2018

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 2-month-old male infant is brought to your office for a health supervision visit. When discussing vaccines, his mother reports that her daughter had an intussusception that was reduced by the radiologist. She would like to delay administration of the rotavirus vaccine for her son until 6 months of age.

Of the following, considering his sibling's history, the MOST accurate information you can provide is that for this infant

A. delaying this vaccine increases the risk of the complication about which the mother is concerned
B. only 1 dose of the vaccine should be administered
C. the 2-dose series is preferred over the 3-dose series of the vaccine, given the family history
D. this vaccine is contraindicated, given the family history
E. this vaccine is not contraindicated, and delaying it decreases its effectiveness

Correct Answer: A

The rotavirus vaccine is a live, orally administered vaccine containing several strains of rotavirus isolated from human and bovine hosts. Two formulations of rotavirus vaccine are available—a 2-dose regimen (RV1) and a 3-dose regimen (RV5). These doses are administered at 2-month intervals starting as early as 6 weeks of age. The maximum age at which the first dose may be administered is 14 weeks, 6 days; the maximum age for administration of the second or third dose is 8 months, 0 days. Although a single dose of the vaccine may confer some protection, the exact level is not known.

In the United States, before the routine administration of rotavirus vaccine, nearly 95% of children acquired at least 1 rotavirus infection by 5 years of age. Rotavirus infection resulted in 55,000 to 70,000 hospitalizations and 20 to 60 deaths each year in young children. The estimated costs of this pathogen, largely because of lost productivity of caregivers of infected children, were approximately $1 billion per year. Routine administration of the rotavirus vaccine has substantially reduced the frequency of office and emergency department visits, hospitalizations, and costs associated with the infection. Evidence suggests that some protection is conferred to nonvaccinated children as well.

The risk of intussusception is slightly elevated after the first dose of the vaccine, with about 1.5 excess cases per 100,000 vaccinated infants. However, because infants younger than 3 months rarely develop intussusception, the benefits of the vaccine outweigh the limited number of excess cases in this age group. As infants reach beyond age 3 months, their risk of intussusception naturally increases; therefore, the number of excess cases associated with a first dose in the vaccine series in this age group would be more substantial. This increasing risk is the reason for the maximum age restrictions for vaccine administration. The vaccine is thought to be effective in older infants, but the increased risk of vaccine-associated intussusception outweighs the benefit.

Contraindications to rotavirus vaccine administration are few. Infants with a personal history of intussusception or a personal history of an anaphylactic reaction to the rotavirus vaccine should not receive the vaccine. However, a family history of intussusception or anaphylaxis is not a contraindication. The RV1 dosing tube contains latex; thus, only the RV5, whose dosing tube is latex-free, should be given to children with spina bifida, bladder exstrophy, and other infants with or who are at high risk of developing a latex allergy. Infants with severe combined immunodeficiency should not receive the vaccine because of the risk of vaccine-acquired rotavirus infection. For infants with other types of immunodeficiency, consultation with an immunologist is recommended before giving the vaccine. Administration of the rotavirus vaccine to infants with active moderate-to-severe gastroenteritis should be delayed until symptoms improve, but for those with mild symptoms, vaccination should not be delayed.

PREP Pearls
- Rotavirus vaccine, an orally administered, live vaccine that is highly effective at preventing gastroenteritis caused by rotavirus, should be administered routinely at the 2-month health supervision visit.
- There are age limits beyond which the vaccine should not be administered (14 weeks, 6 days for a first dose, 8 months, 0 days for the second or third doses); thus, delaying the vaccine could result in missed opportunities for protection.
- There is a small, increased risk of intussusception with the first dose of the rotavirus vaccine, which has an acceptable risk-benefit ratio within the permitted age range.

ABP Content Specifications(s)
- Know the recommendations, contraindications, and schedule for the rotavirus vaccine

Suggested Readings
- Centers for Disease Control and Prevention; Hamborsky J, Kroger A, Wolfe S, eds. Epidemiology and Prevention of Vaccine-Preventable Diseases. 13th ed. Washington DC: Public Health Foundation; 2015.
- Leshem E, Moritz RE, Curns AT, Zhou F, Tate JE, Lopman BA, Parashar UD. Rotavirus vaccines and health care utilization for diarrhea in the United States (2007-2011). Pediatrics. 2014;134(1):15–23. doi: http://dx.doi.org/10.1542/peds.2013-3849.
- Yih WK, Lieu TA, Kulldorff M, Martin D, McMahill-Walraven CN, Platt R, Selvam N, Selvan M, Lee GM, Nguyen M. Intussusception risk after rotavirus vaccination in U.S. infants. N Engl J Med. 2014;370(6):503–512. doi: http://dx.doi.org/10.1056/NEJMoa1303164.

Question 2

A 7-year-old girl was diagnosed with acute B lymphoblastic leukemia 2.5 months ago. Her mother reports that her daughter had been quite ill during the first month of therapy (induction) and required multiple blood transfusions, as well as a 4-week course of parenteral antibiotics that finished 6 weeks ago. The girl's last transfusion of packed red blood cells was 3 weeks ago. She was in a complete remission at the end of induction therapy and is now in consolidation therapy. Five days ago, she started having loose stools that have progressed to watery, voluminous, nonbloody diarrhea occurring 5 to 6 times per day. Three days ago, she developed a rash that started on her upper chest and has worsened daily.

She has a temperature of 37°C, a heart rate of 100 beats/ min, and blood pressure of 85/50 mm Hg. Her examination findings are remarkable for: scleral jaundice; an erythematous, papular, mildly pruritic rash on her trunk; a lacy, pink, macular rash extending down her arms and legs; and erythematous palms and soles. Her liver edge is palpable 3 cm below the costal margin. Her laboratory evaluation shows:

Laboratory test	Result
White blood cell count	1,100/μL (1.1 x 10^9/L)
Hemoglobin	9.1 g/dL (91 g/L)
Platelet Count	89 x 10^3/μL (89 x 10^9/L)
Neutrophils	10%
Lymphocytes	85%
Monocytes	5%
Aspartate aminotransferase	675 U/L (normal, 0-31 U/L)
Alanine aminotransferase	782 U/L (normal, 0-31 U/L)
Bilirubin (total)	4.3 mg/dL (73.5 μmol/L), [normal, 0.2-1.2 mg/dL (3.4-20.5 μmol/L)]

Of the following, the statement MOST consistent with this girl's presentation is that she

   A. has developed Clostridium difficile colitis
   B. is experiencing a relapse of leukemia
   C. received a nonirradiated blood product
   D. received a nonleukodepleted blood product
   E. was exposed to varicella-zoster virus

Correct Answer: C

Typical blood donations consist of whole blood. The whole blood is separated into its components (plasma, platelets, white blood cells, and red blood cells) by centrifugation, which separates substances by density. The individual blood components are then collected separately and stored as transfusion-ready products (fresh frozen plasma, platelets, and packed red blood cells). When a blood product is requested from the blood bank for transfusion, it can be further modified, primarily by leukodepletion and irradiation, to reduce the risk for certain transfusion reactions.

Leukodepletion is the removal of extraneous white blood cells by filtration, which separates particles by size. All packed red blood cell units contain small numbers of donor leukocytes that were unable to be separated from the red blood cells by centrifugation. Leukocytes that are larger than red blood cells (predominantly neutrophils) can be removed by using a filter with pore sizes that are larger than a red blood cell but smaller than a neutrophil. When donor neutrophils are transfused into a recipient, they are lysed and release cytokines that can cause a febrile transfusion reaction. Leukodepletion of the blood product by filtration removes donor neutrophils and thereby reduces the risk of a febrile transfusion reaction.

Medium and large lymphocytes are removed along with the neutrophils during leukodepletion. However, small lymphocytes are the same size as red blood cells and will therefore not be removed through leukodepletion. When presented with a foreign HLA type, lymphocytes are activated and undergo massive replication. Blood products are matched for red blood cell surface antigens (A, B, and O), not HLA types. The immune system of an immunocompetent recipient will recognize HLA-mismatched donor lymphocytes as foreign and eliminate them. However, the immune system of an immunocompromised recipient may be unable to eliminate the donor lymphocytes. In this situation, the donor lymphocytes may recognize the HLA-mismatched host as foreign, undergo massive replication, and cause transfusion-associated graft-vs-host disease (GVHD). Irradiation of a blood product will damage the DNA of donor lymphocytes, thereby rendering them replication incompetent and definitively eliminating the risk for transfusion-associated GVHD.

The girl in this vignette is in the early months of treatment for acute lymphoblastic leukemia and can be expected to be immunocompromised because of chemotherapy. She has typical signs and symptoms of acute GVHD, which most commonly affects the skin (rash), liver (elevated liver function test results and bilirubin levels), and intestines (diarrhea).

Her history of being immunocompromised and receiving multiple transfusions, most recently 3 weeks prior to presentation, greatly raises the concern for transfusion-associated GVHD. Not all blood banks routinely irradiate their blood products prior to release for patient use; therefore, it is critical to order irradiated blood products for all immunocompromised individuals, such as newborns and patients with cancer who are receiving chemotherapy.

Clostridium difficile colitis and leukemia relapse are unlikely to present with hepatomegaly or the described rash. The receipt of a nonleukodepleted blood product would increase the girl's chance of experiencing a febrile transfusion reaction, but it would not put her at risk for transfusion-associated GVHD. If she had contracted varicella-zoster virus, the rash would be different than the rash described in the vignette, and diarrhea and hepatomegaly would not be expected.

PREP Pearls
- Leukodepletion of blood products removes neutrophils by filtration, a process that separates particles based on size.
- Irradiation of blood products damages the DNA of donor lymphocytes, thereby rendering them replication incompetent and definitively preventing transfusion-associated graft-vs-host disease.
- Acute graft-vs-host disease presents with a rash, elevated liver function test results, elevated serum bilirubin levels, and profuse watery diarrhea.

ABP Content Specifications(s)
- Recognize the clinical features of graft-versus-host disease

Suggested Readings
- Blazar BR, Murphy WJ, Abedi M. Advances in graft-versus-host disease biology and therapy. Nat Rev Immunol. 2012;12(6):443–458. doi: http://dx.doi.org/10.1038/nri3212.
- Ferrara JL, Levine JE, Reddy P, Holler E. Graft-versus-host disease. Lancet. 2009;373(9674):1550–1561. doi: http://dx.doi.org/10.1016/S0140-6736(09)60237-3.
- King KE, Ness PM. How do we prevent transfusion-associated graft-versus-host disease in children? Transfusion. 2011;51(5):916–920. doi: http://dx.doi.org/10.1111/j.1537-2995.2010.03011.x.

Question 3

A 28-month-old boy is brought to your office as a new patient. He was adopted from Kazakhstan at the age of 12 months. He received bacillus Calmette-Guérin immunization as an infant. His HIV status has been confirmed as negative. He was seen 14 days ago in a local emergency department with a 1-month history of cough and wheezing. A chest radiograph revealed hilar lymphadenopathy and a consolidation of the left lower lobe. He was treated with high-dose amoxicillin-clavulanate for community-acquired pneumonia. He also received treatment with a short-acting β-agonist and a 3-day course of systemic steroids for associated wheezing. He has not demonstrated interval improvement.

He appears fatigued but otherwise is thriving, and he is in no acute distress. He is afebrile. His respiratory rate is 20 breaths/ min. Shotty lymphadenopathy is appreciated in the anterior cervical chain. Auscultation of the chest reveals decreased aeration at the left base and scattered expiratory wheezing. His abdomen is benign, and his extremities are without cyanosis, clubbing, or edema.

Of the following, the MOST appropriate next step in the care of this child is to

   A. perform computed tomography of the chest
   B. perform routine follow-up after completion of a 10-day course of amoxicillin-clavulanate
   C. place and read a purified protein derivative skin test
   D. repeat chest radiography in 8 to 10 weeks
   E. request urgent bronchoscopy with bronchoalveolar lavage

Correct Answer: C

The child in this vignette is exhibiting clinical and radiographic signs consistent with tuberculosis (TB). Placement of a purified protein derivative skin test is the most appropriate next step in the care of this child.

Signs and symptoms of TB disease in children include cough, fatigue, lethargy, weight loss, fever, and night sweats. Disseminated and meningeal disease are the most severe presentations of TB disease and are more commonly encountered in infants and young children.

Bacillus Calmette-Guérin (BCG) is a live attenuated vaccine strain of Mycobacterium bovis. It is frequently administered to children who are born in areas with endemic TB. In areas of high prevalence, vaccination may prevent primary disease and disease transmission as well as severe manifestations of the disease. Immunization with BCG has approximately 80% efficacy in protecting children from life-threatening forms of TB (miliary TB and TB meningitis) but is much less effective in preventing pulmonary disease and latent TB infection.

Bacillus Calmette-Guérin vaccination is not routinely recommended in the United States because of the low risk of infection with Mycobacterium tuberculosis and the risk for confounding of results from a tuberculin skin test (TST). Although a false-positive TST result may be encountered in the setting of BCG vaccination, receipt of the vaccination is not a contraindication to skin testing. The incubation period between infection and development of a positive TST result or interferon-γ release assay (IGRA) test result is 2 to 10 weeks. The risk of developing tuberculous disease is greatest in the first 6 months to 2 years following infection. Although the risk is lessened by elapsed time, reactivation of latent disease may occur many years after initial infection.

Although other potential etiologies for this boy's clinical symptoms should be considered, he has been adopted from a country that has been identified by the Centers for Disease Control and Prevention (CDC) as at high risk for endemic infection and, as such, meets the criteria for immediate TST with purified protein derivative. A diagnosis of TB disease or latent TB infection in a young child is considered to be a public health sentinel event and often reflects a recent disease transmission.

Tuberculosis testing recommendations for immigrants to the United States were revised in 2007 with subsequent implementation in 2013. For immigrants from areas with a high prevalence of TB disease, the CDC requirements are as follows:
- Chest radiography for individuals 15 years of age and older
- Tuberculin skin test or IGRA for children 2 to 14 years of age
- In individuals with evidence of pulmonary disease, sputum cultures, drug susceptibility testing, and completion of directly observed therapy for TB are indicated prior to immigration.

- Children younger than 2 years of age are not routinely tested unless they are a known contact of a person with active TB, are infected with HIV, or have signs or symptoms suggestive of TB.

Both TST and IGRA are based on specific cellular sensitization after infection. Conditions that decrease the number or function of lymphocyte subsets may reduce the sensitivity of both tests. Other host factors that may decrease TST reactivity include malnutrition, young age, congenital or acquired immunosuppression, viral infection (especially measles, varicella, and influenza), recent infection, and disseminated TB disease.

Interferon-γ release assays are the preferred tests for children 5 years of age and older who have been vaccinated with BCG. These blood tests are approved by the US Food and Drug Administration and measure interferon-γ produced from T lymphocytes in response to stimulation with antigens specific to the M tuberculosis complex (includes M tuberculosis and M bovis).

As with TST, IGRA cannot differentiate between latent infection and active disease. A negative result does not exclude tuberculous disease in an individual with suggestive findings.

The CDC guidelines state that TST is the preferred testing modality in children who are younger than 5 years. Either TST or IGRA may be used in children 5 years of age or older. In BCG-vaccinated children 5 years of age and older, IGRA may be utilized to determine if a positive TST is attributable to the prior BCG vaccination or to latent TB infection.

PREP Pearls
- Infants and young children are at higher risk for severe forms of tuberculous disease, including miliary tuberculous and tuberculous meningitis.
- The diagnosis of tuberculous disease or latent tuberculous infection in a young child is considered to be a public health sentinel event and often reflects a recent disease transmission.
- Tuberculin skin testing is not contraindicated in an individual who has received bacillus Calmette-Guérin vaccination.

MOCA-Peds Objective
- Evaluate a patient with chronic cough

ABP Content Specifications(s)
- Recognize the major clinical features associated with Mycobacterium tuberculosis infection
- Understand the diagnostic tests useful in the evaluation of tuberculosis (both latent and active)
- Understand the epidemiology of Mycobacterium tuberculosis

Suggested Readings

- Centers for Disease Control and Prevention. CDC immigration requirements: technical instruction for tuberculosis screening and treatment. http://www.cdc.gov/immigrantrefugeehealth/pdf/ tuberculosis-ti-2009.pdf..
- Centers for Disease Control and Prevention. Fact sheets: BCG vaccine. http://www.cdc.gov/tb/publications/factsheets/prevention/bcg.htm..
- Starke JR, Committee on Infectious Diseases. Clinical report: interferon-? release assays for diagnosis of tuberculosis infection and disease in children. Pediatrics. 2014;134(6):e1763-e1773. doi: http://dx.doi.org/10.1542/peds.2014-2983.
- Taylor Z, Nolan CM, Blumberg HM, American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR Recomm Rep. 2005;54(RR-12):1-81. .

Question 4

You are seeing an 8-year-old girl in clinic for "twitching." Her parents report that she has had a twitch in her right shoulder for the past month. The twitching happens several times a day, sometimes several times in a row. They see it more often when she is watching TV or reading. The girl reports that she feels like she "has to do it." Her second-grade teacher reports that the girl is doing well academically and socially. Last year, her first-grade teacher told the parents that the girl was defiant, rolling her eyes when asked to do tasks. In clinic, the girl's general physical examination and neurologic examination findings are normal. No twitching is noted.

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

A. educate the girl's parents about motor stereotypies
B. educate the girl's parents about tics and Tourette syndrome
C. evaluate for acute rheumatic fever
D. perform magnetic resonance imaging of the brain
E. start treatment with clonidine

Correct Answer: B

The girl in the vignette has motor tics, and her parents should be educated about this diagnosis. Motor tics are stereotyped motor movements usually involving the face and upper extremities. They are accompanied by an internal compulsion to do the movement and a sense of relief afterwards. Simple motor tics are brief, individual movements such as shoulder twitching, forceful eye blinking, or eye rolling. Complex motor tics are longer in duration, such as lip-licking, reaching out and touching in a certain pattern, or stomping the foot. Phonic tics are noises such as sniffing, throat clearing, barking, or humming. Motor and phonic tics, such as the eye-rolling reported by the girl's first grade teacher, may be misinterpreted as oppositional or defiant behavior. The usual age at onset of tics is 5 to 6 years. Individual tics can resolve over a few weeks or months and new ones oft en appear. When motor and phonic tics have been present over the course of a year, in a patient younger than 18 years, the patient can be diagnosed with Tourette syndrome.

The diagnosis of tics and Tourette syndrome is based on the clinical presentation. In the setting of motor or phonic tics and normal neurologic examination findings, magnetic resonance imaging of the brain or other diagnostic testing is not needed. Children with tics can have comorbid attention deficit/hyperactivity disorder, anxiety, or obsessive-compulsive disorder. These should be treated if present.

Treatment of tics (whether isolated motor or phonic tics, or tics in the setting of Tourette syndrome) is mainly supportive. The first step for the girl in the vignette would be to educate her and her parents about tics and Tourette syndrome. Tics can be transiently suppressed, for instance, during an office visit as in the vignette, but overall, they are involuntary. The girl should not be expected to stop doing them at home or at school. If there is a tic that is particularly bothersome (touching others or loud barking, for example), a trial of medications may be helpful. When starting any medication for tics, the patient and parents should be advised that the tics may diminish but will probably not stop altogether. The 2 medications approved by the Food and Drug Administration for use in tics are haloperidol and pimozide. The side effects of these medications often outweigh the benefit. Many providers first try an α2-adrenergic agonist, such as clonidine or guanfacine, but this is an off-label use. Another treatment for tics is comprehensive behavioral intervention for tics (C-BIT), a behavioral technique or therapy taught by psychologists or other behavioral health specialists that has been shown to reduce tic severity. The girl in the vignette is not having academic or social problems associated with her tics, so she does not need treatment.

Motor stereotypies are stereotyped motor movements that can involve any part of the body. Examples include hand flapping, tonic arm extension, or rocking. They typically start before the age of 3 years, and the same movements persist over time. In contrast to tics, there is no internal compulsion to do the movement or sense of relief afterwards. Motor stereotypies occur in children with autism and in typically developing children. They often decrease as the child ages. Chorea is a random, fast, chaotic motor movement that can occur anywhere in the body. There is no internal compulsion to do the movement or sense of relief afterwards. The diagnostic evaluation of chorea includes testing for evidence of acute rheumatic fever (complete blood cell

count with differential, erythrocyte sedimentation rate, C-reactive protein, antistreptolysin O and antideoxyribonuclease B, and testing for carditis). If this is normal, a magnetic resonance imaging scan of the brain can be obtained to evaluate for vasculitis or other very rare disorders of the basal ganglia. Chorea gravidarum is chorea that occurs during pregnancy, so girls and women of childbearing potential with unexplained chorea should be evaluated for pregnancy. Because the girl in the vignette reports both a compulsion to do the movements and a sense of relief afterwards, the most likely diagnosis is tics and not chorea.

PREP Pearls
- Motor stereotypies typically start before 3 years of age, whereas tics typically begin around 5 to 6 years of age.
- Tics are associated with an urge or compulsion to perform the movement or sound, and a sense of relief afterwards.

ABP Content Specifications(s)
- Recognize clinical findings associated with Tourette syndrome, and manage appropriately

Suggested Readings
- Tourette Association of America. www.tourette.org .
- Zinner SH, Mink JW. Movement disorders I: tics and stereotypies. *Pediatr Rev.* 2010;31(6):223–233. doi: http://dx.doi.org/10.1542/pir.31-6-223.

Question 5

You are seeing a 1-month-old male infant in your office for parental concerns about diarrhea. He was born at term after an uncomplicated pregnancy, passed his first meconium stool at 18 hours of age, and was discharged from the nursery at 36 hours of age. He is breastfed and has been growing adequately. The parents report diarrhea for 1 week, which they describe as 6 loose stools per day with some mucus and occasional small red specks that they think is blood. The infant has had no fever or vomiting, and is feeding and acting normally. No one else at home is sick and there has been no travel. His physical examination shows a vigorous infant with growth parameters at the 50th percentile. He has no skin rashes or anal fissures, and the remainder of his physical examination findings are normal. Although the stool is not grossly bloody, a stool test for blood is positive.

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

  A. change his diet to an amino acid-based formula
  B. change his diet to a lactose-free formula
  C. eliminate cow milk from the mother's diet
  D. obtain serum-specific immunoglobulin E for milk protein
  E. refer to gastroenterology for a colonoscopy

Correct Answer: C

The infant in the vignette demonstrates the characteristic findings of dietary protein-induced colitis: small amounts of blood and mucus in the stool in the presence of normal growth and physical examination findings. Dietary protein induced colitis typically presents in the first few months after birth, with a mean age at onset of 2 months. The most common triggers are cow milk protein and, less commonly, soy protein. Breastfed infants can develop this condition as a result of proteins the mother ingests, therefore, a trial of cow milk and soy elimination from this mother's diet is warranted. Bleeding resolves within 72 hours after this intervention, in most cases.

The diagnosis of this condition is based primarily on the history and physical examination. Anal fissures, another common cause of small amounts of rectal bleeding in otherwise healthy young infants, should be ruled out by physical examination. Further evaluation is not necessary for suspected dietary protein-induced colitis. However, if there are other signs or symptoms, such as vomiting, poor weight gain, large amounts of blood in the stool, fever, or other signs of infection, alternate diagnoses should be considered. Additional evaluation may be required if the symptoms do not resolve with dietary elimination of the offending protein or if additional symptoms occur.

Treatment for dietary protein-induced colitis is elimination of the offending protein. In the case of an infant who is formula fed, changing to a protein hydrolysate or amino acid–based formula would be appropriate, but for a breastfed infant, such as the one in the vignette, continued breastfeeding with changes to the mother's diet is preferred. Because this condition is a response to the protein rather than the carbohydrate component of the feeding, changing to a lactose- free formula would have no effect on the symptoms. Because soy is often a trigger for the condition, changing to soy formula is not appropriate. Dietary protein-induced colitis is not an immunoglobulin E (IgE)-mediated condition, therefore performing serum-specific IgE test is not warranted. Symptoms that suggest IgE-mediated cow milk allergy, such as wheezing and the involvement of other organ systems besides the gastrointestinal system (eg, urticaria), typically occur immediately after milk ingestion. Endoscopy and biopsy are generally reserved for infants whose symptoms worsen after maternal cow milk and soy elimination, or if the bleeding does not resolve.

Parents often seek guidance about their infant's stooling pattern. Normal frequency and consistency can vary widely between individual infants and over time. Soon after birth, breastfed infants typically have more frequent, less formed, sometimes mucous-containing stools compared with formula-fed infants. Most breastfed infants average about 4 stools per day at 1 month of age, whereas formula-fed infants typically have 2 to 3 stools per day. Stooling frequency may occur as often as after every feeding soon after birth, to as infrequently as every few days as the infant matures. Breastfed infants' stools become more formed once they begin taking solids (typically around 6 months of age).

PREP Pearls
- Dietary protein-induced colitis is characterized by small amounts of blood and mucus in the stools of otherwise healthy infants.
- Treatment for dietary protein-induced colitis in infants includes elimination of cow milk and soy protein from the mother's diet for breastfed infants, and feeding an amino acid-based formula for formula-fed infants.
- In cases of suspected dietary protein-induced colitis, poor growth, vomiting, large amounts of blood in the stool, fever or other signs of infection, or failure to respond to the elimination of cow milk or soy from the diet requires further evaluation.

ABP Content Specifications(s)
- Understand the significance of colitis in a breast-fed infant
- Know the normal pattern of feeding and stool frequency in formula-fed infants
- Know the normal pattern of feeding and stool frequency in breast-fed infants

Suggested Readings
- Alvares M, Kao L, Mittal V, Wuu A, Clark A, Bird JA. Misdiagnosed food allergy resulting in severe malnutrition in an infant. *Pediatrics*. 2013;132(1):e229-e232. doi: http://dx.doi.org/10.1542/peds.2012-2362.
- Hyams JS, Treem WR, Etienne NL, et al. Effect of infant formula on stool characteristics of young infants. *Pediatrics*. 1995;95:50-54.
- Sicherer SH. Clinical aspects of gastrointestinal food allergy in childhood. *Pediatrics*. 2003;111(S3):1609-1616.

Question 6

An 11-year-old boy who recently emigrated from Cambodia is brought to your office with jaundice. He reports a gradual onset of poor appetite, fatigue, joint pain, nausea, and abdominal pain. Physical examination reveals scleral icterus and hepatomegaly. Laboratory data are shown:

Laboratory Test	Result
Alanine aminotransferase	310 IU/L (normal, 0-31 IU/L)
Total serum bilirubin	4.6 mg/dL (78.7 µmol/L), [normal, 0.2-1.2 mg/dL (3.4-20.5 µmol/L)]
IgM to hepatitis A virus	Negative
Total IgG and IgM to hepatitis A virus	Positive
Hepatitis B surface antigen	Positive
Antibody to hepatitis B surface antigen	Negative
IgM to hepatitis B core antigen	Negative
Total hepatitis B core antibody	Positive
Hepatitis B e antigen	Positive
IgG antibody to hepatitis C virus	Negative

Of the following, the MOST likely diagnosis is

- A.   acute infection with hepatitis A virus
- B.   acute infection with hepatitis B virus
- C.   chronic infection with hepatitis B virus
- D.   chronic infection with hepatitis C virus
- E.   coinfection with hepatitis B virus and hepatitis A virus

Correct Answer: C

Hepatitis B virus (HBV) infection is a major public health problem and affects an estimated 248 million people worldwide. The disease is endemic in Southeast Asia, Africa, Central Europe, and Eastern Europe. The routes of transmission are sexual, parenteral, and perinatal. In the United States, transmission of HBV among children is rare because of the widespread implementation of universal infant hepatitis B vaccination beginning at birth. In this setting, new infections often occur among unvaccinated individuals. In many HBV endemic countries, infant hepatitis B immunization is not included in the routine childhood immunization schedules. Thus, routine screening for chronic HBV infection is recommended for international adoptees, refugees, and immigrants. In addition, pediatricians must be aware of serologic markers of HBV infection and be able to distinguish acute from chronic HBV infection.

The HBV serologic markers of the patient described in this vignette are consistent with chronic HBV infection because of the presence of hepatitis B surface antigen and hepatitis B core (IgG) antibody (as noted by circulating total hepatitis B core antibody) and the lack of IgM to hepatitis B core antigen (**Item C6**). The presence of hepatitis B e antigen in this child suggests a high level of viral replication and increased risk of HBV transmission. In contrast, acute HBV infection is characterized by the presence of hepatitis B surface antigen without antibodies to the hepatitis B surface antigen and the presence of IgM to hepatitis B core antigen (with or without the presence of hepatitis B e antigen). In individuals with resolved HBV infection, antibody to hepatitis B surface antigen and total hepatitis B core antibody are present. In individuals immunized with hepatitis B vaccine, antibody to hepatitis B surface antigen alone is present.

Chronic HBV infection occurs in 80% to 90% of untreated infants born to mothers with chronic HBV infection who have positive test results for hepatitis B e antigen. Administration of hepatitis B immune globulin and hepatitis B vaccine within 12 hours after birth reduces the rate of mother-to-child transmission of HBV from 90% to 10%. The clinical spectrum of chronic hepatitis B infection in children can vary from an asymptomatic carriage state (in perinatally infected children) to jaundice and elevation of serum alanine transferase levels (in older infected children and adolescents).

* Hepatitis B e antigen.
† Antibody to HBeAg.
§ Antibody to hepatitis B core antigen.
¶ Hepatitis B surface antigen.
** Immunoglobulin M.
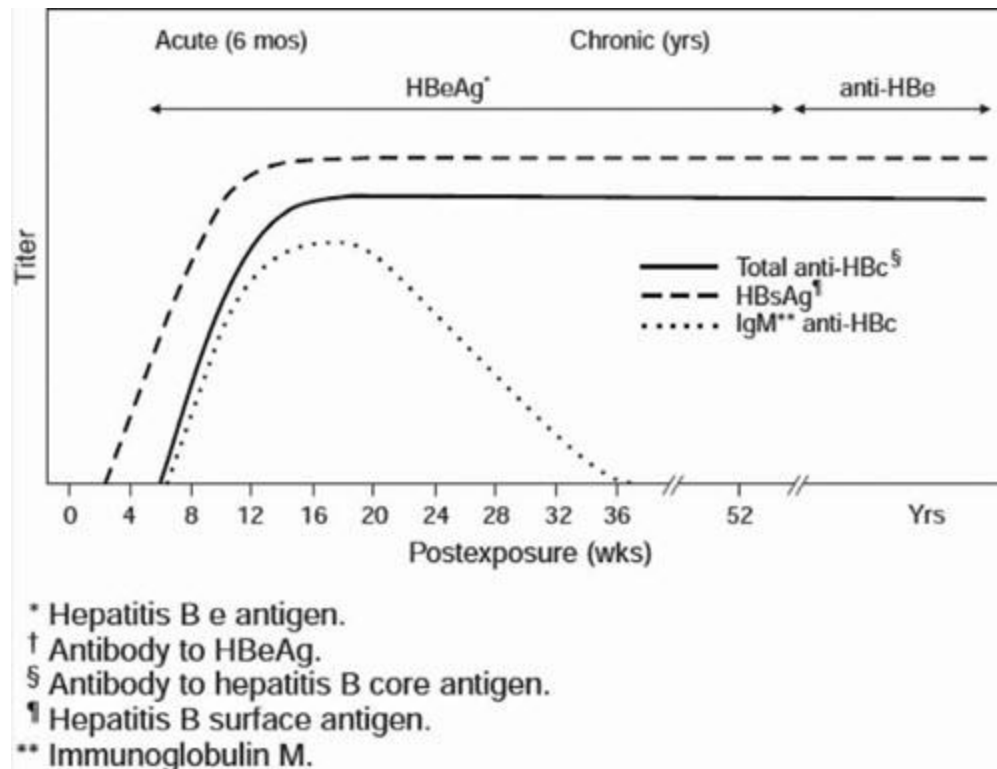
Item C6: Hepatitis B Serologic Markers.

Courtesy of the Centers for Disease Control and Prevention.

Treatment is recommended to reduce the risk of disease progression to cirrhosis and subsequent development of hepatocellular carcinoma. Treatment of chronic hepatitis B infection in childhood can be challenging because of the lack of guidance on initiation of antiviral agents and duration of treatment. Additional challenges include adverse effects of PEGylated interferon-based regimens and concerns of emergent resistance to long-term use of nucleos(t)ide analogues. Levels of hepatitis B e antigen and HBV DNA help to determine the need for treatment initiation and to monitor the response to therapy. Referral to a health care provider with expertise in the management of chronic HBV infection is recommended. The local or state health department must be notified of all children with positive hepatitis B surface antigen test results.

Acute infection with hepatitis A virus would result in IgM to hepatitis A virus. The child described in this vignette has IgG to the hepatitis A virus, which indicates immunization or past infection. The child does not have chronic infection with hepatitis C virus given the absence of anti–hepatitis C virus antibody.

PREP Pearls
- Hepatitis B virus infection is a major global public health problem in Southeast Asia, Africa, Central Europe, and Eastern Europe.

- The presence of hepatitis B surface antigen and total antibody to hepatitis B core antigen without IgM hepatitis B core antibody is indicative of chronic hepatitis B virus infection.
- The presence of hepatitis B e antigen suggests high viral replication and increased risk of hepatitis B virus transmission.
- Screening for chronic hepatitis B virus infection is recommended for international adoptees, refugees, and immigrants.

ABP Content Specifications(s)
- Recognize the clinical features associated with hepatitis B virus infection
- Understand the epidemiology of the hepatitis B virus
- Understand the importance of follow-up screening evaluations for hepatitis B virus infection

Suggested Readings
- American Academy of Pediatrics, Council on Community Pediatrics. Providing care for immigrant, migrant, and border children. *Pediatrics*. 2013;131(6):e2028–e2034. doi: http://dx.doi.org/10.1542/peds.2013-1099.
- 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.
- Christenson JC, Manaloor JJ. Hepatitis A, B, and C. *Pediatr Rev*. 2016;37(10):426–438. doi: http://dx.doi.org/10.1542/pir.2015-0075.

Question 7

A 5-year-old boy is brought to your clinic for evaluation of recurrent episodes of nonbloody, nonbilious emesis. His mother reports that his vomiting episodes began 9 months ago. The boy describes episodes of nausea and vomiting that occur every 4 to 5 weeks with 9 to 15 episodes of nonbloody, nonbilious emesis followed by a return to baseline good health over a 24-hour period. He has generalized abdominal pain that lasts until the emesis has resolved. He reports no associated fever, weight loss, headaches, or diarrhea. The family reports no recent travel, head trauma, cannabis exposure, food triggers, or illnesses preceding the emesis.

The boy has been seen in the emergency department on 3 different occasions, where he was diagnosed with an acute viral illness and treated with intravenous fluid hydration and nausea medication. Laboratory studies at the last emergency department visit included a normal complete blood cell count and electrolyte panel. Abdominal radiographs and ultrasonography results were normal.

Physical examination results are normal, with a body mass index tracking at the 50th percentile and normal vital signs.

Of the following, the BEST choice of medication to address this child's underlying diagnosis is

      A. amitriptyline
      B. cyproheptadine
      C. ondansetron
      D. promethazine
      E. ranitidine

Correct Answer: B

The boy in this vignette has cyclic vomiting syndrome (CVS). The first-line therapy for children 5 years old or younger is cyproheptadine, an antihistamine, used to prevent future episodes. The exact mechanism of action is not clear. Supplementation with coenzyme Q10 and L-carnitine has also shown benefit in prophylaxis.

Cyclic vomiting syndrome is a functional gastrointestinal disorder that can occur at any age, although it most commonly presents in 3- to 7-year-old children. It affects both sexes equally. White individuals are affected more than individuals of other races. Cyclic vomiting syndrome is characterized by episodes of vomiting separated by weeks to months. Potential triggers include stress, fatigue, infections, and foods (monosodium glutamate, chocolate, and aged cheeses). Many children outgrow CVS, but some children develop other functional disorders including migraine headaches and irritable bowel syndrome.

Diagnosis is based on the Rome IV criteria:
- Two or more periods of intense, unremitting nausea and paroxysmal vomiting that last for hours to days occur in a 6-month period.
- Episodes are stereotypical for each patient.
- Episodes are separated by weeks to months with return to baseline health between episodes.
- After appropriate medical evaluation, the symptoms cannot be attributed to another condition.

The initial evaluation for CVS includes a complete history and physical examination. Red flag symptoms that should prompt additional evaluation include age younger than 2 years, bilious emesis, severe abdominal pain, abnormal neurologic symptoms, attacks precipitated by illness or fasting, or progressive worsening. It is recommended that laboratory tests be obtained during an episode prior to intravenous fluid hydration. Laboratory tests (**Item C7A**) are used to screen for infection and hepatic, pancreatic, renal, endocrine, and metabolic diseases. Children may also be screened for pheochromocytoma and acute intermittent porphyria. Pregnancy should be ruled out in female patients. Imaging studies may also be indicated based on the history and physical examination results (**Item C7B**).

Item C7A. Laboratory Evaluation of Suspected Cyclic Vomiting Syndrome.

Complete blood cell count with differential
Erythrocyte sedimentation rate
Hepatic transaminases
Pancreatic amylase
Serum blood urea nitrogen
Serum creatinine
Serum electrolytes
Serum pH
Glucose
Lactic acid
Ammonia
Serum amino acids
Urinalysis
Urine ketones
Urine organic acids
Urine porphobilinogen
Urine aminolevulinic acid
β-Human chorionic gonadotropin

Courtesy of C. Waasdorp Hurtado

Item C7B. Imaging Evaluation of Suspected Cyclic Vomiting Syndrome.

Imaging Test	Purpose
Upper gastrointestinal series with small bowel follow-through	Evaluate anatomy
Abdominal ultrasonography	Evaluate anatomy, pancreas, biliary tree evaluation, renal obstruction
Abdominal computed tomography	Evaluate anatomy, rule out mass
Gastric emptying scan	Evaluate for gastroparesis
Endoscopy	Evaluate for gastritis

Courtesy of C. Waasdorp Hurtado

Most providers will initially obtain the laboratory evaluation and upper gastrointestinal series, proceeding with additional testing as indicated by the history and physical examination results or following a lack of response to conservative therapy. Empiric therapy is often started following normal laboratory results and upper gastrointestinal imaging. The presence of red flag symptoms should prompt additional evaluation.

Amitriptyline is used to treat CVS. However, it is not the first-line therapy because of possible side effects including suicidality and QT prolongation. It is not typically used until after 6 years of age. Ondansetron is a 5-HT3 receptor antagonist that may be used during episodes to treat nausea and vomiting, but it is not effective for prevention. Promethazine is both an antihistamine and an anticholinergic that may be used during episodes, but it has no role in prevention. Ranitidine is a histamine-2 blocker that has no role in the treatment of CVS.

PREP Pearls
- Cyclic vomiting syndrome is a functional gastrointestinal disorder.
- Cyproheptadine is the first-line treatment for cyclic vomiting syndrome in children 5 years old or younger.
- Coenzyme Q10 and L-carnitine are effective in preventing future episodes of cyclic vomiting syndrome.

MOCA-Peds Objective
- Evaluate a patient with chronic abdominal pain

ABP Content Specifications(s)
- Plan the evaluation of recurrent cyclic vomiting

Suggested Readings
- Kaul A, Kaul KK. Cyclic vomiting syndrome: a functional disorder. *Pediatr Gastroenterol Hepatol Nutr*. 2015;18(4):224-229. doi: 10.5223/pghn.2015.18.4.22 .
- Lee J, Wong SA, Li BU, Boles RG. NextGen nuclear DNA sequencing in cyclic vomiting syndrome reveals a significant association with the stress-induced calcium channel (RYR2). *Neurogastroenterol Motil*. 2015;27(7):990-996. doi: 10.1111/nmo.12575 .
- Lee LY, Abbott L, Mahlangu B, Moodie SJ, Anderson S. The management of cyclic vomiting syndrome: a systematic review. *Eur J Gastroenterol Hepatol*. 2012;24(9):1001-1006. doi: 10.1097/MEG.0b013e328355638f .
- Li BU, Lefevre F, Chelimsky GG, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition consensus statement on the diagnosis and management of cyclic vomiting syndrome. *J Pediatr Gastroenterol Nutr*. 2008;47(3):379-393. doi: 10.1097/MPG.0b013e318173ed39 .
- Moses J, Keilman A, Worley S, Radhakrishnan K, Rothner AD, Parikh S. Approach to the diagnosis and treatment of cyclic vomiting syndrome: a large single-center experience with 106 patients. *Pediatr Neurol*. 2014;50(6):569-573. doi: 10.1016/j.pediatrneurol.2014.02.009 .

Question 8

A previously healthy 13-year-old girl is brought to the emergency department because of altered mental status. She had been complaining of abdominal pain, nausea, and vomiting for 3 days before her presentation. For the past month, she has been drinking water and sports drinks excessively, and has been waking up in the middle of the night to urinate. During the day of admission, she became progressively somnolent and then unarousable, prompting her mother to bring her to the emergency department. On arrival, her temperature is 37.0°C; heart rate is 140 beats/min; respiratory rate is 50 breaths/min, and blood pressure is 100/60 mm Hg. Her oxygen saturation is 100% on room air. On physical examination, she is obtunded, responding to only painful stimuli with moaning and withdrawal of extremities. She has no spontaneous eye opening. Her pupils are 3 mm, equal, and reactive. Her eyes are sunken and her lips are cracked and dry. The girl's gag reflex is intact. Her extremities are cool, with a capillary refill of 3 seconds. Pulses are strong. Laboratory results are as follows:

Laboratory test	Result
Sodium	124 mEq/L (124 mmol/L)
Potassium	7.0 mEq/L (7.0 mmol/L)
Chloride	100 mEq/L (100 mmol/L)
Bicarbonate	5 mEq/L (5 mmol/L)
Serum urea nitrogen	38 mg/dL (13.5 mmol/L)
Creatinine	1.4 mg/dL (124 μmol/L)
Glucose	1,350 mg/dL (74.9 mmol/L)
Capillary blood gas pH	6.95
Partial pressure of carbon dioxide	14 mm Hg (1.8 kPa)
Base deficit	−25

Of the following, the BEST management option for this girl is

A. 0.9% sodium chloride (NaCl) bolus, 40 mL/kg intravenously over 20 minutes
B. 3% NaCl bolus, 5 mL/kg intravenously over 20 minutes
C. endotracheal intubation
D. intravenous insulin infusion, 0.1 unit/kg per hour
E. intravenous mannitol, 0.25 g/kg over 15 minutes

Correct Answer: D

The girl in the vignette has diabetic ketoacidosis (DKA) from newly diagnosed type 1 diabetes mellitus. She is encephalopathic and dehydrated, but hemodynamically stable and maintaining her airway, oxygenation, and ventilation. The most appropriate next step in management among the choices listed is to start an intravenous insulin infusion.

With normal physiology, the release of insulin after a dextrose-rich meal leads to the uptake of glucose into fat, liver, and skeletal muscle tissue, as well as cellular glycogen and fat synthesis. In DKA, insulin defi ciency causes decreased glucose uptake, and increased glycogenolysis, and gluconeogenesis. Abnormal glucose metabolism leads to the release of counterregulatory hormones including glucagon, epinephrine, and growth hormone, all of which further increase glycogenolysis and gluconeogenesis. As another counterregulatory mechanism to provide cellular energy in DKA, free fatty acids are released from adipose tissue and converted via beta-oxidation into ketoacids (acetoacetate and beta-hydroxybutyrate). Clinically, this leads to an elevated anion gap metabolic acidosis (bicarbonate level, (<15 mEq/L [<15 mmol/L]), hyperglycemia (>200 mg/dL [11.1 mmol/L]), and the presence of serum or urine ketones. Hyperglycemia causes glucosuria, which in turn leads to osmotic diuresis and dehydration. Polyuria and polydipsia are commonly seen. Hyperosmolarity is caused by ketoacidosis and hyperglycemia, as well as the hypernatremia and elevated urea nitrogen caused by dehydration from osmotic diuresis. Reversal of this physiology is achieved by administration of an insulin infusion.

Encephalopathy from cerebral edema is an important potential complication of DKA. In response to elevated serum osmolarity, neurons produce organic osmolytes (also referred to as "idiogenic osmoles") to maintain osmolar equilibrium, thereby preventing cellular dehydration. As serum osmolarity decreases, cellular edema occurs because of shifting of water toward the higher intracellular osmolality caused by the organic osmolytes. This can occur before presentation from intake of hypotonic fluids, as well as iatrogenically because of overaggressive fluid administration. In DKA, administering 0.9% normal saline, which has an osmolality of 286 mmol/L, will lower serum osmolality. Although the girl in the vignette is dehydrated and needs correction of her fluid deficit, a fluid bolus of 40 mL/kg over 20 minutes would be excessive and could worsen cerebral edema. Most DKA treatment protocols include an initial normal saline bolus of 10 mL/kg over 1 hour, followed by correction of the free water deficit over 48 to 72 hours. For a patient in shock, more aggressive fluid administration is indicated, but should be balanced against potential neurologic complications.

If cerebral edema is severe, intracranial hypertension, herniation, and death can occur. Signs of severely elevated intracranial pressure and impending herniation include systemic hypertension, bradycardia, unreactive and/or unequal pupils, respiratory depression, and loss of cranial nerve function. Computed tomography of the brain is rarely indicated in the acute setting, because a patient's condition can deteriorate in the radiology suite where there is less monitoring, it can delay care, and the clinical examination is reliable enough to direct care.

Osmotherapy, which may include 3% saline or mannitol, can be used to treat the rare patient with severe cerebral edema. However, this is not indicated for the girl in this vignette because her clinical presentation does not support this diagnosis. The rapid increase in serum sodium level that would result from treatment with 3% saline can cause central pontine myelinolysis, and osmotic diuresis from mannitol can worsen dehydration and predispose to venous sinus thrombosis.

Hypoventilation increases cerebral blood volume and intracranial pressure. Normal respiratory compensation for metabolic acidosis follows the Winters' Formula:
$PaCO_2$ (predicted) = $1.5*HCO_3 + 8 \pm 2$

If a patient with metabolic acidosis has a partial pressure of arterial carbon dioxide ($PaCO_2$) higher or lower than the predicted range, there is a concomitant respiratory acidosis or alkalosis, respectively. The girl in the vignette has a $PaCO_2$ of 14 mm Hg, which falls within the range of her predicted $PaCO_2$ of 13.5 to 17.5 mm Hg, so she does not have a respiratory disorder. In addition, because she is protecting her airway, endotracheal intubation is not indicated.

PREP Pearls
- Reversal of diabetic ketoacidosis occurs with the administration of an intravenous insulin drip.
- Early fluid management of diabetic ketoacidosis that is either excessive or hypotonic may worsen cerebral edema and neurologic outcomes.
- Patients with diabetic ketoacidosis rarely benefit from intubation. Indications include respiratory acidosis (which may be present even with partial pressure of arterial carbon dioxide levels below "normal" range), and loss of respiratory drive and airway protective reflexes.
- Patients with diabetic ketoacidosis rarely benefit from osmotherapy. Indications include clinical findings of severe intracranial hypertension.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Recognize the complications associated with diabetic ketoacidosis

Suggested Readings
- Cooke D, Plotnick L. Management of diabetic ketoacidosis in children and adolescents. *Pediatr Rev*. 2008;29:431-436. doi: 10.1542/pir.29-12-431 .
- Glaser NS, Wootton-Gorges SL, Buronocore MH, et al. Subclinical cerebral edema in children with diabetic ketoacidosis randomized to 2 different rehydration protocols. *Pediatrics*. 2013;131:e73-e80. doi: 10.1542/peds.2012-1049 .

Question 9

An 8-year-old girl is brought to your office for a health supervision visit. The mother's only concern is that her daughter has recently developed "acne," and she asks that you recommend treatment. The girl is new to your practice and has had inconsistent medical care in the past. Her medical history is remarkable for "hyperactivity" and "learning problems." She has normal vital signs and growth parameters. The physical examination findings are unremarkable except for the skin; papules and a hypopigmented macule are located on the central area of the face (Item Q9A). There is a similar macule on the trunk and 1 on the thigh (Item Q9B).

Of the following, the topical therapy that is MOST likely to be effective in treating this girl's eruption is

A. ammonium lactate
B. benzoyl peroxide
C. metronidazole
D. mupirocin
E. sirolimus

Correct Answer:E

The girl in this vignette has 2 major features of tuberous sclerosis complex (TSC): 3 or more facial angiofibromas and 3 or more hypomelanotic macules. In addition, she appears to have attention-deficit/hyperactivity disorder and learning difficulties, which are common in individuals who have TSC. The presence of 2 major features is sufficient to make a diagnosis of TSC (**Item C9A**). Facial angiofibromas may become large and disfiguring; treatment with topical sirolimus often causes the lesions to become smaller or resolve (at the time of this writing, the drug did not have US Food and Drug Administration approval for this indication but is commonly used "off label").

Item C9A. Diagnostic Criteria for Tuberous Sclerosis Complex. (a definite diagnosis requires 2 major features or 1 major feature and ≥ 2 minor features)

Major Features	Minor Features
Angiofibromas (≥ 3) or fibrous cephalic plaque	"Confetti" skin lesions: numerous 1- to 3-mm hypopigmented macules often present on the arms or legs
Cardiac rhabdomyoma	Dental enamel pits (>3)
Cortical dysplasias (eg, tubers)	Intraoral fibromas (≥2)
Hypomelanotic macules (3 or more that are ≥ 5 mm)	Multiple renal cysts
Lymphangioleiomyomatosis	Nonrenal hamartomas
Multiple retinal nodular hamartomas	Retinal achromic patch
Renal angiomyolipoma	
Shagreen patch	
Subependymal giant cell astrocytoma	
Subependymal nodules	
Ungual fibromas (≥ 2)	

Reprinted with permisson from Northrup H, Koenig MK, Pearson DA, et al. Tuberous sclerosis complex. *GeneReviews®*.

Tuberous sclerosis complex is a neurocutaneous disorder caused by mutations in TSC1, which encodes hamartin, or TSC2, which encodes tuberin. It is transmitted in an autosomal dominant manner, but two-thirds of affected individuals have a de novo mutation. The mutations result in abnormal cellular proliferation that involves activation of the mechanistic target of rapamycin pathway. This activation promotes tumorigenesis (such as the hamartomas that affect many organ systems) and plays a role in the development of seizures, autism spectrum disorder, intellectual disability, and skin lesions. Tuberous sclerosis complex may impact many systems.

- Skin: Involved in nearly all individuals with TSC. Lesions include hypomelanotic macules, confetti-like hypomelanotic macules, facial angiofibromas, shagreen patches (**Item C9B**), fibrous cephalic plaques, and ungual fibromas (**Item C9C**).
- Central nervous system: brain lesions (subependymal nodules, cortical dysplasias, subependymal giant cell astrocytoma), seizures, developmental delay or intellectual disability, and neuropsychiatric disorders (autism spectrum disorder, attention-deficit/hyperactivity disorder, learning and cognitive impairment, disruptive behaviors)
- Kidneys: benign angiomyolipomas, renal cysts, malignant angiomyolipoma, and renal cell carcinoma
- Heart: cardiac rhabdomyomas
- Lung: lymphangioleiomyomatosis, multifocal micronodular pneumocyte hyperplasia
- Eye: retinal hamartomas

Item C9C: Ungual fibroma in a patient who has tuberous sclerosis.
Courtesy of D. Krowchuk

In the past, managing disfiguring facial angiofibromas was challenging, often involving laser therapy or dermabrasion. However, recent studies have demonstrated that a topical mechanistic target of rapamycin inhibitor (like sirolimus or rapamycin) can improve the appearance of these lesions (as well as ungual fibromas and hypomelanotic macules). Oral mechanistic target of rapamycin inhibitors (sirolimus, everolimus) are often used in the treatment of TSC-related

complications such as subependymal giant cell astrocytomas, pulmonary involvement, renal angiomyolipomas, lymphangioleiomyomatosis, and symptomatic cardiac rhabdomyomas.

The location of the lesions on the central face and the absence of a central keratotic plug make keratosis pilaris (**Item C9D**) unlikely and, therefore, treatment with ammonium lactate is not indicated. Mild acne vulgaris is often treated with benzoyl peroxide, but the absence of inflammatory papules, pustules, and comedones argues against this diagnosis. Periorificial dermatitis, as the name suggests, is characterized by inflammatory papules and pustules on a red background located around the mouth, nose, or eyes (**Item C9E**). Scaling is often present. Because these findings differ from those exhibited by the girl in this vignette, treatment with topical metronidazole is not warranted. Finally, the girl's lesions are not consistent with the inflammatory papules and pustules of folliculitis, making the use of topical mupirocin unnecessary.

PREP Pearls
- Facial angiofibromas in patients who have tuberous sclerosis complex may mimic the lesions of acne vulgaris, can become large and disfiguring, and often respond to treatment with topical sirolimus.
- Oral mechanistic target of rapamycin inhibitors (sirolimus, everolimus) are often used in the treatment of tuberous sclerosis complex-related complications such as subependymal giant cell astrocytomas, pulmonary involvement, renal angiomyolipomas, lymphangioleiomyomatosis, and symptomatic cardiac rhabdomyomas.

MOCA-Peds Objective
- Recognize the genetic syndromes that may present as a learning disability

ABP Content Specifications(s)
- Recognize the clinical findings associated with tuberous sclerosis, and manage appropriately

Suggested Readings
- Northrup H, Koenig MK, Pearson DA, et al. Tuberous sclerosis complex. *GeneReviews*. 2016..
- Section on Dermatology, American Academy of Pediatrics. Tuberous sclerosis complex (TSC). In: Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016:519-526.

Question 10

As a member of your quality improvement team, you are reviewing admission temperatures for premature infants born at your hospital. Delivery room management is identical for premature infants born vaginally and by cesarean section. You note a higher incidence of hypothermia temperature <36.5°C in premature infants born via cesarean section compared with those delivered vaginally.

Of the following, the MOST effective intervention for decreasing hypothermia among premature infants in your hospital is to

    A. apply plastic wrap over neonates' torsos and extremities
    B. cover neonates' heads with caps
    C. increase operating room temperature
    D. place neonates skin to skin with parents immediately
    E. use radiant warmers

Correct Answer: C

Because the premature infants delivered vaginally and by cesarean section are treated identically, increasing operating room temperature is the intervention most likely to improve rates of hypothermia. Neonatal hypothermia, defined as a rectal temperature less than 36.5°C, has been associated with poor neonatal outcomes among both term and premature neonates. Neonates with hypothermia can present with poor perfusion, bradycardia, apnea, hypoglycemia, or hypoxia. Among premature infants born before 37 weeks of gestation, hypothermia has been linked to increased rates of intraventricular hemorrhage, hypoglycemia, and sepsis. Therefore, changing delivery room practices to prevent hypothermia can have a positive impact on long-term health outcomes. Ideally, the operating room temperature should be maintained between 25.0°C and 27.0°C. To accommodate obstetric providers, the temperature may be lowered after the infant is placed under the radiant warmer.

In this scenario, with identical delivery room management, the increased incidence of hypothermia among premature neonates delivered by cesarean section suggests that the environment of the operating room is contributing to hypothermia. Covering exposed skin with plastic wrap to minimize radiant heat loss, using caps, and radiant warmers will prevent hypothermia, but does not explain the difference in hypothermia based on mode of delivery. In low resource settings, immediate skin-to-skin care with a parent may be used to minimize heat loss. However, when other more effective methods are available, skin-to-skin care should not be the primary method used to prevent hypothermia.

PREP Pearls
- Increasing operating room temperature to 25.0°C–27.0°C decreases the risk of neonatal hypothermia among infants born by cesarean section.
- Neonatal hypothermia has been linked to increased rates of morbidity for both term and premature infants.
- Use of radiant warmers, plastic wrap, and caps has been associated with higher admission temperatures among premature infants.

ABP Content Specifications(s)
- Recognize the signs and symptoms of heat loss in a newborn infant, and manage appropriately

Suggested Readings
- Angert R, Adam HM. Care of the very low-birthweight infant. *Pediatr Rev*. 2009;30:32. doi: http://dx.doi.org/10.1542/pir.30-1-32.
- Carlo, WA. Delivery room emergencies. In: Kliegman RM, Stanton BF, St Geme J, Schor NF eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Saunders Elsevier; 2016;chap 100:844–848e.
- Wyckoff MH, Aziz K, Escobedo MB, et al. Part 13: Neonatal resuscitation: 2015 American Heart Association guidelines. update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132(suppl 2):s543-s560.

Question 11

A 14-year-old adolescent is brought to your office for fatigue and decreased appetite that she has experienced over the past month. She has associated nausea but no vomiting, diarrhea, or fever. Her medical history is significant for autoimmune hypothyroidism since age 8 years, for which she takes levothyroxine daily. Physical examination reveals a temperature of 37°C, heart rate of 120 beats/min, blood pressure of 90/48 mm Hg, respiratory rate of 16 breaths/min, weight of 44.6 kg (25th percentile), height of 165 cm (75th percentile), and body mass index of 16.4 kg/m2 (10th percentile). She appears tired, with diffusely hyperpigmented skin. Capillary refill time is 3 seconds. The remainder of her physical examination findings are unremarkable.

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

    A. adrenal insufficiency
    B. anemia
    C. anorexia nervosa
    D. gastroparesis
    E. uncontrolled hypothyroidism

Correct Answer: A

The girl described in the vignette has Addison disease, primary adrenal insufficiency. In primary adrenal insufficiency, there is a deficiency of both glucocorticoid (cortisol) and mineralocorticoid (aldosterone). In response to low cortisol levels, adrenocorticotropic hormone (ACTH) levels are high. The girl's diffuse hyperpigmentation is due to the high ACTH level. Her fatigue, decreased appetite, and nausea are all consistent with Addison disease. Weight loss can be another presenting symptom. Mineralocorticoid deficiency in Addison disease manifests clinically with dehydration, also exhibited by this girl. Her history of autoimmune hypothyroidism suggests an autoimmune etiology for her adrenal insufficiency.

Laboratory findings consistent with primary adrenal insufficiency include hyponatremia, hyperkalemia, hypoglycemia, and metabolic acidosis. Serum cortisol concentration is low and ACTH is high. Eosinophilia may also be seen.

Anemia, anorexia nervosa, gastroparesis, and uncontrolled hypothyroidism can each cause some, but not all, of the signs and symptoms described in the vignette.
If adrenal insufficiency is suspected, a bedside blood glucose test should be performed, because of the high risk for hypoglycemia. Serum electrolyte, glucose, cortisol, and ACTH levels should be obtained.

Children with Addison disease are at risk for adrenal crisis, which typically presents with vomiting, abdominal pain, and hypovolemic shock. The initial treatment of adrenal crisis consists of restoration of intravascular fluid volume and correction of hypoglycemia. A 5% dextrose-containing normal saline bolus of 20 mL/kg may be given intravenously if hypoglycemia is present. Subsequently, a stress dose of hydrocortisone, 100 mg/m^2 of body surface area, should be given intravenously. Hydrocortisone should then be continued intravenously at 100 mg/m^2 per day, either as a continuous infusion or divided every 6 hours, until the child's clinical status is improved. High-dose hydrocortisone has both glucocorticoid and mineralocorticoid activity.

Once the adrenal crisis is resolved, a child with Addison disease requires daily replacement doses of the glucocorticoid hydrocortisone (8–10 mg/m^2 per day divided 2–3 times per day) and the mineralocorticoid fludrocortisone (0.1 mg once per day). Before discharge from the hospital, the child's family should be taught how to administer an appropriate stress dose (double or triple the daily dose divided every 8 hours) of hydrocortisone in case of fever or other moderate stress event. Arrangements should be made to obtain a medical alert tag. The family should be given a prescription for an intramuscular injectable form of hydrocortisone to have at home for use in case of an adrenal crisis, as well as an emergency letter with instructions regarding stress dose steroids.

PREP Pearls
- Fatigue, nausea, weight loss, hypotension, volume depletion, and diffuse hyperpigmentation are common presenting symptoms and signs of Addison disease.
- Laboratory findings of Addison disease include hyponatremia, hyperkalemia, hypoglycemia, metabolic acidosis, low serum cortisol, high adrenocorticotropic hormone level, and eosinophilia.
- Treatment of an adrenal crisis consists of urgent restoration of intravascular fluid volume and correction of hypoglycemia, followed by intravenous administration of stress dose hydrocortisone.
- Long-term treatment of Addison disease consists of replacement of both glucocorticoid and mineralocorticoid deficiencies with hydrocortisone and fludrocortisone.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Recognize the clinical features associated with Addison disease
- Plan the appropriate diagnostic evaluation for Addison disease
- Plan the appropriate management of Addison disease, including an adrenal crisis associated with the disorder

Suggested Readings
- Auron M, Raissouni N. Adrenal insufficiency. *Pediatr Rev*. 2015;36(3):92–102; quiz 103, 129. doi: http://dx.doi.org/10.1542/pir.36-3-92.
- Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2016;101(2):364–389. doi: http://dx.doi.org/10.1210/jc.2015-1710.
- Hsieh S, White PC. Presentation of primary adrenal insufficiency in childhood. *J Clin Endocrinol Metab.* 2011;96(6):E925–E928. doi: http://dx.doi.org/10.1210/jc.2011-0015.

Question 12

A 14-year-old girl comes to your office for a health supervision visit. During the interview, she discloses that on most days over the past month, she has been feeling irritable and sad. She has lost interest in going out with her friends and in playing basketball for her school's team. It has been difficult for her to fall asleep. She feels tired and is finding it hard to pay attention at school. These symptoms have been worsening. The girl reports that she does not drink alcohol, smoke tobacco, or use drugs. She has been healthy and is not taking any medication or supplements. Although she reports no change in appetite, she has lost weight since her last visit. Her review of systems is otherwise negative, and her physical examination findings are within normal limits. You decide to prescribe a medication that has been approved by the US Food and Drug Administration for the treatment of this condition in adolescents, and for which additional medical tests are not indicated.

Of the following, the medication that BEST fits this description is

A. citalopram
B. escitalopram
C. fluoxetine
D. paroxetine
E. sertraline

Correct Answer: C

The adolescent described in the vignette meets *Diagnostic and Statistical Manual of Mental Disorders Fifth Edition* (DSM-5) criteria for depression. She has had more than a 2-week period of above-baseline depressed mood, decreased pleasure in activities, weight loss, insomnia, fatigue, and poor concentration. Depression affects up to 25% of adolescents. Selective serotonin reuptake inhibitors (SSRIs) are recommended as the first-line medications in the treatment of moderate to severe depression. The US Food and Drug Administration (FDA) has approved 2 SSRIs for the treatment of adolescent depression—fluoxetine and escitalopram. SSRIs should be initiated at low doses and then gradually titrated up to achieve the desired effect while minimizing any adverse effects. A medication trial should last at least 6 to 12 weeks. If ineffective, the SSRI should be tapered and a different SSRI tried. Once an effective SSRI has been identified and symptoms have resolved, treatment with the SSRI should be continued for an additional 6 to 12 months. Treatment is effective in most adolescents.

Although SSRIs are generally well-tolerated, patients should be monitored closely for adverse effects. Headache, abdominal pain, and sleep disturbance may occur after dosage changes, but typically improve over time. Electrocardiography (EKG) has been recommended to monitor for QTc prolongation in patients taking higher doses of escitalopram. Fluoxetine does not require monitoring with EKG or other medical test. Patients may become disinhibited and exhibit risk-taking behaviors or increased impulsivity when taking SSRIs. Manic activation may occur in those who are at risk for bipolar disorder. During treatment, it is essential to monitor for suicidal thoughts or behavior. In 2004, the FDA issued a black box warning for the risk of increased suicidal ideation with SSRIs. When prescribing an SSRI, the health care provider should discuss this black box warning with the patient and her family. Adolescents taking SSRIs should be monitored closely for increased suicidal thoughts, agitation, irritability, mania, or worsening mood. For most patients, the risk for suicidal ideation is actually higher with no treatment than with an SSRI. In fact, multiple studies performed since the addition of the black box warning have demonstrated an inverse relationship between rates of SSRI prescriptions and rates of suicide.

Consensus guidelines recommend fluoxetine as the preferred SSRI for the treatment of adolescent depression. Fluoxetine is also FDA-approved for treating childhood depression. Some studies have shown citalopram and sertraline to be effective for treating adolescent depression; however, these medications are not FDA-approved for this indication. Relative to the other options, paroxetine has the least evidence supporting it as an effective treatment for adolescent depression. Dose-dependent QTc prolongation can be seen in patients treated with doses of more than 40 mg of citalopram or 20 mg of escitalopram. EKGs may be obtained to monitor for QTc prolongation with higher doses of these SSRIs.
Depression affects a significant number of adolescents; therefore, it is essential for health care providers to understand the indications for, management of, and risks associated with the use of various antidepressant medications. Guidelines such as the Guidelines for Adolescent Depression in Primary Care (GLAD-PC) are available to support the pediatric health care provider in the care of these patients.

PREP Pearls
- Once an effective selective serotonin reuptake inhibitor (SSRI) has been identified and symptoms have resolved, treatment with the SSRI should be continued for an additional 6 to 12 months.
- Multiple studies performed since the addition of the 2004 US Food and Drug Administration black box warning on SSRIs have demonstrated an inverse relationship between rates of SSRI prescriptions and rates of suicide.
- Dose-dependent QTc prolongation can be seen in patients treated with doses greater than 40 mg of citalopram or 20 mg of escitalopram.

ABP Content Specifications(s)
- Understand the risks associated with the use of various antidepressant drugs

Suggested Readings
- Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein REK. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II, treatment and ongoing management. *Pediatrics*. 2007;120(5):e1313–e1326. doi: http://dx.doi.org/10.1542/peds.2006-1395.
- Maslow GR, Dunlap K, Chung RJ. Depression and suicide in children and adolescents. *Pediatr Rev*. 2015;36(7):299–310. doi: http://dx.doi.org/10.1542/pir.36-7-299.
- Tang MH, Pinsky EG. Mood and affect disorders. *Pediatr Rev*. 2015;36(2):52–61. doi: http://dx.doi.org/10.1542/pir.36-2-52.

Question 13

You are seeing a 4-month-old infant with poor growth and an enlarged abdomen for follow-up care after an emergency department visit. The parents state that they have taken the infant to the emergency department on several occasions for low blood sugar after the baby began to sleep through the night. One of these episodes was associated with a seizure.

The infant has doll-like facies with fat cheeks, protuberant abdomen, hepatomegaly, renomegaly, short stature, and thin arms and legs. No splenomegaly is noted.

You order laboratory tests that reveal elevated lactate, uric acid, and lipid levels, along with a low serum glucose level. Liver transaminases, complete blood cell count, and hemoglobin A1C are within the normal range. You order an echocardiogram that rules out a congenital heart defect with associated congestive heart failure.

The family history is unremarkable, and the infant's developmental milestones are appropriate.

Of the following, the MOST likely disorder to present with these clinical and laboratory findings is

 A. Gaucher disease
 B. glycogen storage disease type I
 C. Hurler syndrome
 D. peroxisomal disorder
 E. Pompe disease

Correct Answer: B

The infant in this vignette has glycogen storage disease type I (GSDI), which classically presents with hepatomegaly, renomegaly, and recurrent episodes of hypoglycemia. The classic appearance consists of doll-like facies with chubby cheeks, thin extremities, distended abdomen, and short stature. In addition to hypoglycemia, children with GSDI have lactic acidosis, hyperlipidemia, hypertriglyceridemia, and hyperuricemia. The 2 subtypes, GSDIb and GSDIa, are clinically difficult to distinguish. Untreated GSDIb patients have recurrent bacterial infections and mucosal ulcerations of the intestinal and oral regions caused by impaired monocyte and neutrophil function. Untreated children with either subtype will experience poor growth, pubertal delays, gout, chronic kidney disease, pulmonary hypertension, osteoporosis, hepatic adenomas, atherosclerosis, pancreatitis, and polycystic ovaries. Children who are treated are likely to have normal growth, and most will survive into adulthood.

Multifactorial treatment is needed to address the laboratory abnormalities and clinical manifestations of GSDI. Treatment components typically include: optimal nutritional therapy to avoid episodes of hypoglycemia; allopurinol; lipid-reducing medications; citrate supplementation; angiotensin-converting enzyme inhibitors; treatment for hepatic adenomas; human granulocyte colony-stimulating factor for recurrent infections; and a diet low in sucrose and fructose. Transplant of the liver, kidneys, or both may be necessary.

Glycogen storage disease type I is an autosomal recessive disorder caused either by a deficiency of glucose-6-phosphatase catalytic activity (GSDIa) or by a defect in glucose-6-phosphate translocase (GSDIb). The genes involved are *G6PC* in GSDIa and *SLC37A4* in GSDIb. Confirmation of a clinical diagnosis requires demonstration of deficient enzyme activity or molecular confirmation of known pathogenic gene mutations.

Gaucher disease is an autosomal recessive lysosomal storage disorder that has a spectrum of presentations but universally includes bone disease, hepatosplenomegaly, cytopenias, and pulmonary disease. Gaucher disease types 2 and 3 also have neurologic involvement.

Hurler syndrome is an autosomal recessive lysosomal storage disorder that presents with coarsening of facial features over time but normal appearance at birth. Common manifestations as the storage material accumulates include umbilical and inguinal hernias, frequent upper respiratory infections, skeletal involvement (dysostosis multiplex), hearing loss, hepatosplenomegaly, valvular cardiac disease, and progressive intellectual disability.

Peroxisomal biogenesis disorders are autosomal recessive disorders caused by impaired peroxisomal fatty acid metabolism. Infants with these disorders exhibit hypotonia, distinctive facies, poor feeding, seizures, and hepatic dysfunction. As the disease progresses, retinal dystrophy, sensorineural hearing loss, and progressive developmental disability occur.

Infantile Pompe disease is another autosomal recessive disorder that presents with severe hypotonia, muscular weakness, cardiomegaly with progression to cardiac failure, failure to thrive, and respiratory distress. It is the only glycogen storage disease that is also a lysosomal

storage disorder. Biochemical testing that supports the diagnosis includes an elevated creatine kinase level and urinary oligosaccharides. Confirmatory testing typically involves demonstration of reduced acid α-glucosidase activity. In Pompe disease, lysosomal glycogen accumulates preferentially in the skeletal muscle, cardiac muscle, and smooth muscle. Enzyme replacement therapy is available for this disorder and should be initiated as soon as possible to improve outcome and save lives.

Hypoglycemia is not a common clinical manifestation of Gaucher disease, Hurler syndrome, peroxisomal disorders, or Pompe disease.

PREP Pearls
- Glycogen storage disease type I classically presents with hepatomegaly, renomegaly, and recurrent episodes of hypoglycemia. Doll-like faces with chubby cheeks, thin extremities, distended abdomen, and short stature are common.
- Children with glycogen storage disease have recurrent episodes of hypoglycemia, lactic acidosis, hyperlipidemia, hypertriglyceridemia, and hyperuricemia.
- Hypoglycemia is not a common in Gaucher disease, Hurler syndrome, peroxisomal disorders, or Pompe disease.

ABP Content Specifications(s)
- Plan the appropriate immediate and long-term management of glycogen storage disease, while considering the long-term prognosis
- Recognize the clinical features associated with glycogen storage disease

Suggested Readings
- Bali DS, Chen Y-T, MD, Austin S, Goldstein JL. Glycogen storage disease type I. *GeneReviews*. 2017. https://www.ncbi.nlm.nih.gov/books/NBK1312/.
- Chou JY, Jun HS, Mansfield BC. Type I glycogen storage diseases: disorders of the glucose-6-phosphatase/glucose-6-phosphate transporter complexes. *J Inherit Metab Dis*. 2015;38(3):511–519. doi: http://dx.doi.org/10.1007/s10545-014-9772-x.

Question 14

A 4-year-old boy is seen in your office for follow-up after he was evaluated and treated at a local emergency department yesterday for right scrotal pain.

Two days ago, the boy began to complain of pain in his right scrotum. At that time, his right scrotum appeared swollen and red to his mother, so she took him to a local emergency department for evaluation. Results available from his emergency department visit yesterday include a urinalysis that was normal, and a urine culture that has yielded no bacterial growth. The child also underwent color Doppler ultrasonography of his scrotum, which revealed slight enlargement of his right epididymis, with increased blood flow to both his right epididymis and right testis. The emergency department physician advised the boy's family that his scrotal pain was due to acute epididymitis.

The boy's medical history includes mild intermittent asthma, with no other documented medical conditions. His asthma has been relatively well-controlled, and he has no history of hospitalizations. Last week, he had an acute asthma exacerbation that seemed to have been triggered by an upper respiratory viral infection. His only current medication is albuterol, which he takes as needed for acute asthma symptoms. He has had no recent fevers, dysuria, increased urinary frequency, or urethral discharge. He is currently attending preschool and has been doing well according to his mother.

In your office today, the child appears well and in no distress. He is afebrile, and his vital signs are within normal limits for his age. Genitourinary examination reveals mild swelling, erythema, and tenderness over the right hemiscrotum (which, the mother informs you, looks slightly improved from yesterday). Both of the boy's testicles lie normally, and his cremasteric reflexes are intact bilaterally. The remainder of his physical examination findings are unremarkable.

Of the following, the best NEXT step in this boy's management would be

A. investigation for sexual abuse because sexually transmitted infections are the most likely cause of this diagnosis in prepubertal boys
B. no further evaluation is necessary because the boy's recent upper respiratory infection most likely caused him to develop this disorder
C. referral to a pediatric oncologist because underlying malignancies exist in more than half of prepubertal boys with this diagnosis
D. referral to a urologist because genitourinary structural abnormalities are present in most boys with this diagnosis
E. repeat urinalysis and urine culture because infection with Escherichia coli is identified in almost all prepubertal boys with this diagnosis

Correct Answer: B

The 4-year old boy in the vignette has been diagnosed with acute epididymitis. The boy needs no further evaluation at this time, because his recent upper respiratory infection most likely led him to develop acute epididymitis.

All pediatric providers should recognize the clinical findings associated with epididymitis and know the most common causes in boys of various ages. Epididymitis is an infection or inflammation of the epididymis. Although it occurs more frequently in sexually active adolescents and adult men, epididymitis can affect prepubertal boys and adolescents who are not sexually active.

Signs and symptoms of epididymitis include unilateral pain and swelling of the scrotum (typically gradual in onset), along with scrotal swelling and erythema. Affected boys may have dysuria, increased urinary frequency, urethral discharge, and fever (though these associated symptoms are not always present). On physical examination, testicles will be lying normally, with intact cremasteric reflexes (which help to distinguish this disorder from testicular torsion). Typically, color Doppler ultrasonography will reveal the affected testis and epididymis with an increase in size and blood flow.

In prepubertal boys, epididymitis arises most commonly as a postviral infectious phenomenon. Associated viral infections may include (but are not limited to) enterovirus and adenovirus, as well as *Mycoplasma pneumoniae*. Although infections with bacterial agents such as *Escherichia coli* can cause epididymitis in prepubertal boys (usually as a result of direct spread of a bacterial urinary tract infection to the epididymis), this etiology is relatively uncommon in this age group.

In sexually active adolescent boys, acute epididymitis is most commonly associated with sexually transmitted infections, including *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Infection with *E coli*, mycobacteria, and viruses are also potential causes in this age group.

For the boy in the vignette, investigation for sexual abuse is not warranted in the absence of other "red flags" for abuse, because sexually transmitted infections are not the most likely cause of epididymitis in his age group and he has a history of a recent viral infection.

Referral to a pediatric oncologist is not indicated for this boy, because an association between underlying malignancies and epididymitis has not been demonstrated in the literature.

Given that the boy in the vignette had negative urinalysis and urine culture results, is improving clinically, and has not had recurrent episodes of epididymitis, referral to a urologist is not indicated. Referral for urologic evaluation for structural abnormalities of the genitourinary tract (such as genitourinary reflux) isindicated for prepubertal boys who are found to have bacterial epididymitis, epididymitis associated with a urinary tract infection, or recurrent epididymitis.

A repeat urinalysis and urine culture is not needed for the boy in the vignette. He has had a recent history of a viral infection, has been afebrile, has had no dysuria or increased urinary frequency, and is improving clinically.

PREP Pearls
- Signs and symptoms of epididymitis include unilateral pain, scrotal swelling and erythema.
- In prepubertal boys, epididymitis arises most commonly from a postviral infectious phenomenon.
- In sexually active adolescent boys, acute epididymitis is most commonly associated with sexually transmitted infections.
- Urologic referral is indicated for prepubertal boys who have bacterial epididymitis, epididymitis associated with a urinary tract infection, or recurrent epididymitis.

ABP Content Specifications(s)
- Recognize the clinical findings associated with epididymitis
- Identify common causes of epididymitis in patients of various ages

Suggested Readings
- Gkentzis A, Lee L. The aetiology and current management of prepubertal epididymitis. *Ann R Coll Surg Engl.* 2014;96:181–183. doi: http://dx.doi.org/10.1308/003588414X13814021679311.
- Perron CE, Bin SS. Pain: scrotal. In: Shaw KN, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2016:chap 56:383–391.
- Somekh E, Gorenstein A, Serour R. Acute epididymitis in boys: evidence of a post-infectious etiology. *J Urol.* 2004;171:391–394. doi: http://dx.doi.org/10.1097/01.ju.0000102160.55494.1f.

Question 15

You are seeing a 15-year-old boy in your office for a sports preparticipation evaluation and annual health supervision visit. The boy is a competitive basketball player and his parents ask if their son should use a mouthguard during sports participation.

Of the following, the MOST accurate statement to include in your discussion with the family is that

    A. basketball has one of the highest rates of dental injuries among high school sports
    B. most dental injuries occur in athletes who were wearing a mouthguard at the time of injury
    C. the rate of dental injuries is higher during sports practice sessions than during competition
    D. the risk of dental injury is much lower if the boy uses a professionally fitted rather than a self-fitted mouthguard
    E. the use of a mouthguard will decrease the boy's risk of sports concussion

Correct Answer: A

The boy in the vignette should use a mouthguard during sports participation because of the high rate of dental injuries during basketball. Dental injuries are common during youth sports. In boys' high school sports, the highest rates of dental injuries occur during basketball, baseball, wrestling, and soccer. Among girls' sports, field hockey, softball, basketball, and lacrosse have the highest rates of dental trauma. Even athletes participating in noncontact sports, such as swimming and track, are at risk for dental injuries. These injuries typically occur as a result of player-to-player contact, getting hit by a ball or sports equipment, or when a player hits the ground.

The American Dental Association recommends that athletes use mouthguards for 29 common sports and physical activities. Use of a mouthguard decreases the risk of various oral injuries, including tooth avulsions, tooth fractures, and lacerations. In sports that do not require the use of a mouthguard by league rules, most dental injuries occur in athletes who were not wearing mouthguards.

Although the rate of dental injury is highest during competition, athletes generally spend many more hours practicing than competing; thus, the overall risk of injury may be higher during practice. Mouthguards should therefore be worn during both practice and competition.

