals pH of 7.5, $PaCO_2$ of 30 mm Hg, and PaO_2 of 50 mm Hg. Chest radiograph is shown in Item Q193 .

Item Q193: *Chest radiograph for the boy described in the vignette. "Reprinted with permission from Durmowicz AG. Pulmonary Edema in 6 Children With Down Syndrome During Travel to Moderate Altitudes. Pediatrics 2001;108(2): 443-447"*

Of the following, the MOST likely cause of his respiratory failure is

A. congestive heart failure
B. pneumonia
C. pulmonary edema
D. surgical bleeding
E. upper airway obstruction

Correct Answer: C
The boy in the vignette has respiratory failure after a tonsillectomy and adenoidectomy procedure, which he underwent due to severe obstructive sleep apnea. The clinical picture of rapid, shallow breathing, crackles, and radiographic appearance indicate that he has pulmonary edema.

Starling's law states that forces favoring filtration out of any capillary bed include increased capillary permeability, intraluminal hydrostatic pressure, and interstitial oncotic pressure, whereas forces preventing filtration include interstitial hydrostatic pressure and intraluminal oncotic pressure. Pulmonary edema, similar to edema in any tissue bed, occurs because of Starling forces favoring filtration out of capillary bed. Pulmonary edema is commonly caused by increased capillary permeability in sepsis and pneumonia, by increased intraluminal hydrostatic pressure in heart failure, and by decreased intraluminal oncotic pressure in hypoproteinemia.

Clinical signs of pulmonary edema include rapid, shallow breathing, hypoxia, retractions, and crackles. Tachypnea is caused by the effect of increased fluid on the pulmonary interstitial stretch receptors, which feed back to the brainstem respiratory center. This can cause respiratory alkalosis, as is seen in the boy in this vignette, unless respiratory failure is so profound as to cause hypercapnia. Primary cardiac etiologies can be ruled out as a cause of this child's pulmonary edema by the lack of significant tachycardia, hepatomegaly, jugular venous distention, diminished peripheral perfusion, and lower extremity edema. Treatment varies widely based on the primary etiology. Radiographic findings also vary based on etiology and can include consolidation in the case of pneumonia, increased interstitial lung markings, and prominent pulmonary vasculature in the case of heart failure.

The child in this vignette has postobstructive pulmonary edema following a tonsillectomy and adenoidectomy. Pulmonary edema can occur during or after the relief of either acute or chronic upper airway obstruction such as seen in croup, epiglottitis, postextubation subglottic edema, or obstructive sleep apnea. The etiology of postobstructive pulmonary edema is uncertain. One theory states that breathing against a severe airway obstruction requires negative intrathoracic pressure that increases venous return and decreases cardiac output, favoring filtration of fluid into the alveoli and pulmonary interstitium. Another possibility is that positive end-expiratory pressure is required to overcome an upper airway obstruction, and its sudden removal after a corrective therapy favors fluid transudation. Treatment of postobstructive pulmonary edema includes oxygen, diuretics, and in more severe cases, application of positive end-expiratory pressure either noninvasively or with intubation and mechanical ventilation.

Congestive heart failure can be a cause of pulmonary edema, but it is less likely for the child in this vignette because there is no hepatomegaly or signs of decreased cardiac output. Pneumonia can occur postoperatively, but it is unlikely to cause new symptoms within 6 hours of the procedure. Surgical bleeding can be a cause of respiratory failure postoperatively after a tonsillectomy and adenoidectomy, but the surgical sites are clean and intact. Upper airway obstruction as a cause of respiratory failure presents with stridor and deep retractions, as opposed to hypoxia, tachypnea, and crackles.

PREP Pearls

- Pulmonary edema presents with rapid, shallow breathing, hypoxia, and crackles.
- Postobstructive pulmonary edema can occur in conditions of upper airway obstruction before and after relief of obstruction.
-

ABP Content Specifications(s)

- Recognize the clinical and laboratory manifestations associated with respiratory failure of various etiologies

Suggested Readings

- Nitu ME, Eigen H. Respiratory failure. *Pediatr Rev.* 2009;30(12):470-478. doi: http://dx.doi.org/10.1542/pir.30-12-470.
- Van Kooy MA, Gargiulo RF. Postobstructive pulmonary edema. *Am Fam Phys.* 2000;62(2):401-404. http://www.aafp.org/afp/2000/0715/p401.html.

Question 194

A 10-year-old previously healthy girl is brought to your clinic for fatigue and excessive hair loss for the past month. She reports chronic dry skin and occasional constipation. Her appetite is normal. Vital signs show a temperature of 36.8°C, blood pressure of 90/56 mm Hg, heart rate of 60 beats/min, respiratory rate of 16 breaths/min, weight of 33 kg (50th percentile), height of 135 cm (32nd percentile), and body mass index of 18 kg/m^2 (68th percentile). Physical examination is significant for pallor and dry, thinning hair. Her thyroid is enlarged twice the normal size, firm and rubbery with heterogeneous texture, and without palpable nodules. She has no cervical lymphadenopathy. Her skin is mildly dry and deep tendon reflexes show a delayed return. The physical examination is otherwise unremarkable.

Of the following, the BEST test to establish the diagnosis is

A. fine-needle aspiration thyroid biopsy
B. thyroid-stimulating hormone
C. thyroid ultrasonography
D. thyroid uptake and scan
E. urinary iodine level

Correct Answer: B
The patient described in the vignette displays signs and symptoms of hypothyroidism. These symptoms include fatigue, hair loss, and constipation. Findings on her physical examination consistent with hypothyroidism include bradycardia, pallor, dry hair and skin, and delayed return of deep tendon reflexes. The description of her thyroid as enlarged, firm, rubbery, and with heterogeneous texture is typical of Hashimoto (or autoimmune) thyroiditis. To diagnose hypothyroidism, thyroid-stimulating hormone (TSH) is the primary test and will be elevated. Free thyroxine (FT4) is also useful and will be low with significant hypothyroidism. In mild cases, the FT4 will be normal at the expense of a mildly elevated TSH level. Many laboratories will reflexively run a FT4 level if the TSH is elevated. Thyroid peroxidase and anti-thyroglobulin antibodies are often detectable in Hashimoto thyroiditis, and would likely be positive in this patient.

Hashimoto thyroiditis is the most common cause of acquired hypothyroidism and results in autoimmune destruction of the thyroid gland. Females in adolescence are more often affected than males. In addition to those described previously, other common signs and symptoms of hypothyroidism include menstrual irregularities in females, poor linear growth, and weight gain that is usually mild. Thyroid function can be normal in Hashimoto thyroiditis, but the individual remains at risk for hypothyroidism in the future. Hashimoto thyroiditis is also the most common cause of goiter in children. Goiter can also occur in Graves' disease, which is autoimmune activation of the thyroid gland and results in hyperthyroidism. The thyroid gland in Graves' disease is usually larger, less firm, and more homogeneous. Other causes of thyroid enlargement include multinodular goiter, iodine deficiency, other thyroiditis, and rarely, thyroid cancer. Thyroid cancer usually presents as a thyroid nodule.

Fine-needle aspiration thyroid biopsy would not make the diagnosis of hypothyroidism. It would make a histologic diagnosis of Hashimoto thyroiditis, but is not used as a diagnostic test for this disorder. It is the preferred preoperative diagnostic test for thyroid cancer. Thyroid ultrasonography may show features of Hashimoto thyroiditis, but would not be diagnostic of hypothyroidism. Thyroid uptake and scan would be diagnostic of Graves' disease, but not hypothyroidism. A urinary iodine level would be informative only in the setting of iodine deficiency, but would not diagnose hypothyroidism.

PREP Pearls

- Thyroid-stimulating hormone level is the best initial test for hypothyroidism and will be elevated in hypothyroidism.
- Hashimoto thyroiditis is the most common cause of acquired hypothyroidism in children and adolescents.
- Hashimoto thyroiditis is the most common cause of thyroid enlargement. A firm, rubbery thyroid gland with heterogeneous texture is typical of Hashimoto thyroiditis.

ABP Content Specifications(s)

- Recognize the clinical features associated with Hashimoto thyroiditis
- Plan the appropriate diagnostic evaluation to distinguish among Hashimoto thyroiditis, other causes of thyroid enlargement, and hypothyroidism

Suggested Readings

- De Luca F, Santucci S, Corica D, et al. Hashimoto's thyroiditis in childhood: presentation modes and evolution over time. *Ital J Pediatr*. 2013;39:8. doi: http://dx.doi.org/10.1186/1824-7288-39-8.
- Diaz A, Lipman Diaz EG. Hypothyroidism. *Pediatr Rev*. 2014;35(8):336-347. doi: http://dx.doi.org/10.1542/pir.35-8-336.

Question 195

A previously healthy 4-year-old boy was brought to your office for evaluation of fever, irritability, and poor oral intake for 3 days. Today, he began drooling and his mother noticed sores in his mouth (Item Q195). In the office, his temperature is 40°C, heart rate is 112 beats/min, and respiratory rate is 24 breaths/min. He is ill appearing and irritable, but consolable. Physical examination reveals numerous vesicles with red halos on the buccal mucosa. The gingiva is intensely erythematous and edematous. He appears mildly dehydrated. The remainder of his examination is unremarkable.

Item Q195: Oral lesions as seen in the boy described in this vignette. Reprinted with permission from Pickering LK, et al.. Red Book Online. Elk Grove Village, IL: American Academy of Pediatrics.

Of the following, the MOST likely diagnosis is

A. acute necrotizing gingivitis
B. aphthous ulcerations
C. hand-foot-mouth disease
D. herpangina
E. primary herpetic gingivostomatitis

Correct Answer: E

The boy in the vignetteexhibits the common features of primary herpetic gingivostomatitis. This condition presents most often in children younger than 5 years of age, though it may occur at any age with the first bout of herpes simplex virus. On physical examination, numerous small vesicles on an erythematous base will be noted (Item C195) on the anterior palate, tongue, buccal mucosa, and gingivae. These lesions are painful and evolve into shallow ulcers. The gingivae may be erythematous, inflamed, and friable. Perioral lesions on the lips and nearby cheeks or chin may be present as well. The enanthem frequently follows several days of high fever, irritability, and malaise. As the lesions progress, many patients develop poor oral intake, drooling, and foul-smelling breath; some may be quite ill-appearing and are at risk for dehydration. Herpetic gingivostomatitis is self-limited and will resolve in 1 to 2 weeks.

Item C195: *Numerous small vesicles noted on the anterior palate, tongue, buccal mucosa, and gingivae in herpetic gingivostomatitis. Reprinted with permission from Pickering LK, et al.. Red Book Online. Elk Grove Village, IL: American Academy of Pediatrics.*

Supportive therapy aimed at relief of pain and fever, plus management of fluid status, is the mainstay of treatment. Antiviral therapy with oral acyclovir may be considered for those with more serious signs or symptoms, and systemic therapy should be used in immunodeficient patients. Treatment is most effective when initiated in the first 3 days of disease.

Healthcare providers must be comfortable differentiating primary herpetic gingivostomatitis from the other common infectious or benign causes of oral lesions in children. Acute necrotizing gingivitis (trench mouth or Vincent stomatitis) is a painful ulcerative condition that primarily affects adolescents and young adults with poor oral hygiene, immunosuppression, or malnutrition. On physical examination, in addition to ulcers, the gingival margins and interdental papillae are markedly inflamed and may be hemorrhagic. A grayish-white pseudomembrane may cover the ulcers. Treatment includes debridement, oral antibiotics, and oral rinses.

Aphthous ulcerations (canker sores) are painful and may be recurrent. These usually occur as 1 to 3 shallow ulcers 3 to 6 mm in diameter, with well-defined borders and a small surrounding rim of erythema, and covered with a grayish white membrane. The etiology is not well understood, but is believed to be multifactorial. Topical steroids and analgesics may improve symptoms until the ulcers heal spontaneously without scarring in 1 to 2 weeks.

Hand-foot-mouth disease, caused by an enteroviral infection, is commonly seen in young children 1 to 4 years of age. It presents with both an exanthem and enanthem. The exanthem consists of gray-white vesicles surrounded by erythema primarily on the palms and soles, and may also involve the buttocks and distal extremities. The enanthem presents as 1- to 3-mm vesicles on an erythematous base involving the buccal mucosa, palate, tongue, uvula, and anterior tonsillar pillars. The oral lesions may be mildly painful, requiring supportive care, and resolve in a few days to a week. Typically, the enanthem of hand-foot-mouth disease occurs concurrently with the exanthem.

Herpangina is an enanthem also caused by enteroviral infection, most often seen in children ages 3 to 10 years. Tiny vesicles and erythematous ulcers occur on the posterior pharynx, involving the soft palate, uvula, and tonsillar pillars, and resolve spontaneously within 1 week.

PREP Pearls

- Primary herpetic gingivostomatitis occurs with a first bout of herpes simplex virus.
- Prodomal high fever and irritability, followed by painful vesicles that ulcerate on the anterior palate, tongue, and buccal mucosa, with intensely inflamed gingivae are characteristic of primary herpetic gingivostomatitis.
- Antiviral therapy may be considered for those with significant illness and is recommended for immunodeficient patients.

ABP Content Specifications(s)

- Differentiate clinically among hand-foot-mouth disease, herpangina, acute herpetic gingivostomatitis, aphthous ulcerations, and benign lesions of the oral cavity

Suggested Readings

- Chayavichitsilp P, Buckwalter J, Krakowski A, Friedlander S. Herpes simplex. *Pediatr Rev.* 2009;30(4):119-130. doi: http://dx.doi.org/10.1542/pir.30-4-119.
- Krol DM, Keels MA. Oral conditions. *Pediatr Rev.* 2007;28(1):15-22. doi: http://dx.doi.org/10.1542/pir.28-1-15.
- Paller AS, Mancini AJ. Exanthematous diseases of childhood. *Hurwitz Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood and Adolescence.* 4th ed. Philadelphia, PA: Saunders Elsevier; 2011:370-389.
- Paller AS, Mancini AJ. Viral diseases of the skin. *Hurwitz Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood and Adolescence.* 4th ed. Philadelphia, PA: Saunders Elsevier; 2011:348-369.
- Ruderfer D, Krilov L. Herpes simplex viruses 1 and 2. *Pediatr Rev*. 2015;36(2):86-90. doi:10.1542/pir.36-2-86.
- Zaoutis T, Klein JD. Enterovirus infections. *Pediatr Rev.* 1998;19(6):183-191. doi: http://dx.doi.org/10.1542/pir.19-6-183.

Question 196

You are seeing a newborn in your office who was noted at birth to have a single congenital abnormality with an otherwise unremarkable physical examination and no obvious facial dysmorphology. You are unsure whether to refer the newborn to a geneticist for evaluation and call the geneticist on staff at your hospital for advice.

Of the following, the isolated clinical finding that MOST warrants referral to this specialist is

A. clubfoot
B. deafness
C. horseshoe kidney
D. polydactyly of the hand
E. single transverse palmar crease

Correct Answer: B
The isolated clinical finding that would most warrant a referral to a geneticist is congenital deafness. Up to 60% of cases of congenital and early-onset hearing loss are caused by genetic factors. In more than 400 genetic syndromes, hearing loss is a feature and more than 100 genes are associated with nonsyndromic genetic hearing loss. Of the patients with hearing loss from a genetic cause, 70% are nonsyndromic and can have an autosomal dominant (15%), autosomal recessive (80%), X-linked (1%), or mitochondrial (1%) inheritance pattern. It is important to take a detailed 3-generation family history to look for a particular genetic etiology.

Approximately 30% of genetic hearing loss is syndromic; thus, a thorough physical examination is essential in evaluating a child with hearing loss. Practitioners should be alert to any of the following abnormal findings:

- Abnormal pigmentary anomalies
- Asymmetry of facial features
- Cardiac anomalies (especially long QT syndrome)
- Cleft lip or palate
- Heterochromia of the irides
- Malformation of an auricle
- Microcephaly
- Renal abnormalities
- Skin tags/ear pits near the auricle
- Thyroid disease

Some physicians advocate for temporal bone imaging in these cases to look for an enlarged vestibular aqueduct, which would be suggestive of Pendred syndrome. If a particular syndrome is suspected, gene sequencing specific to that syndrome is warranted. If the patient is nonsyndromic, then it is commonly recommended to begin with *GJB2* and *GJB6* gene mutation analysis. Fifty percent of autosomal recessive nonsyndromic hearing loss is due to *GJB2* and *GJB6* gene mutations, which encode for connexin 26 and connexin 30 gap junction proteins. If the result of this testing is negative, it is appropriate to perform a hereditary hearing loss next-generation sequencing panel that can test for many known nonsyndromic gene mutations in a single blood test.

Acquired hearing loss can be caused by various infectious diseases. Cytomegalovirus (CMV) is the most common nongenetic cause of hearing loss in children; therefore, a urine CMV test should be performed at the same time as genetic testing in infants presenting with congenital hearing loss. The CMV testing is most accurate when performed in the first 6 weeks after birth. Meningitis is another leading cause of acquired permanent hearing loss, whereas otitis media can result in reversible hearing loss. It is also important to inquire about any history of ototoxic drug use (eg, aminoglycosides, cisplatin), birth hypoxia, or hyperbilirubinemia.

The early identification of hearing loss is important because early intervention has clearly been shown to be effective in promoting speech and language acquisition in deaf and hard-of-hearing

children. As a result, newborn hearing screening is now mandated across the United States. However, not all types of hearing loss are present at birth. Hearing loss can develop throughout childhood and adolescence, making hearing screening a vitally important aspect of health supervision.

Clubfoot, horseshoe kidney, or polydactyly of the hand presenting as an isolated finding would not necessitate a genetics referral, because these anomalies are commonly multifactorial and on their own do not suggest a genetic etiology. The isolated finding of a single transverse palmar crease can be seen in normal individuals, but in pediatrics, trisomy 21 must be considered, especially if other associated dysmorphology is present. Children with intellectual disability, autism spectrum disorder, or multiple congenital anomalies warrant consideration of a genetic diagnosis.

PREP Pearls

- Congenital deafness as an isolated clinical finding warrants referral to a geneticist because up to 60% of cases of congenital and early-onset hearing loss are caused by genetic factors.
- Of patients who have hearing loss with genetic etiologies, 70% are nonsyndromic and 30% are syndromic.
- It is imperative to obtain a detailed 3-generation family history, as well as perform a comprehensive physical examination, to look for clues suggesting a genetic etiology in a patient presenting with congenital or early-onset hearing loss.
- Children with intellectual disability, autism spectrum disorder, or multiple congenital anomalies warrant consideration of a genetic diagnosis.

ABP Content Specifications(s)

- Recognize the need for appropriate referral for genetic counseling

Suggested Readings

- Alford RL, Arnos KS, Fox M, et al. American College of Medical Genetics and Genomics guideline for the clinical evaluation and etiologic diagnosis of hearing loss. *Genet Med.* 2014;16(4):347-355. doi: http://dx.doi.org/10.1038/gim.2014.2.
- Harlor ADB Jr, Bower C, Committee on Practice and Ambulatory Medicin,; Section on Otolaryngology-Head and Neck Surgery. Hearing assessment in infants and children: recommendations beyond neonatal screening. *Pediatrics*. 2009;124(4):1252-1263. doi: http://dx.doi.org/10.1542/peds.2009-1997.
- Smith RJH, Shearer AE, Hildebrand MS, Van Camp G. Deafness and hereditary hearing loss overview. *GeneReviews*. 2014. http://www.ncbi.nlm.nih.gov/books/NBK1434/. Updated January 9, 2014.

Question 197

A 16-year-old adolescent girl presents to your clinic for evaluation of a mass in her left breast, which has been present for 3 months. Her menarche occurred at age 13 years and her last menstrual period ended 2 weeks ago. She reports no change in the mass with her periods. On physical examination, you palpate a 2.5-cm diameter mobile mass in the upper outer quadrant of the patient's left breast.

Of the following, the MOST likely diagnosis for the patient in the vignette is

A. breast abscess
B. breast carcinoma
C. fibroadenoma
D. fibrocystic changes
E. phyllodes tumor

Correct Answer: C
The most likely diagnosis for the adolescent girl in the vignette is a fibroadenoma. Breast masses among adolescent girls are typically benign. In a study of approximately 2,800 young women with breast disease, more than 98% were of benign etiology. On excisional biopsies of breast masses in adolescent girls, most are fibroadenomas. Overall, fibrocystic changes are significantly more common in adolescent girls, but biopsies are rarely performed.

Fibroadenomas are well-circumscribed, smooth, mobile lesions that typically do not change during the course of the menstrual cycle. The diagnosis is typically made by the combination of physical examination and the appearance of clearly defined, homogeneous, hypoechoic densities on ultrasonography. Most fibroadenomas are less than 3 cm in diameter; giant fibroadenomas are more than 5 cm. Management is usually conservative, because many fibroadenomas will spontaneously regress. Giant fibroadenomas may necessitate surgical excision because of breast distortion.

Breast abscesses typically present acutely, with symptoms of inflammation such as erythema, pain, swelling, and fever. Treatment should include coverage for likely skin pathogens (eg, staphylococci, streptococci). Surgical intervention may be required.

Breast cancer is uncommon among adolescents; therefore, both breast carcinoma and phyllodes tumor are unlikely in this scenario.

Adolescents with fibrocystic changes in the breast often complain of breast tenderness, with peak symptoms near the time of menstruation. Physical examination will reveal nodular breasts with indistinct masses. Management includes analgesics; symptoms typically improve with oral contraceptives.

Adolescent boys can also present with the complaint of breast mass. In boys, this complaint is most often secondary to gynecomastia. Physiologic gynecomastia occurs at puberty, and is likely due to a relative delay in testosterone secretion in comparison with estrogen, which stimulates breast development. Pubertal gynecomastia typically resolves in 12 to 18 months.

PREP Pearls

- Breast masses among adolescent girls are typically benign.
- On excisional biopsies of breast masses in adolescent girls, most are fibroadenomas.
- Fibroadenomas are well-circumscribed, smooth, mobile lesions that typically do not change during the course of the menstrual cycle. Management is usually conservative, because many fibroadenomas will spontaneously regress.

ABP Content Specifications(s)

- Understand the significance of a breast mass in an adolescent girl as it relates to puberty

Suggested Readings

- Diamantopoulos S, Bao Y. Gynecomastia and premature thelarche: a guide for practitioners. *Pediatr Rev*. 2007;28(9):e57-e68. doi: http://dx.doi.org/10.1542/pir.28-9-e57.
- Gooding HC, DiVasta AD. Breast disorders and gynecomasia. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. *Neinstein's Adolescent and Young Adult Health Care: A Practical Guide*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:461-470.

Question 198

A 4-year-old girl with cerebral palsy is brought to your office for a health supervision visit. She received early intervention services for delays in language, cognitive, and motor development until 3 years of age. She speaks in 4-word sentences and can ask simple questions. Seventy-five percent of her speech is intelligible. She enjoys playing with other children and can take turns. She is able to copy a square, write her first name, and draw a 6-part person. She wears an ankle-foot orthotic and is able to ambulate with mild difficulty. Her parents are concerned about finding the best placement for their daughter in school. They are worried that she may not be able to keep up with her peers and want her to have as much support as possible.

Of the following, the BEST recommendation is a

A. regular class for art and music and special education class or therapy for the majority of the day
B. regular class for half the day and special education class or therapy for half the day
C. regular class for the entire school day
D. regular class for the majority of the day and a special education class or therapy for part of the day
E. special education class or therapy for the entire school day

Correct Answer: D
The 4-year-old girl in this vignette has relative strengths in her fine motor, cognitive, language, and social development as evidenced by her age-appropriate abilities in copying, writing, drawing, expressive language, receptive language, and interactive play. As such, she does not require specialized academic instruction for cognitive delay or a learning problem and does not require occupational therapy for fine motor problems. On the other hand, this child would benefit from speech therapy, as her speech is less than the 100% intelligibility expected for her age. She may also benefit from physical therapy or adaptive physical education to address her difficulty with ambulation. According to the Individuals with Disabilities Education Act (IDEA), special education services should be provided in the least restrictive environment (LRE), meaning that children should be educated in typical educational settings with children without disabilities as much as possible. For the girl in this vignette, who does not require specialized academic instruction, the best recommendation would be a regular class for the majority of the day, with services for speech therapy and physical therapy or adaptive physical education for part of the day.

The IDEA is an important federal law, which provides for early intervention and special education services for children of various ages with learning or physical disabilities. The IDEA was enacted in 1975 and most recently reauthorized in 2004.

Early intervention (EI) programs are federally funded under Part C of IDEA and serve about 2% of infants and young children. The EI services are provided to children from birth to 3 years of age with delays in development (physical, cognitive, communication, social/emotional, adaptive development) or a condition that results in high probability of developmental delay. Some states also provide services to children who are at high risk for developmental delays. Early intervention programs are multidisciplinary, community-based, and family-centered. As such, services are typically delivered in the child's home. Early intervention starts with identification, screening, and assessment to determine eligibility and needs. Medical services for diagnosis or evaluation can be provided. Services such as special instruction, speech therapy, occupational therapy, physical therapy, family training, and counseling are offered, based on the needs identified through the assessment process. Additional services include home visits and assistance with transitioning to community or special education services as appropriate. A service coordinator assists the family with setting up the services and connecting with resources. Through its family-centered emphasis, EI programs empower parents by providing them with knowledge on how to improve their child's development and by providing resources to address their families' needs. Specific services and goals are outlined in the Individualized Family Service Plan. Short- and long-term outcomes from EI include improved cognitive and social-emotional development, as well as greater academic achievement. Early intervention has been most successful in children with mild delays and those at risk for developmental disability.

From 3 years to 21 years of age, individuals may be eligible for special education services through part B of IDEA. About 13% of children in the United States receive special education services. The IDEA was enacted to ensure that children with disabilities receive a free and appropriate public education. The child is first evaluated to determine if he meets eligibility

criteria under a special education disability category (eg, specific learning disability, speech or language impairment, other health impaired, emotional disturbance, intellectual disability, autistic-like behaviors, hearing impairment, visual impairment, traumatic brain injury). If the child qualifies for special education services, an Individualized Education Program is developed, outlining the services and accommodations that will be provided to the child to meet his educational needs.

Educational inclusion, or the participation of all children including those with disabilities in the same educational settings, is supported by IDEA, which dictates that special education services should be provided in the LRE. This means that the child should be educated in typical educational settings with students without disabilities as much as possible. Although some children will require intensive services in a separate special education classroom or school, a child should receive support in a regular classroom with his typical peers, if feasible. Inclusion can teach students with and without disabilities about the diversity of their community and promotes tolerance, empathy, and collaboration among students. Included students with disabilities may show improvements in their communication and social skills, as well as better educational outcomes. On the other hand, there are challenges to full educational inclusion. General education teachers may feel inadequately prepared to provide optimal instruction to students with disabilities. Although they may receive consultative support from a special education teacher, this may not be sufficient, particularly at the middle school or high school levels when the focus on content is challenging for students who may be struggling with basic academic skills. In addition, children with disabilities may need some time in a less inclusive environment to work on nonacademic functional skills. As adolescents approach the transition to adulthood, educational focus may shift from academic subjects to development of vocational or life skills; however, participation in nonacademic activities with typically developing peers should be maintained. While educational inclusion should be implemented when possible, placement should be made based on what best meets the individual student's needs.

Pediatricians have an essential role in identification and referral to EI and special education programs. Pediatricians can optimize their identification of children with possible delays by using standardized developmental screening instruments at the American Academy of Pediatrics recommended time points of 9 months, 18 months, and 24 or 30 months of age. Children should be referred to their community's EI program on the basis of suspected delay, as prompt treatment improves their outcomes. When a child requires special education, the pediatrician can guide the child's family in navigating the educational process and can advocate for assessment and access to appropriate instruction and services. In this way, pediatricians can positively impact their patients' academic and functional outcomes.

PREP Pearls

- Children should be referred to their community's early intervention program on the basis of suspected delay, as prompt treatment improves their outcomes. Short- and long-term outcomes from early intervention include improved cognitive and social-emotional development, as well as greater academic achievement.
- According to the Individuals with Disabilities Education Act, special education services should be provided in the least restrictive environment, meaning that children should be educated in typical educational settings with children without disabilities as much as possible.
- Inclusion can teach students with and without disabilities about the diversity of their community and promotes tolerance, empathy, and collaboration among students. Included students with disabilities may show improvements in their communication and social skills, as well as better educational outcomes.

ABP Content Specifications(s)

- Understand the advantages and disadvantages of educational inclusion for patients of various ages who have learning or physical disabilities
- Understand the general goals of early intervention programs for children of various ages who have learning disabilities

Suggested Readings

- Rose L, Herzig LD, Hussey-Gardner B. Early Intervention and the role of pediatricians. *Pediatr Rev*. 2014;35(1):e1-e10. doi: http://dx.doi.org/10.1542/pir.35-1-e1.
- Shea SE. Intellectual disability (mental retardation). *Pediatr Rev*. 2012;33(3):110-121. doi: http://dx.doi.org/10.1542/pir.33-3-110.

Question 199

A 15-year-old previously healthy adolescent boy presents to the emergency department for evaluation of an injury that occurred approximately 30 minutes ago when he was trying to catch a fast-moving ball during a high school baseball tournament. The adolescent reports that he fully recalls being hit directly on his right eye with a baseball. His parents brought him to the emergency department for evaluation immediately afterward because of significant pain, bruising, and swelling in his right periorbital area. There was no loss of consciousness at the time of injury, and he has had no vomiting, epistaxis, or drainage from his right eye. He has been holding a cold compress over his injured eyelid since the injury to help with the swelling, so he is unsure about his vision in the right eye.

On physical examination, the adolescent is alert and fully-oriented. He appears uncomfortable, but appropriately answers your questions and follows commands. His vital signs are within normal limits for his age.

His physical examination is significant for marked bruising and swelling over his right eyelid and periorbital area. When you ask him to look at you with both eyes open, his right eye seems to sit slightly lower than the left and his upward gaze is limited on the right. His pupils are 3 mm in diameter, equal, round, and reactive bilaterally. You note slight conjunctival injection in the right eye, but no signs of hyphema. His visual acuity is intact in both eyes. A fluorescein examination is negative for corneal injury. No other abnormalities are seen on a complete neurologic examination.

Of the following, the injury that is MOST likely to be causing the adolescent's clinical findings is

A. fracture of the medial wall of the right orbit
B. fracture of the right orbital floor
C. fracture of the right superior orbital rim
D. traumatic laceration of the right orbital nerve
E. traumatic rupture of the right globe

Correct Answer: B
The 15-year-old adolescent boy in the vignette presents with significant pain, bruising, and swelling of his right eyelid and periorbital area after he was struck directly on his right eye by a fast-moving baseball. Although his visual acuity is intact, his right eye seems to sit lower than the left on examination and he has limited upward movement of his right eye. The injury most likely to be causing these clinical findings is a fracture of the right orbital floor, with associated entrapment of the inferior rectus muscle.

It is critical for all pediatric providers to recognize the clinical findings associated with orbital floor fractures, which may also be referred to as "blow-out" fractures of the orbit. Orbital floor fractures classically occur when relatively small-sized, hard, round objects (such as a baseball) directly strike the eye. Since the volume of the orbital space is fixed, the increased pressure of the infraorbital contents that results from direct trauma may lead to the globe being pushed posteriorly within the orbit, which can result in a linear fracture through the floor of the orbit. This fracture in the floor of the orbit can sometimes act as a "trap-door" through which intraorbital contents can protrude and even become entrapped. Direct trauma to the infraorbital rim may also contribute to the development of orbital floor fractures. In adult patients, the orbital floor is thicker and more likely to shatter as a result of sustaining a traumatic force.

A significant sequela of orbital floor fractures is entrapment of the inferior rectus muscle and orbital fat. Entrapment of muscle within the fracture fragment, or edema and hemorrhage of muscle and extraocular fat that have prolapsed through the fracture site into the maxillary sinus may lead to ischemia and eventual loss of intraocular muscle function.

Clinical findings in children with orbital floor fractures may include a "sunken" appearance to the eye on the affected side, asymmetry in the horizontal level of the eyes, decreased sensation to the cheek, upper lip, and upper gingiva on the affected side (due to injury to the infraorbital nerve), as well as limitation of upward gaze on the affected side due to inferior rectus muscle entrapment.

Urgent operative intervention is indicated in children with orbital blowout fractures with inferior rectus muscle entrapment. A careful ophthalmologic evaluation is indicated in all children with orbital fractures due to the high incidence of associated eye injuries. Visual acuity should be carefully assessed and documented.

Although a fracture of the medial orbital wall could be possible in the patient in the vignette, an orbital floor fracture is much more likely based on his "classic" clinical presentation. The adolescent's inability to look upward indicates entrapment of his inferior rectus muscle, which would be associated with an orbital floor fracture, not a medial orbital wall fracture.
A fracture of the right superior orbital rim would not explain the clinical findings found in the adolescent in the vignette.

Traumatic laceration of the right orbital nerve would be very unlikely in the patient in the vignette, given that he has normal visual acuity. Nevertheless, all children with orbital fractures

should undergo a thorough ophthalmologic examination due to the high likelihood of associated eye injuries.

There are no clinical findings suggestive of a traumatic rupture of the right globe in this adolescent. His pupillary examination is normal, visual acuity is intact, and a flourescein examination is negative for corneal injury. Clinical findings associated with globe rupture may include an abnormally shaped ("teardrop"-shaped) pupil, evidence of associated hemorrhage within the anterior chamber (hyphema), severe subconjunctival hemorrhage, and "streaming" of flourescein on examination of the affected eye with a Wood lamp or slit lamp.

PREP Pearls

- Clinical findings in children with orbital floor fractures may include a "sunken" appearance to the eye on the affected side; asymmetry in the horizontal level of the eye; decreased sensation to the cheek, upper lip, and upper gingiva on the affected side; and limitation of upward gaze on the affected side due to inferior rectus muscle entrapment.
- Urgent operative intervention is indicated in children with orbital blowout fractures with inferior rectus muscle entrapment.
- A careful ophthalmologic evaluation is indicated in all children with orbital fractures due to the high incidence of associated eye injuries.

ABP Content Specifications(s)

- Recognize the clinical findings associated with blow-out fracture of the orbit

Suggested Readings

- Aronson PL, Neuman MI. Facial trauma. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds.*Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:1151-1159.
- Dull KE. Eye: visual disturbances. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. *Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:170-175.

Question 200

A neonatal intensive care nurse presents to the occupational health clinic for evaluation of cough. She recently cared for an infant with respiratory failure who has been confirmed to have pertussis. She was present during his intubation and participated in endotracheal tube suctioning prior to the patient being placed on droplet isolation. Her medical history and immunization records are reviewed.

Of the following, the factor that would allow for the MOST immediate return to work for this nurse is

A. completion of pertussis treatment
B. initiation of pertussis treatment
C. masking for future patient care
D. personal history of pertussis
E. up-to-date Tdap immunization

Correct Answer: A

For the healthcare worker in this vignette who is exposed to and suspected of having pertussis, return to work is permitted after completion of antibiotic therapy. The main goal for treatment of pertussis, typically with a macrolide, is to reduce transmission. Clearance of the organism from the nasopharynx occurs at approximately 5 days of antibiotic therapy. Initiation of a treatment course is not sufficient to allow for return to work in a symptomatic individual given that individuals continue to be contagious at the onset of treatment. Should the healthcare worker forego treatment, the individual should be excluded from work for a period of 21 days.
Since the 1970s, there has been a steady increase in the number of pertussis cases reported in the United States. In 2014, California declared an epidemic and a total of nearly 33,000 cases were reported nationally.

Classic pertussis progresses through 3 stages, though symptoms may be attenuated in certain age groups. The first phase of illness is called the catarrhal phase, which is characterized by upper respiratory tract symptoms. This is followed by the paroxysmal phase characterized by coughing fits. Inspiration between coughing fits can create the classic "whoop" sound. The "whoop" is most common in children, but can be absent in young infants who can present with atypical symptoms such as apnea. The "whoop" is also less common in adolescents and adults. The convalescent phase is characterized by improvement of the coughing episodes.

Despite immunization, some individuals are still at risk for *Bordetella pertussis* infection. Therefore, postexposure prophylaxis is recommended for high-risk exposures irrespective of immunization status, including healthcare workers who are exposed to pertussis and are likely to expose patients at risk of severe pertussis. High-risk patients include infants younger than 1 year of age, women in the third trimester of pregnancy, immunocompromised individuals, and individuals with underlying pulmonary disease. Healthcare workers without high-risk exposures have the option of postexposure prophylaxis and daily symptom monitoring for a period of 21 days.

Masking is not considered sufficient protection for an individual who is symptomatic. A personal history of pertussis in not incorporated into the management algorithms.

PREP Pearls

- Classic pertussis progresses through 3 stages: the catarrhal phase, the paroxysmal phase (when "whooping" may occur), and the convalescent phase.
- The main goal for treatment of pertussis is to reduce transmission.
- Postexposure prophylaxis for pertussis is recommended for high-risk exposures irrespective of immunization status.

ABP Content Specifications(s)

- Recognize the clinical features associated with pertussis in children of various ages
- Understand the epidemiology of Bordetella pertussis

Suggested Readings

- American Academy of Pediatrics. Pertussis (whooping cough). In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:608-621.
- Snyder J, Fisher D. Pertussis in childhood. *Pediatr Rev.* 2012;33(9):412-421. doi: http://dx.doi.org/10.1542/pir.33-9-412 .

Question 201

A 2-week-old female neonate is brought to your office for an urgent visit because bright red blood was noted in her stool this morning. She was born at term by spontaneous vaginal delivery after an uncomplicated prenatal course. She was breastfed and began receiving standard infant formula supplementation because of poor weight gain in the first week after birth. Her parents report that she has had increasing fussiness over the past week. They deny fever or rash.

Of the following, the MOST likely cause for this neonate's presenting symptoms is

A. cow milk protein intolerance
B. infectious colitis
C. ischemic colitis
D. Meckel diverticulum
E. swallowed maternal blood

Correct Answer: A

Cow milk protein intolerance is the most likely cause of blood in stools and fussiness in this 2-week-old neonate. Cow milk protein intolerance is a reaction to cow milk protein found in either breast milk or cow milk–based formulas. Five percent to 15 percent of infants are affected by an allergy or intolerance to cow milk. This may be immunoglobulin E (IgE)- or non-IgE–mediated. Symptoms commonly occur in the first 6 months after birth. Gastrointestinal signs and symptoms (diarrhea, vomiting, and/or guaic-positive stools) are the most common presentation, ranging from a frequency of 50% to 80%. Cutaneous symptoms are seen in 20% to 40%, and respiratory symptoms in 4% to 25% of affected infants. While fussiness is common, weight loss and failure to thrive are uncommon.

Sixty percent of affected infants are exclusively breastfed. Most infants with cow milk protein intolerance experience resolution between 6 months (50%) and 2 years of age (80%-90%). It is rare for the blood loss to result in anemia. In breastfed infants, a maternal elimination diet is often effective. Formula-fed infants should make a transition to extensively hydrolyzed formula (eHF) or an amino-acid formula for those with severe or life-threatening symptoms, such as respiratory distress. Up to 50% of infants with cow milk intolerance will also have soy protein intolerance before age 6 months, and will require a hydrolyzed or amino acid formula. Therefore, a trial of soy formula should be delayed until after 6 months of age if there are financial limitations.

Evaluation should include a detailed history and physical examination and a stool occult blood test to confirm the presence of blood. A maternal elimination diet or food challenge with a non–cow milk diet should be attempted for 2 to 4 weeks. A complete blood cell count should be obtained if blood loss appears to be significant.

The newborn in the vignette has no signs or symptoms to suggest infectious colitis, which is very rare among infants in the developed world. With no evidence of sepsis or congenital cardiac disease, ischemic colitis is unlikely in this newborn. Meckel diverticulum is uncommon in a 2-week-old newborn. Swallowed maternal blood may result in occult positive stools, but would not be visible in stool.

PREP Pearls

- Cow milk protein intolerance may present with diarrhea, fussiness, and/or guaic-positive stools.
- Infants can safely continue to receive cow milk through the intolerance.
- An elimination diet for the infant or breastfeeding mother can be very effective

ABP Content Specifications(s)

- Recognize the clinical and laboratory features associated with milk-protein intolerance, and manage appropriately

Suggested Readings

- De Greef E, Hauser B, Devreker T, Veereman-Wauters G, Vandenplas Y. Diagnosis and management of cow's milk protein allergy in infants. *World J Pediatr.* 2012;8(1):19-24. doi: http://dx.doi.org/10.1007/s12519-012-0332-x .
- Eigenmann PA. The spectrum of cow's milk allergy. *Pediatr Allergy Immunol.* 2007;18(3):265-271. doi: http://dx.doi.org/10.1111/j.1399-3038.2006.00528.x .
- Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee Practical Guidelines. *J Pediatr Gastroenterol Nutr.* 2012;55(2):221-229. doi: http://dx.doi.org/10.1097/MPG.0b013e31825c9482 .
- Ludman S, Shah N, Fox AT. Managing cows' milk allergy in children. *BMJ.* 2013;347:f5424. doi: http://dx.doi.org/10.1136/bmj.f5424 .

Question 202

A 14-year-old adolescent with a history of congenital aortic stenosis presents to your office for a preparticipation sports physical examination. She would like to participate on the school basketball team. She denies palpitations, syncope, presyncope, or exercise intolerance. Six months ago, an echocardiogram demonstrated aortic stenosis with a mild pressure gradient of less than 20 mm Hg and she had a normal response to exercise with treadmill testing.

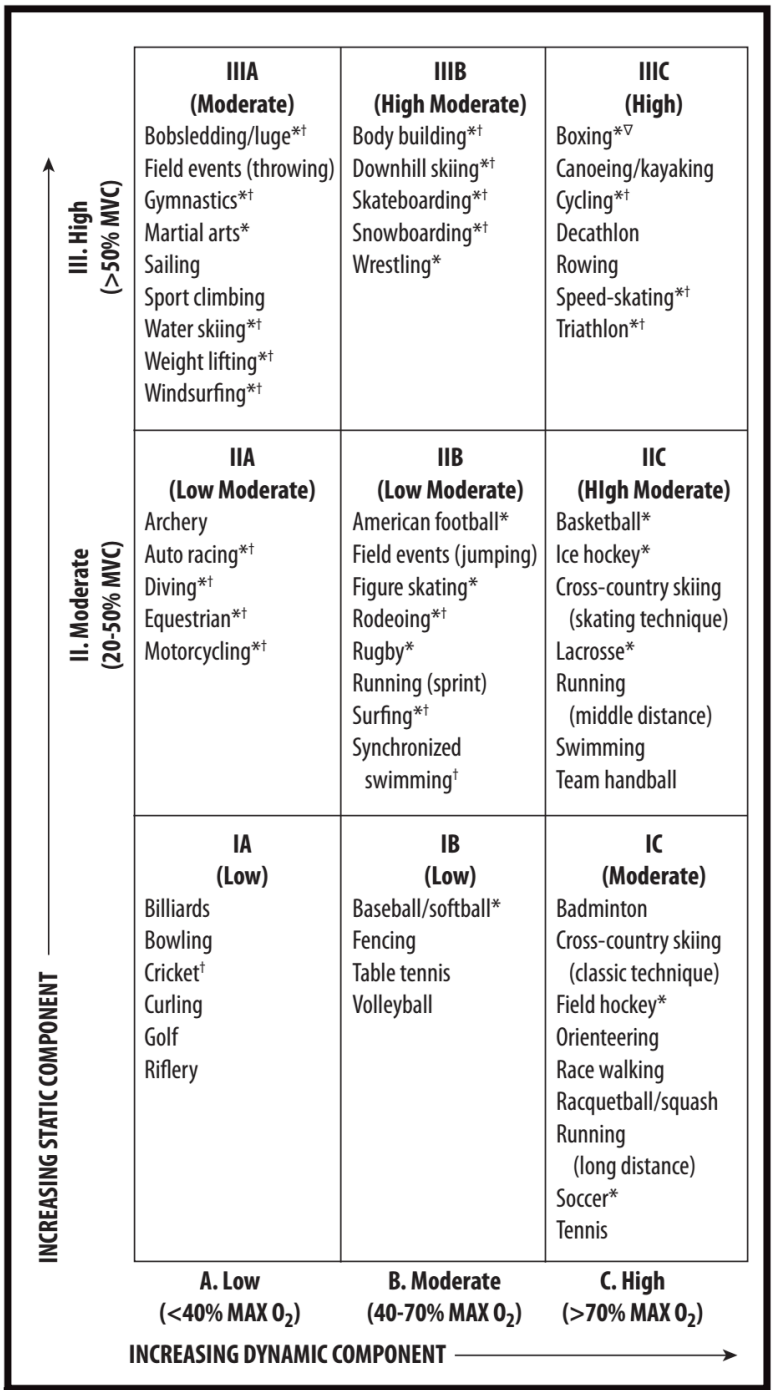
Of the following, the MOST appropriate recommendation for this adolescent is that she

A. can participate in all sports with annual cardiology reassessment
B. cannot be cleared for any sports participation
C. should not participate in any sports without prior cardiac catheterization
D. should participate only in sports with a low or moderate dynamic component
E. should participate only in sports with a low or moderate static component

Correct Answer: A

The patient in the vignette has mild aortic stenosis with a pressure gradient of less than 20 mm Hg. She had a normal response to exercise stress testing. According to guidelines published by the American College of Cardiology (ACC) and the American Heart Association (AHA) in 2015, she can participate in all sports without restriction. However, she should undergo annual echocardiography and exercise testing to assess for changes in her valvular disease. Cardiac catheterization is not required. If her aortic stenosis gradient increases to the moderate category, she should be restricted to sports with low-to-moderate static and dynamic components. Individuals with severe aortic stenosis should be restricted from competitive sports participation (with possible allowance for low static and dynamic sports such as bowling and golf).

The ACC/AHA guidelines provide expert consensus opinion on the types of sports and activities recommended for individuals with various types of heart disease. The guidelines classify sports and activities by both the static component (the percentage of maximal voluntary contraction and concomitant increase in blood pressure) and the dynamic component (percentage of maximal oxygen uptake) (C202).



Adapted and reprinted with permission from Mitchell JH, Haskell W, Snell P, Van Camp SP. 38th Bethesda Conference. *J Am Coll Cardiol.* 2005;45(8):1364-1367

ITEM C202: Classification of sports according to cardiovascular demands.

*Danger of bodily collision.
†Increased risk if syncope occurs.
▽Participation not recommended by the American Academy of Pediatrics.
+The American Academy of Pediatrics classifies cricket in the IB box (low static, moderate dynamic).

In collaboration with 5 other professional societies, the American Academy of Pediatrics (AAP) published the Preparticipation Physical Evaluation (PPE) monograph. The goal of the PPE monograph is to screen athletes for medical conditions that may increase their risk of injury or illness during sports participation. This monograph outlines the components of the PPE and provides a standardized history and physical examination form. In addition, the document summarizes current recommendations for sports participation for individuals with various medical conditions. Among the issues included are recommendations regarding assessment of athletes with a risk of atlantoaxial instability; requirements for protective gear for individuals with the absence of a paired organ (eg, an eye, kidney, or testicle), depending on the type of sport played; and individualized evaluation of athletes with seizure disorders to determine if participation in their chosen activities could increase their risk of injury. The presence of certain acute illnesses (eg, infectious mononucleosis or infectious skin conditions) may require temporary restriction of physical activities.

PREP Pearls

- Athletes with mild aortic stenosis and a normal response to exercise testing can participate in all sports without restriction, with annual cardiology reassessment.
- The American College of Cardiology and American Heart Association provide expert consensus guidelines on the types of sports and activities recommended for individuals with different types of heart disease.

ABP Content Specifications(s)

- Identify which sports are appropriate for athletes with various conditions that may limit sports participation

Suggested Readings

- American Academy of Family Physicians, American Academy of Pediatrics, American College of Sports Medicine, American Medical Society for Sports Medicine, American Orthopaedic Society for Sports Medicine, American Osteopathic Academy of Sports Medicine. Systems-based examination. In: Bernhardt DT, Roberts WO, eds. *PPE: Preparticipation Physical Evaluation*. 4th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2010:39-130.
- Bonow RO, Nishimura RA, Thompson PD, Udelson JE. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 5—valvular heart disease: a scientific statement from the American Heart Association and American College of Cardiology. *Circulation.* 2015;132(22):e292-e297. doi: http://dx.doi.org/10.1161/CIR.0000000000000241 .
- Maron BJ, Zipes DP, Kovacs RJ. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: preamble, principles, and general considerations—a scientific statement from the American Heart Association and American College of Cardiology. *Circulation.* 2015;132(22):e256-e261. doi: http://dx.doi.org/10.1161/CIR.0000000000000236.

Question 203

A 6-month-old infant is brought to your office with excessive tearing in the right eye for the past 4 weeks. He has also had more frequent blinking of the right eye. There is no history of trauma or fever. On physical examination, you note excessive tearing of the right eye and corneal clouding, but no redness. The infant seems particularly upset when you examine the right eye with a light.

Of the following, the MOST appropriate management of this patient is

A. immediate referral to an ophthalmologist
B. patch the right eye and follow-up in 1 day
C. perform a fluorescein examination and irrigate the eye with saline
D. treat with an antibiotic ointment
E. warm compresses and tear duct massage

Correct Answer: A

The infant in this vignette has glaucoma of the right eye and should be referred immediately to an ophthalmologist. Congenital glaucoma is a rare condition, occurring in 1 out of 10,000 live births. Twenty-five percent of infants with this condition will be diagnosed at birth and 80% of infants will be diagnosed by 12 months of age. Glaucoma in children from birth to younger than 3 years of age is referred to as infantile or congenital glaucoma. Infants with an earlier onset of glaucoma tend to have a more severe case than infants who have onset at a later age. Children with glaucoma have an increased intraocular pressure that, if left untreated, may result in permanent vision damage. The type of glaucoma typically seen in infants and children results from an abnormality of the iridocorneal angle that affects the drainage of the aqueous humor from the anterior chamber, leading to an increase in intraocular pressure. This results in corneal and globe enlargement, as well as corneal edema. The corneal edema leads to excessive tearing and photophobia.

The classic presentation of congenital glaucoma includes excessive tearing of the eye, photophobia, and frequent blinking of the eyelid due to muscle spasms. Less than 30% of patients will present with this classic triad. Additional clinical findings include corneal clouding and enlargement of the eye. On funduscopic examination, cupping and atrophy of the optic nerve may be noted.

A child suspected of having glaucoma should have an immediate referral to an ophthalmologist for a thorough funduscopic examination and measurement of intraocular pressure. Normal intraocular pressure is between 10 to 20 mm Hg. Pressures greater than 20 mm Hg are considered elevated, putting the child at increased risk for permanent damage. The treatment of congenital glaucoma is primarily surgical.

Eye patching is one of the treatment options for amblyopia, not glaucoma. A fluorescein examination is used to evaluate for a corneal abrasion or a foreign body. The prolonged nature (4 weeks) of the eye tearing and the associated eyelid spasms make a foreign body or corneal abrasion unlikely. An antibiotic ointment would be an appropriate treatment for conjunctivitis, and this patient has no eye discharge or redness. Warm compresses and tear duct massage are used for the treatment of dacryostenosis, and this patient has no eye discharge.

PREP Pearls

- The classic presentation of congenital glaucoma is excessive tearing, photophobia, and frequent spasms of the eyelid.
- Suspected glaucoma should be referred immediately to an ophthalmologist.
- Treatment for infantile glaucoma is mainly surgical.

ABP Content Specifications(s)

- Recognize the clinical findings associated with congenital glaucoma

Suggested Readings

- Olitsky SE, Hug D, Plummer LS, Stahl ED, Ariss MM, Lindquist TP. Childhood glaucoma. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:3060-3061.
- Rosales T. Excessive tearing. In: Berkowitz CD, ed. *Berkowitz's Pediatrics: A Primary Care Approach.* 5th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:501-504.

Question 204

A 3-year-old girl presents to your office for evaluation of a “lump” in her right neck that was noticed by her mother while she was being bathed. She had an upper respiratory infection 3 weeks ago, with rhinorrhea and cough, which has fully resolved. She has had a normal appetite and energy level. The girl has not had persistent fevers, weight loss, or night sweats. The family has no pets, they have not been in a forest or wooded area, and have not traveled outside the country. The girl is developmentally appropriate, and is at the 40th percentile for both weight and height. On physical examination, a 1.5 × 1.0 cm freely movable and nontender mass is palpable just below the angle of her right mandible. The remainder of her physical examination is unremarkable.

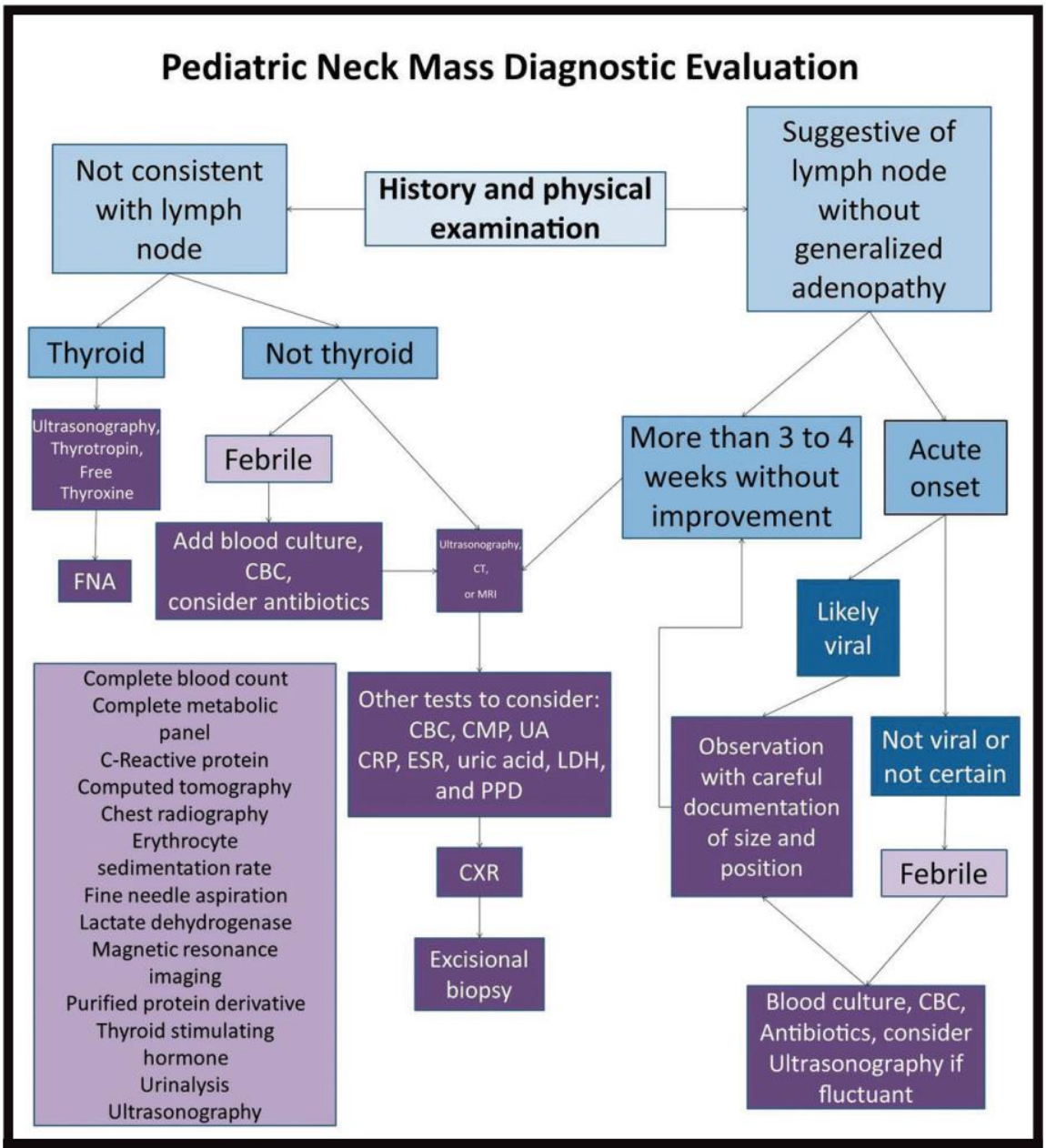
Of the following, the BEST next step in management is to

A. obtain computed tomography scan of the neck with contrast
B. perform a purified protein derivative test
C. provide reassurance to the mother
D. refer to a surgeon for a biopsy
E. treat with oral amoxicillin/clavulanate

Correct Answer: C

Neck masses are a common presenting problem seen by the pediatrician. The differential diagnosis for a neck mass depends on several factors including location, duration, size, and characteristics such as erythema or pain. A useful algorithm for the approach to a neck mass is shown in Item 204 . The girl in the vignette presented with a nontender, nonerythematous, small (<1.5 cm in the greatest diameter) neck mass just below the angle of the right mandible. She has been well, with normal growth and development, and has had no exposures that would raise concern for Lyme disease or cat scratch disease. The location and size of the mass, and the lack of a remarkable history other than the upper respiratory infection that occurred 3 weeks before presentation, suggest that this is a reactive lymph node. As such, no further intervention is warranted.

Diagnostic computed tomography (CT) scans expose children to radiation. Several recent studies suggest that exposure to even a small radiation dose can increase a child's risk for malignancy. Unless there is a strong suspicion of malignancy, CT would not be the imaging method of choice for a child with a neck mass.



Reprinted with permission from Geddes G, Butterly MM, Patel SM, Marra S. Pediatric neck masses. *Pediatr Rev.* 2013;34(3):115-124

ITEM C204: Diagnostic evaluation algorithm for the pediatric neck mass.
CBC, complete blood cell count; CMP, complete metabolic panel;
CRP, C-reactive protein; CT, computed tomography; CXR, chest radiography;
ESR, erythrocyte sedimentation rate; FNA, fine-needle aspiration;
LDH, lactate dehydrogenase; MRI, magnetic resonance imaging;
PPD, purified protein derivative; UA, urinalysis.

With the absence of any historical risk factors or associated symptoms, there is no reason to suspect that the girl in the vignette has tuberculosis and therefore no indication to perform a purified protein derivative test.

Given the constellation of findings suggesting that the girl in the vignette has a simple reactive lymph node, there would be no indication for referral to a surgeon for a biopsy.
Bacterial lymphadenitis presents with erythema and/or pain over an enlarged lymph node, and often with fever. The girl in the vignette had none of these findings, so treatment with amoxicillin/clavulanate (or any antibiotic) would not be indicated. A child with apparent bacterial adenitis that persists despite seemingly adequate antibiotic therapy warrants evaluation by a pediatric oncologist.

PREP Pearls

- Persistent lymphadenopathy despite seemingly adequate therapy for bacterial adenitis warrants evaluation by a pediatric oncologist.
- When evaluating a neck mass, computed tomography (CT) should be reserved for situations in which there is a high index of suspicion for malignancy. Ideally, the patient should be evaluated by a pediatric oncologist before ordering a CT scan.
-

ABP Content Specifications(s)

- Formulate a differential diagnosis of a neck mass

Suggested Readings

- Friedmann AM. Evaluation and management of lymphadenopathy in children. *Pediatr Rev.* 2008;29(2):53-60. doi: http://dx.doi.org/10.1542/pir.29-2-53.
- Geddes G, Butterly MM, Patel SM, Marra S. Pediatric neck masses. *Pediatr Rev.* 2013;34(3):115-125. doi: http://dx.doi.org/10.1542/pir.34-3-115.
- Sahai S. Lymphadenopathy. *Pediatr Rev.* 2013;34(5):216-227. doi: http://dx.doi.org/10.1542/pir.34-5-216.

Question 205

You are seeing a 3-month-old infant in your office for a health supervision visit. He was born at term without perinatal complications. His birthweight was 3.1 kg, and he has been growing and developing normally. His mother reports mild nasal congestion today. His weight today is 5.9 kg (52nd percentile). His heart rate is 145 beats/min and his respiratory rate is 24 breaths/min. On physical examination, the infant is awake, alert, and not in any distress. He has clear breath sounds bilaterally without retractions, stridor, or adventitious sounds. His cardiac examination is significant for a grade 4 harsh systolic murmur loudest at the left upper sternal border. The point of maximum impulse is not displaced. The murmur radiates to both axilla, but not into his neck or back. His oxygen saturation is 89% on room air.

You administer oxygen by nasal cannula and observe that his saturation increases to 91%. On reviewing his chart, you note that on his last physical examination 6 weeks ago, a grade 2 soft systolic murmur was noted at the left upper sternal border.

Of the following, the MOST likely cause of this infant's hypoxemia is

A. Eisenmenger syndrome
B. a patent ductus arteriosus
C. primary pulmonary hypertension
D. pulmonary valve stenosis
E. a ventricular septal defect

Correct Answer: D

The infant described in this vignette has a murmur in the pulmonic position that has increased and is associated with a decrease in oxygen saturation. The murmur described for this infant would be most compatible with valvar pulmonic stenosis (PS) that has worsened and is now severe. As measured by Doppler, mild PS has a gradient across the valve that is less than 30 mm Hg, moderate PS is between 30 and 60 mm Hg, and severe PS is greater than 60 mm Hg. Mild PS may not be progressive. If the pulmonary valve is dysplastic or thickened, as is seen in 10% to 20% of patients with PS, the stenosis may worsen in the first few months after birth. As the stenosis worsens, saturations may gradually decrease because the right ventricular pressure and eventually the right atrial pressure increase. Once the right atrial pressure is higher than that of the left atrium, right-to-left shunting may be noted in the presence of a patent foramen ovale, as is common in a 3-month-old infant. In such cases, the right-to-left shunt will increase as the right ventricular pressure increases, causing systemic desaturation that will respond to some degree to oxygen.

The boy's murmur is not holosystolic, as would be expected with a ventricular septal defect (VSD). It is not heard in the back, as would be expected with a patent ductus arteriosus. This infant is 3 months of age and would not be expected to have Eisenmenger syndrome (reversal of flow through a VSD because of irreversible pulmonary hypertension), as it takes years to develop this condition. If he had primary pulmonary hypertension, he would not have an outflow tract murmur in the right ventricular outflow tract position, but he might have a diastolic murmur of pulmonary insufficiency.

Pulmonic stenosis may cause cyanosis, falling into the category of lesions with decreased pulmonary blood flow, which also includes tricuspid atresia, pulmonary atresia, pulmonary stenosis, tetralogy of Fallot (TOF), and Ebstein anomaly. If this boy had tetralogy of Fallot and he were beginning a hypercyanotic spell, the murmur would become much softer as the oxygen saturation decreased, and the drop in saturation would be pronounced. The physiology of a hypercyanotic spell requires not only PS, but a VSD that allows right-to-left shunting to an overriding aorta with an ever-worsening percentage of desaturated blood returning to the right ventricle. The spell usually begins with the infant crying and thereby decreasing the systemic vascular resistance. Measures such as the knee-chest position to increase the systemic vascular resistance are needed, as well as oxygen administration, to increase the saturation and abort the spell.

Routine pulse oximetry in the newborn nursery has been instituted in many states to screen newborns for cyanotic congenital heart lesions that may be ductal dependent. The goal of screening is to prevent the predicted poor outcome of these infants after discharge. Screening protocols vary slightly among states, with 95% oxygen saturation considered a passing value and less than 90% considered a failed test. If the saturation falls between 90% and 95%, the test is repeated 3 times over at least 3 hours, and the differential saturation between the upper and lower extremities is measured. If the 3 measurements are similar and remain less than 95%, then the infant has not passed the screening test and requires further evaluation.

PREP Pearls

- Pulmonic stenosis (PS) may cause cyanosis if there is significant obstruction and a patent foramen ovale is present.
- Tetralogy of Fallot, with an overriding aorta and ventricular septal defect, has a different physiology from isolated PS. While initial treatment for decreased oxygen saturation will differ between the 2 lesions, both will respond to oxygen administration.
- Many states now require screening of newborns for ductal-dependent cyanotic congenital heart disease with pulse oximetry.

ABP Content Specifications(s)

- Identify cardiac causes of cyanosis in children of various ages, including those who have tetralogy of Fallot

Suggested Readings

- Ardura J, Gonzalez C, Andres J. Does mild pulmonary stenosis progress during childhood? A study of its natural course**.** *Clin Cardiol.* 2004;27(9):519-522. doi: http://dx.doi.org/10.1002/clc.4960270910.
- Bernstein D. Pulmonary valve stenosis with intact ventricular septum. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:2199-2201.
- Mahle WT, Newburger JW, Matherne GP, et al. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the AHA and AAP. *Pediatrics.* 2009;124(2):823-836. doi: http://dx.doi.org/10.1542/peds.2009-1397.
- Maleszewski JJ, Edwards WD. Cardiac anatomy and examination of cardiac specimens. In: Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents.* 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:181-212.
- Prieto LR, Latson LA. Pulmonary stenosis. In: Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents.* 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:983-1008.
- Steinhorn RS. Evaluation and management of the cyanotic neonate. *Clin Pediatr Emerg Med.* 2008;9(3):169-175. doi: http://dx.doi.org/10.1016/j.cpem.2008.06.006.

Question 206

A 3-day-old, full-term, healthy male neonate is brought to your office by his parents for a newborn visit. The family is new to your practice. On reviewing his hospital record, you see that the parents declined the hepatitis B vaccine in the nursery. The parents state that they have significant concerns about vaccine safety and they do not wish to vaccinate their son today.

Of the following, the MOST appropriate next step is to

A. discharge the family from your practice
B. explore with the parents any misperceptions about the safety and efficacy of vaccines
C. hand the parents a brochure explaining the consequences of contracting a vaccine-preventable illness
D. offer the parents a different vaccine schedule
E. report the case to the state child welfare agency for medical neglect

Correct Answer: B

Parents who are hesitant, delay, or refuse to vaccinate their children are common in pediatrics: in 2012, 88% of general pediatricians reported seeing at least 1 family in the past month that refused a scheduled vaccine. Nearly 1 in 3 parents interviewed in a national survey were wary of at least 1 recommended vaccine, and although vaccination rates have risen over the past 2 decades, in some communities, up to 25% of children are incompletely vaccinated. Refusing all vaccines is relatively rare; caregivers who ask to delay or spread out vaccines or express a hesitancy toward some (but not all) vaccines are more common. There are many sources of misinformation about childhood vaccines, and studies of caregivers with doubts about vaccines indicate that discussing their concerns and exploring their misperceptions about safety and efficacy of vaccines with a trusted healthcare professional can be critical to eventual acceptance of recommended vaccines.

A high level of vaccination among populations is an important public health goal. A small number of children do not respond immunologically or have a medical condition where certain vaccines are contraindicated. Vaccinating nearly everyone creates “herd immunity” that may protect these children.

A number of studies of parents and healthcare providers, as well as ethical principles, can guide policies and practices addressing this issue. First, refusing a vaccine constitutes medical neglect only when doing so places the child at substantial risk of serious harm (eg, parents of a child bitten by a stray animal refuse rabies vaccine). Since herd immunity is achieved in a well-immunized community, the neonate in the vignette is not at risk of substantial harm due to his parents’ decision, and the case should not be reported to the state welfare agency. Nevertheless, high levels of vaccination are necessary to control vaccine-preventable disease and the risk of harm from vaccines is very low. Broad public health efforts, including vaccine requirements for school entry and incentives for timely vaccination, are ethical and important societal investments.

While many pediatricians agree to spread out vaccines in at least some cases, it should be discouraged and only considered if discussing the caregivers’ concerns and building a trusting relationship are not effective. Information for caregivers describing children harmed by contracting a vaccine-preventable illness alone does not change the propensity to vaccinate children of caregivers who refuse vaccines. In general, physicians should not discharge families from their care because caregivers refuse vaccines, unless a strong sense of distrust develops that impacts a child’s overall care

PREP Pearls

- Addressing concerns about vaccine safety and efficacy and building a trusting relationship with caregivers are the most effective and ethical approaches to vaccine hesitancy and refusal.
- Information for caregivers that describes disabling or deadly effects of vaccine-preventable illness is not effective in swaying caregivers who refuse vaccines for their children.
- Refusing a vaccine constitutes medical neglect only when doing so places the child at substantial risk of serious harm; most cases of vaccine refusal are not medical neglect.

ABP Content Specifications(s)

- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding religious (philosophical) exemptions for medical treatment/immunizations

Suggested Readings

- Diekema DS. Responding to parental refusals of immunization of children. *Pediatrics*. 2005;115(5):1428-1431. doi: http://dx.doi.org/10.1542/peds.2005-0316 .
- Nyhan B, Reifler J, Richey S, Freed GL. Effective messages in vaccine promotion: a randomized trial. *Pediatrics*.2014;133(4):e835-e842. doi: http://dx.doi.org/10.1542/peds.2013-2365.

Question 207

A 5-year-old boy is brought to the emergency department (ED) 24 hours after treatment in an urgent care center. The boy had been seen for a deep laceration to his right hand following a provoked bite from the aunt's dog. The dog is under observation and the dog's rabies immunizations are up to date. In the urgent care center, the wound was irrigated, cleaned, and sutured. The boy had been started on empiric clindamycin because of a documented penicillin allergy. Overnight, the wound has become red, painful, and warm to touch. The parents were concerned and came to the ED.

Physical examination reveals an anxious, uncomfortable boy. Vital signs show a temperature of 37.2°C, respiratory rate of 20 breaths/min, heart rate of 105 beats/min, and blood pressure of 90/65 mm Hg. A 5 cm sutured laceration on the right palm is noted, along with a large surrounding area of erythema, tenderness, and warmth. A small amount of purulent drainage is emerging from between the sutures. Lymphangitic streaking is noted on the right forearm. The remainder of the physical examination is unremarkable.

The pus is sent for Gram stain and culture that showed small gram-negative coccobacilli (Q207), with the culture pending.

Of the following, the BEST recommendation for an additional antibiotic for this boy is

A. amoxicillin/clavulanate
B. cephalexin
C. erythromycin
D. no additional antibiotic is necessary
E. trimethoprim/sulfamethoxazole

Correct Answer: E

For the boy described in the vignette, the best recommendation for an additional antibiotic is trimethoprim-sulfamethoxazole. Gram-negative coccobacilli found after a dog bite would most likely be *Pasteurella multocida.* One in every 775 Americans will seek emergency care for a dog bite each year, accounting for 1% of emergency department visits. Infection after a dog bite occurs in 15% to 20% of bites in various studies. The usual pathogens include human skin flora and the normal oral and respiratory tract flora of the biting animal. Most bite wound infections are polymicrobial with an average of five distinct bacteria, both aerobic and anaerobic. *Staphylococcus aureus*, including methicillin-sensitive and -resistant *S aureus* (MSSA, MRSA, respectively), and *Streptococcus pyogenes* are the typical human skin organisms found. *Pasteurella* species are normal upper respiratory tract flora of both birds and mammals, and are the most common pathogen isolated from animal bite wounds, representing half of dog bite and three-quarters of cat bite infections.

While *Pasteurella* can cause life-threatening animal diseases such as fowl cholera, shipping fever, hemorrhagic septicemia, fibrinous pneumonia in cattle, and rabbit snuffles, mortality is the exception rather than the rule when these organisms infect humans after an animal bite. Morbidity is still significant, however, from skin and soft tissue infections, and is more likely to occur with cat compared to dog bites. Infection can also occur from cat scratches (distinct from cat-scratch disease), as well as a cat or a dog licking broken skin. Infection is characterized by a rapid and intense inflammatory response, which typically occurs within 24 hours and sometimes within just a few hours of the bite. The wound is purulent in 40% of *Pasteurella* infections, and lymphangitis and adenopathy are common. Besides cellulitis, septic arthritis and osteomyelitis can occur. Septic arthritis usually involves a single joint proximal to the bite, without actual injury to the joint itself. In one-third of cases, there is no history of an animal bite or scratch. Osteomyelitis usually results from extension of the cellulitis or wound infection, but can also occur from direct inoculation of the *Pasteurella* into the periosteum (more often from cat rather than dog bites). *Pasteurella* can be responsible for upper and lower respiratory tract infections such as pharyngitis, sinusitis, otitis media, mastoiditis, epiglottitis, tracheobronchitis, pneumonia, empyema, and lung abscess in patients with pre-existing chronic lung disease. More invasive infections such as meningitis, bacteremia, endocarditis, and peritonitis have also been reported.

Most soft tissue infections from animal bites respond well to oral antibiotics and wound drainage, as needed. Empiric outpatient treatment should address both the most likely pathogens from the animal's mouth *(Pasteurella)* and from the patient's skin (*Staphylococcus aureus*, *Streptococcus pyogenes*). The combination of a penicillin with a β-lactamase inhibitor, such as amoxicillin-clavulanate is widely recommended for patients with no history of penicillin allergy. Patients with nonimmediate hypersensitivity reactions to penicillin can be treated with an oral third-generation cephalosporin such as cefixime or cefpodoxime. Children older than 8 years of age with serious allergic reactions to β-lactam antibiotics should be started on doxycycline, or levofloxacin if 18 years of age or older. Younger children could be placed on trimethoprim-sulfamethoxazole or azithromycin. Antibiotics that are ineffective against *Pasteurella*,such as first-generation cephalosporins (eg, cephalexin), anti-staphylococcal pencillinase-resistant penicillins (eg, nafcillin or dicloxacillin), vancomycin, erythromycin, and

clindamycin, should be avoided. Clindamycin may be added, however, for MRSA coverage. Other bacteria isolated in infected dog bite wounds include *Capnocytophaga canimorsus*, and anaerobes like *Bacteroides* species, fusobacteria, *Porphyromonas, Prevotella*, propionibacteria, and peptostreptococci. In this vignette, the boy is not on effective *Pasteurella* coverage. Since he has a significant penicillin allergy, the only acceptable antibiotic among the choices given is trimethoprim-sulfamethoxazole.

PREP Pearls

- *Pasteurella* is the most common pathogen isolated from animal bite wounds, although infection can also occur through cat scratches and cats or dogs licking non-intact skin. Infection is characterized by an intense inflammatory response occurring within 24 hours of the initial exposure.
- *Pasteurella* infections can cause cellulitis, septic arthritis, osteomyelitis, respiratory infections, meningitis, bacteremia, endocarditis, and peritonitis.
- Empiric treatment of animal bites should cover *Pasteurella, Staphylococcus aureus*, and *Streptococcus pyogenes*. Amoxicillin-clavulanate is recommended, or a third-generation cephalosporin, or trimethoprim-sulfamethoxazole with clindamycin in case of penicillin allergy.

ABP Content Specifications(s)

- Plan appropriate management for a patient with Pasteurella multocida infection

Suggested Readings

- American Academy of Pediatrics. *Pasteurella* infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* American Academy of Pediatrics; 2015:596-597.
- Goldstein EJC, Citron DM, Merriam CV, Tyrrell KL. Ceftaroline versus isolates from animal bite wounds: comparative in vitro activities against 243 isolates, including 156 *Pasteurella* species isolates. *Antimicrob Agents Chemother*. 2012;56(12):6319-6323. doi: http://dx.doi.org/10.1128/AAC.01794-12 .
- Wilson BA, Ho M. *Pasteurella multocida*: from zoonosis to cellular microbiology. *Clin Microbiol Rev*. 2013;26(3):631-655. doi: http://dx.doi.org/10.1128/CMR.00024-13 .

Question 208

You are called by the oncology service to evaluate a 17-year-old adolescent boy who developed fever associated with neutropenia and was found to have acute renal failure 5 days after starting a course of chemotherapy. You review the medications he received during this admission, which include cyclophosphamide, cisplatin, etoposide, vincristine, acetaminophen, and ceftazidime.

Of the following, the medication MOST likely to have contributed to this patient's renal dysfunction is

A. ceftazidime
B. cisplatin
C. cyclophosphamide
D. etoposide
E. vincristine

Correct Answer: B

Of the response choices, cisplatin most likely contributed to this adolescent's renal dysfunction. Cisplatin, a commonly used antineoplastic drug, has the potential to cause progressive renal impairment. Cisplatin-induced tubular toxicity, renal microvasculature vasoconstriction, and renal inflammation have been proposed as mechanisms for its nephrotoxicity. Patients with cisplatin nephrotoxicity may present with renal impairment, Fanconi syndrome (proximal tubular dysfunction with aminoaciduria and glucosuria), hypomagnesemia, and thrombotic microangiopathy (when given along with other chemotherapeutic agents such as bleomycin). Hydration with normal saline and diuresis, along with dosage reduction based on renal function (glomerular filtration rate [GFR]), has been shown to decrease cisplatin-associated nephrotoxicity. In some cases, carboplatin may be substituted for cisplatin because of its lower nephrotoxic potential.

It is important to identify the nephrotoxic potential of different medications used in clinical practice. Drug-induced nephrotoxicity may manifest as a rise in serum creatinine, dyselectrolytemia, tubulointersitial nephritis, and proteinuria or hematuria associated with glomerular injury. Failure to identify drug-induced renal injury may lead to an increased risk of systemic toxicity and adverse effects because many of these drugs are renally excreted. Use of nephrotoxic medications in children with intrinsic renal disease, decreased intravascular volume, or urinary obstruction increases the risk for nephrotoxicity. Once recognized, the basic steps in managing nephrotoxicity include discontinuation of the offending agent, maintenance of adequate hydration, and adjustment of medication dosing for drugs with renal elimination. Nephrotoxicity is not a common adverse effect associated with ceftazidime. It is important to note that cephalosporins may potentiate the nephrotoxicity of aminoglycoside antibiotics. Aminoglycosides are associated with tubular injury, and rarely, acute tubular necrosis. Tubular injury manifests as nonoliguric renal injury, with mild elevations in serum creatinine, polyuria (decreased concentrating ability due to distal tubular injury), and hypomagnesemia. Gentamicin has a higher risk of nephrotoxicity in comparison to tobramycin, with amikacin having the lowest risk. Direct nephrotoxicity is rarely seen with β-lactam antibiotics, which include penicillin, cephalosporin, cephamycin, carbapenems, monobactams, and β-lactamase inhibitors. However, tubulointersitial (allergic) nephritis or glomerulonephritis may be seen with severe hypersensitivity angiitis or serum sickness after β-lactam antibiotic use, with cross-sensitivity among the β-lactam group. Methicillin has been commonly associated with acute tubulointersitial nephritis, along with other systemic features of hypersensitivity such has fever, eosinophilia, and skin rash.

Antifungal agents (amphotericin B, foscarnet) are commonly associated with nephrotoxicity. Renal manifestations with amphotericin B include decreased GFR, hypokalemia, hypomagnesemia, metabolic acidosis, and polyuria (nephrogenic diabetes insipidus). The use of lipid formulations can reduce the incidence and severity of nephrotoxicity with amphotericin B. Nephrotoxicity is commonly seen in association with vancomycin, with increased risk associated with higher trough levels. Antiviral agents (eg, acyclovir) have also been associated with tubular injury and renal dysfunction.

Cyclophosphamide and ifosfamide are alkylating agents frequently used in the treatment of childhood malignancy. Of these, ifosfamide is more commonly associated with nephrotoxicity. Ifosfamide-induced renal toxicity results in proximal tubular dysfunction followed by decreased GFR. Clinical manifestations include metabolic acidosis, hypophosphatemia, hypokalemia, hypomagnesemia, and rickets. The nephrotoxic risk of ifosfamide increases with cumulative dose. The most common urologic toxicity seen with cyclophosphamide and ifosfamide is hemorrhagic cystitis. Hyponatremia, caused by an increased effect of antidiuretic hormone (ADH), is also seen in patients receiving cyclophosphamide.

Adverse effects associated with etoposide, a podophyllotoxin-derived antineoplastic drug include bone marrow suppression, alopecia, ovarian failure, nausea, and vomiting. Hepatotoxicity may occur infrequently, but nephrotoxicity is generally not associated with etoposide.

Vinca alkaloids (vincristine, vinblastine) are not associated with nephrotoxicity. However, hyponatremia, along with inappropriate ADH secretion, may be seen with vinca alkaloid use. Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used medications with analgesic and anti-inflammatory effects. According to current estimates, NSAID-induced renal injury occurs in 1% to 5% of patients using these medications. Renal injury has been reported with the use of nonselective (ibuprofen, naproxen, diclofenac) and selective cyclooxygenase-2 (COX-2) inhibitors (celecoxib). Currently, there is no safe dose or duration for avoiding NSAID-associated renal injury. Infrequent use or doses at less than current recommendations will not reduce the risk of renal injury in high-risk patients. The inhibition of renal prostaglandins by NSAIDs can lead to renal ischemia, with a decreased GFR leading to an acute rise in serum creatinine. Risk is increased in patients with underlying renal vasoconstriction, such as chronic kidney disease; those with hypovolemia from true volume depletion (eg, diuresis, vomiting, or diarrhea) or decreased effective circulation (eg, heart failure, nephrotic syndrome, or cirrhosis) are at increased risk for NSAID-associated renal injury.

Radiocontrast agents have also been associated with tubular injury and renal dysfunction.

PREP Pearls

- Use of nephrotoxic medications in children with intrinsic renal disease, decreased intravascular volume, or urinary obstruction increases the risk for drug-induced nephrotoxicity.
- Cisplatin, a commonly used antineoplastic drug, can cause progressive renal impairment.
- The management of nephrotoxicity includes discontinuation of the offending agent, maintenance of adequate hydration, and adjustment of medication dosing for drugs with renal elimination.

ABP Content Specifications(s)

- Recognize the drug classes that can cause renal toxicity

Suggested Readings

- Jones DP, Spunt SL, Green D, Springate JE. Renal late effects in patients treated for cancer in childhood: a report from Children's Oncology group. *Pediatr Blood Cancer*. 2008;51(6):724-731. doi: http://dx.doi.org/10.1002/pbc.21695.
- Patzer L. Nephrotoxicity as a cause of acute kidney injury in children. *Pediatr Nephrol*. 2008;23(12):2159-2173. doi: http://dx.doi.org/10.1007/s00467-007-0721-x.
- Selewski DT, Symons JM. Acute kidney injury. *Pediatr Rev*. 2014;35(1):30-41. doi: http://dx.doi.org/10.1542/pir.35-1-30.

Question 209

You are seeing a 33-week-gestation male neonate now 6 hours old, born via spontaneous vaginal delivery to a mother with type A2 gestational diabetes. His initial dextrose stick in the delivery room was 50 mg/dL (2.8 mmol/L). At birth, his measurements were a weight of 2.9 kg, head circumference of 32 cm, and length of 46 cm. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	18,600/μL (18.6×10^9/L)
Hemoglobin	20 g/dL (200 g/L)
Platelet count	309×10^3/μL (309×10^9/L)

The neonate is in room air and is taking oral feedings well. The decision is made to transfer him to the level 2 nursery. A medical student with whom you are working asks why he cannot remain in the full-term nursery.

Of the following, the BEST explanation is

A. birth weight less than 3 kg
B. gestational diabetes
C. large for gestational age
D. polycythemia
E. preterm infant

Correct Answer: E

The neonate weighing 2,900 g in the vignette should be transferred to the level 2 nursery because of his gestational age of 33 weeks. In the mid-1970s, the March of Dimes published a report recommending regionalization of obstetric and neonatal care to improve neonatal outcomes. Briefly, a level 1 nursery admits infants with gestational age of 35 weeks or greater with no medical complications. A level 2 nursery cares for infants less than 35 weeks of gestation and can provide assisted ventilation for brief duration. Level 3 and 4 nurseries are best equipped to care for infants less than 32 weeks of gestation, have access to pediatric subspecialty and surgical services, and are able to provide the highest level of respiratory support. In multiple studies, transfer of infants to the appropriate level nursery care has been associated with decreased neonatal mortality and morbidity.

Neonates born to mothers with gestational hypertension or chronic hypertension may have intrauterine growth restriction and be born at lower birthweights for their gestational age. Alternatively, neonates born to mothers with diabetes may be large for gestational age. Gestational age predicts developmental maturity and postnatal outcomes better than birthweight. Birthweight must be plotted against gestational age to confirm appropriate growth and development. For the neonate in this vignette, despite the fact that he is 2,900 g and comfortable in room air, he has an increased risk of complications of prematurity such as hypoglycemia and hypothermia. This neonate should be transferred to the level 2 nursery because of his gestational age.

Neonates weighing less than 3 kg with a gestational age between 35 to 37 weeks of gestation who remain stable in room air and are feeding well by mouth can also remain in a level 1 nursery.

Neonates with gestational diabetes with a normal glucose level can be cared for in a level 1 nursery if greater than 35 weeks of gestation. The neonate in this vignette had a glucose level of 50 mg/dL (2.8 mmol/L), which is acceptable in the first 24 hours after birth.
Large-for-gestational age neonates who have stable blood glucose values can stay in a level 1 nursery if greater than 34 weeks of gestation.

Neonates with polycythemia (hemoglobin ≥ 20 g/dL [200 g/L]) should have a repeat central sample drawn to confirm the diagnosis. If the hemoglobin is greater than 21.6 g/dL (216 g/L) on a central stick, the neonate should be transferred to a level 3 nursery for monitoring and possible partial exchange transfusion.

PREP Pearls

- Regionalization of perinatal care improves maternal and neonatal outcomes.
- Gestational age is a better predictor of complications of prematurity than birthweight.
- Birthweight must be plotted against gestational age to confirm appropriate growth and development.

ABP Content Specifications(s)

- Recognize the need to plot anthropomorphic measurements of a newborn infant against gestational age on a growth chart

Suggested Readings

- Carlo WA. Overview of mortality and morbidity. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:789-793.
- Committee on Fetus and Newborn. Levels of neonatal care. *Pediatrics.* 2012;130(3):587-597. doi: http://dx.doi.org/10.1542/peds.2012-1999.
- Ryan GM Jr. Toward improving the outcome of pregnancy Recommendations for the regional development of perinatal health services. *Obstet Gynecol.* 1975;46(4):375-384.

Question 210

The mother of a 1-year-old girl with cystic fibrosis calls your office for advice. The family is traveling with their daughter to an area with a hot, arid climate with daytime temperatures expected to be above 90°F. The mother asks if you recommend any changes to her daughter's medications or diet during the trip.

Of the following, the MOST appropriate recommendation is

A. decreased vitamin D supplementation
B. increased dose of pancreatic enzyme replacement
C. increased free water intake
D. increased sodium chloride supplementation
E. no alteration in diet or medications

Correct Answer: D

Patients with cystic fibrosis (CF) are at risk for hypochloremic hyponatremic dehydration because of excess epithelial sodium losses. Infants with CF are at higher risk than older children and adults because of their larger relative body surface areas. Routine supplementation with sodium chloride is recommended, with the dose determined by age. Supplementation must be increased in settings of excessive sweating, high ambient temperature or humidity, strenuous exercise, fever, vomiting, or diarrhea.

Patients with CF require vitamin D and other fat-soluble vitamin supplementation, and those with pancreatic insufficiency should also receive pancreatic enzyme replacement. None of these medications needs to be adjusted for ambient temperature or other causes of increased fluid loss. Increased free water intake would increase this patient's risk of hypochloremia and hyponatremia.

PREP Pearls

- Patients with cystic fibrosis are at risk for hypochloremic hyponatremic dehydration because of excess epithelial sodium losses. Routine sodium chloride supplementation is recommended.
- Sodium chloride supplementation must be increased in settings of increased loss, including excessive sweating, high temperature or humidity, strenuous exercise, fever, vomiting, or diarrhea.
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ABP Content Specifications(s)

- Recognize the association of hypochloremic/hyponatremic dehydration in patients who have cystic fibrosis

Suggested Readings

- Borowitz D, Robinson KA, Rosenfeld M, et al. Cystic fibrosis foundation evidence-based guidelines for management of infants with cystic fibrosis. *J Pediatr.* 2009;155(6 suppl):S73-S93. doi: http://dx.doi.org/10.1016/j.jpeds.2009.09.001

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- Guimarães EV, Schettino GC, Camargos PA, Penna FJ. Prevalence of hyponatremia at diagnosis and factors associated with the longitudinal variation in serum sodium levels in infants with cystic fibrosis. *J Pediatr.* 2012;161(2):285-289. doi: http://dx.doi.org/10.1016/j.jpeds.2012.01.052.

Question 211

A 3-week-old neonate born at 28 weeks of gestation develops episodes of apnea and bradycardia in the neonatal intensive care unit. Vital signs show a temperature of 37°C, respiratory rate of 25 breaths/min, heart rate of 110 beats/min, blood pressure of 55/35 mm Hg, and his weight is 1,425 g. On physical examination, he is pale and breathing irregularly. Laboratory data are shown:

Laboratory test	Result
White blood cell count	3,200/µL (3.20×10^9/L)
Segmented neutrophils	59%
Bands	10%
Lymphocytes	20%
Monocytes	11%
Hemoglobin	8.8 g/dL (88 g/L)
Platelet count	87×10^3/µL (87×10^9/L)
Blood culture	*Candida glabrata*
Cerebrospinal fluid (CSF) white blood cells	88/µL
CSF red blood cells	5/µL
CSF glucose	50 mg/dL
CSF protein	150 mg/dL

Of the following, the BEST next study to evaluate for dissemination of this infection is

A. abdominal ultrasonography
B. dilated retinal examination
C. echocardiogram
D. head ultrasonography
E. long bone films

Correct Answer: B

The patient in the vignette has candidemia and meningitis. As in the vignette, lumbar puncture is recommended for all neonates with candidemia. The best next step to evaluate for disseminated infection is a dilated retinal examination. Ophthalmologic evaluation is recommended for all patients with candidemia.

Infections due to *Candida* species have a wide spectrum of presentation. In immunocompetent hosts, *Candida* species cause superficial infections, such as thrush, dermatitis, and onychia. However, very low birthweight neonates and immunocompromised individuals (especially those with neutropenia, neutrophil defects, or T-cell defects) can develop invasive candidiasis, which can lead to infection in nearly any anatomic site. Additionally, individuals with indwelling devices, such as central vascular catheters, peritoneal catheters, and urinary catheters are at risk for invasive *Candida* infections.

Abdominal ultrasonography and echocardiography are recommended in the setting of multiple positive cultures. Abdominal ultrasonography can assess genitourinary tract involvement, as well as fungal nodules in the liver and spleen. Echocardiogram helps assess for endocarditis or an endovascular focus. Head ultrasonography would be needed if a central nervous system complication, such as hydrocephalus, is suspected. While osteomyelitis can occur in the setting of candidemia, plain films would be recommended only if this diagnosis is suggested by physical examination.

Thrush is usually treated with nystatin oral suspension and skin infections with topical antifungals including nystatin and several azole drugs. Refractory mucocutaneous infections are treated with oral agents, usually fluconazole. Invasive infections are treated with parenteral antifungals including the azoles, echinocandins, or amphotericin. Certain *Candida*species have variable susceptibilities to the parenteral drugs and this must be considered when choosing empiric agents. In addition to pharmacologic therapy, management of a patient with an invasive *Candida* infection associated with an indwelling device usually involves removal of the involved device.

PREP Pearls

- Very low birthweight neonates and immunocompromised individuals (especially those with neutropenia, neutrophil defects, or T-cell defects) can develop invasive candidiasis.
- Lumbar puncture is recommended for all neonates and ophthalmologic evaluation for all individuals with candidemia.
- Management of a patient with an invasive *Candida* infection associated with an indwelling device usually includes removal of the involved device.

ABP Content Specifications(s)

- Recognize the clinical features associated with Candida infection
- Identify the risk factors for candidiasis in patients of various ages
- Plan appropriate management for a patient with Candida infection

Suggested Readings

- American Academy of Pediatrics. Candidiasis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:275-280.
- Pappas PG, Kauffman CA, Andres D, et al. Clinical practice guideline for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009;48(5):502-535. doi: http://dx.doi.org/10.1086/596757.

Question 212

A 10-year-old girl is brought to your clinic for a health supervision visit. She has epilepsy, spastic quadriplegic cerebral palsy, is nonambulatory, and receives all nutrition and medications via a gastric tube. She was hospitalized last year for a femur fracture after a seizure, but has otherwise been healthy. You review her medication list, which includes valproate, baclofen, clonazepam, polyethylene glycol, and vitamin D 600 IU/day. You obtain a 25 hydroxyvitamin D level and it is 35 ng/mL (87.4 nmol/L) (normal, > 30 ng/mL).

Of the following, the BEST next step is

A. continue vitamin D 600 IU/day
B. obtain a serum parathyroid hormone level
C. obtain a serum valproate level
D. start a bisphosphonate
E. start supplemental calcium

Correct Answer: A

The girl in the vignette takes an anticonvulsant medication, which is an indication for vitamin D deficiency screening. She should continue taking the recommended daily allowance (RDA) of vitamin D, which for her age is 600 IU. In children taking anticonvulsants, the 25 hydroxyvitamin D level should be checked annually and maintained in the normal range. Vitamin D deficiency can occur regardless of the serum level of the anticonvulsant. Her level is in the normal range, so she does not require additional testing such as calcium or parathyroid hormone levels. Additional calcium supplementation is not necessary for her unless she is unable to absorb her RDA via her current enteral feeds. Obtaining a serum valproate level would not be helpful.

Pediatricians should monitor the bone health of children with conditions that increase the risk of decreased bone mass (Item C212). In addition to taking anticonvulsants and having increased risk of vitamin D deficiency, the girl in the vignette has cerebral palsy, is nonambulatory, and has already had a fracture. She should have a dual-energy x-ray absorptiometry scan to assess bone mineral density and it may be reasonable to start a bisphosphonate. There are limited data about the use of bisphosphonates in children, so referral to a pediatric endocrinologist or other bone specialist is appropriate before empirically starting bisphosphonates.

Many children with severe neurologic deficits will require feeding via gastrostomy tube. Many balanced diets are available that can provide complete nutritional needs of the patient. Consultation with a nutritionist can help in determining the appropriate dietary needs for each child.

PREP Pearls

- In children taking anticonvulsants, the 25 hydroxyvitamin D level should be checked annually and maintained in the normal range.
- The recommended daily allowance of vitamin D for children older than 1 year of age is 600 IU.

ABP Content Specifications(s)

- Plan the dietary management for a patient with a neurologic impairment

Suggested Readings

- Bachrach LK, Sills IN, Section on Endocrinology. Clinical report—bone densitometry in children and adolescents. *Pediatrics.* 2011;127(1):189-194. doi: http://dx.doi.org/10.1542/peds.2010-2961.
- Golden NH, Abrams SA, Committee on Nutrition. Optimizing bone health in children and adolescents. *Pediatrics.*2014;134(4):e1229-e1243. doi: http://dx.doi.org/10.1542/peds.2014-2173.

Question 213

A 13-year-old adolescent girl with diabetes mellitus presents to your office with her mother for a health supervision visit. The mother reports that, over the past 4 months, the adolescent has had loose stools and intermittent abdominal pain. There is no associated emesis. On physical examination, the adolescent appears comfortable. Her heart rate is 71 beats/min, respiratory rate is 18 breaths/min, and weight is at the 9th percentile, with a body mass index at the 4th percentile. One year ago, the adolescent's weight was at the 36th percentile. Her abdomen is distended, nontender, and tympanic, with normal bowel sounds.

Of the following, the MOST sensitive screening test for this diagnosis is

A. deaminated gliadin peptide
B. endomysial antibody
C. HLA DQ2 DQ8
D. immunoglobulin A (IgA)
E. tissue transglutaminase IgA

Correct Answer: E

Celiac disease is an autoimmune disease caused by sensitivity to gluten, which is found in wheat, rye, and barley. The overall prevalence of celiac disease is 1% across all populations, with an increased prevalence (approaching 5%-10%) in children with type 1 diabetes, thyroid disease, Turner syndrome, trisomy 21, and in children with affected family members. Tissue transglutaminase (TTG) immunoglobulin IgA (IgA), elevated in more than 95% of affected individuals, is the best screening test for celiac disease in an IgA-sufficient child (Item C213A). The sensitivity and specificity are 93% to 96% and 96% to 99%, respectively. Although laboratory testing is used to screen for celiac disease, the gold standard for diagnosis remains duodenal biopsy with endoscopy.

Item C213A. Diagnostic Evaluation of Celiac Disease.

Laboratory testing • Immunoglobulin A antibody to tissue transglutaminase • Immunoglobulin A level (screen for immunoglobulin A deficiency) • Antiendomysial antibodies
Endoscopy 4-6 duodenal biopsy samples

Courtesy of C. Waasdorp Hurtado

Deaminated gliadin and gliadin antibody are less sensitive and specific for celiac disease than is TTG IgA testing. Endomysial antibody testing is highly specific for celiac disease, approaching 100%, but the sensitivity is less than 90%. Genetic testing (HLA DQ2 and DQ8) can identify the presence of the genes that place children at risk for the development of celiac disease; however, gene testing cannot identify active celiac disease. Ninety-five percent of affected individuals are positive for DQ2, with the remaining 5% positive for DQ8. The IgA level is an important part of the screening to confirm the accuracy of the TTG IgA testing, but it does not screen for celiac disease.

The classic presentation of celiac disease in childhood is the triad of failure to thrive, bloating, and diarrhea. However, celiac disease can present with a wide variety of gastrointestinal and nongastrointestinal symptoms, especially in older children and adults (Item C213B). Laboratory findings in patients with celiac disease may include iron and folate-deficiency anemia, elevated liver transaminases and fat-soluble vitamin deficiencies. Malabsorption occurs because of injured, shortened villi; this differs from malabsorption in cystic fibrosis, which is caused by pancreatic insufficiency. The shortened villi result in malabsorption of fats and disaccharides, which worsen the diarrhea.

Item C213B. Celiac Disease Signs and Symptoms.

Classic Presentation	Nonclassic Presentation
Diarrhea Failure to thrive Gassiness/Bloating Muscle wasting	Abdominal pain Alopecia Arthritis Constipation Constitutional delay of puberty Dental enamel abnormalities Dermatitis herpetiformis Infertility Intestinal lymphoma Neurologic and psychiatric disorders (ataxia, migraines, depression, fatigue, peripheral neuropathy) Osteoporosis rash Short stature

Courtesy of C. Waasdorp Hurtado

Children with celiac disease should be placed on a gluten-free diet. Nutritional education for both parents and children is critical to success. Vitamin D levels should be assessed, with supplementation as needed.

PREP Pearls

- Tissue transglutaminase immunoglobulin A is the best screening test for celiac disease (CD)
- Duodenal biopsy with endoscopy remains the gold standard for diagnosis of CD.
- Children with CD must be taking a gluten-containing diet at the time of diagnostic testing
- The classic pediatric presentation of CD is the triad of diarrhea, failure to thrive, and bloating.
- There is a wide variety of nonclassic presentations of CD, which are more common in older children and adults.

ABP Content Specifications(s)

- Differentiate the mechanism of absorption in patients with cystic fibrosis from that in patients with celiac disease
- Plan appropriate dietary management for a patient with celiac disease
- Recognize the clinical features associated with celiac disease
- Plan the appropriate diagnostic evaluation for celiac disease

Suggested Readings

- Agardh D, Lee HS, Kurppa K, et al, for the TEDDY Study Group. Clinical features of celiac disease: a prospective birth cohort. *Pediatrics.* 2015;35(4):627-634. doi: http://dx.doi.org/10.1542/peds.2014-3675.
- Barker JM, Liu E. Celiac disease: pathophysiology, clinical manifestations, and associated autoimmune conditions. *Adv Pediatr*. 2008;55:349-365. doi: http://dx.doi.org/10.1016/j.yapd.2008.07.001.
- Ediger TR, Hill ID. Celiac disease. *Pediatr Rev.* 2014;35(10):409-416. doi: http://dx.doi.org/10.1542/pir.35-10-409.

Question 214

A 4-hour-old neonate on the newborn nursery service was noted by nursing to have ambiguous genitalia. The neonate was born at 40 weeks of gestation by spontaneous vaginal delivery to a 38-year-old gravida 2, now para 2 mother after an uncomplicated pregnancy. Given the mother's age, noninvasive prenatal testing was performed and revealed a 46,XY fetal karyotype. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. Birthweight was 3.6 kg. The neonate is doing well and successfully breastfed during the first hour of life. On physical examination, the neonate is vigorous and without dysmorphic features. Examination of the genitalia reveals a 1-cm phallic structure with the urethral opening at the base. There are bilateral labial-scrotal folds. A gonad is palpable in the right labial-scrotal fold, but not on the left (Item Q214). The remainder of the physical examination is unremarkable. The parents want to know if their child is a boy or a girl.

Of the following, the BEST statement to counsel the parents regarding gender of rearing is

A. appearance of the genitalia appear more female and masculinizing surgical intervention would be difficult, so recommend female gender of rearing
B. await further multidisciplinary evaluation and assist the parents in making an informed decision about gender of rearing
C. await a trial of testosterone, and if there is a significant increase in phallic size, recommend male gender of rearing
D. if male genetic sex is confirmed on a repeat postnatal karyotype, recommend male gender of rearing
E. natural history studies show that many infants born with similar-appearing genitalia ultimately identify as male, so recommend male gender of rearing

Correct Answer: B

The neonate described in the vignette has a prenatal 46,XY karyotype and was born with ambiguous genitalia. The decision regarding gender of rearing is complex and should be made ultimately by the parents after a multidisciplinary evaluation to assist them in making the most informed decision possible. Considerations when determining gender of rearing may include, but are not limited to: genetic sex, underlying diagnosis, internal and external anatomy, potential for future urologic and sexual function, response to testosterone, prognosis regarding surgical outcomes, and prediction of future gender identity based on available evidence. The nonpreferred response choices only consider one of these factors.

Ethical principles that can be applied to this situation are autonomy, beneficence, and nonmaleficence. Respect for autonomy is the right for individuals to make their own decisions, or in this case, the right for the parents to make decisions for their child. To assist them in making the decision they feel is best for their child, the parents should be given as much information as possible about their child's diagnosis and prognosis. Beneficence is the benefit to the patient and nonmaleficence is avoiding harm. The diagnostic approach and information provided to the parents should be in the best interest of the infant, with the goal of achieving the most benefit with the least potential for harm. The approach should be multidisciplinary and include psychosocial support for the family. As recommended in the 2006 consensus statement on management of these disorders, the multidisciplinary team should achieve consensus prior to making recommendations to the family.

PREP Pearls

- Decisions regarding gender of rearing for infants with ambiguous genitalia are complex and should ultimately be made by the parents after multidisciplinary evaluation and provision of all available information.
- The 4 principles of medical ethics are respect for autonomy, beneficence, nonmaleficence, and justice.
- The approach to the infant with ambiguous genitalia should be multidisciplinary and include psychological support for the family.

ABP Content Specifications(s)

- Recognize and apply ethical principles involved in using new technologies for sex/gender assignment

Suggested Readings

- Karkazis K, Rossi WC. Ethics for the pediatrician: disorders of sex development: optimizing care. *Pediatr Rev.*2010;31(11):e82-e85. doi: http://dx.doi.org/10.1542/pir.31-11-e82.
- Lee PA, Houk CP, Ahmed SF, Hughes IA. Consensus statement on management of intersex disorders. *Pediatrics.*2006;118(2):e488-e500. doi: http://dx.doi.org/10.1542/peds.2006-0738.
- Lee PA, Wisniewski AB, Baskin L, et al. Advances in diagnosis and care of persons with DSD over the last decade. *Int J Pediatr Endocrinol*. 2014;2014:19. doi: http://dx.doi.org/10.1186/1687-9856-2014-19.

Question 215

A 5-year-old girl is brought to your office because of concerns about her growth. Her mother reports that "it seems like she hasn't grown in forever." She has no significant past medical history. The patient's past and current weight, height, body mass index (BMI), BMI percentile, as well as lower and upper body segment length (U/L ratio) are recorded.

	2 years ago	1 year ago	Current
Height	95 cm	102 cm	110 cm
Weight	14.3 kg	16 kg	18.4 kg
BMI	15.8 kg/m^2	15.4 kg/m^2	15.2 kg/m^2
BMI %	53%	52%	51%
U/L ratio	1.35	1.45	1.55

Of the following, the finding MOST concerning for a growth abnormality in this child is

A. body mass index percentile that has declined over the past 2 years
B. height increase of 8 cm over the past year
C. increase in the upper body/lower body segment ratio over the past year
D. increasing growth velocity over the past 2 years
E. weight increase of 2.4 kg over the past year

Correct Answer: C

The only abnormal feature of growth presented on the patient in this vignette is the increase in the upper body segment/lower body segment (U/L) ratio over the past year. The U/L ratio is an assessment of body proportions that compares the lower body segment (a measure from the top of the pubic symphysis to the floor in a standing patient) and the upper body segment (determined from subtracting the lower body segment from the standing height). The U/L ratio declines from birth and reaches its lowest point during early puberty. Prior to and during puberty, the legs grow faster than the trunk, which accounts for the trend of a decreasing U/L ratio. After pubertal growth, there is often a very slight increase in U/L ratio, as the legs stop growing prior to the trunk. The average U/L ratio is 1.7 for an infant, 1.3 at 3 years of age, and 1.0 for an adult. Several growth disorders and disease processes may be associated with abnormal patterns in the U/L ratio. A decreased U/L ratio for age may be associated with skeletal dysplasias involving the spine and also with disorders involving delayed or incomplete puberty such as Klinefelter, Marfan, and Kallmann syndromes. Increased U/L ratios may be seen in Turner syndrome, skeletal dysplasias involving the long bones (such as achondroplasia), or in patients with precocious puberty.

The body mass index (BMI) and BMI percentile for the patient in the vignette have remained relatively consistent over the past 2 years, which reflects a steady growth pattern. Starting at 3 years of age, linear growth occurs at a rate of about 4 to 7 cm per year and a weight gain of 2.5 kg per year. The average increases in both height and weight remain consistent until the start of puberty. The patient's growth of 8 cm (and her growth velocity over the past year) is slightly higher than average, but still in the normal range. The weight gain of 2.4 kg over the year is normal.

PREP Pearls

- The upper body segment/lower body segment (U/L) ratio decreases from birth and reaches its lowest point during early puberty.
- The average growth and weight gain for a child 3 years of age to the start of puberty is 4 to 7 cm/year and 2.5 kg/year, respectively.
- Measurement of the U/L ratio can aid in the evaluation of children with growth disorders

ABP Content Specifications(s)

- Recognize the differences in upper body segment-to-lower body segment ratio in children compared with that of adults

Suggested Readings

- Keane VA. Assessment of growth. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:84-89.
- Rose SR, Vogiatzi MG, Copeland KC. A general pediatric approach to evaluating a short child. *Pediatr Rev.* 2005;26(11):410-420..
- Turan S, Bereket A, Omar A, Berber M, Ozen A, Bekiroglu N. Upper segment/lower segment ratio and armspan–height difference in healthy Turkish children. *Acta Paediatr.* 2005;94(4):407-413.
- Vogiatzi MG, Copeland KC. The short child. *Pediatr Rev.* 1998;19(3):92-99. doi: http://dx.doi.org/10.1542/pir.19-3-92.

Question 216

A 13-month-old girl presents to the emergency department in July with fever and respiratory distress. Her mother reports that she had been well until 2 days before this presentation when she developed a fever up to 39°C and poor fluid intake. Since then, her breathing has been increasingly labored. The girl was born at full term by normal vaginal delivery, and has had appropriate growth and development. Her immunizations are up to date. The girl's temperature is 38.8°C, respiratory rate is 58 breaths/min, heart rate is 147 beats/min, blood pressure is 102/68 mm Hg, and oxygen saturation is 89% on room air. She has copious rhinorrhea, nasal flaring, and subcostal retractions. A chest radiograph was performed (Item Q216).