Custom mouthguards, made for an individual by a dental health professional, may fit better and be more comfortable than less expensive "boil and bite" or off-the-shelf mouthguards. However, these have not consistently been shown to decrease injury rates compared with off-the-shelf models. Although mouthguards decrease the risk of dental injury, they do not provide protection against sports concussions.

PREP Pearls
- Use of a mouthguard during sports activities decreases oral injuries, including tooth avulsions, tooth fractures, and lacerations.
- Professionally fitted mouthguards have not consistently been shown to decrease oral injury rates compared with "boil and bite" or off-the-shelf mouthguards.

ABP Content Specifications(s)
- Recognize the indications for the use of a mouth guard during sports activities

Suggested Readings
- ADA Council on Access, Prevention and Interprofessional Relations; ADA Council on Scientific Affairs. Using mouthguards to reduce the incidence and severity of sports-related oral injuries. *J Am Dent Assoc.* 2006;137(12):1712–1720.
- Collins CL, McKenzie LB, Ferketich AK, Andridge R, Xiang H, Comstock RD. Dental injuries sustained by high school athletes in the United States, from 2008/2009 through 2013/2014 academic years. *Dent Traumatol.* 2016;32(2):121–127. doi: http://dx.doi.org/10.1111/edt.12228.

- McGuine TA, Hetzel S, McCrea M, Brooks MA. Protective equipment and player characteristics associated with the incidence of sport-related concussion in high school football players: a multifactorial prospective study. *Am J Sports Med.* 2014;42(10):2470–2478. doi: http://dx.doi.org/10.1177/0363546514541926.

Question 16

You are planning a presentation for the parents of incoming 6th grade students at a local middle school regarding the psychosocial component of adolescent development. You have decided to focus your presentation on the development of independence and the influence of peers during early adolescence.

Of the following, the MOST appropriate statement to include in your presentation is

  A. adolescents with authoritarian parents are typically better able to resist peer pressure
  B. peers have increasingly more influence throughout adolescence
  C. relationships with nonfamilial adults have no role in the development of independence
  D. the need for conformity with peers is typically strongest during early adolescence
  E. transitioning to a permissive parenting style is critical for early adolescent development

Correct Answer: D

Adolescent development has 3 components: physical development, cognitive development and psychosocial development. The primary tasks of adolescent psychosocial development are development of a mature self-identity, independence, and mature sexuality. During early adolescence, self-identity development is greatly influenced by peers and the need for group cohesion. However, the influence of peers on self-identity decreases in later adolescence. While there is typically a degree of separation between parents and adolescents during this aspect of development, youth often look to other trusted adults as role models.

Parenting styles can affect adolescent outcomes. Permissive parenting has been associated with higher rates of substance use and school misconduct and less connectedness to school. Authoritative parenting has been shown to better foster adolescent well-being.

PREP Pearls
- The primary task of adolescent psychosocial development is the development of a mature self-identity, independence, and mature sexuality.
- During early adolescence, self-identity development is greatly influenced by peers and the need for group cohesion.
- The influence of peers on self-identity decreases in later adolescence.

MOCA-Peds Objective
- Evaluate the developmental status of adolescents

ABP Content Specifications(s)
- Understand the importance of accepting an adolescent's separation from the family, and the role re-adjustments that may be required
- Identify typical characteristics of a young adolescent's peer group while understanding the influence of that group on behaviors
- Recognize the importance of a peer group in a young adolescent's separation from the family

Suggested Readings
- Hazen E, Schlozman S, Beresin E. Adolescent psychological development: a review. *Pediatr Rev*. 2008;29:161–168. doi: http://dx.doi.org/10.1542/pir.29-5-161.
- Hoskins DH. Consequences of parenting on adolescent outcomes. *Societies* 2014;4:506–531. doi: http://dx.doi.org/10.3390/soc4030506.

Question 17

A 6-month-old infant is brought to your office for a health supervision visit. She was born at 28 weeks of gestation by emergent cesarean delivery after placental abruption. Her neonatal course was complicated with prolonged oral intubation, treatment for necrotizing enterocolitis, and sepsis. Since discharge from the neonatal intensive care unit at 2 months of age, she has been well with appropriate growth. She is developing appropriately for her corrected age. Her parents have questions about teething.

Of the following, the MOST accurate statement is that this infant may have

A. anodontia (absence of teeth)
B. delayed dental eruption
C. early dental eruption
D. hypodontia (missing teeth)
E. supernumerary (extra) teeth

Correct Answer: B

The infant in this vignette, who was delivered prematurely, is most likely to have delayed dental eruption. Infants born before 30 weeks' gestation and infants with birth weights less than 1,000 g are most likely to exhibit delayed dental eruption. This delay is most prominent with primary (deciduous) teeth; many of these children have fairly normal timing for eruption of their permanent dentition. Premature infants do not have an increased likelihood of early dental eruption, anodontia, hypodontia, or supernumerary teeth.

Dental eruption is delayed when it occurs 6 or more months after the expected age range for a specific tooth. There are age- and race-related variations in primary tooth eruption, with girls and African American children showing slightly earlier average eruption ages. Typically, the mandibular central incisors are the first to erupt, and eruption is usually symmetric, with corresponding teeth on the left and right sides erupting at similar times. Average eruption age and variability for primary dentition is shown in **Item C17A**.

Delayed dental eruption can be idiopathic, familial, or associated with local or systemic conditions or genetic disorders. Commonly associated conditions are listed in **Item C17B**.

Item C17A. Average Age and Variability for Eruption of Primary Dentition.
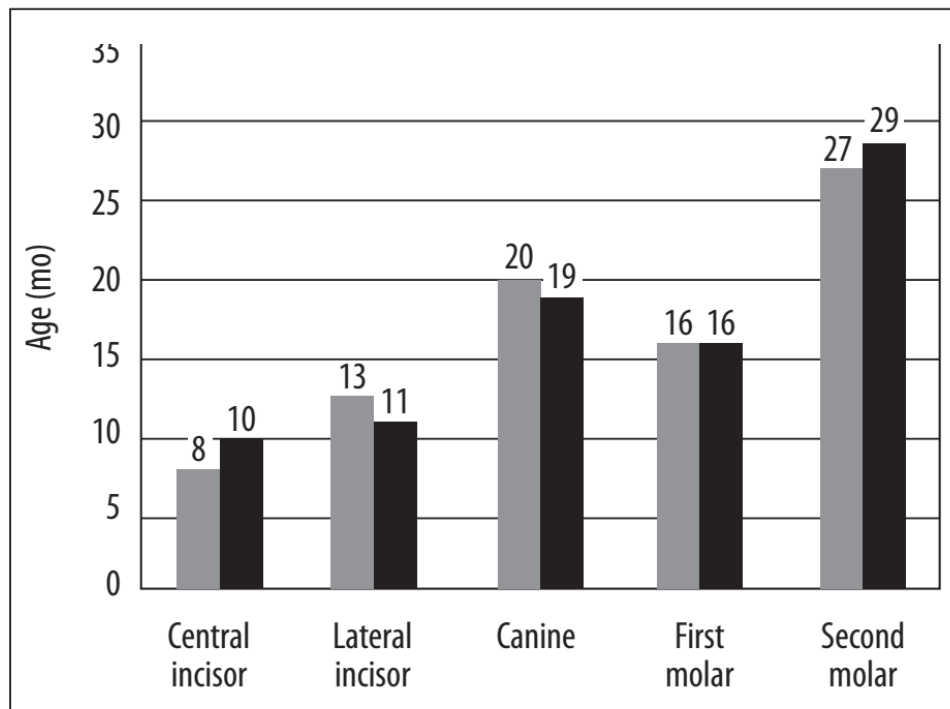
Reprinted with permission from Wright, JT. Normal formation and development defects of the human dentition. *Pediatr Clin North Am*, 47(5), 975-1000.

Item C17B. Conditions Associated With Delayed Dental Eruption.

Local Conditions	Systemic Conditions	Genetic Disorders
Gingival hyperplasia	Anemia	Achondroplasia
Radiation damage	Celiac disease	Amelogenesis imperfecta
Scar tissue	Heavy metal exposure	Apert syndrome
Supernumerary (extra) teeth	Human immunodeficiency virus infection	Chondroectodermal dysplasia
Tumor	Hypoparathyroidism	Down syndrome
	Hypopituitarism	Dyskeratosis congenita
	Hypothyroidism	Mucopolysaccharidosis
	Icthyosis	
	Prematurity	
	Pseudohypoparathyroidism	
	Rickets	

Courtesy of I Larson

PREP Pearls
- Delayed dental eruption can be idiopathic, familial, or associated with local (mucosal or oral) factors, systemic conditions including endocrine abnormalities, or genetic disorders.
- Prematurity and low birth weight can be associated with delayed tooth eruption.

ABP Content Specifications(s)
- Recognize the causes of delayed dental eruption

Suggested Readings
- Klein OD, Oberoi S, Huysseune A, Hovorakova M, Peterka M, Peterkova R. Developmental disorders of the dentition: an update. *Am J Med Genet C Semin Med Genet.* 2013;163C(4):318–332. doi: http://dx.doi.org/10.1002/ajmg.c.31382 .

- Suri L, Gagari E, Vastardis H. Delayed tooth eruption: pathogenesis, diagnosis, and treatment. A literature review. *Am J Orthod Dentofacial Orthop.* 2004;126(4):432–445. doi: http://dx.doi.org/10.1016/j.ajodo.2003.10.031.
- Wright JT. Normal formation and development defects of the human dentition. *Pediatr Clin North Am*. 2000;47(5):975–1000. doi: http://dx.doi.org/10.1016/S0031-3955(05)70254-6.

Question 18

A 17-year-old adolescent girl is brought to your office for follow-up after hypertension was found during her annual sports physical examination. Her average blood pressure of several manual measurements is 133/88 mm Hg. She reports no headache or vision changes. She is otherwise healthy with no significant past medical or surgical history. She takes no medications and reports no illicit drug use. Her family history is significant for maternal grandparents who are both on medication for hypertension starting in their 60s. Her physical examination findings are normal, including comparable blood pressure measurements in all extremities. Her laboratory and imaging evaluation, including urinalysis, metabolic panel, complete blood cell count, fasting lipid levels, urine pregnancy test, and ultrasonography of the kidneys, bladder, and heart, yielded normal results.

Of the following, the BEST initial treatment for this patient is

A. amlodipine
B. atenolol
C. enalapril
D. hydrochlorothiazide
E. salt restriction in her diet

Correct Answer: E

All children should have their blood pressure screened annually beginning at 3 years of age. Other premorbid conditions, such as kidney disease and Kawasaki disease, may warrant earlier blood pressure screening. The patient in this vignette meets the criteria for stage 1 hypertension. Treatment should be initiated with lifestyle modifications, including weight loss, exercise, and decreased sedentary activities, and dietary modifications, including increased consumption of fresh fruit and vegetables and reduced consumption of carbohydrates, fats, processed sugars, salt, and sugar-sweetened beverages. Children whose blood pressure does not normalize after 6 months of these interventions should be started on antihypertensive medications. Therefore, salt restriction is the best initial treatment for the girl in this vignette, and pharmacologic interventions are not indicated at this time.

Pediatric hypertension is defined as the sustained elevation of systolic or diastolic blood pressure above the 95th percentile for a child's age, sex, and height. "Sustained" refers to the need for repeated measurements that are taken by manual auscultation and averaged together. The severity of the blood pressure elevation dictates diagnosis, evaluation, and treatment.

There are 4 categories of blood pressure measurements:
- A normal blood pressure has systolic and diastolic blood pressures less than 120/80 mm Hg or the 90th percentile for the child's age, sex, and height, whichever is lower.
- Prehypertension is defined as systolic or diastolic blood pressure between the 90th and 95th percentiles, or between 120/80 mm Hg and the 95th percentile, if 120/80 mm Hg is lower than the 90th percentile.
- Stage 1 hypertension is defined as systolic or diastolic blood pressure between the 95th percentile and the 99th percentile plus 5 mm Hg.
- Stage 2 hypertension is defined as systolic or diastolic blood pressure above the 99th percentile plus 5 mm Hg. The 95th percentile blood pressures for boys and girls of different ages and heights is shown in **Item C18**.

Blood Pressure at the 95th Percentile for Boys Compared to Height at the 5th, 50th, and 95th Percentiles
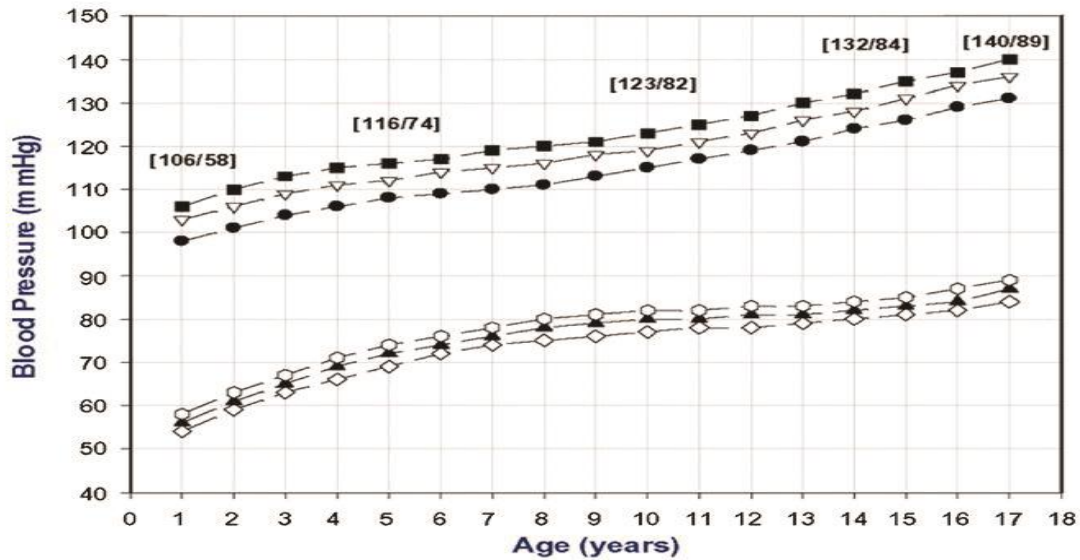
Blood Pressure at the 95th Percentile for Girls Compared to Height at the 5th, 50th, and 95th Percentiles
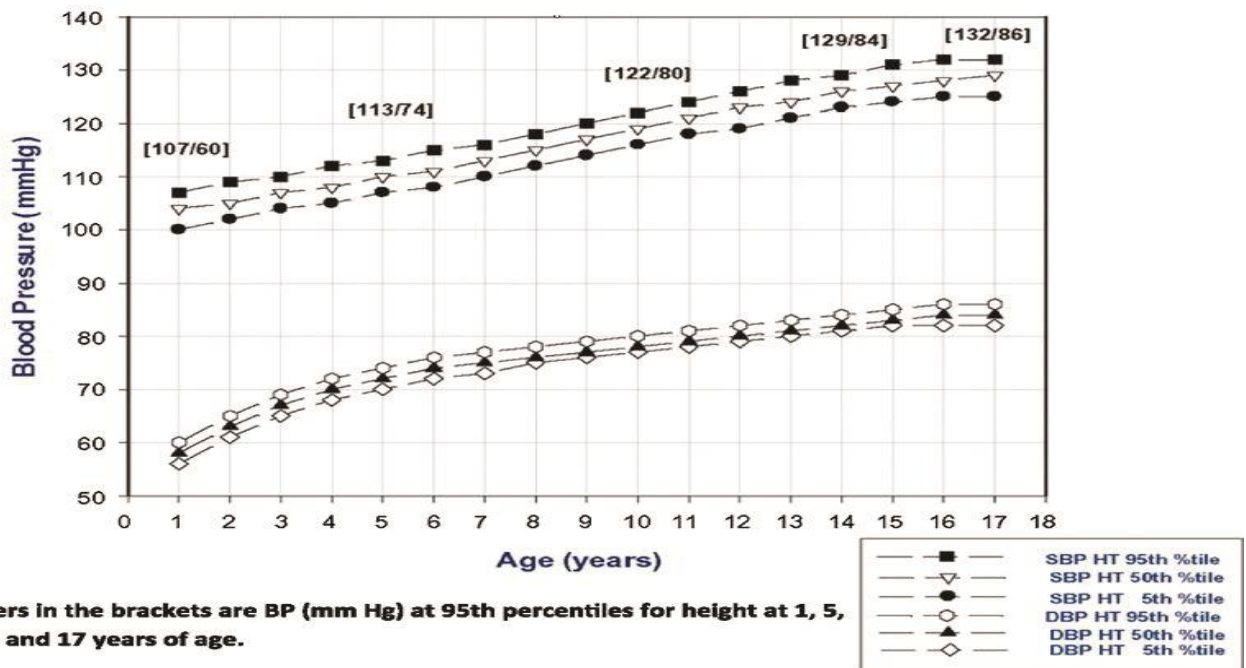
Numbers in the brackets are BP (mm Hg) at 95th percentiles for height at 1, 5, 10, 14, and 17 years of age.

■	SBP HT 95th %tile
▽	SBP HT 50th %tile
●	SBP HT 5th %tile
○	DBP HT 95th %tile
▲	DBP HT 50th %tile
◇	DBP HT 5th %tile

Item C18: Blood pressure (BP) at the 95th percentile for boys and girls.
Reprinted with permssion from Feld LG, Corey H. Hypertension in children. *Pediatr Rev*. 2007; 28 (8) 283-298.

Patients with prehypertension warrant closer monitoring with a repeat blood pressure in 6 months as well as counseling on weight management when appropriate and dietary modifications. Patients who are symptomatic or have secondary hypertension, left ventricular hypertrophy, hypertensive retinopathy, or diabetes mellitus should be started on antihypertensive medications in addition to lifestyle modifications.

PREP Pearls
- Pediatric hypertension is defined as the sustained elevation of systolic or diastolic blood pressure above the 95th percentile for a child's age, sex, and height.
- Stage 1 hypertension is defined as systolic or diastolic blood pressure between the 95th percentile and the 99th percentile plus 5 mm Hg. Treatment with lifestyle changes is indicated for stage 1 hypertension.
- Children who are symptomatic or who have secondary hypertension, ventricular hypertrophy, hypertensive retinopathy, or diabetes mellitus should be started on antihypertensive medications in addition to lifestyle modifications.

ABP Content Specifications(s)
- Formulate a differential diagnosis of essential hypertension
- Plan the appropriate management of essential hypertension

Suggested Readings
- Brady TM. Hypertension. *Pediatr Rev*. 2012;33(12):541–551. doi: http://dx.doi.org/10.1542/pir.33-12-541.
- National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114(2):555–576.

Question 19

A 22-month-old boy is hospitalized in a burn center after a scald injury. The injury was sustained 2 days ago after he pulled a pot of boiling water from the stove top to the floor when his mother stepped away from the kitchen. He has a temperature of 39.1°C, heart rate of 150 beats/min, respiratory rate of 38 breaths/min, blood pressure of 98/66 mm Hg, and oxygen saturation of 100% on 2 L/min of oxygen via nasal cannula. He is distressed. He has decreased breath sounds in both bases, no murmur, abdominal distention, and denuded skin over portions of his right arm, abdomen, and lower legs in a splash pattern. There are newly violaceous edges on the abdominal wound.

Of the following, the BEST indication for starting parenteral antibiotics in this patient is

A. abnormal respiratory examination results
B. discoloration at abdominal wound edges
C. heart rate greater than 120 beats/min
D. temperature greater than 38.3°C
E. wound involving greater than 10% of body surface area

Correct Answer: B

The best indication for starting parenteral antibiotics in the patient in this vignette is discoloration of wound edges. Antibiotics for burn injury patients should be reserved for clinical situations with clear evidence of an active infection. A change in the appearance of the wound, including new discoloration, is the most suggestive of an infection.

Infections are a major contributor to mortality associated with burns. The major infections in patients with burn injuries include pneumonia, burn wound infections, bloodstream infections, and urinary tract infections. The bloodstream infections and urinary tract infections may be associated with indwelling supportive devices.

Extensive burns produce a systemic inflammatory response that results in intravascular hypovolemia from capillary leak and a hypermetabolic state. As a result, vital sign abnormalities, including fever, tachycardia, and tachypnea, are common in patients with burn injuries.

Although pneumonia is an infectious consideration in burn patients, tachypnea and decreased basilar breath sounds are not specific findings for pneumonia. Similarly, tachycardia is not necessarily a sign of septic shock because it can be caused by various etiologies, including hypovolemia and pain. In burn injuries, fever can result from elevated core temperatures and from the systemic inflammatory response that causes a hypermetabolic state. Fever is not an indication for antibiotics because fever is not a specific marker of infection in patients with burn injuries.

Lastly, the extent and severity of a burn influence morbidity and mortality and factors into whether a patient requires treatment at a regional burn center. However, the extent of a burn is not an indication for antibiotics.

PREP Pearls
- Moderate to severe burn injuries create a severe systemic inflammatory response that can cause vital sign abnormalities, including fever, tachycardia, and tachypnea.
- Antibiotics for burn injury patients should be reserved for clinical situations with clear evidence of an active infection.
- A change in the appearance of a burn wound, including new discoloration, is suggestive of an infection.

ABP Content Specifications(s)
- Recognize the major infections seen in patients with burn injuries

Suggested Readings
- Jamshidi R, Sato T. Initial assessment and management of thermal burn injuries in children. *Pediatr Rev.* 2013;34(9):395–403. doi: http://dx.doi.org/10.1542/pir.34-9-395.
- Mayhall C. The epidemiology of burn wound infections: then and now. *Clin Infect Dis.* 2003;37(4):543–550. doi: http://dx.doi.org/10.1086/376993.

- Sharma B. Infection in patients with severe burns: cause and prevention thereof. *Infect Dis Clin North Am.* 2007;21(3):745–759. doi: http://dx.doi.org/10.1016/j.idc.2007.06.003.

Question 20

A 6-year-old boy seen in your office has had chronic nasal congestion and noisy breathing for several months. His parent reports mucoid rhinorrhea that is present every day and worsens intermittently. The boy often has difficulty breathing through his nose, especially when sleeping. Past trials of antihistamines or antibiotics have only provided temporary improvement in symptoms. He has no history of serious bacterial infections, pneumonia, or asthma. His growth and development have been appropriate for his age. He eats a regular diet and has normal stool and urine output. On examination of the nasal passages, you note glistening, bluish-gray, grape-like masses bilaterally. The remainder of the physical examination findings are unremarkable.

The most common cause of this condition in children is BEST evaluated by performing

  A. an aspirin sensitivity challenge
  B. a complete blood cell count with differential
  C. a human immunodeficiency virus immunoassay
  D. an IgE level measurement
  E. a sweat test

Correct Answer: E

The boy in this vignette displays the most common signs and symptoms of nasal polyps, which are persistent mucoid rhinorrhea, chronic nasal congestion, noisy breathing, and disturbed sleep. Cystic fibrosis is the most common cause of nasal polyposis in childhood and should be suspected even in patients without a history of more severe respiratory and digestive symptoms, poor weight gain, or recurrent infections. Therefore, obtaining a sweat test is the best approach to rule out the most common cause of nasal polyps.

Nasal polyps are abnormal pedunculated benign tumors that originate from nasal mucosa or paranasal sinus tissue. The glistening fleshy color of polyps helps to distinguish them from the nasal turbinates. There is a genetic predisposition to developing nasal polyposis, and the pathogenesis is believed to be linked to chronic inflammation. Cystic fibrosis is the most common cause of nasal polyposis in childhood. Nasal polyposis is also associated with aspirin sensitivity, allergic rhinitis, and asthma (components of the Samter triad) and recurrent sinusitis. Although it may be appropriate to evaluate these other conditions, they are not the most common cause of nasal polyposis in children.

Reports of persistent mucoid rhinorrhea, chronic nasal congestion, noisy breathing, and disturbed sleep are often overlooked or minimized. However, it is important to assess potential causes of these symptoms and offer directed intervention to minimize the potential negative effects on quality of life, sleep, and learning. Hyponasal speech and mouth breathing may be evident if the obstruction caused by the presence of polyps is significant (**Item C20**). The mainstay of treatment and prevention of nasal polyposis is the use of glucocorticoids. First-line treatment is intranasal corticosteroid sprays; oral treatment is reserved for patients with severe or refractory disease. Topical or systemic decongestants may provide temporary symptomatic relief, but are not usually effective in decreasing the size of the polyps. Any underlying associated medical conditions should be treated. Surgical intervention should be considered in patients who remain symptomatic despite optimal medical management or in cases of severe obstruction or deformity. There is a tendency for polyps to recur after surgical excision, so ongoing management of the underlying condition is warranted following surgery.
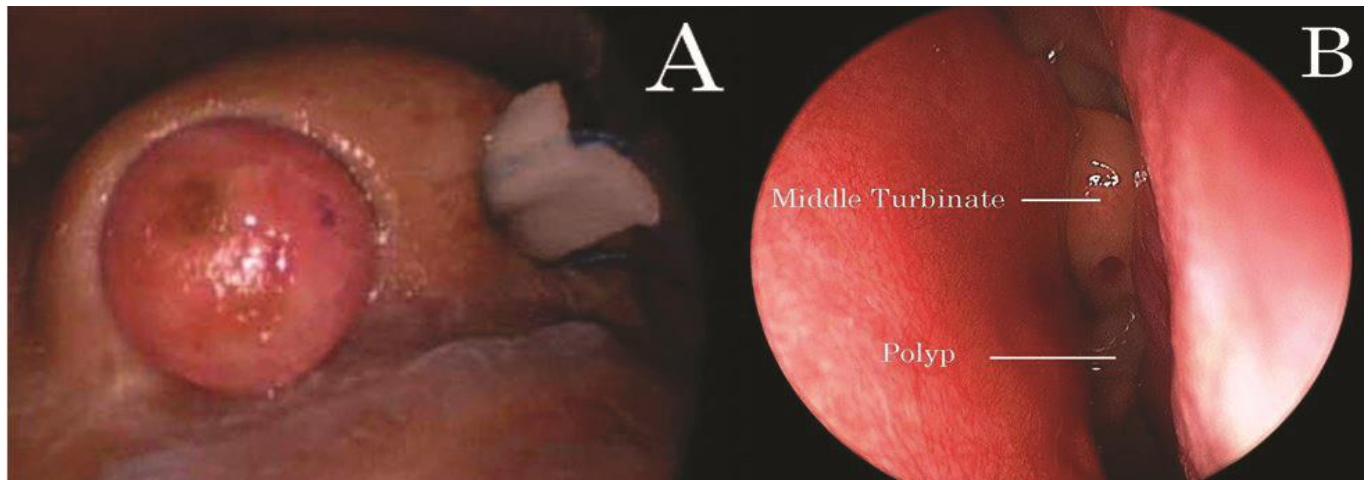
Item C20: Large right nasal polyp (A) and nasal endoscopic view of a small nasal polyp (B). Reprinted with permission from Schoem SR, Darrow DH. *Pediatric Otolaryngology.* Elk Grove Village, IL. American Academy of Pediatrics 2012.

PREP Pearls
- Cystic fibrosis is the most common cause of nasal polyposis in children.
- Nasal polyps are also seen in patients with aspirin sensitivity, allergic rhinitis, recurrent sinusitis, and asthma.
- Intranasal corticosteroid sprays are the first-line treatment for nasal polyps.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of nasal polyps

Suggested Readings
- Gargiulo KA, Spector ND. Stuffy nose. *Pediatr Rev.* 2010;31(8):320–325. doi: http://dx.doi.org/10.1542/pir.31-8-320.
- Haddad J Jr, Keesecker S. Nasal polyps. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Elsevier; 2016:2010–2011.

Question 21

A previously healthy 7-year-old boy is brought to the emergency department for evaluation of decreased urine output. The patient has had diarrhea and vomiting for the past 5 days. Over the last few hours, the patient has become increasingly sleepy. He has a temperature of 38.4°C, heart rate of 150 beats/min, respiratory rate of 24 breaths/min, and blood pressure of 80/40 mm Hg. His weight is 22 kg, and his height is 120 cm. He has mild facial puffiness, pallor, and prolonged capillary refill time (> 3 seconds). A peripheral intravenous catheter is placed, and a blood sample is sent for evaluation.

Of the following, the MOST appropriate intravenous fluid for the initial management of this patient is

A. 5% albumin, 440 mL over 30 min
B. lactated Ringer, 35 mL/h
C. 0.45% normal saline, 35 mL/h
D. 0.9% normal saline, 35 mL/h
E. 0.9% normal saline, 440 mL over 30 min

Correct Answer: E

The patient in this vignette has a history of diarrhea, vomiting, and decreased urine output (oliguria), and his physical examination findings are consistent with hypovolemic shock (tachycardia, hypotension, and prolonged capillary refill time). Serum chemistry results in this patient are most likely to be consistent with acute renal failure (ARF) and associated dyselectrolytemias. Because of the patient's severe dehydration, urgent fluid resuscitation is indicated prior to the availability of serum chemistry results. Fluid management in patients with ARF is aimed at maintaining tissue perfusion (as evaluated by heart rate, blood pressure, and capillary refill time) and preventing volume overload (strict monitoring of input and output, respiratory rate, and edema).

Maintenance of effective circulatory volume is one of the most important steps in the treatment and prevention of ARF. Fluid management in children with ARF is guided by the patient's underlying volume status and the type of renal failure (oliguric or nonoliguric). Fluid resuscitation includes both bolus and maintenance intravenous (IV) fluids. The history of volume loss and clinical features of hypovolemic shock in the patient in this vignette require immediate improvement in circulating volume. Rapid IV fluid bolus with 0.9% normal saline at 20 mL/kg (440 mL for the 22-kg patient in this vignette) within 30 minutes is indicated for fluid resuscitation to improve perfusion. A 5% albumin bolus is appropriate resuscitation fluid in patients with severe hypoalbuminemia and hypovolemic shock. In patients with suspected renal failure and absence of hypovolemic shock, a smaller fluid bolus of 5 to 10 mL/kg could be administered, followed by reassessment of clinical features for repeat infusions.

After improvement in perfusion (decreased heart rate, increased blood pressure, and decreased capillary refill time) the patient will need maintenance IV fluids. Maintenance IV fluid volumes should include insensible water loss plus ongoing losses (eg, urine output, gastrointestinal fluid losses, and chest tube drainage). In children with ARF with no to minimal urine output, the maintenance fluid volume should equal the insensible water loss (40 mL/kg/d for children who weigh < 10 kg; 500 mL/m^2/d for children who weigh > 10 kg). The IV fluids could also be started at a rate of half (31 mL/h) to two-thirds (41 mL/h) of the hourly maintenance requirement fluid (maintenance for the 22-kg patient in this vignette is 62 mL/h by the Holliday-Segar formula). As urine output increases with improvement in renal function, the IV fluid rate can be increased to maintain intravascular volume. Euvolemic ARF patients with adequate urine output should receive full maintenance IV fluids. Volume-overloaded ARF patients should receive no urine replacement or a fraction of urine replacement.

Isotonic fluids (0.9% normal saline and lactated Ringer solution) are preferred over hypotonic fluids (5% dextrose and 0.45 normal saline) for IV fluid resuscitation. 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 solution, should be avoided in patients with renal failure until urine output is established.

PREP Pearls
- Maintenance of effective circulatory volume is one of the most important steps in the treatment and prevention of acute renal failure.
- Rapid intravenous fluid bolus with 0.9% normal saline at 20 mL/kg within 30 minutes is indicated for fluid resuscitation in patients with suspected acute renal failure and hypovolemic shock.
- After improvement in perfusion (decreased heart rate, increased blood pressure, and decreased capillary refill time), the patient will need maintenance intravenous fluids that should include replacement of insensible water loss and ongoing fluid losses (eg, urine output, gastrointestinal fluid loss, and chest tube drainage).
- Fluid management in patients with acute renal failure is aimed at maintaining tissue perfusion and preventing volume overload.

ABP Content Specifications(s)
- Plan the management of fluid depletion in a patient with acute renal failure
- Understand the changing fluid requirements in a patient who has severe 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 renal failure. 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; 2009:2797–2801.
- 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.
- 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 22

A 24-month-old girl is brought to your office for a health supervision visit. When discussing her development, her mother says she denies any concerns and says her daughter is "doing new things all the time. She gets into everything, and she has her good and bad days." When asked if her daughter uses 50 distinct words, her mother says, "Yes, well, probably," and when asked if her daughter can identify colors, her mother says, "Some of them, I think."

Of the following, the BEST next step to evaluate this child's development is to

A. administer the Modified Checklist for Autism in Toddlers-Revised
B. administer the Ages and Stages Questionnaires-3 for 24-month-old children
C. ask the mother further questions regarding her daughter's development
D. engage the child in activities and conversation
E. refer her to an early intervention program

Correct Answer: B

There is a range of ages by which children achieve various developmental milestones. Various screening tests are available to assess whether a child has achieved milestones by what is considered a "normal" age. The Ages and Stages Questionnaires-3 (ASQ-3) are validated questionnaires used as a developmental screening tool for children 1 month to 66 months of age. The typical milestones achieved by the age of 24 months are noted in **Item C22**. Children at risk for delayed milestones in one or more developmental domains include those with chronic health conditions, genetic syndromes, prematurity, neurologic insult, nutritional deficiencies, as well as neglect. Early detection and referral for treatment of delays in development can significantly reduce the impact of such delays, and enable a family to accommodate a child's disability.

Developmental surveillance by observing children in the examination room and obtaining information about their recent achievements from caregivers is an important approach to detecting delays in development, but does not substitute for routine screening with validated tools at key points during infancy and toddlerhood. Proper screening identifies children with delays earlier and more accurately than surveillance alone, and can provide evidence to support a provider's concerns when they are not shared by caregivers. The American Academy of Pediatrics (AAP) recommends screening infants and toddlers for developmental delays with validated tools at 9, 18, and 30 months of age. Because many pediatric offices do not routinely conduct health supervision visits at 30 months, screening for developmental delays at the 24-month visit is a reasonable substitute.

Item C22. Typical Milestones at Age 24 Months.

Socioemotional	Copies others' behaviors, becomes more independent, is occasionally defiant, demonstrates parallel play, and shows limited engagement of other children during play
Language/ communication	Points to objects they want others to notice and to pictures in books, knows several body parts, has at least 50 words, uses 2-4 words in sentences, follows simple verbal instructions
Cognitive	Begins to recognize shapes and colors, remembers the end of favorite rhymes or sayings, finds hidden things, builds 4-block towers
Motor development	Climbs onto furniture, kicks a ball, stands on tiptoe, scribbles, and imitates a drawn straight line and circle.

Adapted from the Centers for Disease Control and Prevention.

The Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) is another validated questionnaire for children aged 16 to 30 months. The M-CHAT-R screens specifically for autism spectrum disorders, whereas the ASQ-3 screens multiple domains of development (communication, gross motor, fine motor, problem solving, and personal-social). In addition to general developmental screening the AAP recommends screening for autism at 18 and 24 months of age. Other validated developmental screening instruments include the Parents' Evaluation of Developmental Status (PEDS) and the Child Development Inventory (CDI). Due to their better specificity and sensitivity, these tools are preferred over the Denver II Developmental Screening Test.

Early intervention programs mandated by the Individuals with Disabilities Education Act allow for timely evaluation and treatment of developmental delays for children up to age 3 years. Referrals to these programs can originate from health care providers as well as families themselves. Although developmental screening is not required for referral, it can effectively assist providers in discerning which children should be referred. Children identified as having developmental delays through routine screening have been shown to enter developmental services at a younger age than those identified with surveillance only.

PREP Pearls
- At age 24 months, children are typically able to kick a ball, imitate a straight line with a crayon, use 2-word sentences, follow simple verbal commands, and point to objects they want others to notice.
- Validated instruments are recommended for use at specific ages to detect delays in motor, socioemotional, language, and cognitive development.
- Children at ages 18 and 24 months should be screened for autism spectrum disorders, in addition to general developmental delays.

ABP Content Specifications(s)
- Evaluate the cognitive and behavioral developmental progress/status of a child at 24 months of age, including recognition of abnormalities
- Evaluate the motor developmental progress/status of a child at 24 months of age

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.
- Guevara JP, Gerdes M, Localio R, et al. Effectiveness of developmental screening in an urban setting. *Pediatrics*. 2013;131(1):30–37. doi: http://dx.doi.org/10.1542/peds.2012-0765.
- Scharf RJ, Scharf GJ, Stroustrup A. Developmental milestones. *Pediatr Rev*. 2016;37;25. doi: http://dx.doi.org/10.1542/pir.2014-0103.

Question 23

An 8-year-old girl is brought to your office by her parents who are concerned because she has been sleeping a lot more. Until 7 days ago, she had been well with normal growth and development. Seven days ago, she had a brief low-grade fever and a transient faint rash that has resolved. Her appetite has been somewhat decreased, but she has seemed otherwise normal.

Her family history is remarkable for her father who had a cholecystectomy, a paternal aunt who reportedly has chronic anemia, and a paternal grandfather who had a splenectomy.

She is at the 40th percentile for height and the 35th percentile for weight. Her temperature is 36.8°C, her heart rate is 122 beats/min, and her blood pressure is 90/62 mm Hg. She is sitting on her mother's lap and is irritable but consolable. She is pale. Her heart, lung, and abdominal examination results are otherwise unremarkable. Her liver and spleen are not palpable. There is no bruising or petechiae.

A laboratory evaluation shows:

Laboratory Test	Result
White blood cell count	5,100/μL (5.1 x 10^9/L)
Hemoglobin	4.1 g/dL (41 g/L)
Platelet count	257 x 10^3/μL (257 x 10^9/L)
Mean corpuscular volume	78 fL
Reticulocytes	0.2%
Hemoglobin A	92%
Hemoglobin A_2	2%
Hemoglobin F	3%

Of the following, the MOST likely cause of this child's severe anemia is

A. decreased red blood cell production caused by acute lymphoblastic leukemia
B. decreased red blood cell production caused by Diamond-Blackfan anemia
C. decreased red blood cell production caused by a parvovirus infection complicating hereditary spherocytosis
D. increased red blood cell destruction caused by acquired autoimmune hemolytic anemia
E. increased red blood cell destruction caused by sickle cell anemia with a hyperhemolytic crisis

Correct Answer: C

Anemia occurs when a patient has a lower than normal level of hemoglobin caused by decreased production of red blood cells, increased destruction of red blood cells, or both. An approach to the differential diagnosis of anemia is shown in **Item C23**.

ITEM C23: Differential diagnosis of anemias.
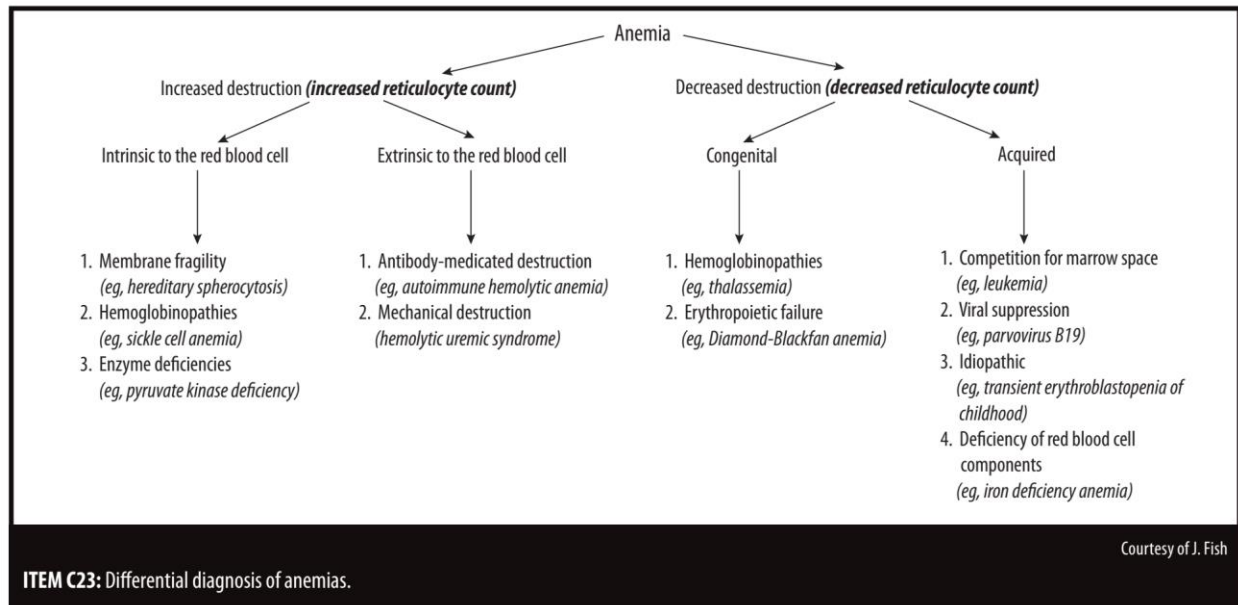
Determining the cause of the severe anemia in the girl in this vignette requires a careful analysis of her history, physical examination results, and laboratory findings. The girl's family history suggests a hereditary process of hemolysis. The paternal family history remarkable for cholecystectomy, chronic anemia, and splenectomy would be expected in a family with hereditary spherocytosis, a genetic disease resulting in fragile red blood cell membranes and a shortened red blood cell lifespan. Although multiple genetic lesions can cause hereditary spherocytosis, the family history in this vignette suggests an autosomal dominant pattern of inheritance with affected family members of both sexes across 3 consecutive generations. The most common form of autosomal dominant hereditary spherocytosis is caused by a defect in the gene encoding the red blood cell membrane protein ankyrin at locus 8p11.2.

Despite the convincing family history for a hereditary hemolytic process, the girl has an abnormally low reticulocyte count, which suggests decreased red blood cell production rather than increased red blood cell destruction. Her recent history of a viral illness with a low-grade fever and transient rash suggests viral suppression of red blood cell production. Her vital signs suggest a gradual-onset, well-compensated process, because her heart rate is only mildly elevated despite a severe anemia.

Taken together, these findings lead to the diagnosis of an underlying heritable hemolytic anemia complicated by viral suppression. The most common cause of severe anemia caused by viral suppression in children with an underlying hemolytic anemia is parvovirus B19 infection. In all people, parvovirus B19 infection can stop red blood cell production for a couple of weeks.

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The normal lifespan of a red blood cell is approximately 120 days; therefore, if red blood cell production stops for 12 to 14 days, there is an approximately 10% drop in hemoglobin, which would be barely noticeable clinically. The lifespan of red blood cells in patients with hereditary spherocytosis can be as short as 10 to 30 days; therefore, a 14-day arrest of red blood cell production can lead to severe anemia, a process called an aplastic crisis. Thus, the girl in this vignette is likely experiencing an aplastic crisis complicating hereditary spherocytosis.

The normal platelet count and white blood cell differential make it very unlikely that the anemia is caused by an underlying leukemia. Although the overall presentation could be consistent with Diamond-Blackfan anemia, a congenital defect of red blood cell production, the girl's family history is much more consistent with a hereditary hemolytic anemia. The low reticulocyte count makes an autoimmune hemolytic anemia or a hyperhemolytic crisis unlikely.

PREP Pearls
- The reticulocyte count is key to distinguishing anemia caused by increased destruction of red blood cells from anemia caused by decreased production of red blood cells.
- Parvovirus B19 is a common cause of aplastic crisis in children with underlying congenital hemolytic anemias.
- Hereditary spherocytosis is caused by genetic defects that influence the structural integrity of the red blood cell membrane, thereby shortening the red blood cell lifespan.

ABP Content Specifications(s)
- Distinguish between a disorder of erythrocyte production and a disorder of erythrocyte destruction based on laboratory results
- Recognize the clinical findings associated with hereditary spherocytosis, and manage appropriately

Suggested Readings
- Christensen RD, Yaish HM, Gallagher PG. A pediatrician's practical guide to diagnosing and treating hereditary spherocytosis in neonates. *Pediatrics*. 2015;135(6):1107–1114. doi: http://dx.doi.org/10.1542/peds.2014-3516.
- Noronha SA. Acquired and congenital hemolytic anemia. *Pediatr Rev*. 2016;37(6):235–246. doi: http://dx.doi.org/10.1542/pir.2015-0053.
- Shah S, Vega R. Hereditary spherocytosis. *Pediatr Rev*. 2004;25(5):168–172. doi: http://dx.doi.org/10.1542/pir.25-5-168.

Question 24

A 12-year-old girl with poorly controlled asthma is brought to the emergency department with wheezing, cough, and dyspnea. She has been seen in the emergency department 6 times in the last year and required admission to the hospital on 4 of these occasions. During 2 episodes, she required admission to the intensive care unit with oxygen or noninvasive ventilatory support. She is nonadherent with prescribed inhaled corticosteroid/long-acting β-agonist and leukotriene inhibitor medications. Her usual triggers are weather changes and viral illness.

She has been using her short-acting β-agonist at a dose of 4 inhalations every 1 to 2 hours for the last 8 hours. She reports that her hands are shaking and her heart is racing.

She is spontaneously breathing but tachypneic and in moderate respiratory distress. She has a heart rate of 160 beats/min, respiratory rate of 44 breaths/min, and oxygen saturation of 95% in room air. Accessory muscles are used in respiratory effort, with retractions noted at suprasternal, subcostal, and substernal sites. Auscultation of the chest reveals no wheezing, crackles, or rhonchi. A radial pulse cannot be palpated during auscultation of cardiac sounds, and systolic blood pressure decreases by 20 mm Hg during inspiration. You have initiated therapy with continuous albuterol at 15 mg/h. The patient has just received prednisone 60 mg orally and intravenous magnesium sulfate.

A chest radiograph reveals bilateral hyperinflation. Arterial blood gas tests reveal a pH of 7.34 and a pCO_2 of 36 mm Hg.

Of the following, the MOST appropriate next step in therapy is to

  A. administer methylprednisolone 40 mg intravenously
  B. increase continuous albuterol to 20 mg/h
  C. initiate bilevel positive airway pressure support
  D. perform endotracheal intubation
  E. place a thoracostomy tube

Correct Answer: C

The patient in this vignette has the signs and symptoms of status asthmaticus. Therapy has appropriately been initiated with albuterol and systemic steroids. Her respiratory status and her clinical examination findings are suggestive of a moderate to severe degree of airway obstruction, and further therapy is warranted to maintain lung volume, prevent atelectasis, optimize oxygenation and ventilation, and prevent respiratory failure. The most appropriate next step in therapy is to initiate support with bilevel positive airway pressure.

This patient's asthma is poorly controlled, and she is at high risk for asthma-related morbidity and mortality. Factors that place a patient at risk for death from asthma include severe asthma, poor perception of asthmatic symptoms, previous asthma attacks with rapid deteriorations, loss of consciousness or hospital admissions, frequent use of short-acting bronchodilator medications, reliance on crisis management in the emergency department, poor adherence to controller therapies, and steroid dependence.

The first-line treatment for asthma is β-adrenergic agents for the relief of bronchospasm. β-adrenergic activation stimulates adenylate cyclase, cyclic adenosine monophosphate, and protein kinase A with resultant smooth muscle relaxation. Albuterol is relatively selective for B_2 receptors and is better tolerated than epinephrine, which nonselectively activates both B_1 and B_2 receptors with associated B_1 effects on heart rate and blood pressure. Even with albuterol, frequent or excessive use may be associated with heart rate elevation, arrhythmia, neuromotor irritability, restlessness, emotional irritability, and tremor.

In the setting of status asthmaticus, the clinician must be mindful of the signs of impending respiratory failure. These signs may include mental status changes or somnolence, decrease in respiratory effort despite worsening hypoxemia, hypercarbia, and respiratory acidosis. The absence of wheezing or a "silent chest" in a patient with asthma is a cause for alarm and denotes severe bronchospasm. A carbon dioxide level that is higher than expected for the degree of tachypnea may reflect worsening respiratory muscle fatigue. An arterial blood gas measurement may provide clarity with regard to acid-base status and adequacy of compensatory mechanisms; in general, a pH less than 7.35 and a PCO_2 greater than 45 mm Hg are reason for concern.

Pulsus paradoxus is a pathologically extreme decrease in systolic blood pressure and pulse amplitude during inspiration. The normal inspiratory fall in blood pressure is less than 10 mm Hg. When the measureable decrease is more than 10 mm Hg, it is referred to as pulsus paradoxus.

Pulsus paradoxus is reflective of diastolic dysfunction with a decrease in left ventricular filling and stroke volume and is a sign of severe cardiopulmonary compromise. Pulsus paradoxus may be caused by cardiac, pulmonary, or other disease states. It is a valuable assessment for the severity of airway obstruction; a pulsus paradoxus greater than 20 mm Hg correlates with moderate to severe obstruction. In addition to the utility of a pulsus paradoxus measurement in status asthmaticus, this finding may be seen with cardiac tamponade, pulmonary embolism, hypovolemic shock, or anaphylaxis.

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The need for endotracheal intubation and mechanical ventilation has been significantly curtailed by careful monitoring and by the availability of less invasive modes of respiratory support, including high-flow nasal cannula oxygen, continuous positive airway pressure, and bilevel positive airway pressure support. The potential benefits of noninvasive positive pressure ventilation include a reduction in work of breathing, direct bronchodilating effects, prevention of atelectasis, and improvements in ventilation/perfusion mismatch.

The patient in this vignette has already received 60 mg of prednisone. The onset of action of the steroids will be delayed by hours and a further increase in dose will not provide short-term relief of bronchospasm nor is it likely to be of physiologic benefit. Given that the patient has a significant degree of airway obstruction, a further increase in the dose of the β-agonist is not likely to provide additional relief. Other adjunctive therapies such as intravenous terbutaline or heliox may be therapeutic options, but these are not included as answer choices. In a conscious adolescent who demonstrates relative normalcy of pulse oximetry, pH, and PCO_2, endotracheal intubation is not indicated at this time. Lastly, there is no evidence of differential aeration or mediastinal shift to suggest a pneumothorax or a pleural effusion. Therefore, placement of a thoracostomy tube would not be expected to be therapeutic in this patient.

PREP Pearls
- Pulsus paradoxus measurements, in addition to clinical signs and symptoms and blood gas measurements, may provide helpful adjunctive evidence of impending respiratory failure in the patient with status asthmaticus.
- Noninvasive modalities of respiratory support may improve ventilation, prevent atelectasis, and support a patient with moderate to severe degrees of airway obstruction without the need for endotracheal intubation and invasive ventilatory support.
- β-adrenergic side effects of albuterol include tremulousness, elevated heart rate, and anxiety. These side effects are generally mild to moderate and well tolerated in the majority of patients.

MOCA-Peds Objective
- Recognize respiratory distress and manage appropriately

ABP Content Specifications(s)
- Recognize the clinical features associated with toxicity to adrenergic agonists in a patient with an acute exacerbation of asthma
- Recognize the signs of severe obstruction during an acute exacerbation of asthma

Suggested Readings
- Galant SP, Groncy CE, Shaw KC. The value of pulsus paradoxus in assessing the child with status asthmaticus. *Pediatrics*. 1978;61(1):46–51.
- National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma—summary report 2007. *J Allergy Clin Immunol.* 2007;120(5 suppl):S94–S138. https://www.nhlbi.nih.gov/files/docs/guidelines/asthsumm.pdf.

- Soroksky A, Klinowski E, Ilgyev E, et al. Noninvasive positive pressure ventilation in acute asthmatic attack. *Eur Respir Rev*. 2010;19(115):39–45. doi: http://dx.doi.org/10.1183/09059180.00006109.

Question 25

A 10-year-old previously healthy girl presents to the emergency department with balance difficulties. She had been at home playing tag with friends and ran into a tree. She remembers hitting her head and falling down. She did not lose consciousness and was able to get up and keep playing, but about 10 minutes later, she suddenly lost her balance. Her mother brought her immediately to the emergency department, where she is complaining of neck pain without headache. The girl's vital signs are normal for age and her general physical examination findings are normal. On neurologic examination, she is alert, without aphasia or dysarthria. Her pupils are equal and reactive to light, extraocular movements are intact in all directions, and there is no nystagmus. Her facial movements are strong and symmetric. She has full motor strength in all 4 extremities with normal tone. Her reflexes are 2/4 throughout, and her toes are down-going on plantar stroking. On finger to nose testing, the girl has mild dysmetria in her right upper extremity. She has a wide-based stance and difficulty walking in a straight line. Within 60 minutes of the injury, computed tomography of the head is performed, which shows a possible hypodensity in the cerebellum. Magnetic resonance imaging of the brain (**Item Q25**) shows diffusion restriction in the right cerebellum in the region supplied by the right posterior inferior cerebellar artery.
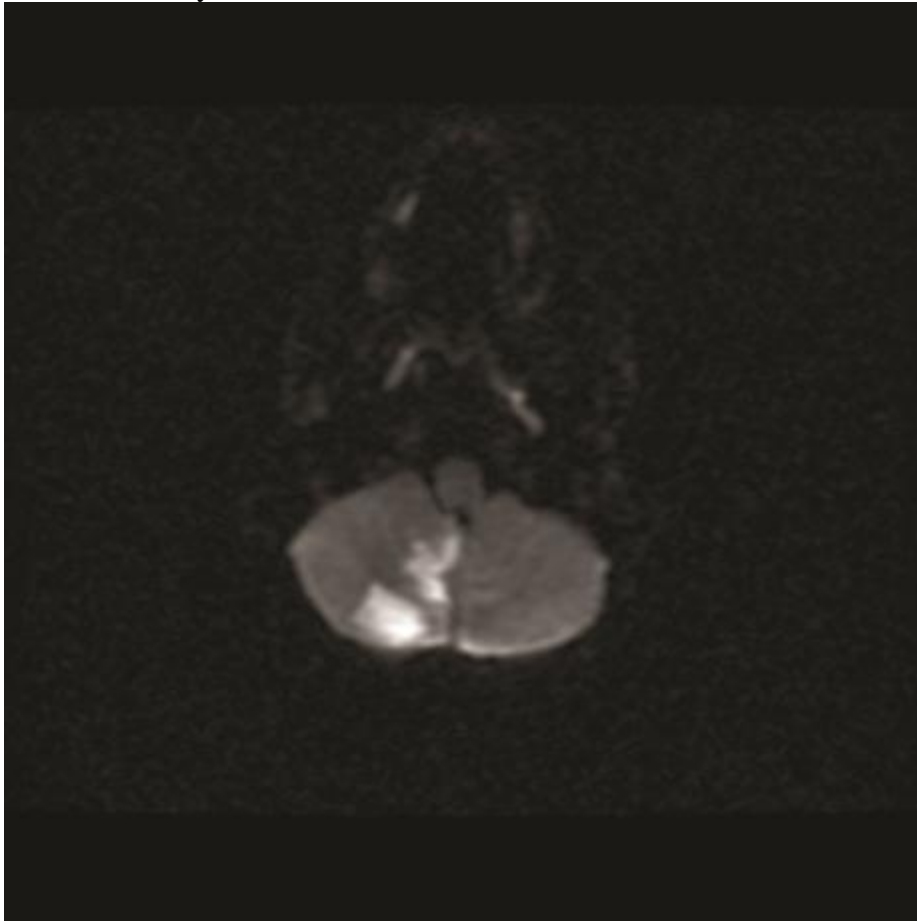
Item Q25: MRI of the brain for the girl described in the vignette.
Courtesy of D. Morita

Of the following, the test MOST likely to yield the underlying diagnosis is

  A. computed tomography angiography of the head and neck with contrast
  B. genetic testing for mitochondrial encephalomyopathy, lactic acidosis, and stroke like episodes (MELAS)
  C. laboratory evaluation for hypercoagulable state
  D. lower extremity venous duplex ultrasound
  E. lumbar puncture for cerebrospinal fluid protein, glucose, cell count, and differential

Correct Answer: A

The girl in the vignette has had an acute, arterial ischemic stroke (AIS) in the cerebellum after an incidental head injury. The magnetic resonance imaging scan shows ischemia in the distribution of the right posterior inferior cerebellar artery (PICA). The most likely mechanism for a stroke in the PICA distribution after a head or neck injury, such as the one sustained by the girl in the vignette, is an artery-to-artery embolism from a vertebral artery dissection. Of the choices listed, computed tomography angiography of the head and neck with contrast is the best test to show a vertebral artery dissection. Magnetic resonance angiography of the head and neck with contrast would also show this finding.

In a child presenting with an acute focal neurologic deficit, stroke should be considered even if the child initially appears well otherwise and has normal vital signs.The causes for AIS in children include embolism, in situ thrombosis, vasculopathy, genetic disorder, and metabolic stroke. Embolic stroke can arise from artery-to-artery embolism resulting from a carotid or vertebral dissection; cardiogenic emboli from intracardiac thrombi; or paradoxical embolism from venous thrombosis embolizing to the arterial circulation through a patent foramen ovale, ventricular septal defect, other cardiac shunt, or through a pulmonary arteriovenous malformation. In situ thrombosis can arise in the setting of a hypercoagulable state such as factor V Leiden deficiency, prothrombin gene mutation, or an inflammatory disorder such as systemic lupus erythematosus or meningitis. Focal cerebral arteriopathy is thought to be a postinfectious process, causing transient narrowing of a cerebral artery, usually the middle cerebral artery. Fabry disease, α-galactosidase A deficiency, is an X-linked disorder that presents with pain crises in childhood and adolescence, angiokeratomas, anhidrosis, and stroke in young adulthood. Causes of metabolic stroke include mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes (MELAS). In MELAS, the area of acute ischemia is in a nonvascular distribution, typically in the posterior parietal and occipital lobes.

Symptoms of acute AIS can include any focal neurologic deficit. Hemiparesis is the most common presenting symptom, but cerebellar strokes may cause just ataxia. Seizure can be a presenting symptom of stroke especially in children younger than 1 year.

For the girl in the vignette, arterial dissection is the most likely cause for stroke. She should be admitted to the pediatric intensive care unit for close monitoring. If vascular imaging does not show arterial dissection, then testing for other causes of childhood AIS should be initiated, such as evaluation for cardiac abnormalities or underlying thrombophilic state. In an acute stroke in the posterior fossa, increasing cerebellar edema can cause compression of the fourth ventricle and obstructive hydrocephalus. Lumbar puncture should not be performed in this setting, because it could cause brain herniation. Evaluation for MELAS is not indicated based on the location of the stroke. There is no evidence in the vignette of deep venous thrombosis; however, if a cardiac or pulmonary shunt were detected, a lower extremity venous duplex ultrasound scan would be indicated.

PREP Pearls
- In a child presenting with an acute focal neurologic deficit, stroke should be considered even if the child initially appears well and has normal vital signs.
- Acute ischemic stroke in the posterior fossa can cause cerebellar edema that can rapidly cause obstructive hydrocephalus.

MOCA-Peds Objective
- Evaluate a child with acute ataxia

ABP Content Specifications(s)
- Recognize the clinical findings associated with childhood stroke
- Understand the pathophysiology of childhood stroke

Suggested Readings
- Mackay MT, Wiznitzer M, Benedict SL, Lee KJ, Deveber GA, Ganesan V; International Pediatric Stroke Study Group. Arterial ischemic stroke risk factors: the International Pediatric Stroke Study. *Ann Neurol.* 2011;69(1):130–140. doi: http://dx.doi.org/10.1002/ana.22224.
- Roach ES, Golomb MR, Adams R; American Heart Association Stroke Council; Council on Cardiovascular Disease in the Young. 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.

Question 26

This morning you received a frantic call from the parents of a 14-year-old girl after they found sexually suggestive pictures of herself on her cell phone. You have arranged to meet with them later today. In preparation you are reviewing the current evidence and recommendations regarding "sexting."

Of the following, the MOST accurate information to provide this family is that

A. adolescents who send more texts overall are more likely to engage in this behavior
B. discussions with children about this behavior should be delayed until high school entrance
C. lesbian, gay, bisexual, and transgender adolescents are less likely to engage in this behavior than heterosexual children
D. this behavior frequently results in legal consequences for the adolescent
E. this behavior is not significantly correlated with other sexual risk behaviors in adolescents

Correct Answer: A

Several studies have looked at risk factors for children's participation in sexting. One of the greatest risks is an adolescent's overall use of texting. Adolescents who send the greatest number of texts overall (>100/day) are the most likely to participate in sexting. Therefore, parents should be encouraged to limit the number of texts per day their child is allowed to send as a possible means to limit sexting.

With the development and widespread availability of electronic media, guidance about personal safety for adolescents has become more complicated. Simply discussing "stranger danger" no longer adequately addresses situations that families might encounter. One of the most common concerns expressed by parents is the impact of sexting on their children, and there is a growing body of evidence about this topic. The definition of sexting varies, depending on whether authors include sending or receiving photographs, sexually explicit texts, or both. This has made it difficult to measure prevalence of the practice. In their study of middle school students, Rice et al defined sexting as "the sending/receiving of sexually explicit cell phone messages." In this study, 20% of subjects reported receiving at least 1 sexting message and 5% reported sending at least 1. However, a 2012 phone survey of 10- to 17-year-old children identified a much lower prevalence: 9.6% reported receiving, forwarding, or creating sexually explicit images of a minor and 2.5% reported creating those images.

The evidence is not clear at this time, but some studies suggest that sexting may be part of the cluster of risky sexual behaviors that includes unprotected sex and multiple partners. Several authors recommend that physicians and other practitioners discuss texting and sexting during health supervision visits as a lead-in to the discussion of risky sexual behaviors. Even early adolescents may be involved in sexting activity, therefore, parents and providers should begin discussing this issue with children well before they reach high school age; certainly as soon as the child is provided with a cell phone.

The American Academy of Pediatrics recommendations for parents regarding children's use of social media, with specific recommendations concerning sexting, are available on the public website safetynet.aap.org. These include:
- *Have a conversation about sexting with your child; find out what they know and think about it.*
- *Discuss in an age-appropriate way what sexting is and that it is inappropriate.*
- *Let children know the consequences of sexting including criminal consequences.*
- *To prevent peer pressure to send texts, collect cell phones when teens and tweens gather.*
- *Discuss news stories with children and rehearse ways to respond if they were in that situation.*
- *Encourage school and town assemblies to educate parents, teachers, and students.*

Demographic studies suggest that lesbian, gay, bisexual, transgender, and queer youth, as well as African American youth, may be at greater risk for sexting activity than other groups. Girls appear to be more engaged in this practice than are boys.

Concern has been raised as to whether children participating in sexting are at risk of prosecution for distributing images that meet the definition of child pornography, even when their motivation is more experimental than criminal. A 2012 study is reassuring. In this survey of law enforcement agencies, most cases that led to prosecution included "aggravating circumstances," such as adult involvement, blackmail, or other malicious behavior. An arrest had been made in just 18% of cases involving experimental or romantic activity among youths, and overall, relatively few cases of sexting came to the attention of law enforcement. Nonetheless, it is a risk that adolescents should be aware of.

Another significant concern regarding sexting is the possibility that explicit images may be distributed without the consent of the subject, may be distributed widely, and may exist indefinitely online. This could have a long-term emotional impact on the individual, and may result in educational and employment impediments in the future. In the 2012 survey mentioned earlier, 21% of adolescents who were the subject of, or who created, a sexually explicit cell phone image, and 25% of those who had received such an image, reported feeling very/extremely upset, embarrassed, or afraid as a result of the event.

PREP Pearls
- Personal safety counseling should include a discussion of texting, sexting, and social media use.
- Adolescents who send the greatest number of texts overall (>100/day) are the most likely to participate in sexting.
- Sexting may be a component of risky sexual behavior, though current evidence is limited.
- Legal action against youth participating in sexting behavior has been rare to date, except in cases with other aggravating circumstances.

ABP Content Specifications(s)
- Counsel parents regarding the importance of personal safety (eg, strangers) for their children

Suggested Readings
- Mitchell KJ, Finkelhor D, Jones LM, Wolak J. Prevalence and characteristics of youth sexting: a national study. *Pediatrics*. 2012;129:13-20. doi: http://dx.doi.org/10.1542/peds.2011-1730.
- Rice E, Gibbs J, Winetrobe H, et al. Sexting and sexual behavior among middle school students. *Pediatrics*. 2014;134:e21-e28. doi: http://dx.doi.org/10.1542/peds.2013-2991.
- Rice E, Rhoades H, Winetrobe H, et al. Sexually explicit cell phone messaging associated with sexual risk among adolescents. *Pediatrics*. 2012;130:667-673. doi: http://dx.doi.org/10.1542/peds.2012-0021.
- Wolak J, Finkelhor D, Mitchell KJ. How often are teens arrested for sexting? from a national sample of police cases. *Pediatrics*. 2012;129:4-12. doi: http://dx.doi.org/10.1542/peds.2011-2242.

Question 27

A 6-year-old girl is seen in the emergency department in July with a 2-day history of fever, headache, and vomiting. There are no sick contacts, no pets at home, and no recent travels. Her immunizations are up-to-date.

She is alert with a temperature of 39.4°C, heart rate of 116 beats/min, and a respiratory rate of 18 breaths/min. Her blood pressure is normal. Her head, ears, eyes, nose, and throat appear normal. There is a blanching maculopapular rash on her neck and upper chest (Item Q27) and pain on neck flexion. Data from an analysis of cerebrospinal fluid are shown:

Item Q27: Rash as described for the girl in the vignette.
Reprinted with permission from the Public Health Image Library. Centers for Disease Control and Prevention.

Laboratory Test	Result
White blood cell count	560/µL
Neutrophils	60%
Glucose	48 mg/dL (2.7 mmol/L)
Protein	65 mg/dL
Gram stain	No organisms seen

Her blood glucose level is 90 mg/dL (5.0 mmol/L). Her headache improves after the lumbar puncture. She is admitted to the hospital with a diagnosis of meningitis.

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

        A.   blood virus serology
        B.   cerebrospinal fluid bacterial culture
        C.   cerebrospinal fluid viral polymerase chain reaction assay
        D.   cerebrospinal fluid virus serology
        E.   skin lesion viral polymerase chain reaction assay

Correct Answer: C

The child in this vignette has clinical and cerebrospinal fluid (CSF) findings consistent with aseptic meningitis. Non-polio enteroviruses (EVs), especially group A and B coxsackieviruses, echoviruses, and numbered enteroviruses, are the most frequent causes of aseptic meningitis in children. The CSF of individuals with viral meningitis has no organisms seen on Gram stain, a relatively low white blood cell count, and mildly elevated protein levels. A neutrophil predominance early in the course of viral meningitis may be noted in the CSF. The CSF profiles of viral meningitis and partially treated bacterial meningitis may be similar. However, the patient in this vignette did not receive previous antibiotic therapy. Patients with bacterial meningitis appear ill, and their CSF pleocytosis and protein levels are significantly higher than in the present case. Nucleic acid amplification tests (ie, reverse-transcriptase polymerase chain reaction [PCR] assays) are rapid and more sensitive than cultures for the detection of EV RNA in the CSF and are the preferred test to confirm the diagnosis of EV meningitis.

The non-polio EVs and human parechoviruses are small nonenveloped RNA viruses in the *Picornaviridae* family. They are ubiquitous with more than 130 identified types, and they commonly cause childhood illnesses. Transmission occurs via fecal-oral contact. Enterovirus infections typically occur during the summer and early fall, and infants and young children are at highest risk. The incubation period usually is 3 to 6 days. The clinical spectrum of infections caused by EVs is varied. Although EVs commonly cause a mild illness with complete recovery, severe illness and death may occur in neonates, infants, and immunocompromised patients.

The disease severity correlates to age and host immunity. Common clinical manifestations include hand-foot-and-mouth disease, herpangina, nonspecific viral exanthems, and gastrointestinal or respiratory infections (**Item C27**). Severe neurologic syndromes associated with EV and human parechoviruses include meningitis, encephalitis, and acute flaccid paralysis. In neonates, EV sepsis is characterized by hepatitis, disseminated intravascular coagulation, and myocarditis. Patients with antibody deficiency syndromes can have persistent central nervous system infection caused by EV. Other clinical syndromes caused by EV include acute hemorrhagic conjunctivitis, pleurodynia, hepatitis, and myopericarditis.

Item C27. Clinical Manifestations of Enterovirus Types.

Syndrome	Predominant Virus	Clinical Features
Nonspecific febrile illness	All types	Febrile illness (occasionally biphasic), with non-specific upper respiratory and gastro-intestinal tract symptoms
Aseptic meningitis	Echovirus and group B coxsackieviruses	Fever, meningeal signs with mild cerebrospinal (CSF) pleocytosis, usually normal CSF glucose and protein, and absence of bacteria
Herpangina	Group A coxsackieviruses	Fever, painful oral vesicles on tonsils and posterior pharynx
Hand-foot-mouth disease	Coxsackievirus A16	Fever, vesicles on buccal mucosa and tongue and on interdigital surfaces of hands and feet
Nonspecific exanthem	Echoviruses	Variable rash (usually rubelli-form but may be petechial or vesicular), +/− fever
Pleurodynia	Coxsackievirus B3, B5	Uncommon, epidemic, fever, and severe muscle pain of chest and abdomen
Carditis	Group B coxsackievirus	Uncommon, myocarditis/peri-carditis, which can present with heart failure or dysrhythmia
Acute hemor-rhagic conjunc-tivitis	Enterovirus 70	Epidemic cause of conjunctivitis with lid swelling, subconjunc-tival hemorrhage, and eye pain without systemic symptoms
Neonatal disease	Group B coxsackie-viruses and echoviruses	Sepsis-like picture, meningoencephalitis, hepatitis, myocarditis

Reprinted with permission form Zoutis T, Klein JD. Enterovirus infections. *Pediatr Rev.* 1998;19(6).

The unique clinical manifestations of outbreaks of specific EV serotypes include: severe neurologic complications (EV71); severe and atypical skin lesions in patients with hand-foot-and-mouth disease (coxsackievirus A6); severe hand-foot-and-mouth disease associated with severe neurologic manifestations in Asia (EV71); acute hemorrhagic conjunctivitis (coxsackievirus A24 variant and EV71); and severe respiratory illness in children with asthma (EV-D68). In addition, acute flaccid myelitis in some children with respiratory illness caused by EV-D68 has been reported by the Centers for Disease Control and Prevention and is the subject of ongoing investigation.

The availability of rapid and sensitive PCR diagnostic testing for EV in CSF has resulted in improved patient care and cost savings because of shortened hospital stays, decreased antimicrobial use, and decreased ancillary diagnostic testing and treatment. Blood, vesicle fluid, and nasopharyngeal, throat, and rectal swabs can also be used for EV PCR. Enterovirus can be isolated by viral culture of stool, throat swabs, and rarely CSF; however, compared to PCR assays, culture methods are less sensitive, time consuming (3-8 days for isolation), and generally unhelpful in patient care decisions. In the present case of aseptic meningitis, CSF PCR testing for EV is more likely to confirm the diagnosis as compared to EV PCR testing from a skin lesion. Diagnosis of acute EV infection by serology is not routinely performed in clinical practice because of the limited sensitivity and poor specificity. Bacterial cultures of CSF would not be diagnostic for a viral illness.

In immunocompetent children, EV meningitis is a self-limited illness. Treatment is supportive. No antiviral agents have been approved for treatment of EV infections. In immunocompromised patients with chronic EV meningoencephalitis, treatment with intravenous immune globulin is recommended. Contact precautions are recommended for hospitalized infants and children with EV infections for the duration of illness. Vaccines against virulent strain EV71 are under development.

PREP Pearls
- Enterovirus infections typically occur during the summer and early fall, and infants and young children are at highest risk. Transmission occurs via fecal-oral contact
- Non-polio enteroviruses (group A and B coxsackieviruses, echoviruses, numbered enteroviruses) are the most frequent causes of aseptic meningitis in children.
- Compared with cultures, reverse-transcriptase polymerase chain reaction assays are rapid and more sensitive for the detection of enterovirus RNA in the cerebrospinal fluid.
- Cerebrospinal fluid polymerase chain reaction assays are the recommended test to confirm the diagnosis of enterovirus meningitis.

ABP Content Specifications(s)
- Understand the epidemiology of the enteroviruses
- Recognize the clinical features associated with echo- and coxsackievirus infection in patients of various ages
- Plan appropriate laboratory evaluation for enterovirus infection

- Recognize the clinical features of associated with enterovirus infection in patients of various ages

Suggested Readings

- American Academy of Pediatrics. Enterovirus (nonpoliovirus). 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; 2015:333–336.
- de Crom SC, Rossen JW, van Furth AM, Obihara CC. Enterovirus and parechovirus infection in children: a brief overview. *Eur J Pediatr*. 2016;175(8):1023–1029. doi: http://dx.doi.org/10.1007/s00431-016-2725-7.
- Robinson CC, Willis M, Meagher A, Gieseker KE, Rotbart H, Glodé MP. Impact of rapid polymerase chain reaction results on management of pediatric patients with enteroviral meningitis. *Pediatr Infect Dis J*. 2002;21(4):283–286.

Question 28

A 3-year-old girl is brought to your clinic for evaluation of diarrhea. Her mother reports that she had been in her usual state of good health until 3 weeks ago, when she developed fever, nausea, vomiting, and diarrhea that lasted for 2 days. Following this event, she has had persistent diarrhea described as 6 to 9 episodes of liquid stools without visible blood or mucus. The episodes are associated with a generalized abdominal pain that peaks prior to each defecation, with some improvement after stooling. Her mother reports she has been distended and flatulent since the acute illness. Her diarrhea is typically worse in the daytime following meals.

Her mother reports no recent travel, reptile exposure, well water use, or ill contacts. Her mother reminds you that she has been worried about her daughter having celiac disease because of a strong family history (the mother and all of her siblings have celiac disease).

The girl has a temperature of 37.5°C, heart rate of 90 beats/min, respiratory rate of 19 breaths/min, and a blood pressure of 87/52 mm Hg. She is alert and well hydrated. Her abdomen is distended and hypertympanic with diffuse tenderness to palpation, but no rebound, guarding, or masses. Her skin is without rash. A complete blood cell count, tissue transglutaminase level, and serum IgA level are normal.

Of the following, the study MOST likely to help confirm your diagnosis is

> A.   fecal fat test
> B.   stool culture
> C.   stool guaiac test
> D.   stool ova and parasite examination
> E.   stool reducing substance test

Correct Answer: E

The child in this vignette has secondary lactase deficiency (following viral acute gastroenteritis), which is diagnosed by the presence of elevated stool reducing substances. When lactose is not digested in the intestine, it typically results in elevated reducing substances and decreased pH in the stool. These findings are caused by the fermentation of lactose in the gut lumen, which produces gas and short chain fatty acids.

Secondary lactose intolerance (lactase deficiency) occurs following damage to the villi in the small intestine. This damage most commonly occurs following acute gastroenteritis (parasitic, viral, and bacterial), but also occurs with celiac disease, inflammatory bowel disease, autoimmune enteropathy, chemotherapy, small bowel bacterial overgrowth, and other causes of small bowel injury. Symptoms include diarrhea, abdominal bloating, abdominal pain, flatulence, and nausea following consumption of lactose-containing food. Lactose is found in all dairy products and mammalian milk. Many processed foods, such as hot dogs, granola, and ramen noodles, commonly contain lactose.

Secondary lactose intolerance is typically best managed by treating the underlying condition. If recovery is slow, avoidance of lactose-containing foods and substitution with non–lactose-containing foods, such as soy, almond, or coconut milk products, is recommended. Alternatively, lactase supplements (available over the counter) can replace natural lactase until the small bowel has healed. Practically, a combination of avoidance and replacement is recommended.

Undiagnosed lactose intolerance can result in chronic abdominal pain caused by persistent bowel dilation from gas and acidic stools. Changes in bacterial flora can also occur, resulting in small bowel bacterial overgrowth. A few small studies have shown a correlation between lactose intolerance and the development of functional gastrointestinal disorders. Lactose intolerance should always be considered in the differential diagnosis of chronic abdominal pain in a child.

A fecal fat test is not appropriate because this child does not have fat malabsorption. Stool guaiac test results are negative in children with lactase deficiency unless it is secondary to bowel inflammation. The results of stool culture and ova and parasite examination would reveal an infection and are unlikely to be positive this distant from initial symptoms.

PREP Pearls
- Secondary lactose intolerance occurs following acute viral, bacterial, and parasitic infections.
- Secondary lactose intolerance can be diagnosed with a full history and physical examination. The diagnosis is supported by a low stool pH and elevated stool reducing substances.
- Secondary lactose intolerance can cause chronic abdominal pain.

MOCA-Peds Objective
- Evaluate a patient with chronic abdominal pain

ABP Content Specifications(s)
- Plan appropriate management of lactose intolerance, taking into consideration the mechanisms causing the disorder
- Recognize the gastrointestinal causes of secondary lactose intolerance
- Understand the role of lactose intolerance in the development of chronic abdominal pain

Suggested Readings
- Berni Canani R, Pezzella A, Amoroso A, Cozzolino T, Di Scala C, Passariello A. Diagnosing and treating intolerance to carbohydrates in children. *Nutrients*. 2016;8(3):157. doi: http://dx.doi.org/10.3390/nu8030157.
- Heyman MB. Lactose intolerance in infants, children, and adolescents. *Pediatrics*. 2006;118(3):1279–1286. doi: http://dx.doi.org/10.1542/peds.2006-1721.
- Shulman RJ. Dietary issues in recurrent abdominal pain. *J Pediatr Gastroenterol Nutr*. 2012;55(suppl 2):S40–S42. doi: http://dx.doi.org/10.1097/01.mpg.0000421412.10999.76.
- Usai-Satta P, Scarpa M, Oppia F, Cabras F. Lactose malabsorption and intolerance: what should be the best clinical management? *World J Gastrointest Pharmacol Ther*. 2012;3(3):29–33. doi: http://dx.doi.org/10.4292/wjgpt.v3.i3.29.

Question 29

A 4-month-old girl presents to the emergency department because of difficulty breathing, which progressively worsened since the mother first noticed it several weeks ago. Her mother states that the infant does not breathe noisily or have pauses in breathing, but does breathe fast. She has had no upper respiratory symptoms, fevers, diarrhea, or sick contacts. The girl spits up 2 to 3 times per day, more frequently than did her older siblings. She usually urinates 4 times per day and has 1 bowel movement per day. She takes 4 oz of formula every 3 hours. The infant was born at 36 weeks' gestation and weighed 2.7 kg at birth (10th–25th percentile). Her current weight is 3.8 kg (<3rd percentile). Her temperature is 37°C, heart rate is 140 beats/min, respiratory rate is 60 breaths/min, blood pressure is 100/60 mm Hg, and oxygen saturation is 100% in room air. The girl's physical examination reveals an undernourished infant with less than normal subcutaneous fat. Her mucous membranes are slightly dry, and her anterior fontanelle is open, soft, and flat. She is in moderate respiratory distress, breathing fast and deeply, with mild intercostal retractions, and no wheezing or stridor. Her heart has a regular rate and rhythm, with no murmurs, and her pulses are equal and strong, with a capillary refill time of 2 seconds. There is no organomegaly and she has normal female genitalia.

Sodium	140 mEq/L (140 mmol/L)
Potassium	5.0 mEq/L (5.0 mmol/L)
Chloride	115 mEq/L (115 mmol/L)
Bicarbonate	14 mEq/L (14 mmol/L)
Urea nitrogen	5 mg/dL (1.8 mmol/L)
Creatinine	0.2 mg/dL (18 µmol/L)
Capillary blood gas pH	7.28
Partial pressure of carbon dioxide	29 mm Hg (3.8 kPa)
Partial pressure of oxygen	60 mm Hg (8 kPa)
Base deficit	–10

Of the following, the MOST likely cause of this infant's acid-base disturbance is

   A.   contraction alkalosis
   B.   lactic acidosis
   C.   renal tubular acidosis
   D.   respiratory alkalosis
   E.   uremic acidosis

Correct Answer: C

The infant in this vignette has a primary metabolic acidosis due to bicarbonate loss, evidenced by acidemia, low serum bicarbonate, normal anion gap, and appropriate respiratory compensation. Bicarbonate can be lost through the gastrointestinal tract and urinary tract. Thus, the most likely cause of this infant's acid-base disturbance is renal tubular acidosis (RTA).

When analyzing a blood gas for acid-base disorders, the clinician must characterize each disturbance as metabolic or respiratory in nature, and determine the contribution of each disturbance to acidosis or alkalosis. A serum bicarbonate (HCO_3) level lower than 22 mEq/L (22 mmol/L) or higher than 26 mEq/L (26 mmol/L) is consistent with metabolic acidosis or alkalosis, respectively. Normal respiratory compensation for metabolic acidosis follows the Winters formula:

$$PaCO_2 \text{ (predicted)} = 1.5*HCO_3 + 8 \pm 2$$

A partial pressure of arterial carbon dioxide ($PaCO_2$) level outside the range predicted by the Winters formula represents a respiratory acidosis or alkalosis. Although respiratory compensation for metabolic acidosis generally occurs within minutes, renal compensation for hypercapnia caused by chronic respiratory failure occurs within days. The rule of thumb for chronic respiratory failure is that the serum bicarbonate rises by 3.5 mEq/L (3.5 mmol/L) for every 10 mm Hg rise in $PaCO_2$.

The infant in this vignette has metabolic acidosis, evidenced by a bicarbonate level of 14 mEq/L (14 mmol/L). According to the Winters formula, the $PaCO_2$ level of 29 mm Hg was within the range of 27 to 31 mm Hg, which indicates no respiratory acid-base disturbance, even though the $PaCO_2$ is below the normal range. The calculated anion gap is 11, which is in the normal range. A normal anion gap implies the loss of bicarbonate, and rules out sources of acidosis that are not measured in the standard chemistry panel, such as in the commonly referenced "MUDPILES" mnemonic (methanol, uremia, diabetic ketoacidosis, paraldehyde, iron/isoniazid, lactate, ethanol/ethylene glycol, salicylates). The most common sources of bicarbonate loss are through the gastrointestinal tract with diarrhea and through the kidneys with RTA. Failure to thrive, hypertension, and vomiting are common presenting signs of RTA. Because there is no evidence in the vignette to support the gastrointestinal tract as the source of bicarbonate loss, RTA is the most likely answer.

It must be noted that a pH in the normal range does not in itself indicate a normal blood gas. For example, a normal pH can be seen when there is concomitant metabolic acidosis and respiratory alkalosis, which can occur in certain life-threatening conditions such as cardiogenic shock, sepsis, and toxic ingestion.

PREP Pearls
- An extremely concerning blood gas, even one that may hint at a life-threatening condition such as cardiogenic shock, sepsis, or toxic ingestion, may have a normal pH.

- A non-anion gap metabolic acidosis indicates losses of bicarbonate from either the gastrointestinal tract or kidneys.
- Respiratory compensation for a metabolic acidosis occurs within minutes, but it may take days for renal compensation for a respiratory acidosis.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Identify factors contributing to metabolic acidosis
- Identify the arterial blood gas abnormalities associated with an acid-base imbalance

Suggested Readings
- Adedoin O, Gottlieb B, Frank R, et al. Evaluation of failure to thrive: diagnostic yield of testing for renal tubular acidosis. *Pediatrics*. 2003;112:e463.
- Chan CM, Scheinman JI, Roth KS. Renal tubular acidosis. *Pediatr Rev.* 2001;22;277–287.

Question 30

You are called to attend the delivery of a 40-week, large-for-gestational age male infant. The mother is a 29-year-old gravida 4, para 2 woman with an elevated glucose level on the glucose challenge test. However, she never completed a glucose tolerance test. Results of her hepatitis B and group B Streptococcus tests were negative. A right choroid plexus cyst was noted on prenatal ultrasonography. At delivery, a tight nuchal cord and shoulder dystocia are noted. The newborn was delivered vaginally with vacuum assistance. Upon delivery, the neonate had poor tone and respiratory effort, requiring positive pressure ventilation, with resulting improvement in tone, activity, and respiratory effort. His birthweight was 4.3 kg (91st percentile), head circumference 36.5 cm (95th percentile), and length 53.5 cm (95th percentile). Physical examination demonstrates a cephalohematoma, decreased abduction of his left shoulder (Item Q30A). No movement is noted at the elbow. Sensation and grasp in the left hand remain intact. His chest radiograph is shown (Item Q30B). A nursing student asks why the neonate is not moving his arm.

Item Q30A: Findings for the neonate described in the vignette.
Courtesy M. LaTuga

Item Q30B: Radiograph for the neonate described in the vignette.
Courtesy M. LaTuga

Of the following, the BEST response to his question is

      A.   brachial plexus injury
      B.   cephalohematoma
      C.   left humeral fracture
      D.   tight nuchal cord
      E.   right-sided choroid plexus cyst

Correct Answer: A

The most likely cause of this neonate's decreased arm movement is brachial plexus injury (BPI). BPI has an incidence of approximately 1 in 1,000 live births. BPI results from a combination of maternal, neonatal, and peripartum factors. It has been associated with maternal diabetes, uterine abnormalities, neonatal macrosomia, transverse lie, and failure to progress. However, most neonates born to mothers with diabetes and macrosomia do not have BPI.

On initial physical examination, neonates with BPI present with decreased movement of the affected arm and an asymmetric Moro reflex. Initial management of suspected BPI includes minimal handling of the affected arm and short-term immobilization. In the absence of fracture, continued immobilization is controversial and passive range of motion exercises are recommended beginning at 7 to 10 days after birth. Affected neonates should receive close follow-up; referral to physical therapy should be ensured to maximize long-term function.

The presentation of BPI varies with the location and degree of cervical nerve root injury. In most cases, swelling of the surrounding nerve sheath causes neuropraxia or temporary loss of motor and sensory conduction in the cervical nerve roots. Less commonly, the nerve sheath ruptures, causing a temporary interruption in nerve conduction. In the unusual case of avulsion of the cervical roots or rupture of the axon, surgical correction may be required to maximize long-term nerve function.

The location of the nerve injury affects the initial clinical presentation. Most cases of BPI result from damage to cervical nerve roots C5-C6, causing Erb-Duchenne paralysis. Affected neonates present with an asymmetric Moro reflex and decreased abduction of the shoulder, external rotation of the arm, and supination of the forearm. Of note, palmar grasp and biceps reflexes on the injured side remain intact. Neonates may also have hemidiaphragmatic paralysis on the affected side from damage to the phrenic nerve. Erb-Duchenne paralysis typically resolves between 2 to 4 weeks after birth. However, phrenic nerve injury is associated with a worse prognosis. For infants, whose symptoms persist beyond 3 months, referral for surgical intervention should be considered.

Klumpke paralysis is caused by damage to cervical roots C7, C8, and T1. Affected neonates may have Horner syndrome on the affected side (ptosis and miosis), and weakness of flexor muscles of forearm and hand. Although the biceps reflex remains intact, palmar grasp will be absent. Neonates with BPI due to axonal rupture or complete nerve root avulsion present with flaccid paralysis of the arm and hand on the affected side, with no biceps reflex or palmar grasp. Long-term prognosis is poor. Magnetic resonance imaging may be helpful in assessing the extent of injury and guiding surgical repair.

Initial evaluation of BPI must include radiographs of the arm and shoulder to ensure no humeral or clavicular fracture is present. In the case of the neonate in the vignette, the humerus and clavicle were intact on the radiograph. Cephalohematoma, tight nuchal cord, and choroid plexus cyst have not been associated with BPI.

PREP Pearls
- Brachial plexus injury (BPI) typically involves swelling of the nerve sheath, resulting in decreased motor and sensory conduction.
- On physical examination, neonates with BPI most commonly have decreased abduction of the shoulder, decreased supination of the forearm, and decreased external rotation of the arm.
- Although most cases of BPI resolve completely, close follow-up and referral to physical therapy should be ensured to maximize long-term function.

MOCA-Peds Objective
- Evaluate and manage a neonate born to a diabetic mother

ABP Content Specifications(s)
- Understand the prognosis associated with brachial plexus injuries
- Recognize the clinical features in an infant whose delivery was complicated by shoulder dystocia
- Recognize the clinical findings associated with brachial plexus injuries, and manage appropriately

Suggested Readings
- Joyner B, Soto MA, Adam HM. Brachial plexus injury. *Pediatr Rev*. 2006;27:238. doi: http://dx.doi.org/10.1542/pir.27-6-238.
- Nelson M. Birth brachial plexus palsy. In: Kliegman RM, Stanton BF, St Geme J, Schor NF eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016; chap 713:3406-3408.e1.

Question 31

A 10-year-old girl with type 1 diabetes diagnosed at age 7 years is brought to your office for frequent episodes of hypoglycemia over the past 2 weeks. She has required oral treatment of low blood glucose levels on 8 separate occasions during this time frame. She is on a flexible basal-bolus insulin regimen with insulin glargine and aspart. Her total daily insulin dose typically averages 0.7 units/kg per day but has averaged 0.5 units/kg per day over the past 2 weeks. There have been no recent changes in her insulin regimen, and her hemoglobin A1c 2 months ago was 7.6%. The girl has had no fever or recent illness, but has been complaining of intermittent "stomach aches." She participates in dance for 1 hour, 1 evening per week. Her physical examination reveals a temperature of 37°C, blood pressure of 102/64 mm Hg, heart rate of 72 beats/min, weight of 32 kg (40th percentile), height of 143 cm (65th percentile), and body mass index of 15.6 kg/m2 (25th percentile). Her weight is unchanged from that documented 8 months ago. The remainder of her physical examination findings are within normal parameters.

Of the following, the MOST likely cause of the girl's hypoglycemia is

    A.   celiac disease
    B.   hypothyroidism
    C.   increased physical activity
    D.   insulin dosing errors
    E.   puberty

Correct Answer: A

The girl described in the vignette most likely has celiac disease, presenting with recurrent hypoglycemia in the context of type 1 diabetes. Celiac disease is an autoimmune disease with an increased incidence in those with type 1 diabetes, occurring in about 5%. Her recurrent hypoglycemia, "stomach aches," and lack of weight gain over the past 8 months are all consistent with celiac disease. Celiac disease is the second most common autoimmune disease associated with type 1 diabetes. The American Diabetes Association recommends screening for celiac disease at the time of diagnosis of type 1 diabetes, and rescreening as indicated for symptoms.

Hypothyroidism does not generally cause hypoglycemia in those with type 1 diabetes. Increased physical activity or insulin dosing errors could cause hypoglycemia, but there is no indication in the vignette that this girl's physical activity level has changed or that insulin dosing errors are being made. Her hemoglobin A1c level measured 2 months ago suggests relatively good glycemic control at that time. Because puberty produces a natural state of insulin resistance, it is more often associated with high blood glucose levels, not hypoglycemia.

Autoimmune thyroid disease, especially Hashimoto thyroiditis with associated hypothyroidism, is the most common associated autoimmune disease seen in children with type 1 diabetes. Approximately one-third of these children have detectable thyroid antibodies and 10% have abnormal thyroid function. The American Diabetes Association recommends screening for thyroid disease with thyroid antibody (thyroid peroxidase, antithyroglobulin antibodies) and thyroid-stimulating hormone (TSH) levels at the time of diagnosis of type 1 diabetes, and rescreening TSH levels every 1 to 2 years.

Addison disease, due to autoimmune adrenal insufficiency, although rare, is the third most common associated autoimmune condition, occurring in less than 1% of pediatric patients with type 1 diabetes. There is no routine recommendation for screening for Addison disease in these children.

Hypoglycemia, in the context of type 1 diabetes, is defined as a blood glucose of less than 70 mg/dL (<3.9 mmol/L). Treatment uses the "rule of 15s": 15 g of fast-acting carbohydrate should be ingested and 15 minutes later the blood glucose level should be tested. Fifteen-gram "doses" of fast-acting carbohydrate include 1/2 cup of juice or regular soda, 1 cup of milk, 3 teaspoons of honey, or 3 to 4 glucose tablets. This treatment and glucose check should be repeated if the blood sugar remains lower than 70 mg/dL. If the next meal will not be eaten within the next 30 to 60 minutes, a small snack of complex carbohydrate, fat, and protein should be eaten to help sustain the blood glucose level. For more severe hypoglycemia, with an inability to take oral glucose, glucagon can be given intramuscularly or subcutaneously. Every patient with diabetes who takes insulin should have a glucagon emergency kit.

PREP Pearls
- Celiac disease may present with unexplained episodes of recurrent hypoglycemia in children with type 1 diabetes
- Autoimmune thyroid disease and celiac disease are the first and second most common autoimmune diseases, respectively, associated with type 1 diabetes.
- Hypoglycemia associated with type 1 diabetes is managed using the "rule of 15s": ingestion of 15 g of fast-acting carbohydrate followed by recheck of the blood glucose level after 15 minutes. This cycle is repeated until the blood glucose level is greater than 70 mg/dL.

ABP Content Specifications(s)
- Recognize the association between type 1 diabetes and other autoimmune disorders
- Plan the appropriate management of hypoglycemia in a patient with type 1 diabetes and other autoimmune disorders (eg, celiac disease, Hashimoto thyroiditis)

Suggested Readings
- American Diabetes Association. 12. Children and adolescents. *Diabetes Care.* 2017;40(suppl 1):S105–S113. doi: http://dx.doi.org/10.2337/dc17-S015.
- Chase HP, Banion C. Chapter 6: Low blood sugar (hypoglycemia or insulin reaction). In: Chase HP, Maahs D, eds. *Understanding Diabetes.* 11th ed. Denver, CO: Paros Press; 2006:35–48. Available at: http://www.ucdenver.edu/academics/colleges/medicalschool/centers/BarbaraDavis/OnlineBooks/Pages/UnderstandingDiabetes.aspx.
- Gregory JM, Moore DJ, Simmons JH. Type 1 diabetes mellitus. *Pediatr Rev.* 2013;34(5):203–215. doi: http://dx.doi.org/10.1542/pir.34-5-203.
- Ly TT, Maahs DM, Rewers A, et al; International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014. Assessment and management of hypoglycemia in children and adolescents with diabetes. *Pediatr Diabetes.* 2014;15(suppl 20):180–192. doi: http://dx.doi.org/10.1111/pedi.12174.

Question 32

A 5-year-old boy with intellectual disability is brought to your office for a health supervision visit. He is making progress in his special education class, but has significant difficulty understanding and using spoken language. His parents report that their son becomes quite upset when things do not go as expected. They have a hard time taking him out in public because his high level of activity is disruptive and his impulsive actions cause his parents to be concerned for his safety. When he is upset, he tends to bite his hands. When you examine him, he averts his gaze and moves about the table, avoiding your touch. His physical examination findings are within normal parameters.

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

      A.   Down syndrome
      B.   fragile X syndrome
      C.   Prader-Willi syndrome
      D.   Rett syndrome
      E.   Smith-Magenis syndrome

Correct Answer: B

The boy in the vignette most likely has fragile X, the most common inherited form of intellectual disability (ID). Boys with fragile X have mild to severe ID, associated with significant receptive and expressive language problems. Autism spectrum disorder or autistic behaviors such as behavioral rigidity (eg, difficulty with change) and sensory sensitivity (eg, avoidance of touch) may be present. Hyperactivity is common in childhood. Hand biting and gaze aversion are characteristic behaviors seen in children with fragile X. Attention-deficit/hyperactivity disorder, anxiety, perseverative speech, and hand flapping may also be seen. Dysmorphic features may be subtle in young boys with fragile X. Classic features such as long face, prominent jaw, and macro-orchidism are seen around the time of puberty. Fragile X is caused by a trinucleotide repeat of greater than 200 CGG repeats in the fragile X mental retardation 1 (*FMR1*) gene. This disorder is seen in 1 in 4,000 males and 1 in 8,000 females. Girls with fragile X may not have physical differences. They tend to be more mildly affected intellectually, presenting with learning disabilities, borderline intellectual functioning, or mild ID. They commonly have problems with inattention and shyness or anxiety. Intellectual disability (ID) is a chronic condition that includes significant deficits in both intellectual and adaptive functioning. The age at presentation is correlated with the severity of ID. The majority have mild ID, and are typically identified when they struggle with learning in school. Children with more severe forms of ID are most often identified earlier in life because of developmental delays in motor and language skills.

Language delay, particularly receptive language delay, can be the first sign of ID in a young child. Language is a symbolic means of communication, which involves cognitive function through effects on memory and the development of concepts. Receptive language is the understanding of another's language, whereas expressive language is the production of language. Assessments of intelligence typically include an evaluation of language. Language skills, particularly receptive language skills, correlate well with cognitive function.

Down syndrome (trisomy 21) is the most common genetic cause of ID, occurring in 1 in 800 births. ID is typically in the mild to moderate range. Clinical features such as hypotonia, epicanthal folds, flat nasal bridge, increased neck tissue, clinodactyly, and wide space between first and second toes are present at birth. About 10% of those affected have an autism spectrum disorder. Adults with Down syndrome have an increased risk of developing Alzheimer's disease in their 50s or 60s.

Prader-Willi syndrome is most commonly caused by a microdeletion on the paternal chromosome 15q11.2-q13, occurring in 1 in 10,000 to 30,000. Intellectual abilities of children with Prader-Willi range from low average cognition to moderate ID. Infants are hypotonic and have failure to thrive. By 2 years of age, as the hypotonia improves, affected children develop obesity and hyperphagia. Physical features include almond-shaped eyes, thin upper lip and downturned mouth, hypogonadism, short stature, and small hands and feet. Obsessive-compulsive behaviors are common. Children perseverate on favorite topics, are stubborn, and have temper outbursts.

Rett syndrome is an X-linked condition almost exclusively seen in girls. It is the result of a mutation of the *MECP2* gene and occurs in 1 in 8,500 females. Development in early infancy is normal, slows in later infancy, and then regresses between 1 and 4 years of age. Acquired microcephaly and stereotypic hand movements (eg, hand wringing, hand washing, clapping, tapping) are characteristic. Children with Rett syndrome often have autistic behaviors. Smith-Magenis syndrome is caused by a deletion of chromosome band 17p11.2, occurring in 1 in 25,000. Most affected children have moderate ID. The physical features of frontal prominence; hoarse, deep voice; and coarse facial features (eg, heavy brows, synophrys, prognathism) may not manifest until late childhood. Children with Smith-Magenis syndrome exhibit unusual behaviors including self-hugging, pulling out fingernails and toenails, and insertion of foreign objects into their body. They typically have sleep problems because of circadian rhythm disturbances. The sleep problems and self-injurious behaviors increase with age. These children can be hyperactive and aggressive.

PREP Pearls
- Language delay, particularly receptive language delay, can be the first sign of intellectual disability (ID) in a young child.
- Children with mild ID are typically identified when they struggle with learning in school. Children with more severe forms of ID are typically identified earlier in life because of developmental delays in motor and language skills.
- Dysmorphic features may be subtle in young boys with fragile X. Classic features such as long face, prominent jaw, and macro-orchidism are generally seen around the time of puberty.
- Autism spectrum disorder or autistic behaviors are commonly seen in children with fragile X syndrome.

MOCA-Peds Objective
- Recognize the genetic syndromes that may present as a learning disability

ABP Content Specifications(s)
- Recognize the age-related clinical findings associated with intellectual disabilities of various etiologies
- Understand the correlation between language development and cognitive function

Suggested Readings
- Fussell JJ, Reynolds AM. Cognitive Development. In: Voigt RG, Macias MM, Myers SM, eds. *Developmental and Behavioral Pediatrics.* Elk Grove, IL: American Academy of Pediatrics; 2011:258–262.
- Shea SE. Intellectual disability (mental retardation). *Pediatr Rev*. 2012;33(3):110–121. doi: http://dx.doi.org/10.1542/pir.33-3-110.
- 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 33

A 42-year-old woman delivers a newborn with unusual features, including brachycephaly, upslanting palpebral fissures, flat nasal bridge, small mouth, low-set small ears, short neck, right single transverse palmar crease, and a sandal toe bilaterally. The newborn has decreased muscle tone. Cardiac examination findings and red eye reflex are normal. You order fluorescence in situ hybridization analysis that reveals the presence of an extra chromosome 21. Newborn screening, including a hearing screen, is pending. A complete blood cell count shows a normal white blood cell count, polycythemia, macrocytosis, and mild thrombocytopenia.

Of the following, the BEST next test to order for this patient is

- A. bone marrow biopsy
- B. brain magnetic resonance imaging
- C. echocardiography
- D. liver function tests
- E. renal ultrasonography

Correct Answer: C

The infant in this vignette has classic dysmorphology consistent with trisomy 21, also known as Down syndrome. Facial characteristics include small head with brachycephaly, epicanthal folds, upslanting palpebral fissures, small posteriorly rotated low-set ears, flat midface, Brushfield spots, and small mouth. In addition, children also commonly have a short neck, single transverse palmar crease, sandal toe, brachydactyly, fifth finger clinodactyly, and short stature. Cognitive impairment typically varies from mild to moderate intellectual disability; only rarely is the cognitive impairment severe. Other associated defects are noted in **Item C33**.

The American Academy of Pediatrics has published guidelines for the health supervision of children with Down syndrome (http://pediatrics.aappublications.org/content/128/2/393). Please refer to these guidelines, including appendix 1 on page 406 (http://pediatrics.aappublications.org/content/128/2/393.figures-only) for detailed age-specific recommendations.

Item C33. Medical Problems Commonly Seen in Down Syndrome.

Condition	Percentage
Hearing problems	75
Vision problems – Cataracts – Refractive errors	 15 50
Obstructive sleep apnea	50-75
Otitis media	50-70
Congenital heart disease	40-50
Hypodontia and delayed dental eruption	23
Gastrointestinal atresias	12
Thyroid disease	4-18
Seizures	1-13
Hematologic problems – Anemia – Iron deficiency – Transient myeloproliferative disorder – Leukemia	 3 10 10 1
Celiac disease	5
Atlantoaxial instability	1-2
Autism	1
Hirschsprung disease	<1

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When first evaluating a newborn with suspected trisomy 21, the pediatrician should perform a comprehensive physical examination to assess for associated anomalies and a fluorescence in situ hybridization analysis for trisomy 21 to quickly confirm the diagnosis for the family. A high resolution chromosome analysis to assess the mechanism of the trisomy 21 is also required. This analysis will reveal if the trisomy 21 is caused by a complete extra chromosome 21 (sporadic trisomy 21) or by an unbalanced translocation; this information allows the family to be informed of recurrence risk. Fluorescence in situ hybridization analysis can indicate that an extra copy of chromosome 21 is present, but it cannot detect a translocation. Advancing maternal age increases the risk for sporadic trisomy 21.

Physical examination of the newborn with trisomy 21 should include careful evaluation for cataracts by looking for a red reflex. Auscultation for a cardiac murmur and pulse oximetry are important initial evaluations for cardiac disease. The child should be observed for stridor, wheezing, or noisy breathing that could indicate cardiorespiratory anomalies or intestinal atresias. A careful history for feeding problems, gastroesophageal reflux, constipation, apnea, bradycardia, cyanosis, or other respiratory difficulties is also needed. A brainstem auditory evoked response or otoacoustic emission should be performed at birth because of increased risk for hearing loss (and per universal newborn hearing screening guidelines). Newborn screening should include measurement of free thyroxine and thyroid-stimulating hormone because many children with trisomy 21 have mildly elevated thyroid-stimulating hormone and normal free thyroxine levels. Because 50% of children with trisomy 21 have congenital heart defects, an echocardiogram should be obtained and read by a pediatric cardiologist even if a normal fetal echocardiogram was obtained. A complete blood cell count is needed to look for hematologic abnormalities, leukemoid reactions, or transient myeloproliferative disorder, which poses an increased risk for leukemia later in life (10%-30%). Leukemia is more common in individuals with trisomy 21 than in the general population, although it is still rare (1%). A bone marrow biopsy would only be indicated if leukemia was suspected. Approximately 3% of children with trisomy 21 have hematologic problems. Magnetic resonance imaging of the brain and renal ultrasonography are not indicated because brain and kidney anomalies are not common in individuals with trisomy 21. The routine serum laboratory values to be followed over time with a diagnosis of trisomy 21 are a complete blood cell count and thyroid function testing, not liver function testing.

PREP Pearls
- When first evaluating a newborn with suspected trisomy 21, the pediatrician should perform a comprehensive physical examination to assess for associated anomalies and a fluorescence in situ hybridization analysis for trisomy 21.
- A high resolution chromosome analysis is required to determine if the trisomy 21 is caused by a complete extra chromosome 21 (sporadic trisomy 21) or by an unbalanced translocation. This informs recurrence risk.
- Common dysmorphology in newborns with trisomy 21 includes small head with brachycephaly, epicanthal folds, upslanting palpebral fissures, small posteriorly rotated

low-set ears, flat midface, Brushfield spots, small mouth, short thick neck, single transverse palmar crease, sandal toe, brachydactyly, and fifth finger clinodactyly.
- Because 50% of children with trisomy 21 have congenital heart defects, an echocardiogram should be obtained and read by a pediatric cardiologist regardless of a normal fetal echocardiogram.

ABP Content Specifications(s)
- Understand the specific management issues in infants with trisomy 21
- Plan the diagnostic evaluation of a patient with trisomy 21
- Recognize the clinical features associated with trisomy 21

Suggested Readings
- Bull MJ, Committee on Genetics. Health supervision for children with Down syndrome. *Pediatrics*. 2011;182(2):393–406. doi: http://dx.doi.org/10.1542/peds.2011-1605.
- National Down Syndrome Society. A promising future together: a guide for new and expectant parents. http://live.ndss.org/resources/publications/printed-materials/a-promising-future-together-additional-translations/ .

Question 34

A 10-year-old girl is brought to your office for a routine health supervision visit. Her mother reports that the girl has a history of recurrent kidney infections and small kidneys. Her last kidney infection was nearly 3 years ago. She has a temperature of 37.4°C, heart rate of 85 beats/min, respiratory rate of 17 breaths/min, blood pressure of 130/85 mm Hg, and normal growth parameters. Her physical examination findings are normal. Her urinalysis results are shown:

Laboratory Test	Result
Specific gravity	1.010
pH	6.0
Protein	3+
Blood, leukocyte esterase, nitrites	Negative

Of the following, the MOST likely cause of this child's urinary findings is

        A.   acute glomerulonephritis
        B.   orthostatic proteinuria
        C.   primary hypertension
        D.   reflux nephropathy
        E.   urinary tract infection

Correct Answer: D

Hypertension, proteinuria, and a history of small kidneys are indicative of underlying chronic kidney disease (CKD) in this patient. The KDIGO (Kidney Disease: Improving Global Outcomes) 2012 clinical practice guidelines diagnose CKD in children based on the presence of 1 of the following criteria:

- Glomerular filtration rate of less than 60 mL/min/1.73 m^2 for greater than 3 months with implications for health, regardless of whether other CKD markers are present
- Glomerular filtration rate greater than 60 mL/min/1.73 m^2 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 by histology or inferred by imaging

The patient in this vignette has CKD based on the second KDIGO criteria. In the early stages of CKD (glomerular filtration rate, 60-90 mL/min/1.73 m^2), patients are often asymptomatic. Symptoms of abnormal voiding patterns (enuresis or polyuria), poor growth, and pallor may be subtle and easily missed. Fixed urine specific gravity of 1.010 confirmed on repeat urinalysis is indicative of an underlying inability to concentrate urine, secondary to tubulointerstitial damage.

Consequently mild changes of increased frequency or thirst may be unrecognized in early stages of CKD. The history of small kidneys and recurrent urinary tract infections in this patient suggests underlying vesicoureteral reflux and associated reflux nephropathy as the cause of her symptoms. In children with vesicoureteral reflux, decreased renal mass and hence small kidneys could be congenital (associated with abnormal renal development) or secondary to renal scars (recurrent urinary tract infections associated with vesicoureteral reflux).

Apart from CKD (in this case caused by reflux nephropathy), of the other choices, proteinuria in children is more likely to be associated with orthostatic proteinuria and acute glomerulonephritis. However, a history of infections and small kidneys is unlikely with orthostatic proteinuria and acute glomerulonephritis. Orthostatic proteinuria is characterized by increased urinary protein excretion during the day when the patient is active and normal urinary protein excretion when the patient is supine/asleep for at least 2 hours. Therefore, to confirm orthostatic proteinuria, a first-morning urine sample is needed. It is important that the patient collect the first urine sample immediately upon waking because even a small amount of activity can lead to proteinuria. A urine protein-creatinine ratio higher than 0.2 in a first-morning sample is abnormal and indicates renal pathology; in these cases, an evaluation by a pediatric nephrologist is required. Acute glomerulonephritis is characterized by glomerular hematuria (cola- or tea-colored urine), hypertension, and renal failure. Acute glomerulonephritis may be associated with hypertension and proteinuria; however, in the absence of hematuria, acute nephritis is unlikely in this patient.

Urinary tract infection is unlikely in this case because of the absence of fever, dysuria, flank pain, or a burning sensation on micturition. The absence of leukocyte esterase, nitrates, and bacteria in the urinalysis excludes urinary tract infection as the underlying cause of proteinuria in this patient.

High blood pressure in the absence of an underlying secondary cause (primary hypertension) is unlikely in this patient. Proteinuria, a history of infections, and a history of small kidneys suggest an underlying renal etiology, which is the most common cause of secondary hypertension in children.

PREP Pearls
- In the early stages of chronic kidney disease (glomerular filtration rate, 60-90 mL/min/1.73 m^2), patients are often asymptomatic.
- Evidence of structural damage or other markers of functional kidney abnormalities, as identified by hypertension, proteinuria, albuminuria, renal tubular disorders, or pathologic abnormalities detected by histology or inferred by imaging, are indicative of underlying chronic kidney disease
- In vesicoureteral reflux, decreased renal mass and hence small kidneys could be congenital (associated with abnormal renal development) or secondary to acquired renal scars (recurrent pyelonephritis associated with vesicoureteral reflux).

ABP Content Specifications(s)
- Recognize the clinical findings associated with reflux nephropathy

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://pedsinreview.aappublications.org/content/31/11/451.full .
- Kidney Disease: Improving Global Outcomes. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013;3(1):v–136. 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 35

You are seeing a 13-month-old boy who is new to your practice for a health supervision visit. The boy recently moved with his family to the rural area where you practice, where his parents have started a strawberry farm. They are currently living in and renovating a farmhouse that was built in 1915. Both their farm and home are supplied with well water. The entire family eats a variety of fresh fruits and vegetables that are grown on their farm.

The child's parents report that he has been very healthy, with no significant medical history. He takes no medications and has no allergies. His immunizations are up to date. His growth and development have been progressing normally. He is breastfed and eats some solid foods, though his mother states that he is a "picky" eater. He does not attend daycare, and loves playing with his 7-year-old twin sisters and 13-year-old brother (who are all healthy and developing normally according to the parents).

In your office, the boy is well-appearing and active. His growth parameters are normal for his age, and findings of a complete physical examination are unremarkable.

His parents ask you to discuss the potential health consequences of exposure to environmental toxins in this boy and his older siblings and how they can reduce the risk of exposure to environmental toxins for their children.

Of the following, the MOST accurate information that you can provide to address the parents' concerns is that

A. all well water that this 13 month old and his siblings consume should be boiled to reduce their risk of exposure to both lead and nitrites
B. the boy's mother should discontinue breastfeeding to reduce his risk of exposure to pesticides
C. the boy's risk of developing asthma after exposure to air contaminants on the farm is the same as the risk of asthma development in his older siblings
D. the boy's risk of exposure to foodborne pesticide residues is lower than the risk of exposure faced by his older siblings because he consumes less food
E. the boy's risk of ingesting lead dust in his home environment is higher than the risk faced by his older siblings

Correct Answer: E

The boy in the vignette lives with his family in an old farmhouse on a farm that is supplied by well water.The most accurate information to provide his parents about minimizing exposure of their children to environmental toxins is that the 13-month-old boy's risk of ingesting lead dust in their home environment is higher than the risk faced by his older siblings. This is because the developmentally normal exploratory behaviors at his age (frequent oral exploratory and hand-to-mouth behaviors), his higher respiratory rate, and his closer physical proximity to the ground and contaminated surfaces (eg, window sills) place him at higher risk for exposure to lead dust than older children.

Pediatric health care providers should know the age- and developmentally specific effects of exposure to a toxic substance in the environment, as well as how to obtain an appropriate exposure history. Children may be exposed to various environmental toxins on a daily basis in air, food, dust, soil, and on surfaces in their home, school, play, and occupational environments. The field of pediatric environmental health is an emerging and rapidly evolving one, with a growing body of literature that is helping to shed light on the effects of various environmental toxins on human health.

According to the World Health Organization, nearly a third of the global burden of disease in children is due to environmental factors. Children have both increased exposure and increased physiologic vulnerability to environmental toxins. Physiologically, children differ from adults in organ system functioning, metabolic capabilities, physical size, and developmental abilities/behaviors. They are particularly susceptible to adverse outcomes from toxic exposures, given their rapid growth and development. Research focusing on the impact of children's unique characteristics on the harm caused to them by environmental toxins is ongoing.

A free resource available to pediatric providers about the effects of environmental toxins on children is the Pediatric Environmental Health Specialty Units (PEHSU) National Classroom, a national resource endorsed by the American Academy of Pediatrics. This resource can be accessed online at http://www.pehsu.net. In addition, the US Department of Health and Human Services Agency for Toxic Substances and Disease Registry has developed an educational module on obtaining a pediatric environmental exposure history, which is available at http://www.atsdr.cdc.gov/csem/pediatric_history/docs/pediatric_history.pdf.

Advising this boy's parents to boil all well water consumed by their children to reduce exposure to both lead and nitrates would not be appropriate. In fact, both lead and nitrates become *more* concentrated in water that is boiled. In homes where there is a concern for contamination of water from lead pipes or lead pipe joints, families should be advised to discard "first-draw" water that has stood overnight in pipes (or to use it for a purpose other than drinking/cooking).

The boy's mother should not be advised to discontinue breastfeeding to reduce his risk of exposure to pesticides. Breastfeeding is encouraged as the optimal form of nutrition for infants

by the American Academy of Pediatrics and the World Health Organization. Although certain lipophilic chemicals can be transmitted through breast milk and result in exposure to nursing infants, instances of harm occurring from chemicals transmitted through breast milk are very rare. The many benefits conferred by breastfeeding, such as enhanced immune function and growth factors that enhance brain development, generally outweigh the risks of exposure to environmental toxins through breast milk.

The boy's risk of developing asthma after exposure to air contaminants on the farm is likely higher than the risk of asthma development in his older siblings. Younger children have higher respiratory rates, resulting in higher weight-adjusted exposure to air contaminants. Furthermore, there is evidence that respiratory exposure to air contaminants during the first years of life have a greater influence on the incidence and severity of asthma compared with exposure later in life.

The statement that the boy's risk of exposure to foodborne pesticide residues is lower than that of his siblings because he consumes less food is incorrect. Young children have higher metabolic rates and generally consume a greater amount of food, water, and air per kilogram than older children. As a result, they have a greater exposure per kilogram of body weight to foodborne toxins. Furthermore, many young children have limited food preferences and may consume the same foods over relatively long periods.

PREP Pearls
- Children are particularly susceptible to adverse outcomes from toxic exposures because of their rapid rate of growth and development.
- Children are at increased risk of harm from environmental toxins because of both increased exposure and increased physiologic vulnerability.
- Young children have higher metabolic rates and generally consume a greater amount of food, water, and air per kilogram than older children. This can result in greater exposure per kilogram of body weight to foodborne and airborne toxins.

ABP Content Specifications(s)
- Understand the effects of a patient's age when exposed to a toxic substance in the environment
- Understand how to obtain a history of exposure to toxic substances in the environment

Suggested Readings
- Etzel RA, Balk SJ, eds; The American Academy of Pediatrics Council on Environmental Health. *Handbook of Pediatric Environmental Health*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2011.
- Pediatric Environmental Health Specialty Units. http://www.pehsu.net. Accessed February 14, 2017.
- US Health and Human Services Agency for Toxic Substances and Disease Registry. Environmental health and medical education: principles of pediatric environmental health. https://www.atsdr.cdc.gov/csem/csem.asp?csem=27&po=0. Accessed April 24, 2016. .

- US Health and Human Services Agency for Toxic Substances and Disease Registry. Pediatric environmental health toolkit. https://www.atsdr.cdc.gov/emes/training/index.html. Accessed April 24, 2016 .
- World Health Organization. Principles for evaluating health risks in children associated with exposure to chemicals. Environmental health criteria 237. http://whqlibdoc.who.int/publications/2006/924157237X_eng.pdf. Accessed April 23, 2016.

Question 36

A 12-year-old girl presents to your office with a 2-month history of anterior knee pain. The pain is present while she is playing basketball and immediately afterwards. She does not recall a precipitating injury. The girl reports localized swelling at the site of pain and denies any feeling of catching, locking, or instability. She is otherwise healthy. On physical examination, you note mild swelling and moderate tenderness at the site of the patellar tendon insertion on the tibia, and pain with resisted knee extension. Physical examination findings of the knee and hip are otherwise unremarkable and her gait is normal.

Of the following, the BEST next step in the evaluation and management of this girl's symptoms is

      A.   complete rest from sports and other physical activities for 6 weeks
      B.   magnetic resonance imaging scan of the knee to evaluate for cartilage injury
      C.   modification of activities to avoid severe pain and use of a patellar strap
      D.   radiography of the knee to evaluate for growth plate injury
      E.   referral to orthopaedic surgery for evaluation and management

Correct Answer: C

The girl in the vignette has history and physical examination findings that are suggestive of Osgood-Schlatter disease (OSD). She should be treated with activity modification. A patellar strap may be applied to relieve the tension caused by the patellar tendon pulling on the tibial tuberosity (**Item C36**).

Item C36: Patellar strap Courtesy of R. Carl

Osgood-Schlatter disease is an apophysitis of the tibial tuberosity. An apophysis is an area of bone growth where a tendon attaches. These areas are susceptible to stress with repeated use of the attached muscle groups or with repeated local impact. OSD typically occurs in girls 10 to 13

years of age and boys 12 to 15 years of age. Up to 20% of children in these age groups are affected. Young athletes with OSD often report pain with running, jumping, and kneeling. Symptoms occur bilaterally in about one-third of cases. On physical examination, affected individuals often have a tender and prominent tibial tuberosity. They may also report pain with extension of the knee against resistance. Treatment involves relative rest; young athletes can participate in sports if they have mild pain, but should refrain from physical activities if they have severe pain or limp. Use of a patellar strap may lessen the tension from the patellar tendon on the tubercle, thereby decreasing pain. Stretching and strengthening exercises may also be helpful. Most children with OSD have no long-term sequelae. However, 10% of affected children will have a persistent bony prominence at the site.

The girl in the vignette does not require complete rest from activities. She can continue to participate in sports as long as she has minimal pain and no change in her gait. OSD can be diagnosed clinically, and is typically managed with conservative measures. Radiography and magnetic resonance imaging are not required to make this diagnosis. Orthopaedic surgery consultation is not usually necessary.

PREP Pearls
- Children and adolescents with Osgood-Schlatter disease can continue to participate in physical activities, unless they have a limp or severe activity-related pain.
- Use of a patellar strap and/or stretching and strengthening exercises may help alleviate symptoms related to Osgood-Schlatter disease.
- Ten percent of individuals with Osgood-Schlatter disease will have a persistent bony prominence at the tibial tuberosity.

MOCA-Peds Objective
- Know the differential diagnosis of knee pain

ABP Content Specifications(s)
- Recognize the clinical findings associated with Osgood-Schlatter disease, and manage appropriately
- Identify the etiology of Osgood-Schlatter disease

Suggested Readings
- de Lucena GL, dos Santos Gomes C, Guerra RO. Prevalence and associated factors of Osgood-Schlatter syndrome in a population-based sample of Brazilian adolescents. *Am J Sports Med.* 2011;39(2):415-420. doi: http://dx.doi.org/10.1177/0363546510383835.
- JF Sarwark CR LaBella, eds. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014.

Question 37

You are discussing the human papillomavirus (HPV) vaccine with a resident who is rotating in your office.

Of the following, the statement that you are MOST likely to include in your discussion is

      A. for children 9 to 14 years of age, a 3-dose schedule is recommended

      B. girls who receive the vaccine are more likely than those who do not to be sexually active and to have an increased number of sexual partners

      C. more than 75% of girls and 50% of boys receive 3 or more doses of the HPV vaccine

      D. the vaccine is associated with an increased risk of developing central nervous system demyelinating disease

      E. the vaccine provides protection against noncervical HPV-associated cancers

Correct Answer: E

Of the response choices, the statement you are most likely to include in your discussion is that the vaccine provides protection against noncervical HPV-associated cancers. Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States. In a study conducted before HPV vaccine licensure, 25% of persons aged 14 to 19 years and 45% of those aged 20 to 24 years were infected. It is estimated that more than 80% of men and women in the United States will be infected with HPV during their lifetime.

Most HPV infections are asymptomatic and resolve spontaneously. Infection with low-risk HPV types (eg, 6 and 11) may cause anogenital warts or mild forms of intraepithelial neoplasia affecting the vulva, vagina, cervix, anus, or penis. Persistent infection with 1 of the 13 oncogenic (high-risk) types may lead to precancerous or cancerous lesions. In the United States, types 16 and 18 are responsible for 63% of HPV-associated cancers (70% of cervical cancers); types 31, 33, 45, 52 and 58 cause an additional 10%. In addition to cervical carcinoma, HPV is associated with other malignancies. In 1 study, HPV DNA was found in 90% of cervical, 75% of vaginal, 69% of vulvar, 63% of penile, and 91% of anal cancers. Approximately 70% of oropharyngeal cancers are believed to result from HPV infection, especially type 16.

Currently, 2 HPV vaccines are licensed and available in the United States: 4-valent (types 6, 11, 16, 18) and 9-valent (types 6, 11, 16, 18, 31, 33, 45, 52, 58). Each of the vaccines is approved for the prevention of HPV-associated cervical, vaginal, vulvar, and anal cancers, and precancerous lesions. The additional coverage provided by the 9-valent vaccine could increase protection against invasive cervical cancer from 70% to 90%.

The 4- and 9-valent vaccines are approved for the prevention of anogenital warts, 90% of which are caused by types 6 and 11. Both vaccines are approved for use in both girls and boys.

The Advisory Committee on Immunization Practices offers the following recommendations regarding HPV immunization:

- Vaccination of girls and boys should begin routinely at 11 or 12 years, but may be initiated as early as 9 years.
    - The vaccine is also recommended for females of ages 13 to 26 years and males of ages 13 to 21 years who were not previously immunized.
    - For men who have sex with men and for persons who are immunocompromised, vaccination is recommended through age 26 years.
- The vaccines are administered with 1 of 2 schedules:
    - For those 9 to 14 years of age, a 2-dose schedule is recommended: the second dose is given 6 or 12 months after the first (if the series is initiated before the 15th birthday, 2 doses are administered)
    - For those 15 to 26 years of age, a 3-dose schedule is recommended: the second dose is administered 1 to 2 months after the first; the third dose is given at least 6 months after the first.
- If the vaccine series is interrupted it may be resumed (ie, the series does not need to be restarted).

- If possible, the same vaccine form should be used to complete the immunization series. However, if this is not possible, another vaccine may be substituted.

The most common adverse effects of HPV vaccination are injection site pain, erythema, and/or edema. Headache, dizziness, fever, nausea, fatigue, or syncope may occur. The vaccine is not associated with an increased risk of developing central nervous system demyelinating disease. Although it is a concern expressed by some parents, studies indicate that girls who receive the vaccine are not more likely than those who do not to be sexually active or to have an increased number of sexual partners.

In the United States, only 39.7% of girls and 21.6% of boys aged 13 to 17 years receive 3 or more doses of HPV vaccine (ie, complete the series). The rate of immunization with 1 or more doses of HPV has increased, but remains lower than for 1 or more doses of tetanus, diphtheria, and pertussis (Tdap) or meningococcal bacteria A, C, W and Y (MenACWY). Although the reasons for this are not fully understood, the lack of a strong provider recommendation is 1 factor. In 1 study, 55% of parents who received a physician's recommendation for HPV immunization had their sons vaccinated compared with only 1% of parents who received no such recommendation. Similarly, in a study published in 2014, the most common reason parents did not vaccinate their daughters against HPV was the lack of a physician recommendation. Resources that may assist clinicians in communicating the importance of HPV vaccine to parents and patients are available at: http://www.cdc.gov/hpv/index.html.

PREP Pearls
- The 9-valent HPV vaccine may protect against HPV types that cause 90% of anogenital warts and 90% of invasive cervical carcinomas.
- A strong provider recommendation is an important factor in a parent's decision to allow the administration of the HPV vaccine to their child.

ABP Content Specifications(s)
- Recognize the clinical features associated with human papillomavirus infection
- Understand the epidemiology of human papillomavirus infection
- Know the recommendations, limitations, and schedule for the human papillomavirus vaccine

Suggested Readings
- Ben-Harush Negari S, Kahn JA. Human papillomavirus infection and anogenital warts. In Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.
- Petrosky E, Bocchini JA Jr, Hairi S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2015;64:300–304.

- Reagan-Steiner S, Yankey D, Jeyarajah J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13-17 years – United States, 2015. *MMWR Morb Mortal Wkly Rep.* 2016;65:850–858.
- Viens LJ, Henley SJ, Watson M, et al. Human papillomavirus-associated cancers – United States, 2008-2012. *MMWR Morb Mortal Wkly Rep.* 2016;65:661–666.

Question 38

A 4-month-old infant is brought to your office for a routine health supervision visit. He was born at term to a primigravida mother after an uncomplicated pregnancy. His parents report that he "lights up" when they enter the room, and he laughs, smiles, and coos. He holds his head steady when he is placed in a seated position and recently began to roll from his back to his abdomen. His parents report that he more consistently reaches for toys with his left hand and preferentially brings this hand in front of his face to gaze at his fingers and place them in his mouth.

Of the following, the MOST appropriate assessment is that this infant's development is

        A.   concerning because he is not yet rolling from his abdomen to his back

        B.   concerning because of a hand preference at this age

        C.   concerning because of global developmental delay

        D.   entirely appropriate for age

        E.   overall advanced for age

Correct Answer: B

The presence of a hand preference or other asymmetry in movement in a 4-month-old infant is a concerning finding that must be evaluated. Consistent handedness does not typically develop until between 4 and 6 years of age, although emerging dominance can be seen between 1 and 3 years of age. As with other asymmetrical movements, handedness that is apparent before 18 months of age may indicate a central or peripheral neurologic abnormality of the opposite side, including hemiparesis.

The remainder of the developmental milestones described for the boy in this vignette are age appropriate. Although each child progresses slightly differently, typically developing 4-month-old infants have the skills and abilities shown in **Item C38**. More information about milestones can be found in *Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents* published by the American Academy of Pediatrics (https://brightfutures.aap.org/materials-and-tools/guidelines-and-pocket-guide/Pages/default.aspx).

Item C38. Typical Developmental Milestones at Age 4 Months.

Gross Motor	Fine Motor	Self-Help	Solving	Emotional	Receptive Language	Expressive Language
• Sits with trunk support • No head lag when pulled to sit • Props on wrists • Rolls front to back	• Hands held predominantly open • Clutches at clothes • Reaches persistently • Plays with rattle	• Briefly holds onto breast or bottle	• Mouths objects • Stares longer at novel faces than familiar • Shakes rattle • Reaches for ring/rattle	• Smiles spontaneously at pleasurable sight/sound • Stops crying at parent voice • To and fro alternating vocalizations	• Orients head in direction of a voice • Stops crying to soothing voice	• Laughs out loud • Vocalizes when alone

Adapted and reprinted with permission from Scharf, RJ, Scharf, GJ, Stroustrup, A. Developmental Milestones. *Pediatr Rev.* 2016; 37(1), 25.

PREP Pearls
- Consistent handedness should not develop before 4 years of age; strong hand preferences at an earlier age may represent relative weakness or neurologic impairment of the "nondominant" side.
- Typically developing 4-month-old infants roll from front to back, reach for objects with their hands, smile spontaneously, initiate social interactions, laugh, and vocalize when alone.

ABP Content Specifications(s)
- Evaluate the cognitive and behavioral developmental progress/status of an infant at 4 months of age, including recognition of abnormalities
- Evaluate the motor developmental progress/status of an infant at 4 months of age, including recognition of abnormalities

Suggested Readings
- Scharf RJ, Scharf GJ, Stroustrup A. Developmental milestones. *Pediatr Rev*. 2016;37(1):25–37. doi: http://dx.doi.org/10.1542/pir.2014-0103.

Question 39

A previously healthy 4-year-old child is brought to your office for follow-up. He was seen in an urgent care center 3 days ago and was diagnosed with an upper respiratory infection. His mother states that he has had daily fevers between 38°C and 39°C over the last week, along with decreased energy and appetite.

He is in mild respiratory distress and appears well hydrated. He has a temperature of 38.6°C, respiratory rate of 35 breaths/min, and heart rate of 140 beats/min. He is warm and well perfused. He has petechiae on his distal extremities. A new 2-3/6 soft, blowing murmur is best heard at the apex. He has no prior history of heart disease. You refer him to the emergency department for blood cultures, inflammatory marker measurement, and admission.

Of the following, the organism that is the MOST likely cause of this child's symptoms is

      A.   Cardiobacterium hominis
      B.   Eikenella corrodens
      C.   Staphylococcus aureus
      D.   Staphylococcus epidermidis
      E.   Streptococcus mitis

Correct Answer: C

The boy in this vignette has persistent fevers, a new cardiac murmur, no history of cardiac disease, petechiae on the extremities, fatigue, and tachycardia. Infective endocarditis (IE) is a very likely diagnosis and further evaluation is needed. Of the choices listed, *Staphylococcus aureus* is the most likely cause of this child's symptoms.

Infective endocarditis is rare in pediatrics. It occurs most often in children with underlying congenital heart disease, but it can also occur in children with normal hearts. Infective endocarditis carries a significant burden of disease relative to morbidity and mortality. Patients with central venous catheters are also at increased risk of IE. Viridans streptococci and *Staphylococcus aureus* are the most common organisms responsible for IE in pediatric patients with or without congenital heart disease. The AACEK organisms (*Aggregatibacter parainfluenzae*, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species) are gram-negative organisms that cause IE, although less commonly than the *Streptococcus* and *Staphylococcus* species. Fungi can also rarely cause IE. Approximately 5% to 10% of IE is culture negative.

Infective endocarditis is the result of a transient bacteremia from the oropharynx, gastrointestinal tract, or genitourinary tract. The bacteremia interacts with damaged cardiac endothelium, platelets, and fibrin resulting in an infected thrombus on the surface of the endothelium. Viridans streptococci (*Streptococcus mitis*) are more often associated with abnormal cardiac valves (congenital heart disease, rheumatic heart disease, postoperative changes) whereas *Staphylococcus aureu*s is the more likely pathogen in an otherwise structurally normal heart, as noted for the boy in this vignette with no prior history of congenital heart disease. *Cardiobacterium hominis*, *Eikenella corrodens*, *Staphylococcus epidermidis*, and *Streptococcus mitis* are less prevalent from an epidemiological perspective and thus not likely the cause of IE in the boy in this vignette.

Infective endocarditis can present in a subacute (over several weeks) or acute (rapidly progressive) fashion. Infective endocarditis tends to present differently in children than in adults; children only rarely have Roth spots (small retinal hemorrhages), Janeway lesions (small painless hemorrhagic lesions on the palms and soles), Osler nodes (small tender intradermal nodules on the fingers and toes), and splinter hemorrhages (linear streaks beneath the nail beds). Most commonly, children with IE develop fever, malaise, anorexia, heart failure, and arthralgias. They often have splenomegaly, embolic phenomenon, murmur (new or changing), and petechiae. The modified Duke criteria (**Item C39**) are used for diagnosis. Treatment is a prolonged course of an appropriate antimicrobial regimen.

Item C39. Stress Dosing Guideline for Hydrocortisone.

Physiologic replacement dosing, oral	6-10 mg/m^2 per day
Oral stress dosing (minor febrile illness, taking oral well)	30 mg/m^2 per day divided three times daily
Intravenous stress dosing (before surgery or major illness, but clinically stable)	50 mg/m^2 1 hour before procedure and then continued 50 mg/m^2 per day divided 4 times daily as needed for continued stress
Intravenous stress dosing (adrenal crisis, sepsis, shock)	100 mg/m^2 initial dose and then 100 mg/m^2 per day divided 4 times daily (100 mg maximum per dose)

Courtesy of J. Pinsker

PREP Pearls
- Infective endocarditis is rare in pediatrics. It occurs most often in children with underlying congenital heart disease, but it can occur in children with normal hearts. Central venous catheters also pose an increased risk for infective endocarditis.
- Viridans streptococci are more often associated with abnormal cardiac valves (congenital heart disease, rheumatic heart disease, postoperative changes) whereas *Staphylococcus aureus* is the more likely pathogen in an otherwise structurally normal heart.
- The AACEK organisms (*Aggregatibacter parainfluenzae, Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species) are gram-negative organisms that cause infective endocarditis, although less commonly than the Streptococcus and Staphylococcus species.

ABP Content Specifications(s)
- Understand the natural history of infective endocarditis
- Recognize pathogens commonly associated with infective endocarditis

Suggested Readings

- Baltimore RS, Gewitz M, Baddour LM, et al; American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young and the Council on Cardiovascular and Stroke Nursing. 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.
- Bragg L, Alvarez A. Endocarditis. *Pediatr Rev*. 2014;35(4):162–167. doi: http://dx.doi.org/10.1542/pir.35-4-162.

Question 40

A 13-year-old adolescent boy with no significant past medical history visits the emergency department in August for evaluation of altered mental status. Three days previously he developed emesis, followed by a severe headache and low-grade fever. Over the next 2 days, he became progressively lethargic. On the day of the emergency department visit, he has had a fever of up to 40°C and altered mental status. His speech is not comprehensible and he is combative. He has a temperature of 38.9°C, heart rate of 110 beats/min, respiratory rate of 28 breaths/min, and blood pressure of 125/68 mm Hg. He is confused and has meningismus but no focal neurologic findings. Laboratory data shows:

Laboratory Test	Result
Serum	
White blood cell count	18,640/µL (18.6 x 10^9/L)
Hemoglobin	11.7 g/dL (117 g/L)
Platelet Count	240 x 10^3/µL (240 x 10^9/L)
Neutrophils	95.2%
Bands	1.6%
Lymphocytes	2.4%
Monocytes	0.8%
Cerebrospinal Fluid	
White blood cell count	763/µL
Neutrophils	32%
Lymphocytes	48%
Monocytes	20%
Red blood cell count	6/µL
Glucose	62 mg/dL
Protein	65 mg/dL

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

- A.   acyclovir
- B.   cidofovir
- C.   ganciclovir
- D.   oseltamivir
- E.   ribavirin

Correct Answer: A

The best next step in management for the patient in this vignette is to start acyclovir. The majority of cases of encephalitis with an identified etiology are viral in origin. Herpes simplex infections should be treated empirically until ruled out with directed testing.

While acute encephalitis is commonly linked to infections, encephalitis can have other etiologies including para-infectious processes (such as acute disseminated encephalomyelitis and acute cerebellar ataxia) and noninfectious causes including autoimmune and paraneoplastic disorders.

Clinical findings associated with encephalitis can include altered mental status, seizures, weakness, and focal neurologic findings. Fever and signs of meningeal irritation are variably present. The diagnostic evaluation of encephalitis includes lumbar puncture for cerebrospinal fluid analysis and directed testing for pathogens of concern. Cerebrospinal fluid pleocytosis is not universally present in the setting of encephalitis but can range from mild to moderate and is usually lymphocytic in origin. Elevated levels of cerebrospinal fluid protein can be observed. Diagnostic imaging is indicated, and the preferred imaging modality is contrasted magnetic resonance imaging of the brain. Electroencephalography must be considered given the possibility of subclinical seizures. Other diagnostic evaluations depend on the etiology being considered.

The management of encephalitis consists principally of supportive care. Patients may demonstrate hemodynamic instability, signs of increased intracranial pressure, or both; such patients should be treated and managed in intensive care units. Seizures should be treated with anticonvulsants. Parainfectious causes have been treated with corticosteroids, intravenous immunoglobulin, and plasmapheresis.

Antimicrobials are available for a variety of organisms that cause infection-related encephalitis, including viral, fungal, and parasitic organisms. Antivirals other than acyclovir can be considered in select scenarios but are not typically considered as empiric treatment in immunocompetent individuals such as the adolescent in this vignette. Cidofovir can be used for cytomegalovirus retinitis and adenovirus. Ganciclovir is the treatment of choice for cytomegalovirus. Oseltamivir could be considered in acute encephalitis caused by influenza. Ribavirin can be considered in severe respiratory syncytial virus infections and viral hemorrhagic fevers.

PREP Pearls
- Clinical findings associated with encephalitis can include altered mental status, seizures, weakness, and focal neurologic findings. Fever and signs of meningeal irritation are variably present.
- The diagnostic evaluation of encephalitis includes lumbar puncture for cerebrospinal fluid analysis, diagnostic imaging (preferably contrasted brain magnetic resonance imaging), and electroencephalography.
- The management of encephalitis consists of supportive care, treatment of seizures with anticonvulsants, and depending on the etiology, antimicrobials.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of encephalitis
- Recognize the clinical findings associated with encephalitis of various causes
- Plan the appropriate management of encephalitis

Suggested Readings
- Falchek S. Encephalitis in the pediatric population. *Pediatr Rev.* 2012;33(3):122–132. doi: http://dx.doi.org/10.1542/pir.33-3-122.
- Tunkel A, Glaser C, Bloch K, et al. The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis.* 2008;47(3):302–327. doi: http://dx.doi.org/10.1086/589747.

Question 41

A 15-year-old adolescent girl is seen in your office for her routine health supervision visit. Her mother reports no concerns, other than her daughter's tendency to be moody and withdrawn, which the family attributes to being a teenager. During the confidential psychosocial interview, the patient reports that she often feels sad. Upon further questioning about her home environment, she tells you that she lives with her mother, stepfather, and younger stepsister. She rarely sees her biological father. Although her stepfather has been present in the home since she was 3 years of age, he is not very involved with her. He often spends time with her stepsister, but leaves her out. He never buys her gifts and has refused to pay for essential items, such as clothing and hygiene products. She hears him state that her own father should be paying for these items. She feels he disciplines her more harshly than her stepsister and reports that he has called her names, but he has never physically harmed her or threatened to injure her.

Of the following, the MOST appropriate management plan is to

       A. acknowledge that differential treatment by the nonbiological parent is understandable and not harmful
       B. agree to keep the patient's conversation confidential and re-evaluate at her next visit
       C. encourage the patient to seek alternative living arrangements
       D. reassure the mother that emotional lability and the desire to spend time alone is typical of teenagers
       E. recommend individual and family counseling

Correct Answer: E

The teenager in this vignette is the victim of psychological or emotional abuse. Individual and family counseling is needed to minimize the negative impact on the girl and to hopefully improve the relationships within the family.

Child maltreatment includes physical abuse, sexual abuse, emotional abuse, and neglect of an individual younger than 18 years by a parent or other custodial caregiver. Physical abuse is the intentional use of physical force, such as hitting, kicking, choking, shaking, and burning. Sexual abuse includes fondling and any other form of sexual activity with a child. Emotional or psychological abuse/maltreatment refers to any behavior that negatively affects one's feelings of self-worth or emotional well-being. Neglect is the failure to have one's basic needs met for shelter, food, clothing, education, and health care.

Psychological maltreatment is the most prevalent form of abuse, yet it is often difficult to identify because it is hidden. Patients and families may rationalize or minimize the abusive behaviors. Often the maladaptive behaviors of the victim, such as the moodiness, sadness, and desire to withdraw, as seen in the girl in this vignette, are mischaracterized as the child's fault or misperceived as related to the child's temperament rather than understood to be a consequence of abuse. Caregiver behaviors that constitute maltreatment of the girl in this vignette are her biological father's abandonment and her stepfather's passive detachment, unresponsiveness, active omission from father-daughter relationships, commission of verbal belittling and name-calling, and refusal to provide for essential needs. This differential treatment is psychologically harmful and requires the physician to address the concern with the family in a sensitive and supportive manner on behalf of the teen. This discussion should occur at the time of the visit. Simply offering reassurance and re-evaluation is not appropriate. In some cases, seeking alternative living arrangements may be in the best interest of the patient, but it would not be the first step in management.

All forms of child maltreatment can negatively affect the cognitive, social, emotional, and physical development of the abused individual. The impact of psychological maltreatment in early childhood is particularly profound; it interferes with the development of secure attachments and healthy peer and intimate relationships. Adults who were abused as children are at greater risk of addiction (alcohol, drugs, or tobacco), mental health problems (including suicide and eating disorders), high-risk sexual behaviors, and other chronic conditions and diseases.

PREP Pearls
- Child maltreatment includes physical abuse, sexual abuse, emotional abuse, and neglect of an individual younger than 18 years by a parent or other custodial caregiver.
- Emotional or psychological abuse/maltreatment refers to any behavior that negatively affects one's feelings of self-worth or emotional well-being.
- Psychological abuse/maltreatment, the most prevalent form of abuse, is difficult to identify and is often under-reported.

- The impact of psychological abuse/maltreatment in early childhood is particularly profound; it interferes with the development of secure attachments and healthy relationships and increases the risk of some chronic conditions in adulthood.

ABP Content Specifications(s)
- Recognize the history, signs, and symptoms indicative of psychological abuse
- Understand the behavioral and emotional consequences of psychological abuse

Suggested Readings
- Hibbard R, Barlow J, MacMillan H; Committee on Child Abuse and Neglect and American Academy of Child and Adolescent Psychiatry, Child Maltreatment and Violence Committee. Psychological maltreatment. *Pediatrics*. 2012;130(2):372–378. doi: http://dx.doi.org/10.1542/peds.2012-1552.
- National Center for Injury Prevention and Control Division of Violence Prevention. Understanding child maltreatment.
2016. https://www.cdc.gov/violenceprevention/pdf/understanding-cm-factsheet.pdf.

Question 42

An 18-month-old girl is brought to the emergency department because of a 2-day history of fever and vomiting. She has a fever (40.1°C) and is mildly dehydrated. Results of a spot urine test strip analysis are shown:

Laboratory Test	Result
pH	7.0
Specific gravity	1.030
Leukocyte esterase	3+
Nitrites	2+
Blood, protein	Negative

You suspect a urinary tract infection as the cause of the patient's symptoms.

Of the following, the MOST appropriate statement regarding the diagnosis and treatment of this patient is

    A. all urinary tract infections must be treated with parenteral antibiotics
    B. bag urine specimens are not valid for the diagnosis of urinary tract infection
    C. minimum duration of treatment for urinary tract infection is 3 days
    D. positive results on either urinalysis or urine culture can establish urinary tract infection diagnosis
    E. renal ultrasonography should not be performed routinely after the first febrile urinary tract infection

Correct Answer: B

The American Academy of Pediatrics has recently published guidelines for the diagnosis and management of initial urinary tract infections (UTIs) in febrile infants and young children (2-24 months old). A properly collected urine specimen for analysis and culture prior to starting antibiotics is paramount to diagnosing and treating UTI. A urine specimen should be collected by catheterization or suprapubic aspiration (SPA) and sent for urinalysis and culture before an antibiotic is started in a febrile infant or young child with no apparent source of infection. Urine specimens collected for culture by catheterization have a sensitivity of 95% and a specificity of 99% for diagnosing UTI. Suprapubic aspiration has limited risks, but it requires expertise and experience; the successful collection rates range from 23% to 90%. Ultrasonographic guidance increases the successful collection rates of SPA. In boys with severe phimosis or girls with tight labial adhesions, SPA is preferred.

Urine culture of specimens collected by a bag applied to the perineum have an unacceptably high false-positive rate (88%) and provide clinically relevant information only when they yield negative results. For bagged urine specimens from febrile boys, the rate of false-positive results is 95% in uncircumcised boys and 99% for circumcised boys. In view of the extremely high false-positive rate, antimicrobial therapy should not be initiated based on positive urinalysis results from bagged urine specimens.

Urinalysis results that suggest infection (pyuria, bacteriuria, or both) and urine culture showing the presence of at least 50,000 colony-forming units of uropathogen per milliliter of an appropriately collected urine specimen (obtained through catheterization or SPA) are both required for confirming the diagnosis of a UTI. Urine test strip analysis cannot substitute for urine culture to document the presence of a UTI; rather, the urine test strip analysis should be used in conjunction with culture. Because urine culture results are not immediately available, a urine test strip analysis suggestive of a UTI helps in presumptively treating a patient at initial presentation. To ensure sensitivity and specificity of the urinalysis, specimens kept at room temperature must be tested within 1 hour after voiding, and specimens kept refrigerated must be tested within 4 hours after voiding. Identification of leukocyte esterase (a marker of pyuria or white blood cells in urine) and nitrites on urine test strip as well as urine microscopic examination for white blood cells and bacteria are used for diagnosing UTIs. A positive result for leukocyte esterase, nitrites, and urine microscopy has the highest sensitivity (99.8%) for diagnosing UTI, followed by leucocyte esterase and nitrites (93%) and leucocyte esterase only (83%).

Adequate treatment of UTI is important in preventing the spread of infection and renal scarring. Oral or parenteral treatment of UTI is equally efficacious, and 7 to 14 days of antimicrobial therapy is recommended. According to the guidelines from the American Academy of Pediatrics, current evidence suggests that a shorter duration of UTI treatment (up to 3 days) is inferior to treatment regimens of 7 to 14 days. Parenteral therapy is preferred in sick patients with poor oral intake or in patients for which there are compliance concerns regarding oral therapy. Initial parenteral therapy is switched to oral treatment with improvement in oral intake; this improvement usually occurs after 24 to 48 hours of parenteral therapy. *Escherichia coli* is the

most common cause of community-acquired UTIs. Third-generation cephalosporins (cefotaxime, ceftriaxone) and aminoglycosides (gentamicin) are appropriate first-line agents for empiric treatment of UTI in children. Cephalosporin, amoxicillin plus clavulanic acid, or trimethoprim-sulfamethoxazole are preferred oral antibiotics for treatment of UTI.

According to the current guidelines, renal bladder ultrasonography is recommended for febrile infants with UTI. Renal bladder ultrasonography is indicated to detect anatomic abnormalities requiring further evaluation, to evaluate the renal parenchyma, and to assess kidney size. The guidelines acknowledge the overall low yield of renal ultrasonography as compared to routine prenatal ultrasound in identifying congenital anomalies of the kidney and urinary tract.

PREP Pearls
- Antimicrobial therapy should not be initiated in infants with suspected urinary tract infections based on positive urinalysis results from bagged urine specimens because of extremely high false-positive rates.
- Catheterization or suprapubic aspiration is the proper technique for collecting urine specimens in infants with suspected urinary tract infections.
- Oral or parenteral treatment of urinary tract infections is equally efficacious, and 7 to 14 days of antimicrobial therapy is recommended.
- Renal bladder ultrasonography is recommended for febrile infants with urinary tract infections.

ABP Content Specifications(s)
- Recognize the clinical findings associated with urinary tract infection in children of various ages
- Understand the natural history of urinary tract infection
- Plan the appropriate prophylaxis for urinary tract infection

Suggested Readings
- American Academic of Pediatrics, 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/10.1542/peds.2011-1330.
- 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.

Question 43

A 7-year-old girl presents to your office for a new patient health supervision visit. She immigrated from Africa 1 week before the visit. She and her family have refugee status and are being resettled by a local agency. Through an interpreter, her mother states that "the girl cannot walk right," and describes progressive difficulty with ambulating that began about 3 years ago, around the time the family fled their home country and settled in a refugee camp in a neighboring country. The girl had several infections while in the refugee camp, mostly self-resolving gastrointestinal illnesses. She denies any recent fevers, rashes, vomiting, or trauma. Her mother states that the girl received some immunizations, including vaccines to prevent polio. Her diet in the refugee camp was limited to mostly gruel, with rare vegetables. The patient's sister has a seizure disorder and developmental delay, and receives a daily medication, but her mother is not sure of the name.

On physical examination, the girl's weight is at the 30th percentile and her height is at the 5th percentile. Her neurologic examination shows normal eye movements with no nystagmus. She has dysmetria and hyporeflexia, poor balance, and great difficulty standing with feet together and her eyes closed. Her gait is wide and she walks unsteadily with a stomping motion. The remainder of the physical examination findings are normal.

Of the following, the test MOST likely to reveal the cause of this child's neurologic problems is a

  A. computed tomography of the head
  B. phenytoin level
  C. serum alpha-fetoprotein level
  D. varicella titer
  E. vitamin E level

Correct Answer: E

The child in the vignette presents with ataxia that has progressively worsened over 3 years, during which time she had a poor diet and limited access to health services. Based on the history and her physical examination, the girl most likely has vitamin E deficiency; therefore, a vitamin E level would be most likely to reveal the cause of her neurologic problems. Other signs and symptoms of vitamin E deficiency include hyporeflexia, abnormal vibratory sensation and proprioception, limitation of eye movement, and muscle weakness.

Ataxia is characterized by a wide-based, swaying gait. There are many causes of ataxia in children; most cases present acutely, with rapid onset of symptoms. The most common cause is acute cerebellar ataxia, a syndrome thought to be associated with recent viral infection, particularly varicella. Other causes of acute ataxia include toxic ingestions (eg, alcohol, benzodiazepines, anticonvulsants), acute infections (eg, viral encephalitis), postinfectious (eg, acute cerebellitis), brain mass, or stroke. Some metabolic neurodegenerative conditions (eg, maple syrup urine disease) exhibit an intermittent ataxia. More progressive ataxias are often the result of inherited conditions (eg, Friedreich ataxia, ataxia-telangiectasia [AT]). Vitamin E deficiency can lead to progressive ataxia. This deficiency usually results from malabsorption or a mutation in the alpha-tocopherol transfer protein gene; it is rarely caused by poor diet. Ataxia from vitamin E deficiency can be treated with the administration of large doses of vitamin E, or by addressing the reason for the malabsorption. Many other causes of progressive ataxia do not have available treatments.

All cases of ataxia warrant a diagnostic evaluation. Acute cases should be evaluated emergently, beginning with a careful history and physical examination. Although acute cerebellar ataxia is the most common cause, it is a diagnosis of exclusion that can be made if tests reveal no more serious and treatable causes. It is self-resolving. Computed tomography of the head can identify brain tumors, and is indicated in patients also presenting with focal neurologic findings, altered consciousness, or new-onset headaches. Toxicology screening tests and drug level measurement can detect ingestions or excessive doses of medications. The cerebrospinal fluid should be evaluated in patients presenting with fever, meningismus, seizures, or altered sensorium to identify meningitis, cerebellitis, or encephalitis. Neuroblastoma can present with ataxia; if suspected, especially in patients with opsoclonus-myoclonus, urine catecholamines should be measured.

Cases presenting with intermittent or progressive ataxia warrant evaluation by a neurologist, but are typically caused by genetic conditions, including mitochondrial disorders or enzymatic defects. Among these, Friedreich ataxia is the most common, typically presenting in adolescence with progressive ataxia in all extremities, diminished tendon reflexes, and lower extremity weakness. It is diagnosed clinically and confirmed with genetic testing. AT presents earlier, typically in toddlerhood, often with abnormal eye movements and oculocutaneous telangiectasias. AT is associated with an elevated serum alpha-fetoprotein level. The diagnosis can be confirmed with genetic testing. The girl in the vignette does not have typical eye and skin findings of AT, making vitamin E deficiency, although rare, more likely in her case. It is

important to investigate this cause of progressive ataxia, because treatment with vitamin E can slow the progression of neurologic symptoms associated with the disorder.

PREP Pearls
- Acute presentation of ataxia warrants an urgent evaluation for a brain mass or cerebrospinal fluid infection.
- Vitamin E deficiency is a rare but treatable cause of chronic, progressive ataxia.
- Signs and symptoms of vitamin E deficiency may include hyporeflexia, ataxia, decreased vibratory sensation and proprioception, muscle weakness, and limitation of eye movement.
-

ABP Content Specifications(s)
- Recognize the signs, symptoms, and causes of vitamin E deficiency, and manage appropriately

Suggested Readings
- Dinolfo, EA. Evaluation of ataxia. *Pediatr Rev*. 2001;22(5):177–178. doi: http://dx.doi.org/10.1542/pir.22-5-177.
- Schuelke M. Ataxia with vitamin E deficiency. *GeneReviews*. http://www.ncbi.nlm.nih.gov/books/NBK1241/. Updated October 13, 2016.

Question 44

A couple brings their 3 children to your office to establish care after moving into the area. They have a healthy 10-year-old boy and a healthy 6-year-old girl who have unremarkable medical histories with normal growth and development. Their third child is a 3-year-old boy whose medical history is remarkable for multiple episodes of otitis media for the last 2 years and 2 episodes of pneumonia, one of which resulted in hospitalization for treatment with parenteral antibiotics. His parents report that he often has oily, foul-smelling stools, although his diet is similar to that of his siblings who have normal stools.

His temperature is 37.1°C, heart rate is 90 beats/min, and blood pressure is 98/60 mm Hg. He is below the third percentile for both weight and height. His lungs are clear bilaterally, and he is not in respiratory distress. His heart examination results are normal, and there is no hepatosplenomegaly.

You obtain complete blood cell counts for the 3 children. The first 2 children have normal results. The third child's complete blood cell count results are shown:

Laboratory Test	Result
White blood cell count	900/µL (0.90 × 10^9/L)
Hemoglobin	10.1 g/dL (101 g/L)
Platelet count	257 x 10^3/µL (257 × 10^9/L)
Mean corpuscular volume	78 fL
Neutrophils	20%
Lymphocytes	75%
Monocytes	5%

Given the historical and laboratory findings, the third child is MOST likely to also have

 A. bilateral absent radii
 B. frontal bossing
 C. a horseshoe kidney
 D. rib cage abnormalities
 E. a transverse palmar crease

Correct Answer: D

The child in this vignette has a history of significant invasive bacterial infections, failure to thrive, and moderate neutropenia. This combination raises concern for a congenital neutropenia syndrome.

Each of the congenital neutropenia syndromes has a unique phenotype, and most of these syndromes are associated with other congenital anomalies in addition to neutropenia. The phenotypes and associations of the most prominent of these syndromes include (but are not restricted to):

- Barth syndrome: cardiomyopathy and proximal skeletal myopathy
- Cartilage-hair hypoplasia:short-limbed dwarfism, fine hair, and impaired immunity
- Chédiak-Higashi syndrome: varying degrees of oculocutaneous albinism
- Dyskeratosis congenita: abnormal skin pigmentation, nail dystrophy, and leukoplakia of the oral mucosa
- Fanconi anemia: many possible congenital abnormalities with highly variable severity
- Shwachman-Diamond syndrome (SDS): failure to thrive, exocrine pancreatic dysfunction, and skeletal abnormalities
- Severe congenital neutropenia: Neutropenia is often the only presenting sign. Severe congenital neutropenia is diagnosed by genetic testing of *ELANE* (the neutrophil elastase gene) on 19p13.3 or *HAX1* on 1q21.3.

The constellation of findings for the boy in this vignette combined with malabsorption and chronic, loose, oily stools are most consistent with SDS, an autosomal recessive disorder caused by a mutation in *SBDS* at locus 7q11. The incidence of SDS is 1 in 75,000 people. The 2 most prominent features of SDS are hematologic abnormalities and exocrine pancreatic dysfunction. Neutropenia is the most common hematologic abnormality associated with SDS, but SDS can present with anemia or thrombocytopenia. More than half of the individuals with SDS are below the third percentile for height. The growth failure is only partially related to malnutrition, and it is likely part of the phenotypic presentation of the genetic lesion. Skeletal abnormalities are common and include metaphyseal dysostosis, thoracic dystrophy with rib cage abnormalities, and costochondral thickening. Hematopoietic stem cell transplant can cure the hematologic abnormalities of SDS but does not improve the remainder of the disease phenotype.

Horseshoe kidneys and absent radii are not associated with SDS, but both occur in thrombocytopenia–absent radius syndrome, which is characterized by severe thrombocytopenia and bleeding but not neutropenia. A transverse palmar crease is not associated with a specific bone marrow failure syndrome, but it occurs in 50% of individuals with trisomy 21, which carries an increased risk for leukemia. Frontal bossing is a deformation of the skull that is caused by stress erythropoiesis in thalassemia.

PREP Pearls
- Shwachman-Diamond syndrome most commonly presents with exocrine pancreatic insufficiency and hematologic abnormalities.
- Shwachman-Diamond syndrome is associated with failure to thrive and skeletal abnormalities.
- Although most congenital neutropenia syndromes are associated with other congenital anomalies, severe congenital neutropenia often presents with isolated neutropenia and is diagnosed through genetic analysis of *ELANE* and *HAX1*.

ABP Content Specifications(s)
- Recognize clinical findings associated with neutropenia
- Plan the appropriate laboratory evaluation of neutropenia, and interpret the results
- Recognize the variable presentation of congenital neutropenia, and manage appropriately
- Recognize aspects of a patient's medical history that may suggest quantitative or qualitative leukocyte disorders

Suggested Readings
- Chirnomas SD, Kupfer GM. The inherited bone marrow failure syndromes. *Pediatr Clin North Am.* 2013;60(6):1291–1310. doi: http://dx.doi.org/10.1016/j.pcl.2013.09.007.
- Myers KC, Davies SM, Shimamura A. Clinical and molecular pathophysiology of Shwachman-Diamond syndrome: an update. *Hematol Oncol Clin North Am.* 2013;27(1):117–128. doi: http://dx.doi.org/10.1016/j.hoc.2012.10.003.
- Walkovich K, Boxer LA. How to approach neutropenia in childhood. *Pediatr Rev.* 2013;34(4):173–184. doi: http://dx.doi.org/10.1542/pir.34-4-173.

Question 45

A 6-week-old infant is brought to your office by her parents. They report that the infant had blueness around the mouth after a period of coughing. Rescue breaths were not required and emergency medical services were not activated. The infant is now alert and pink without labored breathing. She has a 1-week history of clear rhinorrhea and poor feeding. Her father has a cough, which is dry and spasmodic in nature.

The infant appears well and is not in acute distress. An intermittent dry cough is noted. Her respiratory rate is 30 breaths/min, and her lungs are clear bilaterally with good aeration. There is no wheezing or focal auscultatory finding. Cardiac rhythm is regular without murmur. Her abdomen is soft and nontender. Her extremities are warm and well perfused.