Item Q216: Chest radiographs for the girl described in the vignette. Courtesy of J Fish
Courtesy of J Fish

Of the following, the test MOST likely to establish this girl's diagnosis is a

A. flow cytometry test for the phagocyte oxidative burst
B. nasal swab polymerase chain reaction for influenza virus A and B
C. purified protein derivative test
D. serum test for α-fetoprotein
E. spot urine test for homovanillic acid and vanillylmandelic acid

Correct Answer: E

The girl in the vignette has symptoms consistent with a moderately severe viral upper and lower respiratory infection. She presented with fever, poor oral fluid intake, labored breathing, copious rhinorrhea, and subcostal retractions. A chest radiograph was obtained, which was not consistent with pneumonia, but instead showed a posterior mass in the right paraspinal space. Although the initial assessment of the child would appropriately suggest an infectious pneumonia, the finding on the chest radiograph changes the differential diagnosis. Given the age of the child and the location of the mass, the most likely diagnosis is a paraspinal neuroblastoma. The test most likely to establish the diagnosis is therefore a spot urine test for homovanillic acid and vanillylmandelic acid.

Neuroblastoma is the most common extracranial solid tumor in children, with approximately 600 to 800 cases diagnosed in the United States annually. Neuroblastoma is an embryonal tumor of the sympaticoadrenal lineage of the neural crest, and can arise anywhere in the sympathetic chain, including paraspinal ganglia, adrenal glands, and celiac ganglia. Although high-risk neuroblastoma is an aggressive cancer that has poor overall survival, non–high-risk neuroblastoma has an excellent prognosis. Generally, localized disease in children younger than 18 months of age falls into the non–high-risk category. Nonetheless, localized disease in the thorax can lead to significant morbidity because of compression of local structures such as the trachea, bronchi, heart, blood vessels, and spinal cord. A thorough assessment of risk factors and impending morbidity is needed to determine optimal treatment.

Flow cytometry to assess the phagocyte oxidative burst is the test of choice for chronic granulomatous disease (CGD), a diagnosis that is not consistent with the girl's medical history. She has not had recurrent infections, had been well until this acute illness, and is a girl (the most common forms of CGD are X-linked).

Although the initial presentation of the girl could be consistent with an influenza virus infection, the chest radiograph is not consistent with that diagnosis.

The girl has no reported risk factors for tuberculosis and the chest radiograph is not consistent with tuberculosis. Therefore, there is no indication to perform a purified protein derivative test. Serum α-fetoprotein is a marker for germ cell tumors. Germ cell tumors (including teratomas) can present as mediastinal masses, however, they are almost always anterior mediastinal masses. The differential diagnosis of anterior mediastinal masses includes the "4 Ts": teratomas, thymomas, thyroid cancers, and "terrible lymphomas." A mass in the posterior thorax is much more consistent with neuroblastoma.

PREP Pearls

- Neuroblastoma is an embryonal tumor of the sympaticoadrenal lineage of the neural crest, and can arise anywhere in the sympathetic chain, including paraspinal ganglia, adrenal glands, and celiac ganglia.
- The differential diagnosis of a posterior thoracic mass in an infant should include neuroblastoma.

ABP Content Specifications(s)

- Recognize clinical findings associated with neuroblastoma
- Plan the appropriate diagnostic evaluation of neuroblastoma
- Formulate an age-appropriate differential diagnosis of an abdominal mass

Suggested Readings

- Maris JM. Recent advances in neuroblastoma. *N Engl J Med.* 2010;362(23):2202-2211. doi: http://dx.doi.org/10.1056/NEJMra0804577.
- Park JR, Eggert A, Caron H. Neuroblastoma: biology, prognosis, and treatment. *Hematol Oncol Clin North Am.*2010;24(1)65-86. doi: http://dx.doi.org/10.1016/j.hoc.2009.11.011.
- Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015;33(27):3008-3017. doi: http://dx.doi.org/10.1200/JCO.2014.59.4648.

Question 217

A 2-week-old neonate with an atrioventricular canal defect presents to your office for a health supervision visit. She was asymptomatic at birth, as would be expected. The family is very conscientious about bringing their child to her scheduled appointments, and they inform you that they have decided not to pursue surgical treatment of her heart defect. They will be happy to treat her symptoms with medication, but do not want to subject her to hospitalizations or diagnostic testing that is invasive or painful. Her parents are aware that this course of action may shorten her life, but they believe that giving her a life without trauma is more important. You do not agree with this decision and hope to work toward a mutual understanding of these different perspectives.

Of the following, the PRIMARY principle of ethical decision-making the parents are applying is

A. beneficence
B. fidelity
C. justice
D. nonmaleficence
E. veracity

Correct Answer: D

The primary principle being invoked by the parents of the neonate in the vignette is nonmaleficence.

The principle of doing no harm, or nonmaleficence, is one of the major ethical principles in medical decision-making, and was found to be the most important factor in a study of nonmedical psychology students. For these parents, this is the paramount factor in their decision-making. From the physician's point of view, the principle of autonomy (the parent's right to make decisions for their child) will likely be an area of conflict.

Another important principle in ethical decision-making is beneficence, the concept of "doing good for others." In a situation in which parents and physicians or other healthcare providers are not in agreement, it is crucial to determine whether this issue is merely a difference of opinion or one of quality of care and life. The American Academy of Pediatrics (AAP) has published a policy statement that includes the core principle that "all children are entitled to effective medical treatment likely to prevent serious harm or death." The question of whether the parents' decision is considered suboptimal care or likely to cause harm is a distinction with which ethics committees are often faced.

The other response choices are clearly not the most important principles guiding the parents' decision at this time. Fidelity is the principle of maintaining confidentiality. Justice is the principle of being fair. Veracity is the principle of truth telling.

The AAP maintains a comprehensive bibliography of articles and papers on the subject of ethics and medical decision-making.

PREP Pearls

- The ethical principle of nonmaleficence is that of "do no harm."
- Parents are responsible to act for their dependent children and their preferences may sometimes conflict with those of healthcare providers, especially if they are invoking different ethical principles.

ABP Content Specifications(s)

- Recognize and apply ethical principles regarding the care of children and adolescents with disabilities

Suggested Readings

- Adam MB, Diekema DS, Mercurio MR. American Academy of Pediatrics bioethics resident curriculum: case-based teaching guides. American Academy of Pediatrics website. https://www2.aap.org/sections/bioethics/PDFs/BioethicsResidentCurriculum.pdf .
- Cummings CL, Mercurio MR. Autonomy, beneficence, and the rights of parents and children—exploring the application of ethical principles in pediatrics. American Academy of Pediatrics website. https://www2.aap.org/sections/bioethics/PDFs/Curriculum_Session10.pdf.
- Page K. The four principles: can they be measured and do they predict ethical decision making? *BMC Med Ethics.*2012;13:10. doi: http://dx.doi.org/10.1186/1472-6939-13-10.
- Snyder JE, Gauthier CC. The underlying principles of ethical patient care. *Evidence-Based Medical Ethics: Cases for Practice-Based Learning.* Totowa, NJ: Humana Press; 2008:11-16.

Question 218

A 3-year-old girl is brought to your office for a health supervision visit. Her father reports that she is able to dress herself and is about to start a preschool program. During the visit, you see her draw a circle, hop on both feet, balance on 1 foot, and describe what your stethoscope is used for when prompted. Her father asks you if her development is "on track."

Of the following, the BEST way to screen development in this child is

A. administer the Ages and Stages Questionnaire
B. administer the Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R)
C. administer the Pediatric Symptom Checklist
D. office-based surveillance at all visits
E. teacher-based surveillance at preschool

Correct Answer: A

Evaluating development is a key function of pediatric primary care. Routine screening for developmental delays using validated instruments is recommended at 9, 18, 24, and 30 months of age. Periodic screening with formal tools supplements regular surveillance, which should be done at every health supervision visit. This surveillance includes eliciting parental concerns, observing the child, and being familiar with the child's developmental and clinical history. If surveillance suggests a potential risk for developmental delay, screening with an instrument such as the Ages and Stages Questionnaire (ASQ) is indicated. The ASQ is available in different versions for infants and children ages 1 to 66 months. The ASQ tests development in several domains, including fine and gross motor skills, language and communication skills, and socio-emotional skills, and offers sub-scores in each domain to help further characterize any concerns for delays. Caregivers can complete the questionnaire in 10 to 15 minutes.

In addition to the activities reported by the father in the vignette, developmental milestones for a 36-month-old child include self-feeding skills, conversing in 2- to 3-word sentences, building a tower of 6 to 8 cubes, drawing a person with 2 body parts, and walking up stairs with alternating feet. While office-based surveillance can be valuable, many healthcare providers, particularly those in training or with less experience with children, can make inaccurate assessments of development based on surveillance alone. The addition of a formal screening tool improves accuracy. In addition to the ASQ, the Pediatric Evaluation of Developmental Status (PEDS) and the Survey of Wellbeing of Young Children (SWYC) also assess global development in this age group. Children with developmental concerns identified with these tools should be referred to early intervention services and appropriate medical specialists.

The Pediatric Symptom Checklist is a psychosocial screening questionnaire for children aged 4 years and older. The Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) is a tool used to screen for autism spectrum disorder in children ages 16 to 30 months. While input from a child's teacher may be enlightening, teacher-based surveillance has not been formally studied as a means of screening for developmental delays.

PREP Pearls

- The American Academy of Pediatrics recommends developmental screening at 9, 18, 24, and 30 months of age using a formal tool such as the Ages and Stages Questionnaire.
- Formal tools should also be administered at any visit where a developmental concern arises.
- While the Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) screens for autism spectrum disorder, it does not fully assess global development.

ABP Content Specifications(s)

- Evaluate the motor developmental progress/status of a child at 36 months of age
- Evaluate the cognitive and behavioral developmental progress/status of a child at 36 months of age, including recognition of abnormalities

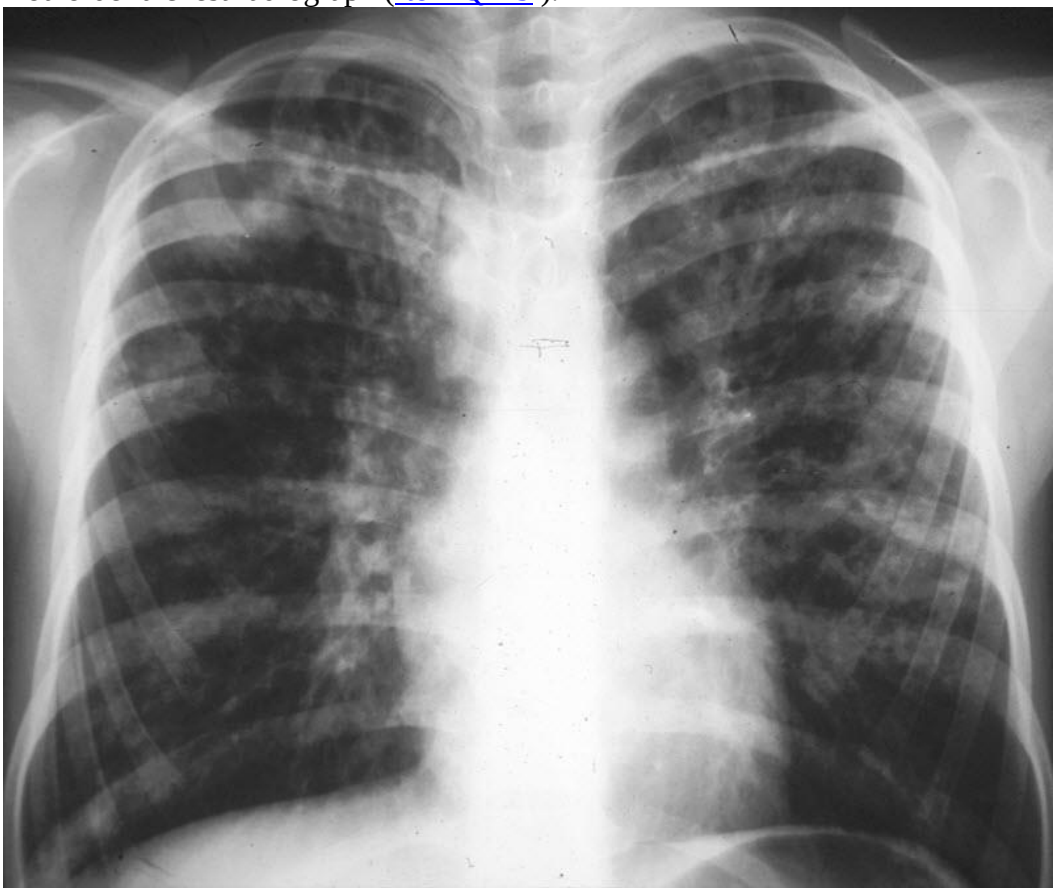
Suggested Readings

- Council on Children With Disabilities, Section on Developmental Behavioral Pediatrics, Bright Futures Steering Committee, Medical Home Initiatives for Children With Special Needs Project Advisory Committee. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. *Pediatrics.* 2006;118(1):405-420. doi: http://dx.doi.org/10.1542/peds.2006-1231.
- Marks KP, LaRosa AC. Understanding developmental-behavioral screening measures. *Pediatr Rev.* 2012;33(10):448-458. doi: http://dx.doi.org/10.1542/pir.33-10-448.

Question 219

An 11-year-old boy is seen for evaluation of a persistent cough and intermittent fevers. He has a long history of atopic dermatitis and asthma diagnosed at 3 years of age. His asthma has required numerous visits to the local emergency department, but no hospitalizations. The boy's asthma has been managed on daily β-agonist and corticosteroid inhalers. Over the past 2.5 months, he has been having intermittent fevers and recurrent episodes of cough, which have not responded to his usual asthma treatments. During this time, he has been treated with 3 courses of antibiotics, including azithromycin, as well as leukotriene receptor antagonists and a short course of systemic corticosteroids without any clear impact on his fevers or cough. He reports malaise, a productive cough with brown mucus, and occasional hemoptysis.

Physical examination reveals a comfortable boy with frequent dry coughs. His vital signs show a temperature of 38.3°C, respiratory rate of 24 breaths/min, heart rate of 90 beats/min, and blood pressure of 110/60 mm Hg. His mucosa are moist and pink, and his nares are clear without rhinorrhea or discharge. The tonsils are 2+. His lungs reveal occasional rhonchi bilaterally and no wheezes. He has no retractions, his heart and abdominal examinations are normal, and his skin is warm and well-perfused.
You order a chest radiograph (Item Q219).



Item Q219: Item Q219. Chest radiograph for the boy described in the vignette. Courtesy of P Lee

Laboratory results are shown:

Laboratory test	**Result**
White blood cell count	18,800/μL (18.8 x 10^9/L)
Neutrophils	70%
Lymphocytes	15%
Monocytes	5%
Eosinophils	10%
Hemoglobin	13.1 g/dL (131 g/L)
Hematocrit	40%
Platelet count	400 x 10^3/μL (400 x 10^9/L)
Serum immunoglobulin E	1,200 μg/L (1.2 mg/L)
Aspergillus fumigatus-specific immunoglobulin E	51 (normal < 0.35)
Aspergillus fumigatus-specific immunoglobulin G	23 (normal < 10)

Of the following, the MOST likely diagnosis for this patient is

A. allergic bronchopulmonary aspergillosis
B. aspergilloma
C. chronic pulmonary aspergillosis
D. disseminated aspergillosis
E. invasive aspergillosis

Correct Answer: A

The boy described in this vignette, most likely has allergic bronchopulmonary aspergillosis. *Aspergillus* is a group of aerobic saprophytic fungi that are ubiquitous in the environment. *Aspergillus* species are molds, that grow in multicellular filaments called hyphae and produce asexual nonmotile spores (conidia) that people routinely inhale. The genus *Aspergillus* consists of multiple subgenera, which are then further divided into sections and species. Mycologists often refer to isolates as a member of an *Aspergillus* species complex because of the hundreds of *Aspergillus*species that exist without available molecular typing or phenotypic differentiating features. *Aspergillus* is found in the air, water, soil, and on decomposing organic material. It grows well on carbon-rich surfaces, such as monosaccharides and polysaccharides, and frequently grows on bread or potatoes. Many *Aspergillus* species are helpful and important in daily life. Miso, soy sauce, and sake are made through fermentation by *Aspergillus oryzae.* Lovastatin, the first US Food and Drug Administration-approved cholesterol-lowering statin medication, was first isolated and is still produced from *Aspergillus terreus.* Essentially all of the world's citric acid used in soft drinks, candy, baking products, and the like is produced by fermentation of *Aspergillus niger*. However, some of these same *Aspergillus* species, such as *A niger,* and *A terreus* can cause invasive disease in immunocompromised patients. *Aspergillus flavus* produces carcinogenic aflatoxins, which can contaminate chili peppers, corn, wheat, rice, peanuts, tree nuts, sunflower seeds, and spices, resulting in severe hepatic necrosis. Children are particularly sensitive to aflatoxin exposure.

Aspergillus fumigatus is responsible for the majority of human aspergillosis including allergic bronchopulmonary aspergillosis (ABPA), aspergilloma, and chronic pulmonary aspergillosis, as well as fungal sinusitis, otomycosis, fungal keratitis, onychomycosis, and primary cutaneous aspergillosis. AspergilIosis primarily occurs in patients with underlying lung diseases such as asthma or cystic fibrosis, or immunocompromised patients. Immunocompromised patients are also prone to invasive aspergillosis (IA), where the fungi spreads from the original conidia colonization site into the surrounding tissues, and disseminated aspergillosis, which spreads throughout the body to distant organs. Although the lung is the usual origin of local disease, invasive disease can originate in the skin and gastrointestinal tract.

Allergic bronchopulmonary aspergillosis results from *Aspergillus fumigatus* conidial colonization creating a hypersensitivity reaction in the airway of patients with either asthma or cystic fibrosis. However, only 1% to 5% of patients with persistent asthma and less than 10% of cystic fibrosis patients will have ABPA. In ABPA, T cells release interleukin-4, interleukin-5, and interleukin-13 in response to the *Aspergillus* antigens, which leads to sharp rises in eosinophils and immunoglobulin E (IgE). Eosinophilic inflammation, combined with proteolytic enzymes and mycotoxins released by the *Aspergillus,* cause damage to the airway, which leads to mucus plugging, central bronchiectasis, bronchocentric granulomatosis, and eosinophilic pneumonias. Clinically, patients with ABPA have recurrent asthma exacerbations, complicated by fever, malaise, bronchial obstruction, productive cough with dark brown mucus plugs, and even hemoptysis. These patients may also have asymptomatic lung consolidations and may not wheeze. Typical laboratory findings are an elevated total blood eosinophil count (generally > 500 cells/μL) and an elevated total serum IgE (generally > 1,000 IU/mL), although this is not specific

for ABPA. Precipitating immunoglobulin G (IgG) antibodies (precipitins) to *Aspergillus* and also specific IgE and IgG antibodies to *Aspergillus* on immunoassay may help pinpointing the actual etiology. Chest radiographs may show upper lobe parenchymal opacities and atelectasis from mucus plugging. Central bronchiectasis of the medial half to two-thirds of the chest is common, as seen in the radiograph in the vignette. There is no single test or agreed upon diagnostic criteria for ABPA, although many experts agree that patients must have a history of asthma or cystic fibrosis, a positive skin test to *Aspergillus* or elevated IgE against *A fumigatus*, and an elevated serum IgE, which should be greater than 1,000 IU/mL. At least 2 additional criteria should be met: precipitating serum antibodies to *A fumigatus* or an elevated serum *Aspergillus* IgG immunoassay, radiographic pulmonary opacities consistent with ABPA, or a total eosinophil count of greater than 500 cells/μL in glucocorticoid-naive patients. The treatment for ABPA focuses on control of the inflammation to prevent lung injury with long-term systemic glucocorticosteroids followed by a very slow taper over 6 months. A triazole antifungal may be used.

Since the patient in this vignette does not have a history of a significant immunocompromised condition or medications, it would be highly unlikely for him to have invasive or disseminated aspergillosis. The chest radiograph does not show any cavities where an aspergilloma might be present. While this clinical picture could be consistent with chronic pulmonary aspergillosis, disease has not been present for more than 3 months. Furthermore, patients with chronic pulmonary aspergillosis often have cavities present on chest radiograph, with or without aspergillomas. Extensive fibrosis, progressive segmental areas of consolidation with or without adjacent pleural thickening, and multiple radiopaque nodular areas may also be seen.

PREP Pearls

- The genus *Aspergillus* consists of hundreds of mold species, whose spores are inhaled on a daily basis, usually without ill effect.
- Aspergillosis is the group of diseases resulting from inhalation of these spores, and usually only occurs in patients with underlying chronic lung disease or an immunocompromising condition. It includes allergic conditions such as allergic bronchopulmonary aspergillosis (ABPA), local disease such as aspergilloma, semi-invasive disease, ie, chronic pulmonary aspergillosis, and invasive disease, such as disseminated aspergillosis.
- Allergic bronchopulmonary aspergillosis is caused by a hypersensitivity reaction to *Aspergillus fumigatus*colonization.

ABP Content Specifications(s)

- Recognize the clinical features associated with Aspergillus infection
- Understand the epidemiology of Aspergillus

Suggested Readings

- American Academy of Pediatrics. Aspergillosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:249-252.
- Greenberger PA, Bush RK, Demain JG, Luong A, Slavin RG, Knutsen AP. Allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol Pract.* 2014;2(6):703-708. doi: http://dx.doi.org/10.1016/j.jaip.2014.08.007.
- Kosmidis C, Denning DW. The clinical spectrum of pulmonary aspergillosis. *Postgrad Med J.* 2015;91(1077):403-410. doi: http://dx.doi.org/10.1136/postgradmedj-2014-206291rep.
- Patterson KC, Strek ME. Diagnosis and treatment of pulmonary aspergillosis syndromes. *Chest.* 2014;146(5):1358-1368. doi: http://dx.doi.org/10.1378/chest.14-0917.

Question 220

A 6-year-old boy presents to the emergency department with the complaint of "body swelling" for the last 3 days that has been worsening. He has no significant medical history and no other complaints. He is afebrile. His respiratory rate is 19 breaths/min, heart rate is 80 beats/min, and blood pressure is 100/60 mm Hg. His physical examination is significant for bilateral periorbital edema, ascites, and diffuse severe pitting edema. His urinalysis demonstrates a specific gravity of 1.025, pH of 6.5, 2+ blood, 3+ protein, with no leukocyte esterase or nitrites. Urine microscopy shows 5 to 10 red blood cells per high-power field, and no white blood cells, crystals, or bacteria. You inform his parents that you suspect that the boy has idiopathic nephrotic syndrome and begin a discussion about treatment options, as well as prognostic factors for renal function.

Of the following, the GREATEST risk of a poor renal prognosis is indicated by

A. anasarca
B. cyclophosphamide resistance
C. hematuria
D. steroid resistance
E. urine protein-to-creatinine ratio greater than 10

Correct Answer: D

The history, physical examination, and laboratory results for the boy in the vignette are consistent with a diagnosis of nephrotic syndrome (NS). The most important determinant of renal prognosis in idiopathic NS is steroid responsiveness.

Nephrotic syndrome is characterized by the triad of edema (facial puffiness or generalized anasarca), proteinuria, and hypoalbuminemia. Serum chemistry will demonstrate hyperlipidemia (elevated cholesterol and low-density lipoprotein cholesterol). Often, on initial presentation with facial puffiness, children are thought to be having an allergic reaction. In the pediatric population, NS is most commonly seen in school-aged children and adolescents. The worldwide prevalence of NS is approximately 16 cases per 100,000 children, with an incidence of 2 to 7 per 100,000 children. Boys are more frequently affected than girls, however this predominance does not persist into adolescence.

Nephrotic syndrome is categorized as primary/idiopathic, secondary, or congenital/infantile (Item C220). The boy in the vignette has idiopathic NS, the most common form encountered in children. Based on renal biopsy findings, children with idiopathic NS are further diagnosed as having minimal change disease, focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis (MPGN), or membranous nephropathy (Item C220). The congenital infantile form of NS presents at birth or before age 1 year, and is associated with genetic abnormalities leading to increased permeability of the glomerular basement barrier.

Item C220. Categorization of Nephrotic Syndrome.

Primary Nephrotic Syndrome
- Focal segmental glomerulosclerosis
- Membranoproliferative glomerulonephritis
- Membranous nephropathy
- Mesangial hypercellularity
- Minimal change nephrotic syndrome

Secondary Nephrotic Syndrome
- Diabetes mellitus (rare in children)
- Drugs and toxins (nonsteroidal anti-inflammatory drugs, gold)
- Inherited diseases (congenital nephrotic syndrome, diffuse mesangiasclerosis, Alport syndrome, nail-patella syndrome, Lowe syndrome)
- Postinfectious (poststreptococcal, human immunodeficiency virus, hepatitis B and C, malaria, syphilis, intrauterine infections, other viruses and bacteria)
- Vasculitides (lupus nephritis, Henoch-Schönlein purpura nephritis, Wegener granulomatosis, Goodpasture syndrome)

Reprinted with permission from Varade WS. Nephrotic syndrome In: McInerny TK, Adam HM, Campbell DE, Kamat DM, Kelleher KJ, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* 19th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009:2296

Minimal change disease is the most common form of NS in children and most cases are treated as such without kidney biopsy. Children with minimal change disease typically present between 2 and 10 years of age, with the classic features of NS and no secondary causes. Urinalysis will demonstrate nephrotic range proteinuria, defined as a spot urine (preferably a first-morning sample) protein-to-creatinine ratio greater than 2 (< 0.2 is normal, 0.2 to 2 is non-nephrotic). The initial episode of NS is treated with oral steroids (60 mg/m^2 per day for 4 to 6 weeks, followed by 40 mg/m^2 per dose every other day for 2 to 5 months, with gradual tapering). The most important determinant of renal prognosis in idiopathic NS is steroid responsiveness. Remission is defined as urine protein-to-creatinine ratio less than 0.2, or urine dipstick negative or trace for protein for 3 consecutive days. A lack of response to steroids after 4 weeks of daily therapy, occurring in approximately 10% of children with idiopathic NS, is considered corticosteroid resistance.

The presence of hypoalbuminemia, marked proteinuria, and generalized anasarca is expected in children with NS and is not an indicator of renal prognosis.
Depending on responsiveness to steroids, children with minimal change disease are categorized as “infrequent relapser” (1–3 relapses annually), “frequent relapser” (≥ 2 relapses within 6 months after initial therapy or ≥4 relapses in any 12-month period), or “corticosteroid dependent” (relapse during taper or within 2 weeks of discontinuation of corticosteroid therapy). Patients with frequent relapsing or corticosteroid-dependent NS are treated with steroid-sparing medications to avoid the complications associated with long-term steroid therapy (eg, cushingoid features, cataracts, growth retardation, glaucoma, peptic ulcer disease, behavioral changes). Cyclophosphamide, an alkylating agent, is used as a steroid-sparing agent and can induce long-term remission. Patients resistant to cyclophosphamide may be treated with other steroid-sparing therapies such as calcineurin inhibitors (cyclosporine, tacrolimus), mycophenolate mofetil, or rituximab. Although resistance to cyclophosphamide is indicative of difficulty in maintaining remission in patients with idiopathic NS, it is not an indicator of poor renal prognosis.

Macroscopic or microscopic hematuria also may be seen in patients with NS. Microscopic hematuria is seen in nearly 20% of children with minimal change disease, and does not predict steroid sensitivity. Microscopic hematuria is seen in 50% to 60% of children with FSGS or MPGN. Gross hematuria is relatively uncommon in children with NS, and should prompt consideration of an alternative diagnosis (Item C220). The presence of renal failure, hypocomplementemia, or clinical features of vasculitis (eg, joint pain and swelling, rash, oral ulcers) should prompt consideration of a diagnosis other than minimal change disease, in a patient with NS.

PREP Pearls

- Nephrotic syndrome (NS) is characterized by the triad of edema (facial puffiness or generalized anasarca), proteinuria, and hypoalbuminemia.
- Minimal change disease is the most common form of NS in children.
- The initial episode of NS is treated with oral steroids.
- The most important determinant of renal prognosis in idiopathic NS is steroid responsiveness.
- Gross hematuria, renal failure, hypocomplementemia, or clinical features of vasculitis should prompt consideration of causes other than minimal change disease in a patient with NS.

ABP Content Specifications(s)

- Understand the natural history of minimal-change nephrotic syndrome
- Formulate a differential diagnosis of nephrotic syndrome with and without hematuria
- Identify the etiology of hyponatremia in nephrotic syndrome
- Understand the various factors that affect the prognosis of nephrotic syndrome
- Recognize complications associated with nephrotic syndrome, including those resulting from diuretic therapy

Suggested Readings

- Andolino TP, Reed-Adam J. Nephrotic syndrome. *Pediatr Rev.* 2015;36(3):117-126. doi: http://dx.doi.org/10.1542/pir.36-3-117.
- Varade WS. Nephrotic syndrome. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DM, eds, *American Academy of Pediatrics Textbook of Pediatric Care.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:2368-2374.

Question 221

You are called to the full-term nursery to examine a term neonate. The mother is a 26-year-old gravida 3, para 2 woman with no significant past medical or prenatal history. The neonate was delivered vaginally at 38 weeks of gestation with a birthweight of 2.82 kg. Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. She is rooming with the mother and is breastfeeding well. Laboratory data are shown:

Laboratory test	**Result**
White blood cell count	18,600/μL (18.6×10^9/L)
Hemoglobin	17.1 g/dL (171 g/L)
Platelet count	309×10^3/μL (309×10^9/L)

The bedside nurse is concerned about the color of the baby's hands (Item Q221).

Item Q221: Hand of the neonate described in the vignette. Courtesy of M LaTuga

Of the following, the BEST explanation for this finding is that it

A. does not correlate with hypoxemia
B. is associated with a bluish-appearing tongue and perioral area
C. is not affected by hypothermia and polycythemia
D. is often found with diminished peripheral pulses
E. is rare among term neonates during the first 24 to 48 hours after birth

Correct Answer: A

The bluish discoloration of the neonate's hand in the vignette is caused by peripheral cyanosis, a finding that does not correlate with hypoxemia. Peripheral cyanosis is marked by bluish discoloration of the extremities only. It is common in newborns during the first 24 to 48 hours after birth and may be exacerbated by hypothermia or polycythemia. Cyanosis is visibly detectable with 3 g/dL (30 g/L) of deoxygenated hemoglobin. Thus, cyanosis may be more difficult to identify in an anemic neonate and more prominent in a neonate with polycythemia. Though the pathophysiology of peripheral cyanosis is not completely understood, it may be related to immature vasomotor control. With vasodilation, there may be slow blood flow with a large difference between the arterial and venous oxygen content. In this situation, the amount of deoxygenated blood present may be high enough to appear cyanotic, though arterial oxygen content remains normal.

In comparison, central cyanosis is usually associated with hypoxemia, which is low levels of dissolved oxygen in the blood. On examination, neonates with central cyanosis will have blue coloring of the tongue and perioral area in addition to bluish discoloration of the distal extremities. Depending on the underlying pathology, poor peripheral perfusion and respiratory distress may also be present. The differential diagnosis for central cyanosis is broad, including ventilation/perfusion mismatch, inadequate ventilation, intracardiac shunting, intrapulmonary shunting, or impaired oxygenation.

PREP Pearls

- Peripheral cyanosis is a common finding in well-appearing term neonates in the first 24 to 48 hours after birth.
- Peripheral cyanosis does not correlate with hypoxemia.
- Peripheral cyanosis may be exacerbated by hypothermia and polycythemia.

ABP Content Specifications(s)

- Recognize that peripheral cyanosis is common in healthy newborn infants

Suggested Readings

- Carlo WA. Clinical manifestation of diseases in the newborn period. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:831-833.
- Tingelstad J. Consultation with the specialist: nonrespiratory cyanosis. *Pediatr Rev*. 1999;20(10):350-352. doi: http://dx.doi.org/10.1542/pir.20-10-350 .

Question 222

The father of a 4-year-old girl with a history of anaphylaxis after egg ingestion calls your office. He has heard that the measles, mumps, and rubella vaccine contains egg antigen and he is wondering if it is safe for his daughter to receive this vaccine. You discuss with the father the most recent Advisory Committee on Immunization Practices and American Academy of Pediatrics immunization recommendations for egg-allergic children.

Of the following, the MOST appropriate plan for this girl is to

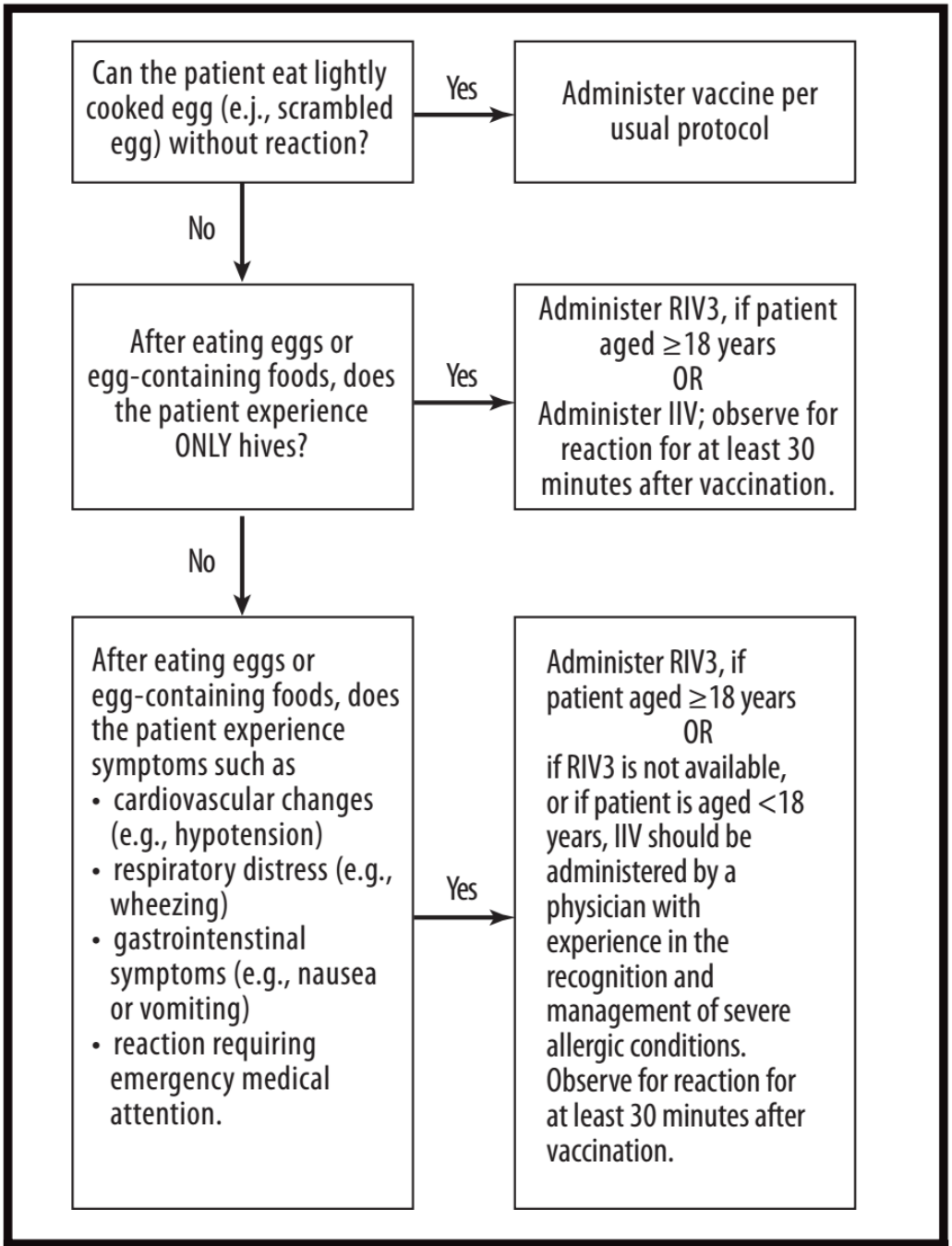
A. administer the vaccine as per routine practice
B. monitor the patient in the office for 2 hours after vaccine administration
C. not administer the vaccine because it is contraindicated
D. perform skin-prick testing with dilute vaccine before vaccination
E. premedicate the patient with oral diphenhydramine

Correct Answer: A

Egg allergy is not a contraindication to the measles, mumps, and rubella (MMR) vaccine. Although the measles and mumps components of the vaccine are produced in chick embryo fibroblast cultures, the risk of serious reaction in egg-allergic individuals is extremely low. Multiple trials have demonstrated MMR vaccine safety, with 1 study demonstrating that more than 99% of egg-allergic children can safely receive the vaccine. Evidence shows that skin-prick testing with the MMR vaccine does not predict a reaction to vaccine administration. Neither premedication nor prolonged monitoring of egg-allergic individuals after vaccination is necessary with the MMR vaccine.

Several other vaccines are also manufactured in egg-derived products, including yellow fever and influenza vaccines. The yellow fever vaccine is recommended for individuals older than 9 months who are living in, or traveling to, countries in South America and Africa where the disease is endemic. The yellow fever vaccine is cultured in chick embryos and, unlike the MMR vaccine, is contraindicated in individuals with hypersensitivity to eggs or chicken proteins. The manufacturer recommends that skin-prick testing be performed before administering the yellow fever vaccine in individuals who are “egg-sensitive” without a history of anaphylaxis. If the vaccine is strongly recommended in an individual with a history of severe reaction to egg or with a positive skin-prick test, desensitization can be performed.

Two types of influenza vaccine are available for administration in children. The intranasal live attenuated influenza vaccine (LAIV) and most formulations of the intramuscular inactivated influenza vaccine (IIV) are cultured in fluid derived from chicken embryos. Although allergy is currently a contraindication for the LAIV, several studies have demonstrated safe administration, with no reported cases of anaphylaxis. Egg allergy is not a contraindication to the IIV, and numerous studies have confirmed its safety. Skin-prick testing is not recommended before the administration of IIV, because a positive skin-prick test does not predict a vaccine reaction. Current guidelines recommend vaccinating egg-allergic individuals in a medical setting with the appropriate staffing and resources to treat an allergic reaction, and monitoring of these patients for 30 minutes after vaccine administration (Item 222).



From Grohskopf LA, Sokolow LZ, Olsen SJ, Bresee JS, Broder KR, Karron RA. Prevention and control of influenza with vaccines: Recommendations of the advisory committee on immunization practices, United States, 2015-16 influenza season. *MMWR Morb Mortal Wkly Rep.* 2015;64(30):818-825

ITEM C222: Recommendations regarding influenza vaccination of persons who report allergy to eggs. Advisory Committee on Immunization Practices, United States, 2015-2016 Influenza Season.

Immunoglobulin E (IgE)–mediated allergic reactions can occur to the other components of vaccines, but are rare. Allergic reactions have been reported to gelatin, casein, latex, and various microbial components of vaccines. These IgE-mediated reactions are immediate, occurring within 5 to 30 minutes after vaccine administration. Delayed reactions may include local effects (eg, redness, swelling, or tenderness at the vaccination site) as well as fever or irritability. None of the delayed reactions should preclude vaccination with additional doses. Delayed, non–IgE-mediated hypersensitivity reactions have been reported to several vaccine components, including thimerosal, aluminum, and phenoxyethanol.

PREP Pearls

- Egg allergy is not a contraindication to the administration of the measles, mumps, and rubella (MMR) vaccine.
- Patients with egg allergy should not receive the yellow fever vaccine.
- The inactivated influenza vaccine (IIV) can be safely administered to patients with egg allergy.
- Allergic reactions to non-egg vaccine components are rare. Local reactions, fever, and irritability are common adverse reactions and should not preclude additional vaccine doses.

ABP Content Specifications(s)

- Plan an immunization regimen for a patient with egg allergy
- Recognize adverse reactions to various vaccine constituents and manage appropriately

Suggested Readings

- Fasano MB, Wood RA, Cooke SK, Sampson HA. Egg hypersensitivity and adverse reactions to measles, mumps, and rubella vaccine. *J Pediatr.* 1992;120(6):878-881 .
- Grohskopf LA, Sokolow LZ, Olsen SJ, Bresee JS, Broder KR, Karron RA. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2015-16 influenza season. *MMWR Morb Mortal Wkly Rep.* 2015;64(30):818-825. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6430a3.htm .
- James JM, Burks AW, Roberson PK, Sampson HA. Safe administration of the measles vaccine to children allergic to eggs. *N Engl J Med*. 1995;332(19):1262-1266. doi: http://dx.doi.org/10.1056/NEJM199505113321904.
- Kelso JM. Allergic reactions to vaccines. *UpToDate.* Available online only with subscription.
- McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the advisory committee on immunization practices (ACIP). *MMWR Recomm Rep*. 2013;62(RR04):1-34. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm.
- Staples JE, Gershman M, Fischer M. Yellow fever vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2010;59(RR07):1-27. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5907a1.htm.

Question 223

You are seeing a 4-month-old infant with cystic fibrosis (CF) for a health supervision visit. The infant was diagnosed with CF on newborn screening, confirmed with sweat testing by pilocarpine iontophoresis and mutation analysis. Pancreatic insufficiency was documented with fecal elastase testing. She is exclusively breastfed and has been prescribed pancreatic enzymes and salt repletion. Preferring a holistic approach, the mother admits that she is somewhat anxious about the recommended therapies for her infant.

On physical examination, the girl is pale with mild edema of the hands and feet. Laboratory data are shown:

Laboratory test	**Result**
Hemoglobin	8.4 g/dL (84 g/L)
Reticulocyte count	5%
Serum albumin	3 g/dL (30 g/L)

A peripheral smear reveals polychromasia with nucleated red blood cells. Additionally, lactate dehydrogenase and indirect bilirubin levels are mildly elevated.

Of the following, the MOST likely cause of this infant's laboratory findings is

A. glucose-6-phosphate-dehydrogenase (G6PD) deficiency
B. congenital spherocytosis
C. thalassemia
D. vitamin E deficiency
E. vitamin K deficiency

Correct Answer: D

The infant in the vignette has clinical and laboratory findings consistent with hemolytic anemia. She had a positive newborn screening test for cystic fibrosis (CF), which was subsequently confirmed with sweat testing via pilocarpine iontophoresis, and has associated pancreatic insufficiency. In this clinical setting, the girl's hemolytic anemia is likely due to vitamin E deficiency resulting from CF-associated steatorrhea and intestinal malabsorption. Thirty-eight percent of infants with CF have evidence of vitamin E deficiency. Vitamin E is an important antioxidant present in cell membranes that reduces free radical damage to unsaturated fatty acids. Low levels of vitamin E may result in hemolytic anemia or other findings, such as muscular weakness and areflexia.

In CF, abnormal CF transmembrane regulator function in the pancreas leads to ductal obstruction, pancreatic autodigestion, and pancreatic insufficiency. As a result, pancreatic enzymes are unable to reach the duodenum, resulting in poor absorption of nutrients in the small intestines. Exocrine pancreatic insufficiency with fat malabsorption results in associated steatorrhea and deficiency of fat-soluble vitamins, including vitamins A, D, E, and K. Deficiencies of fat-soluble vitamins have been described in infants as young as 3 months of age. Therefore, prompt initiation of enzyme replacement therapy and appropriate repletion of vitamins is indicated in infancy to prevent nutritional complications.

Laboratory findings associated with hemolytic anemia include an elevated reticulocyte count and indirect hyperbilirubinemia. In addition, the presence of nucleated red blood cells and/or polychromasia on peripheral smear reflects the release of immature red blood cells from bone marrow. Vitamin E levels may be obtained through chemical serum analysis if deficiency is suspected. A positive Coombs test would support a diagnosis of autoimmune hemolytic anemia. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is most commonly found in males of African or Mediterranean heritage, but has been described in other populations as well. In this condition, oxidative stress to the red blood cell (RBC) and hemolysis occurs with exposure to certain infections, food, or medications. The diagnosis can be confirmed with a finding of a low G6PD level. This infant is female and had no known exposures that would suggest this to be a cause of her anemia.

Congenital spherocytosis is a genetic condition associated with increased fragility of the RBC membrane. Anemia, jaundice, and splenic enlargement are common associated findings. Spherocytes are found on the peripheral smear. A family history is often present. Spherocytosis most commonly occurs in those of northern European descent, but the condition has been described in other populations.

Thalassemia is an inheritable anemia, generally found in those of Mediterranean, African, and Asian descent. Thalassemia affects either the α- or β-globin chain of hemoglobin. Both forms are inherited in an autosomal-recessive pattern. Anemia in thalassemia major is severe, with rapid destruction of RBCs, jaundice, and iron deposition in vital organs. Transfusions are required to sustain life, and stem cell transplantation may offer a cure. In thalassemia trait, the anemia is typically mild, and may be mistakenly diagnosed as iron-deficiency anemia. Thalassemia has no

association with malabsorption, and therefore this infant's low albumin would make this diagnosis less likely.

Syndromes of deficiency of other fat-soluble vitamins have also been well described in patients with CF. Vitamin K deficiency may be associated with abnormal synthesis of vitamin K-dependent coagulation proteins (factors II, VII, IX, and X) and episodes of hemorrhage. Anemia would not be expected in association with vitamin K deficiency in the absence of bleeding, nor would there be evidence of hemolysis. Severe vitamin A deficiency has been implicated in xerophthalmia and night blindness. Vitamin D deficiency is associated with rickets and osteomalacia.

PREP Pearls

- Vitamin E deficiency in infants may result in hemolytic anemia.
- Deficiency of fat-soluble vitamins has been described in infants with cystic fibrosis as young as 6 weeks of age.
- Neurologic abnormalities, including weakness and areflexia, may be associated with vitamin E deficiency.

ABP Content Specifications(s)

- Recognize the specific nutritional problems associated with cystic fibrosis, and manage appropriately

Suggested Readings

- Carr SB, McBratney J. The role of vitamins in cystic fibrosis. *J R Soc Med.* 2000;90(Suppl 38):14-19. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1305879/pdf/10911814.pdf.
- Rana M, Wong-See D, Katz T, et al. Fat-soluble vitamin deficiency in children and adolescents with cystic fibrosis. *J Clin Pathol.* 2014;67(7):605-608. doi: http://dx.doi.org/10.1136/jclinpath-2013-201787 .
- Walkowiak J, Herzig KH, Strzykala K, Przyslawski J, Krawczynski M. Fecal elastase-1 is superior to fecal chymotrypsin in the assessment of pancreatic involvement in cystic fibrosis. *Pediatrics.* 2002;110(1 Pt 1):e7. http://pediatrics.aappublications.org/content/110/1/e7.

Question 224

A 14-day-old female neonate is brought to your office for a 2-week health supervision visit. Her parents report she has been having jerking movements of her right arm for the past day. They last 30 to 60 seconds and happen when she is awake and asleep. The jerking does not stop when they gently hold her arm. She is feeding well. She otherwise seems healthy. Her vital signs and physical examination are normal.

Of the following, the BEST next step is to

A. have parents record the episodes
B. order an electroencephalogram
C. order a serum glucose
D. refer to the emergency department
E. start levetiracetam

Correct Answer: D

The neonate in the vignette is having focal seizures. She should be referred immediately to the emergency department (ED) for evaluation. Seizures in a neonate are almost always caused by an underlying problem or condition, such as infection, hypoglycemia, electrolyte abnormality, acute or subacute intracranial hemorrhage or stroke, hypoxic-ischemic encephalopathy, inborn errors of metabolism, or congenital brain malformations. Many of these conditions require prompt treatment to prevent disease progression. Clinicians should have a high index of suspicion for neonatal seizures. Although neonates can have a variety of nonepileptic paroxysmal movements, if there is a possibility the movement is a seizure, the neonate should be referred immediately to the ED. In neonates, focal seizures may be the only sign of a central nervous system infection, so an otherwise healthy appearance should not deter immediate referral to the ED.

Once in the ED, the initial evaluation starts with a history and physical examination, directed at the potential causes for seizures. For instance, a full fontanelle may indicate intracranial hemorrhage; dermatological findings may indicate a specific infection or genetic syndrome. Initial laboratory testing includes glucose, electrolytes, liver function tests, blood and urine cultures, and almost always, cerebrospinal fluid studies, including viral studies. Treatment with empiric antibiotics and acyclovir should be started at the same time as the initial evaluation, even before laboratory results are available. Early detection and correction of electrolyte abnormalities is also critically important. If the neonate has signs of increased intracranial pressure, such as a full, tense fontanelle, splayed cranial sutures, or persistent downgaze, brain imaging should be obtained before performing a lumbar puncture. Ultrasonography or computed tomography of the head are the most rapid brain imaging tests in this situation.

Additional initial evaluation in the ED includes reviewing newborn screening results and obtaining plasma amino acids, lactate, toxicology screen, ammonia, pH, and urine organic acids. Treatment for neonatal seizures has typically been with phenobarbital or phenytoin; levetiracetam is a newer anticonvulsant that is increasingly used, although there is not a large amount of data for its use in neonates.

If initial testing does not reveal a diagnosis and the neonate is stable, magnetic resonance imaging of the brain is the best test to evaluate for congenital brain malformations. If seizures persist despite anticonvulsants, electroencephalogram can sometimes be helpful in confirming that the movements are epileptic.

PREP Pearls

- A neonate with new onset seizure activity should be referred to the emergency department immediately, even if he or she appears otherwise healthy
- If a neonate with seizures has signs of increased intracranial pressure, such as a full, tense fontanelle, splayed cranial sutures, or persistent downgaze, brain imaging should be obtained before performing a lumbar puncture

ABP Content Specifications(s)

- Formulate a differential diagnosis of neonatal seizures

Suggested Readings

- Hahn JS, Olson DM. Etiology of neonatal seizures. *NeoReviews.* 2004;5(8):e327-e335. doi: http://dx.doi.org/10.1542/neo.5-8-e327.
- Olson DM. Neonatal seizures. *NeoReviews.* 2012;13(4):e213-e223. doi: http://dx.doi.org/10.1542/neo.13-4-e213.

Question 225

A previously healthy 5-year-old boy is brought to the emergency department with fever, a rapidly progressive rash, and increasing lethargy over the past 24 hours. He has not had nausea, vomiting, or sick contacts. He has no allergies or significant past medical history, and is not on any medications. On rapid assessment, he is very difficult to arouse and is moaning and mumbling on painful stimuli, with occasional eye opening. His airway is patent and he is breathing comfortably. He has cool extremities and a capillary refill time of 5 seconds. He has a disseminated purpuric rash involving face, trunk, and extremities. Liver edge is not palpable. Initial vital signs showed a temperature of 39.5°C, heart rate of 170 beats/min, respiratory rate of 24 breaths/min, blood pressure of 70/30 mm Hg, and pulse oximetry of 100% on room air. In the first 30 minutes, he is started on oxygen by non-rebreather facemask, receives 100 mL/kg of 0.9% saline boluses, and a 100 mg/kg dose of intravenous ceftriaxone. Upon re-evaluation, vital signs show a temperature of 39°C, heart rate of 160 beats/min, respiratory rate of 30 breaths/min, blood pressure of 75/40 mm Hg, and pulse oximetry of 100% on 100% non-rebreather facemask. He is still sleepy, but easier to arouse. He is in moderate respiratory distress with intercostal retractions. He has bilateral crackles on auscultation. Heart is regular, with no rubs, gallops, or murmurs. Capillary refill time is 3 seconds. Liver is 4 cm below the costal margin.

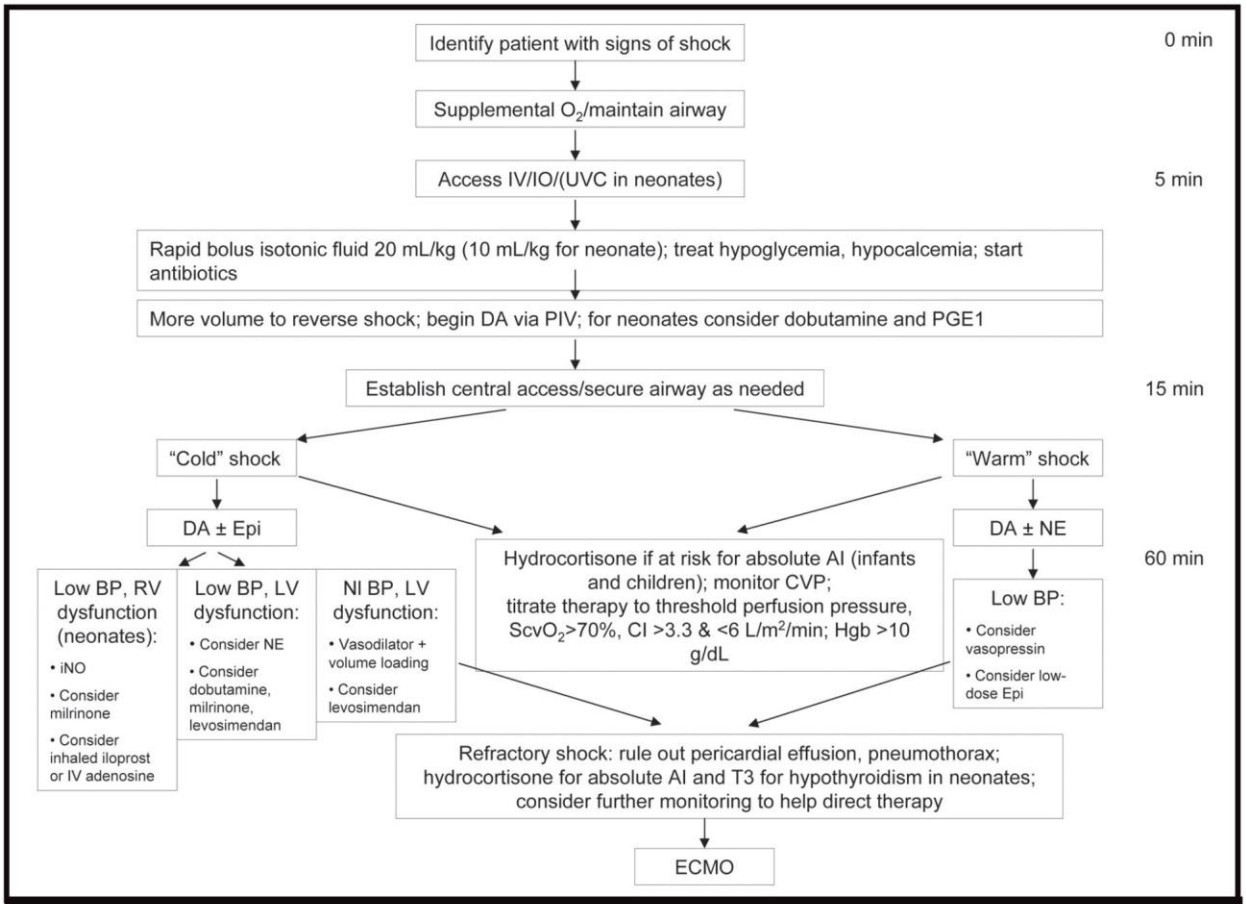
Of the following, the BEST next step to stabilize the patient is

A. administer 0.9% saline bolus, 20 mL/kg intravenously
B. administer 5% albumin bolus, 20 mL/kg intravenously
C. administer hydrocortisone intravenously
D. start double volume whole blood exchange transfusion
E. start intravenous epinephrine infusion

Correct Answer: E

The boy in this vignette has septic shock from meningococcemia. He has received several intravenous fluid boluses but is still in shock, evidenced by persistent tachycardia and hypotension. Since he has hepatomegaly and crackles on lung auscultation, additional fluid administration would worsen his condition, therefore the best next step is to start an epinephrine infusion.

Shock is the condition of oxygen and nutrient delivery insufficient to meet end-organ metabolic demands. Management includes optimizing oxygen delivery, which is the product of cardiac output and oxygen content. Cardiac output is stroke volume multiplied by heart rate, and oxygen content is mostly dependent on hemoglobin concentration and percentage of saturated hemoglobin. Although classifications change, types of shock include hypovolemic, cardiogenic, distributive, and septic. Regardless of the type of shock, fluid management can be assisted by an algorithm such as the one shown in Item C225 ,along with frequent clinical reassessment for hemodynamic status. Once shock is identified in a patient based on signs such as altered mental status, delayed capillary refill, tachycardia, or hypotension, airway and breathing is established, and intravenous or intraosseous access is established in the first few minutes. Rapid boluses of isotonic fluid up to and over 60 mL/kg are given in the first 15 minutes until shock is reversed or until rales or hepatomegaly develop, at which point inotropic medications are started. The 2015 Pediatric Advanced Life Support algorithm for shock should be followed. When these algorithms are followed, patients with cardiogenic shock are identified by the development of pulmonary edema, hepatomegaly, or worsened circulation with heart failure.



Adapted and reprinted with permission from Yager P and Noviski N. "Shock." *Pediatr Rev.* 2010;31;311

ITEM C225: Algorithm for goal-directed management of hemodynamic support in septic shock. Adapted from the 2007 ACCM clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock. AI, adrenal insufficiency; BP, blood pressure; CI, cardiac index; CVP, central venous pressure; DA, dopamine; Dobut, dobutamine; ECMO, extracorporeal membrane oxygenation; Epi, epinephrine; IV, intravenous; iNO, inhaled nitric oxide; IO, intraosseous; LV, left ventricle; NL, normal; PGE1, prostaglandin E1; RV, right ventricle; ScvO2, mixed venous oxygen saturation; UVC, umbilical venous catheter.

Hypovolemic shock is the most common form of shock in children. Findings include tachycardia, tachypnea, delayed capillary refill, and signs of dehydration. Extremities are usually cool because of the compensatory mechanism of vasoconstriction. Hypovolemic shock is usually reversed with fluid administration alone and is less likely to require inotropes. In contrast, septic shock is systemic inflammation caused by an infection leading to shock. The effect of the bacterial toxin, if present, and the host inflammatory cascade cause arteriolar vasodilation, cardiac depression, and increased capillary permeability. This leads to similar signs of intravascular depletion, as in hypovolemic shock. However, septic shock can be distinguished from hypovolemic shock by the presence of fever, decreased cardiac function, vasodilation with "flash" capillary refill, capillary leak, and inotropic requirement. Whereas hypovolemic shock is usually "cold" shock, septic shock may be either "warm" or "cold" depending on the degree of vascular tone.

The boy in this vignette has septic shock evidenced by signs of infection, systemic inflammation, and shock. Since he has rales and hepatomegaly after fluid resuscitation, further increase of

intravascular volume, either with normal saline or 5% albumin, would worsen his condition. Hydrocortisone has been shown to reverse shock in patients at risk of adrenal insufficiency and in patients with catecholamine-resistant shock, but neither is occurring in the boy in this vignette. Double volume whole blood exchange transfusion can be effective in meningococcemia and multiple organ failure, but a more immediate need is to reverse the shock. Starting an epinephrine infusion would be the best next step in reversing the shock.

PREP Pearls

- Hypovolemic shock is usually reversed by restoration of intravascular volume, and is less likely to require inotropes
- In addition to signs of decreased intravascular volume also seen in hypovolemic shock, septic shock can also manifest with fever, "flash" capillary refill, and edema

ABP Content Specifications(s)

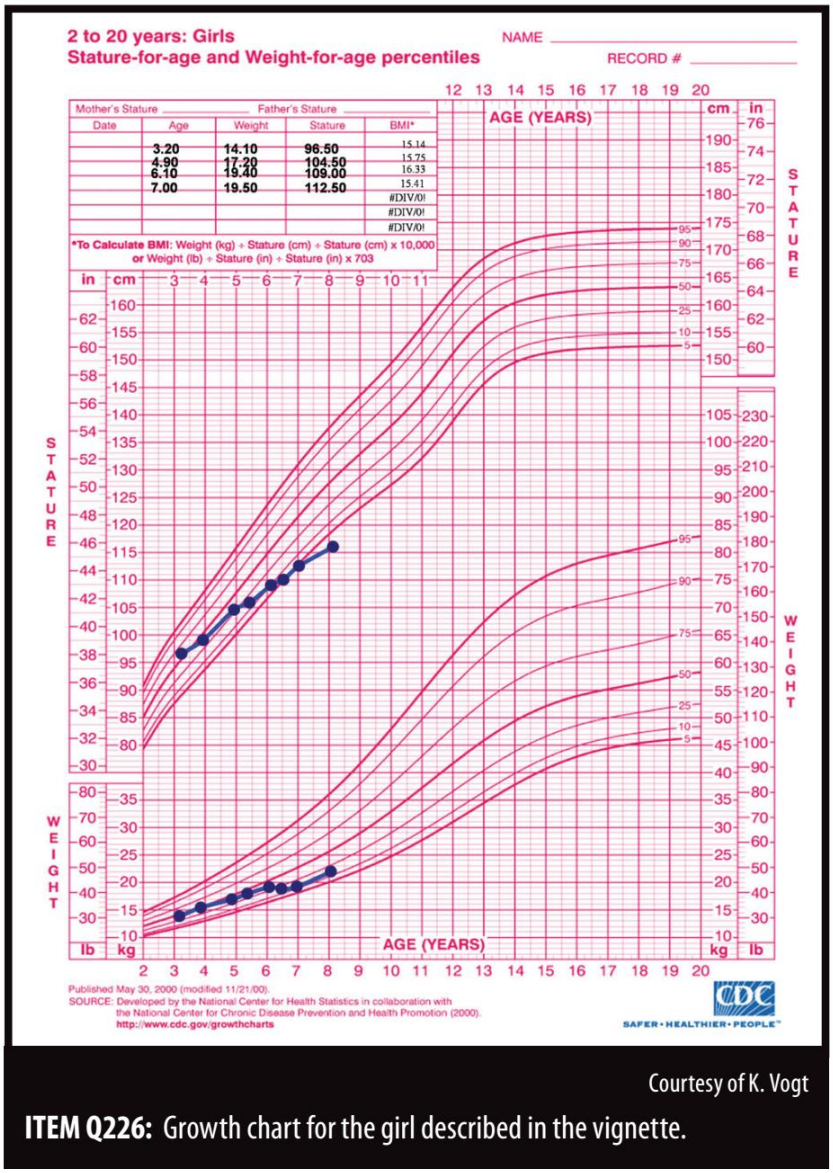
- Differentiate the findings associated with hypovolemic shock from those of septic shock, and manage appropriately

Suggested Readings

- Brierley J, Carcillo JA, Choong K, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med.* 2009;37(2):666-688. doi: http://dx.doi.org/10.1097/CCM.0b013e31819323c6.
- Brierley J, Peters MJ. Distinct hemodynamic patterns of septic shock at presentation to pediatric intensive care. *Pediatrics.* 2008;122(4):752-759. doi: http://dx.doi.org/10.1542/peds.2007-1979.
- de Caen AR, Berg MD, Chameides L, et al. Part 12: pediatric advanced life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation.* 2105;132:S526-S542. doi: http://dx.doi.org/10.1161/CIR.0000000000000266.

Question 226

An 8-year-old girl is brought to the office for a preparticipation physical examination for her summer swim league. She has a history of acute myelogenous leukemia with central nervous system involvement diagnosed at 11 months of age. She was treated with chemotherapy, followed by bone marrow transplant and irradiation that included the central nervous system. She completed therapy 6 years ago. Her parents have noticed that her energy level is not as good as it used to be. She is currently on no medication except for a daily multivitamin. On physical examination, her temperature is 37°C, heart rate is 82 beats/min, blood pressure is 94/52 mm Hg, weight is 22 kg (17th percentile), height is 116 cm (less than third percentile), and body mass index is 16.5 kg/m^2 (61st percentile). She is sexual maturity rating 1 for breast development and pubic hair. The remainder of her physical examination is unremarkable. Her growth curves are shown in Item Q226.



Courtesy of K. Vogt

ITEM Q226: Growth chart for the girl described in the vignette.

Of the following, the MOST likely explanation for her growth failure is
A. cancer recurrence
B. celiac disease
C. growth hormone deficiency
D. hypothyroidism
E. inadequate nutrition

Correct Answer: C

The girl described in the vignette has linear growth failure due to growth hormone deficiency secondary to her history of cranial irradiation. Pituitary hormone deficiencies are common after cranial irradiation and effects are often seen years after therapy has been completed. The growth hormone axis is the most sensitive and the first to be affected. Her decreased energy level is also a manifestation of growth hormone deficiency. Hypothyroidism can have a similar presentation, and she is at risk for hypothyroidism secondary to her cancer therapies, but growth hormone deficiency is more likely. Cancer recurrence would more likely present with additional symptoms such as bruising, fatigue, bone pain, and pallor. Celiac disease and inadequate nutrition usually affect weight prior to height and she does not have any risk factors for celiac disease. Her body mass index at the 61st percentile also makes these unlikely.

Congenital growth hormone deficiency presents with linear growth deceleration after the first 6 to 12 months of life when growth hormone becomes important for linear growth. Weight is not affected as much as length, so weight for length increases. There may also be evidence of altered body composition with increased fat mass and decreased lean body mass. Other pituitary hormone deficiencies may be associated. The presence of nystagmus and mid-line defects suggests septo-optic dysplasia. Males can have micropenis, especially if concomitant gonadotropin deficiency is present. Brain magnetic resonance imaging may reveal pituitary gland or stalk abnormalities, optic nerve hypoplasia, or agenesis of the septum pellucidum/corpus callosum.

Acquired growth hormone deficiency presents with linear growth deceleration after a period of normal growth. Relative weight gain with increased fat mass and fatigue are common. Acquired growth hormone deficiency may be secondary to a brain tumor, cranial irradiation, or head trauma. Other pituitary hormone deficiencies may be associated. Levels of insulin-like growth hormone factor-1 and insulin-like growth factor-binding protein 3 are low and growth hormone levels after stimulation with 2 provocative agents remain less than 10 ng/mL. Bone age is delayed. Magnetic resonance imaging of the brain and sella turcica and testing for other pituitary hormone deficiencies should be undertaken in those found to have growth hormone deficiency.

PREP Pearls

- Consider pituitary hormone deficiencies in those with history of cranial irradiation.
- Linear growth does not become abnormal until after 6 to 12 months of life in those with congenital growth hormone deficiency.
- With acquired growth hormone deficiency, investigation for a brain neoplasm and other pituitary hormone deficiencies should occur.

ABP Content Specifications(s)

- Recognize the clinical features associated with acquired and congenital growth hormone deficiency

Suggested Readings

- Meck MM, Leary M, Sills RH. Late effects in survivors of childhood cancer. *Pediatr Rev*. 2006;27(7):257-263. doi: http://dx.doi.org/10.1542/pir.27-7-257.
- Rogol AD, Hayden GF. Etiologies and early diagnosis of short stature and growth failure in children and adolescents. *J Pediatr*. 2014;164(5 Suppl):S1-S14. doi: http://dx.doi.org/10.1016/j.jpeds.2014.02.027.
- Rose SR, Vogiatzi MG, Copeland KC. A general pediatric approach to evaluating a short child. *Pediatr Rev*. 2005;26(11):410-420. doi: http://dx.doi.org/10.1542/pir.26-11-410.
- Webb EA, Dattani MT. Septo-optic dysplasia. *Eur J Hum Genet*. 2010;18(4):393-397. doi: http://dx.doi.org/10.1038/ejhg.2009.125.

Question 227

A 3-month-old infant is seen in your office for a scheduled follow-up visit. At the 2-month health supervision visit, he was diagnosed with positional plagiocephaly. His parents were instructed to provide more "tummy time" and advised to vary his head position. A 1-month follow-up visit was scheduled. The infant was born at full term without complications and has been well. No problems with feeding or swallowing have been noted. On physical examination, his growth and development are within normal limits. Although the infant prefers to look to the left, his gaze is conjugate and he is able to follow past midline. His head circumference is 39.5 cm. His head shape and face are asymmetric, with flattening of the right parieto-occipital region with the ipsilateral mandible and eye appearing smaller. His ears appear slightly different in shape and position. There is a palpable mass in the right sternocleidomastoid.

Of the following, the BEST next step in this infant's management is

A. cranial orthotics
B. computed tomography of skull and brain
C. plain radiography of neck and cervical spine
D. referral to a physical therapist
E. ultrasonography of the neck

Correct Answer: D

The infant in the vignette has clinical findings consistent with congenital muscular torticollis (CMT). Since the range of motion of his neck has not improved after 4 to 6 weeks of positional intervention in the home environment and craniofacial asymmetry is developing, it is appropriate to refer him for physical therapy. Early treatment is crucial to shortening the duration of the torticollis and limiting the further development of craniofacial asymmetries.

The most common form of congenital torticollis results from an asymmetry in the length and strength of the sternocleidomastoid (SCM) muscles. Physical examination typically reveals restricted range of motion of the neck, with the head tilted toward the shortened SCM and the chin rotated slightly to the opposite side. Often, a firm fusiform mass is palpable, usually in the inferior one-third of the SCM. This interstitial fibrosis of the SCM is likely related to intrauterine malpositioning or perinatal injury.

Most cases of CMT may be treated conservatively with passive stretching of the shortened SCM, positioning (and repositioning) the patient to a midline orientation, and facilitation of active movement. Frequent follow-up is important. Infants with severe cases of torticollis, those whose condition does not resolve spontaneously, or those who are not treated appropriately with early physical therapy may develop positional plagiocephaly that compounds the limited range of motion of the neck. If left untreated, significant craniofacial asymmetry may occur. On the side ipsilateral to the shortened SCM, the eye may appear smaller, the mandible and lower face may be less developed, the frontal area may flatten, and the ear is often smaller and cup-shaped. On the contralateral side, the parietal occipital region will be flattened and the ear may be displaced forward. If torticollis persists, vision and gross motor development may be affected as well. Other causes of abnormal head tilt must be ruled out, including ocular abnormalities (eg, weakness of the superior oblique muscle), congenital vertebral anomalies (eg, Klippel-Feil syndrome), Sandifer syndrome (abnormal posturing because of the pain of esophagitis), craniosynostosis with plagiocephaly, and other neuromuscular disorders that might limit range of motion.

Cranial orthotics may be warranted if significant positional plagiocephaly coexists with CMT; however, the underlying torticollis must be treated with physical therapy. The diagnosis of CMT is usually made clinically and imaging studies are not routinely obtained. Imaging should be considered if CMT persists after 6 months of physical therapy. Computed tomography of the skull or brain may be indicated if craniosynostosis is a concern, if developmental delays raise the question of a brain abnormality, or if the head circumference does not grow at a normal rate. Plain radiography of the neck or cervical spine should be considered if bony abnormalities are suspected. Ultrasonography of the neck mass may be helpful to confirm its muscular nature, however, this is usually recommended only when the mass persists longer than the expected 4 to 6 months.

PREP Pearls

- Early intervention with physical therapy is key to improving outcomes in congenital muscular torticollis (CMT).
- The diagnosis of CMT is usually made clinically and most cases will respond to physical therapy within 6 months.
- The differential diagnosis of CMT includes ocular abnormalities, vertebral anomalies, esophagitis, craniosynostosis, and other neuromuscular causes.

ABP Content Specifications(s)

- Formulate a differential diagnosis of torticollis
- Plan the appropriate management of torticollis

Suggested Readings

- Kuo AA, Tritasavit S, Graham JM Jr. Congenital muscular torticollis and positional plagiocephaly. *Pediatr Rev*. 2014;35(2):79-87. doi: http://dx.doi.org/10.1542/pir.35-2-79.
- Stellwagen L, Hubbard E, Chambers C, Jones KL. Torticollis, facial asymmetry and plagiocephaly in normal newborns. *Arch Dis Child*. 2008;93(10):827-831. doi: http://dx.doi.org/10.1136/adc.2007.124123.

Question 228

You are called to the nursery to evaluate a full-term male newborn noted by the nurses to have apneic episodes and poor feeding. The pregnancy was remarkable for polyhydramnios and abnormal prenatal ultrasonography showing a single umbilical artery, suspected congenital heart defect, and intrauterine growth retardation. Maternal serum quadruple screening at midtrimester revealed low levels of human chorionic gonadotropin and unconjugated estriol. On physical examination, the newborn is small for gestational age with dysmorphic features. He has a small head, eyes, and mouth with low-set malformed ears; micrognathia; rocker bottom feet; a systolic ejection murmur; and generalized hypotonia. His fingers have an unusual posture (Item Q228).

Item Q228: Hand of the neonate described in the vignette. Courtesy of L Parsley

Of the following, the newborn's MOST likely diagnosis is

A. arthrogryposis
B. CHARGE syndrome
C. fetal akinesia
D. trisomy 13
E. trisomy 18

Correct Answer: E

The newborn in the vignette has trisomy 18, which is the second most common autosomal trisomy syndrome. The classic phenotypic features include (Item C228):

- A characteristic facial dysmorphology
  - Dolichocephaly
  - External ear anomalies
  - Micrognathia
  - Short palpebral fissures
  - Small face
- Clenched fist with overriding fingers
- Hypotonia
- Prenatal and postnatal growth deficiency
- Redundant nuchal fold
- Rocker bottom feet

Item C228: Classic phenotypic images of a patient who has triosomy 18. Carey JC. Perspectives on the care and management of infants with trisomy 18 and trisomy 13: striving for balance. Curr Opin Pediatr. 2012; 24:672-678.

Many have major congenital malformations such as kidney and cardiac anomalies.

Many affected children require nutrition via a nasogastric or gastrostomy tube because of poor feeding. Ninety percent of neonates with trisomy 18 die in the first month after birth because of central apnea, severe congenital heart defects, respiratory insufficiency, upper airway obstruction, or a combination of these issues. Only 5% to 10% of affected infants survive beyond the first year. Those who survive will have severe intellectual disability.

Trisomy 18 typically results from a maternal meiotic nondisjunction error with failure of 2 members of a chromosome pair to separate from one another during meiosis. Both chromosomes then go to a single daughter cell, yielding an extra chromosome.

Arthrogryposis-affected infants present with multiple joint contractures. There is no associated facial dysmorphology, and cognition, development, and life span are usually normal.

CHARGE syndrome presents with a combination of findings that include **c**olobomas, **h**eart defects, **a**tresia choanae, **r**etarded growth and development, **g**enital

abnormalities, and **e**ar abnormalities. Fetal akinesia deformation sequence is characterized by decreased fetal movement, intrauterine growth restriction, pulmonary hypoplasia, multiple joint contractures, and facial anomalies. For many affected infants, survival is brief because of the pulmonary hypoplasia. Typical findings in newborns with trisomy 13 include small eyes, cleft lip/palate, microcephaly, cryptorchidism, polydactyly, broad flat nose with hypertelorism, micrognathia, scalp defects, and external ear anomalies. Many have serious brain, cardiac, and renal anomalies; most affected neonates survive for less than 1 month after birth.

PREP Pearls

- The classic phenotypic features of trisomy 18 include a clenched fist with overriding fingers, rocker bottom feet, characteristic facial dysmorphology, prenatal and postnatal growth deficiency, and hypotonia.
- Most newborns with trisomy 18 die within the first month after birth; only 5% to 10% will survive beyond 1 year of age.

ABP Content Specifications(s)

- Recognize the clinical features associated with trisomy 18

Suggested Readings

- Cereda A, Carey JC. The trisomy 18 syndrome. *Orphanet J Rare Dis*. 2012;7:81. doi: http://dx.doi.org/10.1186/1750-1172-7-81.
- Support Organization for Trisomy 18, 13, and Related Disorders. Home page. Support Organization for Trisomy 18, 13, and Related Disorders website. http://www.trisomy.org.
- Wu J, Springett A, Morris JK. Survival of trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome) in England and Wales: 2004–2011. *Am J Med Genet A.* 2013;161A(10):2512-2518. doi: http://dx.doi.org/10.1002/ajmg.a.36127.

Question 229

The parents of a 9-month-old infant ask your opinion about a "spot" that appeared on their daughter's arm several weeks ago. They have observed that when the lesion is rubbed (as when drying the skin after bathing) it may become red and swollen. The infant is well in all respects. Her temperature is 37°C and other vital signs are normal. The physical examination is notable only for an orange-pink, 2-cm oval plaque on the left arm (Item Q229A). After rubbing the lesion, it becomes erythematous (Item Q229B).

Item Q229A: Lesion as described for the infant in the vignette. Courtesy of D Krowchuk

Item Q229B: Appearance of the lesion after it was rubbed. Courtesy of D Krowchuk

Of the following, the MOST likely diagnosis is a

A. café-au-lait macule
B. connective tissue nevus
C. mastocytoma
D. melanocytic nevus
E. nummular eczema

Correct Answer: C

The infant in the vignette has developed a lesion with an orange-peel (peau d'orange) appearance, a finding that indicates the presence of a dermal cellular infiltrate. After rubbing or stroking, the lesion becomes erythematous, often accompanied by swelling (Darier sign). These changes are the result of mast cell degranulation and the release of mediators that cause increased blood flow and fluid leak from vessels. The appearance of the lesion and the presence of a Darier sign indicate a diagnosis of mastocytosis, a group of disorders characterized by the accumulation of mast cells in the skin and, occasionally, other organs. A café-au-lait macule, connective tissue nevus, melanocytic nevus, and nummular eczema would all lack an orange-peel appearance and would not exhibit the Darier sign.

Cutaneous mastocytosis is a spectrum of disease that includes mastocytomas, urticaria pigmentosa, diffuse cutaneous mastocytosis, and telangiectasia macularis eruptiva perstans. Mastocytomas and urticaria pigmentosa are the most common forms encountered in pediatrics. Both are characterized by lesions that have an orange-peel appearance and Darier sign. Mastocytosis may be present at birth or develop any time into middle age. For approximately half of patients, onset occurs in the first 2 years of life and 10% develop the disorder between 2 and 15 years of age. In infants and children, mastocytosis typically is limited to the skin, is not associated with hematologic disorders, and tends to resolve spontaneously by adolescence.

Mastocytomas (the diagnosis for the infant in the vignette) may be solitary or few in number. They appear as yellow to orange-brown papules or plaques (Item C229A). Lesions range in size from a few millimeters to several centimeters and may be found anywhere on the body. There is often a history of pruritus or recurrent blistering, which is the result of mast cell mediator release. Blistering may lead to confusion with disorders like recurrent herpes simplex virus infection or bullous impetigo.

Item C229A: A solitary mastocytoma. Courtesy of D Krowchuk

Urticaria pigmentosa (UP) is the most common form of cutaneous mastocytosis. It is characterized by multiple tan to brown macules or thin plaques, ranging in size from a few millimeters to several centimeters (Item C229B). The lesions of UP may be mistaken for café-au-lait macules or melanocytic nevi because of their color. Pruritus and blistering may occur. If there is sufficient mediator release, patients may experience flushing, hypotension, abdominal discomfort, diarrhea, or respiratory distress.

Item C229B: Urticaria pigmentosa. This patient also manifests dermatographism (arrows), a linear wheal, and flare at the site of skin stroking. Courtesy of D Krowchuk

The diagnosis of mastocytosis is usually made clinically. If uncertainty exists, skin biopsy will demonstrate an accumulation of mast cells in the dermis. For most pediatric patients, no further testing is required. Some advocate measurement of serum tryptase concentration, a mast cell-derived protease that correlates with disease extent. This may be useful if systemic involvement is suspected. If UP is very widespread, screening with a complete blood cell count and blood

chemistries is often recommended to screen for bone marrow or other systemic organ involvement.

Most patients with mastocytosis are asymptomatic and require no intervention. For those experiencing pruritus, a second-generation (eg, loratadine, cetirizine) or third-generation (eg, desloratadine, fexofenadine, levocetirizine) H1 antihistamine may be prescribed. Blistering may be prevented with the application of a potent topical corticosteroid. Patients who have flushing or diarrhea may benefit from cromolyn or an H2 antagonist (eg, cimetidine, ranitidine). A premeasured epinephrine pen is indicated for those who experience hypotensive episodes. Parents should be advised that aspirin, nonsteroidal anti-inflammatory agents, and certain anesthetic agents may cause mast cell degranulation. More information and support are available from http://www.mastokids.org/index.html.

PREP Pearls

- Cutaneous mastocytosis is characterized by orange-brown macules or papules that, upon stroking, develop erythema and swelling (Darier sign).
- Most patients with cutaneous mastocytosis require no treatment and the lesions will resolve spontaneously.

ABP Content Specifications(s)

- Recognize the clinical features of the various forms of mastocytosis and manage appropriately

Suggested Readings

- Carter MC, Metcalfe DD, Komarow HD. Mastocytosis. *Immunol Allergy Clin North Am*. 2014;34(1):181-196. doi: http://dx.doi.org/10.1016/j.iac.2013.09.001.
- Krowchuk DP, Mancini AJ. Cutaneous mastocytosis. *Pediatric Dermatology: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012:407-412.

Question 230

A 15-year-old adolescent girl presents to your clinic with the complaint of painful periods. She reports painful menstrual periods since menarche 2 years ago. The patient states that the pain typically starts 1 or 2 days before her period begins and is so severe that she often misses school. She uses only heating pads for pain control. You diagnose the patient with primary dysmenorrhea and counsel her on how to manage her pain more effectively.

Of the following, the BEST next method for treating this adolescent's pain is to prescribe

A. acupuncture
B. cyclobenzaprine
C. fish oil supplementation
D. ibuprofen
E. leuprolide

Correct Answer: D

The best next method for treating pain for the adolescent in the vignette would be to prescribe ibuprofen.

Primary dysmenorrhea is defined as pain that occurs with menstrual flow in the absence of pelvic disease. An estimated 43% to 93% of postpubertal girls experience some degree of dysmenorrhea. The pain of primary dysmenorrhea is secondary to myometrial contractions because of the secretion of prostaglandin E2 and F2a in the uterus. Anovulatory cycles are associated with lower prostaglandin levels and usually are not associated with dysmenorrhea. The pain of dysmenorrhea may start within a few hours up to several days before starting menses, and is typically described as spasmodic lower abdominal discomfort. The pain may radiate to the back and anterior thighs. Associated symptoms may include headache, nausea, or diarrhea. The differential diagnosis for painful periods includes endometriosis, pelvic inflammatory disease, fibroids, and anatomic abnormalities.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered first-line treatment for primary dysmenorrhea. If the pain is not controlled with NSAIDS, a trial of oral contraceptive pills may be indicated. Patients who continue to have significant symptoms, despite 3 to 6 months of oral contraceptive pill use, should be referred to a gynecologist for evaluation.

Acupuncture and fish oil supplementation have been used in the treatment of dysmenorrhea with unclear benefit. Cyclobenzaprine is sometimes used in conjunction with NSAIDs in the management of chronic pelvic pain, but is not recommended for primary dysmenorrhea. Leuprolide is typically used in the management of endometriosis.

PREP Pearls

- Primary dysmenorrhea is defined as pain that occurs with menstrual flow in the absence of pelvic disease.
- The pain of primary dysmenorrhea is secondary to myometrial contractions due to secretion of prostaglandins E2 and F2a in the uterus after ovulation.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered first-line treatment for primary dysmenorrhea.
- If the pain of primary dysmenorrhea is not controlled with NSAIDS, a trial of oral contraceptive pills may be indicated.

ABP Content Specifications(s)

- Formulate a differential diagnosis of dysmenorrhea
- Understand the pathophysiology of primary dysmenorrhea
- Plan the appropriate management of primary dysmenorrhea

Suggested Readings

- Braverman PK. Dysmenorrhea and premenstrual disorders. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. *Neinstein's Adolescent and Young Adult Health Care: A Practical Guide*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:405-411.
- Gray SH. Menstrual disorders. *Pediatr Rev.* 2013;3(1)4:6-18. doi: http://dx.doi.org/10.1542/pir.34-1-6.

Question 231

An 8-year-old boy is brought to your office for a health supervision visit. He is a polite child who cooperates with your directions and the physical examination. However, his mother complains that she needs to ask him multiple times before he will complete his household chores. He cannot keep his room clean and cannot find his favorite toys in the mess. He enjoys playing with his many friends and particularly likes basketball. He does well at school and his teacher has reported no concerns to his mother.

Of the following, the MOST appropriate next step for his mother to take is to

A. discontinue play dates until he can keep his room clean
B. ignore the messy room as he is doing well academically and socially
C. intermittently reward him with a new toy when his room is cleaned
D. place him in timeout each time he does not clean his room
E. provide feedback while helping him clean his room

Correct Answer: E

The first step to improving compliance is to ensure that the child understands what is expected of him. A request to "clean your room" may need to include specific directions such as put all dirty clothing into the clothes hamper, pick up and throw away trash, place toys into a toy chest, return books to the bookshelf, and make the bed. A child might not understand that all of these components need to be completed unless the parent outlines each step. In order to learn the process, the child may need a parent to help him clean the room and provide guidance or feedback during the process. Techniques to reinforce desired behaviors can be implemented once the child understands what to do.

Behavior modification is the use of techniques to increase or decrease behaviors.
Behavior management works best when parents are positive and are attentive to their children. Time-in and verbal praise are 2 techniques by which parents can encourage appropriate behaviors in their children. Parents first provide nonverbal, physical contact (eg, pat on the back) when noticing desired behaviors (eg, playing quietly), followed by verbal praise once the child has completed or is taking a break in their activity. Parents should clearly state the desired behavior for which the child is being praised. Reward systems, such as those using tokens or points, can also help reinforce wanted behaviors. In the beginning, frequent small rewards are more effective than intermittent large rewards. Rewards can be given less frequently once the desired behavior is consistently present.

Behavior management techniques to decrease undesired behaviors include time-out, planned ignoring, and job grounding. Time-out consists of removing the child from positive interactions and activities. The goals are to stop the undesired behavior and to encourage the development of self-calming skills. To be effective, time-out must be used immediately and every time the undesired behavior occurs. Planned ignoring and extinction involve withdrawal of attention when a child engages in inappropriate behaviors. Of note, these unwanted behaviors typically increase ("extinction burst") when this technique is first used, but will then subside if the parent perseveres. Job grounding can be effective for older children. In this technique, the child is required to complete a randomly chosen predetermined task before his privileges are reinstated.

Behavior modification can be effective in teaching children a variety of beneficial behaviors and skills. However, its success can be limited by lack of consistency and incorrect use of behavior management techniques. Parents must commit time and effort to achieve the desired results. Environmental factors, such as having the right tools or appropriate timing of interventions, may need to be addressed before behavior modification can work. If the child's behavior is severe, persistent, and/or impairing, additional evaluation or multiple modes of treatment (such as psychopharmacology, in addition to behavior modification) may be required.

The boy in this vignette appears to be doing well academically and socially. Completion of household chores is a commonly desired behavior, as this teaches children responsibility and life skills and contributes to the family. First, expectations should be developmentally appropriate and clear. The parent needs to make sure that the child understands these expectations and can complete the task. This can be achieved by providing feedback while helping him clean his

room. The child will learn the task better with practice and guidance. Once this has been done, the desired behavior can be reinforced, such as through rewards. When starting to work on a desired behavior, small rewards given immediately and frequently are more effective than large rewards given intermittently. Positive reinforcement is generally preferred over negative consequences such as timeout or loss of privileges or fun activities. Neither strategy will be effective unless the child understands expectations and is capable of accomplishing the desired task.

Pediatricians who understand the principles of behavior management can assist families by providing advice and counseling on how to address milder problems. They can guide families in accessing group or individual parent training for their child's more significant behavioral problems, and can refer families to mental health professionals for further evaluation and incorporation of multimodal treatment as appropriate.

PREP Pearls

- Behavior modification will not be effective unless the child understands expectations and is capable of accomplishing the desired task.
- When starting to work on a desired behavior, small rewards given immediately and frequently are more effective than large rewards given intermittently. Rewards can be given less frequently once the desired behavior is consistently present.
- Unwanted behaviors typically increase ("extinction burst") when planned ignoring or extinction is first used, but will then subside if the parent perseveres.

ABP Content Specifications(s)

- Understand the advantages and limitations of behavior modification approaches in the overall management of learning and behavioral problems

Suggested Readings

- Christophersen ER, Nyp SS. Behavioral management: theory and practice. In: Augustyn M, Zuckerman B, Caronna EB, eds. *The Zuckerman Parker Handbook of Developmental and Behavioral Pediatrics for Primary Care*. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011:59-65.
- Pipan ME, Blum NJ. Basics of child behavior and primary care management of common behavioral problems. In: Voigt RG, Macias MM, Myers SM, eds. *American Academy of Pediatrics Developmental and Behavioral Pediatrics*. Elk Grove Village, IL: American Academy of Pediatrics; 2011:37-58..

Question 232

A previously healthy 7-year-old boy is brought to the emergency department (ED) after he was noted to be very confused, unsteady on his feet, and having trouble breathing. The parents report that the boy was in good health when he left home this morning to help his grandfather work in his large vegetable garden. Just before lunchtime, the boy complained that "his belly was hurting." He vomited 3 times, followed by nonbloody diarrhea. When his grandfather drove him home for lunch, the boy seemed very sleepy and confused, and he could not get out of the car without assistance because he was stumbling. His parents drove him to the ED immediately. On arrival to the ED, the boy's vital signs include a temperature of 36.8°C, heart rate of 48 beats/min, blood pressure of 76/50 mm Hg, respiratory rate of 40 breaths/min, and pulse oximetry of 88% (room air). On physical examination, he is somnolent and responds to your questions only intermittently. He is drooling profusely and has clear drainage from both of his eyes and nares. His pupils are 2 mm in diameter and minimally reactive bilaterally. Breathing is labored, with coarse breath sounds and diffuse wheezing bilaterally. His skin is pale and diaphoretic, with no rash. The abdomen is soft and diffusely tender with hyperactive bowel sounds. He is moving all of his extremities, but seems generally weak.

You administer 100% oxygen by a non-rebreather mask, obtain intravenous access, and begin preparing for endotracheal intubation because of the boy’s lethargy and respiratory distress.

Of the following, the MOST appropriate therapy to administer to the boy at this time is

A. intramuscular epinephrine
B. intravenous atropine-pralidoxime
C. intravenous naloxone
D. intravenous physostigmine
E. intravenous succinylcholine

Correct Answer: B

The 7-year-old boy in the vignette presents with altered sensorium, ataxia, drooling, lacrimation, gastrointestinal symptoms, respiratory difficulty, bradycardia, miosis, and diaphoresis that manifested acutely after he was assisting his grandfather with garden work. His clinical history and constellation of signs and symptoms are consistent with acute organophosphate poisoning, likely due to pesticide exposure. The most appropriate treatment to administer at this time is intravenous atropine-pralidoxime.

Organophosphates, including pesticides, are an important cause of pediatric poisonings. It is important for all pediatric providers to recognize the signs and symptoms of organophosphate toxicity and to be able to manage them appropriately. Organophosphates are a diverse class of chemical agents that are found in both home and industrial settings. Examples include pesticides (such as malathion and parathion), herbicides, ophthalmic agents, and nerve gases (such as sarin, tabun, VX, and soman) that may be used as agents of biological warfare.

Organophosphates act primarily by inhibiting acetylcholinesterase, resulting in excess accumulation of acetylcholine and overstimulation of both muscarinic and nicotinic acetylcholine receptors. Children can become exposed to organophosphates in their homes or garden/agricultural settings through ingestion, inhalation, injection, or cutaneous absorption. Although most patients exposed to organophosphates become symptomatic quickly, the onset and degree of symptoms vary depending on the specific agent, amount absorbed, route of exposure, underlying health of the patient, and rate of metabolic degradation. Children are especially vulnerable to organophosphate poisoning (particularly from exposure to pesticides) due to their higher body surface area-to-mass ratios and the increased hand-to-mouth activity that is developmentally normal in young children.

Clinical signs and symptoms of organophosphate poisoning can be categorized into 3 types of effects: (1) muscarinic effects, (2) nicotinic effects, and (3) effects on the central nervous system (Item C232).

Item C232. Clinical Signs and Symptoms of Organophosphate Poisoning.

Muscarinic	Nicotinic	Central Nervous System
• Cardiovascular: - bradycardia - hypotension • Respiratory: - rhinorrhea - bronchorrhea - bronchospasm - wheezing - cough - respiratory distress • Gastrointestinal: - increased salivation - abdominal pain - nausea and vomiting - diarrhea - fecal incontinence • Genitourinary: - increased urination - urinary incontinence • Ocular - blurred vision - miosis • Other - increased lacrimation - diaphoresis	• Muscle cramping and fasciculations • Weakness and respiratory failure (due to effects on the diaphragm) • Autonomic manifestations: - Hypertension - Tachycardia - Mydriasis - Pallor	• Anxiety • Confusion • Ataxia • Seizures • Coma

Couurtesy of J. Rose

Muscarinic effects may be recalled by using the familiar mnemonic SLUDGE (**S**alivation, **L**acrimation, **U**rination, **D**iarrhea, **G**astrointestinal upset, and **E**mesis) and DUMBELS (**D**iaphoresis and diarrhea, **U**rination, **M**iosis, **B**radycardia, **B**ronchospasm, **B**ronchorrhea, **E**mesis, **L**acrimation, and **S**alivation).

Respiratory failure is the most common cause of death in victims of organophosphate poisoning. Management of acute organophosphate poisoning involves aggressive support of the airway, breathing, and circulation. Endotracheal intubation is often necessary in patients with respiratory distress due to increased respiratory secretions, laryngospasm, bronchospasm, diaphragmatic failure, coma, and/or seizures. Reducing further exposure of the patient to organophosphates and preventing secondary exposure to healthcare workers is essential in the management of patients with organophosphate poisoning. Clothing should be removed from all exposed patients and skin should be cleansed with soap and water. Healthcare providers must use appropriate personal protective equipment when decontaminating patients. Patients with ocular exposures should undergo ocular irrigation using saline or lactated Ringer's solution.

The mainstays of medical treatment for organophosphate poisoning include atropine and pralidoxime (2-PAM), along with benzodiazepines to treat associated seizures. Physicians should confer with a medical toxicologist or the regional poison center (1-800-222-1222) for recommendations on the most optimal management plan for individual cases of organophosphate toxicity.

Intramuscular epinephrine is the treatment of choice for children presenting with acute anaphylactic reactions. Although some of the signs and symptoms displayed by the boy in the vignette can be seen in children with anaphylaxis, other findings such as miosis, altered sensorium, bradycardia, and excessive lacrimation would not be associated with this diagnosis. The constellation of the boy's clinical manifestations, along with his history of gardening prior to the onset of his illness, point to organophosphate poisoning as the more likely diagnosis. Intravenous naloxone is the antidote for opioid toxicity, which is characterized by the classic triad of central nervous system depression, respiratory depression, and pinpoint pupils. Intravenous physostigmine is an antidote that is recommended for anticholinergic toxicity, which is manifested by central toxicity (delirium, hallucinations, and seizures) or peripheral manifestations (tachycardia, dry skin and mucous membranes, urinary retention, decreased bowel sounds, and hyperthermia). These findings contrast sharply with those seen with organophosphate poisoning.

Succinylcholine is a rapid-acting depolarizing paralytic agent that is used in the process of rapid sequence intubation. Succinylcholine should specifically be avoided in patients with organophosphate poisoning because it is degraded by cholinesterase (which is inhibited by organophosphates), and would have a prolonged duration in patients affected by

organophosphate toxicity. If a paralytic agent is needed for rapid sequence intubation in patients with organophosphate poisoning, then an alternative agent such as rocuronium should be used.

PREP Pearls

- The toxidrome of organophosphate poisoning includes the combination of bronchoconstriction, bronchorrhea, diarrhea, vomiting, salivation, lacrimation, miosis, sweating, and urination. Central nervous system effects may also result from organophosphate poisoning.
- Deaths related to organophosphate poisoning are most often due to respiratory failure. Aggressive support of the airway and breathing is critical to the management of victims.
- The mainstays of medical treatment for organophosphate poisoning include atropine and pralidoxime (2-PAM), along with benzodiazepines to treat associated seizures. Physicians should confer with a medical toxicologist or the regional poison center (1-800-222-1222) for recommendations on the most optimal management plan for individual cases of organophosphate toxicity.
- Reducing further exposure of the patient to organophosphates and preventing secondary exposure to healthcare workers is essential in the management of patients with organophosphate poisoning.

ABP Content Specifications(s)

- Recognize the signs and symptoms of organophosphate poisoning, and manage appropriately

Suggested Readings

- Baer A, Kirk MA, Holstege C. Organophosphates, carbamates, pesticides, and herbicides. In: Erickson TB, Ahrens WR, Aks SE, Baum CR, Ling LJ, eds. *Pediatric Toxicology: Diagnosis and Management of the Poisoning Child*. New York, NY: McGraw-Hill; 2005:352-358..
- Katz KD. Organophosphate toxicity. *Medscape*. 2015. http://emedicine.medscape.com/article/167726. Updated January 27, 2015.

Question 233

A 9-month-old male infant is brought to the pediatric clinic for travel counseling. His family plans to travel to the Philippines to visit relatives in 2 weeks. He has received all recommended vaccines through 6 months of age. His mother is concerned about multiple cases of measles in her home country and would like him to receive any additional vaccines that are indicated prior to their trip.

Of the following, the BEST measles vaccine schedule in this infant is

A. at ages 12 months and 4 years
B. now and at age 4 years
C. now and at age 12 months
D. now and at ages 12 months and 2 years
E. now and at ages 12 months and 4 years

Correct Answer: E

The best measles vaccine schedule for the infant in this vignette is now and at ages 12 months and 4 years.

Giving vaccine according to the routine schedule at 12 months and 4 years would not address the risk of acquiring measles during travel. It is recommended that infants 6 to 11 months of age receive 1 dose of MMR vaccine prior to any international travel; earlier than they ordinarily would under routine vaccination schedules. Due to the presence of maternal antibodies, infants who receive MMR vaccine prior to 12 months of age have lower seroconversion rates compared to those who receive MMR at or after 12 months of age. Therefore, if a dose of MMR is given prior to 12 months of age, the individual should receive an additional 2 doses of vaccine, the first at 12 to 15 months of age, and the second at school entry (4 to 6 years of age). The second dose under the routine schedule can be given before 4 years of age, as long as 28 days have elapsed from the 12 to 15 month dose. The second dose is not considered a booster dose, but is administered in order to allow for seroconversion in individuals who did not seroconvert with their first dose.

Contraindications to measles vaccination include immediate hypersensitivity reaction after the first dose of measles vaccine, pregnancy, and immunocompromised patients, as such individuals should not receive live-virus vaccine. Since vaccine can contain traces of gelatin or neomycin, individuals with a history of anaphylaxis to these components should be evaluated by an allergist prior to administration of vaccine.

In the setting of an outbreak, measles vaccine can be given within 72 hours of the exposure and can provide disease protection in individuals that are susceptible (unimmunized or underimmunized). Vaccine is the principal intervention recommended for outbreaks in schools and childcare centers. Immunoglobulin can also confer protection when administered up to 6 days from the time of exposure. Immunoglobulin is indicated for those at risk of severe measles and complications including infants younger than 12 months of age, pregnant women without evidence of immunity, and immunocompromised individuals. Infants ages 6 to 11 months can receive vaccine instead of immunoglobulin if given within 72 hours of exposure. For those without these risk factors, vaccine is preferred for postexposure prophylaxis.

PREP Pearls

- It is recommended that infants 6 to 11 months of age receive 1 dose of MMR prior to any international travel.
- If a dose of MMR is given prior to 12 months of age, it is recommended that the individual receive an additional 2 doses of vaccine.
- Measles vaccine given within 72 hours of the exposure is the preferred method of controlling measles outbreaks in school and childcare settings in susceptible individuals.

ABP Content Specifications(s)

- Plan appropriate administration of MMR vaccine during an outbreak
- Know the indications, contraindications, limitations, and schedule for the MMR vaccine
- Understand the effects on immunity when MMR vaccine is administered to children younger than 12 months of age

Suggested Readings

- American Academy of Pediatrics. International travel. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:101-107.
- American Academy of Pediatrics. Measles. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:535-547.

Question 234

You are seeing a 4-week-old, first-born male infant in the emergency department. His parents brought him in for evaluation of persistent vomiting, which is now projectile. His emesis is nonbloody and nonbilious. The boy's urine output has decreased over the past several days.

Of the following, the BEST imaging modality to confirm this infant's diagnosis is

A. abdominal computed tomography
B. abdominal radiography
C. abdominal ultrasonography
D. head computed tomography
E. upper gastrointestinal series

Correct Answer: C

The differential diagnosis for vomiting is broad and varies by age (Item C234). A thorough history and physical examination are crucial to defining the differential diagnosis and selecting the appropriate approach to evaluation. For the infant in the vignette with a history of persistent nonbloody, nonbilious emesis, the best initial imaging study is abdominal ultrasonography to evaluate for obstructive lesions. Of the response choices, abdominal ultrasonography is the least invasive and has no radiation exposure, thus it holds the lowest risk.

Item C234. Vomiting in Infants and Children.

Age Group	Differential Diagnosis	Radiographic Evaluation
Infants	• Congenital atresia or stenosis • Food allergy or intolerance • Food protein–induced enterocolitis syndrome • Gastroenteritis • Gastroesophageal reflux disease • Hirschsprung disease • Intussusception • Malrotation • Metabolic disorder • Pyloric stenosis • Sepsis/infection	• Abdominal radiography • Abdominal ultrasonography • Gastrografin enema • Upper gastrointestinal series
Children and adolescents	• Appendicitis • Bezoar • Cyclic vomiting syndrome • Eating disorder • Elevated intracranial pressure • Food allergy or intolerance • Gastroenteritis • Gastroesophageal reflux disease • Intussusception • Malrotation • Pancreatitis • Pregnancy • Sepsis/infection • Strangulated hernia • Toxin ingestion • Tumor/mass	• Abdominal computed tomography • Abdominal ultrasonography • Abdominal radiography • Head computed tomography • Upper gastrointestinal series

Courtesy of C. Waasdorp Hurtado

Abdominal radiography will identify gas patterns suggestive of obstruction, but will not identify the specific location or confirm the diagnosis. Abdominal computed tomography is a more sensitive and specific test, but is associated with significant radiation exposure. Head computed tomography would be helpful in identifying obstructive lesions resulting in hydrocephalus that could stimulate vomiting, but again, would expose the infant to a large amount of radiation. This might be indicated if there were additional central nervous system findings. An upper gastrointestinal series can identify a malrotation and other anatomic etiologies for vomiting, but also involves radiation exposure. Although dysmotility might be suggested by an upper gastrointestinal series, a gastric emptying study is a better test for motility.

PREP Pearls

- Abdominal ultrasonography is the best initial imaging modality to confirm the diagnosis in an infant with nonbloody, nonbilious emesis.
- The differential diagnosis for vomiting is broad and varies by age.
- A thorough history and physical examination are crucial to defining the differential diagnosis and selecting the appropriate evaluation of a child with vomiting.

ABP Content Specifications(s)

- Formulate an age-appropriate differential diagnosis of vomiting

Suggested Readings

- Hryhorczuk AL, Lee EY. Imaging evaluation of bowel obstruction in children: updates in imaging techniques and review of imaging findings. *Semin Roentgenol.* 2012;47(2):159-170. doi: http://dx.doi.org/10.1053/j.ro.2011.11.007.
- Mendez D, Caviness AC, Ma L, Macias CC. The diagnostic accuracy of an abdominal radiograph with signs and symptoms of intussusception. *Am J Emerg Med*. 2012;30(3):426-431. doi: http://dx.doi.org/10.1016/j.ajem.2011.01.010.
- Parashette KR, Croffie J. Vomiting. *Pediatr Rev*. 2013;34(7):307-321. doi: http://dx.doi.org/10.1542/pir.34-7-307.

Question 235

A 13-year-old adolescent presents to your office for a health supervision visit. Her parents are very concerned about her posture, stating that her upper back has a rounded appearance. The adolescent herself is unconcerned. She has no back or neck pain, upper extremity weakness, or paresthesias. She is 6 months postmenarchal. On physical examination, she has a hunched-forward posture with mildly prominent thoracic kyphosis. She is able to correct this posture when prompted. With forward bending, she has a smooth contour of the upper to mid-thoracic spine.

Of the following, the BEST next step in evaluation and management for this patient is to

A. obtain magnetic resonance imaging of the thoracic spine
B. obtain radiographs of the thoracic spine
C. prescribe a custom brace to correct the position of the thoracic spine
D. reassure the family that no further intervention is indicated
E. refer her to an orthopedic specialist for surgical management

Correct Answer: D

The adolescent in the vignette has postural kyphosis, also called postural roundback. She appears to have excessive kyphosis on physical examination, but this position is flexible: she can correct this position when prompted. Since her posture is flexible and she is asymptomatic, no treatment is warranted. She does not require imaging studies, such as radiography or magnetic resonance imaging. No bracing or surgery is indicated.

Kyphosis and lordosis refer to convexity and concavity, respectively, of the spine in the sagittal plane. The normal spine has physiologic curvature in this plane with cervical and lumbar lordosis and thoracic kyphosis. Up to 45 degrees of thoracic kyphosis using Cobb angle measurements on lateral radiographs is considered normal in adolescents.

Individuals with postural kyphosis appear to have excessive thoracic kyphosis but are generally asymptomatic. Often, parents exhibit concern about their child's posture. On physical examination, the excessive kyphosis is somewhat flexible. When bending forward, the contour of the thoracic spine has a rounded appearance without sharp angulation. Families should be counseled that the appearance of the spine generally improves with time. Physical therapy exercises aimed at improving posture may be helpful in the short term. However, adolescents without symptoms may have difficulty adhering to a home exercise program.

The differential diagnosis of postural kyphosis includes Scheuermann disease and congenital kyphosis. Scheuermann disease refers to kyphosis caused by anterior wedging of 3 or more consecutive vertebrae. This disorder typically affects the thoracic spine, causing excessive thoracic kyphosis that becomes apparent during the prepubertal growth spurt. Over half of children with Scheuermann kyphosis will have some back pain before reaching skeletal maturity. Approximately one-third of children and adolescents have associated scoliosis, though this tends to be mild. Affected individuals appear to have a sharp angulation of the spine when bending forward, rather than the smooth contour seen with postural roundback. With mild Scheuermann disease, the kyphotic posture may be flexible. Children and adolescents with mild Scheuermann disease can be observed, with radiographs obtained every 6 months until skeletal maturity to look for progression. Physical therapy may help to alleviate associated back pain. Bracing is controversial, but may help prevent progression of kyphosis in children with moderate to severe Scheuermann disease. Spinal fusion may be considered for severe, symptomatic, progressive cases.

Congenital kyphosis results from vertebral segmentation abnormalities that arise during fetal development. This condition is rare and tends to progress with age. Affected children often exhibit abnormalities on neurologic examination. Surgical treatment is often required.

PREP Pearls

- The normal spine has a physiologic curvature in the sagittal plane with cervical and lumbar lordosis and thoracic kyphosis.
- Postural kyphosis refers to flexible excessive kyphosis that does not cause symptoms, and tends to become apparent during the prepubertal growth spurt.
- Scheuermann disease is defined as anterior wedging of 3 or more consecutive vertebrae, and typically occurs in the thoracic spine, causing excessive kyphosis.

ABP Content Specifications(s)

- Plan the appropriate management of kyphosis
- Recognize the clinical findings associated with kyphosis

Suggested Readings

- Axelrod T, Zhu F, Lomasney L, Wojewnik B. Scheuermann's disease (dysostosis) of the spine. *Orthopedics*. 2015;38(1):4, 66-71. doi: http://dx.doi.org/10.3928/01477447-20150105-01.
- Warner WC Jr, Sawyer JR. Kyphosis. In: Weinstein SL, Flynn HM, eds. *Lovell and Winter's Pediatric Orthopaedics*. 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2013:739-790 .