Of the following, the MOST sensitive test to confirm the diagnosis is

  A. chest radiography
  B. complete blood cell count
  C. culture from nasopharyngeal swab
  D. polymerase chain reaction from nasopharyngeal swab
  E. serologic testing

Correct Answer: D

The infant in this vignette who has a dry, spasmodic cough with related episodes of circumoral cyanosis, is likely to have pertussis or "whooping cough." The most sensitive diagnostic test to confirm this diagnosis is the polymerase chain reaction assay. This test is rapid and sensitive. Pertussis is caused almost exclusively by *Bordetella pertussis*, a gram-negative coccobacillus. Less frequently, *Bordetella parapertussis* infection may be responsible for a pertussis-like illness. The bacteria is transmitted by droplet spread. Individuals can be infected at any age but the highest risk for disease-associated morbidity and mortality occurs in infants younger than 3 months.

Although the frequency of pertussis cases declined sharply after development and introduction of the whole-cell vaccination in the 1940s, a resurgence of the disease has been attributed to more accurate diagnostic methods, transmission to susceptible unvaccinated infants from incompletely vaccinated parents or caregivers, and less robust and waning immunity from newer acellular vaccination types. Vaccination refusal continues to be an additional factor. Updated vaccination guidelines have addressed some of these issues, including routine vaccination of pregnant mothers in the third trimester of each pregnancy and the recommendation for booster immunization of pre-adolescents in whom waning immunity has been demonstrated.

The incubation period for pertussis is 7 to 10 days (range, 5-21 days). The clinical disease manifestations of pertussis are variable but the classic progression of the disease includes early, mild upper respiratory symptoms (catarrhal stage, approximately 5-7 days), progressing to cough, which may be characterized by paroxysmal episodes. In this paroxysmal stage (approximately 7-10 days), there may be a post-tussive inspiratory noise classically identified by its "whooping" sound, and post-tussive emesis may be a prominent feature for many infants and children. Symptoms then gradually wane and resolve over a period of weeks to months. The duration of pertussis is typically 6 to 10 weeks, but as many as half of adolescents with pertussis will cough for more than 10 weeks. During this time, they are at risk for rib fractures, pneumonia, sleep disturbance, and missed educational opportunities. In young infants, the disease may be atypical and severe with apnea, bradycardia, hypoxemia, hemorrhage, and sudden infant death as additional potential complications.

Diagnostic approaches to the confirmation of pertussis infection have evolved. Clinical diagnosis is problematic because the identification of the disease may occur after a cough that was initially attributed to a viral illness fails to resolve as expected. The elapsed time may allow preventable transmission of the disease to susceptible individuals. As a result, a high index of suspicion and early confirmation and treatment of disease with appropriate and targeted therapies are imperative. The traditional approach to diagnosis was with a bacterial culture from nasopharyngeal secretions. Growth of the bacteria is slow, and the sensitivity of culture is low. Culture-based diagnosis has largely been replaced by polymerase chain reaction testing, which is the most appropriate diagnostic tool in the earliest stages of the disease (weeks 1-2) and is favored because of its ability to provide rapid and highly sensitive results. Direct fluorescent antibody testing is no longer recommended. Serologic testing may be beneficial later in the

illness and in older adolescents and adults. However, no commercial serologic test is currently supported by the US Food and Drug Administration as a diagnostic tool.
Although an increase in the white blood cell count and lymphocytosis are suggestive of pertussis in infants and young children, these findings are nonspecific and cannot confirm pertussis infection.

Early identification of pertussis allows directed antimicrobial treatment. When administered during the catarrhal stage of disease, antibiotics may lessen disease burden. After the cough of pertussis is established (paroxysmal stage or later), antibiotics will not be expected to have an impact on disease course but are recommended to prevent the transmission of illness to other contacts. A 5-day course of azithromycin is recommended for both treatment and postexposure prophylaxis. Shorter durations of therapy are not recommended. Azithromycin should be used with caution in individuals with prolonged QT syndromes. In addition, infantile hypertrophic pyloric stenosis has been reported in infants younger than 1 month treated with erythromycin or azithromycin. Azithromycin should only be used in this age group if the risk of severe pertussis and life-threatening complications outweighs the risk of infantile hypertrophic pyloric stenosis. If treatment is required, surveillance for symptoms of developing infantile hypertrophic pyloric stenosis is needed for at least 1 month after completion of therapy.

PREP Pearls
- Pertussis may have an atypical presentation and may be severe and life threatening in infants less than 3 months of age.
- The most sensitive diagnostic tool for pertussis is the polymerase chain reaction, but the efficacy of testing is highest in the first 2 weeks of illness.
- A 5-day course of azithromycin is recommended for the treatment of pertussis and for postexposure prophylaxis.
-

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of a patient in whom pertussis is suspected
- Plan the appropriate management of pertussis in its various stages, including treatment for contacts of infected patients

Suggested Readings
- Centers for Disease Control and Prevention. Updated recommendations for the use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. *MMWR Morb Mortal Wkly Rep*. 2011;60(1):13–15.
- Heininger U. Pertussis: what the pediatric infectious disease specialist should know. *Pediatr Infect Dis J.* 2012;31(1):78–79. doi: http://dx.doi.org/10.1097/INF.0b013e31823b034e.
- Jakinovich A, Sood SK. Pertussis: still a cause of death, seven decades into vaccination. *Curr Opin Pediatr.* 2014;26(5):597–604. doi: http://dx.doi.org/10.1097/MOP.0000000000000139.

Question 46

A 3-year-old boy is brought to the emergency department from his daycare center by emergency medical services. The daycare center staff had found him unconscious in his wheelchair. They have been unable to reach his parents. On physical examination, the boy's blood pressure is 124/80 mm Hg, his heart rate is 108 beats/min, respiratory rate is 20 breaths/min, and his temperature is 36.2°C. He is nonresponsive. His pupils are 3 mm and minimally reactive. He has diffuse spasticity in his limbs, with contractures in his elbows and knees. There are no contusions, soft tissue swelling, or other signs of injury. On examination of the head, shunt tubing is palpable under the scalp in the left occipital parietal area. Computed tomography of the head without contrast is performed (Item Q46).

Item Q46: Computed tomography of the brain without contrast for the child described in the vignette.
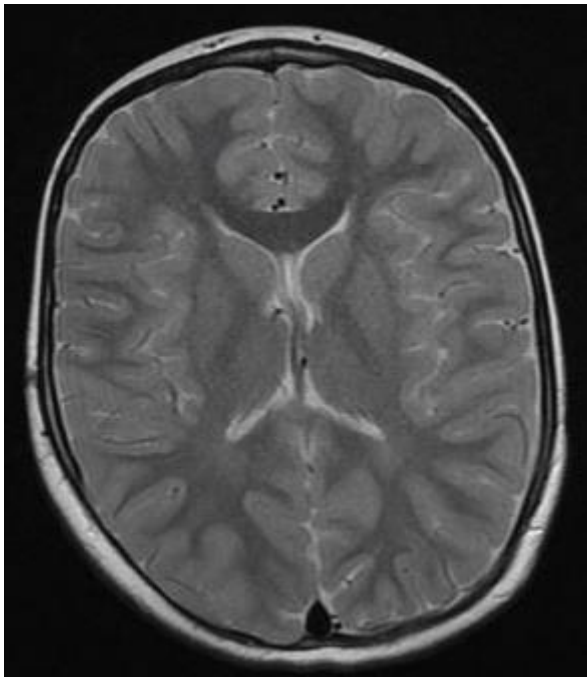
Courtesy of D. Morita

Of the following, the MOST likely cause for unconsciousness in this boy is

  A. cerebral edema
  B. encephalitis
  C. hypertensive encephalopathy
  D. shunt malfunction
  E. traumatic brain injury

Correct Answer: D

The boy in the vignette has acute hydrocephalus, most likely due to a ventriculoperitoneal shunt malfunction. Although all of the conditions in the available responses can cause loss of consciousness, acute hydrocephalus is most consistent with the boy's presentation and computed tomography (CT) results. The CT image in the vignette shows a portion of a shunt catheter, markedly dilated lateral ventricles with rounded horns, and effacement of the sulci. These findings are most suggestive of acute hydrocephalus caused by rapid accumulation of cerebrospinal fluid (CSF) in the ventricular system. This can be differentiated from chronic hydrocephalus, in which case, the ventricular horns are usually not rounded and the sulci are visible. In diffuse cerebral edema, the sulci can be effaced but the ventricles would not be enlarged. Of the other responses, encephalitis is unlikely because he does not have a fever. Hypertensive encephalopathy is unlikely because it does not cause acute hydrocephalus. Traumatic brain injury can present without imaging abnormalities in mild cases; in severe cases, imaging can show evidence of skull fracture or intracranial hemorrhage.

Shunt malfunction occurs when there is a disruption in the flow of CSF anywhere along the shunt pathway. This can be due to mechanical failure or shunt infection. Mechanical failure is the most common cause, and usually occurs within the first year after shunt placement. Causes of mechanical failure include the tip of the ventricular catheter coming to lie against the choroid plexus or the walls of the ventricle, causing the drainage holes to become blocked; fracture of the shunt tubing anywhere along its course; shunt migration; or CSF over drainage. In the case of CSF over drainage, imaging may show slit like ventricles (**Item C46**). Shunt infections also may cause shunt malfunction, usually within the first 6 months after shunt placement.

Item C46: Axial T2 weighted magnetic resonance image of the brain showing 'slit-like ventricles'. Courtesy of D. Morita

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Symptoms of mechanical shunt malfunction can be subtle, such as isolated altered mental status, or there may be overt signs of acute hydrocephalus such as headache, vomiting, seizures, spasticity, and abnormal eye movements. CSF over drainage causes intermittent headaches that improve with lying down. Presenting signs and symptoms of shunt infection include fever, along with various signs of shunt malfunction.

The diagnosis of shunt malfunction is usually made based on imaging studies. When a shunt is functioning appropriately, ventricle size is typically normal or relatively unchanged compared with previous imaging. It is best to review previous images to compare ventricular size and morphology when evaluating a child for shunt malfunction. Shunt malfunction is a neurosurgical emergency, thus, whenever shunt malfunction is suspected, the patient should be sent immediately to the emergency department.

PREP Pearls
- Symptoms of shunt malfunction can be subtle, such as isolated altered mental status, or there can be overt signs of acute hydrocephalus such as headache, vomiting, seizures, spasticity, and abnormal eye movements.
- Shunt malfunction can be due to blocked cerebrospinal fluid (CSF) drainage or due to CSF over drainage.

ABP Content Specifications(s)
- Recognize the clinical findings associated with shunt malfunction or infection in a patient with hydrocephalus and manage appropriately
- Recognize the clinical findings associated with hydrocephalus

Suggested Readings
- Kim TY, Stewart G, Voth M, Moynihan JA, Brown L. Signs and symptoms of cerebrospinal fluid shunt malfunction in the pediatric emergency department. *Pediatr Emerg Care*. 2006;22(1):28–34.
- Patra KP, Lancaster JD, Hogg J, Carpenter JS. Pediatric MRI of the brain: a primer. *Pediatr Rev*. 2014;35(3)106–113. doi: http://dx.doi.org/10.1542/pir.35-3-106.

Question 47

A 13-year-old adolescent boy with Duchenne muscular dystrophy, who is cared for in your practice, was recently hospitalized due to newly symptomatic cardiomyopathy. He is currently stable with medical management and frequent cardiology follow-up. Yesterday he told his older sister that he does not want to undergo procedures and blood tests if he is not going to get better. His parents, however, desire that all available medical care be provided. The family seeks guidance regarding adolescents and personal medical decision making.

Of the following, the MOST appropriate recommendation for this family is to

A. apply for a mature minor exception available through most state court systems
B. delay discussion of end-of-life decisions until the boy's death is imminent
C. participate in a structured interview to promote family agreement about the boy's medical decisions
D. permit the boy to assent/dissent for each medical procedure and treatment
E. permit the boy to have input into his own end-of-life decisions starting at age 16 years

Correct Answer: C

Shared medical decision making is an important component of patient and family-centered care and a key concept of the medical home. The best approach for this family would be to begin open communication early and to participate in a structured process using available resources and tools to promote family agreement about the boy's medical decisions.

This approach is supported by evidence from a study of chronically ill adolescents infected with the human immunodeficiency virus (HIV). The HIV-infected adolescents in this study reported a preference for initiating conversations about their wishes earlier, rather than later, in the course of their life-threatening illness. Electronic media-based tools may be particularly useful in helping some children understand and express their preferences. Based on the results of this study, the adolescent in the vignette would likely benefit from a structured or semi structured interview approach to elicit his preferences, inform him and his family about end-of-life decisions, improve communication, and increase agreement among all involved parties regarding medical decisions, particularly end-of-life care.

Shared medical decision making relies on the concept of autonomy, a major developmental task of adolescence. Many pediatricians believe that, beginning at age 12 to 13 years, children may be developmentally able to understand the consequences of their medical decisions and so should be involved in making them. There is no uniform age at which all children are ready to participate in their medical decisions, such as 16 years. Rather than using age as the determining factor for involving a child in decision making, it is critical to evaluate each individual child's understanding of the information provided and ability to recognize the consequences of his/her decisions.

Although parents or their surrogates are required to give informed permission for medical care, children who are capable should be given the right to assent. However, the limits of assent must be made clear to the child. If a treatment or procedure will proceed despite his/her objection, efforts should be made to help the child to understand what will happen and why, and that the procedure will occur despite his/her objection. It is not practical or even safe to allow a child to overrule each and every medication, blood draw, or medical procedure in the course of treatment. Some ethicists have proposed a model of "constrained parental autonomy," in which parents make decisions, but their decision making is based on respect for the child and his/her perspective.

Most legal standards for consent are based on supporting individual rights of adults, including the right (and obligation) of parents to make decisions for their children. The legal and political support for underage adolescent medical decision making is highly variable. Many states give adolescents the right to consent to care in specialized circumstances, such as the provision of contraception, or the diagnosis and treatment of sexually transmitted infections, drug abuse, and/or mental illness. These rules are based on public health concerns that make this specific medical care a "compelling state interest." In the United States, only 10 states have "mature minor exceptions," granting minors the legal right to consent to general medical care. In states

that have a mature minor doctrine, the state often legislates a specific age at which the doctrine can take effect, ranging from 14 to 18 years of age.

Emancipated minors fall under a different regulation, which also varies by jurisdiction. A minor may be considered emancipated, and thus able to provide informed consent for medical care, if he/she is married, in the military, a parent, self-supporting while not living with parents, a high school graduate, or various other criteria.

PREP Pearls
- The "mature minor doctrine" is a developmental concept that many children, often beginning at age 12 to 13 years, may be able to understand the consequences of their medical decisions and so should be involved in making them.
- The legal standard for consent is based on the right of *adults* to provide consent for themselves or their children. In the United States, only 10 states have "mature minor exceptions," granting minors the legal right to consent to general medical care.
- An "emancipated minor" has the right to provide informed consent for medical care. The criteria vary by jurisdiction and may include marriage, military service, parenthood, being self-supporting while not living with parents, and high school graduation.
- Structured interviews and electronic media–based programs may help support communication and understanding between a child and his/her guardian regarding the child's desires about medical care.

ABP Content Specifications(s)
- Understand when it is appropriate to have a minor involved in making decisions about his or her medical care

Suggested Readings
- American Academy of Pediatrics, Committee on Bioethics. Informed consent, parental permission, and assent in pediatric practice. *Pediatrics*. 1995;95:314-317.
- Berlinger N, Barfield R, Fleischman AR. Facing persistent challenges in pediatric decision-making: new Hastings Center guidelines. *Pediatrics*. 2013;132:789-791. doi: http://dx.doi.org/10.1542/peds.2013-1378.
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- Lee KJ, Havens PL, et al. Assent for treatment: clinician knowledge, attitudes, and practice. *Pediatrics*. 2006;118:723-730. doi: http://dx.doi.org/10.1542/peds.2005-2830.
- Lyon ME, Garvie PA, McCarter R, Briggs L, He J, D'Angelo LJ. Who will speak for me? improving end-of life-decision-making for adolescents with HIV and their families. *Pediatrics*. 2009;123:e199-e206. doi: http://dx.doi.org/10.1542/peds.2008-2379.

Question 48

An 11-year-old boy recently adopted from an orphanage in Burma is brought to your office for a health supervision visit. The child reports no symptoms and is feeling well. No information is known about his biological parents. The results of his physical examination are normal. Laboratory data are shown:

Laboratory Test	Result
White blood cell count	8,000/µL (8.0 x 10^9/L)
Platelet count	185 x 10^3/µL (185 x10^9/L)
Absolute eosinophil count	3,720/µL (3.72 × 10^9/L) (normal, < 0.45× 10^9/L)
Hemoglobin	11.5 g/dL (115 g/L) (normal, 13.5-17.5 g/dL)
Human immunodeficiency virus	Negative

A purified protein derivative skin test for tuberculosis is negative. Three stool samples are negative for ova and parasites.

Of the following, the BEST next test to determine the cause of this child's eosinophilia is serology for

A. Chagas disease
B. hepatitis B virus
C. hydatid disease
D. Strongyloides stercoralis
E. Toxocara canis

Correct Answer: D

Each year, more than 12,000 children from Asia, Latin America, Eastern Europe, and Africa are adopted by parents in the United States. Infectious diseases are the most frequently diagnosed medical problem among immigrant children on arrival to the United States. The American Academy of Pediatrics has published guidelines related to providing care for immigrant children including initial medical evaluation and screening tests for infectious diseases. The guidelines also address immunizations, cultural adjustment, nutrition, growth and development, and psychosocial needs.

The recently immigrated boy from Burma described in this vignette is clinically asymptomatic but has eosinophilia defined as an absolute eosinophil count greater than 450 cells/µl. Stool test results were negative for ova and parasites. In such cases, serologic testing must be considered for tissue-invasive parasitic infections such as strongyloidiasis, schistosomiasis, and lymphatic filariasis. Irrespective of country of origin, all international adoptees and refugees coming to the United States with eosinophilia must undergo serologic testing for *Strongyloides stercoralis* after exclusion of common pathogens associated with eosinophilia. Serologic testing for *Schistosoma* species is recommended for children with eosinophilia immigrating from sub-Saharan Africa, Southeast Asia, or certain regions of Latin America after exclusion of common pathogens associated with eosinophilia. Likewise, serologic testing for lymphatic filariasis should be considered for children aged 2 years and older with eosinophilia immigrating from countries endemic for lymphatic filariasis. Immigrant children should also be screened for hepatitis B and C, syphilis, HIV types 1 and 2, and tuberculosis (**Item C48**).

Table C48. Infectious Diseases Screening Tests Recommended for International Adoptees, Refugees, and Immigrants.

- Hepatitis B virus serologic testing:
    – Hepatitis B surface antigen (HBsAg); the panel should be performed to include hepatitis B surface antibody (anti-HBs) and hepatitis B core antibody (anti-HBc)
- Hepatitis C virus serologic testing
- Syphilis serologic testing:
    – Nontreponemal test (eg, RPR, VDRL, or ART)
    – Treponemal test (eg, MHA-TP, FTA-ABS, EIA, CIA, or TPPA)
- Human immunodeficiency virus (HIV) 1 and 2 serologic testing
- Complete blood cell count with red blood cell indices and differential
- Stool examination for ova and parasites (3 specimens) with specific request for *Giardia intestinalis* and *Cryptosporidium* species testing
- Tuberculin skin test[b] or interferon-gamma release assay
- In children from countries with endemic infection:
    – *Trypanosoma cruzi* serologic testing
- In children with eosinophilia (absolute eosinophil count exceeding 450 cells/µL) and negative stool ova and parasite examinations:
    – *Strongyloides* species serologic testing
    – *Schistosoma* species serologic testing for children from sub-Saharan African, Southeast Asian, and certain Latin American countries
    – Lymphatic filariasis serologic testing for children older than 2 years from countries with endemic infection
- RPR indicates rapid plasma reagin; VDRL, Venereal Disease Research Laboratories; ART, automated reagin test; MHA-TP, microhemagglutination test for *Treponema pallidum*; FTA-ABS, fluorescent treponemal antibody absorption; EIA, enzyme immunoassay; CIA, chemiluminescence assay; TPPA, *T pallidum* particle agglutination.

Reprinted with permission from the American Academy of Pediatrics. Medical evaluation for infectious diseases for internationally adopted refugee, and immigrant children. 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; 2015:194-201.

Strongyloidiasis is an intestinal helminth infection that is endemic in Africa, Asia, areas of Latin America (Argentina, Ecuador, Venezuela, Peru, and Brazil), the Caribbean, and the southeast United States. Humans acquire infection after contact with contaminated soil. Following skin penetration, the infective filariform larvae migrate to the lungs via a hematogenous route, penetrate the alveoli, ascend the bronchial tree, and are then swallowed. After reaching the duodenum, the larvae mature into adult females that release eggs; the eggs hatch into first-stage larvae that are released in feces. The life cycle is maintained when first-stage larvae molt and develop into infective filariform larvae, which penetrate the intestinal mucosa and cause autoinfection. Autoinfection may persist for decades. Chronic infections with *S stercoralis* are usually asymptomatic but eosinophilia is frequently noted. The drug of choice for treating strongyloidiasis is usually ivermectin. However, immigrants from countries endemic for loiasis (a filarial infection caused by *Loa loa*) should be treated with albendazole because ivermectin treatment is associated with toxic encephalopathy in individuals with high blood concentrations of *L loa* microfilariae.

Chagas disease (American trypanosomiasis) is endemic in Latin America, and serologic testing for *Trypanosoma cruzi* should be considered in immigrant children from Chagas disease–endemic nations. Serologic testing for hepatitis B virus is recommended as part of the routine evaluation of internationally adopted or immigrant children but would not be the appropriate test to determine the cause of eosinophilia for the boy is this vignette. Eosinophilia may be noted in other tissue-invasive parasitic infections such as hydatid disease and toxocariasis; however, these infections are less common than intestinal helminth infections (or soil-transmitted helminth infections, such as ascariasis, trichuriasis, and hookworm infection) and schistosomiasis in internationally adopted and refugee children.

PREP Pearls
- All international adoptees and refugees coming to the United States with unexplained eosinophilia must undergo serologic testing for *Strongyloides stercoralis* after exclusion of common pathogens associated with eosinophilia.
- Serologic testing for Schistosoma species and lymphatic filariasis should be considered for children with eosinophilia immigrating from endemic countries after exclusion of common pathogens associated with eosinophilia.
- Immigrant children should also be screened for hepatitis B and C, syphilis, HIV types 1 and 2, and tuberculosis.

ABP Content Specifications(s)
- Plan the appropriate infectious disease screening evaluation of an internationally adopted child
- Plan the appropriate immunizations for an internationally adopted child

Suggested Readings

- American Academy of Pediatrics, Council on Community Pediatrics. Providing care for immigrant, migrant, and refugee children. *Pediatrics*. 2013; 131(6):e2028–e2034. doi: http://dx.doi.org/10.1542/peds.2013-1099.
- American Academy of Pediatrics. Medical evaluation for infectious diseases for internationally adopted refugee, and immigrant children. 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; 2015:194–201 .
- Weatherhead JE, Hotez PJ. Worm infection in children. *Pediatr Rev.* 2015;36(8):341–354. doi: http://dx.doi.org/10.1542/pir.36-8-341.

Question 49

You are working with the resident team in the neonatal intensive care unit caring for a term infant with long-segment Hirschsprung disease. The infant has had a total colectomy with an ileostomy. He is currently receiving both enteral nutrition via a gastrostomy tube and parenteral nutrition via a central venous catheter. The residents ask you how to avoid cholestasis in this infant.

Of the following, the BEST answer is to

  A. cycle the enteral nutrition over 20 hours
  B. cycle the parenteral nutrition over 20 hours
  C. increase the dose of intralipids
  D. increase the glucose infusion rate
  E. increase the trace mineral content

Correct Answer: B

The infant in this vignette with Hirschsprung disease is at risk for the development of cholestasis associated with total parenteral nutrition (TPN). This risk is limited by cycling the TPN over 20 hours or less, with a goal of 12 to 14 hours of infusion. Cycling TPN reduces insulin exposure, allowing for mobilization of fat, which reduces cholestasis risk.

Parenteral nutrition is used in critically ill children who require nutrition but are unable to tolerate enteral nutrition. Use of TPN is associated with many risks:
- Catheter-related problems: sepsis, occlusion, thrombus, dysfunction
- Cholestasis
- Cholelithiasis/gallbladder sludge
- Electrolyte abnormalities
- Hepatitis
- Hyperglycemia
- Hypertriglyceridemia
- Osteopenia/metabolic bone disease
- Vitamin/micronutrient deficiency

Whenever possible, enteral nutrition should be used to avoid the risks and complications associated with TPN. Enteral support is needed in children with failure to thrive or poor growth, a frequent complication of many medical conditions due to inadequate caloric intake or increased metabolic needs. Enteral support may also be indicated in children who cannot take nutrition orally because of the aspiration risk. Children must have a functional gastrointestinal tract to tolerate enteral nutrition.

Enteral nutrition is associated with a healthier gastrointestinal tract with an improved gut immune system and healthier microbiota. Increasing evidence shows substantial benefit to enteral nutrition over parenteral nutrition.

There is no risk for cholestasis associated with continuous enteral feeds over 24 hours, thus there is no benefit associated with cycling enteral feeds. Cholestasis risk increases with increased lipid dosing. Both increased glucose infusion rate and increased trace mineral content make it more likely the patient will experience cholestasis.

PREP Pearls
- Parenteral nutrition is used in critically ill children who require nutrition but are unable to tolerate enteral nutrition.
- Cycling total parenteral nutrition reduces insulin exposure allowing for mobilization of fat, which reduces cholestasis risk.
- Whenever possible, enteral nutrition should be used to avoid the risks and complications associated with total parenteral nutrition.
- Enteral nutrition is associated with a healthier gastrointestinal tract with an improved gut immune system.

ABP Content Specifications(s)
- Understand the indications for providing enteral nutritional support
- Judge the advantages of enteral nutrition over parenteral nutrition

Suggested Readings
- Becker P, Carney LN, Corkins MR, et al. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). *Nutr Clin Pract.* 2015;30(1):147–161. doi: http://dx.doi.org/10.1177/0884533614557642.
- ElHassan NO, Kaiser JR. Parenteral nutrition in the neonatal intensive care unit. *NeoReviews.* 2011;12(3):e130–e140. doi: http://dx.doi.org/10.1542/neo.12-3-e130.
- Lauriti G, Zani A, Aufieri R, et al. Incidence, prevention, and treatment of parenteral nutrition–associated cholestasis and intestinal failure–associated liver disease in infants and children: a systematic review. *JPEN J Parenter Enteral Nutr.* 2014;38(1):70–85. doi: http://dx.doi.org/10.1177/0148607113496280.
- Rangel SJ, Calkins CM, Cowles RA, et al. Parenteral nutrition–associated cholestasis: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. *J Pediatr Surg.* 2012;47(1):225–240. doi: http://dx.doi.org/10.1016/j.jpedsurg.2011.10.007.
- Wales PW, Allen N, Worthington P, et al. A.S.P.E.N. clinical guidelines support of pediatric patients with intestinal failure at risk of parenteral nutrition–associated liver disease. *JPEN J Parenter Enteral Nutr.* 2014;38(5):538–557. doi: http://dx.doi.org/10.1177/0148607114527772.

Question 50

A 2-month-old, 32-week-gestation infant boy with respiratory syncytial virus bronchiolitis is admitted to the hospital with respiratory distress and poor oral intake. His admission vital signs included a temperature of 37.5°C, heart rate of 150 beats/min, respiratory rate of 50 breaths/min, and blood pressure of 80/40 mm Hg. Pulse oximetry was 80% on room air and improved to 96% on 5 L/min of oxygen by nasal cannula. On admission, the infant was breathing fast but comfortably, and his hemodynamic state was adequate. Several hours after admission, on routine assessment, the infant's nurse noticed that he was not breathing, and he was gray around the mouth. At that time, his pulse oximetry was 50% on 5 L/min of oxygen, his heart rate had dropped to 70 beats/min, and his blood pressure was unobtainable. The nurse immediately called a code and started bag valve–mask ventilation. When the code team arrived, they intubated the infant and were able to restore normal vital signs and adequate oxygenation and ventilation.

You review the events preceding the infant's deterioration, and note that a patient care technician had been assigned to respond to alarms for that 24-bed inpatient hospital floor. The system was designed to set off an alarm when pulse oximetry readings drop below 95%. For the first several hours of this infant's admission, the technician silenced his alarm 32 times, while the pulse oximetry measurements ranged from 90% to 94%; during the hour immediately preceding the event, the technician silenced the alarm 5 times, when the infant's pulse oximetry ranged from 70% to 90%.

Of the following, the MOST appropriate step in improving the safety of patients like this infant is to

A. decrease the lower limit of the alarm to a pulse oximetry reading of <90%
B. discipline the responsible patient care technician when such events occur
C. discuss this case at the departmental morbidity and mortality conference
D. implement a system that alerts the physician when an alarm threshold is reached
E. implement hospital-wide education for patient care technicians on respiratory failure

Correct Answer: A

The boy in the vignette, who had been in the hospital with acute respiratory insufficiency from respiratory syncytial virus bronchiolitis, deteriorated on the inpatient unit to the point of near cardiopulmonary arrest, and required bag-valve-mask ventilation and intubation by the code team. A review of the circumstances leading to this event showed that the patient care technician had silenced the alarm many times, including when the patient had concerning pulse oximetry levels. This was likely because of alarm fatigue. The most effective method of mitigating alarm fatigue in similar clinical situations is to decrease the lower limit of the pulse oximeter alarm to less than 90%.

In the current era of skyrocketing health care costs, widespread implementation of electronic health records (EHR), and computerized physician order entry (CPOE), patient safety has become a major focus of research and policy-making. The Joint Commission first established National Patient Safety Goals in 2002; these now include the domains of patient identification, communication among health-care workers, drug safety, alarm systems, infection control, falls, preventing decubitus ulcers, and other in-hospital areas of risk. Other patient safety goals, specific to the EHR, to be considered might include mitigating the risks of EHR downtime, mandates for the universal use of CPOE, minimizing alarm fatigue, and the use of EHR-based triggers for potential safety events.

Alarm fatigue occurs when a high frequency of alerts results in desensitization to the alarm. Especially when most alerts do not require a significant intervention, alarm fatigue can lead the caregiver to miss some alerts that should necessitate an intervention. For the infant in the vignette, a drop-in pulse oximetry from 94% to 90% would not likely represent a change in clinical status sufficient to warrant a change in management. However, a reading of less than 90%, especially when the boy is already receiving significant respiratory support, should initiate a physician evaluation, change in management, or possibly an intensive care unit admission. The high number of alarms for nonconcerning saturation levels likely contributed to the technician becoming desensitized, and thereby led to the silencing of the concerning alerts. In this case and similar instances, reducing the alarm threshold to less than 90% would limit the instances of alerts to those warranting evaluation or a change in management or disposition.

In the case of many patient safety events, it is more beneficial to address systems issues that can help prevent future events as opposed to individual interventions, such as disciplinary actions. Although morbidity and mortality conferences can enhance education, they often do not address systems issues. It would not be appropriate for a physician to be alerted when this overly sensitive alarm threshold is reached, as alarm fatigue could similarly occur. A hospital-wide educational program for pediatric respiratory failure given to patient care technicians, individuals who may not have a medical background, is not practical and even if it were, it would need to be repeated frequently due to staff turnover.

PREP Pearls
- Alarm fatigue occurs when a high frequency of alerts results in desensitization to the alarms. This can be mitigated by avoiding alarm thresholds that would not indicate the need for changes in management or disposition.
- National Patient Safety Goals include the domains of patient identification, communication among health-care workers, drug safety, alarm systems, infection control, falls, preventing decubitus ulcers, and other in-hospital areas of risk.

ABP Content Specifications(s)
- Recognize the use of National Patient Safety Goals to improve patient safety

Suggested Readings
- Lansdowne K, Strauss DG, Scully CG. Retrospective analysis of pulse oximeter alarm settings in an intensive care unit patient population. *BMC Nurs.* 2016;15:36. doi: http://dx.doi.org/10.1186/s12912-016-0149-3.
- Sittig D, Singh H. Electronic health records and national patient-safety goals. *N Engl J Med.* 2012;367(19):1865–1860. doi: http://dx.doi.org/10.1056/NEJMsb1205420.

Question 51

You are called to the newborn nursery to evaluate a neonate with tachypnea. She was born at 38 weeks' gestation to a 29-year-old gravida 6, para 4 woman with a history of mild intermittent asthma and limited prenatal care. She presented to the hospital fully dilated, with meconium-stained amniotic fluid. The infant was delivered vaginally, without assistance, by precipitous delivery. Upon delivery, she had a spontaneous cry with good muscle tone. Her vital signs in the nursery show the following: temperature, 36.7°C; heart rate, 142 beats/min; respiratory rate, 62 breaths/min; and blood pressure, 86/52 mm Hg. Pulse oximetry demonstrates oxygen saturation of 85% on the left foot and 96% on the right wrist. She has mildly increased work of breathing, a 2/6 systolic ejection murmur at the left lower sternal border, and +1 peripheral pulses. The remainder of her examination results are unremarkable. Chest radiography shows decreased lung markings. Her electrocardiogram is shown in Item Q51.
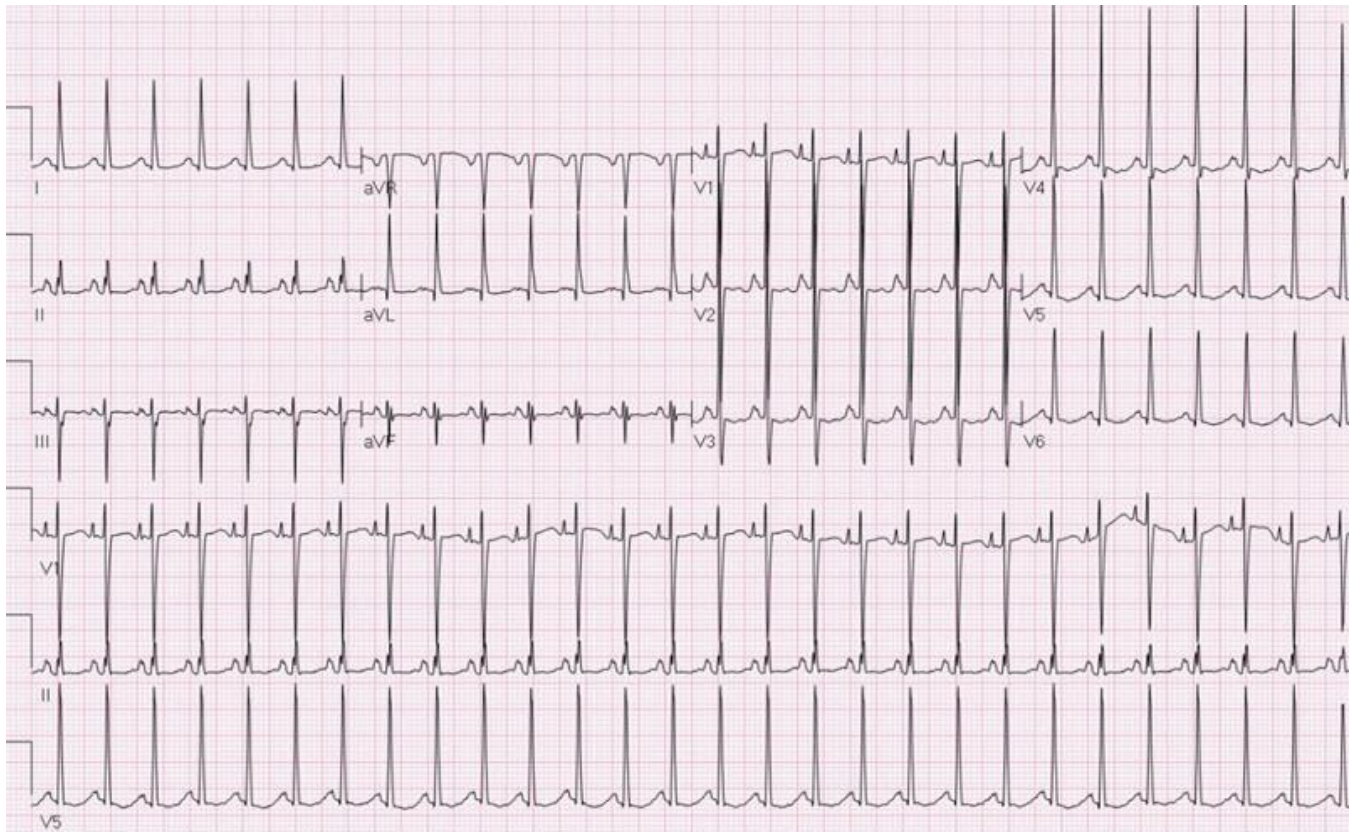
Item Q51: Electrocardiogram for the infant described in the vignette.
Courtesy of M. LaTuga

Of the following, the MOST likely cause of the neonate's tachypnea is

A. congenital diaphragmatic hernia
B. meconium aspiration syndrome
C. respiratory distress syndrome
D. transient tachypnea of the newborn
E. tricuspid atresia

Correct Answer: E

The most likely explanation for the presentation of the neonate in the vignette is tricuspid atresia. The lack of respiratory distress and 11-point differential between her pre- and postductal saturations suggest a cardiac cause of hypoxemia. Her chest radiograph shows decreased pulmonary markings, which is also consistent with tricuspid atresia. In addition, the electrocardiogram has higher voltage in leads V4-V6, seen with left ventricular hypertrophy, which is often seen with tricuspid atresia. In comparison, most neonates have a right-sided dominance with right ventricular hypertrophy (RVH).

Typically, neonates with congenital diaphragmatic hernia (CDH) present with severe respiratory distress, scaphoid abdomen, and audible bowel sounds in the thorax. Intestines are visible in the thoracic cavity on chest radiography. These neonates require immediate intubation to prevent distension of the intrathoracic intestines and compression of lung tissue. Most neonates with CDH do not have cardiac anomalies. Electrocardiography will show RVH.

In comparison, neonates with persistent pulmonary hypertension and meconium aspiration syndrome have labile oxygen saturations and evidence of moderate to severe respiratory distress on physical examination. Meconium obstructs smaller airways, leading to areas of hyperinflation and atelectasis seen as patchy opacities on chest radiography. Because meconium inactivates surfactant, infants with meconium aspiration syndrome may benefit from exogenous surfactant therapy. Meconium also alters pulmonary vasculature, increasing the risk of pulmonary hypertension. Electrocardiography will show RVH.

With respiratory distress syndrome (RDS), neonates do not show evidence of pulmonary hypertension, and chest radiography reveals a homogeneous ground glass appearance, not decreased lung markings. RDS is a disease of inadequate surfactant that occurs most often in premature neonates. In term infants, RDS is typically the result of inactivation of surfactant by infection or meconium. In rare cases, term neonates have inadequate surfactant production because of a genetic abnormality in surfactant or its associated proteins.

Neonates with transient tachypnea of the newborn present with mild to moderate respiratory distress within the first 6 hours after birth. Typically, they have a barrel-shaped chest but do not have a differential between pre- and postductal oxygen saturations. Chest radiography shows increased pulmonary markings with fluid in the right fissure. It occurs because of delayed activation of an epithelial sodium transporter in the lung. Treatment is supportive with continuous positive airway pressure and oxygen therapy as needed. Transient tachypnea of the newborn resolves within the first 24 hours after birth.

Of note, based on the most recent recommendations from the Neonatal Resuscitation Program (**Item C51**) neonates born to mothers with meconium-stained amniotic fluid should not undergo routine endotracheal suctioning. There is insufficient evidence of the benefit of this procedure. Instead, neonates with meconium-stained amniotic fluid with poor muscle tone and decreased respiratory effort should receive positive pressure ventilation. Endotracheal intubation

is reserved for neonates with a heart rate less than 100 beats/min and an inadequate response to positive pressure ventilation.

Item C51. Neonatal resuscitation algorithim.
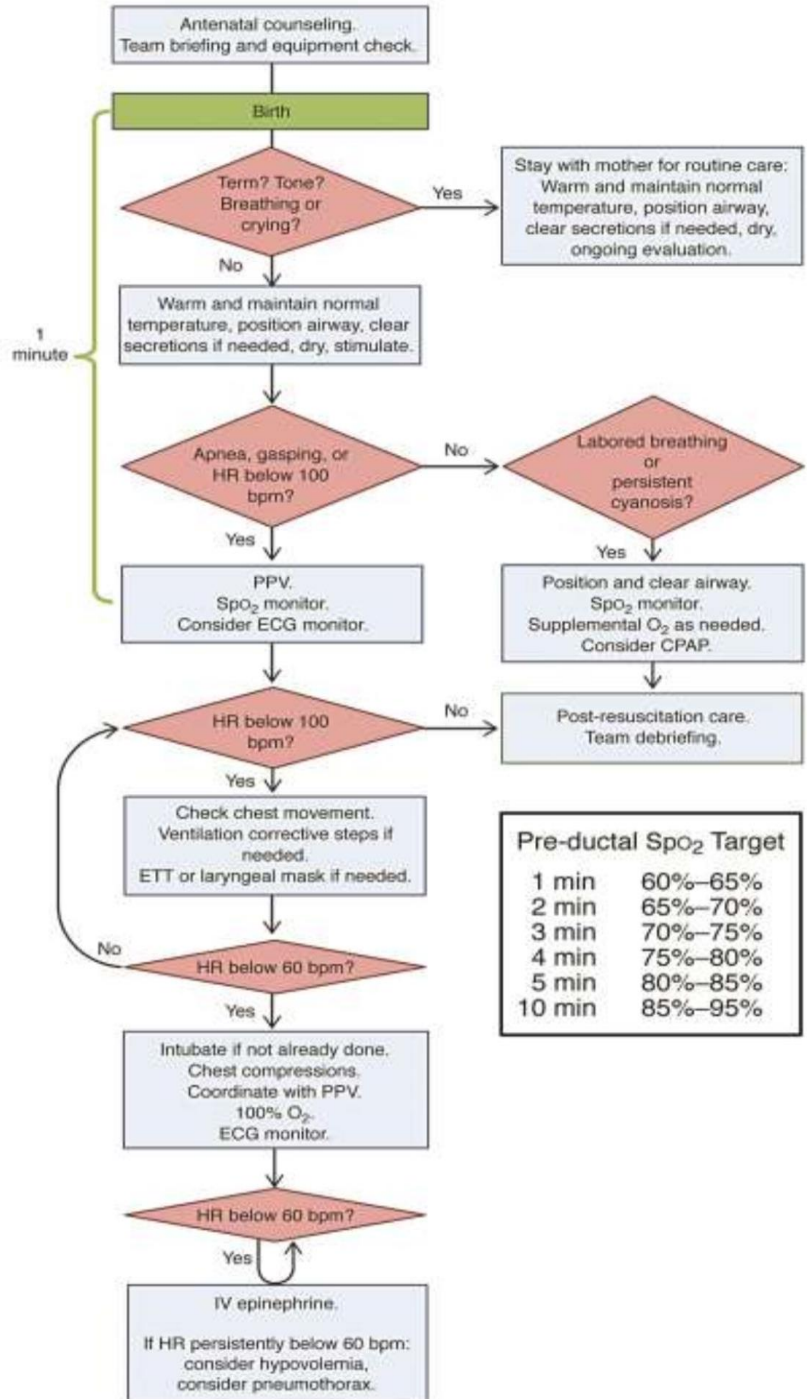
Reprinted with permission from Weiner, GM. Textbook of Neonatal Resuscitation (7th ed.). Elk Grove Village, IL: American Academy of Pediatrics. 2016

PREP Pearls
- Routine endotracheal suctioning at delivery for meconium-stained amniotic fluid is not recommended.
- Neonates with cyanotic congenital heart disease and pulmonary hypertension present with mild to moderate respiratory distress and a fixed differential between pre- and postductal oxygen saturations.
- Neonates with meconium aspiration syndrome have labile oxygen saturations and a chest radiograph with diffuse patchy pulmonary opacities.

MOCA-Peds Objective
- Respond to abnormal results of congenital heart disease screening in a neonate

ABP Content Specifications(s)
- Distinguish between persistent pulmonary hypertension with meconium aspiration and cyanotic congenital heart disease in a neonate
- Recognize the clinical features associated with a neonate who has persistent pulmonary hypertension following meconium aspiration

Suggested Readings
- Dargaville PA, Copnell B. The epidemiology of meconium aspiration syndrome: incidence, risk factors, therapies, and outcome. *Pediatrics*. 2006;117:1712. doi: http://dx.doi.org/10.1542/peds.2005-2215.
- Rothstein R, Paris Y, Quizon A. Pulmonary hypertension. *Pediatr Rev.* 2009;30:39. doi: http://dx.doi.org/10.1542/pir.30-2-39.
- Wyckoff MH, Aziz K, Escobedo MB, et al. Part 13: Neonatal resuscitation: 2015 American Heart Association guidelines: update for cardiopulmonary resuscitation and emergency cardiovascular care. *Pediatrics*. 2015;136;S196. doi: http://dx.doi.org/10.1542/peds.2015-3373G.

Question 52

A 14-year-old adolescent is brought to your office for concerns about short stature. He is interested in trying growth hormone therapy. He has no significant medical history and takes no medication. A comprehensive review of systems yields negative findings. The boy's mother is 173 cm tall and had menarche at age 14 years. His father is 178 cm tall and completed his linear growth in high school. The boy's adjusted midparental height is at the 75th percentile for an adult male. On physical examination, the boy's weight is 39 kg (fifth percentile), height is 148 cm (less than third percentile, -2 SD below the mean), and body mass index is 17.8 kg/m2 (25th percentile). His growth curve is shown (Item Q52). He has a sexual maturity rating of 1 for pubic hair and genital development. The remainder of his physical examination findings are unremarkable. A bone age radiograph is read as 11 years.

Of the following, the MOST accurate statement to include in counseling this boy is that growth hormone therapy is

A. indicated after further testing to determine expected growth response
B. indicated, with a robust growth response expected
C. indicated, with significant individual variation in growth response
D. not indicated because a poor growth response is expected due to his age
E. not indicated because he is likely to achieve normal adult height

Correct Answer: E

The boy 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. There is a family history of delayed puberty in his mother, and he has a delayed bone age. The boy's current height is becoming increasingly discrepant from his peers because he continues to grow at a normal prepubertal height velocity (5 cm/year), while his typically developing peers are growing at pubertal height velocities. His pubertal growth spurt will come later and he will grow for a longer period. If his height is plotted based on his bone age it falls within his target height range percentiles, and predicts catch-up growth. Growth hormone is not indicated in this situation. Based on his bone age and current height, the boy's predicted adult height is 180 cm (71 inches), which is consistent with his target height range of 178 cm (70 inches) ± 5 cm (2 inches).

Growth hormone is approved by the US Food and Drug Administration (FDA) for children with idiopathic short stature whose height is more than 2.25 standard deviations (SDs) below the mean (<1.2%) and who are unlikely to catch up in height. A predicted adult height of less than 63 inches for boys or 59 inches for girls is considered a lack of expected catch-up growth. This boy does not meet these criteria, because his height is currently 2 SDs below the mean and his predicted adult height is well above 63 inches.

Management of constitutional delay consists of reassurance regarding future pubertal development and height, in addition to clinical observation. Constitutional delay can, however, cause significant psychosocial distress. In such cases, referral to a pediatric endocrinologist for a short course of testosterone therapy may be indicated. One approach is to administer testosterone ester 100 mg intramuscularly every month 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.

In addition to growth hormone deficiency and idiopathic short stature, recombinant human growth hormone (rhGH) therapy is FDA-approved in children for the following indications: Turner syndrome, Noonan syndrome, Prader-Willi syndrome, *SHOX* gene haploinsufficiency, children born small for gestational age who have not achieved a height of at least 2 SDs below the mean by age 2 years, and growth failure associated with chronic renal insufficiency (pretransplantation only).

Response to growth hormone therapy depends on the underlying condition, age at initiation of therapy, dose, and duration of therapy. Children with growth hormone deficiency have an excellent growth response to relatively low doses of rhGH. Those without growth hormone deficiency have a less robust growth response and require higher doses. The average gain in final adult height after treatment with rhGH in those with idiopathic short stature is 3.5 to 7.5 cm (1.4–3 inches), but there is considerable individual variation. Longer duration of therapy and initiation before puberty are associated with better height outcomes. The boy in the vignette does not have growth hormone deficiency, so would have a less robust response to rhGH, and his age of 14

years would not allow for a very long treatment duration. Even if he met FDA-approved criteria for rhGH, the therapy would not likely offer any benefit.

PREP Pearls
- Constitutional delay of growth and puberty should be suspected in otherwise healthy children growing at a normal prepubertal growth velocity, and with a family history of delayed puberty.
- Growth hormone is approved by the US Food and Drug Administration for children with idiopathic short stature whose height is more than 2.25 standard deviations below the mean (<1.2%) and who are unlikely to catch up in height.

ABP Content Specifications(s)
- Evaluate constitutional growth delay by growth chart evaluation
- Recognize the effects of growth hormone therapy on growth

Suggested Readings
- Cohen P, Rogol AD, Deal CL, et al; 2007 ISS Consensus Workshop participants. Consensus statement on the diagnosis and treatment of children with idiopathic short stature: a summary of the Growth Hormone Research Society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop. *J Clin Endocrinol Metab.* 2008;93(11):4210-7. doi: http://dx.doi.org/10.1210/jc.2008-0509.
- Kaplowitz PB. Delayed puberty. *Pediatr Rev.* 2010;31(5):189–195. doi: http://dx.doi.org/10.1542/pir.31-5-189.
- 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.e6. 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.
- Wilson TA, Rose SR, Cohen P, et al; Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. Update of guidelines for the use of growth hormone in children: the Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. *J Pediatr.* 2003;143(4):415–421.

Question 53

A 24-month-old boy is brought to your office by his mother who tells you she is concerned about his speech and behavior. She reports that her son uses a total of 10 single words to communicate. He grabs her hand to place it on things that he wants. He does not point or make eye contact. The boy has tantrums when there is any change in his routines or when he hears loud noises. He is fascinated with lights, and does not respond to the presence of other children. His hearing evaluation and physical examination findings are normal. The boy's mother tells you that he has a cousin with "delays."

Of the following, the BEST next management step for this boy is to

A. administer the Childhood Autism Spectrum Test
B. assist the family in accessing an Individualized Family Service Plan
C. order a functional magnetic resonance imaging study
D. order electroencephalography
E. recommend twice-monthly applied behavioral analysis therapy

Correct Answer: B

This boy in the vignette should be referred for early intervention (EI) services, because he is 24 months old and is demonstrating significant delays in his language and social development. EI programs provide services to children from birth to 3 years of age, who have delays in development (physical, cognitive, communication, social/emotional, adaptive development) or a condition with a high probability of developmental delay. An Individualized Family Service Plan, outlining specific services and goals, is developed through the EI program to address the developmental needs of the child.

The boy in the vignette has development and behavior that are highly suggestive of autism. Autism spectrum disorder (ASD) is defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) as having both (1) deficits in social communication and interactions, and (2) restricted, repetitive patterns of behaviors, interests, or activities. The social deficits in ASD include challenges with social-emotional reciprocity, nonverbal social communication, and relationships. The child with ASD may have difficulty navigating conversations and social interactions, using eye contact and gestures, or understanding another person's body language. A 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. These behaviors make it difficult for the child with ASD to develop and maintain friendships. Common findings include repetitive or stereotypical motor movements (eg, hand flapping, rocking, spinning); repetitive speech (eg, immediate or delayed echolalia); behavioral rigidity (eg, significant difficulty with change); abnormally fixated interests (eg, public transportation systems); or abnormal reactions to sensory input 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).

Autism spectrum disorder is a highly heritable neurodevelopmental disorder with a biological basis. For parents with an affected child, the chance of having another child with ASD is 10% to 19%. Genetic abnormalities associated with autism have been found on almost every chromosome. In 10% to 20% of cases of ASD, a genetic syndrome (eg, fragile X syndrome, tuberous sclerosis, Rett syndrome) or genetic difference (eg, mutation, microdeletion, microduplication) can be identified. Gene environment interactions or epigenetic processes are thought to be involved. Neuroimaging demonstrates differences in white matter volume via magnetic resonance imaging (MRI), and problems with cortical connectivity and neuronal activity can be detected via functional MRI. Currently functional MRI is used only for research purposes. Head circumference studies show a pattern of increased brain volume during the first year after birth, and 20% to 30% of children with ASD have macrocephaly. Neuropathological studies show abnormalities in the cerebellum, frontal lobe, temporal lobe, brainstem, and limbic system.

Screening for ASD is essential because autism is relatively common, with a prevalence of 1 in 68, and evidence shows that EI programs improve outcomes. In 2007, the American Academy of Pediatrics (AAP) recommended universal screening for ASD at both the 18- and 24-month health supervision visits and whenever concerns are raised. The 24-month rescreen is

recommended because 20% to 35% of children with ASD regress in language (and sometimes social) development between 15 and 24 months of age. Multiple screening tools are available, and vary in the age at which they should be administered. Screening tools often used include The Infant-Toddler Checklist from the Communication and Symbolic Behavior Scales and Developmental Profile (CSBS-DP) (9-24 months), the Modified Checklist for Autism in Toddlers (16-30 months), and the Childhood Autism Spectrum Test (4-18 years). These 3 screening tools are included in the *AAP Caring for Children with Autism Spectrum Disorders: A Resource Toolkit for Clinicians*.

Concerning results on an autism screen indicate possible autism, but may also occur in other developmental conditions. Referrals and further evaluation should always ensue. A child younger than 3 years should be referred to local EI services, whereas a child 3 years of age or older should be referred to their school district. Children of any age with language or communication problems should be referred for an audiologic evaluation.

The pediatrician should conduct a complete history and physical examination of the child diagnosed with ASD, looking for (1) clues to etiology, such as neurologic findings or dysmorphic features; (2) coexisting medical conditions such as gastrointestinal disease, seizures, and sleep disturbances; and (3) mental health disorders (eg, attention-deficit/hyperactivity disorder, anxiety). An etiologic workup for ASD with intellectual disability or global developmental delay includes a DNA analysis for fragile X syndrome and a chromosome microarray analysis. Magnetic resonance imaging of the brain, electroencephalography, or metabolic studies are not appropriate unless there are clinical indications such as focal neurologic abnormalities, microcephaly, seizurelike behavior, staring episodes where the child is not responsive to touch, episodic decompensation with illness, ataxia, or developmental regression. In children with autism, medical problems may present as increased disruptive behaviors or other behavioral change. Nutritional deficiencies may occur because of the child's limited food repertoire, implementation of a diet-restricted intervention, or may be associated with pica or persistent mouthing behaviors. Coexisting mental health disorders may require treatment with behavioral interventions and/or psychopharmacologic agents. Risperidone and aripiprazole are approved by the US Food and Drug Administration for the treatment of irritability in autism. Pediatricians may need to provide guidance on the use of complementary and alternative treatment modalities.

The mainstay of ASD treatment is intensive behavioral and educational intervention. Educational supports should be provided through special education services or a 504 plan, depending on the child's degree of impairment, coexisting conditions, and educational needs. The treatment best supported by evidence is applied behavioral analysis therapy, which involves analyzing the child's behaviors and systematically teaching skills that reinforce desired actions (eg, communication, prosocial behaviors) and diminish maladaptive behaviors (eg, aggression, noncompliance, elopement). It is an expensive treatment that typically takes place over many hours each week and over years. Additional interventions are available and noted in **Item C53** .

By understanding the principles of autism diagnosis and management, the pediatrician can support families of children with autism through early detection, referrals, and guidance on resources and treatment.

Item C53. Treatment Approaches for Autism Spectrum Disorder

Treatment Approach	Examples
Behavioral	Applied Behavioral Analysis (ABA) Pivotal Response Training (PRT)
Developmental	Developmental Individual-Difference Relationship-based model (DIR)/Floortime
Educational	Treatment and Education of Autistic and related Communication-Handicapped Children (TEACCH)
Speech and language	Picture Exchange Communication System (PECS)
Occupational therapy	Therapy to address fine motor and sensory needs

PREP Pearls
- The American Academy of Pediatrics recommends universal screening for autism spectrum disorder (ASD) at both the 18- and 24-month health supervision visits, and whenever concerns are raised. The 24-month rescreen is recommended because 20% to 35% of children with ASD regress in language (and sometimes social) development between 15 and 24 months of age.
- An etiologic workup for ASD with intellectual disability or global developmental delay includes a DNA analysis for fragile X syndrome and a chromosome microarray analysis.
- The mainstay of ASD treatment is intensive behavioral and educational intervention. The treatment best supported by evidence is applied behavioral analysis.

MOCA-Peds Objective
- Evaluate and manage the behavioral complications of autism spectrum disorder

ABP Content Specifications(s)
- Understand the diagnostic criteria for autism spectrum disorders
- Understand the biologic basis of autistic behavior
- Plan appropriate management for autism spectrum disorders
- Plan age-appropriate screening evaluation for autism spectrum disorders

Suggested Readings
- 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.
- Johnson CP, Myers SM, Council on Children with Disabilities. Identification and evaluation of children with autism spectrum disorders. *Pediatrics.* 2007;120(5):1183–1215. doi: http://dx.doi.org/10.1542/peds.2007-2361.
- Zwaigenbaum L, Bauman ML, Choueiri R, et al. Early identification and interventions for autism spectrum disorder: executive summary. *Pediatrics.* 2015;136(S1):S1–S9. doi: http://dx.doi.org/10.1542/peds.2014-3667B.

Question 54

A 2-year-old boy visits your office for follow-up care after his recent ophthalmologic evaluation for retinal detachment and upward lens subluxation. He is tall for his age and has an increased arm span–height ratio. His upper segment–lower segment ratio is normal for his age. Otherwise, his medical history is unremarkable. His father is 6 ft 2 in and has an increased arm span–height ratio, reduced upper segment–lower segment ratio, high-grade myopia, lens subluxation, flat feet, scoliosis, and a positive wrist and thumb sign. The boy's paternal uncle has aortic root dilation and reduced elbow extension with a negative wrist and thumb sign. His paternal grandmother has aortic root dilation and myopia. Consanguinity is denied.

Of the following, the genetic term that BEST describes the familial presentation in this case is

  A. autosomal recessive inheritance
  B. inbreeding
  C. reduced penetrance
  D. sex-limited expression
  E. variable expression

Correct Answer: E

The family in this vignette has an autosomal dominant disorder with variable expression. Expressivity is a term used to describe the phenotypic expression of a disease among individuals with a particular genotype. The family members in this vignette have Marfan syndrome, which is associated with pathogenic mutations in *FBN1*. Variable expression occurs when the severity and presentation of disease manifestations differs among individuals with the same genotype. The boy in this vignette has retinal detachment and lens subluxation and his paternal grandmother has aortic root dilation and myopia, demonstrating variable systemic involvement among members of the same family.

Another common term in genetics is incomplete penetrance. Penetrance is the probability that a gene will manifest clinically in an individual with a particular genotype. Incomplete or reduced penetrance is an all-or-none phenomenon. Incomplete penetrance occurs when an individual with a specific genotype does not express any signs or symptoms of the disorder. Phenotypic expression can be impacted by modifier genes, aging, or environmental factors. Penetrance is an all-or-none phenomenon. It describes the percentage of people with a predisposing phenotype who actually have clinical effects, even to a small degree, vs the individuals with the same phenotype with no clinical effects. An example is reduced penetrance in individuals with split-hand deformity, a type of ectrodactyly. Some individuals will have the split hand and some will not despite possessing the same genotype. Only 70% of individuals with this gene mutation exhibit the clinical defect.

The patterns demonstrated in single-gene disorders in pedigrees generally depend on several factors.

A disorder is considered autosomal dominant when only one chromosome of the pair carries the abnormal allele and the other chromosome carries a normal allele, but the single abnormal allele is enough to yield an abnormal phenotype in the affected individual.

A disorder is considered autosomal recessive when both chromosomes of the pair carry the abnormal alleles, as in cystic fibrosis or sickle cell disease. A gene mutation on each chromosome in the pair is necessary for the individual to have the disorder. This type of inheritance is called autosomal recessive inheritance. If an individual only carries one gene mutation on a single chromosome that is associated with an autosomal recessive disorder, the individual will be a carrier for the disorder but unaffected.

The chromosome location indicates if the gene is located on an autosome (chromosomes 1 to 22) or on a sex chromosome (chromosomes X or Y).

Autosomal disorders generally affect male and female individuals equally, with the exception of sex-limited disorders. In autosomal dominant disorders, an affected individual has a 50% chance of passing the disorder to his or her offspring. Some disorders have sex-limited expression despite the fact that the disorder is on an autosome rather than a sex chromosome; the disorder will only express itself in a particular sex. Examples of sex-limited expression are male-pattern

baldness and male-limited precocious puberty. Heterozygous females do not manifest the disorder in sex-limited expression disorders.

Inbreeding is a term used to describe mating between individuals from the same small population. Inbreeding could be caused by geographical or cultural reasons. The parents may not consider themselves related but could have a common ancestor within the previous several generations. This shared ancestry predisposes individuals to increased carrier rates for recessive disorders.

PREP Pearls
- Variable expression is when the severity and presentation of a genetic disorder differs among individuals with the same genotype.
- Incomplete or reduced penetrance is an all-or-none phenomenon. Incomplete penetrance occurs when an individual with a specific genotype does not express any signs or symptoms of the disorder.
- Autosomal dominant inheritance is when only one chromosome of the pair carries the abnormal allele and the other chromosome carries a normal allele, but the single abnormal allele is enough to yield an abnormal phenotype in the affected individual. In this case, there is a 50% chance that the individual will pass it on to his or her offspring.

ABP Content Specifications(s)
- Recognize the inheritance pattern associated with an autosomal dominant disorder with variable expressivity
- Recognize the inheritance pattern associated with autosomal dominant disorders
- Recognize the inheritance pattern associated with an autosomal dominant disorder with incomplete penetrance

Suggested Readings
- US National Library of Medicine. What are reduced penetrance and variable expressivity? Genetics Home Reference website. https://ghr.nlm.nih.gov/primer/inheritance/penetranceexpressivity.
- US National Library of Medicine. What are the different ways in which a genetic condition can be inherited? Genetics Home Reference website. https://ghr.nlm.nih.gov/primer/inheritance/inheritancepatterns.

Question 55

You are seeing a 6-year-old girl in the emergency department. Her parents are concerned that she has developed dehydration due to food poisoning. The girl attended a neighborhood picnic, along with the rest of her family, where she consumed various foods including chicken, potato salad, watermelon, and strawberry pie. Within half an hour of eating, the girl told her mother that "her belly hurt really badly," and then proceeded to have multiple episodes of vomiting and diarrhea. These symptoms have continued for 2 hours; she feels very dizzy and cannot stand up. Her mother remarks that the girl's face has appeared flushed since her symptoms began. The girl's 10-year-old brother had an isolated episode of watery diarrhea approximately 1 hour after eating the same food, so the parents are worried that both children were exposed to "bad food" at the picnic.

Other than a history of mild eczema, the girl has been healthy. She takes no medications, and has no known allergies. Her immunizations are up to date.

Her vital signs are as follows: temperature of 36.9°C, heart rate of 145 beats/min, respiratory rate of 30 breaths/min, and blood pressure of 70/45 mm Hg. The girl is awake and responds to your questions and instructions, but seems fatigued and uncomfortable. She retches several times as you are talking with her parents. On physical examination, her entire face and neck appear flushed. She has profuse clear rhinorrhea and watery discharge from both of her eyes. The girl's airway is intact, and you note no angioedema. She has clear lungs bilaterally, and no other signs of respiratory distress. Her abdomen is soft and diffusely tender with hyperactive bowel sounds, but no peritoneal signs. There is no swelling of her extremities. Her hands and feet are cool, with a capillary refill time of 3 seconds. Neurologic examination reveals no focal deficits; however, you cannot assess the girl's gait because she complains of dizziness with any attempt to stand up and prefers to remain lying in bed. You order the administration of a 20 mL/kg intravenous bolus of normal saline.

Of the following, the BEST next step in this girl's management is administration of

A. diphenhydramine, intravenously
B. dopamine, intravenously
C. epinephrine, intramuscularly
D. methylprednisolone, intravenously
E. ondansetron, intravenously

Correct Answer: C

The girl in the vignette displays signs and symptoms that meet the diagnostic criteria for acute anaphylaxis. Administration of intramuscular epinephrine is the best next step in her management.

Acute anaphylaxis is a life-threatening medical emergency that typically affects 2 or more organ systems. The gastrointestinal symptoms (acute nausea, vomiting, diarrhea, and crampy abdominal pain) may be mistakenly attributed to more common etiologies, such as foodborne illnesses. It is imperative for pediatric providers to distinguish between anaphylaxis and food poisoning, because the 2 disorders are managed very differently.

Several important factors can be helpful in distinguishing anaphylaxis from food poisoning. Anaphylaxis is an immunoglobulin E (IgE)–mediated process that generally occurs within minutes (almost always within the first hour) after ingesting a specific food (or after contact with an offending substance). Foodborne illnesses are not IgE-mediated, and tend to manifest within a few hours to as long as 24 hours after ingestion of contaminated food. Most cases of food-related anaphylaxis present with skin manifestations, including hives, flushing, and/or angioedema, whereas these findings are not typical in food poisoning.

The clinical diagnosis of anaphylaxis depends on recognition of its signs and symptoms, which may include urticaria, skin flushing, pruritus, angioedema, rhinorrhea, wheezing, shortness of breath, abdominal pain, vomiting, diarrhea, light-headedness, and even frank syncope. This clinical syndrome is highly likely in patients meeting any 1 of 3 diagnostic criteria established by the World Allergy Organization (**Item C55**).

Item C55. World Allergy Organization's Diagnostic Criteria for Anaphylaxis.

1. Acute onset (within minutes to several hours) of signs/symptoms involving the skin, mucosal tissue, or both (eg, generalized urticaria, itching or flushing of skin, swollen lips/tongue/uvula) AND at least 1 of the following:
   - Respiratory compromise (eg, dyspnea, wheeze/bronchospasm, stridor, hypoxia)
   - Decreased blood pressure or associated symptoms of end-organ dysfunction (eg, fainting, dizziness, incontinence)

2. At least 2 of the following occurring acutely after exposure to a likely allergen:
   - Involvement of the skin and/or mucosal tissue
   - Respiratory compromise
   - Decreased blood pressure or associated symptoms of end-organ dysfunction
   - Persistent gastrointestinal symptoms (eg, crampy abdominal pain, nausea, vomiting, diarrhea)

3. Decreased blood pressure following exposure to a known allergen (low age-specific systolic blood pressure OR a decrease in systolic blood pressure by 30% or more in infants/children)

Adapted and reprinted with permission from Simons FE, Ardusso LR, Bilò MB, et al; World Allergy Organization guidelines for the assessment and management of anaphylaxis. *World Allergy Organ J*. 2011;4:15.

Symptoms of food poisoning typically include abdominal pain, nausea, vomiting, and diarrhea, which develop within 1 to 6 hours of eating contaminated food (although symptom onset can be delayed for up to 24 hours). In the United States, staphylococcal food poisoning is one of the

most common causes. Food poisoning is typically a self-limited illness, though severe cases may require treatment with antiemetics and intravenous fluids to correct dehydration.

Early intramuscular administration of epinephrine has been clearly shown to decrease both hospitalizations and death among patients with anaphylaxis. Although administration of intravenous ondansetron would be appropriate for patients with both anaphylaxis and foodborne illnesses to help alleviate vomiting, intramuscular epinephrine is the first-line treatment recommended for anaphylaxis and should be administered as quickly as possible to all children presenting with the characteristic signs and symptoms.

Intravenous diphenhydramine is commonly used as an adjunctive therapy in the management of anaphylaxis, but there is a lack of evidence supporting its efficacy. Although diphenhydramine may be beneficial for specific anaphylaxis-related symptoms (such as itching), it is not a replacement for epinephrine therapy. Epinephrine should never be deferred or delayed due to administration of antihistamines, such as diphenhydramine, in patients with anaphylaxis.

The girl in the vignette is hypotensive with decreased peripheral perfusion, due to acute anaphylaxis, therefore administration of intramuscular epinephrine rather than intravenous dopamine is the best next management step for her. At least 2 to 3 additional 20-mL/kg boluses of crystalloid fluid would be indicated to address this patient's hemodynamic instability before initiating vasopressor therapy. For patients with persistent hypotension secondary to acute anaphylaxis, intravenous epinephrine would be the pressor of choice.

Intravenous methylprednisolone is sometimes used for treating patients with acute anaphylaxis, though the medical literature does not strongly support its benefit. As with antihistamines, corticosteroids may be used as adjunct treatment for anaphylaxis, but intramuscular epinephrine is always recommended as the initial treatment.

PREP Pearls
- Food-associated anaphylaxis is an immunoglobulin E (IgE)–mediated process that generally occurs within minutes (almost always within the first hour) after ingesting a specific food.
- Foodborne poisoning is *not* IgE-mediated and manifests within a few hours, up to as long as 24 hours, after ingestion of contaminated food.
- Most food-related anaphylaxis cases present with skin manifestations including hives, flushing, and/or angioedema, whereas these findings are not typical in food poisoning.
- The clinical diagnosis of anaphylaxis depends on recognition of its signs and symptoms, which may include urticaria, skin flushing, pruritus, angioedema, rhinorrhea, wheezing, shortness of breath, abdominal pain, vomiting, diarrhea, light-headedness, and even frank syncope.
- Intramuscular epinephrine is the first-line treatment for anaphylaxis, and should be given as quickly as possible to children presenting with the characteristic signs and symptoms.

ABP Content Specifications(s)
- Distinguish between anaphylaxis and food poisoning

Suggested Readings
- Chipps BE. Update in pediatric anaphylaxis: a systematic review. *Clin Pediatr*. 2013;52(5):451–-461. doi: http://dx.doi.org/10.1177/0009922812474683.
- Langley EW, Gigante J. Anaphylaxis, urticaria, and angioedema. *Pediatr Rev*. 2013;34:247. doi: http://dx.doi.org/10.1542/pir.34-6-247.
- Simons FE, Ardusso LR, Bilò MB, et al; World Allergy Organization. World Allergy Organization guidelines for the assessment and management of anaphylaxis. *World Allergy Organ J.* 2011;4:13–37. doi: http://dx.doi.org/10.1097/WOX.0b013e318211496c.

Question 56

A 2-year-old girl presents to your office for evaluation of refusal to bear weight. On the previous day, the girl fell sideways off a slide at the park. She cried at the time of injury, and since then, will not bear weight on her right leg. The girl was seen at an urgent care facility, where radiographs of her right hip, femur, knee, and lower leg were read as normal. Her parents are concerned because she still refuses to walk. The girl has not had any fever, change in appetite, change in energy level, or joint swelling. On physical examination, she has normal range of motion of the hip and knee. She appears to have tenderness over the distal third of the right tibia, but this is difficult to assess, because the girl was very apprehensive during the examination.

Of the following, the next BEST step in evaluation and management for this girl is to

  A. place a cast on the lower extremity and repeat radiography in 2 weeks
  B. obtain laboratory results, including complete blood cell count and inflammatory markers
  C. perform ultrasonography of the hip
  D. perform bone scintigraphy
  E. reassure the family that her examination findings and radiographs are not concerning

Correct Answer: A

The history and physical examination of the girl in the vignette suggests an occult tibia fracture. She should be treated with a cast for 2 weeks, then reassessed with clinical evaluation and repeat radiography.

Children between the ages of 1 and 5 years are especially susceptible to "toddler fractures," oblique fractures of the distal tibia. These fractures can occur with seemingly minor injuries. Tenderness of the distal tibia is often the only sign of toddler fracture, which can be difficult to discern in an apprehensive, young child. Toddler fractures may be difficult to see on anteroposterior and lateral radiographs of the tibia and fibula taken immediately after an injury. The addition of oblique views increases the sensitivity of radiographic studies. Approximately 10 to 14 days after injury, radiographs typically show signs of healing at the fracture site. Therefore, in a child with a history and physical examination that point to the diagnosis of toddler fracture, the affected leg should be placed in a cast and the child should undergo reevaluation about 2 weeks later. Because young children are often unable to give a clear description of their injury and symptoms, any child refusing to bear weight should receive a complete evaluation of the spine and lower extremities.

The girl in the vignette had a witnessed fall and does not exhibit systemic symptoms or joint swelling. This history suggests an acute injury. Laboratory studies are not indicated, because the child does not have any evidence of infection or inflammatory arthritis. Joint infection and arthritis are unlikely given the absence of joint effusion and normal knee and hip motion. Reassurance alone would not be adequate management for this child, given her high likelihood of fracture. Hip ultrasonography can be used to evaluate for effusion in a child with suspected septic arthritis, which should be included in the differential diagnosis for a child with refusal to bear weight and decreased hip range-of-motion. However, the girl in the vignette has normal hip motion. Although bone scintigraphy would show a toddler fracture, this study involves a high dose of radiation and, in a young child, would require sedation; therefore, bone scintigraphy would not be recommended in this case.

PREP Pearls
- Children between the ages of about 1 and 5 years are especially susceptible to "toddler fractures," oblique fractures of the distal tibia.
- Toddler fractures can occur with seemingly minor injuries.
- Oblique radiographs may show toddler fractures that are not seen on anteroposterior and lateral views.

ABP Content Specifications(s)
- Recognize the clinical findings associated with occult fractures that may or may not affect gait in patients of various ages
- Recognize the clinical findings associated with growth plate fractures and injuries

Suggested Readings

- Herman MJ, Martinek M. The limping child. *Pediatr Rev*. 2015;36(5):184-195; quiz 196-197. doi: http://dx.doi.org/10.1542/pir.36-5-184 .
- Sarwark JF, LaBella CR, eds. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014.

Question 57

A resident rotating in your office is about to see a 9-year-old girl for a health supervision visit. In preparation for the encounter, you briefly explain that there is a typical sequence and timing of pubertal events.

Of the following, the sequence of pubertal findings MOST often observed is

A. pubarche, thelarche, menarche, peak height velocity
B. pubarche, thelarche, peak height velocity, menarche
C. thelarche, peak height velocity, pubarche, menarche
D. thelarche, pubarche, menarche, peak height velocity
E. thelarche, pubarche, peak height velocity, menarche

Correct Answer: E

In most girls, the physical changes of puberty occur in the following sequence: thelarche (breast budding), pubarche (the appearance of pubic hair), peak height velocity, and menarche. Thelarche (which defines Sexual Maturity Rating [SMR] breast[B] 2) occurs at an average age of 8.8 years in African American girls, 9.3 years in Hispanic girls, and 9.7 years in white and Asian girls (range 8–13 years). It is the result of ovarian estrogen production. Pubarche generally follows thelarche by 1.0 to 1.5 years, but in a few girls, it is the first sign of puberty. Pubarche primarily results from adrenal androgen production. In girls, the growth spurt begins at about 9.5 years of age, with an average peak height velocity of 8.3 cm/year achieved at age 11.5 years, when most are in SMR B3.

Menarche occurs about 2.5 years after thelarche, at a mean age of 12.1 years in African American girls and 12.6 years in white girls (Hispanic girls are intermediate). Approximately 60% of girls are in SMR B4 at menarche, and 25% are in SMR B3. Menarche occurs about 1 year after peak height velocity is achieved, with limited potential for additional linear growth (mean 7 cm). Failure to reach menarche by age 14 years in the absence of breast development, age 16 years in the presence of breast development, or within 4 years of the onset of breast development, should prompt further evaluation.

PREP Pearls
- In girls, breast development and onset of the growth spurt occur at about 9.5 years of age.
- Menarche occurs around 12.5 years of age when girls are at sexual maturity rating B4 (60%) or B3 (25%).
- Failure to achieve menarche by the age of 14 years in the absence of breast development, or 16 years in the presence of breast development, merits further evaluation.

MOCA-Peds Objective
- Recognize normal variations in pubertal development

ABP Content Specifications(s)
- Understand the sequence of development of secondary sexual characteristics in girls
- Recognize the physiologic changes that commonly precede menarche
- Understand the timing of menarche in female adolescents

Suggested Readings
- Bordini B, Rosenfield RL. Normal pubertal development: part II—clinical aspects of puberty. *Pediatr Rev*. 2011;32:281-291 .
- Carswell JM, Stafford DEJ. Normal physical growth and development. In: Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016 .

Question 58

You are caring for a 2-day-old male neonate in the newborn nursery who was born at term after an uncomplicated pregnancy. His delivery and neonatal course have been similarly uncomplicated. He recently underwent an auditory brainstem response hearing screening as part of the nursery's standard protocol, and he did not pass the screening test of his left ear.

Of the following, the MOST appropriate plan for this neonate is to

A. follow up with his primary care provider and retest his hearing only if he develops signs of hearing loss
B. refer for formal audiologic evaluation only if he has a family history of hearing loss
C. refer for formal audiologic evaluation to be completed before 3 months of age
D. refer for formal audiologic evaluation to be completed between 24 and 36 months of age
E. refer to audiology to be fitted for an age-appropriate hearing aid or assistive device

Correct Answer: C

The newborn in this vignette should be referred for a formal audiologic examination to be completed before he is 3 months old. All infants should undergo newborn hearing screening, and all infants with abnormal screening results should receive confirmatory testing.

All states have universal newborn hearing screening (UNHS) programs, and 97% of infants born in the United States in 2013 were screened for hearing loss. As with all screening, the test is designed to have high sensitivity at the expense of a somewhat lower specificity. A "failed" newborn hearing screen result is not diagnostic of hearing loss; infants who do not pass newborn hearing screening must have additional testing to either diagnose and specify the degree and type of hearing loss or to confirm normal hearing. Because of the overwhelming data that early identification and intervention is crucial to minimizing language, learning, personal-social, and emotional problems associated with hearing loss, UNHS programs aim to identify children with hearing loss before 3 months of age and initiate appropriate interventions prior to 6 months of age. The UNHS programs have decreased the average age of diagnosis for childhood hearing loss from 2.5 years to 3 months.

The auditory system contains 4 main components, all of which must be functional for normal hearing:

- The outer ear (external auditory canal) collects and funnels sound waves.
- The middle ear (tympanic membrane through stapes footplate) functions as a pressure transducer to transfer sound waves from air to fluid.
- In the inner ear (cochlea), sound waves cause opening of ion-gated channels in hair cells leading to action potentials.
- The auditory nerve carries action potentials to the brainstem and auditory cortex.

Problems that disrupt sound from reaching the cochlea are characterized as conductive hearing loss, and problems that affect the inner ear or auditory nerve are considered sensorineural hearing loss. Mixed hearing loss is a combination of the 2 types.