Question 236

A 16-year-old adolescent is brought to the emergency department for unsteadiness and stumbling while walking, which was first noticed 4 days ago. She has a history of cystic fibrosis and has not been seen for medical care or taken any of her routine medications in over 2 years. On physical examination, she appears thin and malnourished. She has an ataxic gait and diminished deep tendon reflexes in the lower extremities, as well as some generalized weakness in the lower extremities.

Of the following, she MOST likely has a deficiency of

A. vitamin A
B. vitamin B3
C. vitamin B6
D. vitamin D
E. vitamin E

Correct Answer: E

The adolescent in this vignette has a deficiency of vitamin E. Patients with cystic fibrosis have difficulty absorbing the fat-soluble vitamins, vitamins A, D, E, and K. Not taking her routine medications (which typically include a supplement containing vitamins A, D, E, and K) puts her at high risk of a vitamin deficiency. Classic manifestations of vitamin E deficiency include generalized weakness, decreased deep tendon reflexes, hemolytic anemia, visual changes, and ataxia.

Vitamin A deficiency is associated with blindness, defective tooth enamel, decreased growth, and a decreased immune response. Vitamin B_3 (niacin) deficiency results in pellagra and is associated with diarrhea, dermatitis, and dementia. Vitamin B_6 (pyridoxine) deficiency results in refractory seizures, dermatitis, peripheral neuropathy, and microcytic anemia. Vitamin D deficiency results in a wide array of clinical presentations, including seizures and tetany (due to hypocalcemia), failure to thrive, hypotonia, widened cranial sutures, bony changes, developmental delay, delayed tooth eruption, and bowed legs.

Vitamins can be classified as being either being water- or fat-soluble (Item C236). The fat-soluble vitamins are A, D, E, and K. These vitamins depend on the secretion of pancreatic enzymes and bile acids from the liver to aid in their absorption. Any disruption in the process of fat digestion, absorption, or transportation can affect the absorption of these vitamins. Fat-soluble vitamins are mainly stored in the liver and in fatty tissues. Water-soluble vitamins include the B complex vitamins, vitamin C, and folate. These vitamins are typically not stored (with the exception of vitamin B_{12}, which has some storage in the liver). Deficiencies in water-soluble vitamins are rare in children in developed countries and typically occur as a result of an inborn error of metabolism; they are not usually due to a dietary deficiency.

Item C236. Fat- and Water-Soluble Vitamins and Their Function.

Vitamin	Absorption	Storage	Main Metabolic Function
A	Fat-soluble; absorbed in the ileum	Stored in the liver	Maintains growth and integrity of epithelial cells in eyes, urinary, respiratory and gastrointestinal tracts
B_1 (thiamine)	Water-soluble	Not stored	Co-enzyme in carbohydrate metabolism, synthesis of nucleic acids and neurotransmitters
B_2 (riboflavin)	Water-soluble	Not stored	Catalyst for mitochondrial oxidative and reductive reactions and hydrogen transfer reaction
B_3 (niacin)	Water-soluble	Not stored	Important in electron transport and glycolysis, forms NAD, NADPH
B_6 (pyridoxine)	Water-soluble	Not stored	Coenzyme in the transport and metabolism of amino acids
B_{12} (cobalamin)	Water-soluble; absorbed in the ileum	Stored in liver; excreted in bile and reabsorbed in the ileum	Involved in conversion of homocysteine to methionine; involved in folic acid metabolism; involved in vitamin A metabolism
Folic Acid	Water-soluble	Not stored	Involved in red blood cell maturation and nucleic acid synthesis
C	Water-soluble	Not stored	Involved in collagen synthesis, metabolism of cholesterol and neurotransmitters; antioxidant functions
D	Fat-soluble; intestinal absorption	Stored in fatty tissues	Increases plasma concentrations of calcium and phosphorus
E	Fat-soluble; absorbed in the ileum	Stored in liver; incorporated into high density lipoproteins and transported to target tissues	Functions as an anti-oxidant
K	Fat-soluble; absorbed in the jejunum	Stored in the liver	Functions as a cofactor involved in the activation of coagulation factors II, VII, IX, and X

Courtesy of D. DeBlasio

It is important to note that the vitamin needs of a preterm infant are different than the vitamin needs of a full-term infant or older child. Preterm infant formulas have a higher concentration of both water-soluble and fat-soluble vitamins given the higher protein requirement for preterm infants and the reduced amount of vitamin storage given the shortened gestational age.

PREP Pearls

- Vitamins A, D, E, and K are fat-soluble vitamins.
- Premature infant formulas contain higher levels of both water-soluble and fat-soluble vitamins than traditional full-term infant formulas

ABP Content Specifications(s)

- Understand the absorption, storage, and metabolism of fat- and water-soluble vitamins in patients of various ages, including those born prematurely

Suggested Readings

- American Academy of Pediatrics. Nutritional needs of the preterm infant. In: Kleinman RE, Greer FR ed. *Pediatric Nutrition.* 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2013:83-122.
- American Academy of Pediatrics. Vitamins and minerals. In: Kleinman RE, Greer FR ed. *Pediatric Nutrition*. 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2013:27.
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- Lauer B, Spector N. Vitamins. *Pediatr Rev*. 2012;33(8):339-352. doi: http://dx.doi.org/10.1542/pir.33-8-339.
- Ross AC, Tan L. Vitamin A deficiencies and excess. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:317-321.
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- Shah D, Sachdev HPS. Vitamin C (ascorbic acid): In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:329-331.

Question 237

A 7-year-old boy presents to the emergency department having had a single temperature measurement of 39°C measured at home with an axillary thermometer. He was diagnosed with B-cell acute lymphoblastic leukemia 1 year ago and is currently receiving "maintenance" chemotherapy. He has a central venous access port.

In the emergency department, the boy is awake, alert, and in no distress. His temperature is 37.8°C, heart rate is 80 beats/min, blood pressure is 92/68 mm Hg, and oxygen saturation is 98% on room air. Other than the hub of his venous access catheter palpable in the left chest wall 4 cm above the areola, the remainder of his physical examination is unremarkable. He was seen earlier in the day in the oncology clinic for a scheduled dose of vincristine. At that time, his complete blood cell count was performed and the results are shown:

Laboratory Test	Patient Result
White blood cell count	560/μL (0.56 x 10^9/L)
Neutrophils	12%
Lymphocytes	81%
Monocytes	6%
Eosinophils	1%
Platelet count	112 × 10^3/μL (112 × 10^9/L)

Of the following, the BEST next step in management would be to

A. access the port, order a blood culture, and start cefepime
B. access the port, order a blood culture, and start ceftriaxone
C. place a peripheral intravenous (IV) line, order a blood culture, and start amoxicillin/clavulanate
D. place a peripheral IV line, order a blood culture, and start ceftriaxone
E. provide reassurance and discharge from the hospital because he does not have a fever

Correct Answer: A

Leukopenia due to bone marrow suppression is a common adverse effect of many chemotherapeutic agents used in the treatment of children with cancer. Often both adaptive immunity (B and T lymphocytes) and innate immunity (neutrophils, monocytes, and natural killer cells) are affected. It is common for these children to develop severe (< 500/μL [0.5 x 10^9/L]), very severe (< 200/μL [0.2 x 10^9/L]), or absolute neutropenia. Children with neutropenia are at markedly increased risk for invasive bacterial infections and the presence of a central venous device further increases that risk.

The occurrence of even a single fever event in a child with neutropenia is a medical emergency and that child should be considered to have bacteremia until proven otherwise. Immunocompromised patients with neutropenia may be unable to mount a normal immune response to severe infections and may not exhibit the expected physical examination findings. All patients with fever and neutropenia should seek immediate medical attention. They should rapidly have their central venous device accessed, have blood cultures sent, and receive a broad-spectrum parenteral antibiotic through their central venous device. Initial antibiotic coverage should include common gram-positive and gram-negative organisms, including *Pseudomonas*. Cefepime is a fourth-generation cephalosporin that would provide appropriate antibacterial coverage for children with febrile neutropenia.

The boy in the vignette presented with the history of a single fever at home, and a leukocyte count of 560/μL (0.56 x 10^9/L) with 12% neutrophils. His absolute neutrophil count is less than 200/μL and therefore he has very severe neutropenia. Despite his well appearance, the boy may have bacteremia and should be treated accordingly. Although ceftriaxone, a third-generation cephalosporin, provides some coverage for gram-positive organisms and good coverage for gram-negative organisms, it does not provide coverage for *Pseudomonas* infections. Ceftriaxone would be a reasonable choice for a non-neutropenic, well-appearing patient with fever and a central venous device, but would not provide adequate coverage for a patient with febrile neutropenia.

Oral amoxicillin/clavulanate would not provide any antibiotic application to the interior of a central venous device and would therefore not be appropriate therapy in this case. Reassurance would not be appropriate for a child with neutropenic fever, even for a single documented fever at home.

PREP Pearls

- Fever with neutropenia is a medical emergency and patients should be treated as if they have bacteremia until proven otherwise.
- Patients with central venous devices, fever, and neutropenia should have their central venous device accessed, a blood specimen sent for culture, and a broad-spectrum, parenteral antibiotic administered as rapidly as possible.
- Treatment for febrile neutropenia should include antibiotic coverage for *Pseudomonas* infection.

ABP Content Specifications(s)

- Plan appropriate antibiotic therapy for a patient with a malignancy who has fever and neutropenia
- Recognize the major infections in patients with cancer

Suggested Readings

- Lehrnbecher T, Phillips R, Alexander S, et al. Guideline for the management of fever and neutropenia in children with cancer and/or undergoing hematopoietic stem-cell transplantation. *J Clin Oncol*. 2012;30(35):4427-4438. doi: http://dx.doi.org/10.1200/JCO.2012.42.7161.
- Meckler G, Lindemulder S. Fever and neutropenia in pediatric patients with cancer. *Emerg Med Clin North Am*. 2009;27(3):525-544. doi: http://dx.doi.org/10.1016/j.emc.2009.04.007.
- Segel GB, Halterman JS. Neutropenia in pediatric practice. *Pediatr Rev*. 2008;29(1):12-24. doi: http://dx.doi.org/10.1542/pir.29-1-12.

Question 238

You are called by a local dentist regarding the need for subacute endocarditis (SBE) prophylaxis for 2 of your patients. The children are scheduled to be seen in his office for dental care. One is a 4-year-old child with mild aortic stenosis (AS) and trivial aortic insufficiency. The other is a 9-year-old child with a small midmuscular ventricular septal defect (VSD), with a gradient of 90 mm Hg as determined with echocardiography.

Of the following, the current American Heart Association recommendation for SBE prophylaxis for these children is that

A. both will require SBE prophylaxis for any dental work
B. both will require SBE prophylaxis, only for major dental work
C. neither will require SBE prophylaxis for any dental work
D. the 4-year-old patient will require prophylaxis for any dental work; the 9-year-old patient will require none
E. the 9-year-old patient will require prophylaxis for any dental work; the 4-year-old patient will require none

Correct Answer: C

In this vignette, one child has mild aortic stenosis with trivial aortic insufficiency, and the other has a small, restrictive (high gradient) ventricular septal defect. Neither of these children requires endocarditis prophylaxis for dental procedures because neither child has cyanotic congenital heart disease or undergone any cardiac procedures involving a device or prosthetic material.
The American Heart Association recommendations for prophylaxis of infective endocarditis (IE) before dental procedures were revised in 2007 (C238A).

Item C238A. American Heart Association's Recommendations for Prophylaxis to Prevent Infective Endocarditis Prior to Dental Procedures.

Prophylaxis is recommended in patients who have:

- had valve replacement or repair with prosthetic material
- had an episode of infective endocarditis with unrepaired cyanotic congenital heart disease (including patients with palliative shunts and conduits)
- had repair of cyanotic congenital heart disease that required use of a device or prosthetic material for the first 6 months after the procedure (as endothelialization of the operative site will not be reliably completed). Continued prophylaxis is required if there is any residual shunt.
- undergone cardiac transplant and have valve disease

Adapted and reprinted with permission from Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation.* 2007;116(15):1736-1754

Recognizing that bacteremia occurs frequently, the recommendations were revised in light of evidence demonstrating that, for many diagnoses, improved oral hygiene was more important in preventing IE than the previously widespread use of antibiotic prophylaxis. The patients who continue to require IE prophylaxis are those at greatest risk for IE. Making the diagnosis of IE requires a high index of suspicion. Symptoms of chronic illness such as intermittent low-grade fever, fatigue, or joint pain should raise concern for IE. Patients may also present acutely ill with high fever, new findings of cardiac valve regurgitation, and congestive heart failure.
In addition to the physical examination, the tests used to make the diagnosis of IE include blood cultures and echocardiography. Blood cultures (2 obtained separately) are crucial in determining the causative organism. Echocardiography is used to evaluate the valves for lesions, such as vegetations or abscesses, in patients with bacteremia. This study is very useful in identifying

patients who may require surgery to drain an abscess or remove a vegetation that is likely to embolize.

The modified Duke criteria (C238B , C238C) can be used to help identify patients with endocarditis.
The 3 major criteria are as follows:

- Two positive blood cultures with pathogens likely to cause IE (such as *Staphylococcus aureus* or viridansstreptococci) or evidence of persistently positive blood cultures with less common organisms; one positive blood culture with *Coxiella burnetii*.
- New findings on echocardiogram consistent with endocarditis, which may include new valve regurgitation, masses, or vegetations.
- New murmur consistent with valve regurgitation.

Minor criteria include the following:

- Underlying heart disease
- Intravenous drug abuse
- Fever
- Positive blood cultures which do not meet major criteria
- Evidence of vasculitis or immunologic effects such as glomerulonephritis

Item C238B. Criteria for Infective Endocarditis (Proposed Modified Duke Criteria, With Modifications Shown in Boldface).

Definite infective endocarditis

Pathologic criteria

(1) Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or

(2) Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis

Clinical criteria*

(1) 2 major criteria; or

(2) 1 major criterion and 3 minor criteria; or

(3) 5 minor criteria

Possible infective endocarditis

(1) **1 major criterion and 1 minor criterion**; or

(2) **3 minor criteria**

Diagnosis Rejected

(1) Firm alternate diagnosis explaining evidence of infective endocarditis; or

(2) Resolution of infective endocarditis syndrome with antibiotic therapy for ≤4 days; or

(3) No pathologic evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for ≤4 days; or

(4) Does not meet criteria for possible infective endocarditis, as above

*See Table **C238C**, for definitions of major and minor criteria.

Reprinted with permission from Li JS, Sexton DJ, Mick N, et al. Proposed modification to Duke criteria of diagnosis of infective endocarditis. *Clin Infect Dis.* 2000;30(4):633-638

Item C238C. Major and Minor Criteria for the Diagnosis of Infective Endocarditis (Duke Criteria: Modifications Shown in Boldface).

Major criteria

- Blood culture positive for infective endocarditis (IE)
  - Typical microorganisms consistent with IE from 2 separate blood cultures:
    - Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*; or
    - Community-acquired enterococci, in the absence of a primary focus; or
  - Microorganisms consistent with IE from persistently positive blood culutres, defined as follows:
    - At least 2 positive cultures of blood samples drawn >12 hours apart; or
    - All of 3 or a majority of ≥4 separate cultures of blood (with first and last sample drawn at least 1 hour apart)
  - **Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer >1 : 800**
- Evidence of endocardial involvement
- Echocardiogram positive for IE **(TEE recommended in patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE [paravalvular abscess]; TTE as first test in other patients)**, defined as follows:
  - Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or
  - Abscess; or
  - New partial dehiscence of prosthetic valve
- New valvular regurgitation (worsening or changing of pre-existing murmur not sufficient)

Minor criteria

- Predisposition, predisposing heart condition or injection drug use
- Fever, temperature >38°C
- Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor
- Microbiological evidence: positive blood culture but does not meet a major criterion as noted above* or serological evidence of active infection with organism consistent with IE
- **Echocardiographic minor criteria eliminated**

TEE, transesophageal echocardiography; TTE, transthoracic echocardiography

*Excludes single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis.

Reprinted with permission from Li JS, Sexton DJ, Mick N, et al. Proposed modification to Duke criteria of diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30(4):633-638

PREP Pearls

- The indications for infective endocarditis (IE) prophylaxis have changed to include fewer diagnoses.
- Infective endocarditis can present with either acute or chronic symptoms.
- Practitioners should have a high index of suspicion for IE in at-risk patients.

ABP Content Specifications(s)

- Plan appropriate prophylaxis for infective endocarditis
- Plan an appropriate diagnostic evaluation of infective endocarditis

Suggested Readings

- Anderson A, Bijlmer H, Fournier PE, et al. Appendix B: Duke Criteria for infective endocarditis. *MMWR Morb Mortal Wkly Rep*. 2013;62(RR03):26. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6203a3.htm. Updated March 29, 2013.
- Baltimore RS, Gewitz M, Baddour LM, et al. Infective endocarditis in childhood: 2015 update a scientific statement from the American Heart Association. *Circulation*. 2015;132(15):1487-1515. doi: http://dx.doi.org/10.1161/CIR.0000000000000298.
- Li JS, Sexton DJ, Mick N, et al. Proposed modification to Duke Criteria of diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30(4):633-638. doi: http://dx.doi.org/10.1086/313753.
- Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116(15):1736-1754. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.106.183095.

Question 239

A 6-year-old girl is seen in your office in late spring for red, watery eyes for 3 days. There is crusting of the eyelids upon wakening, but no purulent drainage. The girl complains of burning but minimal itching. Other children in her class have similar symptoms. On examination, you note erythema along the inferior fornix of the eyes bilaterally. Tympanic membranes are not inflamed.

Of the following, the MOST appropriate next step in managing this child is

A. amoxicillin/clavulanate orally for 7 days
B. cool compresses and artificial tears
C. referral to ophthalmology
D. topical antibiotic eye drops
E. topical antihistamine eye drops

Correct Answer: B

The child in this vignette likely has viral conjunctivitis, which is predominantly caused by adenovirus. Symptoms can last for up to 2 weeks, typically worsening in the first 4 to 7 days. It is best treated with cool compresses and artificial tears, which helps relieve the discomfort. Antibacterial and corticosteroid eye drops are ineffective and contraindicated in viral conjunctivitis.

Viral conjunctivitis caused by adenovirus is highly contagious and may be associated with a viral prodrome and other symptoms of an upper respiratory tract infection. However, conjunctivitis can also be the only symptom. While it is contagious, symptoms are also self-limiting and exclusion from school or daycare is not indicated. Transmission of the virus can be prevented with effective handwashing.

Bacterial conjunctivitis can vary in severity depending on the etiology. Hyperacute bacterial conjunctivitis caused by *Neisseria gonorrhoeae* or *Neisseria meningitidis* is characterized by rapid onset with copious purulent drainage, eyelid edema, pseudomembrane formation, and preauricular adenopathy. It should be treated promptly with intravenous antibiotics and typically requires hospitalization and consultation with an ophthalmologist. *Staphylococcus aureus, Streptococcus pneumoniae, Moraxella catarrhalis,* and other bacteria can also cause conjunctivitis, but infections with these bacteria are often self-limited or easily treated with topical antibacterial drops. They also present with purulent drainage, but it can be minimal. Allergic conjunctivitis also takes several forms: it can be an acute reaction to an environmental allergen (eg, cat dander) or be more subtle (eg, as in seasonal allergies), depending on the trigger. Compared to viral conjunctivitis, pruritus is a more prevalent symptom in allergic conjunctivitis. Topical or systemic antihistamines are first-line therapies and are effective in reducing symptoms in most patients. Referral to an ophthalmologist may be warranted in refractory cases.

PREP Pearls

- Viral conjunctivitis is best treated with cold compresses and artificial tears; topical antibiotics are contraindicated.
- Pruritus is more prominent in allergic conjunctivitis.
- Hyperacute bacterial conjunctivitis caused by *Neisseria* warrants prompt evaluation and intravenous antibiotics; other bacterial etiologies produce less severe symptoms.

ABP Content Specifications(s)

- Differentiate the clinical findings associated with infectious conjunctivitis from those of allergic conjunctivitis
- Plan the appropriate management of conjunctivitis, including prevention of spread to others

Suggested Readings

- Castillo M, Scott NW, Mustafa MZ, Mustafa MS, Azuara-Blanco A. Topical antihistamines and mast cell stabilisers for treating seasonal and perennial allergic conjunctivitis. *Cochrane Database Syst Rev*. 2015;6:CD009566. doi: http://dx.doi.org/10.1002/14651858.CD009566.pub2.
- Richards A, Guzman-Cottrill JA. Conjunctivitis. *Pediatr Rev*. 2010;31(5):196-208. doi: http://dx.doi.org/10.1542/pir.31-5-196.

Question 240

An upset 16-year-old adolescent girl presents to your office. She reports she has been in a sexual relationship with a 17-year-old adolescent boy for a month, but after an argument last night, he informed her that he has hepatitis B. She admits they frequently had sex without condoms and smoked marijuana and tobacco often, but she denies any intravenous drug use and has never witnessed him using any intravenous drugs. She reports that during the month they were together, he appeared healthy with no obvious signs of illness. She met him at a club and does not know much more about him other than his name and phone number.
Physical examination shows a tearful adolescent girl with a temperature of 36.8°C, respiratory rate of 18 breaths/min, heart rate of 95 beats/min, and blood pressure of 130/80 mm Hg. Her sclera are clear, mucosa are moist and pink, lungs are clear to auscultation, and her abdomen is nontender with no hepatomegaly. The skin is warm, well-perfused, and without jaundice. Checking her chart, you see that she completed an appropriate primary hepatitis B vaccination series as an infant, and has no significant medical conditions or past medical history.

Of the following, the BEST recommendation for hepatitis B prophylaxis in this clinical situation is

A. give hepatitis B immune globulin
B. give hepatitis B immune globulin and start a new hepatitis B vaccination series
C. prophylaxis is not recommended
D. start a new hepatitis B vaccination series
E. start oral tenofovir 300 mg once daily

Correct Answer: C

For the adolescent girl in this vignette, no hepatitis B prophylaxis is recommended. Hepatitis B remains a major global health problem with over 2 billion people, or one-third of the world's population, infected with hepatitis B. Around 30 million new infections occur annually, and 5% to 10% of infected individuals will not develop protective antibodies and progress from acute to chronic hepatitis B. This is more common in East Asian and African countries. Ninety percent of infants infected at birth and 25% to 50% of children younger than 5 years of age when they become infected will develop chronic hepatitis B. This results in almost a quarter billion people worldwide living with chronic hepatitis B. Since universal hepatitis B vaccination began in the United States in 1991, the incidence of hepatitis B has fallen dramatically in children and young adults, and is almost 1,000 times lower now than it was in the 1980s.

In countries in Africa, Asia, the Caribbean, most of Eastern Europe, and parts of South America where hepatitis B is endemic, perinatal transmission is primarily responsible for pediatric infections. In the United States and other nonendemic countries, most pediatric cases occur in patients belonging to or exposed to high-risk groups. Item C240lists the pediatric patients who should be screened for hepatitis B because of increased exposure and risk of acquiring infection. For suspected hepatitis B infection, the patient should be screened with 3 tests: the hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs or HBsAb), and immunoglobulin M against hepatitis B core antigen (IgM anti-HBc).

Hepatitis B surface antigen indicates the presence of hepatitis B virus because surface antigens are part of the outer envelope of the virus. Anti-HBs is a specific antibody produced by the patient against the HBsAg, and means the patient is developing or has developed immunity to hepatitis B. Immunoglobulin M anti-HBc indicates active or recent (< 6 months) infection with hepatitis B. The IgM anti-HBc antibody develops against a component of the core, or nucleocapsid (the protein shell surrounding the nucleus) of the hepatitis B virus, and is one of the first antibodies to appear in hepatitis B infection; IgM anti-HBc usually disappears 6 months after initial infection. Anti-HBs can be present in hepatitis B vaccinated individuals and those with hepatitis B infection. Since the hepatitis B vaccine does not contain any core antigens, IgM Anti-HBc should not be present in a vaccinated individual.

If all 3 tests are negative, the patient does not have hepatitis B, but is also not immune and should be vaccinated with a 3-dose series, even if previously vaccinated. If the HBsAg is negative, and the anti-HBs is positive, regardless of the IgM anti-HBc result, the patient is immune to hepatitis B, either through vaccination or natural infection. The HBsAg and IgM anti-HBc are positive early in the course of acute hepatitis B infection. Anti-HBs is negative early on and becomes positive 6 months or more after the infection.

Nonimmune individuals should begin an age-appropriate hepatitis B vaccination series as soon as possible after exposure to hepatitis B. For newborns, vaccination should start within 12 hours of birth and within 24 hours of exposure for all others. In addition, hepatitis B immune globulin (HBIG), prepared from the plasma with donors with high anti-HBs levels, should be given to babies born to mothers who are HBsAg-positive, and people exposed to hepatitis B through

blood contaminated with hepatitis B (highly unlikely today) or sexual contact with an HBsAg-positive person. Newborns should receive HBIG within 12 hours of birth and no later than 1 week after birth, while other individuals with exposure should receive HBIG within 24 hours of exposure, and no later than 14 days after exposure.

If hepatitis B infection develops despite immunoprophylaxis, treatment is basically supportive. There are no data on treatment with nucleoside analogue antivirals in pediatrics, although adult trials showed no clinical benefit.

On first appearance, this 16-year-old adolescent girl fits the profile of an exposed patient in a high-risk group who should have hepatitis B screening laboratory tests and receive HBIG. However, expert guidelines also address the situation where exposure occurs in a person fully vaccinated for hepatitis B. In this case, 1 booster dose of hepatitis B vaccine is recommended for individuals exposed to a HBsAg-positive source. If the source has an unknown HBsAg status (like the adolescent's male partner in this vignette), then no postexposure prophylaxis is recommended because of the low prevalence of hepatitis B in the United States and high efficacy of the vaccine. Anti-HBs seroconversion rates after hepatitis B vaccination are greater than 95% in neonates and around 99% in children and adolescents. Those who are not fully vaccinated should simply complete their series.

PREP Pearls

- In the United States and other nonendemic countries, most pediatric hepatitis B cases occur in patients belonging to or exposed to high-risk groups.
- For suspected hepatitis B infection, the patient should be screened with the hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs or HBsAb) tests, and immunoglobulin M against hepatitis B core antigen (IgM anti-HBc).
- Nonimmune individuals should begin an age-appropriate hepatitis B vaccination series and receive hepatitis B immune globulin as soon as possible after exposure to an HBsAg positive source, while immunized individuals should receive one booster dose of hepatitis B vaccine. Nonimmune individuals should begin an age-appropriate hepatitis B vaccination series as soon as possible after exposure to a source whose HBsAg status is unknown, while immunized individuals require no further treatment.

ABP Content Specifications(s)

- Plan the diagnostic evaluation of suspected hepatitis B virus infection
- Plan the management of a neonate or older child exposed to hepatitis B

Suggested Readings

- American Academy of Pediatrics. Hepatitis B. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:400-423.
- Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the advisory committee on immunization practices (ACIP) part I: immunization of infants, children, and adolescents. *MMWR Recomm Rep.* 2005;54(RR16):1-23. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm.
- US Centers for Disease Control and Prevention. Appendix B: postexposure prophylaxis to prevent hepatitis B Infection. *MMWR Recomm Rep*. 2006,56(RR16):30-31. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a3.htm.

Question 241

A previously healthy 7-year-old boy is brought to the emergency department (ED) for evaluation. He has had diarrhea for 7 days, bloody diarrhea for the past day, and no urine output in the last 16 hours. The boy has become increasingly listless over the past several hours. Physical examination reveals an ill-appearing child with marked pallor and periorbital edema. His temperature is 38.4°C, heart rate is 120 beats/min, respiratory rate is 28 breaths/min, and blood pressure is 130/90 mm Hg. His growth parameters are normal. A complete blood cell count and comprehensive metabolic panel are obtained, with the results shown:

Laboratory Test	**Patient Result**
Sodium	130 mEq/L (130 mmol/L)
Potassium	6.0 mEq/L (6 mmol/L)
Chloride	100 mEq/L (100 mmol/L)
Blood urea nitrogen	50 mg/dL (17.8 mmol/L)
Creatinine	3.4 mg/dL (300 μmol/L)
Albumin	2.9 g/dL (29 g/L)
White blood cell count	20,000/μL (20×10^9/L)
Hemoglobin	8.9 g/dL (89 g/L)
Hematocrit	27%
Platelet count	13×10^3/μL (13×10^9/L)

Of the following, the MOST appropriate choice of intravenous fluid for this patient is

A. 5% dextrose
B. 3% normal saline
C. 0.9% normal saline
D. 0.45% normal saline
E. lactated Ringer's solution

Correct Answer: C

The most appropriate choice of intravenous (IV) fluid for the boy in the vignette would be 0.9% normal saline. The boy presents with a history of bloody diarrhea, pallor, and oliguria. Oliguria is defined as no urine output by 48 hours of age, or a urine output of less than 1 mL/kg per hour in infants or less than 0.5 mL/kg per hour in children (or < 300 mL/m^2 per day). His physical examination is significant for tachycardia, hypertension, and tachypnea, suggesting an underlying volume overload. Laboratory evaluation is consistent with acute renal failure (ARF) (elevated blood urea nitrogen and serum creatinine) dyselectrolytemias (hyponatremia, hyperkalemia, hyperphosphatemia), anemia, thrombocytopenia, and leukocytosis. This child's presentation is consistent with ARF, most likely caused by hemolytic uremic syndrome (renal failure, anemia, thrombocytopenia, and history of bloody diarrhea). His mild hyponatremia is most likely secondary to volume overload.

Management of ARF is based on (1) reversal of the underlying etiology, (2) appropriate supportive therapy, which may include dialysis, and (3) prevention of further injury. Maintenance of effective circulatory volume is one of the most important steps in treating prerenal cases and preventing further injury in intrinsic or postrenal kidney injury.

Fluid management in children with ARF is guided by the child's underlying volume status and whether the renal failure is oliguric or nonoliguric. Fluid administration is aimed at maintaining intravascular volume, preventing volume overload, and managing the associated dyselectrolytemias. Fluid resuscitation includes both bolus and maintenance IV fluids. In the presence of a history of volume loss and clinical features of hypovolemia (dry mucous membrane, tachycardia, hypotension), improvement in circulating volume is indicated. A standard IV fluid bolus for a child with normal renal function would be 0.9% normal saline at 20 mL/kg over 30 to 60minutes. A smaller fluid bolus of 5 to 10 mL/kg should be administered to patients with renal failure, followed by reassessment of clinical features. Of the various options available for maintenance resuscitation IV fluid, isotonic fluids (0.9% normal saline and lactated Ringer's solution) are preferred over hypotonic fluids (5% dextrose and 0.45 normal saline). Recent meta-analyses have shown that IV fluids with sodium concentrations similar to plasma are associated with a reduced risk of hyponatremia and subsequent morbidity and mortality. Potassium-containing fluids, such as lactated Ringer's solution, should be avoided in patients with renal failure until urine output is established. The boy in the vignette has hyperkalemia and no urine output, thus the use of potassium-containing fluid would increase his risk for life-threatening arrhythmias.

Maintenance IV fluid volumes should include insensible water loss (IWL) plus ongoing losses (urine output, gastrointestinal fluid losses, others such as chest tube drainage). In children with ARF with no to minimal urine output, the maintenance fluid volume should equal the IWL (40 mL/kg for children < 10 kg, 500 mL/m^2 for children > 10 kg). As urine output increases with improvement in renal function, the IV rate can be increased to maintain intravascular volume. Euvolemic patients with ARF with adequate urine output may receive full maintenance IV fluids, whereas volume-overloaded patients with ARF should receive a fraction of or no urine replacement.

Hypertonic 3% saline is indicated for management of hyponatremia in patients with a serum sodium concentration less than 120 mEq/L (120 mmol/L), or patients with neurologic manifestations associated with hyponatremia such as headaches, seizures, behavioral changes, obtundation, coma, and respiratory arrest.

PREP Pearls

- Maintenance of effective circulatory volume is one of the most important steps in treating acute renal failure.
- Normal saline (0.9%) is the preferred fluid for intravenous boluses and maintenance fluid in patients with acute renal failure and hyponatremia.
- Patients with acute renal failure with oliguria or decreased urine output should not receive potassium-containing intravenous fluids.

ABP Content Specifications(s)

- Plan the appropriate initial management of acute renal failure, while considering the effects of various therapies on associated physiologic abnormalities
- Plan the appropriate diagnostic evaluation of oliguria

Suggested Readings

- Friedman JN, Beck CE, DeGroot J, Geary DF, Sklansky DJ, Freedman SB. Comparison of isotonic and hypotonic intravenous maintenance fluids: a randomized clinical trial. *JAMA Pediatr*. 2015;169(5):445-451. doi: http://dx.doi.org/10.1001/jamapediatrics.2014.3809.
- Goldstein SL, Androgue HR. Acute kidney failure. In: McInerny TK, Adam HM, Campbell DE, Kamat DM, eds. *American Academy of Pediatrics Textbook of Pediatric Care*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:2895-2898.
- McNab S, Ware RS, Neville KA, et al. Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children. *Cochrane Database Syst Rev*. 2014;12:CD009457. doi: http://dx.doi.org/10.1002/14651858.CD009457.pub2.
- Reid-Adam J. Hyponatremia. *Pediatr Rev*. 2013;34(9):417-419. doi: http://dx.doi.org/10.1542/pir.34-9-417.
- Selewski DT, Symons JM. Acute kidney injury. *Pediatr Rev.* 2014;35(1):30-41. doi: http://dx.doi.org/10.1542/pir.35-1-30.
- Wang J, Xu E, Xiao Y. Isotonic versus hypotonic maintenance IV fluids in hospitalized children: a meta-analysis. *Pediatrics*. 2014;133(1):105-113. doi: http://dx.doi.org/10.1542/peds.2013-2041.

Question 242

You are discussing a possible study with pediatric residents. They have proposed examining the effects of maternal intrapartum antibiotic exposure on the development of childhood asthma. In this retrospective case control study, they will identify a cohort of 18-month-old children with confirmed asthma according to specified criteria from the general pediatric clinic. Healthy, age-matched controls without a diagnosis of asthma will also be chosen randomly from the general pediatric clinic records. They will define intrapartum antibiotic exposure as any maternal antibiotic use in the 24 hours prior to delivery. They will include only vaginal deliveries, as cesarean deliveries have been associated with increased risk of asthma. They will conduct phone interviews of mothers of these two groups of children about emergency department visits and inpatient admissions to identify early pulmonary infections that have also been associated with asthma. They will use funds set aside for research for pediatric residents. They ask for your opinion regarding potential sources of bias in their study design.

Of the following, the source of bias identified in this study design is

A. attrition bias: variable loss of subjects between groups
B. funding bias: funding source affects study design or results
C. misclassification bias: incorrect assignment of exposure to antibiotics
D. recall bias: skewed memory of past events
E. selection bias: enrollment criteria exaggerate differences between subjects and controls

Correct Answer: D

In the study design proposed in the vignette, recall bias may affect the rates of asthma detected between the 2 groups. Briefly, the goal of this study is to evaluate the effect of maternal intrapartum antibiotic exposure on the rate of childhood asthma. The exposure of interest, maternal intrapartum antibiotic exposure, will be obtained from the medical record. The rate of childhood asthma will be obtained from records in the primary care provider clinic. Since early childhood infection has been associated with asthma, the researchers will contact mothers to assess emergency department visits and hospital admissions attributed to respiratory infections. Mothers whose children have a diagnosis of asthma may be more likely to remember past respiratory infections, and therefore this is a source of recall bias between the 2 groups.
Attrition bias suggests a different rate of loss to follow-up between the 2 groups. This may happen when the outcome in question limits a patient's ability to come in for follow-up appointments. There is no evidence of attrition bias in this study design.

Funding bias is present when a group may be treated differently based on the funding sources. Since this is funded by resident research money, there is no funding bias.
Misclassification bias exists when the assignment of exposure or disease may be made incorrectly. Since the medical record will be used to determine antibiotic exposure and the diagnosis of asthma, misclassification bias is minimized in this study design.
Selection bias exists when the patient characteristics between the 2 groups differ. Selection bias can be avoided in this scenario by randomly selecting controls and assuring that the 2 groups are similar, except for the exposure of interest to the study.

If a clinical factor can cause the outcome in the 2 groups, the presumed relationship between the outcome of interest and the finding may be false, ie, there may be confounding. Confounding exists when an associated risk factor in one of the study groups is related to the outcome. Confounding can be controlled in study design or statistical analysis. To control for confounding in study design, subjects in both groups are matched for particular confounders. Another way to control for confounders is to exclude subjects with the confounding factor. In this example, neonates born by cesarean delivery were excluded in an attempt to prevent confounding. Alternatively, during statistical analysis, subjects can be stratified by the presence of confounders. Regression models can also attempt to control for confounders.

PREP Pearls

- Bias is the result of differences between the study groups due to study design and can decrease the ability to find a relationship between the exposure and the outcome of interest.
- Bias should be minimized in study design.
- Some forms of bias can attempt to be accounted for in statistical analysis.

ABP Content Specifications(s)

- Understand bias and how it might distort the estimate of the association between exposure and outcome
- Understand confounding and how to control for it in a study

Suggested Readings

- Jennings JM, Sibinga E. Research and statistics: understanding and identifying bias in research studies. *Pediatr Rev.*2010;31(4):161-162. doi: http://dx.doi.org/10.1542/pir.31-4-161.
- Murray KW, Duggan A. Understanding confounding in research. *Pediatr Rev*. 2010;31(3):124-126. doi: http://dx.doi.org/10.1542/pir.31-3-124.

Question 243

You are seeing a 16-year-old adolescent boy with obstructive sleep apnea and a history of recurrent sinusitis in your office. On physical examination, you note that he has a bifid uvula. You refer him to an otolaryngologist for adenoidectomy and counsel the parents about his risk of postoperative complications.

Of the following, based on physical examination findings, this patient postoperatively is at INCREASED risk of

A. bleeding
B. hypernasal voice
C. nasopharyngeal stenosis
D. surgical site infection
E. torticollis

Correct Answer: B

The adolescent in the vignette has a bifid uvula that is likely associated with an unrecognized submucosal cleft, increasing his risk of velopharyngeal insufficiency (VPI) after an adenoidectomy. Velopharyngeal insufficiency is defined as incomplete closure between the soft palate and the pharyngeal wall during speech, which allows air to escape through the nasal cavity. Velopharyngeal insufficiency leads to a hypernasal voice and in severe cases, nasal regurgitation of fluids. Velopharyngeal insufficiency can be caused by anatomic abnormalities such as hard or soft palate or submucosal clefts, inadequate soft palate length, or paralysis of the soft palate.

Velopharyngeal insufficiency is a known complication of adenoidectomy that occurs because removal of the adenoids increases the size of the nasopharyngeal airway. Individuals with preexisting palatal defects are at much higher risk for postadenoidectomy VPI. It is often a temporary postoperative occurrence, but if persistent, patients should be referred for evaluation by a speech pathologist. Sustained VPI after adenoidectomy is associated with chromosome 22q11 deletion (velocardiofacial) syndrome, and the clinician should strongly consider testing for this syndrome in these patients.

A bifid uvula and possible underlying submucosal cleft do not increase the risk of postoperative bleeding, nasopharyngeal stenosis, surgical site infection, or torticollis.

PREP Pearls

- Velopharyngeal insufficiency (VPI) is the incomplete closure of the soft palate and the pharyngeal wall that allows air to escape through the nasal cavity
- Velopharyngeal insufficiency can lead to a hypernasal voice.
- The risk of VPI is increased after an adenoidectomy, especially in children with preexisting palatal defects or chromosome 22q11 deletion (velocardiofacial) syndrome.

ABP Content Specifications(s)

- Understand the general concept of velopharyngeal insufficiency

Suggested Readings

- Gosain AK, Conley SF, Marks S, Larson DL. Submucous cleft palate: diagnostic methods and outcomes of surgical treatment. *Plast Reconstr Surg.* 1996;97(7):1497-1509.
- Messner AH. Adenoidectomy in children: postoperative care and complications. *UpToDate*. Available online only with subscription.
- Ruda JM, Krakovitz P, Rose AS. A review of the evaluation and management of velopharyngeal insufficiency in children. *Otolaryngol Clin North Am*. 2012;45(3):653-669. doi: http://dx.doi.org/10.1016/j.otc.2012.03.005.

Question 244

You are seeing a 10-year-old boy for a health supervision visit. The boy has a history of asthma, which his parents regard as "mild." He uses short-acting albuterol for his intermittent exacerbations, triggered exclusively by viral illness. His parent have declined controller therapy. The boy is a soccer player who functions at an elite level. He never requires albuterol before playing soccer, nor does he experience exertional dyspnea or fatigue. He has no daily or weekly cough or wheeze. Twice, he had acute dyspnea with wheezing, lost consciousness at home, and required intubation by emergency medical services. In the past year, he was hospitalized on 3 occasions. During each hospitalization, he responded well to aggressive b-agonist and systemic corticosteroid therapies. His medical history is otherwise negative. There is no history of food allergy. He has no respiratory complaints today.

On physical examination, the boy is well appearing and in no respiratory distress. His respiratory rate is 18 breaths/min and unlabored. His cardiac and abdominal examinations are normal. Auscultation of his lungs reveals mild prolongation of the expiratory phase, with a faint end-expiratory wheeze. Spirometry reveals a normal forced vital capacity (FVC), a forced expiratory volume in 1 second (FEV_1) equal to 82% of predicted, and a FEV_1/FVC ratio of 0.71.

Of the following, the MOST accurate statement about this child is that

A. he does not have asthma
B. he is at high risk for asthma-related death
C. he has asthma that can be safely controlled with as-needed use of a short-acting □-agonist
D. his risk for asthma-related death is low on the basis of his intermittent symptoms
E. his risk for asthma-related death is low on the basis of his normal forced expiratory volume in 1 second

Correct Answer: B

The boy in the vignette is at high risk for an asthma-related death. Although his symptoms are exclusively triggered by viral illness, the severity of the associated symptoms and the requirement for hospitalization and oral corticosteroid therapy on 3 occasions in the past year place him in a persistent asthma category.

The absence of chronic cough, wheezing, or exercise intolerance does not preclude an asthma diagnosis. Although there are other etiologies for airway compromise and life-threatening episodes of respiratory distress, the boy's response to short-acting b-agonist and systemic corticosteroids support a diagnosis of asthma.

Asthma severity assessments are made on the basis of both impairment and risk (Item C244). Although the boy in the vignette exhibits a low level of impairment, his risk is significant. His mildly prolonged expiratory phase and end-expiratory wheeze raise concern that he may have poor perception of his asthmatic symptoms, which may be contributing to the rapid and severe decompensation during his exacerbations.

Components of Severity		Classification of Asthma Control (5-11 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤ 2 days/week	> 2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤ 2 times/month	3-4 times/month	>1 times/week but not nightly	Often 7 times/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤ 2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC >85%	• FEV_1 = >80% predicted • FEV_1/FVC >80%	• FEV_1 = 60-80% predicted • FEV_1/FVC = 75-80%	• FEV_1 = <60% predicted • FEV_1/FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year	≥2/year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1.			

EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids

Adapted from the National Heart, Lung and Blood Institute and the National Asthma Education and Prevention Program. Expert panel report 3 (EPR-3): guidelines for diagnosis and management of asthma—summary report. Bethesda, Md: U.S. Department of Health and Human Services. 2007

ITEM C244: Classification of Asthma Severity in Children 5-11 Years of Age.

Controller therapy would be indicated for this child, who has sudden and severe asthma exacerbations. This would be an important aspect of his management, aimed at decreasing his risk for asthma-related death.

A normal forced expiratory volume in 1 second (FEV_1) would not place this boy at low risk for asthma-related death. A normal FEV_1 is common in children, even in those with moderate-to-severe persistent asthma.

Risk factors for asthma-related morbidity and mortality include a severe asthma phenotype, steroid dependence, reliance on frequent use of a short-acting b-agonist, or reliance on crisis management in the emergency department. Significant concern is raised when asthmatic patients have poor symptom perception or when asthma attacks are severe, with rapid clinical deterioration. Loss of consciousness or syncope in association with respiratory symptoms is regarded as a particularly ominous finding.

Corticosteroids are an important component of asthma care. They support bronchodilation by reducing airway hyperresponsiveness and augmenting the b-adrenergic response to short-acting b-agonists. Steroids decrease airway edema by decreasing vascular permeability and inhibiting the release of leukotriene inflammatory mediators. Corticosteroids also have a role in preventing the late-phase allergic reaction by inhibiting the inflammatory response.

Systemic corticosteroids may also have significant adverse effects. These include relatively minor effects such as: mood changes, agitation, and increased appetite. More worrisome side effects include but are not limited to: immune suppression, glucose dysregulation, cataract formation, gastritis, adrenal insufficiency syndromes, and avascular necrosis of bone. Doses of 1 to 2 mg/kg per day for treatment courses of 5 to 7 days are generally well tolerated. Longer treatment courses may necessitate a tapering dose to prevent adrenal crisis.
For persistent asthma, the treatment of choice at all severity levels is an inhaled corticosteroid. Inhaled corticosteroids control the inflammatory response locally, while preventing many of the systemic side effects encountered with oral or parenteral steroid therapy. They reduce asthmatic impairment and risk, and have been shown to achieve better long-term asthma control compared with leukotriene receptor antagonists in both children and adults.

PREP Pearls

- Severity assessments guide treatment decisions, and are based on both asthma related impairment and risk.
- Intermittent asthma symptoms may be associated with significant risk for adverse outcomes.
- Most children with moderate to severe persistent asthma will demonstrate a normal forced expiratory volume in 1 second on spirometric testing.
- The preferred therapy for all levels of persistent asthma is an inhaled corticosteroid.

ABP Content Specifications(s)

- Understand the risks and benefits of corticosteroid therapy in the treatment of a patient who has an acute exacerbation of asthma
- Recognize the signs and symptoms of poorly controlled asthma
- Recognize the characteristics of a child with asthma who is at risk of hospitalization

Suggested Readings

- National Asthma Education and Prevention Program. Expert panel report 3 (EPR-3): guidelines for diagnosis and management of asthma?summary report 2007. *J Allergy Clin Immunol.* 2007;120(5 Suppl):S94-S138. doi: http://dx.doi.org/10.1016/j.jaci.2007.09.029.
- Townley RG, Suliaman F. The mechanism of corticosteroids in treating asthma. *Ann Allergy.* 1987;58(1):1-6.

Question 245

A 10-year-old girl is brought to your office by her parents for evaluation of clumsiness. She had met all the early developmental milestones on time, but over the past year, her parents have noticed that she falls over small obstacles like steps or curbs. They have seen occasional quick jerks of her eyes, especially when she turns her head. Over the past month, she has been coughing when she drinks fluids. The mother reports that she had a cousin who died at 20 years of age of a progressive neurological disorder. Her neurological examination shows an alert girl with upper extremity dysmetria, diffuse areflexia, lower extremity weakness, and an ataxic gait. A brain magnetic resonance image is performed and is normal.

Of the following, the MOST likely test to show the correct diagnosis is

A. 15q11 methylation study (Angelman syndrome)
B. frataxin gene sequencing (Friedreich ataxia)
C. leukocyte lysosomal enzyme panel (leukodystrophy)
D. neurofibromin gene sequencing (neurofibromatosis type 1)
E. serum α-fetoprotein level (ataxia telangiectasia)

Correct Answer: B

The girl in the vignette has Friedreich ataxia. Friedreich ataxia is an autosomal recessive disorder caused by GAA repeat expansion in the frataxin gene on chromosome 9. Of the choices listed, the test most likely to make the diagnosis in this girl is frataxin gene sequencing. In Friedreich ataxia, birth and early developmental milestones are almost always normal. The first signs are gait and limb ataxia, which typically appear in childhood as in the girl in the vignette, but can be earlier or later. Other clinical findings are areflexia, lower extremity weakness, dysarthria, and dysphagia. Eye movement abnormalities such as abnormal saccades (rapid jerky movements of both eyes) may be seen by observant parents. Once the diagnosis is established by genetic testing, the girl will need monitoring for complications of Friedreich ataxia, including cardiomyopathy, diabetes mellitus, and bladder dysfunction, as well as supportive treatment for progressive ataxia, weakness, and dysphagia. Treatment trials are ongoing, but there is currently no known treatment or cure. If symptoms start at an earlier age, life expectancy is shorter.
The evaluation of ataxia should start with chronicity. Chronic, progressive ataxias are more likely to be due to genetic syndromes. In these cases, it is important to obtain a family history and include assessment of eye movements, strength, and reflexes during the neurologic examination. Evaluation typically includes brain imaging, although in genetic ataxias, this is likely to be normal. If a particular genetic syndrome is not identified based on the clinical presentation, a gene panel for hereditary ataxias can be helpful.

Acute ataxias are more likely due to an acute process such as infection, stroke, intracranial mass, or toxicity. In acute ataxias, the history should focus on infections, injuries, and exposures to toxins, and the examination should evaluate mental status and signs of increased intracranial pressure. If there is abnormal mental status or signs of increased intracranial pressure, computed tomography of the head is the quickest test to make a diagnosis. If this does not show signs of edema or mass lesion, lumbar puncture is often needed to obtain cerebral spinal fluid for studies to evaluate for viral and bacterial infection. If there is a clear history of a toxic ingestion, lumbar puncture may not be necessary.

Angelman syndrome is a genetic disorder usually caused by abnormal imprinting on chromosome 15. Symptoms start in infancy or early childhood ages and include gait ataxia, lack of expressive language, microcephaly, and seizures. When Angelman syndrome is suspected, 15q11 methylation study is the best initial test. The girl in the vignette has a later onset of ataxia, so this is not the most likely diagnosis.

Leukocyte lysosomal enzyme panels test for a variety of disorders in which there is an abnormal accumulation of a substance in the lysosomes. Examples include Tay-Sachs disease, metachromatic leukodystrophy, and mucopolysaccharidosis. The clinical presentation of these diseases varies significantly. The girl in the vignette has a very typical presentation of the most common cause of hereditary ataxia, which clinicians should recognize. In her case, the best test is for the most likely disorder, instead of testing for a panel of disorders.

Neurofibromatosis type 1 is an autosomal dominant disorder caused by mutations in the neurofibromin 1 gene on chromosome 17; about half the cases are due to de novo mutations (not

inherited). Symptoms include cutaneous neurofibromas, café-au-lait spots, axillary and inguinal freckling, Lisch nodules, optic nerve gliomas, bone dysplasia, and learning disorders. The girl in the vignette does not have these findings, so this is not the best test.

Ataxia telangiectasia is an autosomal recessive disorder due to mutations in the *ATM* gene on chromosome 11. In most cases, serum α-fetoprotein is elevated. In ataxia telangiectasia, ataxia typically presents in early childhood. Additional signs and symptoms include recurrent respiratory infections, oculomotor apraxia, choreoathetosis, dysarthria, and ocular telangiectasias. The girl in the vignette is older than the typical age at which ataxia telangiectasia presents, and although there is overlap in the signs and symptoms of these 2 disorders, her clinical presentation points more towards Friedreich ataxia than ataxia telangiectasia.

PREP Pearls

- Friedreich ataxia is the most common hereditary ataxia.
- Chronic, progressive ataxias are more likely due to genetic syndromes, whereas acute ataxias are more likely due to infection, stroke, or toxicity.

ABP Content Specifications(s)

- Plan the appropriate evaluation of ataxia

Suggested Readings

- Bidichandani S. Friedreich ataxia. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1281/.
- Kruer MC. Pediatric movement disorders. *Pediatr Rev.* 2015;36(3):104-116. doi: http://dx.doi.org/10.1542/pir.36-3-104.

Question 246

A 5-year-old boy with acute lymphoblastic leukemia receiving induction chemotherapy is in the hospital with fever and neutropenia. Blood culture has grown *Pseudomonas aeruginosa.* He is receiving cefepime. As a result of tumor lysis syndrome, he has developed renal insufficiency.

Of the following, the MOST important factor to consider in the potential adjustment of his antibiotic dosing is

A. creatinine clearance
B. fractional excretion of sodium
C. minimum inhibitory concentration of cefepime
D. serum uric acid level
E. urine output

Correct Answer: A

The child in this vignette has fever and neutropenia, and renal insufficiency from tumor lysis syndrome related to acute lymphoblastic leukemia. Empiric dosing of cefepime, which is a renally cleared antibiotic, should be adjusted based on his creatinine clearance.

Critically ill patients, especially those with acute kidney injury, can exhibit altered drug distribution (pharmacodynamics) and altered drug metabolism (pharmacokinetics). For example, the distribution of hydrophilic drugs can vary in septic patients because of endothelial damage and increased capillary permeability. The volume of distribution of these medications can be further increased by fluid resuscitation and fluid overload from decreased urine output and acute kidney injury. This can lead to subtherapeutic plasma concentration of hydrophilic medications.

Acute kidney injury leads to decreased glomerular filtration. Creatinine is a molecule generated as a byproduct of normal muscle metabolism, and is filtered at the glomerular level and not reabsorbed from or secreted into the renal tubules in large amounts. The clearance of creatinine, the volume of blood cleared of creatinine per minute, is therefore a good approximation of glomerular filtration rate. It can be calculated with data from a 24-hour urine collection and serum creatinine level with the following equation, in which C_{cr} is creatinine clearance in mL/min, V is urine flow in mL/min, U_{cr} is urine creatinine, and P_{cr} is plasma creatinine:

$$Ccr = \frac{Ucr * V}{Pcr}$$

Another commonly used estimate for creatinine clearance that does not require a 24-hour urine collection is the Cockcroft-Gault formula:

$$Ccr = \frac{(140 - Age) * weight\ (kg) * 0.85(if\ female)}{72 * Pcr}$$

Recommended dosing of β-lactam antibiotics based on creatinine clearance is readily available from sources such as the *Harriet Lane Handbook, 20th edition* and *Red Book*: *2015 Report of the Committee on Infectious Diseases, 30th edition*. It should be recognized that acute kidney injury also impairs renal tubular secretion and reabsorption of drugs. Therefore, dosing regimens that only correct for creatinine clearance may lead to increased or decreased drug exposure. Levels of renally cleared antimicrobials with renal toxicity, such as vancomycin and aminoglycosides, should be closely followed, especially in patients with renal impairment. Consideration should be given to culture results, invasiveness of infection, and minimum inhibitory concentration (MIC) of the specific bacterial species to appropriately tailor and dose antibiotics.