The UNHS programs use otoacoustic emission (OAE) testing or auditory brainstem response testing. During OAE testing, an earpiece containing a speaker and a microphone with recorder is placed in the infant's ear canal. The speaker emits sound that produces an expected response in the cochlea that is then measured by the microphone. A normal OAE test result requires a patent outer ear, functioning middle ear, and normal cochlea. The OAE tests are quick, inexpensive, and do not require that an infant be still or sedated. However, they are impacted by debris in the external canal and by middle ear effusions, both of which are common in neonates. They also do not require normal functioning of the auditory nerve and therefore do not detect some causes of sensorineural hearing loss.

Auditory brainstem response testing uses earpieces placed in the external auditory canal to emit clicks or tones and electrodes on the scalp to record the electrical activity of the resulting sound impulses as they are conducted along the auditory nerve to the brainstem. Auditory brainstem

response results can be affected by outer and middle ear conditions, but to a lesser degree than with OAE, and testing requires that the infant be calm and still.

It is crucial to remember that many causes of hearing loss are progressive and therefore may not be identified on UNHS. Children with risk factors for hearing loss (**Item C58**), children with evidence of language delay or other developmental delays, and children whose parents have concerns about their ability to hear should have additional screening and may need diagnostic audiology assessments.

Item C58. Risk Factors for Hearing Loss in Children.

Birth to Age 28 Days

- Family history of congenital or early-onset hearing loss
- Congenital infection known to be associated with hearing loss (eg, cytomegalovirus, rubella, herpes, syphilis, toxoplasmosis, varicella)
- Craniofacial abnormality
- Birth weight<1500 g
- Hyperbilirubinemia requiring exchange transfusion
- Exposure to ototoxic medications
- Bacterial meningitis
- Low Apgar scores at birth (<3 at 5 minutes and <6 at 10 minutes)
- Prolonged mechanical ventilation (>10 days)
- Findings consistent with a syndrome with known hearing loss

Ages 29 Days to 2 Years

- Concern about hearing, speech, language, or other developmental delay
- Bacterial meningitis
- Neonatal risk factors associated with hearing loss
- Head trauma, especially temporal bone fracture
- Findings of syndrome associated with sensorineural hearing loss
- Exposure to ototoxic medications (eg, aminoglycosides, loop diuretics, cisplatin)
- Neurodegenerative disorders
- Infectious diseases associated with hearing loss

Reprinted with permisson from Grindle, CR. Pediatric hearing loss. *Pediatr Rev*. 2014; 35(11), 456-463.

Formal audiologic testing may include OAE or auditory brainstem response, but both of these modalities are essentially tests of the auditory pathway integrity, not true tests of hearing. Definitive tests to confirm normal hearing also require audiograms. Behavioral audiometry, in which examiners observe for behavioral changes such as blinking or pauses in sucking, and visual reinforcement audiometry, in which infants are rewarded with visual stimuli for turning to a sound, can be used in infants as young as 6 to 9 months. Play audiometry, in which children are conditioned to perform a task in response to sound, can be used in children older than 2 years. By 4 years of age, many children can cooperate with conventional audiometry in which a child is asked to raise his or her hand in response to sound. These forms of audiometry assess hearing at a variety of frequencies and decibels, allowing hearing loss to be quantified and specified. The infant in this vignette, who did not pass a newborn hearing screen, must have follow-up testing before he is 3 months old. It would not be acceptable to delay testing until he is older or to pursue additional testing only if risk factors (family history of hearing loss or signs of hearing loss) are present. Newborn hearing screening is not diagnostic; it would also be inappropriate to refer the infant for a hearing aid fitting without confirmatory testing.

PREP Pearls
- All newborns should undergo hearing screening, and confirmatory testing for infants with abnormal screening results should occur before an infant is 3 months of age.
- Children at risk for hearing loss, children with a family history of congenital or early onset hearing loss, and children whose parents have concerns about their hearing should have ongoing hearing screening and may require formal audiologic assessment.

ABP Content Specifications(s)
- Understand how hearing loss is categorized by audiometric testing
- Understand the importance of a screening examination for hearing
- Understand the indications for audiometric testing

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.
- Harlor AD Jr, Bower C, Committee on Practice and Ambulatory Medicine, 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.
- National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention. *Hearing loss in children.* Centers for Disease Control and Prevention website. http://www.cdc.gov/ncbddd/hearingloss/index.html.

Question 59

A 4-year-old boy is brought to your clinic for the first time for a prekindergarten health supervision visit. The family recently moved from another state. The boy is asymptomatic, growing well, and developing normally. His vital signs are unremarkable. His physical examination reveals a heart murmur that occurs just after S1 has completed. The murmur is slightly louder in intensity than S1 or S2 and has a harsh quality to it. It is loudest at the upper right sternal border and is associated with a click. The remainder of his physical examination findings are normal. You explain to the mother that you will refer her son to a pediatric cardiologist for consultation. She becomes anxious and tearful.

To help the mother anticipate, you explain to her that this murmur is MOST consistent with

A. aortic valve stenosis
B. atrial septal defect
C. patent ductus arteriosus
D. pulmonary valve stenosis
E. ventricular septal defect

Correct Answer: A

Although up to 90% of children will have a cardiac murmur detected on physical examination at some point, less than 4 per 1,000 children will actually have heart disease. Determining the characteristics of a murmur, along with a careful history, is important to identify and understand the origin of the murmur and to properly refer children who need further evaluation. From a historical perspective, a provider should evaluate for exercise intolerance, feeding difficulties, cyanosis, syncope, tachypnea, shortness of breath, and dyspnea. A thorough review of the family medical history should look for associated diseases and syndromes such as collagen vascular diseases and maternal toxin exposures. Timing and clinical manifestations of heart murmurs will depend on the lesion and its severity. The patient in this vignette has a loud systolic murmur at the right upper sternal border associated with a click, a description that best fits aortic stenosis.

On physical examination, in addition to looking for signs of syndromes and noncardiac disease associated with congenital heart disease, one must also perform a thorough auscultation of the heart. The following findings on auscultation should always lead to referral for further evaluation: loud pansystolic murmurs, an abnormally loud or single S_2, an S_4 (S_4 gallop), or an ejection or midsystolic click. **Item C59** lists stereotypical heart sounds noted with various pathologies, although there are physiologic variations to these descriptions in actual practice.

An atrial septal defect in and of itself does not cause a murmur, but it can have an associated systolic murmur caused by increased blood flow across the pulmonary valve; this systolic murmur occurs during ejection at the upper left sternal border. Because the pulmonary valve itself is normal, there will not be an ejection click with an atrial septal defect, but a fixed split S_2 is typical. The murmur associated with a patent ductus arteriosus is continuous in nature, not limited to systole. Pulmonary valve stenosis is associated with a systolic murmur at the left upper sternal border and is often associated with a click. A ventricular septal defect results in turbulent blood flow throughout all of systole. The murmur of a ventricular septal defect is heard at the left lower sternal border.

Item C59. Stereotypical Heart Sounds Noted with Various Pathologies.

Lesion	Shape	Timing	Location	Other Findings
Ventricular septal defect (VSD)	Plateau	Holosystolic	LLSB	Apical mid-diastolic murmur with large shunt
Mitral regurgitation	Plateau	Holosystolic	Apex	Higher pitched than VSD murmur
Atrial septal defect	Ejection	Systolic	ULSB	Persistent S_2 split
Patent ductus arteriosus	Diamond	Continuous	ULSB	Bounding pulses
Aortic valve stenosis	Ejection	Systolic	URSB	Ejection click
Subvalvular aortic stenosis	Ejection	Systolic	ML-URSB	No ejection click
Hypertrophic cardiomyopathy	Ejection	Systolic	LLSB-apex	Laterally displaced PMI
Coarctation	Ejection	Systolic	ULSB-Left back	Pulse disparity
Pulmonary valve stenosis	Ejection	Systolic	ULSB	Ejection click; wide S_2 split
Tetralogy of Fallot	Ejection	Systolic	MLSB	Cyanosis

LLSB, lower-left sternal border; ULSB, upper-left sternal border; URSB, upper-right sternal border; MLSB, mid-left sternal border; S_2, second heart sound; PMI, point of maximal impulse.

Reprinted with permission from Harris JP. Evaluation of heart murmurs. *Pediatr Rev*. 1994;15(12); 490-492.

PREP Pearls
- Although up to 90% of children will have a cardiac murmur detected on physical examination at some point, less than 4 per 1,000 children will actually have heart disease.
- A loud systolic murmur at the right upper sternal border and associated with a click best fits a diagnosis of aortic stenosis.
- An atrial septal defect in and of itself does not cause a murmur, but it can have an associated systolic murmur caused by increased flow across the pulmonary valve; this murmur occurs during ejection at the upper left sternal border. A fixed split S_2 is typical.
- A ventricular septal defect results in turbulent flow throughout all of systole. The murmur of a ventricular septal defect is heard at the left lower sternal border.
- Timing and clinical manifestations of heart murmurs will depend on the lesion and its severity.

ABP Content Specifications(s)
- Recognize the major clinical findings associated with the various types of acyanotic congenital heart disease

Suggested Readings
- Harris JP. Consultation with the specialist: evaluation of heart murmurs. *Pediatr Rev.* 1994;15(12):490–492. doi: http://pedsinreview.aappublications.org/content/15/12/490.
- Menashe V. Heart murmurs. *Pediatr Rev.* 2007;28(4):e19–e22. doi: http://dx.doi.org/10.1542/pir.28-4-e19.
- Rao PS. Evaluation of cardiac murmurs in children. *Indian J Pediatr.* 1991;58(4):471–491.
- University of Washington Department of Medicine. Demonstrations: heart sounds and murmurs. https://depts.washington.edu/physdx/heart/demo.html.

Question 60

A previously healthy 5-year-old boy is brought to your office for evaluation of fever and sore throat that began yesterday. In addition, he has mild cough and nasal congestion with minimal rhinorrhea. His oral intake is decreased, and he reports mild abdominal pain.

He has a temperature of 39°C, heart rate of 100 beats/min, and respiratory rate of 24 breaths/min. He appears mildly ill. He has pharyngeal erythema, exudate on the tonsils, moderate palpebral conjunctivitis without discharge, and shotty, nontender, preauricular, and anterior cervical lymphadenopathy. The result of a rapid antigen detection test for group A Streptococcus is negative.

Of the following, the MOST likely etiology is

A. adenovirus
B. coxsackievirus
C. echovirus
D. Epstein-Barr virus
E. parainfluenza virus

Correct Answer: A

The constellation of signs and symptoms present in the boy in this vignette suggests the specific syndrome of pharyngoconjunctival fever caused by adenovirus. The key findings are abrupt onset of pharyngitis, palpebral conjunctivitis, fever, moderate degree of illness, and preauricular lymphadenopathy. Outbreaks of pharyngoconjunctival fever have been associated with swimming pools.

In young children, adenovirus is the most frequent cause of nonstreptococcal pharyngitis. The pharyngitis is exudative in about one-third of patients with adenovirus infection. Erythema of the palpebral conjunctiva can be severe enough to mimic subconjunctival hemorrhage. Mild cough and nasal congestion, minimal infiltrative lobular pneumonia, otitis media, diarrhea, and rash may also be present. Fever and most symptoms should improve within 4 to 7 days, with complete resolution in 10 to 14 days. Various serotypes of adenovirus cause more severe disease. Immunocompromised hosts are at risk for serious complications, even death.

Coxsackievirus and echovirus, which are both enteroviruses, typically produce pharyngitis with vesicles or ulcers; exudate is less commonly seen. A variety of exanthems and enanthems are associated with enteroviruses. Epstein-Barr virus is more common in older children and adolescents and usually presents with a severe exudative pharyngitis, fever, and malaise. Tender cervical lymph nodes, but not preauricular lymphadenopathy, are characteristic of Epstein-Barr virus. Parainfluenza viruses are usually associated with a more prominent cough or stridor and only a mild nonexudative pharyngitis. Clinicians should evaluate each report of sore throat with a thorough history and physical examination. In addition to consideration of the signs and symptoms, epidemiologic factors, such as the seasonality of infections and the age of the patient, should be considered in determining the most likely cause of pharyngitis.

PREP Pearls
- Adenoviruses are the most frequent cause of nonstreptococcal pharyngitis in young children.
- The specific syndrome of pharyngoconjunctival fever is caused by adenovirus.
- The combination of symptoms, physical examination findings, and epidemiologic factors should guide the differential diagnosis of pharyngitis.

ABP Content Specifications(s)
- Understand the natural history of viral infections of the throat

Suggested Readings
- American Academy of Pediatrics. Adenovirus 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; 2015:226–228. http://redbook.solutions.aap.org/chapter.aspx?sectionId=88187092&bookId=1484&resultClick=24.

- Gereige R, Cunill-De Sautu B. Throat infections. *Pediatr Rev.* 2011;32(11):459–469. http://pedsinreview.aappublications.org/content/32/11/459 .
- Weintraub B. Upper respiratory tract infections. *Pediatr Rev.* 2015;36(12):554–556. doi: http://dx.doi.org/10.1542/pir.36-12-554 .

Question 61

An 11-year-old boy with a rash is brought to the emergency department. He was in good health until 2 weeks ago when he had an illness characterized by severe abdominal cramping and bloody diarrhea. At that time, he was treated in the emergency department with pain medication and intravenous fluids. The abdominal pain and diarrhea resolved after 3 days. However, yesterday he had malaise and poor appetite. Today, he appears pale and has a rash. He has a temperature of 37.4°C, heart rate of 130 beats/min, respiratory rate of 24 breaths/min, and blood pressure of 110/65 mm Hg. He is pale and ill, but nontoxic in appearance. He has a petechial rash over his legs. Laboratory data are shown:

Laboratory Test	Result
White blood cell count	6,500/μL (6.5 x10^9/L)
Hemoglobin	7.8 g/dL (78 g/L)
Platelet count	87 x 10^3/μL (87 x 10^9/L)

A peripheral blood smear is shown in Item Q61.
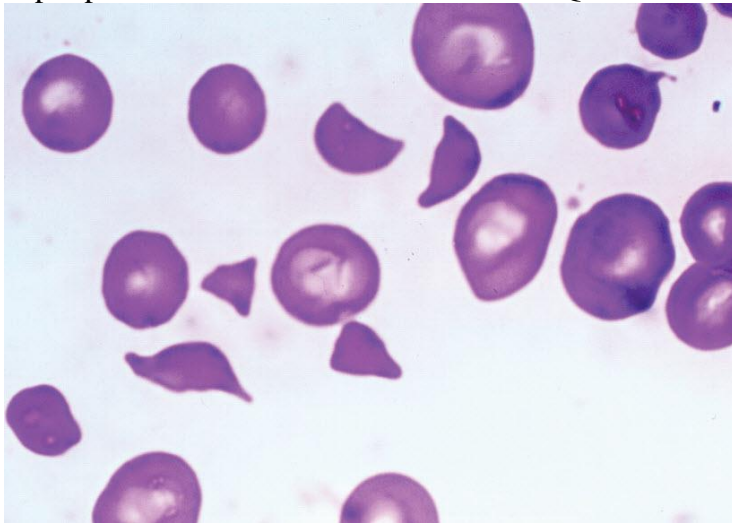
Item Q61: Peripheral blood smear for the boy described in the vignette.
Reprinted with permission from Corrigan JC, Boineau FG. *Pediatr Rev.* 2001, 22(11):366.

Of the following, the test that is MOST likely to confirm the diagnosis is

 A. blood culture
 B. coagulation profile test
 C. electrolytes
 D. hepatic panel
 E. renal function panel

Correct Answer: E

The test that is most likely to establish the diagnosis of the patient described in this vignette is a renal function panel. The patient in this vignette has hemolytic uremic syndrome (HUS) that developed 2 weeks after a diarrheal illness characterized by severe abdominal cramping and bloody diarrhea. Evaluation reveals microangiopathic hemolytic anemia (as evidenced by schistocytes on the peripheral smear) and thrombocytopenia. If the renal function panel reveals abnormalities, then the diagnosis of HUS can be confirmed by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and kidney injury.

Shiga toxin–producing *Escherichia coli* are responsible for the majority of cases of HUS; the most virulent strain is *E coli* 0157:H7. Twenty percent of patients with *E coli* 0157:H7 diarrhea develop HUS. Additional clinical findings of HUS can include neurologic manifestations such as seizures, somnolence, and coma.

The clinical findings associated with *E coli* infections vary by syndrome. Diarrhea caused by *E coli* can be acute or chronic. The diarrhea can range from watery to bloody; the etiology of bloody diarrhea is most likely to be enteroinvasive *E coli* or shiga toxin–producing *E coli*. Fever is characteristic of diarrheal illness caused by enteroinvasive *E coli* and is present in approximately one-third of cases of shiga toxin–producing *E coli* diarrhea.

In addition to causing diarrhea, *E coli* can also cause urinary tract infections, meningitis, and sepsis in neonates. The symptoms of *E coli* urinary tract infections cannot be distinguished from symptoms of other urinary pathogens and can include fever, foul-smelling urine, and urinary urgency, increased frequency, and hesitancy. Leukocytes and nitrites are often detected from urinalysis. If pyelonephritis is present, costovertebral tenderness may be elicited via physical examination. The symptoms of neonatal infection can be protean and include fever or hypothermia, respiratory distress or apnea, tachycardia, lethargy, and irritability. Peripheral white blood cell counts can vary from low to high in patients with sepsis, although cerebrospinal fluid pleocytosis would be expected in patients with meningitis.

Blood culture results are not expected to be positive in patients with HUS. A coagulation profile may be abnormal in patients with sepsis or HUS. Electrolyte levels could be abnormal in patients with diarrhea or renal failure. Abnormalities in the hepatic panel, including transaminitis or elevation of indirect bilirubin as a result of hemolysis can occur in HUS. Although coagulation profiles, electrolyte levels, and hepatic panels could potentially be abnormal in HUS, none of these abnormalities would be specific for the diagnosis.

PREP Pearls
- Hemolytic uremic syndrome is characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and kidney injury.
- Shiga toxin–producing *Escherichia coli* is responsible for most cases of hemolytic uremic syndrome.
- In addition to causing diarrhea, *Escherichia coli* is a cause of urinary tract infections, meningitis, and sepsis in neonates.

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ABP Content Specifications(s)
- Recognize the clinical and laboratory findings associated with *Escherichia coli* infection in children of various ages, including its association with hemolytic-uremic syndrome

Suggested Readings
- American Academy of Pediatrics. *Escherichia coli* and other gram-negative bacilli. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* Elk Grove Village, IL: American Academy of Pediatrics; 2015:340–343 .
- Makvana S, Krilov L. *Escherichia coli* infections. *Pediatr Rev.* 2015;36(4):167–171. doi: http://dx.doi.org/10.1542/pir.36-4-167 .

Question 62

A 4-month-old female infant who was well until 3 days ago is brought to the urgent care center by her parents for increasing difficulty breathing and a cough. She has been breastfeeding less than usual and her urine output is decreased. On physical examination, the infant is awake and fussy but consolable. She is afebrile, with a respiratory rate of 66 breaths/min and pulse oximetry of 92% on room air. She has scattered wheezing and rhonchi bilaterally on auscultation of her lungs, with subcostal and suprasternal retractions. You diagnose her with viral bronchiolitis.

Of the following, the BEST next management step for this infant is to

  A. administer nasogastric or intravenous fluids
  B. administer nebulized albuterol
  C. administer supplemental oxygen
  D. perform polymerase chain reaction for specific viral etiologies
  E. perform chest radiography

Correct Answer: A

The infant in the vignette has viral bronchiolitis, with evidence of increased respiratory effort. Her history is significant for decreased oral intake and urine output. On physical examination, she is tachypneic, has subcostal and suprasternal retractions, and her oxygen saturation is 92%. The infant's most urgent issue is hydration, because she is unlikely to be able to take in adequate fluids at this time. Thus, the best next management step for this girl is to administer nasogastric or intravenous fluids.

Approximately 1 in 5 infants sees a health care provider for bronchiolitis during the first year after birth. Clinical features include fever, rhinorrhea, nasal congestion, and cough. Signs of respiratory distress may be present, such as tachypnea and increased respiratory effort, manifested as nasal flaring and intercostal, subcostal, and supraclavicular retractions. On lung examination, crackles and expiratory wheezing are typically heard. Apnea may occur, particularly in neonates or young infants born prematurely. Although most cases are treated in the outpatient setting, 2% to 3% of all infants are hospitalized for bronchiolitis. Chronic lung disease, congenital heart disease, and immunodeficiency are risk factors for developing more severe disease. Bronchiolitis is a seasonal illness. In most areas of North America, cases are first seen in the late fall, peak in January or February, and cease in the early spring.

Most (50%–80%) bronchiolitis cases requiring hospitalization are attributable to respiratory syncytial virus (RSV). For term infants, maternal immunity to RSV is commonly conferred in the third trimester, but quickly wanes, providing protection only in the first month or so. Depending on their gestational age at delivery, preterm infants may not receive this protection, placing them at increased risk for infection and more severe illness.

The American Academy of Pediatrics guidelines on the diagnosis and treatment of bronchiolitis outline recommendations for infants and children aged 1 to 23 months. Chest radiography and testing for viruses are not recommended for routine diagnostic use; for generally healthy infants, bronchiolitis is diagnosed based on history and physical examination findings. The mainstay of treatment is supportive care, which includes supplemental oxygen for saturations less than 90% and hydration/nutrition support via intravenous line or nasogastric tube for infants whose oral intake is compromised. Bronchodilators, epinephrine, steroid therapy, nebulized hypertonic saline, chest physiotherapy, and antibiotics are not recommended for routine use. Although bronchodilators may decrease symptoms for a select population of infants, there is no way to identify these infants. Conducting a before-and-after assessment of respiratory function, even with a validated scale, is problematic because symptoms are often intermittent, and a natural change in symptoms may lead to a false impression that albuterol is helpful. Supplemental oxygen for neonates or infants with saturations greater than 90% has not been shown to improve clinical outcomes. Continuous pulse oximetry is discouraged. Because oximeter readings often dip below the threshold of 90% only briefly, continuous oximeter monitoring has the potential to falsely suggest a need for continuous oxygen supplementation, and may lead to unnecessary or prolonged hospitalization. There may be a role for home-based oxygen therapy or high-flow air-

oxygen via nasal cannula for hospitalized infants, but the evidence to support broad adoption of these treatments is not yet available.

PREP Pearls
- The mainstay of treatment for viral bronchiolitis is supportive care, which includes supplemental oxygen for saturations less than 90% and hydration/nutrition support via intravenous line or nasogastric tube for infants whose oral intake is compromised.
- Chest radiography and viral testing are typically unnecessary for the diagnosis of viral bronchiolitis.
- Bronchodilators, epinephrine, steroid therapy, nebulized hypertonic saline, chest physiotherapy, and antibiotics are not recommended for routine use in the treatment of bronchiolitis.

ABP Content Specifications(s)
- Plan the appropriate management of bronchiolitis
- Recognize the clinical findings associated with bronchiolitis

Suggested Readings
- Meissner HC. Viral bronchiolitis in children. *N Engl J Med.* 2016;374:62–72. doi: http://dx.doi.org/10.1056/NEJMra1413456.
- Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. *Pediatrics*. 2014;134(5):e1474–e1502. doi: http://dx.doi.org/10.1542/peds.2014-2742.

Question 63

An 11-month-old male infant has been repeatedly seen in your practice over the last 3 months because of an unrelenting rash. The rash started in the diaper area as pink papules with a brownish crust, and then it appeared behind the ears bilaterally as pink flaky lesions. About the same time, the infant developed diffuse erythematous papular lesions on the scalp with gray scales. Topical treatments including nystatin cream and 1% hydrocortisone ointment have yielded no improvement. The application of baby oil to the scalp followed by combing out the flakes also yielded no improvement. There is no rash on the infant's arms or legs. According to his mother, there has been no recent change to his diet, brand of diapers, carpeting, bedding, skin soap, or clothing detergent. His only medication, other than the topical treatments, is a multivitamin.

Until the onset of the rash, the child was healthy. His growth and development are normal. He is at the 45th percentile for height and the 55th percentile for weight, which are consistent with his prior office visits. His vital signs are normal for his age. His heart, lung, abdominal, extremity, and gonadal examination findings are normal. However, there is a clear discharge from the right ear. An otoscopic examination reveals an inflamed, occluded right external ear canal and a normal left ear canal. His skin examination findings are remarkable for the lesions shown in Item Q63. The results of a complete blood cell count and complete metabolic panel are normal.

You refer the infant to a pediatric dermatologist who performs a biopsy.

Item Q63: Rash for the infant described in the vignette.

Of the following, the skin biopsy is MOST likely to show

  A. allergic dermatitis, most consistent with a drug eruption
  B. candidal skin infection
  C. Langerhans cell histiocytosis
  D. Sarcoptes scabiei infection
  E. stage MS (formerly 4S) neuroblastoma

Correct Answer: C

The otherwise healthy infant in this vignette has a dermatologic process involving the diaper area, scalp, and ear canal. Treatments including antifungal and corticosteroid ointments have been tried. This presentation along with the appearance of the rash shown in **Item C63** should raise concern for Langerhans cell histiocytosis (LCH), a rare disease that involves the abnormal proliferation of histiocytes.

Item C63: Rash suggestive of Langerhans cell histiocytosis.
Reprinted with permission from Krowchuk DP, Mancini AJ, eds. *Pediatric Dermatology; A Quick Reference Guide.* 2nd ed. Elk Grove Village, IL; The American Academy of Pediatrics. 2012.

This disease most commonly occurs in children and adolescents between 1 and 15 years of age. The LCH lesions can present in a single site (unifocal) or multiple sites (multifocal) and in single organs or multiple organs. The most commonly affected organs are the bones and skin. The most common presentations are osteolytic, painful bony lesions and eruptions on the scalp, although LCH can present with persistent fevers, weight loss, lethargy, and pancytopenia. In some children, multifocal LCH can involve the pituitary stalk and leads to diabetes insipidus. The pathogenesis of LCH is unclear. Whether LCH is a reactive process or a true malignancy has been the subject of debate; however, the recent identification of *BRAF* mutations in the abnormal histiocyte population suggests a clonal malignancy. Despite the prevalence of *BRAF* mutations within the lesions, LCH is not an inherited disease.

When LCH is suspected, a confirmatory biopsy should be performed, and the child should undergo a complete skeletal survey, magnetic resonance imaging of the pituitary gland, and determination of urine specific gravity and serum sodium concentration, as well as a bone marrow aspirate and biopsy if a cytopenia is present. If LCH presents as a solitary bone lesion, the biopsy should be performed as a curettage, which often stimulates spontaneous regression such that no further therapy is needed. In multisystem disease or solitary bone disease in certain

"risk" areas, systemic chemotherapy with corticosteroids and vinblastine is indicated. Children with single-focus disease have an excellent prognosis. However, up to 60% of children with multifocal or multiorgan disease will have a chronic course with a mortality rate of up to 10%.

Because the infant in this vignette has not been taking medications other than a multivitamin, a drug eruption is unlikely. Although the appearance of the rash in the picture could be consistent with a candidal rash, the lack of improvement with topical antifungal treatment and the involvement of the scalp and the ear canal makes a cutaneous candidal infection less likely. The appearance of the rash and the involvement of the scalp and ear canal are not consistent with a *Sarcoptes scabiei* infection. Stage MS neuroblastoma, a malignant proliferation of embryonal cells of neural crest origin, commonly presents in infants and can involve subcutaneous nodules, but it does not present with an erythematous scaly rash.

PREP Pearls
- Langerhans cell histiocytosis should be considered when skin lesions in the diaper area and scalp persist despite frontline therapy.
- In some children, multifocal Langerhans cell histiocytosis can involve the pituitary stalk and lead to diabetes insipidus with associated increased thirst and urination.
- Children with a confirmed Langerhans cell histiocytosis lesion should undergo a complete evaluation for distant disease, including a skeletal survey and magnetic resonance imaging of the pituitary, as well as bone marrow biopsy if a cytopenia is present.

ABP Content Specifications(s)
- Recognize the clinical findings associated with histiocytosis syndromes of childhood

Suggested Readings
- Allen CE, Kelly KM, Bollard CM. Pediatric lymphomas and histiocytic disorders of childhood. *Pediatr Clin North Am*. 2015;62(1):139–165. doi: http://dx.doi.org/10.1016/j.pcl.2014.09.010.
- Allen CE, Ladisch S, McClain KL. How I treat langerhans cell histiocytosis. *Blood*. 2015;126(1):26–35. doi: http://dx.doi.org/10.1182/blood-2014-12-569301 .
- Badalian-Very G, Vergilio JA, Degar BA, et al. Recurrent BRAF mutations in langerhans cell histiocytosis. *Blood*. 2010;116(11):1919–1923. doi: http://dx.doi.org/10.1182/blood-2010-04-279083 .

Question 64

A 10-year-old boy with a 2-week history of fever up to 38.9°C, cough, malaise, and fatigue is brought to your office. He has experienced a 1-kg weight loss and reports left-side chest pain. The patient and his family returned from a camping trip in the Grand Canyon 4 weeks ago.

The boy appears fatigued. He has mild tachypnea and splinting of respiratory effort. Auscultation of the chest is significant for decreased breath sounds and a pleural rub at the left lung base. A chest radiograph confirms a small left-sided pleural effusion. Examination of the heart, abdomen, and oropharynx are unremarkable. You suspect acute coccidioidomycosis.

Of the following, the finding MOST supportive of this diagnosis is

A. centrilobular nodules with "tree in bud" pattern on computed tomography of chest
B. cutaneous involvement with finding of erythema nodosum
C. detection of coccidioides antigen in urine by enzyme immunoassay
D. detection of serum complement fixation antibody
E. eosinophilia on complete blood cell count

Correct Answer: D

Complement fixation testing is highly specific for a diagnosis of coccidioidomycosis. Coccidioidomycosis or "valley fever" is a disease caused by a fungus, *Coccidioides.* The fungus is most frequently encountered in the soil from the southwestern United States (California, Arizona, New Mexico, Texas, Nevada, and Utah) and also in areas of Mexico, Central America, and South America. The prevalence of coccidioidomycosis in endemic areas increased significantly between 1998 and 2011 with a rise in reported cases from 5.3 to 42.6 per 100,000 population. In some cases, outbreaks of disease may be attributable to events that cause soil disruption or dust generation, such as storms or excavations, but more often, disease occurs sporadically and without apparent antecedent cause.

The 2 species of *Coccidioides* are *C immitis*, which is mostly found in California, and *C posadasii*, which is more commonly encountered in the southwestern United States, northern Mexico, Central America, and South America.

Coccidioides organisms are pathologically identifiable as branching, septate hyphae. Arthroconidia (or spores) from these hyphae may become airborne, and infection occurs almost exclusively through inhalation of fungal spores. Rarely, infection has been spread from cutaneous lesions or through organ transplantation. The incubation period is 1 to 4 weeks. In the pediatric population, infection is asymptomatic or self-limited in 60% of cases. Because associated symptoms may be mild and are often nonspecific, the disease may be overlooked or attributed to more common viral or community-acquired pathogens. The symptoms of primary pulmonary infection with *Coccidioides* include malaise, cough, myalgias, fever, headache, and chest discomfort. During seasonal outbreaks, symptoms may be erroneously attributed to influenza. Pleural and mediastinal disease, including effusion or lymphadenopathy, are complications more commonly encountered in children.

Primary infection may be confined to cutaneous abnormalities. Findings include erythema multiforme or erythema nodosum. Cutaneous manifestations, when present, are generally associated with regional lymphadenopathy or lymphadenitis.

Disseminated infection is rare, occurring in less than 0.5% of infected individuals. In addition to the integument, dissemination may occur to the bones and articular joints or to the central nervous system. Meningeal disease, when encountered, is devastating and nearly uniformly fatal. Risk factors for severe or disseminated disease include age younger than 1 year and impairment of T-cell immunity. Pregnant women in the third trimester and individuals of African and Filipino descent are also at greater risk than the general population. Disseminated disease may occur many years after initial infection.

A diagnosis of coccidioidomycosis may be confirmed through serology or histopathology. Culture analysis may also be used, although fungal growth is slow in culture media. With serologic approaches, a positive IgM response may be detected by enzyme immunoassay or immunodiffusion methods as early as 1 to 3 weeks after infection. A positive IgG response can be detected by immunodiffusion, enzyme immunoassay, or complement fixation methods.

Immunodiffusion and complement fixation tests are highly specific. Serum complement fixation antibody titers are likely to be low and may be transient in mild or asymptomatic disease. When titers are markedly elevated ($\geq$ 1:16), there should be concern for severe disease or disseminated infection.

Enzyme immunoassay testing for detection of *Coccidioides* antigen may be performed on urine, serum, plasma, or bronchoalveolar lavage fluid. Antigen is more likely to be present in patients with more severe forms of disease, but confounding of results may occur in patients with other fungal infections, including histoplasmosis or blastomycosis. A trend of titers is also instructive; rising titers are indicative of progressive disease while falling titers are expected during the recovery phase. In immunocompromised individuals, complement fixation titers may be inaccurate.

Diagnosis may also be confirmed through isolation of *Coccidioides* species in culture from bronchoalveolar lavage, pleural fluid, or other sites of infection (skin, cerebrospinal fluid). Pathologic confirmation is best established with the aid of silver or periodic-acid Schiff staining to visualize mature fungal spherules and endospores. As culture of the fungus can be of potential risk to laboratory personnel, a DNA probe may be utilized to identify the organism with a higher level of safety.

The radiographic finding most associated with coccidioidomycosis is a lobar or multilobar infiltration. Cavitary disease may occur, and while most such lesions will resolve radiographically, a subset may become chronic. A pleural effusion, mediastinal lymphadenopathy, or both can also be seen. Computed tomography may reveal the "tree in bud" pattern of fungal infection. More commonly, computed tomography will allow identification of nodular or cavitary disease and will determine the extent of mediastinal involvement. Eosinophilia may be seen in peripheral blood or in cerebrospinal fluid specimens during active or convalescent disease states. These radiographic and laboratory findings, although suggestive of disease, are less sensitive and specific than complement fixation.

PREP Pearls
- In children with coccidioidomycosis, symptoms are self-limited and mild in 60% of cases.
- Immunodiffusion and complement fixation studies from serum are highly specific for coccidioidomycosis.
- Infants and immunocompromised individuals are at high risk for disseminated or severe forms of infection with *Coccidioides.*

ABP Content Specifications(s)
- Plan the diagnostic evaluation of a suspected Coccidioides infection, and manage appropriately

Suggested Readings

- American Academy of Pediatrics. Coccidioidomycosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. In: *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:302–305.
- Centers for Disease Control and Prevention. Increase in reported coccidioidomycosis—United States, 1998–2011. *MMWR Morb Mortal Wkly Rep.* 2013;62(12):217–221.
- Centers for Disease Control and Prevention. Valley fever (coccidioidomycosis). https://www.cdc.gov/fungal/diseases/coccidioidomycosis/index.html.

Question 65

You are seeing an 11-year-old girl in your office for a health supervision visit. She reports daily headaches that started 2 months ago. The headaches are described as pounding, with nausea and vomiting, but no phonophobia or photophobia. The pain worsens when she leans over to put on her shoes and socks. Occasionally, her vision will turn gray for a few seconds. When her headache is severe, the girl develops double vision. She does not take any medications or supplements. She reports that her weight has increased by more than 20 lbs since her visit 1 year ago. On physical examination, the girl's blood pressure is 102/78 mm Hg and her heart rate is 92 beats/min. Her body mass index is at the 96th percentile. Her neurologic examination shows an inability to abduct her right eye.

Of the following, the MOST likely additional finding on this girl's physical examination would be

A. cataracts
B. nystagmus
C. orbital bruit
D. papilledema
E. ptosis and pupillary miosis

Correct Answer: D

The girl in the vignette has pseudotumor cerebri. Her neurologic examination shows a right cranial nerve VI palsy, which is a sign of increased intracranial pressure. Papilledema may be seen with increased intracranial pressure, so of the choices, this is the most likely finding in this girl. Pseudotumor cerebri is a condition in which there is increased intracranial pressure but no intracranial mass, hydrocephalus, or other structural abnormality. It is sometimes called "idiopathic intracranial hypertension." Risk factors for pseudotumor cerebri include obesity, especially with recent weight gain, and female sex. Medications such as isotretinoin or doxycycline can cause pseudotumor cerebri as well. Symptoms of pseudotumor cerebri include headache, nausea, vomiting, transient visual obscurations (the entire visual field briefly turns gray, as in the girl in the vignette), tinnitus, and headache that worsens with bending over. Neurologic examination findings include papilledema and sometimes a cranial nerve VI palsy. Performing the fundoscopic examination in a darkened room makes it much easier to see papilledema. Untreated pseudotumor cerebri can result in permanent vision loss. In patients with new-onset headaches, clinicians should always assess for evidence of increased intracranial pressure.

None of the other choices listed are associated with increased intracranial pressure. Cataracts are a clouding of the lens in the eye. Symptoms include slowly progressive blurry vision, not transient visual obscurations as described for the girl in the vignette. Nystagmus is a rapid beating movement of the eyes. It can be seen with injury to the brainstem or cerebellum, and sometimes as a medication side effect. It is not a typical finding in increased intracranial pressure, unless the increased pressure is due to a tumor or stroke affecting the brainstem or cerebellum. Orbital bruits, heard on auscultation with the stethoscope bell over the eye, are associated with vascular abnormalities such as carotid stenosis, arteriovenous fistula, or carotid cavernous fistula. The girl in the vignette does not have symptoms of an intracranial vascular abnormality, so this is not the best choice. Ptosis and pupillary miosis are 2 of the 3 findings in Horner syndrome, the third is anhidrosis. Horner syndrome can occur from disruption of the sympathetic pathway that innervates the eye, anywhere along its course from the brain, neck, chest and up to the orbit. It is not a sign of pseudotumor cerebri, and so would not be an expected finding in the girl in the vignette.

PREP Pearls
- Untreated pseudotumor cerebri can result in permanent vision loss.
- Clinicians should always assess patients with headache for signs and symptoms of increased intracranial pressure.
- Signs of increased intracranial pressure include papilledema and cranial nerve VI palsy.

ABP Content Specifications(s)
- Recognize the clinical findings associated with papilledema

Suggested Readings

- Armstrong S, Lazorick S, Hampl S, et al. Physical examination findings among children and adolescents with obesity: an evidence-based review. *Pediatrics*. 2016;137(2):e20151766. doi: http://dx.doi.org/10.1542/peds.2015-1766.
- Puthawala C, Hansen S. Case 1: diplopia in a 15-year-old boy. *Pediatr Rev*. 2016;37(4):169–171. doi: http://dx.doi.org/10.1542/pir.2015-0148.

Question 66

A couple new to your practice recently became foster parents to their 12-year-old nephew. He was removed from a neglectful home with a substance-abusing adult. The boy has been having major behavioral problems with inattention and aggression toward adults and peers, both at home and school. He is now receiving intensive outpatient behavioral health care. The boy's medical history is significant for several extremity fractures. He has been otherwise well, with only minor illnesses, and his physical examination findings are normal. The foster parents ask you about the child's risk for future behavioral and physical health problems as a consequence of his maltreatment.

Of the following, the MOST accurate statement about this family's concern is

- A. a supportive home and consistent discipline is usually sufficient to overcome the effects of these experiences
- B. early childhood experiences such as these have no major effect on the child's subsequent physical health
- C. physiologic changes that result from these early childhood experiences are temporary and reversible
- D. stress from this type of early childhood experience may lead to structural changes in the brain
- E. the physiologic effects of this type of early childhood experience occur only in the brain

Correct Answer: D

Children who are victims of abuse or neglect often grow into adults with more behavioral and physical health problems than the general population. In recent years, a growing body of evidence indicates that chronic or repeated stress, such as occurs with abuse/neglect, can result in physiologic and anatomic changes. The concept of "toxic stress" proposes that strong, frequent, or prolonged activation of stress response systems (the hypothalamic-pituitary-adrenal and sympathetic-adrenomedullary systems) without the buffering presence of a nurturing or supportive adult disrupts brain, neuroendocrine, and immune development during developmentally sensitive periods. This leads to anatomic changes and physiologic dysregulation that may be lifelong, and is the basis for the chronic stress-related physical and behavioral health problems seen in adults who were abused as children. Human and animal studies show that individuals who encounter adverse events such as abuse during early development have lower overall brain volumes with architectural and size differences in the amygdala (necessary for emotional regulation), hippocampus (necessary for encoding and retrieving memory), and prefrontal cortex (the seat of executive function).

In addition to central nervous system effects, there is evidence of immune hyperreactivity among children and adults with a history of abuse and neglect, a likely contributor to the observed increased incidence of asthma and elevated inflammatory markers (eg, C-reactive protein). Adults who were abused as children have higher prevalences of cardiovascular disease, lung and liver disease, hypertension, diabetes mellitus, and obesity compared with the general population. Available evidence, derived largely from retrospective studies, suggests a wide range of behavioral health consequences for children experiencing abuse and neglect, ranging from normal functioning to adverse outcomes such as school failure, unemployment, poverty, incarceration, mood disorders, post-traumatic stress syndrome, interpersonal problems, substance abuse, borderline personality disorder, somatization, psychosis, and dissociative identity disorder. The role of nature versus nurture has long been debated regarding children with these outcomes. A better framework in which to consider early childhood adversity, including abuse and neglect, has been proposed by Shonkoff et al as an "ecobiodevelopmental" approach, which considers multiple factors, including physiological adaptations and disruptions, epigenetics, anatomic development, and children's social and physical environment.

Prevention is the ideal approach to reduce the long-term effects of child abuse and neglect; however, this is not always feasible. Evidence-based approaches to treatment exist, with variable success. A supportive home, with fair and consistent discipline, is recommended for all children. However, for those who experienced early childhood adversity, this approach alone is often not sufficient. Routine discipline that is effective for a child without a history of toxic stress may be perceived as a stress-inducing threat to a previously abused child, and may cause escalation of the behavior rather than extinction. Cognitive behavioral therapy that addresses safety skills, stress management, and emotion regulation, as well as the formulation of an organized and accurate trauma narrative, has proved effective for symptom reduction in other trauma-related situations.

PREP Pearls
- Adults who were abused or neglected as children are at greater risk of physical and behavioral health concerns compared with the general population.
- In "toxic stress," strong, frequent, or prolonged activation of stress response systems (hypothalamic-pituitary-adrenal and sympathetic-adrenomedullary) during developmentally sensitive periods, without the buffering presence of a nurturing or supportive adult, disrupts brain, neuroendocrine, and immune development.
- Individuals who encounter adverse events, such as abuse during early development, have lower overall brain volumes with architectural and size differences in the amygdala (necessary for emotional regulation), hippocampus (necessary for encoding and retrieving memory), and prefrontal cortex (the seat of executive function).
- Cognitive behavioral therapy that addresses safety skills, stress management, and emotion regulation, as well as formulation of an organized and accurate trauma narrative, has the potential to decrease some of the long-term consequences of childhood abuse and neglect.

ABP Content Specifications(s)
- Plan the appropriate evaluation and management of suspected child abuse
- Understand the behavioral and emotional consequences of child physical abuse

Suggested Readings
- American Academy of Pediatrics, Stirling J Jr; Committee on Child Abuse and Neglect and Section on Adoption and Foster Care; American Academy of Child and Adolescent Psychiatry, Amaya-Jackson L; National Center for Child Traumatic Stress, Amaya-Jackson L. Understanding the behavioral and emotional consequences of child abuse. *Pediatrics*. 2008;122:667-673. doi: http://dx.doi.org/10.1542/peds.2008-1885.
- Johnson SB, Riley AW, Granger DA, Riis J. The science of early life toxic stress for pediatric practice and advocacy. *Pediatrics*. 2013;131:319-327. doi: http://dx.doi.org/10.1542/peds.2012-0469.
- Shonkoff JP, Garner AS, Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*. 2012;129:e232-e246. doi: http://dx.doi.org/10.1542/peds.2011-2663.

Question 67

A 16-month-old girl is brought to your office with fever, bloody diarrhea, and vomiting. She lives on a farm and has been drinking unpasteurized cow milk. No other family members are ill. Her temperature is 38°C. She is pale and has mild dehydration. Laboratory data are shown:

Laboratory Test	Result
Hemoglobin	10.6 g/dL (106 g/L)
Sodium	130 mEq/L (130 mmol/L)

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

A. Bacillus cereus
B. Campylobacter jejuni
C. enterotoxigenic Escherichia coli
D. Mycobacterium bovis
E. Shigella sonnei

Correct Answer: B

Campylobacter species are a leading bacterial cause of foodborne gastroenteritis in children. The clinical presentation of the child in this vignette with bloody diarrhea and a history of consumption of unpasteurized cow milk is consistent with gastroenteritis caused by *Campylobacter* species. *Campylobacter jejuni* and *Campylobacter coli* colonize the gastrointestinal tracts of chickens, turkeys, and other farm animals and are present in their environment; rates of *Campylobacter* colonization in chickens are up to 80%. Transmission of *Campylobacter* infection occurs by ingestion of unpasteurized milk, undercooked poultry products, or contaminated water or by contact with infected animals or humans. Outbreaks of *Campylobacter* infection in schools following ingestion of unpasteurized milk have been reported in the United States. Person-to-person spread of *Campylobacter* infection has resulted in outbreaks of gastroenteritis in day care centers and hospital nurseries.

Campylobacter species are gram-negative, spiral, motile, non–spore-forming bacilli. The most commonly implicated diarrhea-causing *Campylobacter* species are *C jejuni* and *C coli*, whereas *C fetus* can cause intestinal infection and severe systemic infection. The Centers for Disease Control and Prevention funds the Foodborne Diseases Active Surveillance Network at 10 United States sites, and this network reported an incidence of 13.8 culture-proven *Campylobacter* cases per 100,000 individuals in 2013. In resource-rich countries, cases of *Campylobacter enteritis* peak during the summer and early fall. Children younger than 5 years have the highest rates of infection with 24.08 cases per 100,000 individuals in 2009.

Infection with *Campylobacter* species typically manifests as an acute gastrointestinal illness with fever, diarrhea, and crampy abdominal pain. The diarrhea may be watery but can become mucoid with frank blood mimicking inflammatory bowel disease. In neonates and young infants, the illness may be characterized by bloody diarrhea without fever. The illness is often self-limited with clinical recovery noted within 1 week without antibiotic therapy. Prolonged or severe disease or relapse occurs in 10% to 20% of patients. Complicated disease (eg, extraintestinal infections, bacteremia) may occur following infection with *C fetus* or other species in immunosuppressed individuals; in addition, a prolonged course and relapses may occur in immunosuppressed individuals. In neonates, *C fetus* can cause sepsis and meningitis. Immune-mediated complications including Guillain-Barré syndrome (and variant Miller Fisher syndrome), reactive arthritis, Reiter syndrome, myopericarditis, and erythema nodosum may occur following *Campylobacter* infection.

Campylobacter species grow slowly, and isolation may be problematic in routine stool cultures. *Campylobacter jejuni* and *C coli* can be isolated from stool specimens by using selective media and a microaerobic environment; these species grow best in 5% to 10% oxygen and at a temperature of 42°C. Direct examination of stool by dark-field microscopy can detect the organism. Non–culture-based methods (such as enzyme immunoassays) are available for rapid diagnosis of *C jejuni* and *C coli*, but false-positive results can occur. Recently, more sensitive multiplex polymerase chain reaction assays have been developed to detect *Campylobacter* species and other common enteric pathogens. In severe infections or infections complicated by

bacteremia or sepsis caused by *C fetus,* it is crucial to isolate the organism by culture to obtain the antimicrobial susceptibility data needed to guide antibiotic therapy.

Most patients with *Campylobacter enteritis* will recover with treatment of dehydration and replacement of fluids and electrolytes, without the need for specific antimicrobial therapy. A 3-day course of azithromycin (10 mg/kg/d) decreases the duration of diarrheal illness and fecal shedding of *Campylobacter* organisms, andearly treatment may prevent relapses. The emergence of antimicrobial resistance in *Campylobacter* species is a major concern. Widespread use of antibiotics by the food industry has compounded this problem. Hospitalized patients with *Campylobacter* gastroenteritis must be placed on contact precautions for the duration of the enteritis illness.

Enterotoxigenic *Escherichia coli* causes watery diarrhea among infants living in low- and middle-income countries. In addition, enterotoxigenic *E coli* is a common cause of traveler's diarrhea in all age groups. *Bacillus cereus* is an important cause of toxin-mediated foodborne illness in the United States and can cause both an emetic and diarrheal syndrome. The emetic syndrome can occur following ingestion of contaminated fried rice containing preformed enteric toxin. The diarrheal syndrome caused by *B cereus* is a severe illness and results in watery diarrhea, vomiting, and abdominal pain. *Mycobacterium bovis* is a rare cause of human infection caused by ingestion of unpasteurized milk and other contaminated dairy products. The principal clinical syndromes of *M bovis* are cervical lymphadenitis, intestinal disease, and meningitis. *Campylobacter* species are a more common cause of bacterial gastroenteritis causing bloody diarrhea in children as compared to infections caused by *Shigella* species, Shiga toxin–producing *E coli*, *Salmonella* species, and *Yersinia* species. *Shigella sonnei* infection is transmitted from person to person via the fecal-oral route and has a higher rate of infection than *Campylobacter* species. The illness is characterized by watery or mucoid stools and/or dysentery, abdominal pain, and tenesmus. Infants with *Shigella* infection can develop high fever, severe dehydration, and self-limited seizures.

PREP Pearls
- *Campylobacter* is a leading bacterial cause of foodborne gastroenteritis in children. The most commonly implicated diarrhea-causing species are *C jejuni* and *C coli*.
- Transmission of *Campylobacter* infection occurs by ingestion of unpasteurized milk, undercooked poultry products, or contaminated water and by exposure to infected animals or humans.
- Infection with *Campylobacter* species typically manifests as an acute gastrointestinal illness with fever, diarrhea, and crampy abdominal pain; in neonates and young infants, the illness may be characterized by bloody diarrhea without fever.
- Treatment with azithromycin or erythromycin decreases the duration of diarrheal illness by hastening eradication of *Campylobacter* organisms in the feces by 2 to 3 days.

ABP Content Specifications(s)
- Understand the epidemiology of Campylobacter infections
- Plan appropriate management for a patient with Campylobacter infection
- Recognize the clinical features associated with a Campylobacter infection

Suggested Readings
- American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Nutrition. Consumption of raw or unpasteurized milk and milk products by pregnant women and children. *Pediatrics*. 2014;133(1):175–179. doi: http://dx.doi.org/10.1542/peds.2013-3502.
- American Academy of Pediatrics. *Campylobacter* infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Disease*s. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:273–275 .
- Centers for Disease Control and Prevention. Incidence and trends of infection with pathogens transmitted commonly through food–Foodborne Diseases Active Surveillance Network, 10 U.S. Sites, 2006-2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(15):328–332.

Question 68

A 13-year-old adolescent girl comes to your office with her mother for her annual health supervision visit. She has lost a significant amount of weight since you saw her last; her body mass index has dropped from the 70th percentile to the 5th percentile over the past year.

She is thin and alert with a heart rate of 43 beats/min, respiratory rate of 23 breaths/min, and blood pressure of 103/58 mm Hg. She has moist mucous membranes with no oral ulceration. Her cardiac examination results are normal with the exception of bradycardia. Her respiratory examination demonstrates good air movement with no wheeze or rhonchi. Her abdomen is scaphoid and soft with hypoactive bowel sounds. She reports intentional significant weight loss following frequent cleanses and multiple diet modifications, including the grapefruit juice diet. She is admitted to adolescent care for continued evaluation and treatment.

Of the following laboratory findings on admission, this patient is MOST likely to demonstrate an elevated

  A. alanine aminotransferase level
  B. bicarbonate level
  C. creatinine level
  D. hematocrit
  E. serum potassium level

Correct Answer: D

The teenage girl in this vignette is malnourished because of significant weight loss associated with recent fad diet use. On admission, her hematocrit is likely to be elevated because of hemoconcentration. Iron deficiency and anemia are not common at the time of initial presentation.

Fad diets often focus on dietary limitation of one nutritional component (eg, gluten, carbohydrates, fat, protein). There is little to no evidence that fad diets work, and there is significant concern for diet failure, harm caused by dietary restriction, and/or risk for development of an eating disorder. Long-term effects and outcomes of fad diets have not been fully studied. Weight loss recommendations for children and adolescents should be holistic and inclusive of the entire family. Nutrition, activity, behaviors, and beliefs must be addressed. The parents must support the diet, or success will be limited.

Fad diets promise dramatic weight loss, however they are associated with many complications (**Item C68**).

Item C68. Potential Fad Diet Complications.

Diet Complication	Mechanism
Dehydration	Gastrointestinal and/or renal losses; inadequate intake
Electrolyte abnormalities	Gastrointestinal and/or renal losses; inadequate intake
Vitamin deficiency	Inadequate intake
Ketosis	Carbohydrate limitation
Thyroid dysfunction	Inadequate iodine intake
Renal dysfunction	High protein intake
Development of eating disorder	Multifactorial

Courtesy of C. Waasdorp Hurtado

Fad diets may also be used to address behavioral concerns such as attention-deficit/hyperactivity disorder. Different diet therapy options include the Feingold diet, sugar restriction, mega-vitamin supplementation, zinc supplementation, and use of fish oil. Only zinc supplementation has shown benefit with improvement in hyperactivity and impulsivity, but without significant change in attention. As with many dietary changes, more study is needed before any dietary intervention can be recommended.

Elevated transaminase levels can be seen in severe malnutrition due to liver injury that resolves with improved nutrition. The mechanism is not clear, but thought to be multifactorial. There is no clinical evidence of severe dehydration in this patient that would result in an elevated bicarbonate level. Similarly, there is no evidence of impaired kidney function that would result in

increased creatinine levels. Elevated creatinine levels may be associated with excess protein consumption or increased muscle mass, which are not likely in this teenager. Hyperkalemia is not frequently seen in children on fad diets. Hypokalemia is more likely in view of significant weight loss and increased stool losses associated with bowel cleanses.

PREP Pearls
- Weight loss recommendations for children and adolescents should be holistic and inclusive of the entire family.
- Fad diets often focus on dietary limitation of one nutritional component (eg, gluten, carbohydrates, fat, protein).
- With significant malnutrition, the hematocrit may be elevated because of hemoconcentration.

ABP Content Specifications(s)
- Recognize the possible adverse effects of "fad" weight loss diets

Suggested Readings
- Brown CA, Sabel AL, Gaudiani JL, Mehler PS. Predictors of hypophosphatemia during refeeding of patients with severe anorexia nervosa. *Int J Eat Disord.* 2015;48(7):898–904. doi: http://dx.doi.org/10.1002/eat.22406.
- Campbell K, Peebles R. Eating disorders in children and adolescents: state of the art review. *Pediatrics*. 2014;134(3):582–592. doi: http://dx.doi.org/10.1542/peds.2014-0194.
- Garber AK, Mauldin K, Michihata N, Buckelew SM, Shafer MA, Moscicki AB. Higher calorie diets increase rate of weight gain and shorten hospital stay in hospitalized adolescents with anorexia nervosa. *J Adolesc Health.* 2013;53(5):579–584. doi: http://dx.doi.org/10.1016/j.jadohealth.2013.07.014.
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- Redgrave GW, Coughlin JW, Schreyer CC, et al. Refeeding and weight restoration outcomes in anorexia nervosa: challenging current guidelines. *Int J Eat Disord.* 2015;48(7):866–873. doi: http://dx.doi.org/10.1002/eat.22390.
- Stratbucker W. Fad dieting and weight loss in children. *Pediatr Rev.* 2016;37(8):357–359. doi: http://dx.doi.org/10.1542/pir.2016-0009.

Question 69

A 5-year-old previously healthy girl presents to your office for evaluation of abdominal pain that has been worsening over the past 12 hours. Three days ago, the girl began to complain of abdominal pain and had a few episodes of nonbilious vomiting, along with a low-grade fever. At that time, she was seen by one of your colleagues, who documented that on physical examination, she had a soft abdomen with active bowel sounds, along with very mild periumbilical tenderness. A rapid Strep test was negative and she was diagnosed with acute viral gastroenteritis. Your colleague advised the family to encourage the girl to drink fluids, and to follow up in 48 to 72 hours if her abdominal pain did not improve.

Today, her abdominal pain is significantly worse. Her pain seemed better last evening, but when she awoke this morning, she complained of severe abdominal pain and has been refusing to walk. She has been refusing to eat or drink anything over the past day, has had intermittent episodes of nonbilious vomiting, and has continued to have fever.

On physical examination, the girl's temperature is 39°C, heart rate is 150 beats/min, respiratory rate is 32 breaths/min, blood pressure is 90/60 mm Hg, and pulse oximetry is 99% on room air. She is ill-appearing and is lying very still on your examination table, with her legs drawn up in a "fetal position." Her mucous membranes appear dry and her eyes are sunken. Her tympanic membranes and oropharynx are normal. Her lungs are clear to auscultation, but she is taking shallow, rapid breaths with intermittent grunting. The girl's abdomen is rigid and her bowel sounds are sparse. She cries in pain as soon as you begin to palpate her abdomen and tries to push your hand away. Her extremities are cool and clammy. You note no rashes. Urinalysis reveals 3+ ketones and 1+ leukocyte esterase, but is otherwise unremarkable.

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

A. appendicitis with perforation
B. diabetic ketoacidosis
C. lower lobe pneumonia
D. malrotation with midgut volvulus
E. mesenteric adenitis

Correct Answer: A

The constellation of signs and symptoms displayed by the 5-year-old girl in the vignette are most consistent with the diagnosis of acute appendicitis complicated by perforation. She is in need of immediate transfer to an emergency department for stabilization, emergent evaluation, and management by a pediatric surgeon.

Acute appendicitis is the most common indication for emergency abdominal surgery in pediatric patients. All pediatric providers must be able to recognize the clinical features associated with appendicitis. Making this diagnosis can be challenging, because the initial signs and symptoms can be quite similar to those of many other common nonsurgical intra-abdominal processes, including self-limited viral syndromes. Furthermore, not all children with appendicitis present with the classic "textbook" manifestations.

Appendicitis results from obstruction of the appendix due to inflammation in the appendiceal wall or a fecalith. This inflammatory process most commonly affects children 9 to 12 years of age. Although it is quite rare in children younger than 2 years, cases of infants with appendicitis have been reported. The diagnosis can be especially challenging in younger children (<5 years of age), because they often have atypical presentations, along with a decreased ability to communicate their symptoms.

The classic abdominal pain associated with acute appendicitis develops gradually, beginning as vague and poorly localized periumbilical pain, which worsens in severity and localizes to the right lower abdomen as the inflammatory process progresses. Commonly associated symptoms include nausea, anorexia, decreased activity level, and fever. Affected patients may also have vomiting (typically preceded by pain) and often experience increased abdominal pain with movement (eg, coughing, hopping, or hitting "bumps" during a car ride).

At the time of appendiceal perforation, there may appear to be a rapid clinical improvement, because of a sudden decrease in intraluminal pressure in the appendix, which transiently decreases the associated pain. Over the subsequent 24 hours, the child's clinical status worsens dramatically with manifestations such as peritoneal signs (abdominal rigidity with marked tenderness, rebound tenderness, and decreased or absent bowel sounds), high fever, systemic toxicity, and even findings of septic shock.

Because the anatomic position of the appendix varies in pediatric patients, localization of pain and abdominal tenderness may not always be at the classic McBurney point in the right lower abdominal quadrant as expected with appendicitis. For example, children with an appendix located in the lateral gutter may present with flank pain and lateral abdominal tenderness, whereas those with an appendix oriented toward the pubis may have tenderness near the pubis, diarrhea, and signs of bladder irritation.

It is important for pediatric providers to understand that, at this point, there is no perfect "test" for ruling out appendicitis, thus a thorough history and physical examination remain critical for identifying the condition. When the diagnosis is highly suspected clinically, pediatric surgical

consultation should be obtained promptly. If the diagnosis of acute appendicitis is equivocal, laboratory studies, including a complete blood cell count with differential, may be useful in supporting the diagnosis; however, laboratory studies cannot be relied upon to definitively confirm or rule out this condition. Although both abdominal ultrasonography and computed tomography (CT) of the right lower quadrant (RLQ) of the abdomen have been used as tools in the evaluation of children with suspected appendicitis, ultrasonography is emerging as the primary imaging modality in many centers. RLQ abdominal ultrasonography can be used to confirm or exclude the diagnosis of appendicitis in children in whom the appendix can be clearly identified. A major advantage of ultrasonography over CT is the avoidance of exposure to unnecessary ionizing radiation.

Diabetic ketoacidosis (DKA) may cause abdominal pain and vomiting in children, along with significant dehydration; however, the presence of peritoneal signs in this patient is not consistent with this diagnosis. Furthermore, the absence of glucosuria on this patient's urinalysis makes a diagnosis of DKA extremely unlikely. In a child presenting for the first time with DKA, the review of systems would typically be positive for polyuria, increased urinary frequency, polydipsia, thirst, and weight loss. Fever is not typically associated with DKA, but affected patients may have fever because of a concurrent infectious process (which may have contributed to the development of DKA).

Children with lower lobe pneumonia may present with referred abdominal pain, along with fever and vomiting. The girl in the vignette, however, has had no cough or other respiratory symptoms (which would typically be seen in patients with pneumonia), and has no pertinent findings on her lung examination. Although pneumonia can cause referred abdominal pain, patients with this diagnosis would not be expected to have focal abdominal tenderness or clinical signs of peritonitis.

Malrotation of the bowel with volvulus is an emergency that requires immediate surgical intervention to avoid significant morbidity (such as bowel ischemia and short bowel syndrome) and mortality. Patients with volvulus most commonly present during the first year after birth, though the condition can present at any age. Classic symptoms include severe abdominal pain (which can be a challenge to identify in infants), along with bilious emesis and signs of abdominal obstruction. The girl in this vignette has no history of bilious vomiting, and her presentation is not consistent with that of volvulus.

Mesenteric adenitis is a self-limited process that occurs because of inflammation of mesenteric lymph nodes in the abdominal RLQ, and can present similarly to acute appendicitis. Patients with mesenteric adenitis would not be expected to present with pain migration, peritoneal signs, or a toxic clinical appearance.

PREP Pearls
- Appendicitis results from obstruction of the appendix due to inflammation in the appendiceal wall or from a fecalith.
- Classic abdominal pain associated with acute appendicitis develops gradually, beginning as a vague and poorly localized periumbilical pain that worsens in severity and localizes to the right lower abdominal quadrant as the inflammatory process progresses.
- Abdominal ultrasonography is emerging as the primary imaging modality for evaluation of suspected appendicitis in many centers.

ABP Content Specifications(s)
- Recognize the clinical features associated with appendicitis
- Plan the appropriate diagnostic evaluation when appendicitis is suspected

Suggested Readings
- Bachur RG. Abdominal emergencies. In: Shaw KN, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2016;chap 124:1313–1333.
- Hansen LW, Dolgin SE. Trends in the diagnosis and management of pediatric appendicitis. *Pediatr Rev.* 2016;37(2):52. doi: http://dx.doi.org/10.1542/pir.2015-0021.
- Ross A, LeLeiko NS. Acute abdominal pain. *Pediatr Rev.* 2010;31(4):135. doi: http://dx.doi.org/10.1542/pir.31-4-135.

Question 70

A 15-month-old previously healthy boy is brought to the emergency department with fever, rash, and increasing lethargy. He was in his usual state of health until he developed a runny nose and cough the day before presentation. On the day of presentation, he has felt warm to the touch, had decreased oral intake, and became progressively lethargic and listless. When he woke up in the morning, his mother noticed a few red spots on his skin. Throughout the day, the rash progressed, significantly covering his trunk, arms, and legs. He has no known allergies.

The boy's temperature is 39.5°C, heart rate is 180 beats/min, respiratory rate is 50 breaths/min, blood pressure is 70/40 mm Hg, and oxygen saturation is 100% on room air. His physical examination reveals a well-nourished but toxic-appearing, lethargic child. He has a nonblanching, purpuric rash evenly distributed over his face, trunk, and upper and lower extremities. His mucous membranes are dry. He is in moderate respiratory distress, with clear lung fields and good bilateral air exchange. His heartbeat is regular, with no murmur. The boy's extremities are cold, with a capillary refill time of 5 seconds. His abdomen is soft with no organomegaly. The nurse places 2 large-bore intravenous catheters, and fluid resuscitation is rapidly initiated.

Of the following, the MOST appropriate antimicrobial therapy in this case is intravenous

 A. acyclovir
 B. amphotericin B
 C. ceftriaxone
 D. chloramphenicol
 E. vancomycin

Correct Answer: C

The boy in this vignette has septic shock from disseminated meningococcemia, evidenced by tachycardia, tachypnea, hypotension, lethargy, and toxic appearance combined with a characteristic purpuric rash. The best antimicrobial choice is ceftriaxone.

Because of its capacity to cause rapidly progressive septic shock and meningitis in healthy children, *Neisseria meningitidis* is one of the most feared bacterial pathogens. It is a gram-negative encapsulated diplococcus that colonizes the nasopharynx. Rates of carriage range from less than 2% in children younger than 2 years of age to as high as 40% in adolescents and young adults. Transmission occurs via respiratory droplets. Individuals in crowded living conditions, such as military barracks and college dormitories, are at higher risk of infection. Younger children are more likely to become ill with meningococcal disease because of less developed innate immune defense mechanisms. Children with acquired or congenital immune defects, such as complement deficiency or functional asplenia, are predisposed to invasive meningococcal disease.

Children with meningococcal disease can deteriorate quickly. Meningococcemia can initially masquerade as a viral syndrome, with presenting signs and symptoms including high fever, rash, chills, and body aches. Within hours, the rash, which can initially be confused with a viral exanthem, will become purpuric (purplish, blotchy, and nonblanching). Endotoxin from the bacterial capsule causes a severe host inflammatory response that can lead to cardiovascular collapse because of myocardial depression and vasodilation, disseminated intravascular coagulation, lethargy, respiratory failure, and death. Pediatricians should be on the alert for signs or symptoms that indicate severe illness. Tachycardia out of proportion to the degree of fever should raise suspicion for shock. A rule of thumb is that the heart rate may increase by 10 beats/min for every degree Celsius above 37 without causing additional concern. A rash that does not blanch (ie, petechiae or purpura) is less likely to be a viral exanthem, rather, it raises concern for thrombocytopenia, sepsis, or disseminated intravascular coagulation. Lastly, signs of meningitis such as vomiting without diarrhea, lethargy, or a stiff neck help differentiate meningococcemia from a viral illness.

Treatment of a child with meningococcemia should focus on the circulation, airway, and breathing, according to guidelines based on pediatric septic shock and pediatric advanced life support (PALS) guidelines. Artificial ventilation should be provided to any child with oxygenation, ventilation, or airway protective reflexes, and should be considered in children who are obtunded or in shock. Intravenous or intraosseous access should be established within the first 2 minutes and aggressive fluid resuscitation should be initiated. Inotropes, vasopressors, and steroids should be considered if the shock is refractory to fluids.

The importance of timely administration of antibiotics cannot be overstated. Although a blood culture and lumbar puncture are important to make the diagnosis, antibiotics should not be delayed. While *N meningitidis* is sensitive to penicillin, ceftriaxone is the appropriate initial therapy when the diagnosis may be uncertain, because it also covers resistant streptococcal disease. Acyclovir and vancomycin could be considered for the broad treatment of meningitis,

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but neither is effective for meningococcal disease. Chloramphenicol is an excellent bactericidal agent for meningococcemia and penetrates the blood-brain barrier, but it has an unfavorable side effect profile. Amphotericin B is an effective antifungal agent for use in immunocompromised patients, but would not be appropriate treatment for the boy in this vignette.

PREP Pearls
- Meningococcemia should be considered in cases of sudden-onset fever and rash.
- Tachycardia out of proportion to the degree of fever should raise suspicion for shock. A rule of thumb is to expect an increase of up to 10 beats/min for every degree Celsius above 37 without additional concern.
- Younger children are more likely to become ill from meningococcal disease; however, rates of carriage are higher among adolescents and young adults, and those in crowded living conditions.
- Children with acquired or congenital immune defects, such as complement deficiency or functional asplenia, are predisposed to invasive meningococcal disease.

ABP Content Specifications(s)
- Understand the epidemiology of Neisseria meningitidis
- Plan appropriate management for a patient with meningococcal disease
- Understand the significance of purpura in a febrile child
- Understand which patients are at increased risk of invasive and recurrent meningococcal disease (eg, asplenia, terminal complement component)
- Recognize the major clinical features associated with Neisseria meningitidis infection

Suggested Readings
- Brayer AF, Humiston SG. Invasive meningococcal disease in childhood. *Pediatr Rev.* 2011;32:152–161. doi: http://dx.doi.org/10.1542/pir.32-4-152.
- 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.
- MacNeil JR, Bennett N, Farley MM, et al. Epidemiology of infant meningococcal disease in the United States, 2006-2012. *Pediatrics* 2015;135:e305–e311. doi: http://dx.doi.org/10.1542/peds.2014-2035.

Question 71

An 8-year-old boy is brought to your office for evaluation of a rash that was first noted 2 months ago. The rash is mildly pruritic. The boy has been otherwise well and is taking no medications. He is afebrile and has normal growth parameters. There are scaling plaques on his trunk and extremities (Item Q71).

Item Q71: Scaling plaques as described for the boy in the vignette. Courtesy of D. Krowchuk

Of the following, the MOST likely diagnosis is

A. nummular eczema
B. pityriasis rosea
C. psoriasis
D. seborrheic dermatitis
E. tinea corporis

Correct Answer:C

The boy in this vignette has an eruption composed of erythematous plaques that have thick scale. Where scale has been removed, there are areas of hemorrhage (ie, Auspitz sign) (**Item C71A**). These findings are consistent with a diagnosis of psoriasis. The lesions of nummular eczema may be round or oval but are not elevated and exhibit crust (dried fluid) rather than scale (**Item C71B**). Unlike in psoriasis, the plaques of pityriasis rosea are thin and have fine scale that is located at the trailing edges of lesions (ie, the scale does not cover the entire lesion) (**Item C71C**). Especially on the scalp, seborrheic dermatitis may mimic psoriasis. However, in seborrheic dermatitis, scale is fine and often "greasy," and the area of involvement is not as well defined as in psoriasis (**Item C71D**). The lesions of tinea corporis are annular with fine scale on the elevated borders and central clearing.

Item C71A: Auspitz sign, arrow.
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Item C71B: Nummular eczema. Courtesy of D. Krowchuk

Scale located at the trailing
edge of the lesion

Item C71C: Pityriasis rosea. Courtesy of D. Krowchuk

Item C71D: Scalp psoriasis.
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Psoriasis is a papulosquamous (ie, elevated lesions with scale) disorder likely caused by a genetic predisposition and an environmental trigger (like infection or trauma). It is believed to be an immune-mediated inflammatory process characterized by epidermal hyperplasia. In 35% to 50% of individuals, the onset is before the age of 20 years. Recently, psoriasis has been linked to comorbidities, including metabolic syndrome and cardiovascular disease. Psoriasis may also occur in some children who have juvenile idiopathic arthritis.

The following variants of psoriasis most often affect infants, children, and adolescents:
- Plaque psoriasis, as exhibited by the boy in this vignette, is the most common form. Lesions typically affect the extensor surfaces of the extremities, but may also occur on the scalp, face, umbilicus, and gluteal cleft. Lesions appear in areas of trauma (the Koebner phenomenon), thus explaining the commonly observed involvement of the extensor surfaces of the elbows and knees.
- Scalp psoriasis (**Item C71D**) may occur alone or accompany plaque psoriasis.
- Nail psoriasis may be an isolated finding or may precede, coincide with, or follow the onset of disease elsewhere on the body. The most common manifestation is pitting (**Item C71E**), but individuals may develop thickening, yellowing, or roughness of the nails.
- Guttate psoriasis (from the Latin *guttātus*, meaning speckled or spotted) occurs commonly in children. It is often precipitated by pharyngeal or perianal *Streptococcus*

pyogenes infection. It begins as a generalized eruption composed of erythematous macules and papules that may mimic a viral exanthem. With time, the lesions become elevated and develop scale (**Item C71F**). Guttate psoriasis may resolve spontaneously or evolve into plaque psoriasis.

- Diaper area psoriasis is characterized by erythematous plaques that involve the convexities and creases. Because the area is occluded, there may be little scale. Psoriasis involving the diaper area may mimic irritant contact dermatitis, seborrheic dermatitis, or candidiasis.

Item C71E: Pitting of the nails in patients with psoriasis. Courtesy of D. Krowchuk

Item C71F: Guttate psoriasis. Courtesy of D. Krowchuk

Psoriasis is a lifelong condition that has a chronic, relapsing course. Treatment is designed to reduce inflammation and normalize epidermal proliferation. First-line therapy for the scalp, trunk, or extremities is a mid-potency topical corticosteroid (eg, triamcinolone 0.1%) applied twice daily as needed. For the face, flexures, or groin, a low-potency preparation (eg, hydrocortisone 1% or 2.5%, or desonide 0.05%) is indicated. If the disease is not controlled with a topical corticosteroid alone, a topical calcipotriene, an agent that normalizes epidermal proliferation, may be added. Other topical agents that may be beneficial are calcineurin inhibitors, retinoids, keratolytics, tars, and anthralin. Phototherapy or systemic agents (eg, methotrexate, cyclosporine A, acitretin, or biologics) are reserved for patients with severe disease that does not adequately respond to topical treatment.

PREP Pearls
- In children and adolescents, psoriasis most often presents with erythematous papules and plaques covered by a thick, adherent scale. The extensor surfaces of the elbows and knees are commonly involved.
- First-line treatment of psoriasis is with an appropriate topical corticosteroid.

ABP Content Specifications(s)
- Recognize the clinical findings associated with psoriasis

Suggested Readings

- Section on Dermatology, American Academy of Pediatrics. Psoriasis. In: Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016:335–340.
- Tollefson MM. Diagnosis and management of psoriasis in children. *Pediatr Clin North Am.* 2014;61(2):261–277. doi: http://dx.doi.org/10.1016/j.pcl.2013.11.003.

Question 72

You are called to admit a 36-week-gestation male newborn to the nursery who was delivered vaginally to a 27-year-old gravida 3, para 1 woman. The mother's prenatal history is significant for an Escherichia coli urinary tract infection and positive group B Streptococcus (GBS) status. Rupture of membranes occurred 8 hours before delivery. The mother received 1 dose of intravenous penicillin 3 hours before delivery, for GBS prophylaxis. The neonate is rooming in with his mother and formula feeding well. The mother has a 4-year-old son at home, and requests that her newborn be discharged 24 hours after birth. You discuss with her the current guidelines for care of neonates born to GBS-positive mothers.

Of the following, the MOST appropriate management plan for this neonate would be

- A. complete blood cell count, blood culture, and cefotaxime administration pending culture results
- B. complete blood cell count and blood culture, with possible discharge at 24 hours of age
- C. complete blood cell count and blood culture, with possible discharge at 72 hours of age
- D. observation in the newborn nursery unit, with possible discharge at 24 hours of age
- E. observation in the newborn nursery unit, with possible discharge at 48 hours of age

Correct Answer: E

In the vignette, a late preterm infant at 36 weeks' gestation was born to a mother who was group B *Streptococcus* (GBS)–positive and treated with 1 dose of penicillin. He should be observed for 48 hours because of premature gestation and inadequate intrapartum antibiotic prophylaxis during labor (<4 hours before delivery). Early-onset sepsis (EOS) continues to be a significant cause of morbidity and mortality for term neonates born in the United States, with a rate of 0.57 per 1,000 live births. Neonates are exposed to microorganisms from the maternal genital and anorectal tract during labor or via ascending spread after rupture of membranes. The primary organisms responsible for EOS are *Streptococcus agalactiae*, also known as GBS, and *Escherichia coli*. Most commonly, EOS due to GBS presents with respiratory distress secondary to GBS pneumonia. However, infected infants may also present with asymptomatic bacteremia.

Pregnant women should undergo vaginal-rectal screening for GBS colonization between 35 and 37 weeks of gestation. Women who screen positive for GBS should receive prophylactic antibiotics during labor, at least 4 hours before delivery, to decrease transfer of GBS from the mother to infant. Since the advent of maternal screening and intrapartum prophylaxis against GBS, rates of EOS due to GBS have decreased. However, intrapartum antibiotic prophylaxis does not eliminate the risk of EOS infection. Other risk factors for EOS include prematurity, prolonged rupture of membranes, and maternal intrauterine infection. Inadequate intrapartum antibiotic prophylaxis in a high-risk group may result in partial treatment and delayed onset of symptoms.

Neither laboratory tests nor the use of broad-spectrum antibiotics, such as cefotaxime, is indicated in a well-appearing infant, despite maternal GBS-positive status.

Discharge from the hospital 24 hours after birth should be reserved for well-appearing term neonates born to mothers without GBS colonization or mothers with GBS colonization who receive adequate intrapartum antibiotic prophylaxis, provided adequate care and follow-up can be assured.

PREP Pearls
- Premature neonates, those born before 37 weeks of gestation, are at increased risk for early-onset sepsis.
- Group B *Streptococcus* (GBS) and *Escherichia coli* remain the most common causes of early-onset sepsis, despite the implementation of GBS screening and intrapartum prophylaxis.
- Inadequate antibiotic prophylaxis before delivery may delay the onset of symptoms of GBS infection, necessitating observation for 48 hours before discharge.
- Women who screen positive for GBS should receive prophylactic antibiotics during labor, at least 4 hours before delivery, to decrease transfer of GBS from the mother to neonate.

ABP Content Specifications(s)
- Recognize the major clinical features associated with group B streptococcal infection, and manage appropriately
- Understand the epidemiology of Streptococcus agalactiae
- Plan the appropriate management of an infant born to a mother with a positive culture for group B streptococcus

Suggested Readings
- Higgins RD, Saade G, Polin RA, et al; Chorioamnionitis Workshop Participants. Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis: summary of a workshop. *Obstet Gynecol.* 2016;127(3):426–436. doi: http://dx.doi.org/10.1097/AOG.0000000000001246.
- Sass L. Group B streptococcal infections. *Pediatr Rev.* 2012; 33:219. 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;127:817. doi: http://dx.doi.org/10.1542/peds.2010-2217.

Question 73

On hospital rounds, you are evaluating a 7-year-old girl who had resection of a mass located in the third ventricle after presenting to the emergency department with worsening headaches and vomiting. Now on postoperative day 3, she is recovering well. She is able to drink fluids, is beginning to eat soft foods, and her pain is well-controlled. Physical examination reveals a temperature of 37°C, blood pressure of 125/78 mm Hg, heart rate of 74 beats/min, and weight of 22 kg, up 1 kg from her preoperative weight. Her craniotomy incision is clean, dry, and intact. The remainder of her examination findings are unremarkable.

Laboratory investigation reveals the following:
•Serum sodium, 128 mEq/L (128 mmol/L)
•Serum potassium, 3.9 mEq/L (3.9 mmol/L)
•Serum chloride, 98 mEq/L (98 mmol/L)
•Serum bicarbonate, 22 mEq/L (22 mmol/L)
•Blood urea nitrogen, 8 mg/dL (2.9 mmol/L)
•Serum creatinine, 0.3 mg/dL (26.5 µmol/L)
•Plasma glucose, 92 mg/dL (5.1 mmol/L)
•Serum albumin, 3 g/dL (30 g/L) (reference range, 3.9–5 g/dL [39–50 g/L])
•Hematocrit, 26%
•Serum osmolality, 264 mOsm/L (264 mmol/L) (reference range, 285–300 mOsm/L [285–300 mmol/L])
•Urine osmolality, 730 mOsm/L (730 mmol/L)
•Urine specific gravity, 1.020
•Urine sodium, 248 mEq/L (248 mmol/L)

Of the following, the MOST likely cause of the girl's hyponatremia is

 A. cerebral salt wasting
 B. hyponatremic dehydration
 C. infusion of excess hypotonic fluid
 D. pseudohyponatremia
 E. syndrome of inappropriate antidiuretic hormone secretion

Correct Answer: E

The girl described in the vignette has syndrome of inappropriate antidiuretic hormone secretion (SIADH) as a postoperative complication after removal of her brain mass. The proximity of her tumor to the posterior pituitary likely resulted in the inappropriate release of antidiuretic hormone. Her SIADH is expected to be transient.

The hyponatremia seen in SIADH is due to water retention. Volume status is euvolemic or hypervolemic. This girl's elevated blood pressure, weight gain, and normal to low blood urea nitrogen (BUN) and creatinine indicate mild hypervolemia. Her serum sodium and osmolality are low because of the water retention. Similarly, her urine osmolality and urine specific gravity are high because of increased water retention in the kidney. The hypervolemia is suppressing her aldosterone, causing sodium excretion in the kidney and thus leading to relatively high urine sodium levels.

The girl's volume status indicates that she does not have cerebral salt wasting or hyponatremic dehydration, as total volume is depleted in these conditions. Urine sodium is also low in hyponatremic dehydration, because of total body sodium loss with normal sodium reabsorption in the kidney. Pseudohyponatremia occurs when glucose or lipid levels are high. She does not have any evidence of other disorders that would cause pseudohyponatremia. The infusion of excess hypotonic fluids would not result in elevation of urine osmolality, specific gravity, or sodium levels.

It is important to make the correct diagnosis in cases such as the girl in the vignette, so proper management can be implemented. Although the treatment for SIADH is fluid restriction, the treatment of cerebral salt wasting and hyponatremic dehydration is hydration with isotonic fluids. The distinguishing features of SIADH, cerebral salt wasting, and hyponatremic dehydration are highlighted in **Item C73**.

Item C73. Causes of Secondary Osteoporosis.

Neuromuscular Disorders and Inborn Errors of Metabolism	Chronic Diseases	Endocrine Disorders	Gastroenterologic and Nutritional Disorders	Iatrogenic
• Cerebral palsy • Muscular dystrophy • Prolonged immobilization • Spinal cord injury • Homocystinuria • Glycogen storage disease • Galactosemia • Gaucher disease	• HIV infection • Cystic fibrosis • Organ transplants • Thalassemia • Chronic inflammatory conditions • Inflammatory bowel disease • Systemic lupus erythematosis • Juvenile idiopathic arthritis • Rheumatoid arthritis • Chronic renal insufficiency • Nephropathy • Multiple myeloma • Lymphoma • Ectopic ACTH syndrome • Leukemia • Mastocytosis • Alcoholism	• Delayed puberty • Hypogonadism • Hyperprolactinemia • Growth hormone deficiency • Hyperthyroidism • Juvenile diabetes mellitus • Hypophosphatasia • Cushing syndrome • Hyperparathyroidism • Cushing disease	• Vitamin D deficiency • Calcium deficiency • Protein intolerance • Malnutrition • Chronic liver disease • Primary biliary cirrhosis • Anorexia nervosa • Malabsorption syndromes • Gastric bypass surgery	• Glucocorticoids • Methotrexate • Cyclosporine • Heparin • Anticonvulsants • Medroxyprogesterone injections • Diuretics • Radiotherapy • Chemotherapy

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Syndrome of inappropriate antidiuretic hormone secretion may be associated with central nervous system and pulmonary disorders, hypothyroidism, glucocorticoid deficiency, and certain medications. The more commonly used medications that can cause SIADH include carbamazepine, selective serotonin reuptake inhibitors, tricyclic antidepressants, vincristine, and cyclophosphamide.

PREP Pearls
- The hallmarks of syndrome of inappropriate antidiuretic hormone secretion (SIADH) include hyponatremia, hypo-osmolality, euvolemia or mild hypervolemia, inappropriately concentrated urine, and urine sodium excretion.
- SIADH is associated with euvolemia or mild hypervolemia, in contrast to cerebral salt wasting and hyponatremic dehydration, which are associated with hypovolemia.
- The treatment for SIADH is fluid restriction. The treatment for cerebral salt wasting and hyponatremic dehydration is hydration with isotonic fluid.
- SIADH can be associated with central nervous system and pulmonary disorders; hypothyroidism; glucocorticoid deficiency; and medications, including carbamazepine, selective serotonin reuptake inhibitors, tricyclic antidepressants, vincristine, and cyclophosphamide.

ABP Content Specifications(s)
- Recognize disease conditions and medications associated with SIADH
- Recognize how to differentiate SIADH from hyponatremic dehydration
- Recognize the clinical and laboratory features associated with SIADH, and manage appropriately

Suggested Readings
- Moritz ML, Ayus JC. Disorders of water metabolism in children: hyponatremia and hypernatremia. *Pediatr Rev*. 2002;23(11):371–380.
- Ranadive SA, Rosenthal SM. Pediatric disorders of water balance. *Pediatr Clin North Am.* 2011;58(5):1271–12780, xi-xii. doi: http://dx.doi.org/10.1016/j.pcl.2011.07.013.
- Reid-Adam J. Hyponatremia. *Pediatr Rev*. 2013;34(9):417–419. doi: http://dx.doi.org/10.1542/pir.34-9-417.

Question 74

A 7-year-old boy is brought to your office by his parents who are concerned that he is having problems with learning. Although he managed to keep up with his peers last year in kindergarten, this year he has struggled with his classwork. He is attentive, well-behaved, and appears to be making good effort. An evaluation through the school did not uncover any learning disabilities or intellectual disability. Testing demonstrated consistently low-average scores in aptitude, achievement, and adaptive functioning, and he has no problems with memory or processing. His parents have scheduled a meeting at his school next week to discuss what help their son might need. They ask for your advice on how to proceed.

Of the following, the BEST next step is to recommend

 A. changing schools to find a better fit for his learning style
 B. enrolling their son in summer school and afterschool tutoring
 C. hiring an advocate to get an Individualized Education Program
 D. repeating first grade to give their son time to mature
 E. requesting a section 504 plan for accommodations

Correct Answer: B

Although the 7-year-old boy in the vignette does not have a learning disability, he is clearly struggling with learning. While some might consider grade retention for this child, this would not address the problems with this child's learning. This boy is most likely to achieve academic success if given additional instruction from trained educators, such as through summer school and after school tutoring.

The rate of grade retention is estimated to be approximately 10% to 20% of students. Boys are more likely to be retained than girls. Black and Hispanic students are more likely to be retained than students of other backgrounds. Children who are doing poorly in school may be considered for grade retention. It was believed that repeating a grade level will allow children time to catch up to their peers. However, while some studies show that these children may do well academically and emotionally at the beginning of their repeated year, these positive effects do not persist.

Current evidence does not support grade retention. Most studies show that grade retention at any grade level is ineffective and potentially harmful, resulting in lower levels of academic achievement, a higher likelihood of dropping out of high school, and lower ultimate educational attainment and employment success. In contrast, students who are low achieving but not grade retained have comparable employment outcomes to their peers. Furthermore, students view their grade retention as progressively more stressful as the grade level at which they are retained increases. Self-esteem and social development are more likely to be affected when a child is retained at higher grade levels.

Grade retention does not address underlying learning problems and thus does not meet the educational needs of students who are struggling academically. In most cases, the students are instructed in the same unsuccessful manner and environment. Unless additional or different educational strategies are used, these children are likely to continue with low achievement and school failure.

Students who are struggling academically are best served by early identification and implementation of evidence-based interventions. These include methods to address the individual child's areas of academic weakness by increasing the amount of instruction time (eg, summer school, after school programs, tutoring) and by providing supplemental instruction by trained personnel (eg, early reading programs). Programs which involve parents and those which support the mental health of children (eg, school-based mental health programs, behavioral modification) are also helpful interventions.

The boy in the vignette does not have a learning disability, so he would not qualify for an Individualized Education Program. He does not have a condition, such as attention-deficit/hyperactivity disorder, that would qualify him for accommodations designated through a section 504 plan. Although changing schools to find one that better fits his learning style might address the boy's learning challenges, in many cases, this would not be feasible or would be difficult to accomplish.

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Pediatricians can help and support families making decisions about their children's education. Awareness of educational resources, as well as knowledge about the lack of evidence to support (and evidence of harm from) grade retention can help pediatricians advocate for strategies that can make a difference in the child's future academic and employment success.

PREP Pearls
- Most studies show that grade retention at any grade level results in lower academic achievement, higher likelihood of dropping out of high school, and lower ultimate educational attainment and employment success.
- While some studies show that children who are retained a grade may do well academically and emotionally at the beginning of their repeated year, these positive effects do not persist.
- Students who are struggling academically are best served by early identification and implementation of evidence-based interventions that include increasing the amount of instruction time (eg, summer school, after school programs, tutoring) and providing supplemental instruction by trained personnel (eg, early reading programs), rather than grade retention.

ABP Content Specifications(s)
- Understand the advantages and disadvantages of grade retention

Suggested Readings
- Jimerson SR, Pletcher SMW, Graydon K, Schnurr BL, Nickerson AB, Kundert DK. Beyond grade retention and social promotion: prompting the social and academic competence of students. *Psychol Schools.* 2006:43(1):85–97.
- Von Hahn LE. Specific learning disabilities in children: educational management. https://www.uptodate.com/home .

Question 75

A 14-year-old boy presents to your office for a preparticipation sports physical examination. He is a freshman in high school and would like to play for his school's hockey and soccer teams in the upcoming year. His parents report that the boy has a history of 2 concussions. The first occurred 2 years ago when he jumped off a swing. The second occurred 4 months ago while he was wrestling with his brother. He did not lose consciousness with either event, but experienced headaches and sensitivity to light for 2 weeks after the recent incident.

The boy reports that he feels "fine" now. However, his parents report that he seems more forgetful and has had difficulty concentrating since the second concussion. He is otherwise healthy. You counsel the family regarding the boy's current condition and the risks of sports participation based on his history.

Of the following, the MOST accurate statement to include when counseling this family is that

    A. he can be cleared for both soccer and football participation, but will have to stop contact sports permanently if he has a third concussion
    B. he can be cleared for soccer participation, but should not play hockey until his cognitive symptoms resolve
    C. neuropsychological testing is recommended to identify any cognitive deficit
    D. the boy's difficulty with concentration and forgetfulness are unrelated to his injury history
    E. the boy's recent injury does not meet the criteria for diagnosis of a concussion

Correct Answer: C

The adolescent in the vignette sustained a sports-related concussion 4 months before his preparticipation visit. His parents have concerns about persistent neurocognitive functional deficits after his injury. Neuropsychological testing could identify areas of impaired cognitive function. This would be important information to consider when making a sports participation clearance decision.

A concussion is a neurologic injury that results from a rotational (side-to-side) or linear (back-and-forth) force applied to the head or from direct contact to the head. By definition, a concussion does not cause visible brain structural abnormalities, but instead can cause somatic symptoms, sleep disturbance, mood symptoms, and/or cognitive problems. Although most children recover from sports-related concussion within 6 weeks of injury, some individuals experience prolonged symptoms.

There are no gold-standard tests to identify persistent cognitive dysfunction after concussion; however, neuropsychological testing may identify memory and concentration deficits. For the boy in the vignette, in the absence of baseline neuropsychological testing, any deficits identified could not be conclusively linked to his concussion. However, low test scores that are inconsistent with prior school performance would be suggestive of concussion-related functional impairment.

The boy's parents report that he has had onset of memory and concentration difficulties since his recent concussion, and these concerns should be taken seriously. His history of headache, light sensitivity, and cognitive symptoms after a wrestling injury meet the criteria for sports concussion. He should not return to contact sports (eg, soccer, basketball) or collision sports (eg, football, hockey) without additional evaluation. A history of 3 concussions is not, by itself, an absolute contraindication to contact or collision sport participation. Withholding sports clearance should be considered when an athlete has had multiple concussions, along with a history of increasingly prolonged recovery times, a history of multiple concussions occurring after short intervals, and/or concussions that occurred with seemingly minor contact.

PREP Pearls
- Although most children recover from sports-related concussion within 6 weeks of injury, some individuals experience prolonged symptoms.
- There are no gold-standard tests to identify persistent cognitive dysfunction after concussion, but neuropsychological testing may identify functional deficits

ABP Content Specifications(s)
- Understand the importance of assessing and documenting neurocognitive function prior to sports participation

Suggested Readings

- Halstead ME, McAvoy K, Devore CD, Carl R, Lee M, Logan K. Returning to learning following a concussion. *Pediatrics*. 2013;132(5):948-957. http://pediatrics.aappublications.org/content/132/5/948.
- McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med.* 2013;47(5):250-258. doi: http://dx.doi.org/10.1136/bjsports-2013-092313.

Question 76

In the last 3 months, there have been several violent incidents at a high school near your office. As the director of the school-based health center located there, you have been asked to lead a coalition charged with addressing school violence.

Of the following, the MOST accurate information you can provide the coalition regarding this issue is that

- A. implementing a School Resource Officer program would have the strongest positive impact
- B. mentoring programs do not have a direct effect
- C. prevention programs should not address risk factors such as low commitment to school
- D. school level interventions should address the role of the student bystander
- E. strategies targeting high-risk youth will have the greatest positive impact

Correct Answer: D

Of the response choices, the most accurate information you can provide the coalition regarding this issue is that school level interventions should address the role of the student bystander. School violence refers to violence occurring on school property, on the way to or from school or school-sponsored events, or during a school-sponsored event. According to the 2015 Youth Risk Behavior Survey (YRBS) which monitors health risk behaviors, nearly 8% of high school students were involved in a fight, 6% were threatened or injured with a weapon, and 20% were bullied on school property within the last 12 months. Exposure to school violence can lead to problems such as alcohol and drug use, depression, anxiety, and suicide.

Risk factors that have been associated with youth violence include a prior history of violence, substance use, association with delinquent peers, family dysfunction, poor academic performance, and community poverty.

Recommended approaches to the prevention of youth violence include:
- Universal, school-based prevention programs delivered to all students that focus on topics such as emotional self-awareness and control, positive social skills, problem solving, conflict resolution, and building positive relationships with caring adults in their community.
- Parent- and family-based programs designed to educate parents about child development and teach communication skills and nonviolent conflict resolution skills.

Despite the popularity of School Resource Officer programs, rigorous evaluations to show their effectiveness are not available.

Mentoring programs have been shown to decrease adolescent risk behaviors to include violence and delinquency.

Universal prevention approaches that have a positive impact on all youth are more likely to be effective in eliminating youth violence than are programs targeting only at-risk youth.

PREP Pearls
- Exposure to school violence can lead to problems such as alcohol and drug use, depression, anxiety, and suicide.
- Risk factors that have been associated with youth violence include a prior history of violence, substance use, association with delinquent peers, family dysfunction, poor academic performance, and community poverty.
- Universal prevention approaches that have a positive impact on all youth are more likely to be effective in eliminating youth violence than programs targeting only at-risk youth.
- Mentoring programs have been shown to decrease adolescent risk behaviors to include violence and delinquency.

ABP Content Specifications(s)
- Recognize factors associated with risk-taking in adolescents
- Understand age-appropriate non-violent strategies for conflict resolution in adolescence
- Recognize and apply ethical principles regarding violence in society
- Identify the various roles of adolescents with regard to school violence

Suggested Readings
- Centers for Disease Control and Prevention. Trends in the prevalence of behaviors that contribute to violence on school property. National YRBS: 1991—2015. www.cdc.gov/yrbss.
- Centers for Disease Control and Prevention. https://www.cdc.gov/violenceprevention/youthviolence/index.html.
- David-Ferdon C, Simon TR. *Preventing Youth Violence: Opportunities for Action*. Atlanta, GA: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention; 2014.

Question 77

You receive a call from the family of one of your patients. The family has a 3-week-old healthy infant who was delivered at term and has been exclusively breastfed since birth. The mother of your patient has been experiencing pain and lower extremity weakness since the delivery. Her physician has ordered magnetic resonance imaging with gadolinium-based contrast to evaluate for lumbosacral plexus nerve injury. When she scheduled the imaging procedure, she was advised by the radiology nurse to avoid breastfeeding for 48 hours after the contrast administration. The patient's family is interested in your advice.

Of the following, the MOST appropriate recommendation is that this mother

 A. avoid breastfeeding for 24 hours after contrast administration
 B. avoid breastfeeding for 48 hours after contrast administration
 C. cease breastfeeding entirely after contrast administration
 D. continue to breastfeed or express her breast milk without interruption
 E. request that the imaging study be performed without contrast

Correct Answer: D

Both the American Academy of Pediatrics and the American College of Radiology have published reports supporting the safety of gadolinium-based contrast agents in breastfeeding mothers. They recommend that mothers continue breastfeeding without interruption after contrast administration. The mother in this vignette can continue to breastfeed or express her milk after receiving contrast; she does not need to avoid breastfeeding for any length of time and should not cease breastfeeding because of contrast administration.

Gadolinium-based contrast agents have a relatively large molecular weight and are water soluble; very low levels (less than 0.04% of the intravenous [IV] dose given to the mother) are detected in breast milk after IV administration to lactating women. Furthermore, gadolinium contrast agents are not absorbed by the infant (or adult) gut in an appreciable manner. Therefore, the expected systemic dose in the breastfed infant is estimated to be less than 0.0004% of the IV dose given to the mother and is less than 1% of the recommended dose for an infant receiving IV gadolinium for a magnetic resonance imaging study.

In general, drugs with small molecular weight, low protein binding in maternal serum, low volume of distribution, and high lipid solubility are more readily excreted in breast milk, and drugs with a long half-life may accumulate in breast milk. Drugs with high oral bioavailability are more likely to be absorbed in the infant gut, whereas drugs with limited or no oral bioavailability may be excreted into breast milk in high concentrations but not actually absorbed by the infant.

Pediatricians are often asked about infant safety with maternal medications during lactation. Besides characteristics of the drug itself, we should also consider the breastfeeding infant's age, health status, and feeding volume and frequency; potential alternative maternal medications; and the parents' preferences and concerns. LactMed (https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm) is a free and widely available database provided by the National Institutes of Health that includes information on drug levels in breast milk, possible effects on lactation, infant serum or urine drug concentrations after exposure through breast milk, and potential adverse events in exposed infants. Although this data is not known for all medications, information from the LactMed database can be used to guide decision-making.

The American Academy of Pediatrics recommends exclusive breastfeeding as the normative and best feeding method for about the first 6 months after birth. Among other benefits, breastfeeding decreases an infant's risk of acute otitis media, upper and lower respiratory tract infections, gastroenteritis, necrotizing enterocolitis, obesity, diabetes, atopic dermatitis, and sudden infant death syndrome. Health benefits for breastfeeding mothers include decreases in maternal postpartum blood loss as well as decreases in the rates of type 2 diabetes mellitus, hypertension, hyperlipidemia, rheumatoid arthritis, and ovarian and breast cancers. Interruptions in exclusive breastfeeding, even for short periods of time, can interfere with milk production, maternal confidence, mother-infant bonding, and in some situations can lead to premature weaning.

There are very few contraindications to breastfeeding; these contradictions include classic galactosemia, maternal human T-lymphotropic virus type 1 or 2 infections, active untreated maternal tuberculosis infection, maternal HIV infection in areas outside the developing world, and the use of some maternal medications and recreational drugs.

PREP Pearls
- The LactMed database (https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm) is a free and evidence-based resource regarding medication safety during lactation.
- Lactating mothers who receive gadolinium-based contrast agents can safely breastfeed their infants without interruption.

MOCA-Peds Objective
- Manage breast-feeding difficulties

ABP Content Specifications(s)
- Understand factors that could interfere with breast-feeding
- Recognize the effects of maternal ingestion of drugs on breast-fed infants

Suggested Readings
- ACR Committee on Drugs and Contrast Media. ACR Manual on Contrast Media. Version 10.2. American College of Radiology; 2016. American College of Radiology.
- Sachs HC, Committee on Drugs. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. *Pediatrics*. 2013;132(3):e796–e809. doi: http://dx.doi.org/10.1542/peds.2013-1985.
- Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics*. 2012;129(3):e827–e841. doi: http://dx.doi.org/10.1542/peds.2011-3552.

Question 78

You are seeing a 1-day-old, full-term baby in the newborn nursery for the first time. The prenatal testing and course was unremarkable. Apgar scores were 9 at 1 minute and 9 at 5 minutes. There were no complications at birth. Vital signs are all appropriate for age. On physical examination, you note a 2/6 low-pitched, musical, midsystolic ejection murmur at the lower left sternal border. The liver edge is palpable 1 cm below the right costal margin. There is cyanosis of both feet (Item Q78). The remainder of the physical examination findings are unremarkable.

Of the following, the BEST next step in management is

  A. initiation of prostaglandin infusion
  B. performance of an echocardiogram
  C. reassurance
  D. referral to pediatric cardiologist
  E. transfer to neonatal intensive care unit

Correct Answer: C

The newborn in this vignette has completely age-appropriate examination findings. The murmur described is a classic description of a benign, innocent murmur. The liver edge is in a typical location for a newborn. The skin examination reveals acrocyanosis, which is normal in the newborn (**Item C78A** and **Item C78B**). Therefore, reassurance is all that is warranted.

The murmur described is a normal finding, as is the acrocyanosis, making an echocardiogram, prostaglandin infusion, or referral to a pediatric cardiologist unnecessary. There is no indication for transfer to the neonatal intensive care unit.

Item C78A: Acrocyanosis.
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Item C78B: Acrocyanosis.
Courtesy of M. LaTuga

Cyanosis is caused by the presence of hemoglobin that is not bound to oxygen in the blood (deoxyhemoglobin) and is typically seen when there is greater than 5 g/dL of deoxygenated hemoglobin. The ability to detect cyanosis is dependent upon hemoglobin concentration (easier to detect with a higher hemoglobin concentration, as noted in newborns, compared to a patient with severe anemia), the site of observation, and the experience of the observer. Peripheral cyanosis (acrocyanosis) is caused by the slow flow of blood through an area with a relatively large arteriovenous oxygen difference. In the newborn, acrocyanosis is commonly seen in the hands and feet and is a normal finding. Central cyanosis, however, would be seen at the lips and mucous membranes. Central cyanosis is a serious finding that warrants prompt evaluation of the respiratory, cardiac, and neurological systems.

PREP Pearls
- Peripheral cyanosis (acrocyanosis) is caused by the slow flow of blood through an area with a relative large arteriovenous oxygen difference and is a normal finding in newborns, most commonly seen in the hands and feet.
- Central cyanosis is a serious finding that warrants prompt evaluation of the respiratory, cardiac, and neurological systems.
- Cyanosis is caused by the presence of hemoglobin that is not bound to oxygen in the blood (deoxyhemoglobin) and is typically seen when there is greater than 5 g/dL of deoxygenated hemoglobin.

**ABP Content Specifications(s)**
- Distinguish between central cyanosis and acrocyanosis

Suggested Readings
- Kitterman JA. Cyanosis in the newborn infant. *Pediatr Rev.* 1982;4(1):13–23. http://pedsinreview.aappublications.org/content/4/1/13.
- Lees MH, King DH. Cyanosis in the newborn. *Pediatr Rev.* 1987;9(2):36–42. http://pedsinreview.aappublications.org/content/4/6/183.1.

Question 79

A 6-year-old girl is brought to your office for evaluation because she has been scratching her bottom and experiencing painful urination for about 2 weeks. The girl has no history of fever, vomiting, abdominal pain, abnormal urinary frequency, or vaginal discharge. Her appetite is normal, and her urine and stool output are unchanged. She attends kindergarten and has remained playful. Her mother reports that the girl seems fidgety at night and has been tired during the day. The girl is well-developed and well-nourished. She has a few superficial abrasions on her buttocks near the gluteal cleft and anus, plus mild vulvar erythema. The remainder of the physical examination findings are normal. You ask the mother to collect specimens by touching the perianal skin with transparent adhesive tape and applying the tape to a glass slide. This collection should be performed for 3 consecutive mornings when the girl wakes up. At a follow-up appointment, you examine the specimen slide under a microscope (Item Q79).
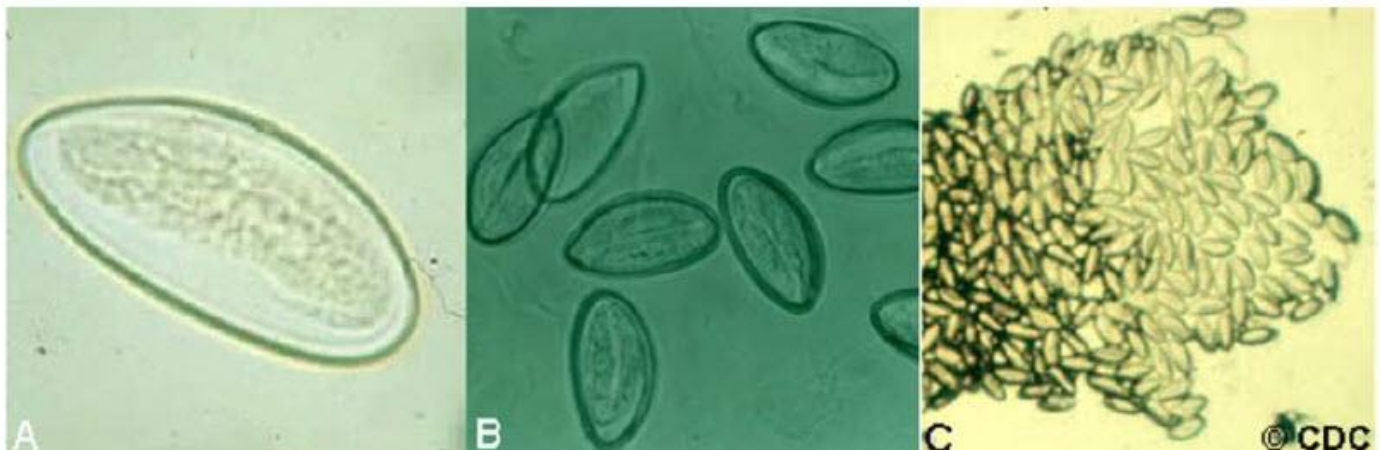
Item Q79: Microscopic findings for the girl described in the vignette. (A, B) Enterobius egg(s). (C) Enterobius eggs on cellulose tape prep. Courtesy of the Centers for Disease Control and Prevention

Of the following, the MOST accurate statement regarding the epidemiology of this condition is

A. contact with contaminated toys, bedding, and toilet seats may lead to disease
B. the incubation period from ingestion until perianal findings is 2 weeks
C. it occurs more often in rural settings
D. the prevalence is highest in children younger than 3 years
E. transmission can occur to humans from infected cats or dogs

Correct Answer: A

The girl in this vignette has characteristic signs and symptoms of pinworm infection (*Enterobius vermicularis*), which can be transmitted by the fecal-oral route indirectly from contact with toys, bedding, clothing, and toilet seats that are contaminated with eggs. Because enterobiasis is common worldwide, it is important for medical providers to understand its epidemiology and clinical manifestations.

Pinworm infection occurs in a variety of climates and across all socioeconomic levels. It is most common in young school-aged children (5 to 10 years of age), and transmission is most frequent in crowded living conditions or in people who are institutionalized. Humans are the only natural host of *E vermicularis*.

Enterobius vermicularis is a nematode (roundworm). Gravid adult female worms migrate out of the rectum and deposit up to 10,000 fertilized eggs on the perianal folds at night, which leads to pruritus ani, restless sleep, and occasionally vulvitis associated with dysuria. The female pinworms die within 24 hours of laying their eggs. The life cycle continues because autoinfection is common, especially in children, as the perianal area is scratched and eggs are transferred back to one's own mouth. Other person-to-person transmission occurs indirectly through contaminated food or fomites. Eggs may survive in indoor environments for 2 to 3 weeks. It is believed that eggs may also be inhaled and swallowed if airborne or transmitted via sexual contact. After ingestion, larvae hatch from the eggs while in the small intestine and then move to the cecum and mature into adult worms in about 1 month. If the worm burden is high, abdominal pain, nausea, and vomiting may develop. Although adult pinworms have been found in pathologic specimens of normal and inflamed appendices, a causative role in appendicitis has not been determined. The incubation period from ingestion of eggs until the adult female begins to lay eggs is 1 to 2 months or longer. The entire lifespan of the adult worms is 2 to 3 months. Retroinfection, or the migration of newly hatched larvae back into the rectum from the perianal area may occur, but the prevalence is unknown.

The diagnosis of pinworm infestation is often made clinically, and medical providers may choose to treat pinworm infestation empirically if the clinical scenario is consistent. Adult worms may be visualized in the perianal region 2 to 3 hours after the onset of sleep. Alternatively, the cellophane tape collection technique described in this vignette may be used to collect eggs prior to awakening if diagnostic confirmation is desired. Simultaneous treatment of the entire household, along with improved hygienic measures and concurrent environmental cleaning, is necessary to reduce reinfection and spread of disease. Anthelmintic treatment options for enterobiasis include:

- Albendazole, 400 mg orally once, repeat in 2 weeks
- Mebendazole, 100 mg orally once, repeat in 2 to 4 weeks
- Pyrantel pamoate, 11 mg/kg orally once (maximum dose, 1 g), repeat in 2 weeks

PREP Pearls
- Pinworms (*Enterobius vermicularis*) may be transmitted by the fecal-oral route indirectly from contact with toys, bedding, clothing, and toilet seats that are contaminated with eggs.
- Autoinfection from scratching the perianal area and transferring eggs back to one's own mouth is common.
- Pinworm infestation is often clinically diagnosed, and medical providers may choose to treat pinworm infestation empirically if the clinical scenario is consistent.

ABP Content Specifications(s)
- Recognize the clinical features associated with Enterobius vermicularis infestation, and manage appropriately
- Understand the epidemiology of Enterobius vermicularis

Suggested Readings
- American Academy of Pediatrics. Pinworm infection (Enterobius vermicularis). 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; 2015:621–622.
- Centers for Disease Control and Prevention. Parasites: *enterobiasis* (also known as pinworm infection). http://www.cdc.gov/parasites/pinworm/index.html .
- Dent AE, Kazura JW. *Enterobiasis* (Enterobius vermicularis). In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Elsevier; 2011:1737–1738 .

Question 80

A full-term female neonate weighing 3,700 g is born to a 32-year-old woman with hepatitis C virus infection. The mother was diagnosed during this pregnancy and has not received antiviral therapy. Her human immunodeficiency virus test results are negative. Her husband's test results for hepatitis C virus infection are negative. She has never used intravenous drugs. As a child, she received a blood transfusion after sustaining an injury during a motor vehicle collision. She inquires about the long-term prognosis if the baby were to acquire hepatitis C virus infection from her.

Of the following, you are MOST inclined to inform the mother that

A. decompensated cirrhosis in adulthood is likely
B. hepatocellular carcinoma without cirrhosis is likely
C. rapidly progressive fibrosis in adulthood is likely
D. slowly progressive fibrosis in childhood is likely
E. spontaneous clearance of the virus in infancy is likely

Correct Answer: D

The expected course of hepatitis C virus (HCV) infection acquired via maternal to fetal transmission is slowly progressive liver fibrosis.

Only 5% of infants born to mothers with HCV infection acquire the virus. Coinfection with HIV increases the percentage to 10%. Spontaneous resolution of infection in infancy can occur in 25% to 40% of infected infants. Although the proportion of infected infants is low, a large portion will go on to develop chronic infection.

The possible long-term outcomes of patients who have HCV infection include cirrhosis, liver failure, and hepatocellular carcinoma. Hepatitis C virus infection is the most common condition leading to liver transplant in adults in the United States.

Spontaneous clearance of the virus in infancy does not occur in most cases of perinatal infection. Although comorbid conditions and behaviors (such as alcohol consumption) have been associated with accelerated progression of disease, the natural history of HCV infection is for slow progression. It is estimated that 5% to 30% of chronically infected adults develop cirrhosis over 2 to 3 decades. Hepatocellular carcinoma without cirrhosis has been reported; however, in most cases cirrhosis precedes hepatocellular carcinoma. The risk of developing hepatocellular carcinoma is 0% to 3% per year after cirrhosis ensues.

Individuals that are chronically infected with HCV should have regular monitoring of hepatic enzymes and function. The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition recommends annual evaluation. Individuals with significant liver disease should undergo at least annual screening for hepatocellular carcinoma through ultrasonography and measurement of α-fetoprotein levels.

Only 1 regimen, a combination of peginterferon and ribavirin, is Food and Drug Administration–approved in children for treatment of HCV infection. However, this regimen can have significant toxicity and its efficacy for the common HCV genotype in the United States is modest at best. Additionally, severe disease is not common in childhood. Given the toxicity and modest efficacy of this regimen and the slowly progressive nature of fibrosis, children in the United States do not commonly receive therapy. However, persistent elevation of hepatic enzymes or progressive disease can be considered as an indication for treatment.

PREP Pearls
- Only 5% of infants born to mothers with hepatitis C virus infection acquire the virus.
- Although the likelihood of vertical transmission of hepatitis C virus is low, a large portion of infected infants will develop chronic infection.
- The possible long-term outcomes of patients who have chronic hepatitis C virus infection include cirrhosis, liver failure, and hepatocellular carcinoma.
- Individuals with chronic hepatitis C virus infection should have annual evaluation of hepatic enzymes and function, and children with significant liver disease should undergo

at least annual hepatocellular carcinoma screening through ultrasonography and α-fetoprotein measurement.

ABP Content Specifications(s)
- Understand the possible long-term outcomes of patients who have hepatitis C virus infections
- Understand the importance of follow-up screening evaluations for complications of hepatitis C virus infection

Suggested Readings
- American Academy of Pediatrics. Hepatitis C. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* Elk Grove Village, IL: American Academy of Pediatrics; 2015;423–430.
- Christenson J, Manaloor J. Hepatitis A, B, and C. *Pediatr Rev.* 2016;37(10):426–438. doi: http://dx.doi.org/10.1542/pir.2015-0075.
- Mack C, Gonzalez-Peralta R, Gupta N, et al. NASPGHAN Practice Guidelines: diagnosis and management of hepatitis C infection in infants, children, and adolescents. *J Pediatr Gastroenterol Nutr*. 2012;54(6):838–855. doi: http://dx.doi.org/10.1097/MPG.0b013e318258328d.

Question 81

A 4-year-old boy is brought to the urgent care center for fever, vomiting, diarrhea, and reduced urine output. On physical examination, the boy is alert and able to answer some questions. He has a mildly elevated heart rate, normal blood pressure, dry mucous membranes, and sunken eyes. You diagnose him with acute gastroenteritis, and begin treatment with oral ondansetron and frequent, small aliquots of oral rehydration solution (ORS). However, he resists any oral intake and after 1 hour, has taken only 5 mL/kg of ORS. You order placement of an intravenous (IV) line for hydration. Despite the staff's best efforts, 3 attempts at placing an IV failed. His father is visibly upset and asks if there is another option for giving his son fluids.

Of the following, the BEST next step in managing this child's dehydration is to

A. administer ORS via nasogastric tube
B. place an intraosseous line for hydration
C. reattempt oral rehydration using small aliquots of ORS
D. reattempt oral rehydration using small aliquots of water
E. request that a nurse from the intensive care unit place the IV line

Correct Answer: A

Of the response choices, the best next step in managing this child's dehydration is to administer an oral rehydration solution (ORS) via nasogastric tube. The boy in the vignette is volume depleted as a result of vomiting and diarrhea caused by viral gastroenteritis, a condition that nearly every child experiences by 2 years of age. Based on the clinical history and physical examination, this child has a 5% to 9% volume loss. His level of dehydration can be categorized as moderate (**Item C81A**), and these losses should be replaced. Severe dehydration (>9% volume deficit) requires immediate intravenous fluid therapy, with repeated boluses of 20 mL/kg of normal saline until adequate tissue perfusion is achieved. However, the recommended first step in a health care setting for mild to moderate dehydration is to initiate oral rehydration therapy (ORT), even if caregivers report that they have been trying this at home to no avail. Compared with intravenous fluid therapy, ORT can be more rapidly initiated and is equally clinically effective in treating mild to moderate dehydration.

Table C81A. Clinical Signs and Symptoms of Dehydration.*

Clinical Signs	Mild (3%-5%)	Moderate (6%-9%)	Severe (≥10%)
Systemic	Increased thirst	Irritable	Lethargic
Urine Output	Decreased	Decreased (<1 mL/kg/hr)	Decreased (oliguria/anuria)
Mucous Membranes	Tacky	Dry	Parched
Skin Turgor[†]	Normal	Reduced	Tenting
Capillary Refill[†]	Normal	Mildly delayed	Markedly delayed
Skin Temperature	Normal	Cool	Cool, mottled
Anterior Fontanelle	Normal	Sunken	Markedly sunken
Heart Rate	Normal	Increased	Markedly increased or ominously low
Blood Pressure	Normal	Normal to low	Low
Respirations[†]	Normal	Deep, rate may be increased	Deep, rate may be increased, decreased or absent

* These findings for isonatremic dehydration overestimate the degree of dehydration with hyponatremia and underestimate the degree of dehydration with hypernatremia.

[†] Best predictors of dehydration.

Reprinted with permission from Powers KS. Dehydration: isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev.* 2015, 36 (7) 274-285.

Oral rehydration solution should be given in small aliquots every 5 minutes, based on weight, degree of dehydration on presentation, and any ongoing fluid losses (**Item C81B**). ORS has a specific sodium and glucose ratio. The use of fluids lacking the proper sodium and glucose balance (eg, apple juice, soda, water) puts volume-depleted patients at risk for hyponatremia. Treatment with ondansetron can reduce nausea and vomiting, increasing the chance of success with ORT, and reducing the need for intravenous fluid therapy and hospitalization.

Table C81B. Guidelines for Administration of Oral Solutions to Replace Fluid Deficit over 4 Hours.

Weight (kg)	Mild Dehydration (3%–5%)		Moderate Dehydration (6%–9%)	
	Total Volume Over 4 Hours	Volume per Administration	Total Volume Over 4 Hours	Volume per Administration
5	150-250 mL	5 mL every 5-8 min	300-450 mL	6-9 mL every 5 min
10	300-500 mL	6-10 mL every 5 min	600-900 mL	12-18 mL every 5 min
15	450-750 mL	10-15 mL every 5 min	900-1,350 mL	18-28 mL every 5 min
20	600-1,000 mL	12-20 mL every 5 min	1,200-1,800 mL	25-37 mL every 5 min
25	750-1,250 mL	15-25 mL every 5 min	1,500-2,250 mL	30-45 mL every 5 min
30	900-1,500 mL	18-30 mL every 5 min	1,800-2,700 mL	37-55 mL every 5 min
40	1,200-2,000 mL	25-40 mL every 5 min	2,400-3,600 mL	50-75 mL every 5 min

Reprinted with permission from Powers KS. Dehydration: isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev.* 2015, 36 (7) 274-285.

If a child with moderate dehydration fails to take the required amount of ORS, or continues to vomit, nasogastric or intravenous fluid administration should commence. If an intravenous line is being placed, many experts recommend obtaining serum glucose and sodium levels to help direct the type of intravenous fluid used for rehydration. For isotonic dehydration, experts recommend 2 different strategies for intravenous rehydration. Some advocate giving a 20mL/kg bolus of

normal saline and then reattempting ORT in the emergency department. A more traditional approach is to admit the child to the hospital, and replace the calculated fluid deficit intravenously with D5 half-normal saline over a 24-hour period. Critics of this latter approach cite the risk of hyponatremia and recommend using only isotonic saline for volume replacement. It is important to note that children with a number of medical conditions, such as congenital heart disease and chronic kidney disease, require tailored fluid therapy, for which ORT may not be the best option. ORT may be inappropriate or unlikely to be successful in infants younger than 6 months of age; children with other chronic conditions, such as neurodevelopmental disabilities; and when a cause other than infectious gastroenteritis, such bowel obstruction, pancreatitis, or intussusception, is suspected.

Placing an intraosseous line is appropriate for patients with severe dehydration or shock when rapid intravenous access cannot be obtained, but would be too aggressive an approach for the boy in the vignette. Asking experienced staff from other units to place intravenous lines can delay treatment and disrupt care in the other unit. Although it may be appropriate in certain clinical settings, it is not so when a nasogastric route is readily available.

PREP Pearls
- The first line treatment for mild-moderate dehydration is to attempt oral rehydration, with or without administering ondansetron, even if caregivers report that this has failed at home.
- If a child with moderate dehydration fails to take the required amount of oral rehydration solution, or continues to vomit, nasogastric or intravenous fluid administration should commence.
- Severe dehydration (>9% volume deficit) requires immediate intravenous fluid therapy, with repeated boluses of 20 mL/kg of normal saline until adequate tissue perfusion is achieved.

ABP Content Specifications(s)
- Plan fluid therapy for a patient with acute gastroenteritis unresponsive to oral rehydration

Suggested Readings
- Bellemare S, Hartling L, Wiebe N, et al. Oral rehydration versus intravenous therapy for treating dehydration due to gastroenteritis in children: a meta-analysis of randomised controlled trials. *BMC Med*. 2004;2:11 .
- Moritz ML, Ayus JC. Misconceptions in the treatment of dehydration in children. *Pediatr Rev*. 2016;37(7):e29–e31. doi: http://dx.doi.org/10.1542/pir.2016-003.
- Powers KS. Dehydration: isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev*. 2015;36(7):274–285. doi: http://dx.doi.org/10.1542/pir.36-7-274.

Question 82

You are leading a small group discussion with pediatric residents about strategies hospitals use to reduce medical errors. You discuss approaches for improving the patient handoff process between day shift inpatient care teams and on-call residents.

Of the following, the MOST accurate statement to include is that

    A. this process should be individualized based on each care provider's preference
    B. only team members handing off patients to the receiving team should discuss patients during this process
    C. printed patient summary documents used in this process remain accurate for an average of 12 hours
    D. standardization of this process increases the time required to hand off patients to the on-call team
    E. use of a mnemonic to remember the important elements of this process leads to fewer miscommunication events

Correct Answer: E

Medical errors are common, and can have a negative impact on patients' health outcomes. Poor communication is a major cause of medical error. The accurate transmission of clinical information between clinicians transferring and receiving care responsibility, the patient handoff process, is crucial to preventing medical errors. Using a mnemonic to guide the handoff process decreases the risk of miscommunication, and ensures that all important elements of the process are included.

The resident duty hour restrictions implemented several years ago have increased the frequency of patient handoffs. Graduate medical education training programs are required to educate residents and fellows on the optimal approaches to the handoff process. Standardization of handoffs decreases the risk that important information will be omitted, and generally aims to do so without increasing the demand on practitioner time. Elements that improve handoff quality include face-to-face communication, using a mnemonic to ensure that all important elements are included, and having the receiving team summarize information provided by the team handing over care.

Printed patient summary documents can help with the transfer of information during the handoff process. Use of both a sign out document and verbal communication is preferable to verbal communication alone. However, these documents generally remain accurate for only a short period. One study found that the half-life of printed patient summaries (the time before half of the summaries will contain inaccuracies) was 6 hours or less. Use of an electronic summary that is continuously updated to reflect clinical changes is recommended as the ideal method to keep patient handoff information up to date.

PREP Pearls
- Using a mnemonic as a guide during patient handoffs decreases the risk of miscommunication, and helps to ensure that all important elements are included.
- Printed patient summary documents can help with the transfer of information during the handoff process; however, these documents generally remain accurate for only a short period.

ABP Content Specifications(s)
- Understand the importance of assessment and redesign of health-care processes before error occurs
- Understand the importance of assessment and redesign of health-care processes before error occurs
- Understand the importance of leadership in creating a culture of safety in the health-care system
- Promote effective team functioning in the prevention of medical error
- Apply knowledge of human factors in the design of systems and processes promoting patient safety

Suggested Readings

- Rosenbluth G, Jacolbia R, Milev D, Auerbach AD. Half-life of a printed handoff document. *BMJ Qual Saf.* 2016;25(5):324-328.
- Starmer AJ, Spector ND, Srivastava R, et al. Changes in medical errors after implementation of a handoff program. *N Engl J Med.* 2014;371(19):1803-1812.

Question 83

A 2-year-old boy is brought to your office for evaluation of a persistent cough. The cough has been present since 3 weeks of age and is wet in quality. Produced phlegm has been swallowed rather than expectorated, and the cough is worse in the morning upon waking. The child has had intermittent wheezing during respiratory illnesses. He has been admitted to the hospital 3 times with bronchiolitis and has demonstrated short-term improvement with short-acting β-agonists, systemic steroids, and parenteral antibiotics.

The child also has chronic rhinitis. He recently had surgical adenoidectomy and bilateral myringotomy tube placement due to chronic otitis media with speech delay. There is no history of failure to thrive or dysphagia. Results of a sweat test were normal.

The child is well nourished, active, and playful. Height and weight are at the 50th percentile for age. Mucopurulent drainage is noted from both nares. Serous drainage is present from both myringotomy tubes, and postnasal drip is visible at the posterior oropharynx. Auscultation of the lungs reveals bilateral end expiratory wheezing and coarse breath sounds throughout. The abdominal and cardiac examination findings are unremarkable.

Of the following, the finding that MOST strongly supports the likely diagnosis is

 A. bronchiectasis of upper lobes on computed tomography of the chest
 B. chronic pansinusitis on sinus computed tomography
 C. culture of sputum for Moraxella catarrhalis
 D. heterotaxy
 E. homozygous presence of DNAH11 mutation

Correct Answer: E

The child in this vignette has a constellation of symptoms and signs that should raise concern for a suppurative lung disease. Given that the results of sweat testing by pilocarpine iontophoresis were normal, the most likely diagnosis is primary ciliary dyskinesia (PCD). The finding that will most clearly establish the diagnosis is confirmation of the homozygous presence of a known disease-causing mutation, including mutations in *DNAH11*.

The diagnosis of PCD is challenging; symptoms that include chronic cough, intermittent wheezing, and upper airway congestion may be attributed to more common childhood illnesses such as bronchitis, allergic rhinitis, sinusitis, or asthma. As such, the consideration of a ciliopathy as the etiology for symptoms is often delayed. Furthermore, testing for ciliary dyskinesia is not available at every center, and results may be difficult to interpret without the assistance of a specialist. Therefore, referral to a regional center with clinical and research expertise may be indicated.

The suggestive symptoms of ciliary dyskinesia include:
* A history of neonatal respiratory distress, tachypnea, hypoxemia, or respiratory failure. Often, these findings may be attributed to transient tachypnea of the newborn or other inciting factors, such as amniotic fluid aspiration.
* Chronic, daily nasal drainage that is nonseasonal, may be purulent, and may be present as early as the first weeks after birth; chronic or recurrent sinusitis may be a clinical complication once the sinuses are developed.
* Chronic wet or productive cough, often worse in the early morning. The cough, along with the nasal drainage, may originate early in postnatal life.
* Chronic otitis media or otorrhea, often requiring tympanostomy tube placement; complications include regional spread of chronic middle ear infection (eg, mastoiditis) and hearing loss.
* Recurrent or chronic bronchitis or pneumonia
* Bronchiectasis
* Male infertility

The classic description of Kartagener syndrome or triad, first described in the early 20th century, includes situs inversus totalis, chronic sinusitis, and bronchiectasis. Subsequent investigations have provided additional insights regarding the prevalence and etiology of associated laterality defects in patients with ciliary disorders. Laterality defects are more common (approximately 50%) than initially suspected in patients with PCD. The spectrum of laterality defects is not limited to situs inversus totalis. Rather, up to 6% of individuals with PCD may demonstrate heterotaxy syndromes with or without associated congenital heart disease. In addition, certain genetic syndromes (eg, Bardet-Biedl syndrome) are associated with ciliary dysfunction. As such, the clinical spectrum of symptoms and comorbidities that must be considered in this suspected patient population has continued to evolve.

In the diagnostic approach to a suspected ciliopathy, the terminology "immotile cilia syndrome" is no longer favored because ciliary samples from many individuals with ciliopathic disorders

may demonstrate normal or near-normal motility on wet preparation or high power magnification inspection. Newer technology, which includes high-speed video-microscopy, may allow a collaborating pathologist to detect more subtle abnormalities of ciliary beat frequency or "stiffness" of beat patterns.

The gold standard for the diagnosis of ciliary defects has long been electron microscopic analysis of ciliary samples extracted from the nose or airway. The classic normal ciliary ultrastructure includes 9 outer doublets in a circular pattern and surrounding a central pair of microtubules. The expected 9 + 2 structure is maintained by radial spokes and intertubular linkage. Additionally, inner and outer dynein arms are visible as appendages to each of the outer doublets; these large protein complexes are responsible for ciliary movement, which is affected through sliding of microtubules. Pathognomonic abnormalities in ciliary ultrastructure include absence of inner and/or outer dynein arms, absence of radial spokes, or absence of the central microtubular pair, resulting in related disorganization of the complex. Recently, a specific genetic defect responsible for PCD (*DNAH11* mutation) has been confirmed as being associated with ciliary ultrastructure. Although cilia beat frequency may show subtle abnormalities, this discovery has confirmed that ultrastructural analysis will not identify all patients with PCD.

Nasal nitric oxide is under investigation to determine its validity as a screening tool in patients with suspected PCD and ciliopathic disorders.

The identification of genetic mutations that cause or predispose to ciliopathy is under continuous study. More than 30 disease-causing mutations have been identified.

Moraxella catarrhalis, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus* are commonly isolated from the airway of individuals with bronchitis, pneumonia, sinusitis, and/or bronchiectasis. However, none of these radiographic or laboratory findings are individually or collectively diagnostic of primary ciliary dyskinesia.

PREP Pearls
- The symptoms of primary ciliary dyskinesia often mimic more common childhood respiratory illness such as bronchitis, pneumonia, or asthma, and a high index of suspicion is required to recognize disease-associated signs and symptoms.
- The diagnosis of primary ciliary dyskinesia presents an ongoing challenge. The diagnosis may be suspected on the basis of clinical or radiographic findings but must be confirmed by ultrastructural analysis of cilia or by genetic mutation analysis.
- Heterotaxy and other laterality defects are seen with increased frequency in patients with primary ciliary dyskinesia. Therefore, an individual with congenital heart disease or laterality defect and suggestive upper or lower airway symptomatology should be evaluated for evidence of a ciliopathy.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of primary ciliary dyskinesia
- Recognize disorders associated with primary ciliary dyskinesia

Suggested Readings
- www.genetests.org.
- Fitzgerald DA, Shapiro AJ. Primary ciliary dyskinesia. *Paediatr Respir Rev.* 2016;18:1–2. doi: http://dx.doi.org/10.1016/j.prrv.2015.11.010.
- Leigh MW, Zariwala MA, Knowles MR. Primary ciliary dyskinesia: improving the diagnostic approach. *Curr Opin Pediatr.* 2009;21(3):320–325. doi: http://dx.doi.org/10.1097/MOP.0b013e328329cddb.

Question 84

A 15-year-old boy with trisomy 21 is brought to your office for evaluation of "tiredness." His mother reports that, over the past several months, he has not been as active as usual. He prefers to sit and watch his siblings play soccer rather than play with them, as he had in the past. When he goes shopping with her, he stops and rests frequently. The boy has recently been complaining of headaches, neck aches, and muscle aches. His sleep pattern is unchanged and he does not have daytime sleepiness. His academic performance is unchanged. On physical examination, his weight is 170 pounds, which is increased by 20 pounds from his visit 6 months ago. His blood pressure is 118/68 mm Hg and his heart rate is 92 beats/min. His general physical examination findings are normal, other than common stigmata of trisomy 21. There is no bruising, paleness, petechiae, or dry skin. His neurologic examination shows low tone in his upper extremities and increased tone in his lower extremities. His patellar reflexes are brisk and his toes extend on plantar stroking. Laboratory studies show a white blood cell count of 5,000/μL (5.0×10^9/L) with 45% neutrophils, 45% lymphocytes, 3% eosinophils, and 7% monocytes; hemoglobin, 13 g/dL (130 g/L); platelets, 300×10^3/μL (300×10^9/L).

Of the following, the boy's MOST likely underlying diagnosis is

- A. anemia
- B. atlantoaxial instability
- C. hypothyroidism
- D. leukemia
- E. obstructive sleep apnea

Correct Answer: B

The boy in the vignette has trisomy 21, and at baseline, would have decreased muscle tone and hyporeflexia or areflexia. His lower extremity increased tone and hyperreflexia are unexpected, and suggest a spinal cord lesion such as cervical cord compression due to atlantoaxial instability. Increased tone in his legs is making it difficult for him to participate in his usual physical activities. Taking breaks and decreasing overall activity make him seem "tired" to his family even though he is not sleepy. Asking for examples of "tiredness" or "fatigue" during the history can help distinguish exercise intolerance from sleepiness, depression, encephalopathy etc.

Atlantoaxial instability occurs when there is increased mobility between vertebrae C1 (atlas) and C2 (axis). Although patients with atlantoaxial instability can be asymptomatic, there is a risk of spinal cord compression. Symptoms of spinal cord compression include increased tone or spasticity in the limbs, hyperreflexia, bowel or bladder incontinence, torticollis, or neck pain. These symptoms can have a slow onset, as in the boy in the vignette, or they can present abruptly, especially if there is sudden neck hyperextension or flexion as can happen in active sports, falls, or during a procedure such as intubation. If acute spinal cord compression is suspected, the patient should be referred immediately to the emergency department for neurosurgical evaluation.

Anemia, hypothyroidism, leukemia, and obstructive sleep apnea can all cause fatigue and decreased exercise tolerance, but none of these cause spasticity or hyperreflexia.

PREP Pearls
- Patients with atlantoaxial instability are at risk for spinal cord compression.
- Symptoms of spinal cord compression include new-onset limb spasticity, hyperreflexia, bowel or bladder incontinence, torticollis, or neck pain.

ABP Content Specifications(s)
- Understand the association between atlantoaxial instability and potential neurologic complications

Suggested Readings
- Hobson-Rohrer WL, Samson-Fang L. Down syndrome. *Pediatr Rev.* 2013;34(12):573–574. doi: http://dx.doi.org/10.1542/pir.34-12-573.
- Leonard JR, Jaffe DM, Kuppermann N, Olsen CS, Leonard JC, for the Pediatric Emergency Care Applied Research Network (PECARN) Cervical Spine Study Group. Cervical spine injury patterns in children. *Pediatrics*. 2014;133(5):e1179–e1188. doi: http://dx.doi.org/10.1542/peds.2013-3505.

Question 85

You are seeing a 4-year-old boy for recurrent purulent otorrhea. He had frequent episodes of acute otitis media as an infant and had myringotomy tubes placed at age 2 years, after which he had only occasional ear infections. Since an episode of acute otitis media 3 months ago, he has had frequent recurrences of purulent ear drainage from his left ear, which improved when treated with topical fluoroquinolone/glucocorticoid drops. The boy has been otherwise well. His left ear currently has purulent drainage obscuring the tympanic membrane. The remainder of his physical examination findings are normal. Screening shows a mild decrease in hearing in the left ear, with normal hearing in the right ear.

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

- A. avoidance of water in the ears and reevaluation in 2 weeks
- B. treatment with oral amoxicillin and topical bacitracin-polymyxin-hydrocortisone drops
- C. referral to an allergy/immunology specialist for evaluation
- D. referral to an otolaryngology specialist for evaluation
- E. repeat administration of topical fluoroquinolone/glucocorticoid drop

Correct Answer: D

The boy in the vignette has had recurrent purulent otorrhea for several weeks, and thus an underlying cause, such as cholesteatoma, foreign body, histiocytosis, and other inflammatory or malignant conditions, should be considered (**Item C85**). Persistent purulent otorrhea for more than 2 weeks despite treatment is an indication for referral to otolaryngology. Thus, the most appropriate next step in management would be referral to an otolaryngologist, who can thoroughly clean and examine the ear under the operating microscope.

Item C85. Causes of Purulent Otorrhea in Children.

Infectious
- Acute otitis media with perforation
- Chronic suppurative otitis media
- Necrotizing otitis media
- Otitis externa
- Otomycosis

Structural/Mechanical
- Cholesteatoma
- Foreign body
- Granuloma
- Polyp
  - Ventilation tube complication

Other
- Histiocytosis
- Immune deficiency
- Neoplasm (rhabdomyosarcoma)

Courtesy of K Bowen

Cholesteatoma, composed of squamous epithelium and keratin and appearing as a white mass behind the tympanic membrane (TM), is the cause of persistent otorrhea in 25% to 60% of children. Cholesteatoma may be congenital or acquired. Most cases of cholesteatoma are acquired and occur as a result of chronic eustachian tube dysfunction, which creates a vacuum that pulls TM surface epithelium into the middle ear, forming a cyst. The epithelial cells then produce and deposit keratin and other debris inside the cyst, causing the lesion to grow. The most common form is a "retraction pocket cholesteatoma," which occurs in the posterior-superior portion of the TM, in the pars flaccida, or at the site of a previous ventilation tube. More rarely, epithelium can enter the middle ear through a TM perforation, or by creeping along the side of a retained ventilation tube.

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Congenital cholesteatoma is rare. It occurs in the absence of prior history of ear disease; this includes no history of prior ear surgery, TM perforation, or TM retraction. On physical examination, a white mass is visible behind an intact TM. Hearing loss may be present, and precedes TM perforation and drainage by months to years.

Treatment of cholesteatoma is surgical removal. In developed nations, lethal complications of cholesteatoma are very rare, but permanent hearing loss may occur in untreated cases. Purulent otorrhea in children is defined as acute (< 6 weeks duration) or chronic (≥6 weeks duration). The most common cause of acute purulent otorrhea is infection, frequently acute otitis media with TM perforation. The most common organisms isolated are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Rarely, *Streptococcus pyogenes* may be found. Other frequent causes of acute purulent otorrhea include otitis externa, ventilation tube placement complication, cholesteatoma, and foreign body.

Chronic suppurative otitis media is the most common cause of chronic purulent otorrhea, with biofilm-producing *Staphylococcus aureus* and *Pseudomonas aeruginosa* being the most commonly isolated organisms. Neoplasm, histiocytosis, and infection related to immunodeficiency states are much rarer causes of purulent otorrhea.

Debate exists regarding the impact of water exposure on the development of otorrhea. Generally, ear plug use and strict water avoidance for children with ventilation tubes are no longer recommended. However, in children older than 6 years, otorrhea occurs most often during the summer swimming season. Thus some practitioners still recommend that precautions be taken for children in this age group when swimming.

Given the duration and recurrent nature of his symptoms, water avoidance is unlikely to be curative for the boy in the vignette. Although treatment with amoxicillin and an ototopical antibiotic would be appropriate for a child with acute otitis media with perforation, it is not appropriate for a child with chronic symptoms such as the boy in the vignette. The role of allergy in otitis media with effusion and chronic suppurative otitis media remains controversial, with inadequate data on which to base a recommendation for referral to allergy/immunology at this time. Failure to resolve purulent otorrhea despite adequate treatment is an indication to search for an underlying condition. It is not appropriate to administer repeated courses of fluoroquinolone/glucocorticosteroid drops.

PREP Pearls
- Among children with persistent otorrhea, 25% to 60% are found to have a cholesteatoma, a collection of squamous epithelial cells and keratin within the middle ear.
- Acute purulent otorrhea, lasting less than 2 to 6 weeks, is most commonly associated with acute otitis media with tympanic membrane perforation.
- Chronic suppurative otitis media is the most common cause of chronic purulent otorrhea.
- The causative organisms for acute and chronic purulent otorrhea are different.
- Less common causes of persistent otorrhea include foreign body, polyp, granuloma, histiocytosis, neoplasm, and immune deficiency.

ABP Content Specifications(s)
- Understand the significance of otorrhea
- Identify the various causes of purulent otorrhea

Suggested Readings
- Harris KC, Conley SF, Kerschner JE. Foreign body granuloma of the external auditory canal. *Pediatrics*. 2004;113:e371-e373.
- Isaacson G. Diagnosis of pediatric cholesteatoma. *Pediatrics*. 2007;120:603-608. doi: http://dx.doi.org/10.1542/peds.2007-0120.
- Isaacson G. Why don't those ear drops work for my patients? *Pediatrics*. 2006;118:1252-1253. doi: http://dx.doi.org/10.1542/peds.2006-0826.
- Van Dongen T, Schilder AG, Venekamp RP, deWit A, van der Heijden GJ. Cost-effectiveness of treatment of acute otorrhea in children with tympanostomy tubes. *Pediatrics*. 2015;135:e1182-e1189. doi: http://dx.doi.org/10.1542/peds.2014-3141.

Question 86

You are evaluating a 10-day-old term newborn who is in the emergency department because of decreased activity, poor feeding, and respiratory distress. The baby was born by normal spontaneous vaginal delivery with no pregnancy or delivery complications. Maternal history is negative for premature or prolonged rupture of membranes, group B Streptococcus colonization, genital herpes, hepatitis B surface antigen, human immunodeficiency virus, and rapid plasma reagin.

The newborn is critically ill and has a temperature of 35.3°C. He is in respiratory failure and shock. Skin examination findings are normal. Laboratory data are significant for leukopenia, thrombocytopenia, disseminated intravascular coagulation, and severe hepatitis. A chest radiograph shows bilateral pulmonary infiltrates. Blood and urine cultures were obtained, but the newborn is not stable enough for lumbar puncture.

Of the following, the BEST initial antimicrobial treatment is ampicillin, cefotaxime, and

  A. acyclovir
  B. amphotericin B
  C. oseltamivir
  D. trimethoprim-sulfamethoxazole
  E. vancomycin

Correct Answer: A

The neonate described in this vignette has a clinical picture suggestive of severe sepsis with shock, respiratory failure, pneumonitis, hepatitis, and disseminated intravascular coagulation. These findings are concerning for both viral or bacterial sepsis. Physicians must recognize that herpes simplex virus (HSV) can present in neonates with severe hepatitis, disseminated intravascular coagulation, pneumonitis, and sepsis syndrome. Thus, initiating empiric intravenous acyclovir therapy after obtaining diagnostic studies for HSV, in addition to antibacterial treatment with ampicillin and cefotaxime, is the preferred treatment for the neonate in this vignette. In addition to HSV, other viruses such as enterovirus and adenovirus can also cause severe sepsis with hepatitis and coagulopathy.

The incidence of neonatal herpes in the United States is estimated to vary from 1 in 3,000 to 20,000 live births. Approximately 70% of newborns with perinatal HSV infection are born to mothers with asymptomatic genital herpes infection near delivery. Neonatal herpes can be caused by HSV1 or HSV2; approximately 75% of cases are caused by HSV2. Approximately 85% of neonatal HSV infection is acquired at delivery by fetal exposure to the virus in the maternal genital tract. Additionally, HSV may be acquired via ascending infection with membrane rupture or with apparently intact membranes. In 5% of cases, HSV transmission occurs during pregnancy. Postnatal transmission from a parent or other caregiver (often from nongenital infection) occurs in 10% of cases. The risk of neonatal herpes is highest (25%-60%) from mothers with primary genital HSV infection as compared to mothers with recurrent genital HSV infection (< 2%).

Neonatal herpes manifests as skin, eye, and mouth disease in 45% of cases; disseminated disease in 25% of cases; and central nervous system (CNS) disease with or without skin lesions in 30% of cases. Disseminated disease, which often presents around 10 to 12 days after birth, is the most severe form of neonatal HSV infection and affects many organ systems, especially the lung, liver, and brain. The clinical presentation is often characterized by sepsis syndrome with pneumonitis, hepatitis, severe coagulopathy, and encephalitis. Skin lesions may be absent at disease onset, but approximately 66% of disseminated disease cases have cutaneous vesicles. Early clinical diagnosis of disseminated neonatal HSV infection is difficult because the clinical presentation is often nonspecific and confused with bacterial infection. Skin vesicles may be absent in disseminated disease, as seen in the patient in this vignette.

Neonatal HSV disease may be diagnosed by detection of virus from vesicles (if present) or surface swabs (conjunctivae, mouth, nasopharynx, or anus) by culture or polymerase chain reaction (PCR). Lumbar puncture should be performed in all cases of suspected neonatal herpes to evaluate for CNS involvement. The diagnostic evaluation of neonatal HSV infection should include HSV PCR assays of cerebrospinal fluid and whole blood and determination of serum alanine transferase levels. Positive PCR test results or viral cultures from surface swabs collected more than 12 to 24 hours after delivery are indicative of neonatal HSV infection. Neuroimaging and ophthalmologic evaluation is recommended to exclude HSV ocular disease.

All neonates with suspected or confirmed HSV infection must receive intravenous acyclovir (60 mg/kg/d in 3 divided doses). The recommended length of acyclovir therapy is 21 days for CNS or disseminated disease and 14 days for skin, eye, and mouth disease. A repeat lumbar puncture is recommended for infants with CNS disease at the completion of a 3-week acyclovir course to demonstrate negative cerebrospinal fluid HSV PCR test results. If the HSV PCR results remain positive, intravenous acyclovir is continued for 1 additional week and followed by repeated cerebrospinal fluid testing. In such cases, a pediatric infectious disease consultation is recommended.

Following completion of intravenous acyclovir, all infants with neonatal HSV infection (disseminated disease; skin, eye, and mouth disease; or CNS disease) must receive oral acyclovir suppressive therapy for 6 months. Improvement in neurodevelopmental outcomes in babies with CNS disease and prevention of cutaneous recurrences in all 3 forms of HSV disease have been reported with oral acyclovir suppressive therapy. Infants must be closely monitored with serial complete blood cell counts for neutropenia while receiving acyclovir suppressive therapy. With receipt of intravenous acyclovir therapy, the risk of mortality in disseminated neonatal HSV infection has decreased from 85% to 30%, and neurologic development is normal in 85% of survivors. The risk of mortality is greatest when the neonatal HSV infection presents with lethargy and severe hepatitis.

In a term infant, the differential diagnosis of sepsis must include late-onset bacterial sepsis. However, the clinical presentation and laboratory findings in the neonate described in this vignette are more consistent with disseminated herpes than methicillin-resistant *Staphylococcus aureus* infection. Initiating acyclovir therapy in conjunction with intravenous ampicillin and cefotaxime to cover for common pathogens associated with neonatal sepsis (such as group B *Streptococcus*, *Escherichia coli*, *Listeria monocytogenes,* or *Enterococcus*) is the preferred response over vancomycin for empiric treatment of this infant.

Candidiasis is a major cause of morbidity and mortality among low birth-weight infants in the neonatal intensive care unit. However, invasive fungal infection would be very unusual in an otherwise healthy term infant during the first weeks after birth. Thus, amphotericin therapy to empirically treat fungal infection would not be recommended for the neonate in this vignette. Rarely, influenza infection in infants can manifest as a sepsis-like syndrome associated with pneumonia; however, initiating empiric oseltamivir would not be a preferred response in this case. *Pneumocystis jirovecii* infection, an opportunistic infection in immunocompromised individuals, is rare in the first month after birth and an unlikely diagnosis in this infant given the negative maternal HIV antibody serology. Thus, trimethoprim-sulfamethoxazole therapy to empirically treat *P jirovecii* pneumonia would not be recommended.

PREP Pearls
- Sepsis caused by herpes simplex virus should be in the differential diagnosis of any critically ill infant with an acute presentation of sepsis syndrome, rapidly progressive pneumonitis, hepatitis, and disseminated intravascular coagulation.

- Disseminated neonatal herpes simplex virus infection is the most severe form of neonatal herpes and is associated with high morbidity and mortality.
- Early recognition of disseminated herpes simplex virus disease in the neonate can be difficult, because the clinical presentation often mimics bacterial sepsis with the absence of cutaneous vesicles.
- Neonates with suspected or confirmed herpes simplex virus infection must receive intravenous acyclovir. Infants with neonatal herpes simplex virus infection must receive oral acyclovir suppressive therapy for 6 months after completion of intravenous acyclovir for acute herpes simplex virus infection.

MOCA-Peds Objective
- Recognize respiratory distress and manage appropriately

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation for herpes simplex virus infection
- Plan the appropriate management of herpes simplex virus infection in children of various ages, taking into account appropriate timing of therapy
- Recognize the clinical features associated with herpes simplex virus infection in children of various ages

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, Lin CY, Jacobs RF, et al. Natural history of neonatal herpes simplex virus infections in the acyclovir era. *Pediatrics*. 2001;108(2):223–229. doi: http://dx.doi.org/10.1542/peds.108.2.223.
- 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.

Question 87

You are seeing a 4-month-old breastfed male infant for a health supervision visit with a resident. The infant's mother reports frequent effortless regurgitation of food that follows most liquid meals. She reports no pain or fussiness with the episodes and no correlation with changes in maternal diet.

The infant has a heart rate of 118 beats/min, respiratory rate of 26 breaths/min, and temperature of 37°C. He is alert and well nourished. His examination findings are unremarkable. The resident asks what education she should provide this mother about when regurgitation is likely to resolve.

Of the following, it is MOST likely that these events will stop by

 A. 6 months
 B. 8 months
 C. 9 months
 D. 10 months
 E. 12 months

Correct Answer: E

There are many terms for the movement of stomach contents up the esophagus and to or out of the mouth. These terms include regurgitation, gastroesophageal reflux, gastroesophageal reflux disease, rumination, and vomiting.

Regurgitation is the involuntary effortless return of stomach contents to the mouth and is common in infants. Regurgitation is associated with the transient relaxation of the lower esophageal sphincter. The stomach contents are often expelled, and the process is commonly referred to as "spitting up." Sixty-seven percent of infants aged 4 months will experience regurgitation daily. Regurgitation is a physiologic process that resolves in 95% of infants by 12 months of age. Gastric distention, as seen in infants feeding large volumes, increases the frequency of the the lower esophageal sphincter relaxation and therefore increases regurgitation around meal times.

Rome IV criteria for infant regurgitation include regurgitation 2 or more times per day for 3 or more weeks without retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulty, or abnormal posturing in an otherwise healthy infant 3 weeks to 12 months of age.

Vomiting is defined by a central nervous system reflex involving skeletal muscles and the autonomic nervous system resulting in the forcible expulsion of gastric contents through the mouth. This process is accomplished with coordination of musculature in the diaphragm, small bowel, stomach, and esophagus.

Gastroesophageal reflux is the regurgitation of stomach contents into the esophagus without associated symptoms. It occurs in all infants, children, and adults and is not associated with harm in most people. It is difficult to differentiate gastroesophageal reflux and regurgitation. Gastroesophageal reflux disease is regurgitation of stomach contents into the esophagus with associated tissue damage or symptoms (eg, pain, failure to thrive, irritability, cough, dental erosions).

Rumination is the effortless, voluntary, habitual regurgitation of recently swallowed stomach contents without associated heartburn, discomfort, or nausea. It is a rare disorder. Rome criteria for diagnosis include repetitive contractions of the abdominal muscles, diaphragm, and tongue followed by regurgitation of stomach contents, which are then expectorated or chewed and re-swallowed. Three of the following criteria are required for diagnosis: onset between 3 and 8 months of age; does not respond to management for gastroesophageal reflux disease, anticholinergics, formula changes, gavage, or gastrostomy tube feedings; unaccompanied by signs of nausea or distress; and does not occur during sleep and when the infant is interacting with individuals. Complications of rumination can include weight loss, electrolyte abnormalities, malnutrition, dental erosions, halitosis, and inability to function.

PREP Pearls
- Regurgitation is the involuntary effortless return of stomach contents to the mouth and is common in infants. Regurgitation resolves in 95% of infants by 12 months of age.
- Gastroesophageal reflux is regurgitation of stomach contents into the esophagus without associated symptoms.
- Gastroesophageal reflux disease is regurgitation of stomach contents into the esophagus with associated tissue damage or symptoms.
- Rumination is the effortless, voluntary, habitual regurgitation of recently swallowed stomach contents without associated heartburn, discomfort, or nausea.

ABP Content Specifications(s)
- Recognize the significance of regurgitation in infants
- Distinguish between rumination and regurgitation

Suggested Readings
- Di Lorenzo C. Other functional gastrointestinal disorders in infants and young children. *JPGN J Pediatr Gastroenterol Nutr.* 2013;57(suppl 1):S36–S38. doi: http://dx.doi.org/10.1097/01.mpg.0000441933.15093.c3.
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- Vandenplas Y, Hauser B, Devreker T, Salvatore S. Infant regurgitation and pediatric gastroesophageal reflux disease. In: Faure C, Di Lorenzo C, Thapar N, eds. Pediatric Neurogastroenterology: Gastrointestinal Motility and Functional Disorders in Children. New York, NY: Humana Press; 2013:331–346 .

Question 88

A 2-year-old previously healthy girl is brought to the urgent care center where you are working about 20 minutes after she was stung on her right foot by a yellow jacket. The girl was running barefoot through the grass at a local park when she suddenly began screaming and sat down on the ground, clutching her right foot. Her mother noticed several bees flying around her and saw a dead insect on the ground near the girl. She collected the dead insect in a plastic bag, and drove the girl to urgent care center for evaluation.

The girl is crying loudly. Her vital signs are normal for her age. You note no stridor, angioedema, drooling, or facial swelling on physical examination, and she displays no signs of respiratory distress. The girl's lung sounds are clear and equal bilaterally with good aeration, and her abdomen is soft without distention or tenderness. Her extremities are warm and well-perfused, without swelling. You note a 0.5-cm area of erythema on the sole of the child's right foot. No generalized rash or other skin lesions are present. An insect's stinger is visible near the center of the erythematous area on the sole of her foot; you remove the stinger with fine-tipped sterile forceps without difficulty.

The girl's mother shows you the plastic bag containing the dead insect, which you identify as a yellow jacket (Vespula malculifrons). She is very worried because the girl's father had a serious anaphylactic reaction after being stung by a wasp a few years ago.

Of the following, the MOST appropriate recommendation regarding further evaluation and management for this girl is

 A. application of cool compresses to the right foot and oral analgesics
 B. a short course of oral corticosteroids and oral analgesics
 C. observation in the urgent care center over the next 6 hours
 D. referral to an allergist for venom immunotherapy
 E. use of an epinephrine autoinjector if future Hymenoptera stings occur

Correct Answer: A

The young girl in the vignette presents after sustaining a Hymenoptera sting to her foot. She has localized erythema at the site of her recent sting, but no other findings of systemic illness. Only supportive care, including application of cool compresses to the girl's foot and mild oral analgesics, are indicated at this time. Pediatric providers must recognize the clinical findings associated with life-threatening reactions to Hymenoptera stings, as well as reactions that require no further intervention in children.

Bees (*Apidae)*, wasps (*Vespidae*), and ants (*Formicidae*) are insects that comprise the order known as Hymenoptera. All members of this order can sting and cause a wide range of reactions—from minor localized redness and swelling to severe systemic anaphylactic reactions. The most common reactions to Hymenoptera stings in children include localized pain, itching, erythema, and mild swelling at the site of the sting, without any signs of systemic illness (as observed in the girl in the vignette). In such cases, the recommended treatment involves removing the stinger (using tweezers or gently scraping the skin), application of cool compresses or ice packs, mild oral analgesics (eg, acetaminophen), and oral antihistamines to help alleviate pruritus. Minor local reactions to Hymenoptera stings generally resolve within a few hours to a few days.

More severe local reactions to Hymenoptera stings can present with marked swelling, redness, and pain near the sting site. This may prompt clinicians to suspect cellulitis, but infection is unlikely in the first 48 hours after a sting, and antibiotics are generally not required. Large localized reactions to Hymenoptera stings can take more than a week to resolve, and affected patients often have similar reactions with future stings. Patients who have this type of local response to Hymenoptera stings have a relatively low risk of future anaphylactic reactions (≤10%).

The most severe and life-threatening reactions to Hymenoptera stings are immunoglobulin E–mediated, systemic anaphylactic reactions. These cases typically involve rapid development of symptoms involving 2 or more body systems, which may include skin and/or mucous membrane (urticaria, angioedema, flushing), respiratory (wheezing, cough, stridor, dyspnea), cardiovascular (hypotension, dizziness, syncope, shock), and gastrointestinal (colicky abdominal pain, nausea, vomiting, diarrhea) manifestations. Reactions of this type are fortunately rare; anaphylaxis due to insect stings occurs in 0.5% to 5% of the general population, and is less commonly observed in children than in adults. Children presenting with anaphylaxis should be treated immediately with intramuscular epinephrine and aggressive supportive measures to maintain the airway, breathing, and circulation. In addition, all children presenting with acute anaphylaxis should be transported to an emergency department by trained emergency medical personnel.

Oral corticosteroids may be warranted as a component of treatment in patients with either severe local reactions or acute anaphylaxis following Hymenoptera stings. The girl in the vignette presents with a minor local reaction, therefore, treatment with systemic corticosteroids is not indicated in her case.

Observation in the urgent care center over the next 6 hours is not necessary for the girl in the vignette, given that her reaction to a Hymenoptera sting was limited to a minor local reaction. Children who are treated for acute anaphylactic reactions do require close clinical monitoring for a period of at least 4 to 6 hours (generally in an emergency department setting) and may need to be hospitalized in certain cases.

Referral to an allergist for venom immunotherapy would not be warranted in this patient, given the very mild degree of her reaction. Prospective studies involving pediatric participants have found that fewer than 1% of Hymenoptera sting victims have more severe subsequent reactions to stings.

Use of an epinephrine autoinjector in case of future Hymenoptera stings would not be an appropriate recommendation for the girl in the vignette. Prescription of injectable epinephrine (as well as referral for venom immunotherapy) is indicated for children who have presented with systemic anaphylactic reactions due to Hymenoptera stings, but not for patients with local reactions.

PREP Pearls
- Common reactions to Hymenoptera stings include localized pain, itching, erythema, and mild swelling at the site of the sting, without any signs of systemic illness. In such cases, the recommended treatment involves removal of the stinger, application of cool compresses or ice packs, and the use of mild oral analgesics and oral antihistamines to help alleviate pruritus.
- The most severe and life-threatening reactions to Hymenoptera stings are immunoglobulin E–mediated, systemic anaphylactic reactions. Anaphylaxis due to insect stings occurs in 0.5% to 5% of the general population, and is less common in children.
- Children presenting with anaphylaxis should be treated immediately with intramuscular epinephrine and aggressive supportive measures to maintain the airway, breathing, and circulation.