Fractional excretion of sodium is a useful method of characterizing the etiology of renal failure into prerenal, intrinsic renal, and postrenal, but is not helpful in determining antibiotic dosing. The MIC of cefepime is helpful in determining the susceptibility of the *Pseudomonas aeruginosa* organism and therefore antibiotic selection, but is not as important a factor on dosing as invasiveness of infection or creatinine clearance in the setting of renal failure. Serum uric acid level is a marker of tumor lysis syndrome, but not a measure of renal failure. Urine output is a useful marker of renal failure, but is not as indicative of drug metabolism as creatinine clearance.

PREP Pearls

- Creatinine clearance is a good estimate of glomerular filtration rate and the basis of dosing antibiotics in acute kidney injury.
- Volume of distribution of hydrophilic medications can be increased in critically ill patients and can lead to inadequate drug levels.

ABP Content Specifications(s)

- Understand the circumstances that require adjustment of renally excreted antibiotic doses in patients of various ages

Suggested Readings

- Eyler RF, Mueller BA. Antibiotic dosing in critically ill patients with acute kidney injury. *Nat Rev Nephrol.* 2011;7(4):226-235. doi: http://dx.doi.org/10.1038/nrneph.2011.12.
- Mix MC, Engorn B. Drugs in renal failure. In: Engorn B, Flerage J, eds. *The Harriet Lane Handbook.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:994-1017.
- Patel N, Scheetz MH, Drusano GL, Lodise TP. Determination of antibiotic dosage adjustments in patients with renal impairment: elements for success. *J Antimicrob Chermother.* 2010;65(11):2285-2290. doi: http://dx.doi.org/10.1093/jac/dkq323.

Question 247

A 5-year-old previously healthy boy is brought to your office for concerns of precocious puberty. Two months ago, during a bath, his mother first noted the presence of pubic hair and that his penis size seemed large. She feels these signs are progressing. He also has adult body odor and acne on his forehead. He takes no medication and there is no exogenous exposure to androgen. He has no headaches or visual changes and review of systems is otherwise unremarkable. His mother had menarche at 12 years of age and his father had average timing of his puberty. There is no family history of precocious puberty. On physical examination, temperature is 37°C, heart rate is 89 beats/min, blood pressure is 98/56 mm Hg, weight is 22 kg (90th percentile), and height is 117 cm (97th percentile). He appears older than his chronologic age and has well-defined muscle tone. He has moderate inflammatory acne over his forehead and comedonal acne on his nose. Examination of the genitalia reveals an adult-size phallus, pubic hair at sexual maturity rating 3, and prepubertal sized testes measuring approximately 2 mL that are palpable bilaterally in the scrotum. He has a small amount of axillary hair bilaterally. The findings on neurologic examination are unremarkable.

Of the following, the test MOST likely to lead to the diagnosis is

A. dehydroepiandrosterone sulfate (DHEA-S)
B. human chorionic gonadotropin (hCG)
C. luteinizing hormone (LH)
D. testosterone
E. thyroid-stimulating hormone (TSH)

Correct Answer: A

The boy described in the vignette has precocious puberty due to an androgen-secreting adrenal tumor. The adrenal source of his excess androgen is evidenced by prepubertal sized testes and lack of exogenous androgen exposure. The excess androgen is not coming from the testes, so it is not due to central precocious puberty. The other endogenous source of androgen is the adrenal gland. Dehydroepiandrosterone sulfate (DHEA-S) is a marker of adrenal androgen production and would be markedly elevated in this case.

Testicular size is an important discriminator between central and peripheral precocious puberty in boys. Testes are pubertal in volume (≥ 4 mL) in central precocious puberty, as they are stimulated by luteinizing hormone (LH). A pubertal LH level of 0.3 IU/L or greater is consistent with central precocious puberty. Although an adrenal tumor may produce testosterone, DHEA-S is a more specific marker of adrenal androgen production. Testosterone is primarily secreted by the testes and a pubertal testosterone level (≥ 30 ng/dL, depending on laboratory) would most likely indicate central precocious puberty. Human chorionic gonadotropin (hCG)-secreting tumors can also cause precocious puberty in males by stimulating the LH receptor on the testis. However, the testes would be pubertal in size. Severe, long-standing hypothyroidism can cause precocious puberty due to structural similarity of thyroid-stimulating hormone (TSH) with LH and follicle-stimulating hormone (FSH). In such a case, other clinical features of hypothyroidism would be present.

The traditional definition of precocious puberty is signs of puberty before age 8 years in girls and age 9 years in boys. Newer evidence suggests that the lower age limit for onset of normal puberty may be 7 years for white girls and 6 years for black girls. When evaluating precocious puberty, it is important to distinguish central from peripheral etiology. Central precocious puberty results from activation of the hypothalamic-pituitary-gonadal axis and can be determined by an increase in size of the testes (measured on physical examination) or ovaries (by ultrasonography) to pubertal volumes. Biochemically, central precocious puberty can be detected by a pubertal LH level, basal or stimulated. In contrast to girls, where central precocious puberty is most often idiopathic, in boys, it is more often due to underlying central nervous system pathology. A diagnosis of central precocious puberty should prompt magnetic resonance imaging of the brain. Peripheral precocious puberty may originate from the adrenal gland, gonad, an hCG-secreting tumor (in males), exogenous hormone exposure, or severe hypothyroidism. The differential diagnosis of precocious puberty is shown in Item C247 . Important historical information in the evaluation of precocious puberty includes onset and progression of pubertal signs, potential exposure to exogenous sex steroids, family history, and neurologic review of systems. In addition to pubertal signs and staging on examination, a neurologic, abdominal (for palpable tumor), and skin examination is also important. Café-au-lait spots may be suggestive of McCune-Albright syndrome or neurofibromatosis type 1, both of which can be associated with precocious puberty.

Item C247. Differential Diagnosis of Precocious Puberty.

Central precocious puberty
• Central nervous system (CNS) neoplasm (hypothalamic hamartoma, optic glioma, others) • CNS irradiation • CNS anatomic abnormality • CNS infection • CNS trauma • Familial (*MKRN3* mutation) • After treatment for congenital adrenal hyperplasia or other sex steroid exposure (secondary to maturation of the hypothalamic-pituitary-gonadal axis) • Idiopathic
Peripheral precocious puberty
• Congenital adrenal hyperplasia (virilizing) • Adrenal tumors (most commonly androgen-producing, less commonly estrogen producing) • Gonadal tumors • McCune-Albright syndrome (precocious puberty more commonly associated in girls than boys) • Hypothyroidism (severe, long-standing) • Exogenous hormone exposure
Boys only
• Familial male-limited precocious puberty (activating mutation of the LH receptor) • hCG-secreting tumor (liver, gonad, mediastinum, retroperitoneum, pineal gland)

Courtesy of K. Vogt

An initial evaluation includes measurement of LH, FSH, TSH, estradiol in girls, and testosterone in boys, and a bone age radiograph. Stimulation of LH with gonadotropin-releasing hormone agonist may be necessary to detect central precocious puberty. In boys, a quantitative hCG level is indicated. Pelvic ultrasonography in girls is helpful in determining ovarian volume and if there is concern for an ovarian tumor. In girls with signs of excess androgen exposure and in boys with prepubertal sized testes, measurement of 17-hydroxyprogesterone (for congenital adrenal hyperplasia due to 21-hydroxylase deficiency), DHEA-S (marker of adrenal androgen production), and testosterone (in girls) is indicated. Testicular ultrasonography is indicated if a testicular tumor is suspected. In cases of central precocious puberty, brain magnetic resonance imaging should be performed.

PREP Pearls

- In boys with precocious puberty, size of the testes is an important discriminator between central and peripheral precocious puberty.
- Biochemically, a pubertal luteinizing hormone level of 0.3 IU/L or greater is consistent with central precocious puberty.
- Central nervous system pathology is much more common in boys with central precocious puberty than in girls.

ABP Content Specifications(s)

- Formulate a differential diagnosis for precocious puberty
- Plan an appropriate diagnostic evaluation to differentiate the various causes of precocious puberty, including that associated with an adrenal etiology

Suggested Readings

- Fuqua JS. Treatment and outcomes of precocious puberty: an update. *J Clin Endocrinol Metab.* 2013;98(6):2198-2207. doi: http://dx.doi.org/10.1210/jc.2013-1024.
- Kaplowitz PB. Precocious puberty. *Medscape*. http://emedicine.medscape.com/article/924002-overview. Updated September 4, 2015.
- Kaplowitz PB. Precocious puberty. *Medscape*. http://emedicine.medscape.com/article/924002-overview. Updated September 4, 2015.
- Long D. Precocious Puberty. *Pediatr Rev.* 2015;36(7):319-321. doi: http://dx.doi.org/10.1542/pir.36-7-319.
- Sinha S. Precocious pseudopuberty. *Medscape*. http://emedicine.medscape.com/article/923876-overview. Updated October 30, 2015.

Question 248

A 6-year-old girl is brought to your office for evaluation of "swollen glands." For the past 2 days, she has had a low-grade fever, cough, and sore throat, and her activity level and appetite have decreased. The mother reports that, with several illnesses this year, the girl has had noticeable swelling of the glands in her neck. She was tested for strep throat several times, but the result was always negative. Each time, the swelling improved as the acute illness resolved. Her mother has a history of Hodgkin lymphoma, so she is worried that these recurring infections with lymphadenopathy may indicate something more serious.
On physical examination, her vital signs are normal for age and her temperature is 37.5°C. Her tonsils are erythematous without exudate. Her bilateral jugulodigastric nodes are slightly tender to palpation and measure 1 cm in diameter. They are discrete and mobile, with no overlying erythema or warmth. The remainder of her examination is unremarkable, with no other significant lymphadenopathy or hepatosplenomegaly. You inform the mother that the girl's pattern of lymphadenopathy is not concerning and that lymphadenopathy in specific other locations would merit concern for malignancy.

Of the following, the lymphadenopathy location you would find MOST concerning is

A. posterior cervical
B. preauricular
C. submandibular
D. submental
E. supraclavicular

Correct Answer: E

Lymphadenopathy, defined as an abnormality in size and consistency of lymph nodes, is common in childhood. Recurrent and transient lymphadenopathy that is related to intermittent viral illnesses, as seen in the girl in the vignette, is almost always benign. The presence of supraclavicular lymphadenopathy on physical examination should always raise concern for malignancy.

It is understandable that parents may be alarmed by the presence of enlarged lymph nodes in their child, especially when there is a family history of malignancy or immunodeficiency. It is important for pediatric healthcare providers to be aware of the broad range of disease processes, both infectious and noninfectious, that may be associated with lymphadenopathy. A thorough history and physical examination is the first step in determining a differential diagnosis of lymphadenopathy and plan for evaluation and treatment.

When evaluating lymphadenopathy, the history and physical examination should include:

- age and general health of the patient, including immunization status
- location, number, and distribution of enlarged lymph nodes
- characteristics of the lymph nodes: size, consistency, tenderness, mobility, matting
- onset of lymphadenopathy
- associated constitutional signs and symptoms: presence of conjunctivitis, arthritis, bone pain, rash, pallor, petechiae, fevers, night sweats, weight loss, generalized lymphadenopathy, or hepatosplenomegaly
- progression and duration of illness: rapid progression or duration of more than 4 weeks (defined as chronic) deserves further investigation
- exposures: contact with ill individuals, pets/animals/insects, travel, medications
- close inspection for localized lesions that would drain directly to the involved nodes

Infection is the most likely cause for lymphadenopathy in young children, with the likelihood of malignancy increasing in adolescents. The location of enlarged lymph nodes is an important factor in determining the cause. It is helpful to consider the lymphatic drainage pattern when conducting the physical examination and considering potential causes. Cervical lymphadenopathy is commonly associated with upper respiratory infections. The jugulodigastric nodes are often enlarged and tender in reaction to acute pharyngitis. Supraclavicular lymphadenopathy should always be considered abnormal and may be enlarged in cases of mycobacterial infection or sarcoidosis, as well as malignancy. Lymphadenopathy in the preauricular, submandibular or submental areas is frequently associated with infectious or inflammatory processes and do not in themselves indicate a higher likelihood of malignancy.

Characteristics that suggest benign reactive lymphadenopathy include nodes that are localized, discrete, mobile, not matted, less than 2 cm in diameter, and with no overlying erythema or warmth. Associated constitutional signs and symptoms such as bone pain, pallor, petechiae, recurrent fevers, weight loss, hepatosplenomegaly, or generalized lymphadenopathy raise the suspicion for a malignant cause.

PREP Pearls

- Lymphadenopathy in the supraclavicular region should always raise concern for malignancy.
- Transient recurring lymphadenopathy that is temporally related to intermittent viral illnesses is almost always benign in young children.
- A thorough history and physical examination is the first step in determining the cause of lymphadenopathy.
- Lymphadenopathy with rapid progression in size or duration of more than 4 weeks merits further investigation.

ABP Content Specifications(s)

- Plan the appropriate clinical evaluation of acute cervical lymphadenopathy

Suggested Readings

- Chesney PJ. Cervical adenopathy. *Pediatr Rev*. 1994;15(7):276-284. doi: http://dx.doi.org/10.1542/pir.15-7-276.
- Peters TR, Edwards KM. Cervical lymphadenopathy and adenitis. *Pediatr Rev*. 2000;21(12):399-405. doi: http://dx.doi.org/10.1542/pir.21-12-399.
- Putnam TC. Lumps and bumps in children. *Pediatr Rev.* 1992;13(10):371-378. doi: http://dx.doi.org/10.1542/pir.13-10-371.
- Sahai S. Lymphadenopathy. *Pediatr Rev*. 2013;34(5):216-227. doi: http://dx.doi.org/10.1542/pir.34-5-216.

Question 249

You are seeing a 5-day-old newborn in your office for an initial health supervision visit. The mother reports an unremarkable pregnancy and delivery, with a brief period of hypoglycemia after delivery that resolved quickly with the first feeding. The newborn has been feeding well without signs of lethargy since that time. His physical examination is unremarkable. The mother is anxious, having had an infant 10 years ago who died of sudden infant death syndrome after a 2-day respiratory illness while the family was living abroad. You received notification today that this newborn's screening test was flagged for elevations of C6, C8, and C10 acylcarnitines, with the C8 level most significantly elevated. As prescribed in the ACT algorithm published by the American College of Medical Genetics, you order a blood glucose and electrolyte levels, blood gas, liver function tests, urine organic acids, urine acylglycines, and a plasma acylcarnitine profile.

The laboratory results reveal:

- Plasma acylcarnitine profile: elevated C8
- Urine organic acids: slightly elevated dicarboxylic acids
- Urine acylglycines: elevated hexanoylglycine

Blood glucose, liver function tests, blood gas, and electrolyte levels were all normal.

Of the following, this newborn's MOST likely diagnosis is

A. carnitine-palmitoyltransferase-2 deficiency
B. maple syrup urine disease
C. medium-chain acyl-coenzyme A dehydrogenase deficiency
D. phenylketonuria
E. propionic aciduria

Correct Answer: C

The laboratory abnormalities for the newborn in the vignette are consistent with medium-chain-acyl-coenzyme A dehydrogenase (MCAD) deficiency, an autosomal recessive fatty acid oxidation disorder. Elevations in C6, C8, and C10 acylcarnitines are the diagnostic laboratory findings. Medium-chain-acyl-coenzyme A dehydrogenase is the most common fatty acid oxidation disorder. Children with this disorder are normal at birth and typically present between 3 and 24 months of age, with an episode of hypoketotic hypoglycemia, vomiting, and lethargy triggered by a minor illness. Seizures, hepatomegaly, and liver dysfunction are common and, if not treated appropriately, can lead to coma and death. Prognosis can be excellent if appropriate management is implemented. Management involves the prevention of hypoketotic hypoglycemia events. Children are provided with frequent feedings to avoid any prolonged period of fasting, especially with intercurrent illness. Young children are placed on a low-fat diet (< 30% fat) and should ingest 2 g/kg of uncooked cornstarch at bedtime to ensure adequate glucose during the overnight period. During periods of illness, affected children should be treated with simple carbohydrates by mouth or intravenously, if necessary, to maintain an anabolic state.

A family history of sudden death in childhood, especially in the first 2 years of life, or Reye syndrome in siblings is a clue suggesting MCAD. The inclusion of MCAD on newborn screening is critical in preventing morbidity and mortality in affected children, allowing the implementation of recommended management guidelines as early as the newborn period, thereby increasing the likelihood of a normal lifespan and outcome.

In the 1960s, Dr. Robert Guthrie developed newborn screening to identify newborns with phenylketonuria (PKU). Phenylketonuria is an inherited metabolic disorder that can result in severe intellectual disability, unless appropriate dietary interventions are initiated in early infancy. A primary goal of newborn screening is to detect newborns with serious but treatable disorders. Early identification allows timely implementation of interventions necessary to prevent or ameliorate negative consequences of these disorders, leading to significant reductions in death and disease-associated disabilities. The specific disorders tested on newborn screening varies by state, but all states have expanded the number of diseases included, and now routinely test for 30 or more metabolic, endocrine, and genetic disorders, including PKU, galactosemia, organic acidemias, fatty acid oxidation disorders, congenital adrenal hyperplasia, congenital hypothyroidism, and sickle cell disease.

The American College of Medical Genetics has developed Newborn Screening ACT (ACTion) sheets for many genetic and metabolic disorders identified on newborn screening. These sheets guide physicians on how to communicate with the family and determine the appropriate referrals and laboratory testing needed when an infant screens positive for a disorder. This allows healthcare personnel to act in a timely manner to confirm a suspected diagnosis and initiate treatment as soon as possible, improving outcomes. Most primary care physicians will work in collaboration with their state newborn screening program. The state program will manage all cases of newborns with abnormal screening by contacting their families and physicians and coordinating management in an expedient manner. If an inherited disorder is identified, the family may be referred for genetic counseling about recurrence risk.

Newborn screening programs also screen for the other response choices listed. The laboratory abnormalities and clinical presentations associated with those disorders are noted in Item C249 .

Item C249. Laboratory Abnormalities and Clinical Presentations Associated With Metabolic Disorders.

Metabolic Disorder	Laboratory Abnormalities	Clinical Presentation
Carnitine palmitoyltransferase-2 deficiency	Elevated C16 and/or C18:1 acylcarnitine	• Liver failure, hypoketotic hypoglycemia, cardiomyopathy, seizures, muscle pain and weakness, myoglobinuria • Adult and infantile forms dependent on level of enzymatic function
Medium-chain acyl-CoenzymeA dehydrogenase deficiency	Elevated C8 with lesser elevations of C6 and C10 acylcarnitine	• Normal infancy/childhood with exacerbations of hypoketotic hypoglycemia, vomiting, and lethargy during periods of intercurrent illness • Increased risk of seizures, liver dysfunction, and sudden death
Maple syrup urine disease	Elevated leucine, isoleucine, alloleucine, and valine	• Poor feeding, lethargy, tachypnea, seizures, ketonuria, lethargy, opisthotonus, coma, and central respiratory failure during the neonatal period • Brief asymptomatic period in the first 2 to 3 days after birth, with rapid decompensation thereafter
Phenylketonuria	Elevated phenylalanine without increased tyrosine	• Untreated PKU leads to a progressive irreversible intellectual disability, mousy odor, fair skin and hair, hyperactivity, autism, and seizures • Treated PKU leads to a relatively normal cognitive outcome and lifespan
Propionic acidemia	Elevated C3 acylcarnitine	• Metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, hepatomegaly, and failure to thrive in the neonatal period

PKU = phenylketonuria

Courtesy of L. Parsley

PREP Pearls

- Medium-chain acyl coenzyme A dehydrogenase (MCAD) deficiency is an autosomal recessive fatty acid oxidation disorder that presents with elevations in C6, C8, and C10 acylcarnitines on newborn screening tests.
- Children with MCAD are normal at birth, typically presenting between 3 and 24 months of age with an episode of hypoketotic hypoglycemia, vomiting, and lethargy triggered by a minor illness.
- Children with MCAD are at increased risk for liver dysfunction, seizures, coma, and sudden death.
- A primary goal of newborn screening is to detect infants with serious but treatable disorders and implement interventions to prevent or ameliorate negative consequences.
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ABP Content Specifications(s)

- Recognize when genetic counseling is appropriate for the family of a child who has a metabolic disease
- Plan the appropriate initial response to a positive neonatal screening test for metabolic diseases

Suggested Readings

- American College of Medical Genetics and Genomics. Newborn screening ACT sheets and confirmatory algorithms. American College of Medical Genetics and Genomics website. https://www.acmg.net/ACMG/Publications/ACT_Sheets_and_Confirmatory_Algorithms/NBS_ACT_Sheets_and_Algorithm_Table/ACMG/Publications/ACT_Sheets_and_Confirmatory_Algorithms/NBS_ACT_Sheets_and_Algorithms_Table.aspx?hkey=e2c16055-8cdc-4b22-a53b-b863622007c0.
- American College of Medical Genetics and Genomics. Tandem mass spectrometry in newborn screening. *Genet Med*. 2000;2(4):267-269. doi: http://dx.doi.org/10.1097/00125817-200007000-00011.
- Levy PA. An overview of newborn screening. *J Dev Behav Pediatr*. 2010;31(7):622-631. doi: http://dx.doi.org/10.1097/DBP.0b013e3181eedf01.
- Matern D, Rinaldo P. Medium-chain acyl-coenzyme a dehydrogenase deficiency. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1424/. Updated March 5, 2015.
- Newborn Screening Authoring Committee. Newborn screening expands: recommendations for pediatricians and medical homes-implications for the system. *Pediatrics*. 2008;121(1):192-217. doi: http://dx.doi.org/10.1542/peds.2007-3021.

Question 250

While working in the emergency department (ED), you are supervising the resident caring for an 18-year-old young woman who was sexually assaulted 6 hours earlier. She gives consent for appropriate medical and forensic examinations. You ask the ED staff to contact social services to assist with notification of legal authorities and then review the management of victims of sexual assault with the resident.

Of the following, an essential component of the evaluation and management of this case is

A. human immunodeficiency virus postexposure prophylaxis
B. postexposure hepatitis B vaccination virus postexposure prophylaxis
C. prophylactic treatment for gonorrhea, chlamydia, and Trichomonas
D. screening for drugs of abuse
E. testing for gonorrhea and chlamydia

Correct Answer: C

An essential component of the evaluation and management of the girl in this vignette would be prophylactic treatment for gonorrhea, chlamydia, and *Trichomonas*.

A sexual assault victim should be examined by a clinician with sexual assault care training to ensure proper evidence collection and documentation of findings. After an acute assault, decisions regarding testing for sexually transmitted diseases should be made on an individual basis. Initial evaluation may include tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* at the sites of penetration, tests of vaginal specimens for *Trichomonas vaginalis*, as well as serum samples for evaluation of HIV, hepatitis B, and syphilis infections. Adherence with follow-up visits is generally poor among sexual assault survivors. Therefore, empiric treatment for chlamydia, gonorrhea, and *Trichomonas* is recommended at the time of initial evaluation.

Postexposure HIV prophylaxis should be individualized according to risk. Postexposure hepatitis B vaccination is recommended if the hepatitis status of the assailant is unknown and the survivor has not been previously vaccinated. Screening for drugs of abuse is not recommended as part of the evaluation of a victim of sexual assault. Emergency contraception should be considered when the assault could result in pregnancy.

According to national data, adolescents and young adults have the highest rates of sexual assault. On the 2013 National Youth Risk Behavior Survey, 7.3% of high school students reported that they had been physically forced to have sexual intercourse. The prevalence was 10.5% among girls and 4.2% among boys. Up to 75% of adolescent sexual assaults are perpetrated by an acquaintance or relative. According to Kaufman M, adolescent female victims are more likely to delay seeking medical care and are less likely to press charges than are adult women. Male victims are less likely to report sexual assault than female victims.

PREP Pearls

- Empiric treatment for chlamydia, gonorrhea, and *Trichomonas* is recommended at the time of initial sexual assault evaluation.
- In cases of sexual assault, postexposure human immunodeficiency virus prophylaxis should be individualized according to risk.
- The examination of a sexual assault victim should be performed by a clinician with sexual assault care training to ensure proper evidence collection and documentation of findings.
- Adolescents and young adults have the highest rates of sexual assault.

ABP Content Specifications(s)

- Recognize the medical and emotional needs of an adolescent victim of sexual assault, and manage appropriately

Suggested Readings

- Kann L, Kinchen S, Shanklin SL, et al. Youth risk behavior surveillance — United States, 2013. *MMWR Morbid Mortal Wkly Rep*. 2014;63(SS04):1-168. http://www.cdc.gov/mmwr/pdf/ss/ss6304.pdf.
- Kaufman M. Care of the adolescent sexual assault victim. *Pediatrics*. 2008;122(2):462-470. doi: http://dx.doi.org/10.1542/peds.2008-1581.
- Rickert VI, Etter DJ, Chacko MR. Sexual assault and victimization. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. *Neinstein's Adolescent and Young Adult Health Care: A Practical Guide*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:610-619.
- Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64(RR03):1-137. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6403a1.htm.

Question 251

A 4-year-old boy is brought to your office for concerns about his behavior. He gets into trouble for fighting with his younger siblings and for refusing to follow directions. He gets frustrated easily and will throw things when upset. When you greet the boy, he makes good eye contact and smiles. He speaks in 2-word phrases and can follow a single step direction if given with gesture. He enjoys playing with the puzzles and cars in your office, but shows no interest in looking at books. When you praise him for solving a puzzle, he smiles and looks to his mother. His physical examination is within normal limits.

Of the following, the MOST appropriate next step in management is to

A. engage the child in play therapy
B. enroll the child in a preschool program
C. order an electroencephalogram
D. refer the child to early intervention services
E. request an evaluation through his school district

Correct Answer: E

The boy in this vignette has delayed language development. Since a typical 4-year-old child can speak in sentences and follow multistep commands, this child's expressive and receptive language are less than expected for his age. On the other hand, this child's social skills and play appear appropriate and his challenging behaviors may be secondary to frustration from difficulty communicating. Of the choices provided, the most appropriate next step is to request an evaluation through the child's school district to evaluate his development and learning so that appropriate educational services can be initiated. The boy in this vignette would qualify for speech and language therapy and may also qualify for specialized academic instruction (eg, placement in a special education preschool program) if cognitive or other learning concerns are identified.

The Individuals with Disabilities Education Act (IDEA) is an important federal law, which provides for early intervention (EI) and special education services for children with learning or physical disabilities. The IDEA was enacted in 1975 and most recently reauthorized in 2004. Individuals aged 3 to 21 years may qualify for special education services through part B of IDEA. An evaluation is first conducted to determine if the child meets eligibility criteria under one of the special education disability categories (eg, specific learning disability, speech or language impairment, other health impaired, emotional disturbance, intellectual disability, autistic-like behaviors, hearing impairment, visual impairment, traumatic brain injury). If the child qualifies for special education services, an Individualized Education Program (IEP) is developed, outlining the services and accommodations that will be provided to the child to meet his educational needs. About 13% of children in the United States receive special education services.

Early intervention programs are federally funded under Part C of IDEA. They provide services to children from birth to 3 years of age with delays in development (physical, cognitive, communication, social/emotional, adaptive development) or a condition that results in high probability of developmental delay. Some states also provide services to children who are at high risk for developmental delays. The EI programs are multidisciplinary, community-based, and family-centered. Early intervention starts with identification, screening, and assessment to determine eligibility and needs. Services such as special instruction, speech therapy, occupational therapy, physical therapy, family training, and counseling are offered, based on the needs identified through the assessment process. Additional services include home visits and assistance with transitioning to community or special education services as appropriate. A service coordinator assists the family with setting up the services and connecting with resources. Specific services and goals are outlined in the Individualized Family Service Plan. Early intervention serves about 2% of infants and young children.

Children younger than 3 years of age with developmental or learning concerns should be referred to their state's EI program or to their local school district if older than 3 years of age. The 4-year-old child in this vignette would benefit from an evaluation through his school district. While enrollment in a preschool program would be helpful, an evaluation of this child through his school district will help determine if his needs can be met in a typical preschool program or if a

special education preschool is a better fit. The evaluation would also determine if additional therapies (eg, speech therapy) are necessary and if the child qualifies for an IEP. Play therapy, a form of psychotherapy used to allow children to express their feelings and experiences through play, would not address this child's developmental or educational needs. Landau-Kleffner syndrome, or acquired epileptic aphasia, is a neurological disorder where children develop normally and then lose language skills. An electroencephalogram is not indicated in this child who does not have a history of language regression. However, this child should be referred for audiology, speech/language, and developmental/psychological evaluations (through school, insurance, or private pay).

Pediatricians can be instrumental in guiding families to appropriate community services for their children with learning and behavioral problems. Children younger than 3 years of age with confirmed or suspected developmental delay should be referred to their community's EI program, and if older than 3 years of age, to their local school district for needed special education services. The pediatrician can advocate for assessment and access to appropriate instruction and services. Prompt treatment improves the outcomes of these children.

PREP Pearls

- The Individuals with Disabilities Education Act (IDEA) is an important federal law, which provides for early intervention and special education services for children with learning or physical disabilities.
- Individuals aged 3 to 21 years may qualify for special education services through part B of IDEA.
- Children younger than 3 years of age for whom there are developmental or learning concerns should be referred to their state's early intervention program or, if older than 3 years of age, to their local school district.

ABP Content Specifications(s)

- Identify the types of community services available to families of children who have learning and behavioral problems

Suggested Readings

- Lipkin PH, Okamoto J, Council on Children with Disabilities and Council on School Health. The Individuals with Disabilities Education Act (IDEA) for children with special educational needs. *Pediatrics*. 2015;136(6):e1650-e1662. doi: http://dx.doi.org/10.1542/peds.2015-3409.
- Rose L, Herzig LD, Hussey-Gardner B. Early intervention and the role of pediatricians. *Pediatr Rev*. 2014;35(1):e1-e10. doi: http://dx.doi.org/10.1542/pir.35-1-e1.

Question 252

The mother of a 17-year-old previously healthy adolescent girl calls your office. Two nights ago, the adolescent came home very late from a party. She seemed extremely anxious and emotionally labile. Yesterday, she admitted to her mother that she had tried lysergic acid diethylamide (LSD) at the party and that it had made her feel "really strange." Although she is now asymptomatic, the mother is concerned about the potential for her daughter experiencing delayed health consequences after using LSD. She asks you about possible delayed adverse effects.

Of the following, this adolescent is MOST at risk for

A. cardiac conduction abnormalities
B. development of renal insufficiency
C. persistent hypertension
D. persistent perceptual disturbances
E. seizure activity due to hallucinogen withdrawal

Correct Answer: D

The 17-year-old adolescent girl in the vignette recently used lysergic acid diethylamide (LSD). Of the possible delayed adverse effects listed, she is most at risk for persistent perceptual disturbances.

All providers of pediatric care should understand the major physiologic and behavioral consequences associated with hallucinogen abuse. According to the 2013 National Survey on Drug Use and Health, 229,000 individuals aged 12 years and older reported use of LSD within the month prior to the survey. Hallucinogens are a class of drugs that alter perception, cognition, and mood. These substances act primarily by activating serotonin receptors in the central nervous system. The most widely-recognized hallucinogen is LSD. Naturally occurring hallucinogens include psilocybin, mescaline (derived from peyote), N,N-dimethyltryptamine (DMT), and lysergic acid amide (LSA) (derived from morning glory seeds).

Acute physiologic effects of hallucinogen use include paresthesias, dizziness, weakness, drowsiness, nausea, and blurred vision. Individuals typically experience alteration in perception, distortion of shapes and colors, visual hallucinations, distorted cognition and time sense, and alterations in mood (ranging from euphoria to extreme anxiety or fear). Direct end-organ damage has not been found to result from hallucinogens. Users are at increased risk for traumatic injuries occurring due to impaired judgment while they are under the influence of these substances.
A potential long-term consequence of hallucinogen use is hallucinogen persisting perception disorder, which involves recurrence of perceptual distortions that were previously experienced when the individual was under the effects of the hallucinogenic substance ("flashbacks") in the absence of another disorder, such as schizophrenia. Hallucinogen persisting perception disorder is fortunately relatively rare, and does not affect every individual after hallucinogen use. Hallucinogen use has not been associated with the subsequent development of cardiac conduction abnormalities, renal insufficiency, or persistent hypertension.

There is no evidence that hallucinogens are physiologically addictive or produce a withdrawal syndrome. Therefore, seizure activity due to withdrawal would not be an expected long-term effect of LSD use in this patient.

PREP Pearls

- Acute physiologic effects of hallucinogen use include paresthesias, dizziness, weakness, drowsiness, nausea, and blurred vision. Users typically experience alteration in perception, distortion of shapes and colors, visual hallucinations, distorted cognition and time sense, and alterations in mood (ranging from euphoria to extreme anxiety or fear).
- Direct end-organ damage has not been found to result from hallucinogens.
- Hallucinogen persisting perception disorder is a potential long-term consequence of hallucinogen use. It involves recurrence of perceptual distortions that were previously experienced when the individual was acutely under the effects of the hallucinogenic substance ("flashbacks") in the absence of another disorder (such as schizophrenia) that would explain these symptoms.

ABP Content Specifications(s)

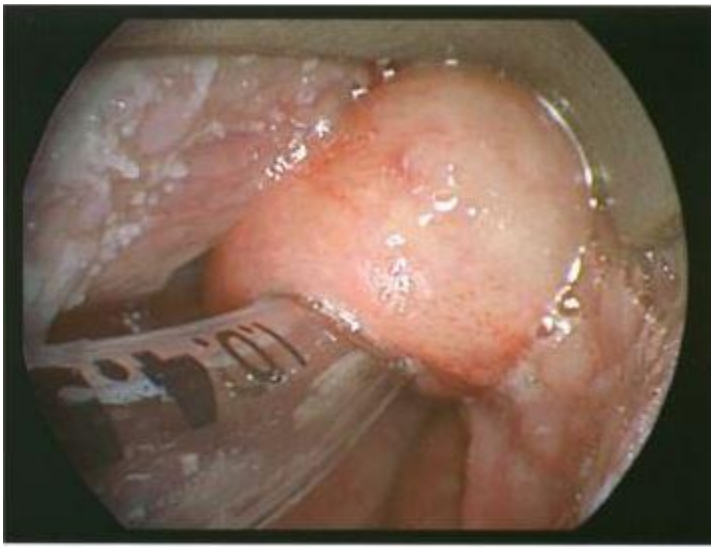
- Recognize the major behavioral consequences of hallucinogen use/abuse
- Recognize the clinical findings associated with an acute hallucinogen intoxication, and manage appropriately
- Identify the major physiologic consequences associated with hallucinogen use/abuse, including those associated with the various means of administration

Suggested Readings

- Eldridge DL, Hillenbrand K. Hallucinogens. *Pediatr Rev*. 2006;27(8):314-315. doi: http://dx.doi.org/10.1542/pir.27-8-314.
- Gussow L. LSD and other hallucinogens. In: Erickson TB, Ahrens WR, Aks SE, Baum CR, Ling LJ, eds. *Pediatric Toxicology: Diagnosis and Management of the Poisoning Child*. New York, NY: McGraw-Hill; 2005:398-402.
- National Institute on Drug Abuse, National Institutes of Health. Hallucinogens and dissociative drugs. National Institute on Drug Abuse website. https://www.drugabuse.gov/publications/research-reports/hallucinogens-dissociative-drugs/director. Updated February 1, 2015.

Question 253

A 4-year-old fully vaccinated boy presents to the pediatric emergency department with fever and respiratory distress. His past medical history includes recurrent otitis media and 2 hospitalizations for pneumonia. Vital signs show a temperature of 39.4°C, respiratory rate of 40 breaths/min, heart rate of 150 beats/min, and blood pressure of 95/65 mm Hg. On physical examination, he has marked stridor and is drooling. Anesthesia is called for airway management and, on intubation, they observe the image shown in Item Q253 . A blood culture is positive for *Haemophilus influenzae* type b.



Item Q253: Findings for the boy described in the vignette. Courtesy of L Marquez

Of the following, the study that would BEST assess vaccine response in this patient is

A. delayed cutaneous hypersensitivity
B. humoral immune panel
C. lymphocyte proliferation assay
D. phagocytic oxidative response
E. total hemolytic complement

Correct Answer: B

The best study to assess vaccine response is a humoral immune panel. The child in the vignette is fully immunized, but has an invasive infection, epiglottitis, and bacteremia due to *Haemophilus influenzae* type b. This raises concern for an inadequate vaccine response. The humoral immune panel would allow one to measure antibody titers to several vaccine antigens, allowing for an assessment of vaccine response.

Generally, immunity is divided into 2 components, the innate and adaptive immune system. The adaptive immune system is further divided into the cellular and humoral immune systems. The complement system functions in both innate and adaptive immunity. The innate immune system is comprised of proteins and cells, including monocytes, neutrophils, macrophages, and natural killer cells. The cellular and humoral immune systems is composed of T- and B-lymphocytes, respectively. However, this is a simplistic approach to the immune system because there is cross-talk between components of the various systems and defects can occur that affect several aspects of immunity simultaneously.

Defects of the cellular immune system or T-lymphocyte function tend to present with failure-to-thrive, chronic diarrhea, and recurrent opportunistic infections, including cytomegalovirus, *Candida*, and *Pneumocystis jirovicii*. Disorders of T-lymphocyte function include severe combined immunodeficiency, DiGeorge syndrome, and X-linked hyperimmunoglobulin M. A complete blood cell count is the first test for assessing a defect of the cellular immune system, as some disorders are characterized by lymphopenia. If there is concern for an acquired defect of the cellular immune system, HIV testing should also be pursued. Absence of lymphopenia does not rule out a cellular defect, as qualitative or functional defects can be present. Delayed cutaneous hypersensitivity and the lymphocyte proliferation assay are 2 means of assessing T-lymphocyte function.

Defects of the humoral immune system present as recurrent sinopulmonary infections with encapsulated bacteria. Disorders of the humoral immune system include X-linked aggamaglobulinemia and common variable immunodeficiency. Defects in humoral immunity can be detected by measuring serum immunoglobulins. Additionally, some disorders are characterized by low to absent B cells, detectable by flow cytometry.

Defects of the innate immune system have varied presentations and include disorders such as chronic granulomatous disease (CGD), leukocyte adhesion defects, and complement deficiencies. Phagocyte oxidative response evaluates the neutrophil defect of CGD and total hemolytic complement (CH50) determines complement activity.

PREP Pearls

- The humoral immune panel assesses vaccine response by measuring antibody titers to several vaccine antigens.
- A complete blood cell count is the first test for assessing a defect of the cellular immune system, as some disorders are characterized by lymphopenia.
- Defects in humoral immunity can be detected by measuring serum immunoglobulins.

ABP Content Specifications(s)

- Recognize the clinical findings associated with combined antibody and cellular immunodeficiency
- Plan the laboratory evaluation of antibody function
- Plan the laboratory evaluation of cell-mediated immunity

Suggested Readings

- Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol.* 2015;136(5):1186-1205. doi: http://dx.doi.org/10.1016/j.jaci.2015.04.049.
- Fleisher TA. Primary immune deficiencies: windows into the immune system. *Pediatr Rev.* 2006;27(10):363-372. doi: http://dx.doi.org/10.1542/pir.27-10-363.

Question 254

While working in the pediatric clinic, you discuss newborn screening with a group of residents and medical students. You review a recent clinical case with them of a 15-month-old boy followed in the well child clinic since 3 months of age. He has a chronic cough and has had 3 episodes of pneumonia in the past 12 months. He was brought in for evaluation of pale foul-smelling diarrhea. His mother described bulky and greasy stools, gassiness, and abdominal distention. Review of the growth chart demonstrated decreasing weight from the 38th percentile at birth to the 10th percentile.

Of the following, the cause of diarrhea in children with this disorder is

A. cow milk protein intolerance
B. disaccharidase deficiency
C. endocrine pancreatic insufficiency
D. exocrine pancreatic insufficiency
E. small bowel bacterial overgrowth

Correct Answer: D

The child in the vignette has chronic respiratory issues, failure to thrive, and fat malabsorption consistent with cystic fibrosis (CF). The malabsorption and resulting diarrhea seen in CF are caused by exocrine pancreatic insufficiency. Malabsorption of fat and disaccharides are most commonly involved, and clinically present with diarrhea, failure to thrive, gassiness/bloating, and fat-soluble vitamin deficiency.

The differential diagnosis for malabsorption and diarrhea in children includes the following:

- Abetalipoproteinemia
- Celiac disease
- Cholestasis
- Cystic fibrosis
- Dysbiosis (small bowel bacterial overgrowth)
- Eosinophilic gastrointestinal disease
- Exocrine pancreatic insufficiency
- Infectious etiology
- Inflammatory bowel disease
- Lactose intolerance
- Short bowel syndrome
- Sucrase deficiency
- Toddler's diarrhea

Evaluation for malabsorption requires stool analysis, which should include fecal fat, reducing substances, pH, cultures, ova and parasites, and occult blood. Endoscopy and/or colonoscopy may be considered, depending on the clinical picture. Fecal fat testing measures the amount of fat in the stool, either in a spot evaluation or with a 72-hour test. Elevated fecal fat is consistent with fat malabsorption.

Screening for infectious etiologies of malabsorption is performed with stool culture, ova and parasite testing, and occult blood testing. Disaccharide malabsorption can be identified with a low stool pH and positive stool-reducing substances. Upper endoscopy and colonoscopy can be used to identify bowel inflammation that may result in malabsorption, and small bowel biopsies can quantify disaccharidase levels. This is particularly helpful in the evaluation for lactase and sucrase deficiency. Biopsies may also help diagnose inflammatory bowel disease and eosinophilic gastrointestinal disease.

It would be unusual for a child to develop cow milk protein intolerance after 1 year of age. Disaccharidase deficiency presents with gassiness and diarrhea, but without pulmonary symptoms. Endocrine pancreatic insufficiency is associated with diabetes and does not present with gastrointestinal symptoms. Small bowel bacterial overgrowth presents with gassiness and diarrhea after antibiotic exposure, or during an acute illness with associated dysbiosis.

PREP Pearls

- Cystic fibrosis is associated with exocrine pancreatic insufficiency, resulting in fat malabsorption.
- Malabsorption is clinically identified by chronic diarrhea.
- Lactase and sucrase deficiency result in malabsorption of lactose and fructose, respectively, and present with abdominal cramping and diarrhea.

ABP Content Specifications(s)

- Plan the appropriate diagnostic evaluation for malabsorption

Suggested Readings

- Jones HF, Butler RN, Moore DJ, Brooks DA. Developmental changes and fructose absorption in children: effect on malabsorption testing and dietary management. *Nutr Rev* 2013;71(5):300-309. doi: http://dx.doi.org/10.1111/nure.12020.
- Siddiqui Z, Osayande AS. Selected disorders of malabsorption. *Prim Care.* 2011;38(3):395–341. doi: http://dx.doi.org/10.1016/j.pop.2011.05.002.
- Van de Vijver E, Desager K, Mulberg AE, et al. Treatment of infants and toddlers with cystic fibrosis–related pancreatic insufficiency and fat malabsorption with pancrelipase MT. *J Pediatr Gastroenterol Nutr*. 2011;53(1):61-64. doi: http://dx.doi.org/10.1097/MPG.0b013e31820e208e.

Question 255

A 4-year-old boy presents to your office for evaluation of leg pain. He feels pain behind his knees about once per week, generally at night as he is falling asleep. Occasionally, the pain wakes him from sleep. His parents have been treating the pain with acetaminophen and massage, which generally alleviates the pain within 20 to 30 minutes. The parents deny any history of limp, joint swelling, fevers, or skin changes in their son. The boy occasionally reports leg pain when walking more than 4 blocks, but his activity level is age appropriate. His appetite is normal. His physical examination is unremarkable.

Of the following, the BEST next step in evaluation and management for this boy is to

A. obtain radiographs of the hips
B. obtain radiographs of the knees
C. obtain serum C-reactive protein levels and complete blood cell count
D. reassure the family that no further intervention is needed
E. re-examine him after restriction of physical activity for 4 weeks

Correct Answer: D

The boy in the vignette has the classic history for benign nocturnal limb pains of childhood, often referred to as growing pains. Given this history, lack of constitutional symptoms, and normal physical examination findings, he does not require additional evaluation.

A French physician first described the clinical syndrome of growing pains in the 1800s. Affected children, typically between the ages of 3 and 10 years, report cramping limb pain generally in the evening or at night. Pain is typically bilateral and self-limited, involving the knees, shins, or calf muscles, and awakens some children from sleep. Most affected children experience pain up to 1 or 2 times per week. Despite the term growing pains, the peak age of incidence does not correspond with a time of rapid growth, and the etiology of this syndrome remains unclear. Up to one-third of young children are affected. Massage and over-the-counter analgesics are often helpful for accelerating pain relief. The term benign nocturnal limb pains of childhood is now used to describe this syndrome.

When taking a history for a child with limb pain, the practitioner should ask about associated symptoms, gait changes, history of travel, and family history of autoimmune conditions. Children who exhibit activity-related pain, increasing pain intensity, joint swelling, limp, or constitutional symptoms (eg, fever, malaise, or a decrease in activity) should be evaluated for other conditions such as idiopathic arthritis or infection. Leukemia should be considered in a child with limb pain and constitutional symptoms because 25% of children with leukemia have extremity pain as a presenting symptom. When the history or physical examination findings are inconsistent with benign nocturnal limb pains of childhood, an initial evaluation should include laboratory and radiographic testing. For young children, radiographs should be obtained of the site of reported pain, as well as the joint above and below the site to evaluate for sources of referred pain. A complete blood cell count and C-reactive protein or erythrocyte sedimentation rate should be obtained to evaluate for infection and other inflammatory conditions. Although some children with growing pains tend to have pain on days when they are especially active, a 4-week rest period is unlikely to significantly alter nighttime pain episodes.

PREP Pearls

- Benign nocturnal limb pains of childhood, often referred to as growing pains, refers to a recurrent pattern of cramping lower extremity pain in young children that typically occurs in the evening or at night.
- Despite the term growing pains, the peak age of incidence does not correspond with a time of rapid growth, and the etiology of this syndrome remains unclear.

ABP Content Specifications(s)

- Plan the appropriate management of functional joint complaints

Suggested Readings

- Pavone V, Lionetti E, Gargano V, Evola FR, Costarella L, Sessa G. Growing pains: a study of 30 cases and a review of the literature. *J Pediatr Orthop*. 2011;31(5):606-609. doi: http://dx.doi.org/10.1097/BPO.0b013e318220ba5e.
- Uziel Y, Chapnick G, Jaber L, Nemet D, Hashkes PJ. Five-year outcome of children with "growing pains": correlations with pain threshold. *J Pediatr*. 2010;156(5):838-840. doi: http://dx.doi.org/10.1016/j.jpeds.2009.11.078.

Question 256

An 18-month-old girl is brought to your office for a health supervision visit. Her parents report that she is starting to climb the stairs by herself and ask for your advice on how to avoid stair climbing injuries.

Of the following, the BEST advice that you would give the parents is to

A. carry the child up and down the stairs until she is steadier
B. encourage the child to use the handrail at all times
C. install a flexible accordion style gate at the top and the bottom of the stairs
D. redirect the child when she attempts to climb the stairs by herself
E. remove the carpeting from the stairs

Correct Answer: B

Encouraging a child to use the handrail on a stairway at all times is an important piece of safety advice to relay to caregivers. Stairway accidents are a frequent cause of injury in young patients, especially as their mobility increases. Stairway accidents are the most common cause of injury in 12-month-old children. The most common injuries sustained in stairway accidents are soft tissue injuries, closed head injuries, and lacerations. The most common anatomic locations of injuries are the head and neck, upper extremities, and lower extremities. The most frequent mechanism of injury is the child falling down the stairs (without mention of another action or object), followed by the child being carried down the stairs by an adult who loses his or her balance. The injuries that result from an adult carrying a child down the stairs tend to be more serious, given the potential for crush injuries from the adult falling on top of the child. Other common mechanisms of stairway injuries include jumping on the stairs, riding a toy down the stairs, tripping down the stairs, and injuries involving baby walkers and strollers.

In addition to encouraging children to use the handrail at all times and advising caregivers against carrying children on the stairs, there are several other key steps to promote stairway safety. If caregivers must carry children on the stairs, they should avoid carrying other objects, as this increases the risk the caregiver may lose his/her balance and fall. Stairs should be well-lit and free from clutter, and approved safety gates should be installed at both the top and bottom of the stairs. Accordion-style gates should be avoided because the neck or arm may become entrapped in the gate. Caregivers should discourage children from playing on or near stairs and from carrying objects while on the stairs. Caregivers should be advised to remove their children from strollers before going up or down stairs.

Carpeting on stairs reduces slipping and can help prevent stairway falls. Instead of redirecting a child when he/she attempts to climb the stairs, it is more important to demonstrate the correct way to use the stairs, reinforce the appropriate safety techniques, and observe closely.

PREP Pearls

- Most stairway injuries result from children falling down the stairs with no association with an object.
- Caregivers carrying children up or down the stairs is also an important cause of stairway injuries.
- Important safety practices include advising caregivers against carrying children on the stairs, keeping stairs free from clutter and well-lit, using approved gates at the top and bottom of stairs, and using handrails at all times.

ABP Content Specifications(s)

- Counsel parents regarding stairway safety

Suggested Readings

- Haderspeck J. Safety pitfalls: Stairs are a leading cause of injury for small children. American Academy of Pediatrics News website. http://www.aappublications.org/content/33/9/36.6.
- Zielinski AE, Rochette LM, Smith GA. Stair-related injuries to young children treated in US emergency departments, 1999–2008. *Pediatrics*. 2012;129(4):721-727. doi: http://dx.doi.org/10.1542/peds.2011-2314.

Question 257

A 3-month-old infant is brought to your office to establish care after having recently immigrated to the United States. On physical examination, you note that her right arm and leg are significantly larger than her left arm and leg, and that the right side of her tongue protrudes from between her lips. She is at the 95th percentile for both weight and height. Her mother reports that she has been breastfeeding without difficulty and has been well since birth.

Of the following, the MOST appropriate test to incorporate into her care plan is

A. abdominal ultrasonography every 3 months
B. complete blood cell count every 3 months
C. immunoglobulin levels every month
D. spot urine test for vanillylmandelic acid and homovanillic acid every 6 months
E. transcranial Doppler every year

Correct Answer: A

Although the cause of the vast majority of childhood cancers is not known, a landmark study published in 2015 found cancer-predisposing genetic mutations in approximately 9% of children with cancer and that number is likely a very conservative estimate. There are several well-described cancer predisposition syndromes that are important to recognize as early in life as possible, to implement screening plans that may lead to earlier cancer diagnosis, and thereby better outcomes.

The infant in the vignette has global macrosomia (95th percentile for height and weight), macroglossia, and hemihyperplasia (an enlarged left side of the body and face). This presentation suggests an overgrowth syndrome such as Beckwith-Wiedemann syndrome (BWS). Beckwith-Wiedemann syndrome is caused by genetic or epigenetic abnormalities involving chromosome 11p15. Affected children have an increased risk of cancer through age 7 to 8 years, with embryonal tumor types such as hepatoblastoma and nephroblastoma (Wilms tumor) most commonly reported. Given that these embryonal solid tumors have a higher rate of cure when identified at an earlier stage, screening for these tumors in patients with BWS is appropriate. Screening recommendations typically include serum a-fetoprotein measurements every 3 months until age 4 years to screen for hepatoblastoma and complete abdominal ultrasonography every 3 months through age 7 to 8 years to screen for Wilms tumor.

Overgrowth syndromes are not associated with an increased risk of leukemia, humoral immunodeficiency, or neuroblastoma. Therefore, screening with a complete blood cell count, immunoglobulin levels, or urine vanillylmandelic acid and homovanillic acid levels would not be recommended. Transcranial Doppler measures the flow velocity in cranial arteries. It is used in young patients with sickle cell disease to predict the risk of stroke. The patient in the vignette did not present with any stigmata of sickle cell disease, therefore this screening test would not be appropriate.

PREP Pearls

- Cancer predisposition syndromes should be recognized as early in life as possible so that appropriate screening plans can be put in place to improve outcomes.
- Children with hemihyperplasia, including Beckwith-Wiedemann syndrome, should undergo screening for embryonal tumors via serum α-fetoprotein measurement every 3 months until age 4 years, and abdominal ultrasonography every 3 months through age 7 to 8 years.

ABP Content Specifications(s)

- Recognize the risk factors for hematologic or oncologic disorders that may require screening or evaluation

Suggested Readings

- Gill J. Inherited hematologic and oncologic syndromes. *Pediatr Rev.* 2011;32(9):401-404. doi: http://dx.doi.org/10.1542/pir.32-9-401.
- Puumala SE, Hoyme HE. Epigenetics in pediatrics. *Pediatr Rev*. 2015;36(1):14-21. doi: http://dx.doi.org/10.1542/pir.36-1-14.
- Ricafort R. Tumor markers in infancy and childhood. *Pediatr Rev*. 2011;32(7):306-308. doi: http://dx.doi.org/10.1542/pir.32-7-306.

Question 258

A 12-year-old boy is brought to the emergency department following a motor vehicle collision. He complains of headache, but has had no vomiting or seizure activity. He is awake and conversant, but cannot remember the details of the accident. His Glasgow coma scale score is 15. He has a history of myringotomy tube placement for frequent ear infections at 2 years of age. On examination, he has bloody otorrhea on the left.