ABP Content Specifications(s)
- Recognize the reactions to insect stings that require no further management in patients younger than 16 years of age
- Recognize the clinical findings associated with life-threatening reactions to Hymenoptera stings, and manage appropriately

Suggested Readings
- Golden DB, Moffitt J, Nicklas RA, et al; Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma & Immunology (AAAAI); American College of Allergy, Asthma & Immunology (ACAAI); Joint Council of Allergy, Asthma and Immunology. Stinging insect hypersensitivity: a practice parameter update 2011. *J Allergy Clin Immunol.* 2011;127:852–854. doi: http://dx.doi.org/10.1016/j.jaci.2011.01.025 .

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- Zirngibl G, Burrows HL. Hymenoptera stings. *Pediatr Rev.* 2012;33:534. doi: http://dx.doi.org/10.1542/pir.33-11-534.

Question 89

You are called to the newborn nursery to evaluate a 1-day-old newborn who has developed progressive respiratory distress. There were no complications, illnesses, or toxic exposures during the pregnancy. Prenatal care was appropriate, and no abnormalities were noted on routine screening or prenatal ultrasonography at 18 weeks of gestation. Maternal screening was negative for perinatal infectious diseases. Labor and delivery were uncomplicated. The amniotic fluid was clear, and the Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. By 2 hours after birth, the neonate took 15 mL of formula without difficulty. Subsequent feedings have taken longer, and by 12 hours of age, he was no longer interested in feeding. He has had occasional cough and spit-ups, but no increase in oral secretions. Since then, he has had progressive tachypnea and now is grunting. His temperature is 37°C, heart rate is 180 beats/min, respiratory rate is 60 breaths/min, blood pressure is 60/40 mm Hg, and oxygen saturation is 90% on room air. Physical examination reveals a male newborn in moderate respiratory distress. His skin has a grayish appearance. He has intercostal retractions and is grunting. His lungs have crackles bilaterally with good air entry. He has a grade 3 continuous murmur that is heard throughout the precordium. His liver edge is palpable 3 cm below the right costal margin. His extremities are cool, with capillary refill time of 4 seconds.

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

  A. arterial blood gas analysis
  B. chest radiography
  C. echocardiography
  D. pre- and postductal pulse oximetry
  E. urine organic acids

Correct Answer: C

The neonate in the vignette presents with shock, hypoxia, and respiratory failure that rapidly progressed over the first day after birth. Because he does not have risk factors for or signs of sepsis, the most likely cause of his condition is congenital heart disease with ductal-dependent systemic blood flow. The diagnostic test most likely to reveal the boy's diagnosis is echocardiography.

Shock is the failure of circulation or cellular respiration to meet the metabolic demands of end organs. Oxygen delivery is equal to the product of oxygen content (oxygen bound to hemoglobin plus oxygen dissolved in blood) and cardiac output (stroke volume multiplied by heart rate). Stroke volume is affected by preload, afterload, and cardiac contractility.
Cardiogenic shock occurs when cardiac output is decreased because of primary pump failure. Causes include arrhythmias resulting in either inadequate preload or low heart rate, hypertension or obstructive lesions causing high afterload, and primary defects in contractility. Arrhythmias often occur in the context of family history, such as Wolff-Parkinson-White and long QT syndromes, or other conditions causing electrolyte disturbances. Pericardial tamponade can be caused by trauma or inflammatory conditions such as inflammatory arthritis and systemic lupus erythematosus.

Specific etiologies of cardiogenic shock vary by age. Myocarditis and dilated cardiomyopathy can occur in any pediatric age group. Single ventricle congenital heart disease can manifest as shock in the neonatal period, as in the case of the child in the vignette. The boy has hypoplastic left heart syndrome, in which the left ventricle does not develop, and the aortic arch and/or mitral valve annulus is often atretic. The right ventricle, therefore, supplies both the pulmonary circulation and systemic circulation via the ductus arteriosus, which inserts into the distal arch. This is known as ductal-dependent systemic blood flow. As the ductus arteriosus begins to close, systemic circulation decreases and shock ensues. Although there is mixing of deoxygenated and oxygenated blood, there is enough pulmonary blood flow such that cyanosis is not always obvious. Affected infants appear gray, poorly perfused, and tachypneic. Rales and hepatomegaly are common. The treatment for a neonate with ductal-dependent circulation is to start a prostaglandin infusion, which opens the ductus arteriosus. This therapy should be started without delay if a ductal-dependent lesion is suspected, even before echocardiography results are available. If an alternative diagnosis such as sepsis or inborn error of metabolism is certain, prostaglandins are not indicated.

Congenital heart disease lesions with left-to-right shunting, such as ventricular septal defects, atrioventricular canal defects, and anomalous pulmonary venous return often manifest at approximately 2 months of age. As the pulmonary vascular resistance decreases, the amount of shunted blood increases. Because the left ventricle pumps blood through the shunt, as well as the forward systemic flow, congestive heart failure ensues.

For cases of cardiogenic shock, the most important consideration for clinicians is timely recognition. Some clinical signs and symptoms of heart failure in adults are not reliable in children, such as chest pain, orthopnea, jugular venous distention, and peripheral edema. Heart

failure in children is often heralded by less concerning signs and symptoms such as poor feeding, vomiting, or difficulty breathing, masquerading as less serious gastrointestinal or respiratory illnesses. It is thus important for the clinician to maintain a high index of suspicion for cardiac illness, paying special attention to tachycardia, narrow pulse pressure, cool extremities, and hepatomegaly.

Although arterial blood gas analysis is useful in children with shock, to detect problems with circulation, acid-base balance, and ventilation, it is not specific enough to diagnose single ventricle heart disease. Chest radiography and pre- and postductal pulse oximetry are important components of the workup of congenital heart disease, but are also not specific enough to make the diagnosis. Urine organic acids can be helpful in the workup of a neonate in shock, but the most likely diagnosis for the neonate in the vignette is congenital heart disease.

PREP Pearls
- Heart failure in children is often heralded nonspecific signs and symptoms such as poor feeding, vomiting, or difficulty breathing.
- Congenital heart disease with left to right shunting, such as ventricular septal defects, atrioventricular canal defects, and anomalous pulmonary venous return often manifest with heart failure at approximately 2 months of age.
- A prostaglandin infusion should be started immediately for any neonate with shock, unless ductal-dependent systemic blood flow lesions are excluded.

MOCA-Peds Objective
- Respond to abnormal results of congenital heart disease screening in a neonate

ABP Content Specifications(s)
- Recognize findings associated with cardiogenic shock in children of various ages
- Plan an appropriate diagnostic evaluation of cardiogenic shock

Suggested Readings
- Bhat BV, Plakkal N. Management of shock in neonates. *Indian J Pediatr.* 2015;82(10):923–929. doi: http://dx.doi.org/10.1007/s12098-015-1758-7.
- Hsu DT, Pearson GD. Heart failure in children: part I, history, etiology, and pathophysiology. *Circ Heart Fail.* 2009;2:63–70. doi: http://dx.doi.org/10.1161/CIRCHEARTFAILURE.108.820217.
- Reynolds HR, Hochman JS. Cardiogenic shock: current concepts and improving outcomes. *Circulation.* 2008;117(5):686–697. doi: http://dx.doi.org/10.1161/CIRCULATIONAHA.106.613596.

Question 90

You are evaluating a lesion on the eyelid of a 4-week-old infant. The parents report that the lesion first appeared as faint redness at 5 days of age. Since then, the lesion has become elevated. The infant has normal vital signs and growth parameters. Physical examination findings are unremarkable, except for the lesion. Overlying the left upper eyelid and brow is an erythematous plaque (Item Q90). The infant is unable to open the eye completely. A pediatric ophthalmology consultation confirms that the ptosis caused by the lesion is partially obstructing the visual axis.

Item Q90: Erythematous plaque affecting the left upper eyelid of the infant described in the vignette. Courtesy of D. Krowchuk

Of the following, the MOST appropriate course of action for this infant is

  A. active nonintervention
  B. intralesional corticosteroid injection
  C. prednisone orally
  D. propranolol orally
  E. pulsed-dye laser therapy

Correct Answer: D

The infant in this vignette has an enlarging superficial hemangioma, also known as an infantile hemangioma (IH), that involves the left upper eyelid and prevents the eye from fully opening. A pediatric ophthalmology consultation confirms partial obstruction of the visual axis that could lead to amblyopia. As a result, intervention is indicated, and the most appropriate treatment is oral propranolol. Propranolol is the most effective agent available (95% clearance rate), has a rapid onset of action, has few contraindications, and is well tolerated. For many years, oral corticosteroids (like prednisone or prednisolone) were considered first-line therapy for problematic IH. However, they are less effective than propranolol (43% clearance rate), slower to work, and have significant adverse effects. They are reserved for infants who have contraindications or inadequate response to propranolol. Intralesional corticosteroids may have a role in the management of refractory periocular hemangiomas, but their use has been associated with rare but serious adverse effects, including blindness caused by central retinal artery occlusion. Because the pulsed-dye laser penetrates to a depth of just 1.2 mm, it is useful only in the management of very superficial lesions. This procedure can be technically challenging and may require general anesthesia.

Infantile hemangiomas occur in approximately 5% of infants and are more common in girls than boys; other risk factors include prematurity, white race, multiple gestation pregnancy, placenta previa, and preeclampsia. They usually are not present at birth but appear within the first 4 weeks of age. Before an IH appears, an area of blanching and dilated blood vessels may be observed (**Item C90A**). Infantile hemangiomas have the potential to proliferate, especially during the first 5 months after birth. Most growth occurs in the first 1 to 2 months, and 80% is complete by 3 months of age. By 6 to 12 months of age, growth slows and lesions begin to involute (**Item C90B**). In most children, residual skin changes persist, including telangiectasias, redundant skin, fibrofatty tissue, and scars.

Item C90A: Area of blanching and dilated blood vessels. Courtesy of D. Krowchuk

Item C90B: Localized combined hemangioma with central gray-white discoloration of early stage of involution. Courtesy of D. Krowchuk

Infantile hemangiomas may be classified based on their depth.
- Superficial: as exhibited by the infant in this vignette, these lesions appear red with little or no evidence of a subcutaneous component (formerly called strawberry hemangiomas).
- Deep: the lesion appears blue and is located below the skin surface (formerly called cavernous hemangiomas).
- Combined: both superficial and deep components are present (**Item C90B**).

Infantile hemangiomas may also be classified based on their anatomic appearance.
- Localized: well-defined, focal lesions (**Item C90B**)
- Segmental: large plaques that occupy a large anatomic region (**Item C90C**)
- Multifocal: multiple discrete lesions

Item C90C: Segmental infantile hemangioma. Courtesy of D. Krowchuk

Most IHs are small, uncomplicated, and require no intervention. However, some raise concern and are best managed in consultation with a pediatric dermatologist or other appropriate IH specialist. Most IH proliferation occurs in the first 1 to 2 months after birth; therefore, for potentially problematic IH, frequent observation and timely intervention are essential. Infantile hemangiomas located in the following areas may require intervention:

- Periocular: may cause amblyopia by compressing the globe (causing astigmatism or myopia), occluding the visual axis, or producing strabismus.
- Nasal tip: without intervention these IHs rarely resolve with a satisfactory appearance and may damage nasal cartilage.
- Lip: without intervention these IHs rarely resolve with a satisfactory appearance and may interfere with feeding (especially if ulcerated, **Item C90D**).
- Beard area: involvement of the lower lip, chin, and mandibular areas (**Item C90C**) may be associated with hemangiomas involving the airway (symptoms include stridor or hoarseness).
- Midline lumbosacral: may be associated with underlying spinal dysraphism, particularly when accompanied by another abnormality (prominent sacral dimple, gluteal cleft deviation, mass).

Item C90D: Ulcerated infantile hemangioma involving the upper lip. Courtesy of D. Krowchuk

Other potentially problematic IHs include:
- Ulcerated lesions: ulceration is the most common complication and is most likely with IH that involve the perioral or diaper areas (**Item C90D**) or are segmental. Ulcers are painful, may become infected, and may leave scars.
- Multiple lesions: the presence of 5 or more cutaneous IH may indicate the presence of systemic involvement, most often of the liver (hemangiomas in the liver may cause high-output congestive heart failure).
- Large segmental (ie, that occupy a large anatomic area) IHs involving the face or lumbosacral areas: may be associated with extracutaneous manifestations.
    - PHACE association: **P**osterior fossa defects, **H**emangiomas, **A**rterial anomalies, **C**ardiovascular abnormalities, **E**ye anomalies
    - LUMBAR association: **L**ower extremity hemangioma, **U**rogenital anomalies and **U**lceration, **M**yelopathy, **B**ony deformities, **A**norectal malformations and **A**rterial abnormalities, and **R**enal anomalies (also described as SACRAL or PELVIS association)

PREP Pearls
- Most infantile hemangiomas are small, uncomplicated, and require no intervention.
- Most infantile hemangioma growth occurs in the first 1 to 2 months after birth. For potentially problematic infantile hemangiomas, frequent observation and timely intervention are essential.
- Infantile hemangiomas that should raise concern and may require intervention include: lesions near the eye, on the nasal tip, on the lip, in the beard area, or in the midline lumbosacral spine; ulcerated lesions; multiple lesions (5 or more); and large segmental lesions (on the face, in the lumbosacral area).

ABP Content Specifications(s)
- Recognize hemangioma and manage appropriately

Suggested Readings
- Chinnadurai S, Fonnesbeck C, Snyder KM, et al. Pharmacologic intervention for infantile hemangioma: a meta-analysis. *Pediatrics*. 2016;137(2):e20153896. doi: http://dx.doi.org/10.1542/peds.2015-3896.
- Darrow DH, Greene AK, Mancini AJ, et al. Diagnosis and management of infantile hemangioma: executive summary. *Pediatrics*. 2015;136(4):786–791. doi: http://dx.doi.org/10.1542/peds.2015-2482.
- Drolet BA, Frommelt PC, Chamlin SL, et al. Initiation and use of propranolol for infantile hemangioma: report of a consensus conference. *Pediatrics*. 2013;131(1):128–140. doi: http://dx.doi.org/10.1542/peds.2012-1691.
- Spence-Shishido AA, Good WV, Baselga E, Frieden IJ. Hemangiomas and the eye. *Clin Dermatol*. 2015;33(2):170–182. doi: http://dx.doi.org/10.1016/j.clindermatol.2014.10.009.

Question 91

You are called to attend a vaginal delivery requiring forceps. The mother is a 37-year-old gravida 3, para 0 woman with a history of multiple sclerosis. Due to maternal infertility, this pregnancy was the result of in vitro fertilization, and had an uncomplicated course. The mother received pulse corticosteroids during the third trimester. The infant was delivered with forceps due to arrest of descent. Upon delivery, the newborn had a spontaneous cry and active flexion of the arms and legs. On physical examination, you note an asymmetric cry and incomplete closure of the left eyelid. Forehead movement is decreased on the left compared to the right.

Of the following, the MOST likely cause of this physical finding is

  A. congenital myasthenic syndrome
  B. congenital myotonic dystrophy
  C. facial nerve palsy
  D. hypoxic-ischemic encephalopathy
  E. maternal corticosteroid use

Correct Answer: C

The physical examination findings in the neonate in the vignette are most consistent with a left facial nerve (cranial nerve VII) palsy. These neonates typically present with an asymmetric cry and partial eye closure on the affected side. Decreased movement of the forehead muscles may be found as well. The differential diagnosis for facial nerve palsy includes birth trauma and congenital nerve palsy. Neonates with congenital facial nerve palsy frequently have other craniofacial abnormalities consistent with a genetic syndrome such as Moebius syndrome or Goldenhar syndrome. Congenital hypoplasia of the depressor anguli oris muscle causes an isolated decrease in movement of the corner of the mouth and typically resolves without intervention; this may be confused with facial nerve palsy. Though facial nerve palsy is associated with delivery assisted by forceps or vacuum, the injury likely results from positioning and the duration of labor rather than direct nerve damage from instrumentation.

Neonates with congenital myotonic dystrophy or congenital myasthenic syndrome present with generalized weakness, including respiratory depression, rather than the isolated facial findings seen in the infant in the vignette. Neonates with hypoxic-ischemic encephalopathy have an abnormal alert state, ranging from hyperactivity to stupor, abnormal muscle tone, and impaired respiration. The neonate in the vignette has no evidence of these systemic abnormalities. Maternal corticosteroid use is not associated with facial nerve palsy.

In addition to facial nerve palsy, a number of other injuries are associated with birth trauma (**Item C91**). Birth trauma occurs more frequently in neonates with macrosomia, instrumentation-assisted delivery, prematurity, or abnormal presentation during delivery. One injury that creates a degree of urgency is subgaleal hemorrhage. This injury must be recognized promptly, because neonates have the potential to rapidly lose large quantities of blood into the subaponeurotic space. A subgaleal hemorrhage presents as a boggy mass at the nape of the neck, which increases in size after delivery. The diagnosis can be made with ultrasonography or computed tomography. Concern for a subgaleal hemorrhage requires prompt consultation with a pediatric neurosurgical team.

Item C91. Injuries Associated with Birth Trauma.

Type of Injury	Examples
Soft tissue	Abrasions, bruising, fat necrosis, lacerations
Extracranial bleeding	Cephalohematoma, subgaleal
Intracranial bleeding	Subarachnoid, epidural, subdural, cerebral, cerebellar
Nerve	Facial, cervical nerve roots (brachial plexus palsies, phrenic), Horner syndrome, recurrent laryngeal
Spinal cord	Epidural hemorrhage of the cervical cord
Fracture	Clavicle, humerus, femur, skull
Dislocation	
Torticollis*	
Eye	Subconjunctival and/or retinal hemorrhage
Solid organ	Liver, spleen

*Secondary to bleeding in the sternocleidomastoid muscle

Adapted and reprinted with permission from Rosenberg AA. Traumatic birth injury. *NeoReviews*.

PREP Pearls
- Facial nerve palsy is associated with instrumentation-assisted delivery, macrosomia, prematurity, and abnormal presentation during delivery.
- Neonates with facial nerve palsy present with asymmetric cry and partial eye closure on the affected side.
- Congenital facial nerve palsy that presents with additional craniofacial anomalies is seen with genetic syndromes such as Moebius syndrome.

ABP Content Specifications(s)
- Recognize situations that may increase the risk of birth injuries
- Identify and manage the neurologic injuries that may occur at birth

Suggested Readings
- Carlo WA, Ambalavanan N. Nervous system disorders. In: Kliegman RM, Stanton BF, St Geme J, Schor NF, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016;chap 99:834–844.e1.
- Rosenberg AA. Traumatic birth injury. *NeoReviews*. 2003;4:e270. doi: http://dx.doi.org/10.1542/neo.4-10-e270.
- VanderPluym J, Vajsar J, Jacob FD, Mah JK, Grenier D, Kolski H. Clinical characteristics of pediatric myasthenia: a surveillance study. *Pediatrics*. 2013;132:e939. doi: http://dx.doi.org/10.1542/peds.2013-0814.

Question 92

You discuss laboratory results with the mother of a 16-year-old adolescent whom you recently evaluated for primary amenorrhea. You suspected complete androgen insensitivity based on her tall stature, Sexual Maturity Rating 5 breast development, and absence of pubic hair, axillary hair, acne, and body odor. In addition, 2 of her maternal aunts are infertile. The laboratory results show a 46,XY karyotype and testosterone level in the normal male adolescent range, confirming your suspected diagnosis. The mother also suspected this diagnosis and understands that her daughter will not be able to carry a pregnancy. She asks that you not reveal the diagnosis to her daughter because she does not feel her daughter will be able to handle the information.

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

    A. contact the girl's father and elicit his help in revealing the diagnosis to his daughter
    B. encourage both parents to come to the office with their daughter to discuss the diagnosis
    C. honor the mother's request and not mention the diagnosis to her daughter
    D. refer the girl for further subspecialty care and ask the subspecialists to assist in revealing the diagnosis
    E. wait until her next health supervision visit and ask the girl if she would like to know the test results

Correct Answer: B

The vignette describes the ethical dilemma faced when a parent does not want a diagnosis revealed to an adolescent. The ethical principles of veracity, fidelity, and confidentiality are in conflict among the girl, her mother, and the provider. These principles are important in developing a therapeutic patient-parent-provider relationship. Veracity is the quality of being truthful or honest. Fidelity is the quality of being faithful. Confidentiality requires that the health professional not divulge a patient's personal information without his or her permission.

For the case described in the vignette, the provider has an obligation of veracity (truthfulness), and fidelity (faithfulness) to the girl. These principles are in conflict with fidelity to the mother regarding her request that the information remain confidential, and not revealed to her daughter who is a minor. Encouraging both parents to come to the office with their daughter to discuss the diagnosis is the best next step toward resolving these conflicts. When discussing disclosure with the mother, it is important to acknowledge her concern, elicit any additional concerns, discuss the potential adverse effects of not disclosing, and collaborate on the approach to disclosure.

Contacting the girl's father violates the obligation of fidelity and confidentiality to the mother. Honoring the mother's request violates the obligation of veracity and fidelity to the girl. Asking subspecialists to reveal the diagnosis violates the obligation of fidelity to the family. Asking the girl if she would like to know the test results violates the obligation of fidelity and confidentiality to the mother.

The girl in the vignette has complete androgen insensitivity syndrome (CAIS), which is caused by a mutation in the *AR* gene on the X chromosome, rendering the androgen receptor unresponsive to androgen. Those affected have a 46,XY karyotype with a female external phenotype. They typically have a female gender identity. Testes are present but remain intra-abdominal because response to testosterone is required for testicular descent. The developing testes appropriately secrete anti-müllerian hormone, which results in regression of the müllerian structures: the uterus, fallopian tubes, and upper vagina. At the time of puberty, the increased testosterone produced in the testes is aromatized to estrogen, resulting in breast development. As the androgen receptors do not respond to testosterone, only sparse, or no, pubic and axillary hair develops. Gonadectomy is indicated for these children because of the risk of malignancy in undescended testes, and subsequent hormone replacement should be provided. In the vignette, the girl's infertile maternal aunts are also affected, reflecting the X-linked inheritance pattern.

It was common practice as late as the 1990s to not reveal the karyotype or true diagnosis of CAIS to the patient or family. Full disclosure at the time of diagnosis is now standard of care.

PREP Pearls
- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding issues of veracity
- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding issues of fidelity
- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding issues of confidentiality

ABP Content Specifications(s)
- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding issues of veracity
- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding issues of confidentiality
- Recognize and apply ethical principles involved in the patient-parent-pediatrician relationship regarding issues of fidelity

Suggested Readings
- Adam MB. Session 9: Pediatrician-parent-patient relationship: obligations of veracity, fidelity, and confidentiality. In: Adam MB, Diekema DS, Mercurio MR, eds. *American Academy of Pediatrics Bioethics Resident Curriculum: Case-Based Teaching Guides.* 2011.
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- Lantos J. The patient-parent-pediatrician relationship: everyday ethics in the office. *Pediatr Rev*. 2015;36(1):22–29; doi: http://dx.doi.org/10.1542/pir.36-1-22 .
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- Sigman GS, Kraut J, La Puma J. Disclosure of a diagnosis to children and adolescents when parents object: a clinical ethics analysis. *Am J Dis Child*. 1993;147(7):764–768.

Question 93

A 3-year-old boy is brought to your office by his parents for concerns about his behaviors. His parents have observed him to have several episodes of facial flushing and irregular breathing. They report that they have noticed him reaching into the front of his pants when this happens. When his parents touch him or distract him, the boy resumes his usual play. The episodes occur both at home and in public. He is a healthy child whose development has been within normal limits. His physical examination findings are normal.

Of the following, the MOST appropriate advice you can provide the boy's parents is that

A. their son is likely to continue these behaviors in public
B. their son needs an evaluation by a child abuse expert
C. these behaviors indicate a serious health concern
D. they should guide him to limit these behaviors
E. they should ignore these behaviors

Correct Answer: D

Masturbation is a common childhood behavior. Facial flushing, sweating, and irregular breathing may occur during self-stimulation of the genitalia. The behavior stops when the child is distracted. The young boy in the vignette should be guided to understand that masturbation is a normal behavior, but one that should be limited to private settings.

Most children will engage in masturbation at some point in their lives. Overt masturbation increases through early childhood, peaking at age 5 years. Infants and toddlers may posture their lower extremities or seek pressure on the perineum. These behaviors are sometimes mistaken for seizures, movement disorders, or abdominal pain as the child may grunt, breathe irregularly, and sweat during these episodes. A distinguishing feature of masturbation is that the behavior stops when the child is distracted. Curious preschoolers may touch their genitals as they explore their bodies, or they may attempt to view and touch other children's genitals as they recognize the difference between genders. They may rub their body against other people.

Overt masturbation decreases when children become aware of what is socially acceptable. Private masturbation increases during adolescence, particularly in boys.

Children typically cease masturbating in public when they become aware of social norms. This 3-year-old boy's sexual behaviors are in the range of normal and are not concerning for possible child abuse. Behaviors that would be concerning include oral contact with or insertion of objects, finger(s), or penis into another's genitalia. The boy's behaviors are not suggestive of seizures or movement disorders, in which case, he would not be able to stop the behaviors when distracted. Parents should not ignore a child's public sexual behaviors, because that will reinforce the child's belief that masturbation is acceptable in those settings. Parents should guide their children on what is socially acceptable.

Pediatricians should provide anticipatory guidance and reassurance to families that masturbation is a normal behavior. They should direct parents to avoid punishing the child for these normal behaviors. Redirection and behavior modification may be used to help limit the behaviors to private settings. Masturbation can be ignored when done in an appropriate location (eg, child's bedroom).

PREP Pearls

- Overt masturbation increases through early childhood, peaking at age 5 years. Children cease masturbating in public when they become aware of social norms.
- A distinguishing feature of masturbation is that the behavior stops when the child is distracted.
- Redirection and behavior modification may be used to help limit masturbation behaviors to private settings.

ABP Content Specifications(s)
- Understand the natural history of self-exploration and masturbation

Suggested Readings
- Kellogg ND. Clinical report: the evaluation of sexual behaviors in children. *Pediatrics*. 2009;124(3):992–998. doi: http://dx.doi.org/10.1542/peds.2009-1692.
- Mallants C, Casteels K. Practical approach to childhood masturbation: a review. *Eur J Pediatr*. 2008;167:1111–1117. doi: http://dx.doi.org/10.1007/s00431-008-0766-2.
- Strachan E, Staples B. Masturbation. *Pediatr Rev*. 2012;33(4):190–191. doi: http://dx.doi.org/10.1542/pir.33-4-190 .

Question 94

A 2-week-old newborn is brought to your office for the first health supervision visit. A review of the newborn screening results shows phenylketonuria.

Of the following, the MOST appropriate next step in management for this newborn is to implement

A. administration of ammonia-reducing agents
B. aspartame supplementation
C. a high-protein diet with a high phenylalanine-containing medical formula
D. a low-protein diet with a phenylalanine-free medical formula
E. no treatments

Correct Answer: D

The newborn in this vignette has phenylketonuria (PKU) detected via universal newborn screening. This metabolic disorder is caused by an enzymatic deficiency of phenylalanine hydroxylase. Without dietary restriction of phenylalanine implemented in early infancy, PKU will cause irreversible intellectual disability in most children. Newborn screening can detect PKU in nearly 100% of cases; thus, cognitive deficits can be prevented by treatment with a low-protein diet and a phenylalanine-free medical formula as soon as possible after birth.

In the 1960s, Dr Robert Guthrie developed a blood test that could detect PKU, thus beginning newborn screening. Over time, many more screening tests have been added to newborn screening, including galactosemia, amino acid disorders, maple syrup urine disease, sickle cell disease, hearing screening, cystic fibrosis, hypothyroidism, and urea cycle disorders. Newborn screening is a public health service that allows rapid identification of babies potentially at risk for a disease before any observable symptoms are present. This approach allows for rapid intervention and medical treatment that ultimately improves outcomes. The number and types of conditions included on the newborn screening panel vary by state and are determined by each state's public health department. Most states include the 32 core conditions that are recommended by the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children. Some states include up to 150 conditions on the newborn screening panel. Importantly, screening is not a diagnostic test that confirms a particular condition. Further definitive testing is indicated after an abnormal result from newborn screening. Newborn screening includes 3 components: a dried blood spot sample obtained from a heel stick, pulse oximetry to assess for cyanotic congenital heart defects, and a hearing screen. Ideally, the blood test is performed when the newborn is 24 to 48 hours of age. For a disorder to be included in the core panel of recommended disorders for newborn screening, the following criteria should be met:

- The disorder should be identifiable in the first 24 to 48 hours after birth.
- A screening test should be available with a high level of sensitivity and specificity.
- Early detection will result in a clinical benefit with timely intervention and treatment.

Since the implementation of newborn screening programs, many children's lives have been saved or impacted in a positive manner through early recognition and initiation of treatment. Ammonia-reducing agents or aspartame supplementation is not an appropriate medical treatment for PKU. A high-protein diet and a high phenylalanine-containing formula would be very dangerous for a child with PKU because it would cause high serum levels of phenylalanine that would lead to cognitive disability. A child who is not treated and maintains a normal diet with no medical interventions would also develop permanent cognitive disability.

PREP Pearls
- The conditions included on the newborn screening panel vary by state and are determined by each state's public health department. Most states include the 32 core conditions that are recommended by the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children.
- Newborn screening includes a dried blood spot sample obtained from a heel stick, pulse oximetry to assess for the possibility of a cyanotic congenital heart defect, and a hearing screen.
- Newborn screening identifies newborns at risk for particular disorders. Secondary definitive testing is indicated if a newborn screening result is abnormal.

ABP Content Specifications(s)
- Recognize that newborn screening identifies conditions that affect a child's long-term health or survival while recognizing that testing requirements vary from state to state

Suggested Readings
- American College of Medical Genetics. Newborn screening ACT sheets and confirmatory algorithms. ACMG website. https://www.acmg.net.
- Newborn Screening Saves Lives Reauthorization Act of 2014, HR 1281, 113th Cong (2014). https://www.congress.gov/bill/113th-congress/house-bill/1281?q=%7B%22search%22%3A%5B%22H.R.+1281%22%5D%7D&r=3.
- What your state offers (links to state-specific sites for inclusion of disorders on newborn screening protocols). Baby's First Test website. http://babysfirsttest.org/.

Question 95

You are seeing a 16-year-old girl with a history of mild scoliosis for a preparticipation examination before the start of her volleyball season. The girl's height is 71 inches and weight is 145 lb. Her physical examination is notable for marked pes planovalgus, pectus carinatum, hypermobility of the wrist and finger joints, and long, thin fingers.

Of the following, the MOST appropriate test to perform before considering clearance for sports participation for this girl is

 A. cervical spine radiography
 B. echocardiography
 C. genetic testing
 D. magnetic resonance imaging of the spine
 E. no additional evaluation

Correct Answer: B

The girl in the vignette exhibits several features that are characteristic of Marfan syndrome. Before participating in volleyball, she should undergo echocardiography to assess for aortic root dilation.

Marfan syndrome is a connective tissue disorder that typically leads to musculoskeletal, cardiovascular, skin, and eye abnormalities. This condition is caused by a mutation in the fibrillin-1 (*FBN1*) gene and is inherited in an autosomal dominant fashion. In about one-quarter of affected individuals, Marfan syndrome occurs because of a spontaneous mutation. The signs and symptoms of Marfan syndrome are generally apparent by adolescence. Typical musculoskeletal features include tall stature (women over 70 inches at skeletal maturity, men over 75 inches), long thin face, arachnodactyly, scoliosis, pectus excavatum or carinatum, and joint hypermobility. Common cardiac manifestations include aortic root dilation and aortic dissection. Skin findings, such as striae, and ocular findings, especially, ectopia lentis, are also characteristic of Marfan syndrome. The revised Ghent criteria are used to diagnose Marfan syndrome, in conjunction with genetic testing to identify *FBN1* gene mutations.

Athletes with Marfan syndrome are at risk for aortic root rupture and aortic dissection. In a young athlete who exhibits signs and symptoms suggestive of Marfan syndrome, echocardiography can aid in the diagnosis. Individuals with a diagnosis of Marfan syndrome without aortic dilation or significant valvular disease may be cleared to participate in sports but should avoid high-intensity sports, especially those with intense isometric activity such as weight-lifting.

Although genetic testing may be indicated for the adolescent in the vignette, it would not be the most appropriate test to perform when considering clearance for sports participation. Individuals with Marfan and other connective disorders have an increased risk of scoliosis and spondylolisthesis, and spinal radiography would be the best initial study for these conditions. However, these diagnoses are not significant when determining clearance to play sports. Magnetic resonance imaging of the spine and radiography focused on the cervical spine would not be indicated in this case.

PREP Pearls
- Individuals with Marfan syndrome are at risk for aortic root rupture and aortic dissection.
- Athletes with suspected Marfan syndrome should undergo echocardiography before clearance for sports participation is granted.

ABP Content Specifications(s)
- Recognize the implications for sports participation in a patient with Marfan syndrome

Suggested Readings

- Cheng A, Owens D. Marfan syndrome, inherited aortopathies and exercise: what is the right answer? *Br J Sports Med.* 2016;50(2):100–104. doi: http://dx.doi.org/10.1136/bjsports-2014-306440rep.
- Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology Consensus Recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol.* 2008;52(24):1990–1996. doi: http://dx.doi.org/10.1016/j.jacc.2008.08.055.
- von Kodolitsch Y, De Backer J, Schuler H, et al. Perspectives on the revised Ghent criteria for the diagnosis of Marfan syndrome. *Appl Clin Gen.* 2015;8:137–155. doi: http://dx.doi.org/10.2147/TACG.S60472.

Question 96

You are seeing a 17-year-old girl in the emergency department. She has had a 3-day history of lower abdominal pain that is worse with ambulation and abnormal vaginal discharge. Her last menstrual period was 2 weeks ago. The girl has had 3 lifetime male sexual partners and was last sexually active about 1 week ago, at which time she did not use a condom. Physical examination reveals a temperature of 37.2°C; other vital signs are normal. The girl appears to be in mild discomfort, and abdominal examination reveals left lower quadrant pain on palpation.

Of the following, the MOST appropriate next step in this girl's evaluation is to perform a

  A. complete blood cell count
  B. pelvic examination
  C. pelvic ultrasonography
  D. rectal examination
  E. urinalysis

Correct Answer: B

The girl in the vignette has symptoms and signs suggestive of pelvic inflammatory disease (PID); therefore, a pelvic examination is the most appropriate next step in her evaluation. The white blood cell (WBC) count may be elevated in those who have PID, but often is normal in mild to moderate disease. Pelvic ultrasonography may be useful if the clinician is unable to evaluate the adnexa, appreciates an adnexal mass, or has concerns about ectopic pregnancy. In the absence of symptoms suggestive of gastrointestinal or urinary tract disease, performance of a rectal examination or urinalysis, respectively, will be of limited benefit. In patients suspected of having PID, a pregnancy test is useful to evaluate for ectopic pregnancy.

The pelvic examination begins with inspection of the external genitalia for anatomic abnormalities, as well as evidence of sexually transmitted infestations or infections (eg, pubic lice or nits, genital warts, or ulcers). During the speculum examination, a cervical swab specimen is obtained for nucleic acid amplification testing (NAAT) for *Chlamydia trachomatis* and *Neisseria gonorrhoeae,* and a sample of vaginal secretions is obtained for a saline wet mount. Wet mount examination is performed to evaluate for increased numbers of WBCs (supporting a diagnosis of PID), candidiasis, bacterial vaginosis, or trichomoniasis. If the bimanual examination reveals cervical motion, uterine, or adnexal tenderness and no other diagnosis is likely, treatment for PID should be initiated. Testing for HIV and syphilis should be offered.

The recent change in recommendations for cervical cytology screening (initial screening at age 21 years) and the availability of NAAT performed on urine or vaginal swab specimens, have dramatically reduced the need for pelvic examination in adolescents. At present, indications for such examination include:
- Persistent vaginal discharge (rule out foreign body)
- Pelvic pain (rule out PID)
- Desire to use an intrauterine device or diaphragm
- Sexual abuse

Pelvic examination occasionally may be useful in the evaluation of amenorrhea, abnormal vaginal bleeding, or dysmenorrhea unresponsive to standard therapy.

PREP Pearls
- Changes in recommendations for cervical cytology screening and the availability of nucleic acid amplification tests have reduced the need for pelvic examination in adolescents.
- In sexually active girls who have lower abdominal or pelvic pain, pelvic inflammatory disease should be considered and a pelvic examination performed.

ABP Content Specifications(s)
- Understand the indications for a pelvic examination in an adolescent girl

Suggested Readings
- Braverman PK, Breech L, and the Committee on Adolescence. American Academy of Pediatrics: clinical report—gynecologic examination for adolescents in the pediatric office setting. *Pediatrics*. 2010;126:583–590. doi: http://dx.doi.org/10.1542/peds.2010-1564.
- Committee on Gynecologic Practice. Committee opinion No. 534: well-woman visit. *Obstet Gynecol* 2012;120:421–424 (reaffirmed 2016). doi: http://dx.doi.org/10.1097/AOG.0b013e3182680517.
- Kaskowitz A, Quint E. A practical overview of managing adolescent gynecologic conditions in the pediatric office. *Pediatr Rev* 2014;35:371–380. doi: http://dx.doi.org/10.1542/pir.35-9-371.
- Shrier LA. Pelvic inflammatory disease. In Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016 .

Question 97

You are reviewing the medical records of a patient who is entering your practice. This 2-week-old male newborn was born at term to a 20-year-old, gravida 1 para 1 mother who did not receive prenatal care. At delivery, the baby was found to have micrognathia, glossoptosis, and a cleft palate consistent with Pierre Robin sequence. He was cared for in the neonatal intensive care unit, and at the time of discharge he was being fed breast milk through a nasogastric tube. Notes report that he is able to breathe comfortably and maintain adequate oxygen saturation when he is positioned prone or on his side. Genetics consultation and testing during his hospital stay confirm Stickler syndrome.

Of the following, the condition MOST commonly associated with this syndrome, other than those conditions already noted, is

  A. autism spectrum disorder
  B. cardiac anomaly
  C. intestinal malrotation
  D. renal anomaly
  E. vision impairment

Correct Answer: E

Stickler syndrome is a group of genetic conditions characterized by the Pierre Robin sequence (cleft palate, glossoptosis, and micrognathia or retrognathia) and severe myopia or other ocular abnormalities (**Item C97**). Many patients with Stickler syndrome also have sensorineural hearing loss or skeletal abnormalities including hypermobility, scoliosis, or early arthritis. Stickler syndrome is not associated with an increased risk of autism spectrum disorder or cardiac, intestinal, and renal anomalies.

Item C97: Girl with Stickler syndrome. Courtesy of T. Jewett

Mandibular abnormalities, including the micrognathia or retrognathia seen in patients with Pierre Robin sequence, can lead to airway obstruction and feeding difficulties. Treatment strategies depend on factors including individual anatomy and physiology, palatal structure, and noncraniofacial comorbidities. In some infants, airway compromise can be expected to improve as they grow; treatment may therefore include temporary interventions such as nasal airways, palatal obturators, and/or feeding through a nasogastric or gastrostomy tube. In other patients, glossopexy (surgical adhesion of the tongue to the lower lip to prevent posterior malpositioning),

mandibular distraction osteogenesis (in which the mandible is surgically displaced anteriorly), or tracheostomy may be indicated.

Patients with Pierre Robin sequence typically also have palatal abnormalities including orofacial clefts. Clefts can involve the lip, philtrum, nose, gums, hard or soft palate, or uvula. They can be isolated or associated with a syndrome. Genetic causes of orofacial clefts include trisomy 13, velocardiofacial syndrome (22q11.2 deletion), Smith-Lemli-Opitz syndrome, Treacher Collins syndrome, and Stickler syndrome.

Children with palatal clefts are at increased risk for chronic middle ear effusion and conductive hearing loss associated with eustachian tube dysfunction. Although infants with isolated labial clefts may be able to breastfeed, infants with palatal clefts cannot achieve effective suction and therefore typically require feeding by bottle, oftentimes with special bottle nipples. Children with orofacial clefts are at increased risk of language and articulation disorders; this outcome tends to be improved with earlier surgical correction. Lip clefts are typically repaired before 6 months of age, with palatal cleft repair occurring around 1 year of age.

The infant in this vignette has Stickler syndrome and demonstrates common complications of the associated craniofacial abnormalities, including airway obstruction and feeding difficulties. He should be assessed by a pediatric ophthalmologist for evaluation of myopia or other ocular issues. If he has myopia, corrective lenses will aid his visual development. Surgical intervention may be indicated if he has glaucoma or cataracts. The patient should also have a thorough audiologic evaluation given the increased risk of hearing impairment in children with craniofacial anomalies.

PREP Pearls
- Stickler syndrome is a group of genetic conditions characterized by Pierre Robin sequence (cleft palate, glossoptosis, and micrognathia or retrognathia) and severe myopia or other ocular abnormalities, as well as potential sensorineural hearing loss and skeletal abnormalities.
- Children with mandibular abnormalities often have airway obstruction and feeding difficulties.
- Children with palatal clefts are at increased risk of eustachian tube dysfunction, middle ear effusion, and conductive hearing loss. They may also experience feeding and language difficulties.

ABP Content Specifications(s)
- Plan the appropriate management of a cleft palate in patients of various ages
- Recognize conditions commonly associated with cleft palate
- Recognize the clinical findings associated with cleft palate, including submucous cleft and ear sequelae of poor eustachian tube function
- Recognize the clinical findings associated with mandibular abnormalities, and manage appropriately

Suggested Readings

- Abbott MA. Cleft lip and palate. *Pediatr Rev*. 2014;35(5):177–181. doi: http://dx.doi.org/10.1542/pir.35-5-177.
- Butow KW, Naidoo S, Zwahlen RA, Morkel JA. Pierre Robin sequence: subdivision, data, theories, and treatment–part 4: recommended management and treatment of Pierre Robin sequence and its application. *Ann Maxillofac Surg*. 2016;6(1):44–49.
- Robin NH, Moran RT, Ala-Kokko L. Stickler syndrome. *GeneReviews*. 2014. https://www.ncbi.nlm.nih.gov/books/NBK1302/.

Question 98

A 16-year-old adolescent girl visits your clinic with a chief symptom of fatigue. She describes the fatigue as being present over the prior 1 or 2 weeks and increasing in severity. She has not been to soccer practice during this time and has been too fatigued to attend school over the last few days. She reports more hair loss than usual in the shower. She has a heart rate of 100 beats/min and blood pressure of 135/60 mm Hg. The remainder of her vital signs are normal. Neck examination shows an enlarged thyroid with a bruit on auscultation. Her heart rate is regular. The lungs are clear to auscultation bilaterally. Her skin is warm and moist. She has a decreased level of thyroid-stimulating hormone and an increased level of thyroid-stimulating immunoglobulin.

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

  A. administration of methimazole
  B. administration of nonsteroidal anti-inflammatory drugs
  C. administration of propylthiouracil
  D. radioactive iodine therapy
  E. thyroidectomy

Correct Answer: A

The patient in this vignette has hyperthyroidism given her history, physical examination results, and laboratory evaluation results. Fatigue and hair loss, although nonspecific, can be seen with hyperthyroidism. Physical examination reveals tachycardia, hypertension with a wide pulse pressure, skin that is warm to touch and moist, and an enlarged thyroid with a bruit noted on auscultation. Her laboratory evaluation reveals a decreased thyroid-stimulating hormone level and an increased thyroid-stimulating immunoglobulin level, which are consistent with Graves disease. Most patients (90%) with Graves disease will have a positive thyroid-stimulating immunoglobulin test result. Thyroid peroxidase antibodies may be measured and are present in 10% of patients with Graves disease as well as in patients with autoimmune thyroiditis. Additionally, liver function tests and a complete blood cell count are often performed in the initial evaluation to help monitor adverse effects of therapy.

Therapies for children with Graves disease include antithyroid drugs (methimazole), radioactive iodine therapy, and thyroidectomy. The first-line therapy for children with Graves disease is methimazole. Propylthiouracil has an increased risk of hepatotoxicity and is reserved for individuals with allergy or adverse reactions to methimazole or complications related to surgery or radioactive iodine therapy. Because some children experience disease remission with medication, surgery and radioactive iodine therapy are not first-line therapies, although many pediatric patients will ultimately require these interventions. Nonsteroidal anti-inflammatory medications have no specific role in the treatment of Graves disease.

Hyperthyroidism can cause tachycardia, increased cardiac output, and hypertension with a wide pulse pressure because of a decrease in peripheral vascular resistance. Palpitations and arrhythmias (such as atrial fibrillation) can occur, although arrhythmias are much more common in adults than children.

Given the sinus tachycardia seen with Graves disease and hyperthyroidism in general, β-blockers are often initiated at diagnosis and continued until the methimazole takes effect, which may be several weeks. β-Blockers such as propranolol are indicated in patients with a heart rate greater than 100 beats/min, palpitations, hypertension, or tremors. Neurologic symptoms associated with hyperthyroidism can also improve with β-blockers.

PREP Pearls
- The therapies for children with Graves disease include antithyroid drugs (methimazole as the first-line treatment), radioactive iodine therapy, and thyroidectomy.
- Hyperthyroidism can cause persistent sinus tachycardia.
- β-Blockers are often initiated at the time of diagnosis of hyperthyroidism.
- β-Blockers such as propranolol are indicated in patients with a heart rate greater than 100 beats/min, palpitations, hypertension, or tremors.

ABP Content Specifications(s)
- Recognize the role of hyperthyroidism in persistent sinus tachycardia

Suggested Readings
- Sills I. Hyperthyroidism. *Pediatr Rev.* 1994;15(11):417–421. doi: http://pedsinreview.aappublications.org/content/15/11/417 .
- 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 99

You are seeing an 8-year-old girl for a new patient evaluation. Two weeks ago, she was placed into foster care. The foster parent reports that child protective services is investigating the child's father for maltreatment and possible sexual abuse. Her mother is currently incarcerated. The child has been timid and sad, but seems to be acclimating to her new setting. She has difficulty falling asleep and has one episode of enuresis nightly. She reports no acute injury or pain. She is shy but able to engage in developmentally appropriate conversation. Her weight is at the 25th percentile and her height is at the 50th percentile for age. She has fading bruises on the back of her legs. You perform a complete physical examination and the recommended screening tests for any child newly placed into foster care.

Of the following, the condition that is MOST likely to be found by screening in this patient is

  A. dental caries
  B. human immunodeficiency virus
  C. impaired vision
  D. mental health problems
  E. tuberculosis

Correct Answer: D

The girl in this vignette is typical of the children and adolescents who are involved with the child welfare system. Many of these children have been exposed to multiple adverse childhood experiences and may have a variety of physical, mental, developmental, and psychosocial problems. Among these problems, mental health issues are the most common.

Pediatric health care providers are challenged to provide compassionate and comprehensive care to this special health care needs group. Although barriers can exist in caring for this transitory, medically complicated population with multiple caregivers, the role played by pediatricians in care coordination and advocacy on behalf of these vulnerable children is crucial to their well-being. An initial assessment should occur within 72 hours of foster care placement and includes evaluation for abuse, neglect, acute infections, mental health issues, and immediate concerns related to chronic medical conditions. Dental problems, human immunodeficiency virus infection, vision impairment, and tuberculosis infection are some of the conditions screened for during the initial assessment.

A comprehensive evaluation to identify all physical, mental, developmental, and dental health problems and to develop a coordinated management plan should be completed within 1 month of foster care placement. The frequency of follow-up visits to monitor progress and provide ongoing support should be determined by the acuity and severity of the child's physical, mental, developmental, and socioemotional problems. Preventive health care should be performed in accordance with the recommendations for routine health supervision.

The American Academy of Pediatrics (Council on Foster Care, Adoption, and Kinship Care; the Committee on Adolescence; and the Council on Early Childhood) published a technical report and policy statement in 2015 that outlines the pediatrician's role in addressing the health care issues of children and adolescents in foster or kinship care (http://pediatrics.aappublications.org/content/136/4/e1131). Also, the American Academy of Pediatrics and its partners have created the Healthy Foster Care America initiative as an excellent online resource for health care providers "to improve the health and well-being outcomes of children and teens in foster care" (www.aap.org/fostercare).

PREP Pearls
- Many children and adolescents who enter the child welfare system have been exposed to multiple adverse childhood experiences.
- Mental health and behavioral problems are the most common conditions seen in this uniquely vulnerable population.
- An initial assessment should occur within 72 hours of foster care placement and include evaluation for abuse, neglect, acute infections, mental health issues, and immediate concerns related to chronic medical conditions.
- A comprehensive evaluation to identify all physical, mental, developmental, and dental health problems and to develop a coordinated management plan should be completed within 30 days of entrance into the child welfare system.

ABP Content Specifications(s)
- Recognize the needs of youth aging out of the foster care system, and manage appropriately
- Recognize and apply ethical principles regarding children in foster care
- Understand the basic functions of the child welfare and foster care systems and the pediatrician's role in that system
- Plan the appropriate evaluation of children of various ages who are in the foster care system, and manage appropriately

Suggested Readings
- American Academy of Pediatrics. Fostering Connections to Success and Increasing Adoptions Act: health oversight and coordination plans—recommendations and resources. https://www.aap.org/en-us/advocacy-and-policy/state-advocacy/Documents/HOCPs-AAP-Resources-and-Recommendations.pdf.
- Council on Foster Care, Adoption, and Kinship Care and Committee on Early Childhood. Health care of youth aging out of foster care. *Pediatrics*. 2012;130(6):1170–1173. doi: http://dx.doi.org/10.1542/peds.2012-2603.
- Szilagyi M. The pediatric role in the care of children in foster and kinship care. *Pediatr Rev*. 2012;33(11):496–508. doi: http://dx.doi.org/10.1542/pir.33-11-496.
- Szilagyi MA, Rosen DS, Rubin D, Zlotnik S; Council on Foster Care, Adoption, and Kinship Care, Committee on Adolescence, and Council on Early Childhood. Health care issues for children and adolescents in foster care and kinship care. *Pediatrics*. 2015;136(4):e1142–e1166. doi: http://dx.doi.org/10.1542/peds.2015-2656.

Question 100

A premature neonate born at 34 weeks of gestation is admitted to the neonatal intensive care unit. She was born to a 26-year-old gravida 2 para 1 to 2 mother via spontaneous vaginal delivery. The mother was well until 1 week prior to delivery when she developed an illness characterized by emesis and diarrhea. Her illness lasted for 3 days, and she improved when she developed contractions and had spontaneous rupture of membranes. She received a dose of a corticosteroid and penicillin in the labor and delivery unit prior to the birth of the baby. The neonate has a temperature of 35.8°C, heart rate of 120 beats/min, respiratory rate of 34 breaths/min, blood pressure of 88/45 mm Hg, and oxygen saturation of 98% with continuous positive airway pressure of 4 cm H2O. She is appropriately sized for her gestational age but appears ill. Her fontanelle is full, and she has mild retractions, abdominal distention, and a papular red rash. Laboratory data show:

Laboratory Test	Result
Blood	
White blood cell count	4,500/µL (4.5 x10^9/L)
Cerebrospinal Fluid	
White blood cell count	825/µL
Red blood cell count	24/µL
Glucose	20 mg/dL
Protein	235 mg/dL

A cerebrospinal fluid Gram stain is shown in Item Q100.
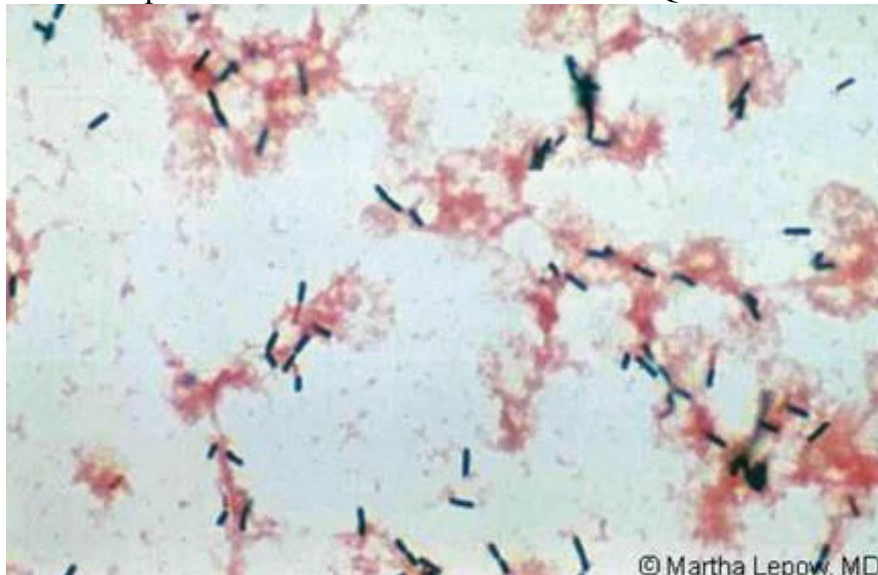
Item Q100: Cerobrospinal fluid Gram stain findings for the neonate described in the vignette. Copyright Martha Lepow, MD Reprinted with permission from Kimberlin DW, et al. Red Book Online. Elk Grove Village, IL. American Academy of Pediatrics 2015.

Of the following, the infection MOST likely to be responsible for this neonate's illness is

A. Escherichia coli
B. Klebsiella pneumoniae
C. Listeria monocytogenes
D. Staphylococcus aureus
E. Streptococcus agalactiae

Correct Answer: C

The infection most likely to be responsible for the illness of the neonate in this vignette is *Listeria monocytogenes*. The mother's preceding gastrointestinal illness, the infant's premature delivery in the setting of the maternal illness, and most specifically, the gram-positive rods in cerebrospinal fluid are suggestive of *L monocytogenes* infection.

Listeria can survive in refrigerated, acidic, and salty foods, and ingestion of contaminated food is usually the principal form of transmission. However, the key exceptions to foodborne origin are fetal or neonatal infections. If a pregnant woman ingests contaminated food, maternal bacteremia can ensue. The organism has the ability to cross the placenta and directly infect a fetus. Severe infections caused by *L monocytogenes* tend to occur in select groups, including neonates, the elderly, pregnant women, and immunocompromised individuals.

The nonspecific symptomatology (fever, myalgias, back pain) of invasive infections with *L monocytogenes* in pregnant women makes diagnosis difficult. The infant in this vignette was born prematurely, which is common in the setting of in utero infection, and had early onset disease, which usually manifests as sepsis. Infants can develop a diffuse erythematous papular rash called granulomatosis infantisepticum. *Listeria* infection in neonates can also manifest as late-onset disease, typically meningitis, that is thought to be caused by peripartum transmission of the organism. Disease in immunocompromised individuals and the elderly usually manifests as bacteremia or meningitis. Central nervous system infections can present as rhombencephalitis. Endocarditis and brain abscesses have also been reported.

Neonatal infections are treated with a combination of ampicillin and gentamicin. In patients with β-lactam allergies, the combination regimen can be substituted by monotherapy with trimethoprim-sulfamethoxazole or a fluoroquinolone. Cephalosporins do not have activity against *L monocytogenes*.

Escherichia coli and *Klebsiella pneumoniae* are gram-negative rods in the Enterobacteriaceae family that are well-recognized pathogens in neonates and can cause various illnesses, including urinary tract infections, bacteremia, and meningitis. *Staphylococcus aureus* and *Streptococcus agalactiae* are gram-positive cocci that also cause neonatal illness. *Staphylococcus aureus* can cause skin and soft tissue infections, bacteremia, musculoskeletal infections, and device-associated infections in neonates. Like *Listeria*, *S agalactiae* can manifest with early or late-onset disease in the neonate.

PREP Pearls
- Severe infections caused by *Listeria monocytogenes* tend to occur in select groups, including neonates, the elderly, pregnant women, and immunocompromised individuals.
- In neonates, early onset disease caused by *Listeria monocytogenes* usually manifests as sepsis whereas late-onset disease usually presents as meningitis.
- Neonatal infections caused by *Listeria monocytogenes* are treated with a combination of ampicillin and gentamicin.

ABP Content Specifications(s)
- Recognize the clinical features associated with Listeria monocytogenes infection
- Understand the epidemiology of Listeria monocytogenes
- Plan appropriate management for a patient with Listeria monocytogenes infection

Suggested Readings
- American Academy of Pediatrics. Listeria monocytogenes 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; 2015:513–516 .

Question 101

been healthy over the previous year, with only minor upper respiratory infections, 1 ear infection, and 1 visit to the emergency department for a forehead laceration. His developmental screening results are appropriate for his age. On physical examination, white lines are seen along the bases of several teeth. His mother states that she brushes her son's teeth daily, but he has not yet seen a dentist. The boy has not had any tooth pain or problems with eating. His mother had several cavities when she was a young girl.

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

A. add daily fluoride rinses to his oral health routine
B. continue current management and reevaluate in 3 months
C. perform a fluoride wash in your office
D. recommend decreasing sugar intake
E. refer him to a dentist for evaluation

Correct Answer: E

White spots or lines, often at the base where the tooth meets the gum, are one of the first signs of dental caries. The evolution from early caries to cavities can sometimes be prevented at this stage, with careful brushing and fluoride treatment. However, a child with this physical examination finding should be referred to a dentist promptly, ideally within 2 to 3 weeks, for a more detailed evaluation and prevention strategy. Caries can progress to cavities quickly, so a management plan of reevaluation after 3 months without referral to a dentist is not appropriate.

Demineralization of teeth occurs when the oral microbiome encounters a supply of sugar, which is then consumed by the oral bacteria, producing acid, which then breaks down tooth enamel. This initially presents as white lines or spots. As tooth decay progresses to cavities, the white lines and spots turn yellowish with the loss of tooth enamel. Brown discoloration can subsequently result when decayed areas are stained with food. As teeth decay further, the damage becomes visually more obvious, which should always prompt an urgent dental referral. Severe dental decay can predispose a child to a dental abscess, and requires immediate evaluation and treatment.

Dental caries is a common chronic condition of early childhood. It is more prevalent among children living in poverty. Because infants and children have frequent health supervision visits, especially in infancy, the pediatrician should play a prominent role in oral health and caries prevention. A child's risk of caries can be assessed early in life; prematurity, conditions or medications that prevent or reduce saliva production, chronic medications containing sugar, and tooth decay in caregivers can predispose a child to developing early caries. Sugar consumption, particularly when sugary residue can remain in the mouth for several hours (eg, sleeping with a bottle of juice) is a major risk factor for developing caries, and anticipatory advice should be given at health supervision visits regarding sugar consumption.

Fluoride toothpaste is recommended for all tooth-brushing children. Infants and young children typically swallow toothpaste when brushing teeth, putting them at risk for fluorosis, which manifests as subtle white lines across teeth. Therefore, before age 3 years, the application of only a very small amount of toothpaste, equivalent to a grain of rice, is recommended. At 3 years of age and older, a pea-sized amount is recommended. Mouthwash is not recommended for children who are too young to expectorate the liquid.

The United States Preventive Services Task Force recommends that primary care clinicians apply fluoride varnish every 3 to 6 months in children age 5 years and younger, depending on risk factors. Fluoride applied topically reduces demineralization and promotes the remineralization of tooth enamel. It also inhibits the bacterial enzymes implicated in the caries process. Most state Medicaid programs will reimburse separately for this service, which involves painting the teeth with a clear substance. After application, children are instructed to avoid tooth brushing for several hours and to eat only soft foods; this maximizes the contact time between the varnish and teeth.

PREP Pearls
- White spots or lines at the base of teeth are a sign of early childhood caries and should prompt a referral for dental evaluation.
- Because infants and children have frequent health supervision visits, the pediatrician can play a large role in caries prevention. This includes anticipatory guidance and periodic fluoride varnish applications.

ABP Content Specifications(s)
- Recognize the clinical findings associated with caries in patients of various ages
- Recognize the various clinical findings associated with dental and periodontal disease

Suggested Readings
- Clark MB, Slayton RL, Section on Oral Health. Fluoride use in caries prevention in the primary care setting. *Pediatrics*. 2014;134(3):626–633. doi: http://dx.doi.org/10.1542/peds.2014-1699.
- Section on Oral Health. Maintaining and improving the oral health of young children. *Pediatrics*. 2014;134(6):1224–1229. doi: http://dx.doi.org/10.1542/peds.2014-2984.

Question 102

You are seeing a 4-year-old boy with moderate intellectual disability and autism. His physical examination findings are normal. He is nondysmorphic. Both parents have normal intelligence. The mother inquires about further testing for her son to discover why he has cognitive delays. You agree that further testing is warranted and order a fragile X test.

Of the following, an additional genetic test that should be ordered in this child is

A. fluorescence in situ hybridization for trisomy 21
B. karyotype
C. microarray
D. serum amino acids
E. serum ammonia

Correct Answer: C

The patient in this vignette has intellectual disability without evident dysmorphology or other syndromic features. In this situation, the American College of Medical Genetics and the American Academy of Pediatrics recommend baseline genetic testing that includes a chromosomal microarray and fragile X testing. A chromosomal microarray would detect a gross chromosomal deletion or duplication as well as microdeletions or microduplications that could be missed on a high-resolution karyotype. A microarray would also identify specific breakpoints and genes involved in a particular copy number variation. This information is helpful when researching specific clinical associations seen with a particular microdeletion or microduplication. A microarray is typically ordered in cases involving a patient with autism, intellectual disability, or multiple congenital anomalies without a unifying diagnosis; microarray testing has replaced the karyotype as first-line testing in these situations.

A karyotype would not be indicated because this test is used to detect sex chromosome disorders, trisomies, and chromosomal rearrangements. Fluorescence in situ hybridization analysis is a cytogenetic mapping technique whereby a fluorescent tag (the probe) is used to map specific chromosomal aberrations; it is commonly used for rapid diagnosis in cases of suspected trisomies or various microdeletion disorders including cri du chat syndrome, 22q11 microdeletion (DiGeorge syndrome), and Smith-Magenis syndrome. Fluorescence in situ hybridization for trisomy 21 would not be indicated because the child lacks the classic dysmorphology commonly noted in trisomy 21. Serum amino acids and ammonia levels would be indicated if an inborn error of metabolism is suspected or potentially as second-tier testing if the first-tier testing results are unremarkable. A metabolic disorder is the cause of intellectual disability in 1% to 5% of cases.

PREP Pearls
- Chromosomal microarray and fragile X testing are recommended as first-line tests by the American College of Medical Genetics and the American Academy of Pediatrics for children with global developmental delay and intellectual disability of unknown etiology.
- A karyotype detects sex chromosome disorders, trisomies, chromosomal rearrangements, and gross deletions/duplications.
- Fluorescence in situ hybridization analysis is a cytogenetic mapping technique that detects specific chromosomal aberrations; it is commonly used for rapid diagnosis of trisomies or specific microdeletion disorders (eg, 22q11.2 deletion syndrome, cri du chat syndrome).

MOCA-Peds Objective
- Recognize the genetic syndromes that may present as a learning disability

ABP Content Specifications(s)
- Understand the role of microarray testing in postnatal diagnosis
- Understand the role of karyotyping in postnatal diagnosis
- Understand the role of fluorescence in situ hybridization studies in postnatal diagnosis

Suggested Readings
- Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. *Am J Hum Genet.* 2010;86(5):749–764. doi: http://dx.doi.org/10.1016/j.ajhg.2010.04.006.
- 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.
- South ST, Lee C, Lamb AN, Higgins AW, Kearney HM, Working Group for the American College of Medical Genetics and Genomics (ACMG) Laboratory Quality Assurance Committee. ACMG Standards and Guidelines for constitutional cytogenomic microarray analysis, including postnatal and prenatal applications: revision 2013. *Genet Med.* 2013;15(11):901–909. doi: http://dx.doi.org/10.1038/gim.2013.129.

Question 103

A 5-year-old boy is brought to your office for evaluation of recurrent allergies and eye swelling. The patient is currently taking diphenhydramine prescribed by a pediatrician. The patient has no other significant medical history. He has a temperature of 37.2°C, respiratory rate of 17 breaths/min, heart rate of 84 beats/min, and blood pressure of 110/74 mm Hg. He has bilateral periorbital edema (Item Q103) and mild pitting edema. Urinalysis results are shown:

Item Q103: Periorbital edema as described for the boy in the vignette Courtesy of M. Rimsza

Laboratory Test	Result
Specific gravity	1.025
pH	6.5
Blood	2+
Protein	4+
Leukocyte esterase, nitrites	Negative

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

A. cetirizine
B. diphenhydramine
C. furosemide
D. reassurance
E. steroid

Correct Answer: E

Nephrotic syndrome (NS) should be considered in a patient with recurrent episodes of eye swelling and facial puffiness, as seen in the boy in this vignette. Initially, these patients are often mistaken as having an allergic reaction and treated with a short course (3-5 days) of oral steroids or antihistamine. The short course of steroids may be associated with some or no improvement in symptoms in a patient with NS.

Nephrotic syndrome is characterized by edema (facial puffiness or generalized anasarca), proteinuria, hypoalbuminemia, and hyperlipidemia (elevated cholesterol levels and low-density lipoprotein cholesterol levels). 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. Overall, 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. Idiopathic NS is the most common form encountered in children. Based on renal biopsy findings, children with idiopathic NS are further diagnosed with minimal change disease (most common), focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, or membranous nephropathy. Microscopic hematuria may be present in nearly 20% of patients with minimal change disease and 50% to 60% of children with focal segmental glomerulosclerosis or membranoproliferative glomerulonephritis. Gross hematuria is uncommon in children with NS and should prompt consideration of an alternative diagnosis. In a patient with NS, the presence of renal failure, hypocomplementemia, or features of vasculitis (eg, joint pain and swelling, rash, oral ulcers, serological evidence) should prompt consideration of a diagnosis other than minimal change disease. The congenital/infantile form of NS presents at birth or before 1 year of age, and it is associated with genetic abnormalities that lead to increased permeability of the glomerular basement barrier.

Minimal change disease is the most common form of NS in children; as such, the majority of cases are treated without kidney biopsy. Minimal change disease typically presents between 2 and 10 years of age with the classic features of NS and a negative evaluation result for 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 (< 0.2 is normal, 0.2-2 is non-nephrotic).

The initial episode of NS is treated with oral steroids (60 mg/m^2/d for 4-6 weeks, followed by 40 mg/m^2/d given every other day for 2-5 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 urinalysis results of negative or trace for protein for 3 consecutive days. A lack of response to steroids after 4 weeks of daily therapy is considered corticosteroid resistance and occurs in approximately 10% of children with idiopathic NS.

Depending on responsiveness to steroids, children with minimal change disease are categorized as infrequent relapsers (1-3 relapses annually), frequent relapsers (≥ 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 who are frequent relapsers or corticosteroid dependent 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.

Mild edema in patients with NS can be managed with salt and water restriction (two-thirds of maintenance requirements) and steroids. Once the steroids decrease proteinuria (induce remission), the edema rapidly resolves. Diuretics (furosemide) alone or in combination with intravenous albumin are indicated for severe edema that interferes with ambulation or is associated with respiratory distress or tissue breakdown. It is important to note that aggressive diuretic therapy in the presence of intravascular volume depletion adds to the already increased risk for thrombosis in patients with NS. Patients with NS are at increased risk for thrombosis because of increased plasma levels of procoagulants, urinary loss of anticoagulants, and thrombocytosis.

The patient history, physical examination findings, and urinalysis results are consistent with a diagnosis of NS for the patient in this vignette; therefore, reassurance or treatment with cetirizine or diphenhydramine is not appropriate.

PREP Pearls
- Nephrotic syndrome is characterized by edema (facial puffiness or generalized anasarca), proteinuria, hypoalbuminemia, and hyperlipidemia.
- Initially these patients are often mistaken as having an allergic reaction and therefore treated with a short course (3-5 days) of oral steroids or antihistamine.
- Proteinuria on urinalysis differentiates nephrotic syndrome from allergies.

ABP Content Specifications(s)
- Plan the appropriate initial management of the first episode of minimal-change nephrotic syndrome
- Recognize the clinical and laboratory findings associated with minimal-change nephrotic syndrome

Suggested Readings

- Andolino TP, Reid-Adam J. Nephrotic syndrome. *Pediatr Rev*. 2015;36(3):117–125. doi: http://dx.doi.org/10.1542/pir.36-3-117.
- 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; 2009:2296–2303.

Question 104

A 14-month-old girl is referred to the emergency department by her pediatrician for bruising. The pediatrician called ahead of the child's arrival and expressed concern for possible child abuse. The family of 3 live together in a single-family home, and the mother is the primary caregiver. The child was born at term following an uncomplicated pregnancy and delivery and was discharged home with her mother after 2 days. Her parents report that she has a normal, age-appropriate diet and consumes not more than 2 cups of whole milk per day.

The child's parents report that she has always bruised very easily. Since she became mobile and started crawling, they noticed intermittent but frequent and large bruises on her knees, elbows, buttocks, and forehead. They report that she also experiences at least 2 nosebleeds per week and that the nosebleeds sometimes last longer than 10 minutes before they stop with pressure. She has otherwise been well, without any hospitalizations or surgeries. The parents report no history of trauma, other than occasional falls while cruising. Five days prior to this visit, she fell from a stand while cruising and hit her head on a ceramic floor. She did not lose consciousness, cried immediately, and was soothed when she was picked up. Her behavior has been normal since then. She does not take any medications.

She is a happy, well-developed girl who looks appropriate for her age. She is sitting comfortably in her mother's lap. Her height is at the 25th percentile and her weight is at the 20th percentile for her age. Her heart rate and blood pressure are normal for her age. When put down, she is able to cruise. She happily babbles and can say "mama." There is a faded, flat bruise approximately 3 cm in diameter on her glabella that tracks under her eyes as a green discoloration. There are also bruises of various sizes and ages on her knees, elbows, and sacral area. There is dried blood in her right nare. The remainder of her physical examination findings are unremarkable.

An initial laboratory evaluation shows:

| Laboratory Test	Result
White blood cell count	5,100/μL (5.10×10^9/L)
Hemoglobin	11.1 g/dL (111 g/L)
Platelet count	257×10^3/μL (257×10^9/L)
Mean corpuscular volume	73 fL
Reticulocytes	1.2%
Prothrombin time	12.1 s (normal range, 10.8-13.9 s)
Partial thromboplastin time	46 s (normal range, 26.6-30.3 s)
Mixing studies	The partial thromboplastin time corrects.

Of the following, the BEST next step in the management of this child is to immediately

  A. call child protective services
  B. determine factor VII, VIII, and IX levels
  C. determine factor VIII, von Willebrand antigen, and von Willebrand activity levels
  D. perform computed tomography of the head
  E. perform flow cytometry on peripheral blood to assess for lymphoblasts

Correct Answer: C

The toddler in this vignette exhibits normal development but has an abnormal bleeding history. She has been incurring large bruises in locations of pressure, including the knees and elbows while crawling, the buttocks when she falls from a stand, and her forehead when she loses her balance because of her normal toddler gait. She has also experienced epistaxis of abnormal frequency and duration. A spontaneous nosebleed longer than 10 minutes is concerning for an abnormal intranasal blood vessel or a coagulopathy. Her history and physical examination results are concerning for a coagulopathy. The abnormal partial thromboplastin time that is corrected in a mixing study confirms an abnormality of the coagulation cascade, specifically the intrinsic cascade (**Item C104**). A deficiency of von Willebrand factor would be most consistent with the history, physical examination results, and laboratory abnormalities detailed for the girl in this vignette.
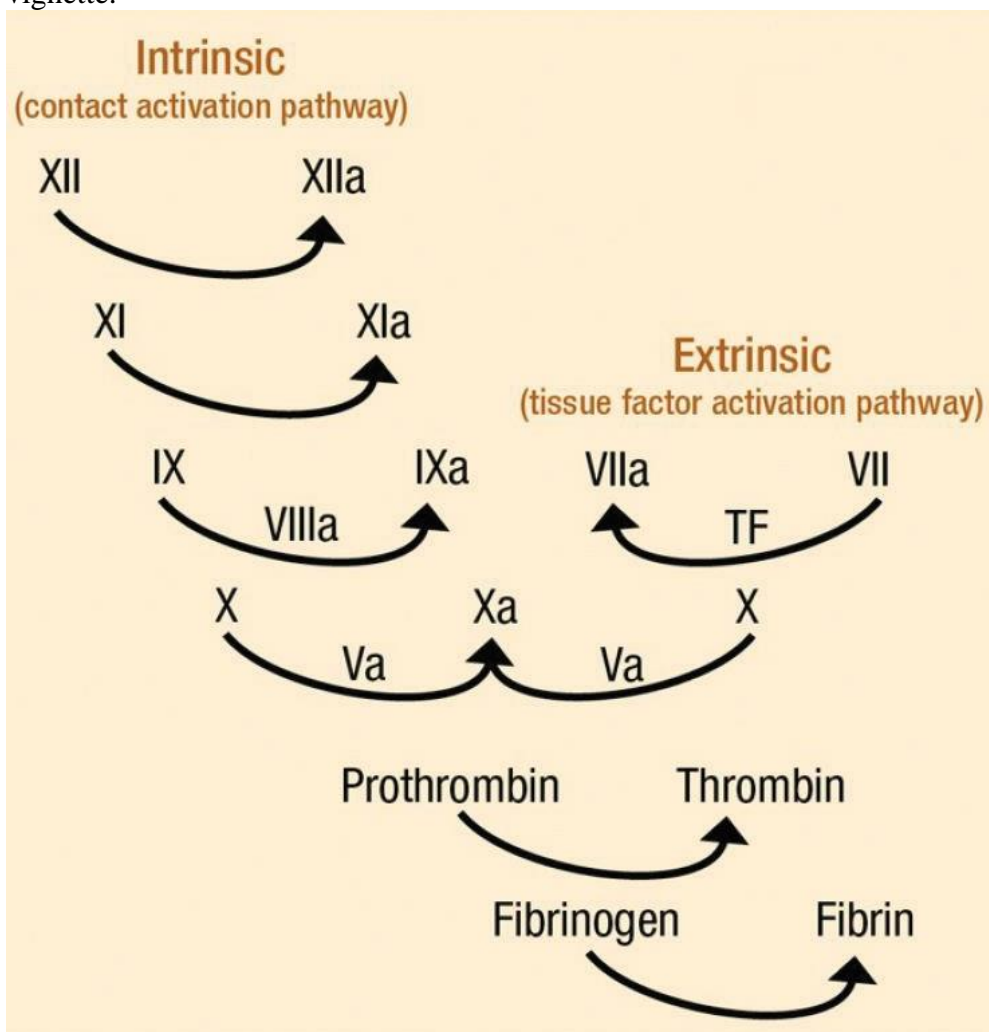
Item C104: Coagulation Pathways.

Von Willebrand factor is a key component of coagulation that lies outside the traditional coagulation cascade and allows platelets to bind to fibrin to form a clot. Von Willebrand disease occurs when there is decreased function or inadequate production of von Willebrand factor. This disease is the most common heritable bleeding disorder; therefore, a detailed family bleeding history is essential. However, the absence of a significant family bleeding history does not exclude von Willebrand disease because the genetic lesion can occur spontaneously. The disease phenotypes range from mild to severe bleeding disorders that reflect the degree of dysfunction or absence of the von Willebrand factor. The types of von Willebrand disease include 1, 2A, 2B, 2M, 2N, and 3. Type 1 is the most common and least severe. Type 3 is rare and characterized by a severe deficiency or total absence of functional von Willebrand factor; therefore, it presents with a very severe bleeding phenotype.

Given the child's remarkable history, physical examination results, and laboratory findings, it is extremely likely that she has a coagulopathy. There would therefore be no indication to call child protective services. Her last known head trauma was 5 days prior to the visit, and she appears well; thus, there is no indication for computed tomography of the head. The normal prothrombin time confirms a normal extrinsic coagulation cascade, and therefore a normal factor VII level. Her sex makes factor VIII and IX deficiencies unlikely, as both conditions are X linked.
A patient with a suspected coagulopathy should have an evaluation of the intrinsic and extrinsic pathways of coagulation (partial thromboplastin time and prothrombin time), platelet count, platelet function, von Willebrand factors, and fibrinogen.

PREP Pearls
- Von Willebrand disease is the most common heritable bleeding disorder.
- Von Willebrand factor links fibrin to functional platelets, thereby enabling the formation of a stable clot.
- The types of von Willebrand disease are correlated with phenotypes of variable severity.
- A patient with a suspected coagulopathy should have an evaluation of the intrinsic and extrinsic pathways of coagulation (partial thromboplastin time and prothrombin time), platelet count, platelet function, von Willebrand factors, and fibrinogen.

ABP Content Specifications(s)
- Plan an appropriate screening evaluation for a coagulation disorder
- Plan the general therapeutic approach for a patient with a bleeding diatheses
- Plan the appropriate diagnostic evaluation for increased bruising

Suggested Readings

- Acharya SS. Rare bleeding disorders in children: identification and primary care management. *Pediatrics*. 2013;132(5):882–892. doi: http://dx.doi.org/10.1542/peds.2012-3662.
- Carpenter SL, Abshire TC, Anderst JD, Section on Hematology/Oncology and Committee on Child Abuse and Neglect. Evaluating for suspected child abuse: conditions that predispose to bleeding. *Pediatrics*. 2013;131(4):e1357–e1373. doi: http://dx.doi.org/10.1542/peds.2013-0196.
- Rodriguez V, Warad D. Pediatric coagulation disorders. *Pediatr Rev*. 2016;37(7):279–291. doi: http://dx.doi.org/10.1542/pir.2015-0062.

Question 105

A 3-year-old boy is brought to your office for a follow-up visit. Developmental screening at his most recent health supervision visit was significant for language and mild fine and gross motor delays. Subsequent developmental evaluation identified additional cognitive and adaptive delays. Testing for a genetic cause for the boy's developmental delays reveals 300 CGG repeats in the FMR-1 gene. His physical examination is notable for hypotonia and prominent ears. As a child, the boy's mother received special education for a learning disability. She asks you, based on his diagnosis, what she should expect for his future intellectual development.

Of the following, the boy is MOST likely to have

  A. borderline intellectual disability
  B. mild intellectual disability
  C. moderate intellectual disability
  D. profound intellectual disability
  E. severe intellectual disability

Correct Answer: C

The boy in the vignette has fragile X syndrome, and as a result, will most likely have moderate intellectual disability (ID). Fragile X is the most common inherited cause of ID. It affects 1 in 3,600 to 4,000 boys and 1 in 4,000 to 8,000 girls. The condition is the result of a mutation in the fragile X mental retardation gene (*FMR-1*) on the X chromosome. An expansion of the trinucleotide, CGG, to greater than 200 repeats in this gene results in hypermethylation of the gene, reduced *FMR1* protein, and the phenotypic features of fragile X. Cognitive deficits in patients can vary from learning disability to borderline intellectual function to severe ID. Boys with a full mutation typically have moderate ID (average IQ ~ 41), whereas girls are more mildly affected.

Prenatal causes of ID include infection, toxins and teratogens, congenital hypothyroidism, inborn errors of metabolism, and genetic abnormalities. Infections of note include rubella, cytomegalovirus, syphilis, toxoplasmosis, and herpes simplex virus. In utero exposure to alcohol is important to ascertain; fetal alcohol syndrome is the most common preventable cause of ID. Phenylketonuria is an inborn error of metabolism which, when untreated, can cause ID.