Of the following, the MOST likely reason for this patient's symptoms is

A. basilar skull fracture
B. chronic otitis externa
C. chronic otitis media
D. middle ear trauma
E. traumatic brain injury

Correct Answer: D

Otorrhea is drainage coming from the ear and can be caused by a variety of conditions. Following trauma to the face and head, it is important to assess for otorrhea, as it can be associated with a basilar skull fracture and middle ear trauma. The boy in the vignette has unilateral bloody otorrhea, without other signs of a serious head injury. While a basilar skull fracture can still present with Glasgow coma scale score of 13 to 15, the most likely reason for the bloody otorrhea in this boy is middle ear trauma.

Basilar skull fractures can produce a tear in the dural membrane, which can cause a cerebrospinal fluid leak. This can manifest as clear or bloody otorrhea or rhinorrhea. It is important to distinguish between a basilar skull fracture and other causes of otorrhea; when suspected, patients should undergo a computed tomography of the head.

Middle ear trauma can result from direct trauma over the ears from a motor vehicle collision, sporting accident, penetrating trauma, or barotrauma. Associated symptoms can include hearing loss, nausea, vertigo, ataxia, and facial nerve paralysis. Many of the presenting symptoms overlap with basilar skull fracture.

Nontraumatic causes of otorrhea include infection, cholesteatoma, and foreign body. Acute and chronic otitis media can cause otorrhea, which is typically cloudy or purulent and occasionally foul-smelling. There is often a history of pain, but rupture of the tympanic membrane and drainage of middle ear fluid often brings symptomatic relief. Otitis externa also causes otorrhea, associated with pain on manipulation of the pinna. Patients who have undergone myringotomy tube placement will often have episodes of otorrhea that are sometimes bloody and typically foul-smelling. For the boy in the vignette, his history of being in a motor vehicle collision makes infectious causes less likely. He may have sustained a minor traumatic brain injury, but that alone would not account for his symptoms.

PREP Pearls

- Bloody otorrhea following trauma can be a sign of basilar skull fracture or middle ear trauma.
- Basilar skull fracture, if suspected, should be evaluated with computed tomography of the head.
- Otitis media and otitis externa can also cause bloody otorrhea. While the otorrhea may be bloody, it is typically cloudy, not clear

ABP Content Specifications(s)

- Identify the various causes of bloody otorrhea

Suggested Readings

- Long M. Otitis externa. *Pediatr Rev.* 2013;34(3):143-144. doi: http://dx.doi.org/10.1542/pir.34-3-143.
- Nguyen CV, Parikh SR. In brief: cholesteatoma. *Pediatr Rev*. 2008;29(9):330-331. doi: http://dx.doi.org/10.1542/pir.29-9-330.

Question 259

A 13-year-old adolescent girl and her 4-year-old brother are brought to your office because of diarrhea that has lasted over 2 weeks. The diarrhea is watery, brown, with no obvious blood, and occurs over 10 times daily. Both children have mild abdominal discomfort, but have been able to go to school. Neither child reports fever, chills, nausea, or vomiting. The children have 2 additional siblings, 11 and 7 years of age, respectively, who have no symptoms. There is no significant past medical or family history for any of the children or parents. The family was on vacation 1 month ago and spent most of the time in the resort's swimming pool. The family ate at several different restaurants. The mother reports the groundskeeper was meticulous about checking and maintaining the pool's chlorine concentration daily.
Physical examination shows a female adolescent and young boy with normal vital signs and no abnormal findings on physical examination.

Of the following, the MOST likely pathogen responsible for the symptoms in these children is

A. Clostridium difficile
B. Cryptosporidium
C. Endolimax nana
D. Norovirus
E. Salmonella species

Correct Answer: B

The most likely pathogen responsible for the symptoms in the children in this vignette is *Cryptosporidium*. Recreational water illnesses (RWIs) can occur when people swim and participate in water-related activities in contaminated water. Exposure occurs in swimming pools, hot tubs, water parks, water play areas, lakes, rivers, and oceans. Although some RWIs can be caused by chemicals in the water, most are caused by pathogens individuals swallow, inhale in mists or aerosol, or with which they have physical contact. The most common RWI is diarrheal illness, but skin, ear, respiratory, eye, and neurologic diseases can also occur. By far, the leading cause of swimming pool-related diarrheal illness is the microscopic parasite *Cryptosporidium*.

Cryptosporidium species are ubiquitous and found on every continent. Over the past 20 years, it has been recognized as one of the leading causes of waterborne disease in the United States, in both fecally contaminated drinking water and recreational water. It is highly contagious, and ingestion of 10 to 50 *Cryptosporidium* oocysts can result in severe disease. In 1993, over 400,000 Milwaukee residents developed gastroenteritis from *Cryptosporidium* in contaminated city drinking water. While most pathogens are killed by water sanitization through chlorination within an hour, *Cryptosporidium* oocysts are relatively resistant to chlorine and can survive for over a week in a properly chlorinated swimming pool. Submicron filtering of drinking water will trap the oocysts, but this is not achievable through normal swimming pool filtering methods. Cryptosporidium disease, or cryptosporidiosis, typically presents as a mild watery, nonbloody diarrhea 7 to 10 days after infection, although 30% of pediatric infections can be asymptomatic. Symptomatic patients often report low-grade fevers, malaise, anorexia, nausea, and abdominal cramps, in addition to the diarrhea. Diarrhea usually self-resolves within 2 weeks, but can persist much longer. Certain groups, such as young children, pregnant women, and particularly immunocompromised individuals are at higher risk for developing severe or chronic disease.

Most reported cryptosporidiosis cases in the United States are in 1- to 9-year-old children. Prevention of RWI is 2-fold: minimize fecal contamination and maintain proper water sanitization. The first is accomplished by staying out of the water if having diarrhea, regular bathroom breaks for children and adults to avoid urinating or defecating in the water, checking infant swim diapers frequently and not changing them near the recreational water source, showering before entering the water, good handwashing after using the toilet, and not swallowing the water. The second is by monitoring and taking appropriate measures to keep the free chlorine or bromine level in the water high, as well as maintaining an appropriate pH to maximize their germicidal potency.

The watery brown diarrhea without blood lasting for 2 weeks in relatively well-appearing afebrile children, such as in this vignette, whose recreational water exposure was properly chlorinated is a classic description of *Cryptosporidium* diarrhea. This is the leading cause of swimming pool-related diarrhea. *Clostridium difficile* colitis could present with watery brown diarrhea without blood lasting for weeks, but abdominal pain, malaise, and fever would be expected on examination, along with a history of antibiotic usage. *Endolimax nana* is a nonpathogenic parasite in humans. Since the introduction of rotaviral vaccines,norovirusis the

most common cause of acute gastroenteritis in the United States and the leading cause of medically attended acute gastroenteritis in American children younger than 5 years of age. Norovirus is highly contagious and exposure to less than 20 viral particles can cause abrupt onset of watery nonbloody diarrhea with abdominal cramping, nausea, and vomiting. Fever, headaches, and myalgias are common, but the symptoms usually resolve within 72 hours, although it might take a few days in younger children. Like *C difficile*, *Salmonella* infection (salmonellosis) could cause typical symptoms of a bacterial colitis such as abdominal pain and fever, but the *Salmonella* diarrhea should be mucopurulent and bloody. Also, salmonellosis usually lasts less than a week. Appropriate swimming pool chlorination is highly effective against norovirus and *Salmonella*.

Other causes of RWI diarrhea are bacteria like *Shigella* and *Escherichia coli* O157:H7, and parasites like *Giardia*, which is a leading cause of waterborne illness in the United States because of its ubiquity. *Giardia* can also cause a self-limited but prolonged watery diarrhea lasting several weeks.

Not all RWI are diarrheal. Hot tub folliculitis is caused by *Pseudomonas aeruginosa*. Pneumonia can result from inhalation of steam or mist containing *Legionella*, while the majority of otitis externa (swimmer's ear) cases are due to *P aeruginosa* and *Staphylococcus aureus*.

PREP Pearls

- Recreational water illnesses (RWIs) occur when people swim and participate in water-related activities in contaminated water. The most common RWI is gastroenteritis, primarily caused by *Cryptosporidium*. Ingestion of only a few *Cryptosporidium* oocysts can cause severe disease, especially in young children, pregnant women, and immunocompromised individuals, although asymptomatic infection is seen in up to 30% of children.
- Chlorine kills recreational water pathogens, but the time it takes to do so varies. Most pathogens are killed within an hour, but *Cryptosporidium* can survive for days in a properly chlorinated swimming pool.
- There are nondiarrheal RWI such as hot tub folliculitis, legionellosis, and otitis externa.

ABP Content Specifications(s)

- Recognize which pathogens can be transmitted by contaminated recreational water, while providing guidance about prevention of such infections

Suggested Readings

- American Academy of Pediatrics. *Giardia intestinalis* (formerly *Giardia lamblia* and *Giardia duodenalis*) infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed*. Elk Grove Village, IL: American Academy of Pediatrics; 2015:353-355.
- American Academy of Pediatrics. Cryptosporidiosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:312-315.
- Sanborn M, Takaro T. Recreational water-related illness: office management and prevention. *Can Fam Physician.* 2013;59(5):491-495. http://www.cfp.ca/content/59/5/491.full.pdf+html.
- US Centers for Disease Control and Prevention. Recreational water illnesses (RWIs). US Centers for Disease Control and Prevention website. http://www.cdc.gov/healthywater/swimming/rwi/. Updated February 5, 2015.

Question 260

You are called by the surgical service to see a 3-year-old girl with fever and vomiting. She was born with a cloacal anomaly, and 4 days ago underwent an elective anorectal urethral vaginoplasty. Her temperature is 39°C, respiratory rate is 24 breaths/min, heart rate is 120 beats/min, and blood pressure is 90/62 mm Hg. On physical examination, she appears mildly dehydrated. Her surgical wound is nonerythematous, with no drainage. The remainder of her examination is unremarkable. An indwelling urinary catheter was placed intraoperatively and there is cloudy urine in the drainage bag. You suspect that the girl has an *Enterococcus* urinary tract infection.

Of the following, the MOST accurate statement is that this type of infection is

A. associated with urinary catheterization
B. caused by gram-negative bacteria
C. characterized by a positive test for nitrites on urinalysis
D. characterized by a negative test for leucocytes on urinalysis
E. usually associated with bacteremia

Correct Answer: A

The girl in the vignette has an indwelling catheter, which puts her at increased risk for a urinary tract infection (UTI) with *Enterococcus*. Enterococci are commonly isolated from the urinary tract and there is an increased risk for enterococcal UTI associated with catheterization, instrumentation, and obstruction of the genitourinary tract. Enterococci, gram-positive cocci normally present in the intestines, are a common cause of hospital-acquired UTI. The risk of hospital-acquired infection with enterococcus is increased in patients with prolonged hospitalization, treatment with multiple antibiotics, and catheterization of the urinary tract.

Enterococcal infection should be suspected in a high-risk patient with clinical features suggestive of UTI (fever, cloudy urine), and a urinalysis showing bacteriuria, pyuria (positive leucocyte esterase), and negative nitrites. Bacteremia is not commonly seen in association with enterococcal UTI. Antibiotic therapy administered while the urine culture and sensitivity results are pending should include coverage for both *Escherichia coli* and *Enterococcus* because, although *Enterococcus* is most common in high-risk patients, *E coli* is the most common overall cause of UTI. Third-generation cephalosporins (eg, cefotaxime, ceftriaxone) and aminoglycosides (eg, gentamicin) are appropriate first-line agents for empiric treatment of UTI in children, but should not be used as monotherapy in children with suspected enterococcal UTI. For enterococcal coverage, amoxicillin or ampicillin should be added to the treatment regimen until urine culture/sensitivity results are available.

Management of catheter-related UTI should include consideration of catheter removal, if clinically appropriate. Removal of the urinary catheter has been shown to improve recovery time and decrease colonization in enterococcal infections.

PREP Pearls

- Enterococcal urinary tract infection (UTI) should be suspected in any child with an indwelling catheter and a urine dipstick analysis negative for nitrites.
- Empiric antibiotics in patients suspected of having an enterococcal UTI should include a combination of ampicillin or amoxicillin and a third-generation cephalosporin or aminoglycoside.

ABP Content Specifications(s)

- Recognize pathogens commonly associated with urinary tract infection in children of various ages

Suggested Readings

- Feld LG, Mattoo TK. Urinary tract infections and vesicoureteral reflux in infants and children. *Pediatr Rev.*2010;31(11):451-463. doi: http://dx.doi.org/10.1542/pir.31-11-451.
- Haslam DB. Enterococcus. In: Kleigman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:1342-1344.
- Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics*. 2011;128(3);595-610. doi: http://dx.doi.org/0.1542/peds.2011-1330.

Question 261

You are called to the cesarean delivery of a 39-year-old gravida 1, para 0 woman with a history of obesity and fibroids with chorioamnionitis. Maternal laboratory tests were significant for blood type O positive and negative for group B *Streptococcus*. She was admitted for induction of labor because of preeclampsia. She developed a temperature of 39.3°C associated with uterine tenderness and was begun on vancomycin, clindamycin, and gentamicin. The duration of rupture of membranes was 8 hours. A live female neonate is delivered without assistance. The neonate's vital signs show a temperature of 37.1°C, heart rate of 156 beats/min, respiratory rate of 40 breaths/min, and a blood pressure of 70/42 mm Hg. She is alert with good tone and no respiratory distress.

Of the following, the BEST next step in her management is to

A. allow the neonate to room in with the mother
B. observe closely in nursery for signs of infection
C. obtain blood culture, complete blood cell count, and start ampicillin and gentamicin
D. obtain blood culture, complete blood cell count, cerebrospinal fluid culture, and start ampicillin and gentamicin
E. start cefotaxime

Correct Answer: C

For the term neonate born to the mother with chorioamnionitis in this vignette, the best next step in management is to obtain a complete blood cell count (CBC), blood culture, and begin ampicillin and gentamicin. Early-onset sepsis (EOS) is defined by a positive blood or cerebrospinal fluid culture within 72 hours after birth. Among term neonates, group B *Streptococcus* (GBS) is the most common cause of EOS. Since 2002, when the US Centers for Disease Control and Prevention recommended prenatal maternal screening and prophylaxis for GBS colonization, the risk of EOS caused by GBS has decreased. Concurrently, rates of EOS caused by *Escherichia coli* may be increasing. While the rates of EOS are low (GBS is 0.35/1,000 live births, *E coli* is 0.07/1,000 live births), the mortality from both infections is high: 10% for infants with EOS caused by *E coli* and 2% for EOS caused by GBS. Risk factors for EOS include maternal chorioamnionitis, premature gestation, maternal colonization with GBS, and rupture of amniotic membranes for greater than 18 hours.

In the neonate in the vignette, the mother was GBS-negative and did not have prolonged rupture of membranes. The presence of maternal fever and uterine tenderness suggests maternal chorioamnionitis. At a minimum, neonates born to mothers with chorioamnionitis should be evaluated with a blood culture and a CBC. The initial CBC can be sent at birth or at 6 to 12 hours of life. A later CBC may more accurately predict risk of infection. Although clinical tests such as C-reactive protein lack the sensitivity to predict EOS in term neonates, they may be helpful to determine when to stop antibiotic therapy.

Based on local antibiotic resistance patterns, empiric coverage for *E coli* must be chosen. In most institutions, ampicillin and an aminoglycoside provide coverage against GBS, *E coli,* and *Listeria monocytogenes*. Use of a third-generation cephalosporin as initial empiric treatment for EOS has been associated with increased rates of antibiotic resistance. Thus, cefotaxime should be reserved for gram-negative bacteremia or meningitis.
For a well-appearing neonate, the risk of meningitis is low. Thus, cerebrospinal fluid culture is not required. Lumbar puncture should be performed in neonates with bacteremia, a clinical picture consistent with sepsis, or clinical deterioration while on antimicrobial therapy.

PREP Pearls

- The most common causes of early-onset sepsis (EOS) in term infants are group B *Streptococcus* (GBS) and*Escherichia coli.*
- Risk factors for EOS include prematurity, prolonged rupture of amniotic membranes greater than 18 hours, maternal GBS colonization, and maternal chorioamnionitis.
- Neonates born to mothers with chorioamnionitis should be evaluated with a complete blood cell count and blood culture. Depending on clinical status, these neonates could be started on empiric antibiotic coverage.

ABP Content Specifications(s)

- Plan the appropriate management of an infant born to a mother with chorioamnionitis

Suggested Readings

- Polin RA, Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. *Pediatrics*. 2012;129(5):1006-1015. doi: http://dx.doi.org/10.1542/peds.2012-0541.
- Sass L. Group B streptococcal infections. *Pediatr Rev*. 2012;33(5):219-224. doi: http://dx.doi.org/10.1542/pir.33-5-219.
- Stoll BJ, Hansen NI, Sánchez PJ, et al. Early onset neonatal sepsis: the burden of group B streptococcal and E. coli disease continues. *Pediatrics*. 2011;127(5):817-826. doi: http://dx.doi.org/10.1542/peds.2010-2217.

Question 262

The father of a 3-year-old patient mentions at his son's health supervision visit that the family recently purchased a motorboat to use on a local lake. In addition to your typical safety recommendations, you counsel the family regarding safe boat use.

Of the following, the intervention MOST likely to reduce this child's risk of drowning is

A. cardiopulmonary resuscitation training for the supervising adults
B. inflatable arm bands ("water wings")
C. personal flotation device ("life jackets")
D. supervision by a responsible adult
E. swimming lessons

Correct Answer: C

The intervention most likely to reduce the risk of drowning for the boy in the vignette is a personal flotation device (PFD). Drowning is the second most common cause of death in children ages 1 to 4 years, surpassed only by congenital anomalies. After motor vehicle crashes, drowning is the second leading cause of injury-related death in all children younger than 14 years. Boys, young children, adolescents, African-Americans, and those with a history of seizure are at higher risk of drowning than the general pediatric population. Among adolescents and adults, alcohol use is involved in up to 70% of deaths associated with water recreation.

Personal flotation devices or "life jackets" are key to preventing drowning, especially in open water or boating-related incidents. One matched cohort study analyzing US Coast Guard data showed that wearing a PFD reduced the risk of drowning in a boating accident by nearly 50%. Children should wear PFDs that are approved by the US Coast Guard and are the appropriate size for the user.

Cardiopulmonary resuscitation (CPR) training for supervising adults is important because effective and timely CPR is associated with improved outcomes in drowning victims. However, primary prevention of drowning is the most important intervention. Inflatable arm bands ("water wings"), pool toys, and other foam or inflatable objects are not effective in reducing the risk of drowning. Personal flotation devices alone cannot prevent drowning; constant, focused adult supervision is also important. There are no data demonstrating that swimming lessons decrease the risk of drowning in children younger than 4 years of age.

PREP Pearls

- Drowning is a common cause of death in children.
- Appropriately fitted personal flotation devices can significantly reduce the risk of drowning in open water and boating-related incidents.
- Swimming lessons have not been shown to decrease the risk of drowning in children younger than 4 years of age.

ABP Content Specifications(s)

- Counsel parents and children regarding safe boat use (eg, flotation devices, supervision)

Suggested Readings

- Cummings P, Mueller BA, Quan L. Association between wearing a personal floatation device and death by drowning among recreational boaters: a matched cohort analysis of United States Coast Guard data. *Inj Prev.* 2011;17(3):156-159. doi: http://dx.doi.org/10.1136/ip.2010.028688.
- Meyer RJ, Theodorou AA, Berg RA. Childhood drowning. *Pediatr Rev.* 2006;27(5):163-168. doi: http://dx.doi.org/10.1542/pir.27-5-163.
- US Centers for Disease Control and Prevention. Unintentional drowning: get the facts. US Centers for Disease Control and Prevention website. http://www.cdc.gov/HomeandRecreationalSafety/Water-Safety/waterinjuries-factsheet.html. Updated October 24, 2014.
- Weiss J, American Academy of Pediatrics Committee on Injury, Violence, and Poison Prevention. Prevention of drowning. *Pediatrics*. 2010;126(1):e253-e262. doi: http://dx.doi.org/10.1542/peds.2010-1265.
- Yuma P, Carroll J, Morgan M. A guide to personal flotation devices and basic open water safety for pediatric health care practitioners. *J Pediatr Health Care.* 2006;20(3):214-218. doi: http://dx.doi.org/10.1016/j.pedhc.2006.02.008.

Question 263

You are planning a multicenter randomized, controlled clinical trial to evaluate the efficacy and safety of a proposed new drug. Your study design will use an intention-to-treat analysis.

Of the following, this method of analysis is EXPECTED to result in a(n)

A. bias in estimate of treatment effect
B. increase in statistical power
C. loss of randomized subjects because of nonadherence
D. low tolerance for protocol deviation
E. minimization of type II error

Correct Answer: B

"Intention to treat" (ITT) is a strategy that may be used in the analysis of randomized controlled trials. In this approach, every subject is analyzed according to his or her randomized group assignment; noncompliance, protocol deviation, withdrawal, and other events that may follow randomization are ignored. Intention to treat has been referred to as "once randomized, always randomized." Intention to treat analysis preserves sample size and statistical power is therefore maintained.

Intention to treat is best regarded as a comprehensive strategy for study design, conduct, and analysis rather than a mode of analysis alone. This approach maintains similarity in treatment groups, thus, as noncompliance among study participants is recognized and these results are included in the analysis, an unbiased estimate of treatment effect results. Intention-to-treat analysis minimizes type I error, or the incorrect rejection of a true null hypothesis.

Generalizability in study results is a benefit of ITT; statements on the efficacy of interventions in patients who received treatment strictly according to protocol are not the intent. Full application of ITT is only achieved when complete outcome data can be analyzed for all randomized subjects.

PREP Pearls

- In an intention-to-treat analysis, study participants are analyzed according to their randomized assignment, regardless of changes that may occur after randomization.
- Intention-to-treat analysis prevents the loss of statistical power that may be encountered with a failure to complete study protocols (dropout) or noncompliance.

ABP Content Specifications(s)

- Understand the concept of intention-to-treat analysis to maintain the power of a study

Suggested Readings

- Gupta SK. Intention to treat concept: a review. *Perspect Clin Res*. 2011;2(3):109-112. doi: http://dx.doi.org/10.4103/2229-3485.83221.
- Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomized controlled trials. *BMJ*. 1999;319(7211):670-674. doi: http://dx.doi.org/10.1136/bmj.319.7211.670.
- Sheiner LB, Rubin DB. Intention-to-treat analysis and the goals of clinical trials. *Clin Pharmacol Ther*. 1995;57(1):6-15. doi: http://dx.doi.org/10.1016/0009-9236(95)90260-0.

Question 264

A previously healthy 8-year-old girl presents to the emergency department with an unprovoked generalized tonic-clonic seizure lasting 20 minutes. She has never had a seizure or head injury before and there is no family history of seizures. Her physical examination shows a mildly sleepy girl, with no other neurological abnormalities. Electrolytes, glucose, and a complete blood cell count are normal. Magnetic resonance imaging of the head is also normal. She is admitted for observation and the next day has an electroencephalogram that is normal. You are planning to discharge her home.

Of the following, the BEST statement about her seizure recurrence risk is it

A. is 25% to 45%
B. is greater than 45% because she had a prolonged seizure
C. is greater than 45% because she is prepubertal
D. will stay the same over the next 2 years, then decrease
E. will stay the same over the next 14 years, then decrease

Correct Answer: A

Between 40% to 50% of adults and children with a first, unprovoked seizure will have a recurrent seizure. Factors that increase the risk of recurrent seizure include abnormal findings on electroencephalogram and abnormal results from magnetic resonance imaging of the brain, such as remote brain injury or brain malformation (which may not be seen on computed tomography). A prolonged first seizure does not increase the risk of recurrent seizure. In a typically developing child with a first, unprovoked seizure whose electroencephalogram and magnetic resonance imaging of the brain are normal, the recurrence risk is as low as 25%. For the girl in the vignette, the seizure recurrence risk is 25% to 45%; it will be at the lower end of the range if her magnetic resonance imaging results are normal. About half of recurrent seizures occur in the first 6 months after the first seizure, and almost 90% of recurrent seizures happen in the first 2 years. Identifying an etiology for the seizure can help predict the risk of recurrence.

Seizures and epilepsy in childhood can be due to an epilepsy syndrome or to an underlying etiology. Underlying etiologies can be subdivided into 6 categories: genetic, structural, metabolic, immune, infectious, and unknown. This classification scheme is currently being updated by the International League Against Epilepsy (www.epilepsydiagnosis.org). Examples of epilepsy syndromes include childhood absence epilepsy and juvenile myoclonic epilepsy. Examples of underlying etiologies of epilepsy include traumatic brain injury, mitochondrial disorders and genetic disorders. In a particular child, more than 1 epilepsy syndrome or etiology may apply. For example, a child younger than 4 years of age who develops absence seizures may also have glucose transporter deficiency, a metabolic and genetic cause for epilepsy; or, a child with tuberous sclerosis has both a genetic and structural cause for epilepsy.
Clinicians should be aware of the increased risk of developing seizures in children with one or more underlying etiologies, but it is rarely necessary to start anticonvulsants prior to the onset of clinical seizures.

PREP Pearls

- Seizure recurrence risk is as low as 25% in a typically developing child with a first, unprovoked seizure whose electroencephalogram and magnetic resonance imaging of the brain are normal.
- About half of recurrent seizures occur in the first 6 months after the first seizure, and almost 90% of recurrent seizures happen in the first 2 years.

ABP Content Specifications(s)

- Recognize factors associated with an increased risk of a seizure disorder

Suggested Readings

- Camfield P, Camfield C. Special considerations for a first seizure in childhood and adolescence. *Epilepsia*. 2008;49(Suppl 1):40-44. doi: http://dx.doi.org/10.1111/j.1528-1167.2008.01449.x.
- International League Against Epilepsy: www.EpilepsyDiagnosis.org .
- Sidhu R, Velayudam K, Barnes G. Pediatric seizures. *Pediatr Rev*. 2013;34(8):333-342. doi: http://dx.doi.org/10.1542/pir.34-8-333.

Question 265

A previously healthy 2-year-old boy is brought to the emergency department with 5 days of fever, progressive lethargy, vomiting, and poor oral intake. Vital signs show a temperature of 38.5°C, heart rate of 180 beats/min, respiratory rate of 50 breaths/min, blood pressure of 70/50 mm Hg, and pulse oximetry of 95% on room air. He does not have a significant past medical history, take any medications, or have any allergies. Physical examination reveals a well-nourished boy in a state of anxiety. He is pale around the mouth and has dry mucous membranes. Neck examination shows jugular venous distention and no lymphadenopathy. He is in respiratory distress with grunting, tachypnea, and intercostal retractions. Lungs have scattered crackles bilaterally. Liver is 5 cm below the costal margin. Extremities are cool with capillary refill time of 5 seconds. Arterial blood gas analysis shows a pH of 7.40, PCO_2 of 24 mm Hg, and PaO_2 of 95 mm Hg. Serum bicarbonate level is 15 mEq/L (15 mmol/L) and lactate level is 8 mg/dL (0.9 mmol/L) (normal, < 2 mg/dL).

Of the following, the condition revealed by the blood gas in this boy is

A. hypoxemia with appropriate respiratory compensation
B. metabolic acidosis and respiratory alkalosis
C. metabolic acidosis with appropriate respiratory compensation
D. metabolic alkalosis with appropriate respiratory compensation
E. respiratory alkalosis with appropriate metabolic compensation

Correct Answer: B

The child in this vignette has fever, lethargy, and cardiogenic shock. He has metabolic acidosis based on his levels of serum bicarbonate and lactate, as well as respiratory alkalosis based on hypocapnia out of proportion to normal respiratory compensation for his degree of metabolic acidosis.

There are few clinical scenarios in pediatrics more dangerous than the combination of metabolic acidosis and respiratory alkalosis. The underlying etiology can include congestive heart failure, toxic ingestion, increased intracranial pressure, sepsis, and pulmonary embolism. In addition to the life-threatening conditions on this differential diagnosis, the false sense of security some clinicians may adopt with a blood gas pH result in the "normal" range makes this combination even more concerning. Although the pH of the child in this vignette is normal, the blood gas as a whole is very abnormal. Separate from the blood gas results, the clinician should recognize that the boy is in cardiogenic shock, based on tachycardia, delayed capillary refill time, and hepatomegaly. As a result, he has metabolic acidosis due to lactic acidosis from poor end-organ perfusion. If ventilation is intact, the cerebral respiratory center causes an increase in minute ventilation to compensate for metabolic acidosis. Expected respiratory compensation for a given degree of metabolic acidosis is predicted based on the Winters formula:

$$pCO2 = (1.5 * HCO3 + 8) \pm 2$$

If PCO_2 falls within the expected range according to the Winters formula, it is considered appropriate compensation and not a separate disorder. If PCO_2 is higher than expected, it represents a concomitant respiratory acidosis. In some cases of severe metabolic acidosis, even PCO_2 levels lower than normal but not quite low enough to satisfy the Winters formula can represent respiratory acidosis. This is often seen in severe diabetic ketoacidosis, especially with neurologic impairment, in which minute ventilation cannot keep up with the severity of metabolic acidosis. It should be noted that mechanical ventilation sometimes cannot keep up either, so extreme caution should be taken before intubating a child with diabetic ketoacidosis.

If PCO_2 is lower than expected, as in the boy in the vignette, it represents a concomitant respiratory alkalosis. Since the lower PCO_2 brings the pH closer to the normal range, this scenario represents a major pitfall for some clinicians. Although there are 2 discrete disorders, the clinician may not recognize either disorder and underestimate the severity of illness. In congestive heart failure, pulmonary edema activates the lung stretch receptors that feed back to the respiratory center to stimulate tachypnea. In pulmonary embolism, tachypnea can be caused by hypoxia and alveolar ischemia. Tachypnea is one of the major criteria for systemic inflammatory response syndrome and sepsis. Neurologic effects of some toxic ingestions, such as salicylates and tricyclic antidepressants, can stimulate the respiratory center. Lastly, increased minute ventilation to lower PCO_2 is a compensatory mechanism to limit cerebral blood volume in increased intracranial pressure. These are all life-threatening conditions that independently lead to respiratory alkalosis. If they also occur in the setting of metabolic acidosis, the blood gas could be in the normal range.

Hypoxia can lead to an increase in minute ventilation, but there is no expected level of compensation. An expected PCO_2between 28.5 and 32.5 mm Hg would represent metabolic acidosis with appropriate respiratory compensation. The child does not have metabolic alkalosis because the bicarbonate level is lower than the normal range. Metabolic compensation for respiratory alkalosis can occur, but the primary metabolic derangement in this vignette is lactic acidosis from cardiogenic shock.

PREP Pearls

- The combination of metabolic acidosis and respiratory alkalosis can be seen with a blood pH approaching the normal range and can represent life-threatening conditions.
- Expected PCO_2 levels from appropriate respiratory compensation for metabolic acidosis can be estimated using the Winters formula.

ABP Content Specifications(s)

- Recognize the arterial blood gas values associated with various conditions

Suggested Readings

- Lewis JL III. Acid-base disorders. Merck Manual Professional Version website. http://www.merckmanuals.com/professional/endocrine-and-metabolic-disorders/acid-base-regulation-and-disorders/acid-base-disorders. Updated February 1, 2013.
- Sarnaik AP, Heidemann SM, Clark JA. Interpretation of blood gases. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:1989.

Question 266

You are seeing a 2-day-old female neonate in the newborn nursery. She was born at 39 weeks of gestation by spontaneous vaginal delivery to a 26-year-old gravida 1, now para 1 mother. The birthweight of the neonate was 2.5 kg. The pregnancy and delivery were uncomplicated. Her mother took levothyroxine and prenatal vitamins during pregnancy. Routine prenatal laboratory test results were normal, including a negative group B *Streptococcus* culture. On physical examination, the neonate has a temperature of 37°C, heart rate of 180 beats/min, respiratory rate of 30 breaths/min, and blood pressure of 100/70 mm Hg. She appears thin with decreased subcutaneous fat, but is awake and alert with her eyes wide open. She has a prominent Moro reflex. The remainder of the physical examination is unremarkable.

Of the following, the test MOST likely to establish the diagnosis is

A. anti-thyroglobulin antibody
B. blood culture
C. glucose
D. thyroid function panel
E. thyroid peroxidase antibody

Correct Answer: D

The neonate described in the vignette displays signs and symptoms of hyperthyroidism, which would be confirmed with a thyroid function panel. The etiology of her hyperthyroidism is neonatal Graves disease. Although not revealed in the vignette, the mother has a history of Graves disease that was treated with radioactive iodine ablation, so the mother now requires levothyroxine replacement. Despite definitive treatment for her Graves disease, thyroid-stimulating immunoglobulins are still present and cross the placenta where they stimulate the baby's thyroid gland. Neonatal Graves disease is rare, but when it occurs, can cause significant morbidity and mortality.

Anti-thyroglobulin antibody and thyroid peroxidase antibody are associated with Hashimoto thyroiditis and are not pathologic. Although a blood culture and glucose level may be indicated based on symptoms, they would not reveal the diagnosis of hyperthyroidism. The effect of maternal levothyroxine on the fetus is minimal and would not cause hyperthyroidism in the baby. Clinical features of infants with hyperthyroidism may include increased wakefulness, jitteriness, tachycardia, decreased subcutaneous fat, exaggerated Moro reflex, and ultimately heart failure. Older children and adolescents may experience weight loss, increased appetite, palpitations, increased stooling, difficulty sleeping, exercise intolerance, decreased school performance, menstrual irregularities, tremor, exophthalmos, warm, moist skin, exaggerated deep tendon reflexes with clonus, and systolic hypertension.

The diagnosis of hyperthyroidism occurs when the thyroid-stimulating hormone (TSH) level is low, often below the detection limit of the assay, and free thyroxine (FT4) and tri-iodothyronine (T3) levels are elevated. The most common etiology of hyperthyroidism in children is Graves disease. Other etiologies include hashitoxicosis, other thyroiditis, an autonomously functioning thyroid nodule, states of high human chorionic gonadotropin (hCG) levels, and exogenous thyroid hormone intake. Once hyperthyroidism is confirmed, further evaluation determines the etiology. Elevated thyroid-stimulating immunoglobulins confirms Graves disease. Elevated thyroid peroxidase and anti-thyroglobulin antibodies are consistent with autoimmune thyroiditis, although they can also be elevated in Graves disease. A nuclear medicine thyroid uptake and scan shows increased, uniform uptake in Graves disease and decreased uptake with thyroiditis or exogenous thyroid hormone intake. An autonomously functioning thyroid nodule is detected on the scan as a concentrated area of uptake. Thyroid ultrasonography is useful in detecting thyroid nodules.

The management of hyperthyroidism depends on the etiology. For Graves disease, treatment options include the anti-thyroid medication, methimazole, radioiodine ablation, and thyroidectomy. The latter two are considered definitive therapies, ultimately requiring thyroid hormone replacement. Propylthiouracil is no longer recommended as first-line therapy due to reports of serious liver injury. β-blockers are used as adjunctive therapy until symptoms of hyperthyroidism are controlled. Babies with neonatal Graves disease may require methimazole and a β-blocker for a few months until the maternal thyroid-stimulating antibodies wane. Hyperthyroidism due to thyroiditis tends not to be as severe as with Graves disease. Thyroid function tests should be followed for the resolution of hyperthyroidism and for the possible

development of hypothyroidism. The hyperthyroidism may be treated symptomatically with β-blockers. Autonomously functioning thyroid nodules are most often surgically removed.

PREP Pearls

- Neonatal Graves disease is caused by maternal thyroid-stimulating immunoglobulins acting at the baby's thyroid gland. Although rare, it can cause significant morbidity and mortality if not recognized.
- Graves disease is the most common etiology of hyperthyroidism in children and adolescents.
- Treatment options for Graves disease include methimazole, radioiodine ablation, and thyroidectomy. β-blockers are used as adjuvant therapy to control symptoms.

ABP Content Specifications(s)

- Plan the appropriate diagnostic evaluation of hyperthyroidism
- Recognize the clinical features associated with hyperthyroidism, including that occurring in neonates
- Plan the appropriate management of hyperthyroidism

Suggested Readings

- Léger J, Carel JC. Hyperthyroidism in childhood: causes, when and how to treat. *J Clin Res Pediatr Endocrinol*. 2013;5(Suppl 1):50–56. doi: http://dx.doi.org/10.4274/Jcrpe.854.
- Srinivasan S, Misra M. Hyperthyroidism in children. *Pediatr Rev.* 2015;36(6):239-248. doi: http://dx.doi.org/10.1542/pir.36-6-239.

Question 267

A 4-month-old infant with trisomy 21 is brought to your office for a health supervision visit. She was born by elective cesarean delivery at 38 weeks of gestation to a 37-year-old gravida 2 para 1 mother. A small, asymptomatic ventricular septal defect was diagnosed at birth. Her parents report a new concern of abnormal eye movements, described as occasional rhythmic beating followed by a normal focused gaze. The infant has been clinically well, with growth and development appropriate for her genetic condition.

On physical examination, the infant has facial features consistent with trisomy 21. Her pupils are equal, round, and reactive to light. There is a subtle asymmetry of the brightness of the red reflexes. The corneal light reflex is centrally located. The infant is able to fix and follow past midline horizontally with conjugate eye movement. You do not appreciate any abnormal eye movements.

Of the following, BEST next management step for this infant is

A. computed tomography of the brain and eyes
B. thyroid function tests
C. urgent referral to ophthalmology
D. urine specimen for reducing substances
E. watchful waiting and follow-up in 2 months

Correct Answer: C

The infant in the vignette has clinical findings suggestive of congenital cataracts, for which an urgent referral to ophthalmology is warranted. The clinical presentation of congenital cataracts in infants may include:

- Asymmetric retinal red reflexes
- Leukocoria
- Photophobia
- Strabismus
- Nystagmus
- Decreased visual acuity

Parental report of abnormal eye movements should always be taken seriously, even when the findings are reported as intermittent and are not evident on physical examination.
Many pediatric disorders, including trisomy 21, are associated with cataracts. A cataract is an opacification of the lens that may occur bilaterally or unilaterally, and may vary in size and location. The larger the cataract, the greater the risk is that it will negatively affect visual development. Trisomy 21 is also associated with nystagmus, which this infant's history suggests; however, nystagmus may also be a sign of poor vision. Although this infant has the ability to fix and follow past midline with conjugate eye movements, centralized corneal light reflexes, and pupils that are equal, round, and reactive, the possibility of a serious ophthalmologic disorder is not excluded. Urgent referral to a pediatric ophthalmologist is the next best step in management. Watchful waiting with follow-up in 2 months is not appropriate because early detection and prompt intervention are critical to optimize visual outcomes.

The performance of a thorough, age-appropriate eye examination is crucial at each health supervision visit, as well as at any time a concern is raised. This examination should include assessment of the external eye anatomy, ocular motility, and ability to fix and follow, as well as direct ophthalmoscopic examination of the pupil and evaluation of the retinal red reflex. The examiner should view the eyes simultaneously for comparison. The color of the normal retina varies between individuals, but should be consistent for both of an individual’s eyes. If the retina appears black, white, asymmetric, or dim, then concern for an abnormal red reflex is raised. The red reflex represents the reflection of the examiner's light from the retina, so an abnormal red reflex can be caused by retinal disorders (eg, retinoblastoma) or anterior eye disorders (eg, cataract).

The infant in the vignette has been clinically well, with growth and development appropriate for her genetic condition. Therefore, evaluation for causes of cataract with computed tomography of the brain and eyes or a urine specimen for reducing substances is not appropriate at this time. Although it is important to screen routinely for hypothyroidism in patients with trisomy 21, hypothyroidism is not a cause of cataracts.

PREP Pearls

- A concern for congenital cataract warrants an urgent ophthalmologic evaluation.
- Clinical features of congenital cataracts include asymmetric retinal red reflex, leukocoria, photophobia, strabismus, nystagmus, and decreased visual acuity.

ABP Content Specifications(s)

- Recognize the clinical findings associated with congenital cataracts

Suggested Readings

- Olitsky SE, Hug D, Plummer LS, Stahl ED, Ariss MM, Lindquist TP. Abnormalities of the lens. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2015:3044-3047.
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Question 268

A 13-year-old adolescent is brought to your office for a health supervision visit. When you ask if there are any changes at home, she tells you that her parents are getting a divorce. She does not know with whom she will live and is worried about how things will change. She is concerned that she may need to change schools and move to a new home. Her younger brother has been acting out and her parents have been arguing more. Things have been quite tense at home.

Of the following, your patient is MORE likely than her unaffected peers to have

A. fewer household responsibilities
B. a higher perception of self-efficacy
C. later sexual experiences
D. a less active dating life
E. a marriage that will end in divorce

Correct Answer: E

The adolescent in this vignette is dealing with the events leading up to the divorce of her parents. Once the divorce is finalized, its impact does not end. This adolescent will be subject to both short- and long-term consequences. These include the influence of her parents' dissolving marriage on her own subsequent intimate relationships. Children whose parents have divorced are at higher risk of becoming divorced themselves.

Approximately half of first marriages end in divorce. While 85% of divorced adults remarry, 40% of these new marriages also end in divorce. Divorce affects over 1 million children per year, causing multiple changes in these children's lives. Not only does the family structure change, but the child's living circumstances also change. The child's home environment, school placement, childcare arrangements, extracurricular activities, community, routines, peer groups, and available supports may all be affected. The child's lifestyle may change due to decreased income and resources. Older children and adolescents may be required to take on more responsibilities with household and childcare duties.

Children adjust to these changes with varying degrees of success. They are at risk for academic underachievement, depression, delinquency, and high-risk behaviors such as drug use and early sexual activity. These children may have decreased self-esteem and lower perceptions of self-efficacy. Those with an easy temperament and at least average cognition tend to do better with divorce of their parents. Girls may do better with adjustment emotionally and academically closer to the time of the divorce, but may have problems 5 to 10 years later as they enter into adulthood.

Children of divorce have more disruption in their interpersonal relationships, including with their peers and parents. Romantic relationships are particularly affected. The adolescent's ideas about and understanding of relationships may be influenced by their parents' divorce. They are more likely to date and to engage in earlier and more frequent sexual activity. As they enter adulthood, they are more likely to have difficulty with intimacy and commitment in their romantic relationships. As adults, they are more likely to have marriages that end in divorce.

The adolescent in this vignette is more likely than her unaffected peers to have more household responsibilities, particularly if there is just one parent at each household. She is at risk of having lower perception of self-efficacy, earlier sexual experiences, and a more active dating life, in addition to a marriage that will end in divorce.

It is important to recognize that divorce is not a single event to a child and that the time leading up to divorce and the time after has significant and enduring impact on children. Pediatricians have an important role in helping children and their parents through these difficult times and can counsel those affected in what to expect.

PREP Pearls

- Divorce is not a single event to a child. The time leading up to a divorce and the time after has significant and enduring impact on children.
- Children of divorce are at risk for academic underachievement, depression, delinquency, and high-risk behaviors such as drug use and early sexual activity.
- Adolescents with divorced parents are more likely to date and to engage in earlier and more frequent sexual activity. As adults, they are more likely to have marriages that end in divorce.

ABP Content Specifications(s)

- Understand the effects of divorce on a patient's subsequent intimate relationships

Suggested Readings

- Cohen GJ, American Academy of Pediatrics, Committee on Psychosocial Aspects of Child and Family Health. Helping children and families deal with divorce and separation. *Pediatrics*. 2002;110(5):1019-1023. http://pediatrics.aappublications.org/content/110/5/1019.
- Kaplan-Sanoff M. Divorce. In: Augustyn M, Zuckerman B, Caronna EB, eds. *The Zuckerman Parker Handbook of Developmental and Behavioral Pediatrics for Primary Car*e. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011:446-449.
- Kleinsorge C, Covitz LM. Impact of divorce on children: developmental considerations. *Pediatr Rev*. 2012;33(4):147-155. doi: http://dx.doi.org/10.1542/pir.33-4-147.

Question 269

A 15-year-old adolescent girl presents to your office for her annual health supervision visit. During the review of systems, the patient reports heavy menstrual periods requiring 8 to 10 pads per day for the first 3 to 5 days. She often soaks the pads and at times will use 2 pads to try to prevent leakage. Her periods typically last for 10 days. Her last menstrual period ended 2 weeks ago. She reports sexual activity once 2 months ago. Her physical examination is unremarkable. You perform a complete blood count in your office, which reveals a hemoglobin of 8.3 g/dL (83 g/L).

Of the following, the BEST initial step in this adolescent's evaluation and management would be

A. dilation and curettage
B. intravenous conjugated estrogens
C. iron supplementation
D. oral contraceptive pills
E. pregnancy testing

Correct Answer: E

The best initial step in the evaluation and management of the adolescent in the vignette would be pregnancy testing. Clinicians should first consider the possibility of pregnancy in the initial evaluation of a patient with abnormal vaginal bleeding because pregnancy complications such as ectopic pregnancy can be life-threatening.

Dysfunctional uterine bleeding, also referred to as abnormal uterine bleeding, is a common menstrual complaint among adolescent girls. It is defined as irregular or prolonged vaginal bleeding in the absence of structural pathology. Typical menstrual cycles vary from 21 to 35 days long, with 3 to 7 days of bleeding and 20 to 80 mL of blood loss per cycle. An excessive amount of bleeding is defined as menorrhagia. Metrorrhagia is irregular bleeding; menometrorrhagia is heavy and irregular bleeding.

The differential diagnosis for abnormal vaginal bleeding is broad, and includes abnormal uterine bleeding, pregnancy-related complications, infections (eg, cervicitis, endometritis), bleeding disorders, endocrinopathies, structural abnormalities, systemic diseases, and medications. Abnormal uterine bleeding occurs because of a maturational delay in the negative feedback loop, whereby rising estrogen levels suppress follicle-stimulating hormone secretion. The most common cause of abnormal bleeding in an adolescent girl is abnormal uterine bleeding caused by a constantly proliferative endometrium that irregularly sheds tissue when the feedback mechanism is immature.

The treatment of abnormal bleeding is largely determined by the severity of anemia. Surgical intervention, such as dilation and curettage, is rarely indicated; medical management with the goal of endometrial stabilization (eg, intravenous conjugated estrogens, oral contraceptive pills) is preferred. Iron replacement is another important aspect of medical management.

PREP Pearls

- Dysfunctional uterine bleeding, also referred to as *abnormal uterine bleeding*, is irregular or prolonged vaginal bleeding in the absence of structural pathology.
- Clinicians should first consider the possibility of pregnancy in the initial evaluation of a patient with abnormal vaginal bleeding, because pregnancy complications, such as ectopic pregnancy, can be life threatening.
- Medical management with the goal of endometrial stabilization is preferred.

ABP Content Specifications(s)

- Plan the appropriate management of dysfunctional uterine bleeding
- Plan the appropriate evaluation of dysfunctional uterine bleeding
- Recognize the various etiologies of menometrorrhagia
- Formulate a differential diagnosis of dysfunctional uterine bleeding

Suggested Readings

- Gray SH. Menstrual disorders. *Pediatr Rev*. 2013;34(1):6-18. doi: http://dx.doi.org/10.1542/pir.34-1-6.
- Mitan LAP, Schwartz BI. Abnormal uterine bleeding. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. *Neinstein's Adolescent and Young Adult Health Care: A Practical Guide*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:412-214.

Question 270

A 10-year-old girl is brought to your office for follow-up of learning problems. Her parents have worked closely with her teacher to implement classroom accommodations and a modified workload. She is receiving specialized academic instruction to target her difficulties with reading. Her parents have begun a reminder and reward system for homework and chores. Despite these efforts, their daughter continues to struggle with inattention and academic performance. Her parents are not interested in prescription medication and ask which special diet or other nonpharmacologic treatment is most likely to help.

Of the following, the BEST response to the parents' question is

A. electroencephalographic biofeedback
B. a restricted sugar diet
C. sensory integration techniques
D. vision therapy
E. zinc supplementation

Correct Answer: A

Although none of the treatments listed have sufficient high-quality research needed to be established as a standard-of-care, electroencephalographic biofeedback (neurofeedback) has the most scientific evidence supporting its efficacy. In the American Academy of Pediatrics' (AAP) *Addressing Mental Health Concerns in Primary Care: A Clinician's Toolkit*, biofeedback is listed as an evidence-based child and adolescent psychosocial intervention for attention and hyperactivity behaviors. Neurofeedback uses technology that monitors specific brain waves to allow the patient to train their brain to function more efficiently.

Complementary and alternative (CAM) treatments are frequently used in children, particularly in those with special healthcare needs. Complementary therapies are those therapies that are used along with conventional therapies, whereas alternative therapies are those used instead of conventional therapies. The CAM treatments commonly considered for learning and behavioral problems such as dyslexia and attention-deficit/hyperactivity disorder (ADHD) include dietary modifications or supplements, vision therapy, and sensory integration treatments.

Dietary treatments for conditions such as ADHD have included sugar-restricted, additive/preservative-free (Feingold diet), oligoantigenic/elimination, and polyunsaturated fatty acid supplements. Whereas parents often report increased hyperactivity after their children consume sugar, multiple controlled studies have not supported this claim in children with or without ADHD. The Feingold diet, in which artificial colors, flavors, preservatives, and salicylates are removed, has not been supported by research. Studies of diets eliminating food antigens or allergens and studies of omega-3-fatty acid supplements have had mixed results. Zinc supplementation has been shown to improve ADHD symptoms in Middle Eastern children with endemic zinc deficiency, but its role in treating ADHD in other children is unclear.

Sensory integration therapy, using tools such as brushes, swings, and balls, is typically provided by occupational therapists to address problems managing or processing sensory inputs (eg, tactile, vestibular, proprioceptive). These difficulties are seen in some children with ADHD, autism spectrum disorders, and anxiety disorders. Sensory integration therapy is based on the concept that problems with development, learning, and emotional regulation occur when the body is unable to handle sensory inputs from the environment appropriately. It has been difficult to establish sufficient evidence for sensory integration therapy due to lack of standardized diagnostic criteria, standardized treatment, and studies with small sample sizes. The AAP specified in a 2012 policy statement that sensory processing disorder generally should not be diagnosed and that other developmental and behavioral disorders (eg, autism spectrum disorders, ADHD, developmental coordination disorders, childhood anxiety disorders) must be considered instead.

Families have used vision-based treatments such as tinted filters or lenses, muscle and ocular pursuit-and-tracking exercises, and vision therapy to treat learning disabilities. However, children with learning disabilities do not differ from children without learning disabilities in their ocular health and function. There is insufficient evidence that subtle eye or vision problems, such as refractive errors or jerky eye movements, affect the degree of learning disability. These

therapies do not address the impairment in phonologic processing underlying dyslexia or the difficulties in understanding and retrieval of basic math facts involved in learning disabilities in mathematics. For these reasons, the AAP, the American Academy of Ophthalmology, the American Association for Pediatric Ophthalmology and Strabismus, and the American Association of Certified Orthoptists have recommended against using these vision-based treatments to treat learning disabilities.

Data are limited and results have been inconsistent for most CAM treatments. Studies have been limited by small sample size, lack of placebo or control group, lack of randomization, and poor study design. There are few randomized controlled trials of sufficient size to make appropriate conclusions about the efficacy of these treatments. However, CAM treatments provide parents with hope for improvement or cure and a feeling of control over their child's condition. Parents can implement these interventions independently and may find the adverse effects more acceptable than those of conventional treatments. Families may be motivated to use CAM treatments when their child has a chronic condition that does not have a cure and when conventional treatment may not have been fully successful.

Pediatricians have an essential role in guiding families in developing a comprehensive treatment plan for their children. Pediatricians should ask in a nonjudgmental manner about the use of CAM treatments because most parents do not volunteer this information. Pediatricians should be familiar with commonly used CAM treatments and should consider both the safety and the evidence for their effectiveness in discussions with families. Pediatricians can recommend therapies that are safe and effective, tolerate therapies that are safe but may not be effective, monitor closely or discourage therapies that are not safe but are effective, and discourage therapies that are not safe or effective. Treatments with CAM should be considered in relation to conventional treatments, but should not replace or delay proven conventional treatments that are safe and more efficacious. They should be reasonable in both the time commitment of the family and cost. When using CAM, the pediatrician should guide families in determining specific treatment goals, a process to monitor and track change, and a time frame for determining if the therapy is helpful in achieving the targets. Throughout these discussions, pediatricians should respect the family's beliefs, values, and goals, and should consider the family's perspective.

PREP Pearls

- Complementary therapies are those therapies that are used along with conventional therapies, whereas alternative therapies are those therapies used instead of conventional therapies.
- Data are limited and results have been inconsistent for most complementary and alternative medicine treatments. Studies have been limited by small sample size, lack of placebo or control group, lack of randomization, and poor study design. There are few randomized controlled trials of sufficient size to make appropriate conclusions about the efficacy of these treatments.
- Pediatricians can recommend therapies that are safe and effective, tolerate therapies that are safe but may not be effective, monitor closely or discourage therapies that are not safe but are effective, and discourage therapies that are not safe and not effective.

ABP Content Specifications(s)

- Evaluate available data regarding dietary or controversial perceptual/therapeutic interventions for children with learning and behavioral problems, and provide appropriate guidance while understanding a family's motivation for seeking such treatment

Suggested Readings

- American Academy of Pediatrics. Sensory integration therapies for children with developmental and behavioral disorders. *Pediatrics*. 2012;129(6):1086-1189. doi: http://dx.doi.org/10.1542/peds.2012-0876.
- Galicia-Connolly EZ, Shamseer L, Vohra S. Complementary, holistic, and integrative medicine: therapies for learning disabilities. *Pediatr Rev.* 2011;32(2):e18-e24. doi: http://dx.doi.org/10.1542/pir.32-2-e18.
- Handler SM, Fierson WM, Section on Ophthalmology and Council on Children with Disabilities, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orhoptists. Learning disabilities, dyslexia, and vision. *Pediatrics*. 2011;127(3):e818-e856. doi: http://dx.doi.org/10.1542/peds.2010-3670.
- Kember KJ, Vohra S, Walls R. The use of complementary and alternative medicine in pediatrics. *Pediatrics*. 2008;122(6)1374-1386. doi: http://dx.doi.org/10.1542/peds.2008-2173.
- Millichap JG, Yee MM. The diet factor in attention-deficit/hyperactivity disorder. *Pediatrics*. 2012;129(2):330-337. doi: http://dx.doi.org/10.1542/peds.2011-2199.

Question 271

A 12-year-old previously healthy girl presents to your office for evaluation 4 hours after her friend's pet cat scratched her on the right forearm multiple times and bit her on the right hand. The girl takes no medications and she has no known allergies. A review of her chart reveals that she has had 4 prior DTaP immunizations; the most recent one was when she was 5 years of age. The girl is afebrile and appears well. Her vital signs are within normal limits for her age. Her physical examination is significant only for multiple superficial linear abrasions on her right forearm, and a 4-mm puncture wound on the dorsum of her right hand with no surrounding erythema, warmth, or tenderness. There is no bleeding from the wound. The girl tells you that she washed the wound immediately with soap and water, and you also thoroughly clean the wound in your office.

Of the following, the MOST appropriate treatment for this girl is

A. oral amoxicillin-clavanulate
B. Tdap
C. Tdap and oral amoxicillin-clavulanate
D. Tdap and tetanus immune globulin (TIG)
E. Tdap, TIG, and oral amoxicillin-clavulanate

Correct Answer: C

The girl in the vignette presents for care after sustaining a puncture wound to her right hand from a cat bite. She completed a series of 4 DTaP immunizations earlier in childhood, and her last dose was given about 7 years ago. Although the wound on her right hand does not appear to be infected, she is at high risk for wound infection, given that her wound resulted from a cat bite. The most appropriate care regimen for this patient includes administration of Tdap and oral amoxicillin-clavulanate.

Puncture wounds are a common type of injury sustained by children, accounting for approximately 3% to 5% of all traumatic injuries presenting to pediatric emergency departments. Although most children sustaining puncture wounds have uncomplicated courses, serious complications can arise. It is essential for all pediatric providers to identify the sequelae of puncture wounds of various etiologies, as well as to plan the appropriate management for these injuries.

Puncture wounds may arise from a variety of circumstances. While over half involve the plantar surface of the foot, other affected sites include the legs, arms, hands, and, less commonly, the trunk and head. Glass, wood, plastic, and other metal objects can be involved as the offending objects. In addition, puncture wounds may arise from mammalian bites, as in the adolescent in the vignette. The majority of bite wounds are caused by dogs and cats.

Of the complications that may arise from puncture wounds, development of infection is the most common. Wound infection is more likely when puncture wounds are deep, when there is more devitalized tissue, and in cases involving retained foreign bodies. Other factors that have been identified as increasing risk for puncture wound infection include wounds involving the forefoot and hand, punctures occurring through shoes, and an underlying history of diabetes mellitus or other disorders compromising immunity. Puncture wounds arising from bites, particularly cat bites, are also complicated by the frequent development of infection, occurring in 30% to 80% of cases. In contrast to dogs (who have broader, flatter teeth that primarily involve the superficial tissues and become infected in no more than 25% of cases), cats have sharper teeth that lead to deeper inoculation of bacteria and subsequent infection of the soft tissues and/or underlying joints. Human bites are also high risk in terms of subsequent development of wound infections.

Bacterial agents most commonly implicated in puncture wound infections include *Staphylococcus aureus*, β-hemolytic streptococci, and anaerobic bacteria. Infections from *Pasteurella multocida* are often seen in puncture wounds arising from animal bites. *Pseudomonas aeruginosa* has been commonly isolated in patients sustaining plantar puncture wounds while wearing tennis shoes at the time of injury. Aside from infection, complications that may arise from puncture wounds include retained foreign bodies, injury to neurovascular structures, and tattooing of skin from debris, which can lead to permanent cosmetic deformity.

For all children presenting with puncture wounds, a careful history is essential to guide appropriate management and to identify risk factors for complications. Physical examination should include a complete evaluation of the injured area, including assessment of circulation and motor function distal to the wound. The wound must be inspected for retained foreign material and signs of infection. Diagnostic imaging should be obtained if there is any consideration that a foreign body may be present. A plain radiograph should pick up most metal or glass particles, as well as animal teeth fragments.

Tetanus immunization status should be reviewed for all children presenting with puncture wounds, and tetanus-containing immunizations and tetanus immune globulin should be administered when indicated. While any open wound may be a possible source for tetanus infection, those wounds contaminated with dirt, fecal matter, or saliva are at increased risk. Puncture wounds, along with crush injuries, avulsions, burns, and wounds involving necrotic tissue, are particularly prone to tetanus infection, so immunization status is of high importance. Administration of tetanus immunoglobulin is recommended for those patients with "high-risk" wounds (such as those contaminated with dirt, feces, soil, and/or saliva; puncture wounds; avulsions; crush injury-related wounds; burns; and frostbite) who have received 3 or fewer tetanus toxoid-containing immunizations (or who have an unknown immunization history). Guidelines for tetanus prophylaxis as a component of wound management (including puncture wound management) are summarized in Item C271 .

Item C271. Guidelines for Tetanus Prophylaxis as a Component of Wound Management.

History of tetanus toxoid (doses)	Clean, minor wounds		All other wounds	
	DTaP, TdaPP, OR TD	TIG	DTaP, TdaP, OR TD	TIG
Fewer than 3 or unknown	Yes	No	Yes	Yes
3 or more	**No if <10 years** since last tetanus-containing vaccine dose	No	**No if <5 years** since last tetanus-containing vaccine dose	No
	Yes if >10 years since last tetanus-containing vaccine dose	No	**Yes if >5 years** since last tetanus-containing vaccine dose	No

Reprinted with permission from Kimberlin DW, Brady, MT, Jackson, MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL American Academy of Pediatrics; 2015:775

Uninfected puncture wounds should be irrigated with copious amounts of sterile saline, cleansed with an antiseptic solution, and debrided whenever jagged edges are present. Skin should be cleansed of foreign material to avoid permanent tattooing. Foreign bodies should be removed to reduce the risk of wound infection, reduce pain, and avoid subsequent damage to underlying neurovascular structures.

Although prophylactic antibiotic coverage is *not* required for all puncture wounds, it is recommended for puncture wounds that are grossly contaminated, those with devitalized tissue, puncture wounds to the feet occurring through shoes (due to risk of infection with *Pseudomonas*), and many mammalian bite wounds, especially cat and human. Administration of Tdap immunization only would not be the most appropriate course of management for the adolescent in the vignette. She has a puncture wound to her hand from a cat bite that puts her at high risk for development of infection. Initiation of prophylactic antibiotics should be a component of her management.

Administration of tetanus immunoglobulin would not be necessary for the patient in the vignette because she has a confirmed history of receiving more than 3 immunizations containing tetanus toxoid.

Administration of amoxicillin-clavulanate only would not be appropriate. Although the adolescent in the vignette did receive 4 doses of DTaP earlier in her childhood, it has been more than 5 years since she received the last dose of a tetanus-toxoid containing vaccine. Since cat bite wounds are considered “higher risk” in terms of infection potential, immunization with Tdap is indicated at this time for the patient in the vignette.

PREP Pearls

- Of the complications that may arise from puncture wounds, development of infection is the most common.
- Aside from infection, less common complications that may arise from puncture wounds include retained foreign bodies, injury to neurovascular structures, and tattooing of skin from debris, which can lead to permanent cosmetic deformity.
- Administration of tetanus immunoglobulin is recommended for those patients with “high-risk” wounds (such as those contaminated with dirt, feces, soil, and/or saliva; puncture wounds; avulsions; crush injury-related wounds; burns; and frostbite) who have received 3 or fewer tetanus toxoid-containing immunizations (or who have an unknown immunization history).

ABP Content Specifications(s)

- Identify the sequelae of puncture wounds of various etiologies
- Plan the appropriate use of tetanus immune globulin

Suggested Readings

- Black KD, Cico SJ, Caglar D. Wound management. *Pediatr Rev.* 2015;36(5):207-215. doi: http://dx.doi.org/10.1542/pir.36-5-207.
- Spiro DM, Zonfrillo MR, Meckler GD. Wounds. *Pediatr Rev*. 2010;31(8):326-334. doi: http://dx.doi.org/10.1542/pir.31-8-326.

Question 272

A 40-year-old pregnant nurse presents to the occupational health clinic for annual influenza vaccination. She works at a teaching hospital and has recently been assigned to the bone marrow transplant unit. She has a history of asthma and has had hives when she consumes eggs. She inquires about appropriate influenza prevention.

Of the following, the MOST appropriate preventative measure for this nurse is

A. amantadine orally during influenza season
B. inactivated influenza vaccine
C. live attenuated influenza vaccine
D. no immunizations or oral prophylaxis
E. oseltamivir orally during influenza season

Correct Answer: B

The most appropriate preventative measure for the nurse in the vignette is inactivated influenza vaccine. Immunization is the best preventative measure against influenza.

As a matter of patient safety, the American Academy of Pediatrics recommends mandatory influenza vaccination for all healthcare providers. Vaccination rates need to reach at least 90% in healthcare personnel in order to prevent healthcare-associated influenza infections. Voluntary vaccination programs fail to achieve such rates, thus necessitating the recommendation for mandatory programs.

The nurse in the vignette has 3 contraindications to live attenuated influenza vaccine (LAIV): pregnancy, asthma, and egg allergy. Of note, her egg allergy alone does not preclude her from receiving inactivated influenza vaccine because her reaction is mild. For severe (anaphylactic) reactions to eggs, consultation with an allergist prior to vaccination with inactivated vaccine is recommended. Despite her inability to receive LAIV, she remains eligible for inactivated influenza vaccine.

While antivirals, including oseltamivir, are recommended for chemoprophylaxis in outbreak settings for certain high-risk groups, they are not recommended as a substitute for vaccination. Furthermore, amantadine is no longer recommended for influenza infections for 2 reasons: high levels of resistance against the adamantanes in influenza A viruses and lack of activity against influenza B viruses.

PREP Pearls

- Immunization is the best preventative measure against influenza.
- Mild allergic reactions to eggs are not considered a contraindication to vaccination with inactivated influenza vaccine.
- Antivirals are not recommended as a substitute for vaccination.

ABP Content Specifications(s)

- Recognize the importance of annual influenza immunizations for medical office and hospital personnel and medical staff

Suggested Readings

- American Academy of Pediatrics. Influenza. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report Of The Committee On Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:476-493.
- Committee on Infectious Diseases. Influenza immunization for all health care personnel: keep it mandatory. *Pediatrics*. 2015;136(4):809-818. doi: http://dx.doi.org/10.1542/peds.2015-2922.
- Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2015-2016. *Pediatrics*. 2015;134(4):1-17. doi: http://dx.doi.org/10.1542/peds.2015-2920.

Question 273

You are seeing a 2-year-old girl in your office for evaluation of diarrhea, which has persisted for 8 weeks. Her mother describes 5 to 7 liquid stools per day, with no visible blood. She denies any abdominal symptoms, fevers, or constitutional symptoms. There was no recent travel, well water use, exposure to reptiles or ill contacts, or recent viral illness. On physical examination, the girl appears well nourished and well hydrated, and is growing appropriately.

Of the following, this girl's MOST likely diagnosis is

A. celiac disease
B. chronic nonspecific diarrhea
C. cow milk protein intolerance
D. infectious colitis
E. inflammatory bowel disease

Correct Answer: B

The young girl in the vignette has chronic nonspecific diarrhea, also known as toddler's diarrhea. Chronic nonspecific diarrhea affects approximately 15% of children, with onset between 6 and 36 months of age. It is defined by intermittent or regular passage of 2 to 6 watery bowel movements daily, typically during the daytime. Stools will contain mucus and undigested food particles. There is no blood in the stools and infectious evaluation is negative. Affected children continue to grow appropriately. Their review of systems is negative, with the exception of the stooling pattern. Chronic nonspecific diarrhea is a functional process without inflammation, maldigestion, or malabsorption. Treatment involves control of symptoms through increased fiber and limiting sucrose and fructose in the diet.

The evaluation of a child with chronic diarrhea should be determined by the clinical situation, and may include testing stool for fecal fat, reducing substances, pH, cultures, ova and parasites, and occult blood. Endoscopy and/or colonoscopy may be considered, depending on the clinical picture. In the case of chronic nonspecific diarrhea, all studies will be negative.
The child in the vignette has no other associated symptoms, or any evidence of failure to thrive, that would suggest a diagnosis of celiac disease. Cow milk protein intolerance is unlikely to develop at this age. Infectious colitis is typically associated with profuse, voluminous diarrhea with or without blood, and children with infectious colitis are often quite ill. Inflammatory bowel disease typically presents with an ill-appearing patient who, in addition to diarrhea, may suffer from fevers, rash, joint pain, weight loss, and often presents with abnormal laboratory values such as anemia and elevated inflammatory markers.

PREP Pearls

- Toddler's diarrhea, or chronic nonspecific diarrhea, is a functional gastrointestinal disease.
- The prognosis for children with chronic nonspecific diarrhea is excellent, with anticipated resolution of symptoms by school age.
- The evaluation of chronic nonspecific diarrhea includes testing stool for fecal fat, reducing substances, pH, cultures, ova and parasites, and occult blood, all of which will be negative. Endoscopy and colonoscopy may be considered if clinically indicated.

ABP Content Specifications(s)

- Recognize the clinical features associated with chronic nonspecific diarrhea, and the prognosis for affected patients
- Plan the initial evaluation of an infant with protracted diarrhea
- Identify possible causes of chronic nonspecific diarrhea

Suggested Readings

- Di Lorenzo C. Other functional gastrointestinal disorders in infants and young children. *J Pediatr Gastroenterol Nutr*. 2013;57 Suppl 1:S36-S38. doi: http://dx.doi.org/10.1097/01.mpg.0000441933.15093.c3.
- Guarino A, Lo Vecchio A, Berni Canani R. Chronic diarrhoea in children. *Best Pract Res Clin Gastroenterol.*2012;26(5):649-661. doi: http://dx.doi.org/10.1016/j.bpg.2012.11.004.
- Zella GC, Israel EJ. Chronic diarrhea in children. *Pediatr Rev.* 2012;33(5):207-218. doi: http://dx.doi.org/10.1542/pir.33-5-207.

Question 274

A 13-year-old adolescent is brought to the office for evaluation of a rash on his chest and back that developed 2 weeks ago. The rash is pruritic, but the patient is well in other respects and takes no medications. His temperature is 37°C and other vital signs are normal. His physical examination is remarkable only for a rash on the chest and back with sparing of the extremities, face, and groin (Q274A , Q274B).

Q274A: Rash as described for the boy in the vignette. Lesions are shown involving the chest and abdomen. Courtesy of D Krowchuk

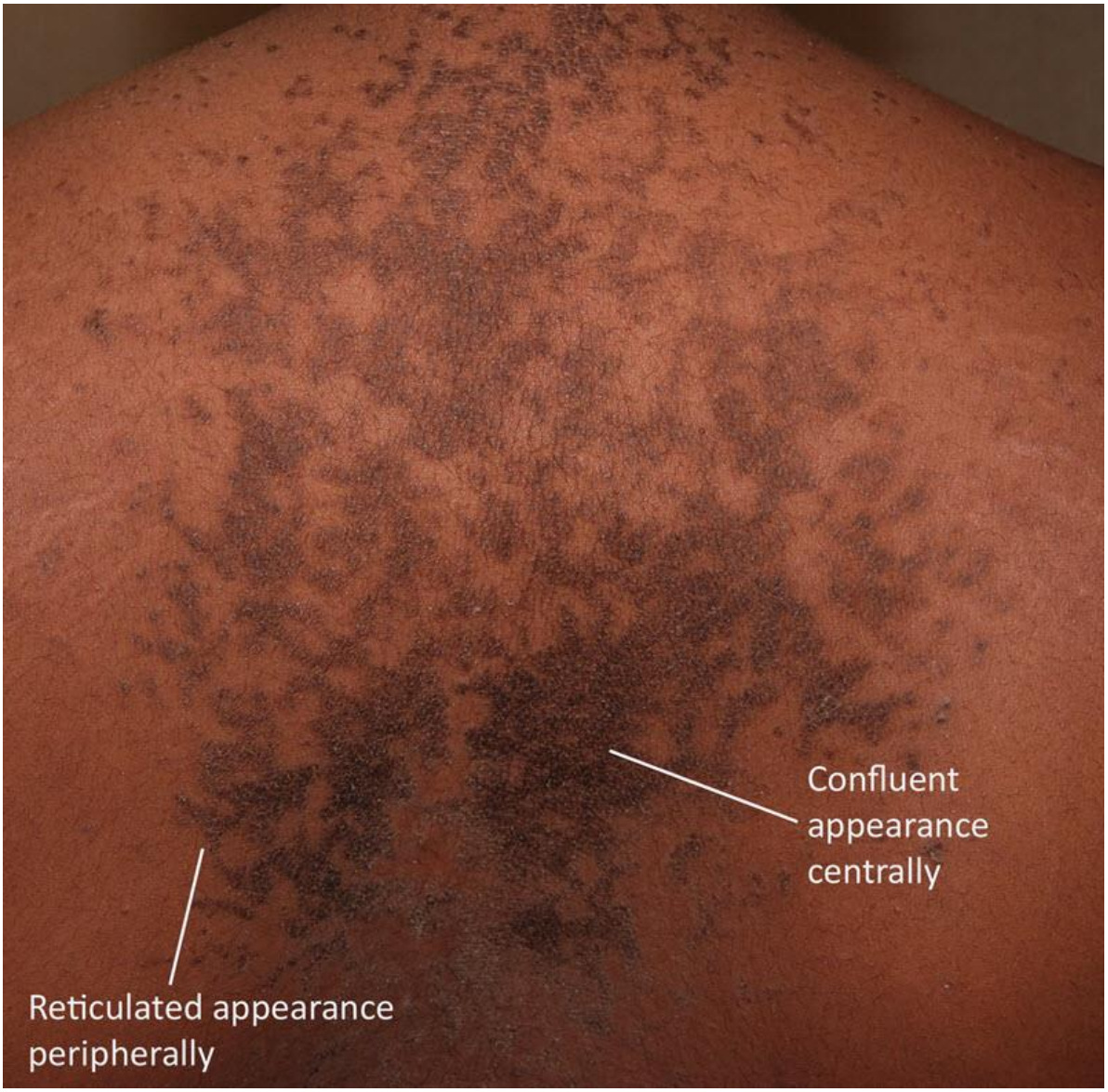
Q274B: Close-up view of the lesions on the left chest. Courtesy of D Krowchuk

Of the following, the MOST appropriate treatment is
A. griseofulvin orally
B. hydroxyzine orally
C. minocycline orally
D. penicillin intramuscularly
E. selenium sulfide topically

Correct Answer: B

The adolescent in the vignette has an eruption involving the trunk. Individual lesions are oval thin plaques oriented with long axes parallel to Langer lines of skin stress (C274A). The plaques have scale that is located at the trailing edge of lesions, unlike at the leading edge, as is the case in tinea corporis. Together, these features are characteristic of pityriasis rosea (PR), and accordingly, symptomatic management with hydroxyzine is indicated. Several other disorders cause eruptions that are limited to or prominently involve the trunk. Among these are confluent and reticulated papillomatosis (often treated with minocycline) (C274B), secondary syphilis (treated with intramuscular penicillin) (C274C), tinea versicolor (treated with topical selenium sulfide) (C274D), and tinea corporis (if multiple lesions are present, oral treatment is needed with griseofulvin).

C274A: The lesions of pityriasis rosea are aligned with long axes oriented parallel to lines of skin stress. Courtesy of D Krowchuk



C274B: Confluent and reticulated papillomatosis: papules, patches, or thin plaques located on the trunk, especially the central chest. Individual lesions have a rough texture. Courtesy of D Krowchuk

C274C: Secondary syphilis: Widespread erythematous macules and papules. The extremities, including the palms and soles are involved. Patients often are ill with fever, malaise, and generalized lymphadenopathy. Courtesy of D Krowchuk

C274D: Tinea versicolor: round, hyper- or hypopigmented, scaling macules located on trunk. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL; American Academy of Pediatrics: 2012

Pityriasis rosea is a self-limited papulosquamous disorder (ie, lesions are elevated and have scale) that has a characteristic rash and course. Clinical and epidemiologic data support an infectious etiology. Human herpesvirus-7 and -6 have been implicated and PR and PR-like eruptions have been reported following administration of several vaccines. Pityriasis rosea usually occurs in the spring and fall, and most often affects adolescents and young adults. In as many as 80% of patients, the initial lesion is a round or oval erythematous scaling patch with central clearing (herald patch) (C274E). The herald patch may be confused with tinea corporis, although border elevation is common in the latter. Within 2 weeks, a generalized eruption appears that is composed of erythematous papules and plaques (C274A). Since lesions are arranged along lines of skin stress, they may mimic the boughs of a fir tree ("Christmas-tree" appearance) (C274F). In individuals of color, the eruption may differ: it may have an "inverse" distribution (with lesions concentrated on the extremities and relative sparing of the trunk) or lesions may be papules with fewer plaques (C274G). New PR lesions appear for 2 to 3 weeks and the eruption resolves in 4 to 8 weeks.

C274E: Herald patch of PR: erythematous, round or oval, with scale at the trailing edge. Courtesy of D Krowchuk

C274F: On the back, the alignment of pityriasis rosea lesions along lines of skin stress (and the ribs) may mimic the appearance of the boughs of a fir tree ("Christmas-tree" appearance). Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL; American Academy of Pediatrics: 2012

C274G: An African-American child with pityriasis rosea. There are numerous small papules. Reprinted with permission from Krowchuk DP, Mancini AJ, eds. Pediatric Dermatology. A Quick Reference Guide. 2nd ed. Elk Grove Village, IL; American Academy of Pediatrics: 2012

Most individuals with PR require no therapy. If pruritus is significant, a topical corticosteroid may be applied or a sedating antihistamine may be taken at bedtime. An emollient containing phenol or menthol may be applied as needed as a counter irritant to mask the perception of pruritus. Judicious sun exposure may reduce pruritus and hasten resolution of the eruption. Both erythromycin and acyclovir have been proposed as possible treatments, although current evidence does not support their use.

PREP Pearls

- The lesions of pityriasis rosea are oval scaling thin plaques, with the long axes oriented parallel to lines of skin stress.
- In pityriasis rosea, the scale is located on the trailing edge of lesions.
- On the back, pityriasis rosea lesions appear along lines of skin stress and the ribs, and may mimic the appearance of the boughs of a fir tree ("Christmas-tree" appearance).
- In individuals of color, pityriasis rosea may have an "inverse" distribution, with plaques or papules concentrated on the extremities and relative sparing of the trunk.

ABP Content Specifications(s)

- Recognize the clinical findings associated with pityriasis rosea, and manage appropriately

Suggested Readings

- Chuh AA, Dofitas BL, Comisel G, et al. Interventions for pityriasis rosea. *Cochrane Database Syst Rev*. 2007;18(2):CD005068. doi: http://dx.doi.org/10.1002/14651858.CD005068.pub2.
- Drago F, Vecchio F, Rebora A. Use of high-dose acyclovir in pityriasis rosea. *J Am Acad Dermatol*. 2006;54(1):82-85. doi: http://dx.doi.org/10.1016/j.jaad.2005.06.042.
- Krowchuk DP, Mancini AJ. Tinea corporis. *Pediatric Dermatology: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012:241-246.
- Sharma PK, Yadav TP, Gautam RK, Taneja N, Satyanarayana L. Erythromycin in pityriasis rosea: a double-blind, placebo-controlled clinical trial. *J Am Acad Dermatol*. 2000;42(2 Pt 1):241-244. doi: http://dx.doi.org/10.1016/S0190-9622(00)90132-4.

Question 275

A 3-month-old infant is brought to your office because he has been very irritable, and feeding poorly over the past 2 days. He vomited once this morning. The infant has had no fever or symptoms of an upper respiratory infection. He is a full-term infant with no significant past medical history and he has been growing and developing appropriately. His mother just returned to work last week and his father, who is unemployed, has been caring for the infant during the day. She thinks that the baby's fussiness may be due to the recent change in his routine.
In your office, the baby's vital signs include a temperature of 37.2°C, heart rate of 160 beats/min, respiratory rate of 36 breaths/min, and pulse oximetry of 96% on room air. On physical examination, the baby is very fussy and the mother is having difficulty consoling him. There are several circular bruises on his right forehead and left forearm. The remainder of his physical examination is unremarkable. His mother denies any history of trauma.
You advise the baby's mother that he should undergo further evaluation in the emergency department because of his concerning symptoms of irritability, poor feeding, vomiting, and bruising. Your differential diagnosis includes child abuse.

At this point, the MOST appropriate manner to proceed given your concern for abuse is to

A. discuss with the mother, but do not report to child protective services unless additional injuries are identified
B. discuss with the mother, but leave reporting to child protective services to emergency department providers to avoid conflicting information
C. report to child protective services and discuss with the mother during the current office visit
D. report to child protective services, but do not discuss with the mother until the emergency department evaluation has been completed
E. report to child protective services only if the mother grants consent due to federal privacy legislation

Correct Answer: C

The infant in the vignette presents with a clinical picture that is concerning for abusive head trauma, along with unexplained bruising that should raise suspicion for child abuse. Further evaluation in the emergency department is indicated at this time. The most appropriate manner to proceed given the concerns for abuse is to report the concerns to Child Protective Services and discuss them with the mother during the current office visit.

Child abuse is unfortunately quite common and can result in significant morbidity and even mortality. For this reason, prompt reporting and appropriate management of cases of suspected child abuse is essential to the health and safety of children.

All physicians should understand their duty and ethical obligation to report suspected child abuse and neglect and to provide appropriate guidance and support to families during an investigation. Identifying and reporting suspected child abuse to Child Protective Services can be one of the most challenging responsibilities for pediatricians who have a unique and important opportunity to recognize the signs and symptoms of abuse and intervene in order to protect victims.

When pediatricians have a reasonable suspicion that a child is a victim of abuse, the law mandates reporting to Child Protective Services. Failure to report suspected abuse can result in further injury to the patient involved (and to other children in the same environment) and can result in civil or criminal penalties for the physician. It is important to discuss the concern and requirement to report suspected child abuse with the child's parents whenever a pediatrician reports a concern to Child Protective Services. While such a discussion may be very difficult, it will enable more honest, open dialogue with parents during and following the ensuing investigation. In discussing suspected child abuse with parents, it is helpful to explain concern about an injury while not placing blame and to inform the parents that a report to Child Protective Services is required by law. Preparing the family for what will happen next is important. Though some families may choose not to return to a pediatrician's practice once a report is made, pediatricians should continue to offer support to parents throughout the entire process. It is important for pediatricians to realize that the parents bringing the child to medical attention may or may not be the perpetrators responsible for inflicting the identified injuries.

For the infant in the vignette, deferring reporting of suspected abuse to Child Protective Services until additional injuries are identified is not an appropriate approach. The presence of unexplained forearm and forehead bruising in this nonambulatory 3-month-old infant should prompt reporting to Child Protective Services, whether or not any additional injuries are identified on further evaluation. Any injury to a young preambulatory infant, including bruises, mouth injuries, fractures, and intracranial or abdominal injury, is suggestive of abuse and should be reported to Child Protective Services. Bruises are the most common and apparent injuries due to physical abuse, but are missed as a "sentinel injury" in nearly half of fatal and near-fatal abusive injuries. Even if the infant's further evaluation in the emergency department is negative for additional occult injuries, this should not be interpreted as false reassurance that child abuse can be ruled out.

Leaving it up to emergency department providers is not the most appropriate course of action, even if concerns are discussed with the mother during the office visit. If any physician suspects that a patient is a victim of abuse, transferring the child to another physician or facility does not release him or her from the requirement to report suspected abuse. As an advocate for children, the pediatrician must report suspected abuse to the appropriate Child Protective Services and law enforcement authorities, regardless of the decision to transfer the child for further care. Reporting suspected abuse without discussing with the mother is also not the most appropriate course of action. As explained previously, it is important for pediatricians to discuss the need to report suspected child abuse to Child Protective Services with the child's parents whenever possible.

Finally, obtaining consent from the patient's mother to report suspected child abuse is unnecessary and does not need to occur before making a report. The Health Insurance Portability and Accountability Act rules allow disclosure of protected health information to Child Protective Services without legal guardian authorization when the physician makes a mandatory report.

PREP Pearls

- Reporting to Child Protective Services is mandated by law whenever pediatricians have a reasonable suspicion that a child is a victim of abuse. Failure to report suspected abuse can result in further injury to the patient involved and civil or criminal penalties for the physician.
- It is important to discuss the concern and requirement to report child abuse to Child Protective Services with the child's parents.
- Any injury to a young preambulatory infant, including bruises, mouth injuries, fractures, and intracranial or abdominal injury are suggestive of abuse and should be reported to Child Protective Services.
- If any physician suspects that a patient is a victim of abuse, transferring the child to another physician or facility for further care does not release him or her from the requirement to report suspected abuse.

ABP Content Specifications(s)

- Understand the physician’s duty and ethical obligation to report suspected child abuse or neglect
- Provide apporpriate guidance and support to a family during an investigation of child abuse or neglect

Suggested Readings

- Christian CW, American Academy of Pediatrics Committee on Child Abuse and Neglect. The evaluation of suspected child physical abuse. *Pediatrics*. 2015;135(5):e1337-e1354. doi: http://dx.doi.org/10.1542/peds.2015-0356.
- Wood JN, Callahan JM, Christian CW. Child abuse/assault. In: Shaw KN, Bachur RG, Chamberlain J, Lavelle J, Nagler J, Shook JE, eds. *Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2015:657-670.

Question 276

A 7-year-old girl is admitted to the hospital for an asthma exacerbation. The girl typically experiences moderate exacerbations with viral illnesses and has been treated in the emergency department on 3 occasions over the past 6 months. She has a chronic dry cough that is worse with exertion, and at night her coughing wakes her parents 3 times per week. She routinely uses albuterol before gymnastics, and additional short-acting b-agonist therapy 4 to 5 times per week for dyspnea and fatigue with vigorous exertion.

On admission, the girl is treated with 6 puffs of albuterol every 2 hours and 2 mg/kg of prednisone daily. Overnight, she is transferred to the pediatric intensive care unit (PICU) for increased oxygen requirement, tachypnea, and anxiety. In the PICU, she has mild tachycardia, and is found to be in moderate respiratory distress with a respiratory rate of 36 breaths/min and suprasternal and substernal retractions. Her oxygen saturation is 92% on 0.5 L/min oxygen via nasal cannula. Lung auscultation reveals a prolonged expiratory phase with diffuse expiratory and end-inspiratory wheezing, with no focal crackles. The remainder of her physical examination is unremarkable. Chest radiography demonstrates a diffuse hazy opacification of the right hemithorax with mediastinal shift toward the right side and hyperinflation.

Of the following, the MOST likely cause of this girl's findings is

A. atelectasis due to mucus plugging
B. atelectasis due to acute foreign body aspiration
C. pneumonia due to chronic foreign body aspiration
D. pneumonia due to Mycoplasma infection
E. tension pneumothorax

Correct Answer: A

The girl in the vignette has symptoms that are consistent with status asthmaticus, in the setting of underlying moderate persistent asthma. The radiographic findings affecting the right hemithorax, with hyperinflation and mediastinal shift toward the affected right side, suggest that volume loss or atelectasis is most likely due to mucus plugging. The most common etiology for atelectasis in status asthmaticus is mucus plugging.

According to the most recent expert guidelines, the following criteria should be used to establish a diagnosis of asthma:

- Presence of episodic symptoms of airflow obstruction or airway hyperresponsiveness
- Demonstration that airflow obstruction is at least partially reversible
- Exclusion of alternate diagnoses

In children ages 5 years or older, spirometry is recommended to demonstrate obstruction and reversibility. Reversibility is determined either by an increase in forced expiratory volume in 1 second (FEV_1) of more than or equal to 12% from baseline or by an increase of 10% or more of predicted FEV_1 after inhalation of a short-acting bronchodilator. It should be noted that FEV_1 measurements are often within normal range for children with moderate-to-severe persistent asthma, and may be an insensitive measure for making an asthma diagnosis when used in isolation. A comprehensive approach to diagnosis, incorporating the history, physical examination, risk, and pulmonary function (when applicable), is recommended.

The absence of wheezing does not preclude a diagnosis of asthma; symptoms may include exercise intolerance, chest tightness, lingering cough with viral infections, or recurrent shortness of breath. Symptoms are often worse at night, with associated sleep disruption. When making the diagnosis of asthma, alternate diagnoses associated with airway obstruction must be considered. These include, but are not limited to, tracheomalacia, foreign body aspiration, bronchopulmonary dysplasia, vascular malformations, chronic pulmonary aspiration, and vocal cord dysfunction. Once an asthma diagnosis is established, an assessment of asthma severity is required to guide treatment decisions. National Heart, Lung and Blood Institute guidelines recommend that an asthma severity assessment include presence of cough, nighttime awakening, interference with normal activities, requirement for short-acting b-agonist use, and risk assessments.

Severity assessments are based on both impairment and risk. For example, the girl in the vignette has required 3 emergency department visits in the past 6 months for asthma exacerbations. This history alone documents persistent asthma. Her cough, which wakes her parents 3 times per week, places her in the moderate-persistent level of severity. Her pretreatment course of short-acting b-agonist (SABA) for athletics is not relevant for severity classification, but her need for additional dosing of SABA to address symptoms 4 to 5 times per week places her in the mild category. Final severity classification corresponds to the highest severity assessment obtained. This girl's asthma severity assessment would therefore be regarded as moderate-persistent. Chest radiography performed during asthma exacerbations generally will not provide clinically relevant information. The most common inciting factor for an asthma exacerbation is a viral illness. Confounding the diagnosis is that findings of viral illnesses often mimic those seen in

chronic asthma. Atelectasis, or volume loss due to mucus plugging, is a common finding and may be lobar or subsegmental. Other common findings on chest radiography include peribronchial thickening and peribronchial infiltration, which reflect inflammation of the bronchial mucosa and peribronchial tissue. Chest radiography, although of low yield, may be considered when there is concern for a complication such as pneumothorax or pneumomediastinum.

Right middle lobe syndrome is described when atelectasis or an infiltrate recurrently affects the right middle lobe. This is most commonly associated with asthma. However, bronchiectasis may affect any lobe of the lung with chronic or recurrent infection. In patients with recurrent or chronic radiographic disease, bronchoscopy may be warranted to rule out foreign body aspiration or a mass lesion.

The girl in the vignette has chronic symptoms of asthma. Her age and lack of acute onset of symptoms make atelectasis due to acute foreign body aspiration less likely. Although a chronically retained foreign body may be associated with obstructive pneumonia, in this case, the volume loss seen on chest radiography is more consistent with atelectasis. *Mycoplasma* infection is a common illness associated with status asthmaticus, which may also be associated with atelectasis or infiltration. A child with tension pneumothorax would be expected to present in severe respiratory distress, often with cardiorespiratory insufficiency. Findings on chest radiograph include a lucent lung with contralateral mediastinal shift.

PREP Pearls

- Symptoms of asthma may include cough, chest tightness, and exercise intolerance; wheezing may not be a prominent clinical feature
- Severity assessments are used to guide treatment decisions and should be determined based on both asthma-related impairment and risk.
- Most children with moderate to severe persistent asthma will demonstrate a normal forced expiratory volume in 1 second on spirometric testing.
- The most common etiology for asthmatic exacerbation is a viral illness.
- Most chest radiographs obtained during asthmatic exacerbations will not yield clinically relevant information.

ABP Content Specifications(s)

- Know the classifications of asthma and their components
- Know the diagnostic criteria for asthma
- Recognize the development of atelectasis during an acute exacerbation of asthma, and manage appropriately

Suggested Readings

- Livingston GL, Holinger L, Luck SR. Right middle lobe syndrome in children. *Int J Pediatr Otorhinolaryngol.*1987;13(1):11-23.
- Narayanan S, Magruder T, Walley SC, et al. Relevance of chest radiography in pediatric inpatients with asthma. *J Asthma.* 2014;51(7):751-755. doi: http://dx.doi.org/10.3109/02770903.2014.909459.
- National Asthma Education and Prevention Program. Expert panel report 3 (EPR-3): guidelines for diagnosis and management of asthma?summary report 2007. *J Allergy Clin Immunol.* 2007;120(5 suppl):S94-S138. doi: http://dx.doi.org/10.1016/j.jaci.2007.09.029.
- Spahn JD, Cherniack R, Paull K, Gelfand EW. Is forced expiratory volume in one second the best meaure of severity in childhood asthma? *Am J Respir Crit Care Med*. 2004;169(7):784-786. doi: http://dx.doi.org/10.1164/rccm.200309-1234OE.
- Swischuk LE. Asthma attack: is a chest x-ray necessary? *Pediatr Emerg Care*. 2005;21(7):468-470.

Question 277

You are caring for a 2-year-old girl in the intensive care unit who has progressively worsening pneumonia and acute respiratory distress syndrome. The pressures required to maintain oxygenation and ventilation have been increasing. She is currently intubated with a size 4.0 mm uncuffed endotracheal tube, on pressure-controlled ventilation with the following settings: rate of 30, peak inspiratory pressure of 30 cm H_2O, positive end-expiratory pressure of 10 cm H_2O, and FiO_2 of 1.0. Exhaled tidal volumes are inadequate. Arterial blood gas results are a pH of 7.15, PCO_2 of 70 mm Hg, and PaO_2 of 50 mm Hg. There is an audible leak of air at the glottic level during inspiration. When peak inspiratory pressure is increased to 35 cm H_2O, the leak becomes louder, but the tidal volume does not increase.

Of the following, the BEST next step in management is to

A. increase ventilator positive end-expiratory pressure
B. increase ventilator rate
C. reintubate with a 5.0 mm endotracheal tube
D. start extracorporeal membrane oxygenation
E. start inhaled nitric oxide

Correct Answer: C

The girl in this vignette has respiratory failure and worsening acute respiratory distress syndrome (ARDS) from pneumonia. She is not achieving adequate oxygenation and ventilation on mechanical ventilation. One reason for this is the diameter of the endotracheal tube is too small, evidenced by the air leak at the glottic level. The best step is to reintubate with a larger endotracheal tube.

The goals of mechanical ventilation in respiratory failure are to achieve adequate oxygenation and ventilation. PaO_2 levels of 60 mm Hg or higher represent oxygenation sufficient to maintain oxygen delivery. If arterial blood gas levels are not available, pulse oximetry readings of 90% or greater can be used as a benchmark. Adequate $PaCO_2$ levels can vary based on the setting. For example, the normal $PaCO_2$ range is between 40 to 45 mm Hg, but higher $PaCO_2$ levels (known as "permissive hypercapnia") are often accepted in ARDS management, as long as the pH is greater than 7.25. The girl in this vignette is hypoxic and her hypercapnia has caused respiratory acidosis.

In respiratory failure, hypoxia occurs when alveoli are collapsed or filled with fluid. If deoxygenated blood from the right ventricle flows past alveoli without exchanging oxygen, pulmonary venous return is desaturated, leading to hypoxia. Oxygenation is achieved if alveoli remain open throughout the respiratory cycle. Alveolar recruitment is maintained in mechanical ventilation with airway pressure and positive end-expiratory pressure (PEEP). A ventilator achieves airway pressure by regulating flow in and out of a circuit connecting the ventilator, tubing, endotracheal tube, airway, and lungs. If there is a leak in the system, pressure may not be maintained at prescribed levels. A common place for a leak in the system is at the glottic level if the endotracheal tube diameter is significantly smaller than the airway. The resulting release of pressure can lead to alveolar de-recruitment. This is a likely contributor to the hypoxia of the girl in this vignette. Similarly, a leak around the endotracheal tube occurring during inspiration represents the escape of air that would be involved in alveolar ventilation. If significant, as in the girl in this vignette, this could lead to impaired ventilation, hypercapnia, and respiratory acidosis. Since inspiratory pressures on the ventilator are higher than the PEEP, the air leak is usually louder during inspiration.

If oxygenation and ventilation are impaired despite high ventilator settings, measures should be taken to eliminate the air leak. If the endotracheal tube includes an inflatable cuff, air can be injected into the cuff to seal the airway. If an uncuffed tube is in place, it should be replaced with a wider endotracheal tube. A useful rule of thumb for endotracheal tube size is diameter (mm) = 4 + age/4. Depending on the discretion of the physician, sizes of 4.0 mm, 4.5 mm, or 5.0 mm would all be appropriate. The selection of a cuffed or uncuffed endotracheal tube is also subjective.

Increasing the PEEP would not be helpful because it would not be maintainable due to the air leak. Increasing the ventilator rate may increase minute ventilation, but because the rate is already close to maximum for age, it would not be the best choice. Extracorporeal membrane

oxygenation and inhaled nitric oxide are therapies for severe hypoxic respiratory failure, but are invasive and expensive when there are simpler options available.

PREP Pearls

- A rule of thumb for selection of endotracheal size is diameter (mm) = 4 + age/4.
- A leak around the endotracheal tube at the glottic level can lead to impaired oxygenation and ventilation, and may necessitate reintubation with a larger tube.

ABP Content Specifications(s)

- Plan appropriate ventilatory management in patients of various ages, especially with regard to selecting the appropriate tube size

Suggested Readings

- Carlo WA, Ambalavanan N. Conventional ventilation: traditional and new strategies. *Pediatr Rev*. 1999;20(12):e117-e126. doi: http://dx.doi.org/10.1542/pir.20-12-e117.
- Nitu ME, Eigen H. Respiratory failure. *Pediatr Rev*. 2009;30(12):470-478. doi: http://dx.doi.org/10.1542/pir.30-12-470.
- Sarnaik AP, Mastropietro CM. Mechanical ventilation. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:536-544.

Question 278

A 15-year-old adolescent presents to your office for evaluation 3 days after he sustained a neck injury while playing football. During a tackle, he hit the right side of his neck against another player's thigh and had immediate, burning, right-sided neck pain that radiated down the right arm with associated weakness. The symptoms lasted for 2 hours. His history is significant for a similar injury approximately 1 year ago. His parents ask you when he can be cleared to return to football. On physical examination, the adolescent has full range of motion of the neck and upper extremities. He has no tenderness to palpation of the neck. Upper extremity strength and reflexes appear normal and symmetric.

Of the following, the MOST appropriate recommendation regarding clearance to play football is that he

A. may play after an additional 4 weeks of rest
B. may play if electromyography and nerve conduction velocity studies are normal
C. may play if neck radiographs are normal
D. may play without restriction
E. should not play, given his history of a prior similar injury

Correct Answer: D

The adolescent in the vignette experienced a transient upper brachial plexus neuropraxia, commonly referred to as a stinger or burner. He has normal neurologic examination findings and normal strength. Since his unilateral symptoms completely resolved after 2 hours and he has only 1 prior similar injury, he should be allowed to return to football without restrictions. It is estimated that one-third to one-half of American football and rugby players have experienced a stinger, in which compression or traction of the upper brachial plexus causes pain radiating down the affected upper extremity. There are 3 mechanisms of injury that cause stingers: (1) hyperextension and ipsilateral lateral flexion causing compression of the brachial plexus, (2) traction on the brachial plexus because of contralateral lateral flexion, or (3) a direct blow to the lateral neck.

The athlete in the vignette does not require additional evaluation or a period of rest because he is currently asymptomatic and did not have prolonged or bilateral symptoms. He has only 1 prior stinger and 1 year has elapsed since that injury. A history of bilateral upper extremity symptoms after a neck injury suggests spinal cord involvement, which requires urgent additional evaluation. Although symptoms lasting more than 24 hours or a history of multiple prior stingers are not uncommon in benign cases, spine imaging may be warranted before allowing a return to play in such cases. Electromyography, nerve conduction studies, and neck radiographs are not needed before this patient may return to play.

Medical providers making decisions about allowing an athlete to return to play after a musculoskeletal injury must consider various factors, including the demands of the sport. The athlete must be able to use the affected body part as required for the sport without changes in mechanics. For example, a swimmer who has to alter his or her stroke pattern in response to persistent shoulder pain after an injury should not be allowed to return to full participation. Children and adolescent should not return to impact sports if they have an alteration in gait. Athletes should not be allowed to return to sports activity if there is a high risk of injury to themselves or others. If supportive devices or padding are used, they must not pose a hazard to other competitors. Returning athletes must also demonstrate psychosocial readiness; after an injury, an athlete should not participate in practice or competition until he or she feels ready to handle the physical and emotional demands of the sport.

PREP Pearls

- Transient upper brachial plexus neuropraxia, commonly referred to as a stinger or burner, is a common injury in football.
- A history of bilateral upper extremity symptoms after a neck injury suggests spinal cord involvement and requires urgent additional evaluation.

ABP Content Specifications(s)

- Understand the criteria for return to play in sports after various orthopedic injuries
- Understand the criteria for return to play in sports after a neck injury

Suggested Readings

- Herring SA, Kibler WB, Putukian M. The team physician and the return-to-play decision: a consensus statement: 2012 update. *Med Science Sports Exer*c. 2012;44(12):2446-2448. doi: http://dx.doi.org/10.1249/MSS.0b013e3182750534.
- Kawasaki T, Ota C, Yoneda T, et al. Incidence of stingers in young rugby players. *Am J Sports Med.* 2015;43(11):2809-2815. doi: http://dx.doi.org/10.1177/0363546515597678.

Question 279

It is your office's policy to ensure that a portion of each appointment with an adolescent patient is designated to interview and counsel the patient without a parent present. A premedical student shadowing you in your clinic asks if there are situations in which you would suggest that the parents accompany the adolescent during the entire visit. You explain the importance of providing confidential services to adolescents. You then discuss times when having a parent present during the entire visit is essential.

Of the following, the MOST appropriate time for such involvement would be if the adolescent is

A. being evaluated for a life-threatening illness
B. being evaluated for substance abuse
C. being seen for a simple complaint like a cold
D. hearing impaired and relies on the parent for communication
E. intellectually disabled with an IQ of 45

Correct Answer: E

When providing care to adolescents, 2 important concepts must be kept in mind: (1) consent¾who is authorized to give consent for care, and (2) confidentiality¾who has the right to control the release of information.

An intellectually disabled adolescent with an IQ of 45 is unlikely to be capable of providing informed consent or a reliable history; therefore, having a parent present during the entire visit would almost always be appropriate. None of the other situations would preclude the practitioner from providing an opportunity for confidential services.

Emancipated minors have adult status and can provide full consent for their own health care. Criteria for emancipation typically include marriage, military service, or living apart from parents while being self-supporting. Many states have procedures for recognizing minors as emancipated.

All states have provisions that authorize minors to give consent for certain services such as contraceptive services, pregnancy care, evaluation and treatment for sexually transmitted infections, or substance abuse. In the vast majority of states, minors can receive emergency carewithout the prior consent of a parent. Furthermore, most states recognize the “mature minor doctrine.” This doctrine permits consent for treatment (or refusal) by minors if they are at least 15 years old, able to understand the risks and benefits of the proposed treatment, the care is not high risk, is of benefit to the minor, and is a part of established medical management.
In most states, minor consent laws also address confidentiality, and the disclosure of information, when a minor is authorized to give consent for care. In addition, under the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPPA), when minors legally consent to health care the parent does not necessarily have the right to access that health information. Ensuring confidentiality in the delivery of health care services for adolescents is vital, because this may encourage adolescents to seek timely medical care and provide complete information when they do seek care.

PREP Pearls

- When providing care to adolescents, 2 important concepts must be kept in mind: (1) consent—who is authorized to give consent for care, and (2) confidentiality—who has the right to control the release of information.
- Emancipated minors have adult status and can give full consent for their own health care.
- Criteria for emancipation typically include marriage, military service, or living apart from parents while being self-supporting.

ABP Content Specifications(s)

- Recognize factors that determine when parents may/should accompany their adolescent during medical visits
- Recognize the circumstances that constitute an emancipated minor with regard to ability to accept or reject medical treatment

Suggested Readings

- Center for Adolescent Health and the Law. State minor consent laws: a summary, third edition. Center for Adolescent Health and the Law website. http://www.cahl.org/state-minor-consent-laws-a-summary-third-edition/.
- English A, Gudeman R. Understanding legal aspects of care. In: Neinstein LS, Katzman DK, Callahan T, Gordon CM, Joffe A, Rickert V, eds. *Neinstein's Adolescent and Young Adult Health Care: A Practical Guide.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016:90-94.

Question 280

You are called urgently to the newborn nursery to assess a neonate with a change in neurologic status. The female neonate was born at full term after an uncomplicated pregnancy and delivery. Her first 24 hours after birth were symptom-free, after which she developed a poor suck with difficulty feeding. Her condition continued to worsen, progressing to vasomotor instability, lethargy, seizures, and then obtundation on day 4 after birth. Chest radiography, lumbar puncture, and head ultrasonography yielded normal results. Blood, urine, and cerebrospinal fluid cultures are pending. Her C-reactive protein level is normal. A complete blood cell count shows thrombocytopenia and neutropenia. Further laboratory testing reveals a metabolic acidosis with a high anion gap, hyperammonemia, ketonuria, and hypoglycemia. On day 5 after birth, you are notified that her newborn screen has been flagged for an elevated C3 acylcarnitine.

Of the following, the laboratory test MOST likely to determine this neonate's diagnosis is

A. 17-OH-progesterone level
B. biotinidase level
C. carnitine profile
D. lactate level
E. urine organic acids

Correct Answer: E

The neonate in the vignette has proprionic acidemia (PA). Metabolic acidosis is a relatively common presentation in pediatrics. It can be caused by a number of acquired conditions, including:

- Catabolic states
- Diabetic ketoacidosis
- Infections
- Intoxications
- Severe dehydration
- Tissue anoxia

Each of these should be considered in children presenting with metabolic acidosis. In a neonate, it is important to also consider an inborn error of metabolism (IEM). Neonates with an IEM will present with a brief symptom-free period after birth, followed by rapid decompensation, leading to lethargy, seizures, coma, and potentially death within the first week after birth. Immediate recognition of the possibility of an IEM is vitally important because a matter of hours could have a drastic impact on the child's long-term morbidity and mortality. Treatment varies depending on the specific type of metabolic disorder.

Proprionic acidemia frequently presents with laboratory abnormalities including metabolic acidosis with a high anion gap, ketonuria, hypoglycemia, hyperammonemia, and cytopenias. Proprionic acidemia may also have a late-onset presentation with developmental regression, frequent emesis, protein intolerance, failure to thrive, low tone, dystonia, and cardiomyopathy. Late presentations typically occur when a catabolic stress, such as an infection or surgery, triggers an acute metabolic decompensation. Most cases of PA are identified on expanded newborn screening because of an elevated C3 (propionylcarnitine). Testing of urine organic acids is recommended in children who are either symptomatic or identified on newborn screening. An elevated 3-hydroxypropionate level and the presence of methylcitrate, tiglylglycine, and priopionylglycine will be noted on the urine organic acid test in cases of PA and not in the urine of unaffected individuals. Therefore, because the newborn in the vignette had an elevated C3 acylcarnitine level on newborn screening, urine organic acids would be the best test to confirm a suspected organic acidemia.

Measuring the 17-OH progesterone level would be indicated in the case of suspected congenital adrenal hyperplasia (virilization, salt-wasting crisis). A biotinidase level would be indicated for a child presenting with developmental regression, eczema, hypotonia, ataxia, vision problems, hearing loss, alopecia, and seizures in association with a biotinidase deficiency. A carnitine profile or lactate level would be indicated as part of a basic metabolic workup, but neither would be diagnostic in this situation.

When a physician suspects an IEM, a basic metabolic workup should be undertaken, which typically includes:
A serum analysis for:

- Acylcarnitine panel
- Amino acids
- Ammonia
- Blood glucose
- Carnitine profile
- Electrolytes
- Lactate
- Pyruvate

Urinalysis for:

- organic acids
- ketones

It is very important to test for ketonuria because the absence or presence of ketonuria clues the diagnosis of the various types of metabolic disorders. Results can be obtained in an expedient manner, allowing for appropriate interventions to be initiated quickly. Genetic sequencing is appropriate, but the results would not be back in time to make life-saving decisions.

PREP Pearls

- Proprionic acidemia (PA) typically presents in neonates, with a brief symptom-free period that progresses to feeding problems, vomiting, seizures, coma, and eventually death, if appropriate interventions are not initiated.
- Laboratory abnormalities seen in children with PA include metabolic acidosis with a high anion gap, ketonuria, hypoglycemia, hyperammonemia, and cytopenias.
- On urine organic acid testing, propionic acidemia will demonstrate an elevated 3-hydroxypropionate level and the presence of methylcitrate, tiglylglycine, and priopionylglycine.
- When an inborn error of metabolism is suspected, a basic metabolic workup should be undertaken, which includes serum analysis for lactate, pyruvate, ammonia, blood glucose, complete blood count, electrolytes, carnitine profile, acylcarnitine panel, and amino acids, as well as urine analysis for organic acids and ketones.

ABP Content Specifications(s)

- Plan the evaluation of a patient with suspected metabolic disease who is acidotic
- Plan the evaluation of a patient with suspected metabolic disease who is comatose

Suggested Readings

- Carrillo-Carrasco N, Venditti C. Propionic acidemia. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK92946/. Updated May 17, 2012.
- Levy PA. Inborn errors of metabolism: part 1: overview. *Pediatr Rev.* 2009;30(4):131-138. doi: http://dx.doi.org/10.1542/pir.30-4-131.
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