The degree of ID varies between and within genetic syndromes. Down syndrome is the most common genetic cause of ID. Although ID in Down syndrome can range from mild to severe, most people with Down syndrome have mild to moderate ID. As noted before, boys with fragile X typically have moderate ID whereas girls are more mildly affected. Children with Prader-Willi syndrome have low average cognition to moderate ID. Severe cognitive impairment is seen in Angelman syndrome.

Perinatal causes of ID include prematurity, low birthweight, hypoxia, intracranial hemorrhage, perinatal central nervous system infection, and perinatal trauma. Postnatal causes of ID include acquired brain injury, central nervous system hemorrhage, central nervous system infection (eg, meningitis, encephalitis), intracranial tumors, asphyxia, severe psychosocial deprivation, severe malnutrition, chemotherapy, and toxins (eg, lead).

PREP Pearls
- Prenatal causes of intellectual disability (ID) include infection, toxins and teratogens, congenital hypothyroidism, inborn errors of metabolism, and genetic abnormalities.
- Fetal alcohol syndrome is the most common preventable cause of ID.
- Genetic etiologies of ID include conditions such as Down syndrome, the most common genetic cause, and fragile X, the most common inherited cause.

MOCA-Peds Objective
- Recognize the genetic syndromes that may present as a learning disability

ABP Content Specifications(s)
- Recognize the range of intellectual disabilities associated with common genetic syndromes
- Identify the prenatal and perinatal causes of intellectual disabilities, including factors associated with family history

Suggested Readings
- Moeschler JB, Shevel M; Committee on Genetics. Comprehensive evaluation of the child with intellectual disability or global developmental delays. *Pediatrics*. 2014;124(3):e903–918. doi: http://dx.doi.org/10.1542/peds.2014-1839.
- 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 106

A 12-year-old girl is brought to your office after possibly having a seizure. Her mother reports that while she was braiding the girl's hair for a dance competition, the girl complained of feeling dizzy, then her face turned pale, and her eyes rolled upward. She collapsed onto the floor and convulsed for 10 seconds. She then woke up and complained of nausea and a headache. After 10 minutes, she was back to normal. In your office, the girl's vital signs and physical examination findings are normal. The mother tells you that her sister, the girl's aunt, had childhood epilepsy.

Of the following, the BEST next step in the evaluation and management for this girl is to

  A. advise increasing fluid and salt intake
  B. assess for an anxiety disorder
  C. order computed tomography of the head
  D. order electroencephalography
  E. order polysomnography with multiple sleep latency test

Correct Answer: A

The girl in the vignette had hair grooming syncope with an associated syncopal convulsion. Hair grooming syncope is a situational syncope that occurs when the person's hair is being brushed, cut, braided or pulled tightly in some way. It is more common in girls, but can happen in boys. Syncopal convulsions are brief convulsions that can occur after syncope of any cause; they are not epileptic seizures. Compared with generalized tonic-clonic seizures, syncopal convulsions are shorter in duration, usually lasting only a few seconds, and there is no significant postictal period. Clinically, syncopal convulsions occur *after* the person has lost consciousness, not at the same time, as occurs in a generalized tonic-clonic seizure. Hair grooming syncope may be related to vasovagal syncope, and increasing fluids and salt intake may help prevent episodes. The best advice to provide regarding future events is to make sure the girl is sitting down when her hair is being braided or pulled tightly, so that she is protected from serious injury if she has another syncopal episode.

In cases in which the clinical presentation is typical of situational syncope, extensive diagnostic evaluation is not needed. This girl has no symptoms of psychogenic syncope or conversion disorder, so assessing for anxiety is not the best next step. Because her physical examination findings are normal, brain imaging is not needed. The girl's history is very suggestive of hair grooming syncope, and the syncopal convulsion was brief; therefore, epileptic seizure is very unlikely and electroencephalography would not be helpful. Polysomnography with multiple sleep latency test would only be helpful if the episode was suggestive of cataplexy. In cataplexy, sudden emotions, such as fright or laughter, cause a collapse of the body, but consciousness is preserved. The girl's event is not consistent with cataplexy.

PREP Pearls
- Compared with generalized tonic-clonic seizures, syncopal convulsions are shorter in duration, usually lasting only a few seconds, and there is no significant postictal period.
- Syncopal convulsion occurs *after* the person has lost consciousness, not at the same time as in a generalized tonic-clonic seizure.
- Increasing fluids and salt intake may help prevent vasovagal syncope.

ABP Content Specifications(s)
- Differentiate the features of epileptic seizures from those of paroxysmal non-epileptic events

Suggested Readings
- Cannon B, Wackel P. Syncope. *Pediatr Rev.* 2016;37(4):159–168. doi: http://dx.doi.org/10.1542/pir.2014-0109.
- Stewart JM. Common syndromes of orthostatic intolerance. *Pediatrics*. 2013;131(5):968–980. doi: http://dx.doi.org/10.1542/peds.2012-2610.

Question 107

A 5-month-old asymptomatic infant is brought to your office after her parents were notified by the health department that she may have been exposed to an unvaccinated day care worker with measles. You call the health department and find out that the index patient is an unvaccinated adult who works at the day care center and developed fever, cough, and generalized rash after returning from travel to the Philippines, where a large measles outbreak was ongoing. Your patient has received the 2-month and 4-month immunization series, and the parents report no symptoms at this visit. Her physical examination findings are normal.

Of the following, the BEST measles control strategy for this infant is

  A. administration of acyclovir
  B. administration of immune globulin
  C. administration of measles vaccine
  D. isolation
  E. reassurance and close observation

Correct Answer: B

Measles is a highly communicable acute viral illness characterized by a febrile rash that can cause considerable morbidity and mortality among children, especially in lower and middle income countries. Although measles was eliminated in the United States in 2000 (defined as interruption of year-round endemic transmission) because of high rates of 2-dose measles vaccine coverage, imported measles cases have caused small, poorly sustained outbreaks. From 2009 to 2014, a total of 1,264 confirmed measles cases were reported in the United States, including 275 imported cases from 58 countries and 66 different outbreaks. Over 60% of measles cases in the United States occurred in vaccine-eligible residents who were intentionally unvaccinated. In 2014 alone, the United States experienced 23 measles outbreaks and 668 measles cases. The problem of vaccine refusal in certain vulnerable communities increases the risk of measles transmission among completely vaccinated individuals. Data from recent measles outbreaks indicate that unvaccinated United States residents who return from travel to measles-endemic countries are at high risk for acquiring measles and spreading the disease to others in their communities.

Measles virus is transmitted from person to person via respiratory droplets or direct contact with infected nasal or pharyngeal secretions. The measles virus is highly infectious with an estimated basic reproductive number (R0) of 12 to 16 (ie, the number of secondary cases generated by a single index case in a fully susceptible population). Secondary attack rates up to 90% can occur in susceptible household contacts. Population-level herd immunity thresholds must reach approximately 95% to prevent the reestablishment of indigenous measles transmission. Patients with measles are contagious from 4 days before to 4 days after the onset of the rash. Individuals are considered to have presumptive evidence of immunity to measles if they meet any of the following 4 criteria: documented receipt of age-appropriate vaccination with a live measles virus–containing vaccine; serological evidence of immunity; laboratory confirmation of disease; or birth before 1957.

Pregnant women without evidence of measles immunity, neonates, infants younger than 12 months, and severely immunocompromised patients are at risk for developing severe disease and complications from measles. The Advisory Committee on Infectious Diseases at the Centers for Disease Control and Prevention have published guidance on the administration of postexposure prophylaxis (PEP) to prevent measles in exposed susceptible contacts. Studies suggest that PEP with measles-mumps-rubella (MMR) vaccine (administered within 72 hours of measles exposure) or immune globulin (administered within 6 days of exposure) to susceptible contacts will confer protection or modify the clinical course of disease.

In the United States and other high income countries, most mothers have evidence of vaccine-induced immunity. Infants born to mothers with vaccine-induced immunity lose transplacentally acquired measles antibodies at an earlier age than infants born to mothers with naturally acquired immunity. For infants aged 6 months and younger who are exposed to measles, PEP with intramuscular immune globulin is recommended at a dose of 0.5 mL/kg (maximum dose, 15 mL). Intramuscular immune globulin must be administered as soon as possible after exposure but may be given within 6 days of exposure. For exposed infants aged 6 through 11 months, MMR

vaccine can be given in place of intramuscular immune globulin and would offer protection if given within 72 hours of exposure. Infants receiving MMR vaccine before their first birthday should be revaccinated at 12 through 15 months of age and receive a third dose at least 28 days later, usually at 4 through 6 years of age.

The MMR vaccine as PEP must be considered in all exposed, vaccine-eligible contacts who are unvaccinated or have received only one MMR dose. In community-wide measles outbreaks involving households, schools, and day care centers where the transmission risk is very high, PEP with MMR vaccine is recommended for exposed infants aged 12 months and older. Intravenous immune globulin as PEP is recommended for pregnant women without evidence of measles immunity and for severely immunocompromised patients, regardless of vaccination history or immune status.

Acyclovir has no antiviral activity against measles and is not recommended for postexposure chemoprophylaxis. Individuals who receive MMR vaccine or immune globulin as PEP should be monitored closely for symptoms of measles for at least one incubation period (through 21 days after exposure). In hospital or ambulatory settings, patients with suspected measles should be immediately isolated and placed on airborne transmission precautions.Immunocompetent patients with measles must be isolated until 4 days after rash onset, whereas isolation is recommended for the duration of illness in infected immunocompromised patients. Clinicians must report every suspected measles case to the health department. The continued threat of imported measles cases coupled with large outbreaks in communities with low vaccine coverage warrants the urgent need for pediatricians to address vaccine hesitancy and effectively communicate the safety and public health benefit of vaccines.

PREP Pearls
- Measles is a highly communicable acute viral illness characterized by a febrile rash. The illness can result in serious complications among pregnant women without evidence of measles immunity, infants younger than 12 months, and severely immunocompromised patients.
- For infants aged 6 months and younger who are exposed to measles, postexposure prophylaxis with intramuscular immune globulin is recommended within 6 days of exposure.

ABP Content Specifications(s)
- Plan appropriate use of intramuscular immune globulin in immunocompromised and unimmunized patients who have been exposed to measles
- Recognize the clinical features associated with measles, including complications
- Plan appropriate control measures to prevent the spread of measles

Suggested Readings

- 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.
- Centers for Disease Control and Prevention. 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(RR-04):1–34.
- Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between vaccine refusal and vaccine-preventable diseases in the United States: a review of measles and pertussis. *JAMA*. 2016;315(11):1149–1158. doi: http://dx.doi.org/10.1001/jama.2016.1353.

Question 108

An 8-day-old term male neonate is brought for an urgent visit because of maternal concerns of stooling problems. She reports that the pregnancy and delivery were uncomplicated. Her son had been breastfeeding well, approximately every 2 to 3 hours; however, the frequency is now decreasing. The mother feels that her milk supply is in. While the neonate's urine output has been good, he seems to have difficulty with stooling. He stooled at 54 hours after birth following a glycerin suppository and has not stooled since. The mother is concerned that his abdomen is distended and he seems uncomfortable. The newborn screening results are normal.

The neonate is alert and fussy, but consolable with a pacifier. He has a heart rate of 148 beats/min and respiratory rate of 27 breaths/min. He is afebrile. His weight is down 120 g from his birth weight. His anterior fontanelle is open, soft, and flat. He has moist mucous membranes. His abdomen is distended and hypertympanic with good bowel sounds and no hepatosplenomegaly. His rectal examination demonstrates normal placement of the anus. A digital rectal examination demonstrates a mildly tight sphincter and empty rectal vault, with a large volume of foul fecal material exploding out with removal of your digit.

Of the following, the MOST likely diagnosis is

A. anal stenosis
B. cystic fibrosis
C. Hirschsprung disease
D. infantile inflammatory bowel disease
E. intestinal volvulus

Correct Answer: C

Hirschsprung disease (HSD) is the most likely diagnosis for the infant in this vignette with delayed meconium passage and abnormal digital rectal examination findings with an empty rectal vault, contracted anal sphincter, and explosive foul smelling output with removal of the finger. Other symptoms may include poor feeding, abdominal distention, diarrhea, infrequent bowel movements, and bilious emesis. Most children will become symptomatic in the first days to weeks after birth.

Hirschsprung disease is caused by a lack of craniocaudal migration by ganglion cell precursors that would normally migrate from the neural crest along the gastrointestinal tract during gestational weeks 5 through 12. The aganglionic segment starts at the internal anal sphincter and extends proximally. Approximately 75% to 80% of affected patients have short-segment HSD with the aganglionic segment distal to the splenic flexure, and 20% have long-segment HSD with the affected segment extending proximally to the splenic flexure. A very small number of patients have total bowel aganglionosis.

Hirschsprung disease causes abnormalities in affected bowel motility. Enterocolitis is the major cause of morbidity and mortality in children with HSD. Enterocolitis presents with abdominal distention, explosive watery stools, fever, and hypovolemic shock. Enterocolitis is most often seen in children with HSD who are younger than 2 years, but it can be seen in children up to 10 years of age. Additional complications of HSD include neonatal constipation and failure to thrive.

The gold standard for diagnosis of HSD is a suction or full-thickness rectal biopsy with submucosa present that is taken 2 cm above the dentate line and shows an absence of ganglion cells. Acetylcholinesterase staining will demonstrate hyperplasia of axons. Additional evaluation may include an unprepared barium enema (no cleanout prior to the study) (**Item C108**). Affected individuals will demonstrate a transition zone between the contracted affected bowel and the dilated proximal ganglionated segment. Absence of a transition zone does not rule out HSD. Anorectal manometry can also suggest HSD with absence of reflex relaxation of the internal anal sphincter.
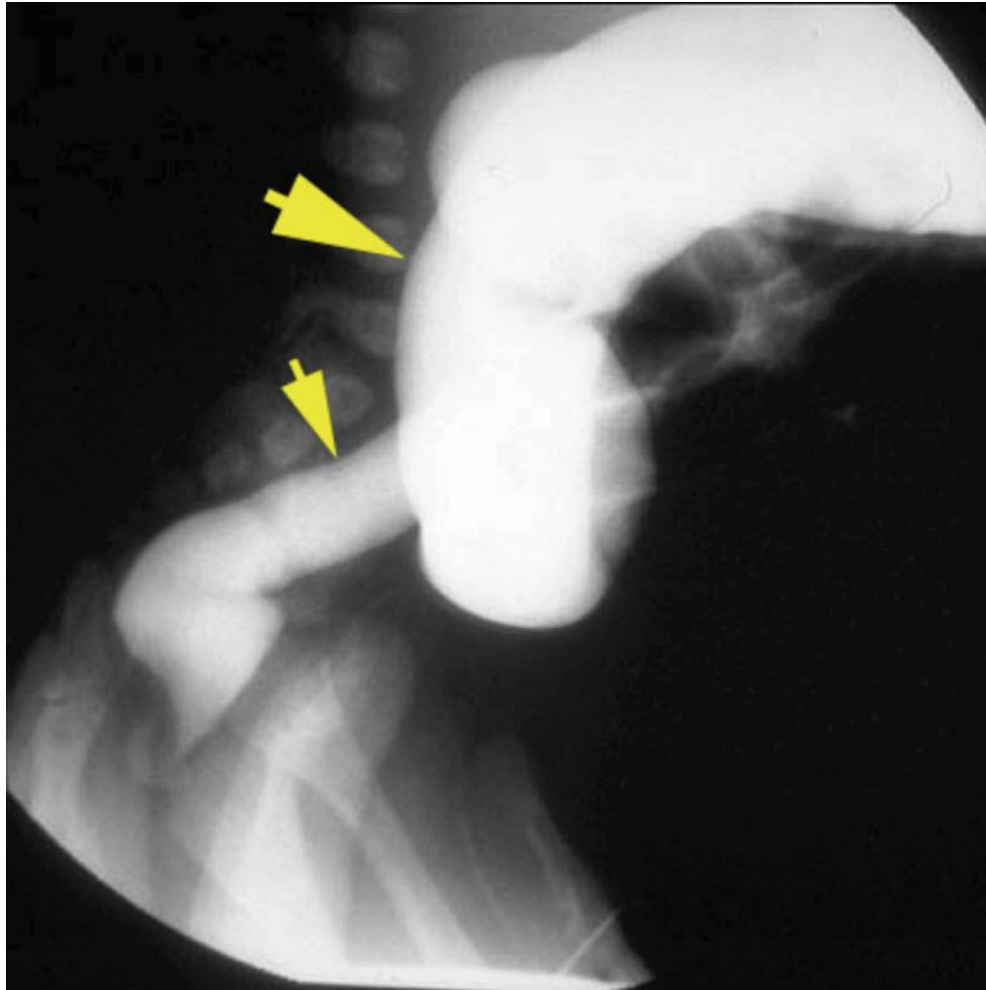
Item C108: Barium Enema in a child with Hirschsprung Disease. The small arrow identifies the aganglionic portion of the colon. The large arrow identifies the dilated colon proximal to the segment affected by Hirschsprung disease.
Courtesy S. Schwarz

Anal stenosis is an incorrect diagnosis given the physical examination findings with the empty rectal vault and explosive stools. In anal stenosis, the sphincter is typically very tight and there is usually stool in the rectal vault and no explosive burst of fluid with removal of the finger. Cystic fibrosis may present with a delay in meconium passage, but with normal rectal examination findings. Infantile inflammatory bowel disease is rarely seen at 8 days of age and presents with a very ill-appearing child with copious bloody stools and failure to thrive. Intestinal volvulus will present with abdominal distention, decreased bowel sounds, bilious emesis, and extreme fussiness; children with intestinal volvulus have a surgical abdomen caused by bowel obstruction and appear ill.

PREP Pearls
- Hirschsprung disease presents with abnormal digital rectal examination findings with an empty rectal vault, contracted anal sphincter, and explosive foul-smelling output with removal of the finger.
- The gold standard for diagnosis of Hirschsprung disease is rectal biopsy with the absence of ganglion cells.
- Barium enema may demonstrate a transition zone in Hirschsprung disease
- Rectal manometry will not demonstrate reflex relaxation of the internal anal sphincter in children with Hirschsprung disease.

ABP Content Specifications(s)
- Identify complications associated with Hirschsprung disease
- Plan the appropriate diagnostic evaluation in a patient in whom Hirschsprung disease is suspected

Suggested Readings
- Arshad A, Powell C, Tighe MP. Hirschsprung's disease. *BMJ*. 2012;345:e5521. doi: http://dx.doi.org/10.1136/bmj.e5521.
- Burkardt DD, Graham JM Jr, Short SS, Frykman PK. Advances in Hirschsprung disease genetics and treatment strategies: an update for the primary care pediatrician. *Clin Pediatr (Phila)*. 2014;53(1):71–81. doi: http://dx.doi.org/10.1177/0009922813500846.
- Feldman T, Wershil BK. In brief: Hirschsprung disease. *Pediatr Rev*. 2006;27(8):e56–e57. doi: http://dx.doi.org/10.1542/pir.27-8-e56.
- Frongia G, Günther P, Schenk JP, et al. Contrast enema for Hirschsprung disease investigation: diagnostic accuracy and validity for subsequent diagnostic and surgical planning. *Eur J Pediatr Surg*. 2016;26(2):207–214. doi: http://dx.doi.org/10.1055/s-0035-1546755.
- Rudolph C, Benaroch L. Hirschsprung disease. *Pediatr Rev*. 1995;16(1):5–11. doi: http://dx.doi.org/10.1542/pir.16-1-5.

Question 109

During a health supervision visit for her biological child, a mother mentions that the family is considering adopting 2- and 4-year-old brothers who have been in foster care for more than 1 year. The mother asks for information about health and behavior issues that may arise with these children.

Of the following, the MOST accurate information to provide the mother is that

    A. international adoptees have more health problems than domestic adoptees
    B. sleep and feeding problems are anticipated as these children adjust to their new environment
    C. the incidence of special health care needs among these children is equivalent to that in the general population
    D. these children are likely to recognize that this family may be "different" from their friends' families
    E. these children often have minor developmental delays initially, but nearly always catch up within a few months

Correct Answer: B

Approximately 2% of children in the United States come to their families through adoption: 38% are adopted from foster care, 38% through private domestic adoption, and 25% through international adoption. The family in the vignette should anticipate adjustment issues as their adopted children transition to their new home. In addition to problems such as temper tantrums or emotional withdrawal, these children may experience difficulty with the timing, duration, and quality of sleep and feeding problems such as food refusal, hoarding, or overeating. Besides evaluating and managing an adopted child's physical issues, the pediatrician's role is to provide the support, counseling, and referrals that will help families develop healthy attachments and resolve adjustment issues.

In one survey, parents described the health of their adopted children as excellent or very good 85% of the time. However, compared with the general population, these children more commonly have special health care needs (39% vs 19% in the general population). Their health care issues range from physical problems, such as asthma or complex medical conditions to developmental delays and behavioral health problems, such as attention-deficit/hyperactivity disorder, autism, and mood disorders. This is particularly true of children adopted through the foster care system, 54% of whom have special health care needs. International adoptees are less often referred for behavioral health services than are domestic adoptees.

Prenatal, perinatal, and environmental factors before adoption are presumed to have a continuing impact on performance even after adoption. A meta-analysis of studies on IQ, school achievement, language development, and learning problems among adoptees indicated that although adopted children's IQs often closely matched their adoptive siblings, over time, they did not catch up to peers in their new environment in terms of school achievement, language development, and learning abilities. This appears to be particularly true for children adopted at an older age, who were noted to be more similar to their birth parents than their adoptive parents in regard to performance and achievement.

Most children form strong and loving relationships with their adoptive family, but the fact of adoption affects their psychosocial development in different ways throughout their childhood, depending on their developmental stage. The story of their adoption should be introduced to the child early, rather than waiting for some anticipated "right time." Young children do not recognize a difference between their family and families composed of only biological children, but by 3 years of age they often begin to ask questions about adoption and their own adoption story. By kindergarten entry, adoptees realize that most children are not adopted. They may assume that they are responsible for their biological parents not living with them, and they may experience separation issues. School-aged children may appear unconcerned about their adoption, but even if they do not raise questions about their adoption story, adjustment difficulties may occur. They may identify with and fantasize about a perfect biological family, and if adopted across racial or cultural lines, may have difficulties reconciling their identity. During adolescence, with the age-appropriate task of developing a separate identity, these issues may affect a child's relationship with their adoptive parents and family. Some adolescents will

identify more with their biological family (whether known or imagined) than their adoptive family. Encouraging open communication about adoption may mitigate some of these problems.

PREP Pearls
- Approximately 2% of children in the United States are adopted, and nearly 40% of these children have special health care needs.
- Initial adjustment issues seen as a child transitions to an adoptive home may include withdrawal, temper tantrums, and sleep and feeding problems.
- Although the IQs of adopted children are similar to that of their adoptive siblings, they may not catch up to peers in school achievement, language development, and learning ability.
- Psychosocial response to adoption may change as a child progresses through various developmental stages.

ABP Content Specifications(s)
- Understand the psychosocial issues surrounding adoption
- Understand the pediatrician's role in the adoption process

Suggested Readings
- Child Trends.org website. http://www.childtrends.org/?indicators=adopted-children.
- Jones VF, Committee on Early Childhood, Adoption and Dependent Care. Comprehensive health evaluation of the newly adopted child. *Pediatrics*. 2012;129:e214-e223. doi: http://dx.doi.org/10.1542/peds.2011-2381.
- Jones VF, Schulte EE, and the Committee on Early Childhood and Council on Foster Care, Adoption, and Kinship Care. The pediatrician's role in supporting adoptive families. *Pediatrics*. 2012;130:e1040-e1049. doi: http://dx.doi.org/10.1542/peds.2012-2261.
- Juffer F, van Ijzendoom MH. Behavior problems and mental health referrals of international adoptees a meta-analysis. *JAMA*. 2005;293:2501-2515. doi: http://dx.doi.org/10.1001/jama.293.20.2501.
- Van Ijzendoorn MH, Juffer F, Klein Poelhuis CW. Adoption and cognitive development: a meta-analytic comparison of adopted and nonadopted children's IQ and school performance. *Psychological Bulletin.* 2004; 131:301-316. doi: http://dx.doi.org/10.1037/0033-2909.131.2.301.

Question 110
You have been treating a 10-year-old boy with a long-acting stimulant medication for attention-deficit/hyperactivity disorder. Since starting the medication, his school performance and self-efficacy have improved significantly. He takes the medication in the morning only on school days. His teacher has noticed that his work output and behavior are optimal in the morning, so she has arranged his schedule accordingly. The boy is able to complete homework with the help of one-on-one tutoring and enjoys participating in sports. His sleep habits and growth are adequate. Due to changes in his health insurance, his current medication will no longer be covered.

Of the following, the MOST appropriate substitute medication, when administered at the same dose, would have the same

 A. active ingredient in an intermediate-acting form
 B. area under the curve of concentration versus time
 C. peak serum concentration
 D. rate and extent of absorption
 E. volume of distribution and rate of elimination

Correct Answer: D

The boy in the vignette has attention-deficit/hyperactivity disorder (ADHD) that is well-managed on a particular stimulant medication. Because the medication will no longer be covered by insurance, he would benefit from a medication that is bioequivalent, which indicates a similar rate and extent of absorption.

When an oral medication is administered, concentration as a function of time of the active ingredient depends on several factors. The formulation of a medication can determine how quickly the active ingredient is absorbed. For example, several narcotic agents, ADHD medications, and antihypertensives have different immediate-release and sustained-release formulations. Medications are distributed to varying degrees in fatty tissues compared with plasma. Also, drugs in plasma can either be free or protein bound. These factors determine the volume of distribution as well as the concentration of different medications. Furthermore, kinetics of elimination via the liver, kidney, and metabolism in the plasma are important in determining the concentration profile of drugs. The body's total exposure to a medication is best determined by the area under the curve (AUC) of a plot of the drug concentration as a function of time. This curve is dependent on the rate of absorption, extent of absorption, and kinetics of elimination.

Bioequivalence is defined as 2 drugs having a similar rate and extent of absorption. This can be estimated by studying the concentration profile and AUC of the active ingredient of the drugs. The concept is used in the pharmaceutical industry to demonstrate similar action of 2 different medications, for example, a brand-name and a generic medication.

The initial medication used to treat the ADHD of the child in the vignette resulted in improved school performance and self-efficacy, and there is evidence that the effect wears off later in the day, as his sleep habits and growth are adequate. Because he can no longer receive this medication, he would benefit from a bioequivalent drug, as opposed to one with different concentration versus time curve. Of the choices, an active ingredient in an intermediate-acting form would likely be absorbed and eliminated more slowly. A similar area under the curve of concentration versus time would yield the same amount of total drug exposure, but would not indicate the same rate of absorption. The same peak concentration also would not predict a similar time profile of the active ingredient. Lastly, similar volume of distribution and rate of elimination would not determine how quickly the drug is absorbed.

PREP Pearls
- Bioequivalence is defined as the property of 2 medications to have a similar rate and extent of absorption.
- Area under the curve of concentration as a function of time expresses the total amount of exposure of the body to a medication.
- The concentration versus time curve is affected by the rate and extent of absorption and kinetics of elimination.

ABP Content Specifications(s)
- Understand factors that influence bioequivalence of drugs

Suggested Readings
- Chen ML, Davit B, Lionberger R, et al. Using partial area for evaluation of bioavailability and bioequivalence. *Pharm Res*. 2011;28(8):1939–1947. doi: http://dx.doi.org/10.1007/s11095-011-0421-x.
- Haidar SH, Dabit B, Chen ML, et al. Bioequivalence approaches for highly variable drugs and drug products. *Pharm Res.* 2008;25(1):237–241. doi: http://dx.doi.org/10.1007/s11095-007-9434-x.
- Scheff JD, Almon RR, DuBois DC, et al. Assessment of pharmacologic area under the curve when baselines are variable. *Pharm Res.* 2011;28(5):1081–1089. doi: http://dx.doi.org/10.1007/s11095-010-0363-8.

Question 111

You are called to the cesarean delivery of a 39-week-gestation male neonate with a category 3 fetal monitor tracing and suspected placental abruption. The mother is a 23-year-old gravida 1, para 0 woman with a history of seizure disorder controlled by levetiracetam. The amniotic fluid is bloody. Upon delivery, the neonate is floppy, pale, and apneic, with a heart rate of 50 beats/minute. There is no improvement in tone with warming, drying, and stimulation. You intubate the neonate 2 minutes after birth, with the heart rate improving to 120 beats/min but no change in tone, perfusion, or responsiveness after 15 minutes of resuscitation. You arrange for immediate transfer to a level 3 nursery in the neighboring town for possible therapeutic hypothermia.

Of the following, this treatment will MOST likely benefit the neonate by

A. decreasing apoptosis and damage from oxidative stress
B. depleting adenosine triphosphate stores
C. improving glomerular filtration rate
D. increasing heart rate and perfusion
E. increasing lactic acid production

Correct Answer: A

The neonate in the vignette is at risk for hypoxic-ischemic encephalopathy (HIE) because of placental abruption and physical examination findings consistent with encephalopathy with an ongoing need for ventilation 10 minutes after birth. If an umbilical cord blood gas or blood gas measurement is obtained within the first hour after birth, a neonate with suspected HIE will have a metabolic acidosis. Neonates with moderate to severe encephalopathy who receive therapeutic hypothermia (TH) within the first 6 hours of birth have decreased morbidity and mortality compared with normothermic controls. Based on animal data, TH improves outcomes by decreasing apoptosis and damage caused by oxygen free radicals. Potential side effects of TH include bradycardia, coagulopathy, and fat necrosis.

Hypothermia has been used as treatment following injury and disease for centuries, dating back to ancient Egyptian, Roman, and Greek civilizations. More recently, using animal models of neonatal brain injury, TH has been shown to decrease brain infarct size and improve neurocognitive outcomes. Clinical trials of TH have demonstrated decreased morbidity and mortality for neonates with moderate encephalopathy compared with normothermic controls. As such, TH has become the standard of care for neonates with suspected HIE in the United States. Neonates with suspected moderate HIE should be treated with therapeutic hypothermia (TH), cooling to 33.5°C for 72 hours, to reduce the risk of morbidity and mortality.

However, an increased risk of disability still exists for those who received TH. Trials of adjuvant treatments including xenon gas, erythropoietin, and cord blood cell infusion are ongoing. Neonates with suspected HIE frequently have systemic signs affecting all organ systems. They may require respiratory support with mechanical ventilation. Hypotension and persistent pulmonary hypertension are common. Neonates may be oliguric or anuric after renal damage and/or hypoperfusion of the kidneys. They are at risk of developing syndrome of inappropriate antidiuretic hormone with oliguria and hyponatremia. Many will develop seizures in the immediate postnatal period.

Therapeutic hypothermia lowers the metabolic rate and adenosine triphosphate usage, and decreases lactic acid production. While TH can cause cold diuresis and increased GFR, the benefit of TH is related to neurodevelopmental outcomes.

PREP Pearls
- Hypoxic-ischemic encephalopathy (HIE) is suspected in neonates with an acute perinatal event, continued need for ventilation 10 minutes after birth, and abnormal neurologic examination.
- Neonates who have been treated with TH are at increased risk of morbidity, and require close follow-up for developmental delays.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Recognize the effects of intrapartum asphyxiation on multiple organ systems

Suggested Readings
- Gillam-Krakauer M, Carter BS. Neonatal hypoxia and seizures. *Pediatr Rev.* 2012;33:387. doi: http://dx.doi.org/10.1542/pir.33-9-387.
- Perlman JM. Summary proceedings from the Neurology Group on hypoxic-ischemic encephalopathy. *Pediatrics*. 2006;117:S28. doi: http://dx.doi.org/10.1542/peds.2005-0620E.

Question 112

A 16-year-old Hispanic girl is brought to your office for a 3-day history of thick white vaginal discharge associated with pruritus. She was treated for vaginal candidiasis 1 month ago with oral fluconazole and feels that the symptoms have returned. She is not sexually active. You note that she has lost 2 kg since you saw her 1 month ago. Her medical history is unremarkable and she takes no medication. Physical examination reveals a temperature of 37°C, blood pressure of 138/90 mm Hg, heart rate of 104 beats/min, weight of 98 kg (>95th percentile), height of 167 cm (75th percentile), and body mass index of 35 kg/m2 (>95th percentile). She has acanthosis nigricans over the nape of her neck and in her groin area. Genital examination shows erythema of the labia and vaginal opening, and thick, white vaginal discharge. The remainder of the examination findings are normal. You perform a potassium hydroxide smear of the vaginal discharge, which demonstrates hyphae. You plan to treat her again with fluconazole.

Of the following, the BEST additional test to order is a(n)

 A. complete blood cell count
 B. fasting glucose level
 C. fasting insulin level
 D. human immunodeficiency virus antibody test
 E. immunoglobulin levels

Correct Answer: B

The girl described in the vignette has metabolic syndrome and is at risk for type 2 diabetes. Her recurrent vaginal candidiasis and weight loss are most likely symptoms of diabetes. Thus, a fasting plasma glucose level is indicated to screen for this condition.

Although the girl's obesity and acanthosis nigricans are consistent with insulin resistance, a fasting insulin level would not be particularly informative in this situation. A complete blood cell count, human immunodeficiency virus antibody test, and immunoglobulin levels may be indicated in the workup for recurrent infections. However, for the girl in the vignette, these are not the best additional tests to order, because diabetes is the most likely diagnosis based on her history and physical examination findings.

Metabolic syndrome is a constellation of risk factors for cardiovascular disease and type 2 diabetes. The components of metabolic syndrome exhibited by this girl include obesity, high blood pressure, and evidence of insulin resistance (acanthosis nigricans). Polycystic ovary syndrome and dyslipidemia can also be associated with insulin resistance. The pathogenesis of type 2 diabetes includes both insulin resistance and relative pancreatic ß-cell failure.
Options for screening for diabetes include obtaining a:
1. fasting plasma glucose level (≥125 mg/dL [6.9 mmol/L] is diagnostic)
2. 2-hour plasma glucose level during a 75-g oral glucose tolerance test (≥200 mg/dL [11.1 mmol/L] is diagnostic)

OR
1. hemoglobin A1c level (≥6.5% is diagnostic)

A random plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher with classic symptoms of diabetes is also diagnostic. Unless there is unequivocal hyperglycemia, testing should be repeated on a different day before the diagnosis of diabetes is made. A 2-hour plasma glucose level after a 75-g oral glucose load is the most sensitive screening method; however, the fasting plasma glucose and hemoglobin A1c levels are easier to obtain. It is important to note that the hemoglobin A1c diagnostic level of more than or equal to 6.5% has been confirmed for adults, but it remains unclear if the same diagnostic level should be used for adolescents.

PREP Pearls
- Consider diabetes in the setting of recurrent vaginal candidiasis, especially when other risk factors are present.
- Screening tests for diabetes include a fasting plasma glucose (≥125 mg/dL [6.9 mmol/L] is diagnostic), 2-hour plasma glucose during a 75-g oral glucose tolerance test (≥200 mg/dL [11.1 mmol/L] is diagnostic), or hemoglobin A1c (≥6.5% is diagnostic).
- Acanthosis nigricans is a marker of insulin resistance. Obesity, polycystic ovary syndrome, hypertension, and dyslipidemia can also be associated with insulin resistance.

ABP Content Specifications(s)
- Recognize the clinical features associated with insulin resistance
- Plan an appropriate screening evaluation for a patient in whom type 2 diabetes is suspected

Suggested Readings
- American Diabetes Association. Standards of medical care in diabetes: 2, classification and diagnosis of diabetes. *Diabetes Care.* 2017;40(suppl 1):S11-S24.
- Dileepan K, Feldt MM. Type 2 diabetes mellitus in children and adolescents. *Pediatr Rev.* 2013;34(12):541-8. doi: http://dx.doi.org/10.1542/pir.34-12-541.
- Wittcopp C, Conroy R. Metabolic syndrome in children and adolescents. *Pediatr Rev.* 2016;37(5):193-202. doi: http://dx.doi.org/10.1542/pir.2014-0095.

Question 113

A 15-year-old boy is brought to your office for behavioral concerns. His parents report that they have been struggling with their son's lack of respect toward adults and his disregard for household rules. He frequently returns home after curfew and his parents are concerned that he may be involved with a gang. The adolescent has been referred to his school's attendance review board for skipping multiple days of school and has been in trouble for vandalism of school property. He often intimidates his siblings and children in their neighborhood. The boy's parents are worried that their son will turn out like his uncle, who has been incarcerated and has "anger management" issues.

Of the following, the BEST next management step for this boy's behavior is to

 A. prescribe a mood stabilizer
 B. prescribe an atypical antipsychotic
 C. recommend a family and community-based treatment program
 D. recommend a wilderness camp or boot camp
 E. recommend participation in a Scared Straight program

Correct Answer: C

The adolescent in this vignette is demonstrating several antisocial behaviors—defiance, rule-breaking, vandalism, and aggression. Of the options provided, participation in a family and community-based treatment program would be the best next step in addressing this boy's behaviors.

Delinquent behaviors may be seen before 10 years of age, may increase between ages 10 and 16 years, and may decrease in late adolescence and early adulthood. Children with significant noncompliant, defiant, and argumentative behaviors may meet the criteria for oppositional defiant disorder. As they enter adolescence, those with persistent violation of major societal rules and the rights of others (eg, aggression toward others, property destruction, fire-setting, deceit, theft) may meet the criteria for conduct disorder.

Most adolescents report participation in at least 1 delinquent act. Studies demonstrate that 6% to 8% of juvenile offenders commit 50% to 70% of all juvenile crimes. Compared with girls, boys are more likely to be arrested, have had multiple arrests, and have committed more serious offenses. Risk factors for antisocial behavior include low socioeconomic status, history of abuse, exposure to violence, parental substance abuse, and parents with antisocial behaviors. Disturbed peer relationships is another important factor. Gang involvement is particularly associated with both nonviolent and violent offenses. Chronic offenders are more likely to have had aggressive behaviors, associations with antisocial peers, and poor school commitment. Youth with callous-unemotional traits (limited guilt, remorse, and empathy) have a poorer prognosis and are more difficult to treat. Common comorbidities include school problems, substance use, attention-deficit/hyperactivity disorder (ADHD), and mental health problems such as depression.

When evaluating the child or adolescent with antisocial behaviors, information should be gathered from multiple sources. Parents and other adults (eg, teachers) should be asked about the frequency, severity, and persistence of the disruptive behaviors. The specifics of the behavior (eg, type of aggression, target of aggression), triggers for the behavior, adult responses to the behaviors, and impact on functioning should be determined. Risk factors, psychosocial stressors, substance use, and family psychiatric history should be identified. Teachers can provide information on the child or adolescent's school behaviors and academic performance. In addition, the child or adolescent should be interviewed regarding their view of their behaviors and circumstances. Assessments should be performed for coexisting conditions such as ADHD, oppositional defiant disorder, conduct disorder, anxiety, depression, and learning disabilities. Standardized rating scales (eg, Child Behavior Checklist, Behavior Assessment System for Children, Youth Self-Report, Conners 3) may be helpful.

Evidence-based psychosocial interventions are the recommended first-line treatment for juvenile delinquency. Individual therapy for the child can include skill building in problem-solving, anger management, social interactions, and emotional regulation via cognitive-behavioral techniques. These techniques can also be used to decrease aggressive reactions to perceived threats for those with anxiety. Parent or caregiver training on behavior modification, parent-child interactions, communication, and supervision of the child should be included, as appropriate, in the treatment

plan. School-based programs may teach conflict resolution to the child and parenting skills to the caregivers. Multimodal treatments are particularly successful. Multisystemic therapy, an effective intervention that is family- and community-based, uses cognitive behavioral therapy, family therapy, and behavior management training to address factors in the home, school, and neighborhood. When antisocial behaviors occur in the setting of a diagnosed condition, treatment of that condition may help decrease aggressive and disruptive behaviors. When there is significant safety concern, involvement with law enforcement, or other severe consequences, a referral should be made to a mental health professional.

Psychopharmacologic treatment is not the primary treatment for delinquent behaviors. However, medications, such as stimulants or alpha-agonists for those with ADHD or selective serotonin reuptake inhibitors to treat anxiety, may be considered for treatment of identified coexisting disorders. Although psychiatrists may consider use of antipsychotic medications or mood stabilizers to manage severe behaviors, evidence supporting their use for the treatment of delinquent behaviors is limited. Research has shown wilderness camps and boot camps to be ineffective in addressing delinquency and group treatment with other troubled children to be detrimental. Furthermore, skills learned outside of his typical environment may not generalize when the child returns home. The Scared Straight program attempts to prevent criminal behavior through in-person visits to prisons and interactions with inmates; research has found this intervention ineffective and possibly harmful.

Pediatricians can help address the problem of antisocial behaviors by counseling parents on behavioral management strategies and connecting families with evidence-based psychosocial treatments.

PREP Pearls
- Delinquent behaviors may be seen before age 10 years, may increase between ages 10 and 16 years, and may decrease in late adolescence and early adulthood.
- Evidence-based psychosocial interventions (eg, cognitive behavioral therapy, behavior management training) are the first-line treatment for juvenile delinquency.
- Research has shown that wilderness camps, boot camps, and the Scared Straight program are ineffective in addressing delinquency.

ABP Content Specifications(s)
- Plan the appropriate management of antisocial behavior/delinquency
- Plan the appropriate evaluation of antisocial behavior/delinquency

Suggested Readings
- Blair RJ, Leibenluft E, Pine DS. Conduct disorder and callous-unemotional traits in youth. *N Engl J Med.* 2014;371(23):2207–2216. doi: http://dx.doi.org/10.1056/NEJMra1315612.
- Hawkins JD, Smith BH, Catalano RF. Delinquent behavior. *Pediatr Rev.* 2002;23(11):387–391.
- Zart DM, Keizer-Lange MD. Aggressive behavior in children and adolescents. *Pediatr Rev.* 2011;32(8):325–331.

Question 114

A mother brings her 14-year-old son with moderate intellectual disability to your office for a routine health supervision visit. He has a large head, long face, prominent jaw, large ears, and macroorchidism. The family history is notable for a mother with mild learning disability, a maternal uncle with moderate intellectual disability and similar facies, along with the patient's 3-year-old brother who has signs of global developmental delay. The mother inquires about a potential genetic cause.

Of the following, the testing that will MOST likely confirm the diagnosis for this patient is

 A. ammonia level
 B. chromosomal microarray
 C. fragile X DNA analysis
 D. serum amino acids
 E. urine organic acids

Correct Answer: C

The patient in this vignette has fragile X syndrome, a common form 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. Diagnosis is confirmed by *FMR1* molecular analysis. Fragile X syndrome is an X-linked, autosomal-dominant, trinucleotide repeat disorder characterized by a phenomenon 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 increasing severity is caused by the expansion of an unstable trinucleotide repeat that is prone to errors during cell division. In fragile X syndrome, an intellectually normal premutation carrier 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. Approximately 25% 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 macroorchidism. In full-mutation individuals, the dysmorphology becomes more evident as the child ages, whereas premutation carriers have normal intellect and appearance. Male premutation carriers (55-200 CGG repeats) have an increased incidence of fragile X–associated tremor/ataxia syndrome, which resembles a Parkinson-like disorder with intention tremor, gait ataxia, and eventual dementia. Female premutation carriers are at risk for primary ovarian insufficiency, with cessation of menses before 40 years of age. The pedigree in this vignette is consistent with an X-linked dominant disorder, with both male and female family members affected, but the male individuals 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 as first-tier testing for all children with intellectual disability. A chromosomal microarray would be recommended for the patient in this vignette; however, the diagnosis based on his pedigree, history, and classic dysmorphology is most consistent with fragile X syndrome. Therefore, *FMR1* molecular analysis would be the best test to confirm this diagnosis.

Chromosomal microarray, now a first-line test, has replaced the standard karyotype and fluorescence in situ hybridization testing for patients with global developmental delay, intellectual disability, and multiple congenital anomalies. There are certain instances where fluorescence in situ hybridization and a karyotype may still be indicated, such as in suspected Down syndrome, 22q11.2 deletion, or Williams syndrome. The higher resolution capabilities of a chromosomal microarray allow it to detect very small microdeletions and microduplications that

would ordinarily be missed on a standard karyotype. Its diagnostic rate is at least twice that of the standard karyotype. However, it cannot detect chromosomal rearrangements, such as balanced and unbalanced translocations, which can be important in the determination of recurrence risk.

It is always important to obtain a detailed medical history, family history including a pedigree of 3 or more generations, and a physical and neurologic examination with specific attention to dysmorphology when deciding on specific genetic testing. For instance, if a child had typical trisomy 21 features, a karyotype and fluorescence in situ hybridization testing may be most appropriate. However, in cases of intellectual disability or multiple anomalies of unknown etiology, a chromosomal microarray would be the initial best test.

Approximately 1% to 5% of patients with intellectual disability have an identifiable metabolic disorder; some of these disorders are treatable and should not be missed. Red flags for a metabolic disorder include recurrent episodes of decompensation, progressive coarsening of features, unusual neurologic findings (eg, ataxia, tremor, dystonia, impairment of extraocular eye movements) or developmental regression. The newborn screening results must be confirmed because many but not all metabolic disorders are detected by this screening. If a metabolic disorder is suspected in association with intellectual disability, the following tests should be considered: serum amino acids, urine organic acids, urine oligosaccharides, urine glycosaminoglycans, purines/pyrimidines, acylcarnitine profile, ammonia level, total homocysteine, and creatine-guanidinoacetate ratio. If first-tier fragile X testing and a chromosomal microarray are normal in association with a pedigree that suggests X-linkage, then an X-linked intellectual disability panel should be considered.

Serum amino acids, ammonia level, and urine organic acids would not be initially recommended in a clinical setting highly suggestive of a fragile X diagnosis. If the child's presenting history was suspect for an inborn error of metabolism, these tests would be indicated.

PREP Pearls
- The American Academy of Pediatrics and the American College of Medical Genetics recommend chromosomal microarray and fragile X testing as first-tier testing for children with intellectual disability.
- Fragile X syndrome is an X-linked dominant condition that results in moderate to severe intellectual disability in male individuals along with a classic dysmorphology. In female individuals, 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.
- Metabolic screening tests should be considered in a patient with intellectual disability and clinical findings suggestive of an inborn error of metabolism.

MOCA-Peds Objective
- Recognize the genetic syndromes that may present as a learning disability

ABP Content Specifications(s)
- Identify common chromosomal causes of intellectual disabilities
- Identify common metabolic causes of intellectual disabilities
- Identify common inheritance patterns of intellectual disabilities

Suggested Readings
- 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 .
- Saul RA, Tarleton JC. FMR1-related disorders. *GeneReviews*. 2017.

Question 115

A 12-year-old boy presents to your office for evaluation after sustaining a puncture wound to his left foot from a rusty nail. Two days ago, while helping his father clean out an old barn, the boy stepped on a rusty nail, which pierced through his tennis shoe and punctured his left forefoot. Within an hour after this injury, he cleansed the wound with tap water and applied a bandage to it. His mother convinced him to come to your office for evaluation today after she noticed that the skin surrounding the wound was becoming red and warm. The patient denies any history of fever.

A review of his chart reveals that he has a history of well-controlled type 1 diabetes, as well as mild intermittent asthma. He receives subcutaneous insulin via an insulin pump, and uses albuterol only occasionally for his asthma symptoms. He has had 4 prior tetanus-containing immunizations; the most recent one was administered when he was 5 years of age.

In your office, the patient is afebrile and appears well. His vital signs are within normal limits for his age. His physical examination findings are significant for a 5-mm puncture wound on the sole of his left forefoot, which is surrounded by an area of erythema that is about 1 cm in diameter. His skin feels warm and is tender to palpation in this area. There is no bleeding from the wound, but the patient reports that he noticed some yellow drainage on the bandage that he changed earlier today. The remainder of his physical examination findings are unremarkable.

You thoroughly irrigate the wound in your office, and debride a small amount of necrotic tissue around the puncture wound.

Of the following, the MOST appropriate care regimen for this patient includes

A. administration of tetanus toxoid, diphtheria toxoid, and acellular pertussis (Tdap) immunization and prescription of oral ciprofloxacin
B. administration of Tdap immunization and tetanus immune globulin (TIG), and prescription of mupirocin topical ointment
C. administration of Tdap immunization and TIG, and prescription of oral ciprofloxacin
D. administration of TIG and prescription of mupirocin topical ointment
E. administration of Tdap adsorbed immunization and prescription of mupirocin topical ointment

<u>**Correct Answer:A**</u>

The boy in the vignette presents with a puncture wound to his left foot after a rusty nail penetrated through his tennis shoe while he was working in an old barn. The erythema surrounding his puncture wound and yellow drainage indicate development of an infection. Because this child's puncture wound occurred through a tennis shoe, he is at risk for infection with *Pseudomonas aeruginosa*. Of the options listed, the most appropriate care regimen for this boy includes administration of tetanus toxoid, diphtheria toxoid, and acellular pertussis (Tdap) immunization and prescription of oral ciprofloxacin.

Pediatric providers need to understand and recognize the sequelae of puncture wounds occurring due to various etiologies. Puncture wounds occur relatively commonly in children, accounting for approximately 3% to 5% of all traumatic injuries presenting to pediatric emergency departments. Although more than half involve the plantar surface of the foot, puncture wounds may also involve the legs, arms, hands, and, less commonly, the torso and head. Glass, metal, wood, and plastic objects may be involved. Puncture wounds can also occur due to mammalian bites, most commonly from dogs and cats. Although most children with puncture wounds have uncomplicated courses, serious complications can arise.

Wound infection, the most common complication of puncture wounds, is more likely to occur in wounds that are deep, with devitalized tissue, and with retained foreign bodies. Other risk factors include wounds affecting the forefoot, wounds involving penetration of the foot through shoes, and the presence of underlying medical disorders compromising immunity (including diabetes mellitus). Puncture wounds caused by bites, especially cat bites, are also quite susceptible to infection. Infection has been reported in 30% to 80% of cat bites, and up to 25% of dog bites. Human bites are also highly prone to wound infection.

The bacterial species most frequently implicated in puncture wound infections include *Staphylococcus aureus,* beta-hemolytic streptococci, and anaerobic bacteria. *Pasteurella multocida* is a common cause of infection in puncture wounds caused by animal bites. For patients sustaining a puncture wound to the foot through the sole of a tennis shoe (like the boy in the vignette), infections caused by *Pseudomonas aeruginosa* may arise.

In addition to infection, complications associated (though less commonly) with puncture wounds include retained foreign bodies, injury to underlying neurovascular structures, and tattooing of the skin from debris (which may result in permanent cosmetic deformity).

A careful history and physical examination are essential to determine the appropriate management of puncture wounds. Physical examination should include a thorough evaluation of the affected area, including assessment of circulatory and motor function distal to the wound. Puncture wounds must be meticulously inspected for retained foreign material and signs of infection. If there is any suspicion for a retained foreign body, diagnostic imaging should be obtained. Most glass and metal objects, as well as animal teeth, can be identified on plain

radiography. Ultrasonography may also be useful in identifying and localizing retained foreign bodies.

Puncture wounds, along with crush injuries, avulsions, burns, and wounds involving necrotic tissue, are prone to tetanus infection (particularly those contaminated with dirt, fecal matter, or saliva); therefore, tetanus immunization status must be determined for all children with puncture wound injuries. When indicated, tetanus-containing immunizations and tetanus immune globulin should be administered as early as possible. A summary of guidelines for tetanus prophylaxis as a component of wound management can be found in **Item C115**.

Item C115. Guidelines for Tetanus Prophylaxis.

History of Adsorbed Tetanus Toxoid (Number of Doses)	Tetanus Prophylaxis Recommended			
	Clean, Minor Wounds		All Other Wounds*	
	DTaP, Tdap, or Td	TIG	DTaP, Tdap, or Td	TIG
< 3 or unknown number	Yes	No	Yes	Yes
≥ 3	No, if <10 years since last dose of tetanus-containing vaccine Yes, if ≥10 years since last dose of tetanus-containing vaccine	No	No, if <5 years since last dose of tetanus-containing vaccine Yes, if ≥5 years since last dose of tetanus-containing vaccine	No

Adapted from Black KD, Cico SJ, and Caglar D. Wound management. *Pediatr Rev*. 2015;36(5):215.

Puncture wounds should be irrigated with profuse amounts of sterile saline, cleansed with an antiseptic solution, and debrided whenever jagged edges or necrotic tissue are present. Foreign

material must be cleaned off the skin to avoid permanent tattooing. Foreign bodies must be removed to help prevent wound infection, reduce pain, and avoid subsequent damage to underlying neurovascular structures.

Prophylactic antibiotic coverage is *not* required for all simple, uninfected puncture wounds, however, there are circumstances when prophylactic antibiotics are indicated. These include (but are not limited to) puncture wounds that are grossly contaminated, those with devitalized tissue, puncture wounds to the feet occurring through the soles of shoes, and many mammalian bite wounds. Patients presenting with wounds that appear infected should be treated with the appropriate antibiotic therapy.

Administration of tetanus immune globulin (TIG) alone or with a prescription of mupirocin topical ointment would not be appropriate for the boy in this vignette. Because he has received more than 3 tetanus-containing immunizations in the past, TIG is not indicated. He has an infected puncture wound that is at risk for infection with *Pseudomonas aeruginosa*, therefore, topical mupirocin would not be an appropriate antibiotic choice.

PREP Pearls
- Infection is more likely to occur in puncture wounds that are deep, wounds with devitalized tissue, wounds with retained foreign bodies, and puncture wounds caused by mammalian bites.
- Other complications associated with puncture wounds include retained foreign bodies, injury to underlying neurovascular structures, and tattooing of the skin from debris (which may result in permanent cosmetic deformity).
- Wound infections associated with puncture wounds to the feet occurring through the sole of a tennis shoe are commonly caused by *Pseudomonas aeruginosa.*

ABP Content Specifications(s)
- Understand the principles of wound cleansing
- Identify the sequelae of puncture wounds of various etiologies

Suggested Readings
- Black KD, Cico SJ, Caglar D. Wound management. *Pediatr Rev.* 2015;36(5):207–216. doi: http://dx.doi.org/10.1542/pir.36-5-207.
- Kimberlin DW, Brady MT, Jackson MA, Long SS, eds; Committee on Infectious Diseases. Tetanus. In: *Red Book Online: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015:773–778.
- Spiro DM, Zonfrillo MR, Meckler GD. Wounds. *Pediatr Rev.* 2010;31:326–331. doi: http://dx.doi.org/10.1542/pir.31-8-326.

Question 116

You are seeing a 16-year-old male wrestler in your office for a sports preparticipation evaluation. The boy asks about diet and exercise practices that could lead to a competitive advantage during the wrestling season. The boy's height is 69 inches and he weighs 175 lb. His body mass index is 25.8 kg/m^2 (91stpercentile). The boy has a very muscular build.

Of the following, the MOST appropriate statement to include in your discussion with this boy is that

A. he is overweight and should begin a gradual weight loss program for improved performance and general health
B. he should attempt to change his body composition with a goal of attaining 5% body fat
C. he should limit acute weight loss by dehydration to less than 3% of his body weight
D. he should limit weight loss to 2% per week if he desires to compete in a lower weight class
E. his elevated body mass index is not a cause for concern given his muscular build

Correct Answer: E

Body mass index (BMI) is calculated as weight (kg)/(height [m]^2). Individuals with BMI values less than the 5th percentile are considered underweight and those with a BMI between the 85th and 94th percentile are considered overweight, and those at or above the 95% percentile are obese. However, BMI calculations do not take body composition into account. An adolescent athlete with high lean muscle mass and low body fat percentage may have an elevated BMI without being at an increased risk for adverse health effects. The boy in the vignette likely falls into this category, given his history of participation in wrestling and muscular build, so his elevated BMI is not a cause for concern.

Wrestling is a weight class sport that emphasizes a lean, muscular physique. Within the wrestling community, there is a strong perception that athletes have a competitive advantage when they compete at the lowest possible weight. Therefore, wrestlers are at increased risk of engaging in unhealthy methods of losing weight and building lean body mass. Unhealthy practices aimed at acute weight loss include decreasing fluid and food intake, increasing sweat production (through exercise or exposure to heat, eg, saunas), increasing urine or stool output (eg, with diuretics or laxatives), use of stimulant medication, spitting, and vomiting. Engaging in these practices can have severe, negative health consequences. While athletes use these methods in the belief that acute weight loss to "make weight" will convey a competitive advantage, in fact, dehydration and even mild hypohydration actually impair performance. When caring for athletes in weight class sports or sports that favor a thin build, pediatricians should ask specifically about unhealthy weight loss practices as well as the use of substances that promote weight loss or changes in body composition.

The National Federation of High School Associations (NFHS) and the National College Athletic Association (NCAA) have implemented rule changes designed to restrict the use of harmful weight loss methods. The NFHS sets the minimum acceptable body fat percentage as 7% (about the 5th percentile for a 16-year-old boy). The boy in the vignette should not be encouraged to decrease his body fat percentage to the 5th percentile. Despite having a BMI above the 85th percentile, the boy should not be encouraged to lose weight, because his weight is probably appropriate given given his muscular build. He should be encouraged to avoid suboptimal hydration, because this could adversely affect both health and sports performance. Athletes with excess body fat who wish to lose weight should be advised regarding healthy diet and exercise plans that lead to no more than 1 lb/week of weight loss in skeletally immature adolescents, and up to 2 lbs/week in individuals who have completed skeletal growth.

PREP Pearls
- Body mass index (BMI) calculations do not take body composition into account. Therefore, an adolescent athlete with high lean muscle mass and low body fat percentage may have an elevated BMI without being at an increased risk of adverse health effects.
- Unhealthy practices aimed at acute weight loss include decreasing fluid and food intake, increasing sweat production (through exercise or exposure to heat, eg, saunas), increasing urine or stool output (eg, with diuretics or laxatives), use of stimulant medication,

spitting, and vomiting. Engaging in these practices can have severe negative health consequences.

ABP Content Specifications(s)
- Recognize inappropriate weight-loss regimens for athletes who participate in sports with weight categories
- Understand the role of fluids in weight control for athletes

Suggested Readings
- Carl R, Johnson, MD, Martin T. American Academy of Pediatrics Council on Sports Medicine and Fitness. Promotion of healthy weight-control practices in young athletes. *Pediatrics*. 2017;140(3):e20171871.
- Wilk B, Yuxiu H, Bar-Or O. Effect of body hypohydration on aerobic performance of boys who exercise in the heat. *Med Sci Sports Exerc*. 2002;34(5 suppl):S48.
- Williams MH, Anderson DE, Rawson ES. *Nutrition for Health, Fitness, & Sport*. 10th ed. New York, NY: McGraw Hill; 2012.

Question 117

A 4-week-old twin infant is brought to your office for a follow-up visit. The patient and his twin sister were born via vaginal delivery at 38 weeks of gestation after an uncomplicated pregnancy. They are the first children for their parents. During the visit, the baby's father expresses concern that the male twin does not make eye contact with his parents like his twin sister. He notes that although both twins will occasionally have eye crossing, his son's eyes seem to wander more often. Both twins will raise their chins off the floor when placed prone. The babies are breastfeeding well and are gaining weight appropriately. Both twins startle to loud noises, and their parents think that both will preferentially calm when they hear their mother's voice.

Of the following, the MOST accurate assessment of the twins' development is

 A. although their progress differs, both twins are developing normally
 B. both twins show evidence of global developmental delay
 C. both twins show evidence of isolated developmental delay
 D. the female twin shows evidence of development that is advanced for her age
 E. the male twin shows evidence of isolated developmental delay

Correct Answer: E

The male twin in this vignette, who has abnormal eye movements and is not making eye contact with his parents, shows evidence of an isolated developmental delay. Developmental skills are classified into the following domains:

- Gross motor (large muscle movements)
- Fine motor (small muscle, mouth, and hand movements)
- Language (receptive and expressive language)
- Cognitive (problem-solving, reasoning, and memory)
- Social-Emotional (attachment and self-regulation)

Children with isolated developmental delay have problems in just 1 of these domains, although atypical development in 1 domain can certainly affect development in other domains. In contrast, children with global developmental delay have atypical development across all domains.

At 1 month of age, typically developing infants have the skills and abilities shown in **Item C117**
More information about milestones can be found in *Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents* published by the American Academy of Pediatrics (https://brightfutures.aap.org/materials-and-tools/guidelines-and-pocket-guide/Pages/default.aspx).

Item C117. Typical Developmental Milestones at Age 1 Month.

Gross Motor	Fine Motor	Self-Help	Problem Solving	Social/ Emotional	Receptive Language	Expressive Language
• Chin up in prone position • Turns head in supine position	• Hands fisted near face	• Sucks well	• Gazes at black-white objects • Follows face	• Discriminates mother's voice • Cries out of distress	• Startles to voice/ sound	• Throaty noises

Adapted and reprinted with permission from Scharf, RJ, Scharf, GJ, Stroustrup, A. Developmental Milestones. *Pediatr Rev.* 2016;37(1), 25.

The boy in this vignette is not making eye contact with his parents and has disconjugate gaze, but he demonstrates normal gross motor, self-help, social-emotional, and receptive language skills. These findings raise concern for an isolated delay in the problem-solving or cognitive domain, and more specifically, are concerning for problems within his visual pathway. His twin sister, in contrast, shows typical development across all domains.

PREP Pearls

- Children with global developmental delay have atypical development across domains (gross motor, fine motor, language, cognitive, and social-emotional). Children with isolated developmental delay have atypical development in just 1 domain.
- A typically developing 4-week-old infant lifts her chin when prone, holds her hands fisted near her mouth, sucks well, makes eye contact, follows a face with her eyes, recognizes her mother's voice, startles to voice or loud sound, and cries when in distress.

ABP Content Specifications(s)
- Distinguish between isolated, global, and atypical developmental delay
- Evaluate the developmental progress/status of a neonate through the first four weeks after birth

Suggested Readings
- Scharf RJ, Scharf GJ, Stroustrup A. Developmental milestones. *Pediatr Rev*. 2016;37(1):25–37. doi: http://dx.doi.org/10.1542/pir.2014-0103.

Question 118

A 9-year-old girl is brought to your office for evaluation of increased urination for the last 3 months. She has been using the bathroom more frequently. She had daytime accidents last week and has been having nighttime accidents for the last month. According to her mother, the patient attained bladder and bowel control by 4 years of age. The patient has reported headaches for 4 months, and the headaches have increased in severity for the last 2 weeks. There is no history of encopresis. She has a temperature of 37.7°C, heart rate of 80 beats/min, respiratory rate of 16 breaths/min, and blood pressure of 96/46 mm Hg. She has normal neurological examination results and growth parameters. Her fundus could not be visualized.

Of the following, the test MOST likely to explain the cause of the patient's urinary symptoms is

A. cystourethrography
B. renal ultrasonography
C. serum creatinine
D. urine culture
E. urine osmolality

Correct Answer: E

Polyuria is characterized by an increased total urine volume resulting from an underlying defect in water balance. Children with 24-hour urine output greater than 2 L/m^2 have polyuria. A functional definition for polyuria is an inappropriately high urine output compared to circulatory volume and serum osmolarity (increased total urine volume caused by an underlying defect in water balance in patients with hypernatremic dehydration).

Polyuria presents with the excretion of large volumes of dilute urine, as seen in patients with chronic kidney disease (CKD), diabetes mellitus (osmotic diuresis), diabetes insipidus (DI) (antidiuretic hormone disorders), and psychogenic polydipsia (**Item C118**). Enuresis is diagnosed in children aged 5 years or older who void in bed or on clothes twice or more per week for 3 consecutive months. Primary enuresis occurs in children with no period of sustained dryness. Secondary enuresis is identified in children with a period of sustained dryness for 6 months (for nocturnal enuresis) or 3 months (for diurnal enuresis).

Item C118. Differential Diagnosis of Polyuria in Childhood.

Neurogenic Vasopressin Deficiency
- Familial
- Idiopathic
- Congenital malformations (septo-optic dysplasia, holoprosencephaly, encephalocele)
- Acquired
  – Head trauma
  – Vascular event (thrombosis or hemorrhage)
  – Postinfection (meningitis, encephalitis, congenital cytomegalovirus, toxoplasmosis)
  – Tumor (craniopharyngioma, germinoma, optic glioma)
  – Systemic infiltrative diseases (histiocytosis, syphilis, tuberculosis, sarcoidosis
  – Inflammatory (lymphocytic hypophysitis)
  – Guillain-Barré syndrome
  – Autoimmune disorders

Renal Vasopressin Insensitivity
- Familial nephrogenic diabetes insipidus
  – V2 receptor gene defect (X-linked)
  – Aquaporin-2 gene defect (autosomal recessive)
- Acquired
  – Postobstructive
  – Drug-induced (lithium, amphotericin B)
  – Associated with systemic disease (sickle cell disease, sarcoidosis, amyloidosis)
  – Metabolic (hypercalcemia, hypokalemia)

Other Renal Disorders
- Renal tubular defects
  – cystinosis
  – distal renal tubular acidosis
  – Bartter syndrome
  – renal Fanconi syndrome
  – ARC [arthrogryposis, renal tubular dysfunction, and cholestasis] syndrome
- Nephronophthisis

Excessive Fluid Intake
- Primary polydipsia
- Water intoxication

Osmotic Diuresis
- Diet-induced
- Drug-induced
- Diabetes mellitus (type 1 or 2)

Recent onset of secondary enuresis (nighttime and daytime) and increased urinary frequency in the patient in this vignette suggests increased urinary volume needing further evaluation. Children with polyuria may have nocturia or enuresis; however, symptoms of urinary frequency, nocturia, or enuresis may not be associated with increased urinary volume (or polyuria). Therefore, to confirm an underlying defect in water balance, urine osmolality should be measured. A low urine osmolality (< 250 mOsm/kg) would indicate renal losses of hypotonic fluid as seen in CKD, diabetes mellitus (osmotic diuresis), DI (antidiuretic hormone disorders), and diuretic therapy.

Diabetes insipidus occurs secondary to decreased secretion of antidiuretic hormone (central DI) or secondary to renal resistance to antidiuretic hormone effects (nephrogenic DI). Patients with DI exhibit polyuria, polydipsia, and increased thirst. They may exhibit varying degrees of dehydration, and laboratory evaluation usually reveals hypernatremia in association with dilute urine (urine osmolality < plasma osmolality). Central DI is characterized by decreased antidiuretic hormone secretion and can be idiopathic (most common) or secondary to central nervous system tumors, infiltrative lesions (histiocytosis), and trauma (surgical or nonsurgical). Recent onset of headaches and increased frequency of headaches suggest an underlying central nervous system tumor or infiltrative lesion as the most likely cause of the polyuria in the child in this vignette.

Nephrogenic DI in children is secondary to a mutation in either the antidiuretic hormone receptor, arginine vasopressin receptor 2, or the aquaporin 2 channel. The arginine vasopressin receptor 2 mutations have an X-linked inheritance and account for 90% of cases; male individuals are more severely affected than female individuals. Neonates and infants with nephrogenic DI exhibit irritability, failure to thrive, a preference for water, and clinical findings of dehydration. These patients may be brought to the emergency department for evaluation of recurrent episodes of hypernatremic dehydration.

Congenital anomalies of the kidney and urinary tract and cystic kidney diseases (nonglomerular CKD) account for nearly 60% of pediatric CKD. Neonates with renal dysplasia/congenital anomalies of the kidney and urinary tract are identified by prenatal ultrasonography. Abnormalities noted on renal ultrasonography can include hydronephrosis (unilateral versus bilateral), increased echogenicity of renal parenchyma, renal size abnormalities (small or enlarged), cysts, and bladder abnormalities. Tubulointerstitial injury associated with congenital anomalies of the kidney and urinary tract leads to reduced urinary concentration (acquired nephrogenic DI), and these patients usually exhibit polyuria with or without enuresis. Proteinuria can occur in patients with underlying glomerular disease, tubulointerstitial injury, or both. It is important to note that persistent proteinuria may be the only indication of renal disease in asymptomatic patients. Persistent proteinuria on urinalysis or a urine protein to creatinine ratio higher than 0.2 on a first-morning sample is considered abnormal.

Children with CKD usually have poor growth as a manifestation of decreased renal function. Reduced renal erythropoietin production with CKD leads to anemia. The anemia is normocytic and normochromic consistent with anemia of chronic disease; however, these patient are at

increased risk for iron- and vitamin B_{12}–deficient anemia because of the poor nutritional status associated with advanced stages of CKD. Urinary osmolality is low (< 250 mOsm/kg) in patients with advanced CKD. However, for the patient in this vignette, absence of growth retardation, absence of pallor, and a normal blood pressure make CKD a less likely cause of the symptoms as compared to DI. Further evaluation in patients suspected of having CKD would include urine analysis, serum chemistry (creatinine, serum electrolytes, complete blood count with iron profile, and lipid profile) and ultrasonography of the kidneys.

The serum creatinine level and the subsequently calculated glomerular filtration rate (GFR) are measures of kidney function and indicative of the stage of kidney disease in a patient with CKD. The GFR is indicative of the number of functioning nephrons; however, GFR is not a good indicator of loss of functioning nephrons as seen in CKD because of the compensatory increased function in the remaining nephrons. Therefore, a patient with half the number of functioning nephrons may have a normal GFR because of the compensatory hyperfiltration in the functioning nephrons. As the GFR decreases with progressive glomerular injury, the rise in the serum creatinine level is also counteracted by increased tubular secretion of endogenous creatinine, leading to no or minimal increase in the serum creatinine level. In the girl in this vignette, in the absence of any other signs of CKD, the serum creatinine level is more likely to be normal and therefore unhelpful in explaining the cause of her symptoms. Renal ultrasonography will not establish renal losses as the underlying cause of the patient's symptoms.

In the patient in this vignette, urinary tract infection is unlikely in the absence of fever or urinary symptoms such as dysuria, flank pain, or burning micturition. Urine culture and cystourethrography are thus not indicated.

PREP Pearls
- Children with polyuria may have nocturia or enuresis; however, the symptoms of frequency, nocturia, or enuresis may not be associated with increased urinary volume (or polyuria).
- A low urine osmolality (< 250 mOsm/kg) would indicate excess renal losses of hypotonic fluid leading to polyuria.
- Patients with polyuria excrete large volumes of dilute urine (low urine osmolality), as seen in chronic kidney disease, diabetes mellitus (osmotic diuresis), diabetes insipidus (antidiuretic hormone disorders), and psychogenic polydipsia.

MOCA-Peds Objective
- Evaluate a child with secondary enuresis

ABP Content Specifications(s)
- Recognize the clinical and laboratory findings associated with daytime and nocturnal urinary incontinence in male and female patients
- Plan the appropriate diagnostic evaluation and management of incontinence

Suggested Readings

- Miller RS, Libber SM, Plotnick L. Polyuria. 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; 2017:1528–1533.
- Saborio P, Tipton GA, Chan JC. Diabetes insipidus. Pediatr Rev. 2000;21(4):122–129. doi: http://dx.doi.org/10.1542/pir.21-4-122.

Question 119

You are evaluating an 18-year-old young man who has a 1-week history of a painless "sore" on his penis. He has no dysuria, urethral discharge, or fever. The patient reports 3 lifetime sexual partners who were men and that he uses condoms inconsistently. He practices insertive anal intercourse. Physical examination is remarkable only for a 5-mm ulcer on the shaft of the penis (Item Q119). The lesion has an indurated border but is not painful to palpation. There is no inguinal lymphadenopathy.

**Item Q119:** Lesion for the patient described in the vignette.
Courtesy of Fiumara, NJ and the Public Health Image Library, Centers for Disease Control and Prevention.

Of the following, the test that is considered DEFINITIVE for diagnosis is

 A. bacterial culture
 B. dark-field examination
 C. Gram stain
 D. rapid plasma reagin test
 E. VDRL test

Correct Answer: B

The patient described in the vignette has a painless ulcer with an indurated border located on the penile shaft. These findings favor the diagnosis of primary syphilis. Herpes simplex virus infection, chancroid, or nonsexually transmitted infections (eg, Epstein-Barr virus infection) all typically produce painful ulcers. The test that provides a definitive diagnosis of syphilis is dark-field microscopic examination of transudate from the ulcer demonstrating *Treponema pallidum* spirochetes (**Item C119**). Bacterial culture and Gram stain are not useful in diagnosing syphilis. Because dark-field microscopy is not widely available, a presumptive diagnosis often is made using 1 of 2 types of assays: nontreponemal tests, such as the rapid plasma reagin (RPR) or VDRL tests, and treponemal tests, such as fluorescent treponemal antibody absorbed (FTA-ABS), *T pallidum* passive particle agglutination (TP-PA), and others.
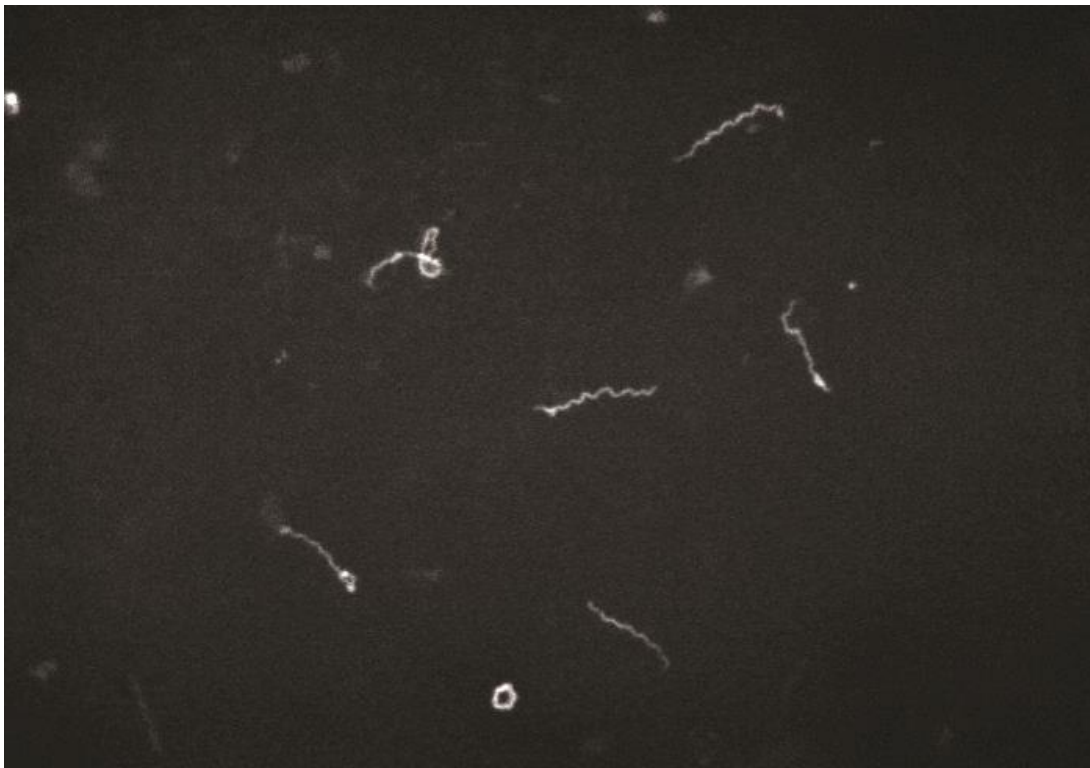
Item C119: *Treponema pallidum* spirochetes seen on darkfield microscopy.
Courtesy of the Public Health Image Library, Centers for Disease Control and Prevention, and Dr. WF. Schwartz

Nontreponemal tests are used to both screen for syphilis and monitor response to treatment. The sensitivity of these tests depends on the duration of infection. When an ulcer is present, the test will be positive in 25% of patients; at 2 weeks, 3 weeks, and 4 weeks after infection, the positivity rates rise to 50%, 75%, and 100%, respectively. As many as 40% of positive nontreponemal tests are false positive, which may be caused by infections (including human immunodeficiency virus), autoimmune disease, pregnancy, injection drug use, or older age. For

this reason, a positive nontreponemal test result should be confirmed by performing a treponemal test.

In the year 2000, syphilis was on the verge of elimination in the United States, with the number of cases being the lowest since reporting began in 1941. Since then, the rate has increased 3-fold, reaching 6.3 cases/100,000 population in 2014. The rise is primarily in the number of cases among men who have sex with men, especially those who are 20 to 29 years of age, reside in the West and South, and are black. However, increases were observed in every age subgroup between 15 and 44 years, and in nearly every race/ethnic group. Of additional importance is the increased number of cases seen among women, raising concern about the potential for increasing numbers of congenital syphilis cases and the attendant risk of perinatal death.

PREP Pearls
- A painless genital ulcer with an indurated border should prompt consideration of primary syphilis.
- Although dark-field examination provides a definitive diagnosis of primary syphilis, due to availability, in most settings, a presumptive diagnosis will be made using a nontreponemal test; positive results should be confirmed with a treponemal test.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation when Treponema pallidum infection is suspected
- Understand the epidemiology of Treponema pallidum

Suggested Readings
- Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2014. Atlanta, GA: US Department of Health and Human Services; 2015. http://www.cdc.gov/std/stats14/syphilis.htm.
- Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64(No. RR-3):1–137.
- Fortenbery JD. Syphilis. In: Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.
- Patton ME, Su JR, Nelson R, Weinstock H. Primary and secondary syphilis – United States, 2005-2013. *MMWR Morb Mortal Wkly Rep*. 2014;63:402–406.

Question 120

The mother of a 6-month-old female infant who is a patient in your practice calls for advice. The infant is healthy, aside from a hemangioma for which she is undergoing medical therapy with oral propranolol. In the last few days, she has developed a febrile illness. The infant continues to breastfeed, although she seems to be taking in less volume. The mother asks about the appropriateness of continuing the propranolol during this illness.

Of the following, you explain to the mother that the MOST likely adverse effect of propranolol is

A. hypoglycemia
B. hypokalemia
C. hypothermia
D. prolonged duration of febrile illness
E. tachycardia

Correct Answer: A

β-Blockers are used in pediatrics in the context of hypertension, tachyarrhythmias, and hemangiomas as well as other less common indications. β-Blockers have been less studied in children than in adults, but they are known to have a unique side effect profile in children as compared to adults. Knowledge of the side effect profile of β-blockers comes mostly from case reports and retrospective analyses. β-Blockers have side effects of bradycardia, hypotension, hypoglycemia, hypoglycemia-induced seizures, and hyperkalemia. Additionally, β-blockers can exacerbate bronchospasm and should be used with caution in children with asthma. β-Blockers are not associated with hypokalemia, hypothermia, or prolongation of febrile illness.

There have been no reports of asymptomatic hypoglycemia with the use of routine screening. A dose-dependent relationship regarding hypoglycemia has also not been demonstrated in children. Children on corticosteroids and preterm infants are at higher risk of hypoglycemia with β-blockers. β-Blockers can mask some signs and symptoms of hypoglycemia including tachycardia, anxiety, and hunger. Hypoglycemia-related sweating is not masked by β-blockers. Hypoglycemia associated with β-blockers is more frequent with decreased oral intake, as seen in the infant in this vignette. To minimize hypoglycemia, β-blockers should be administered during the daytime with a feeding shortly thereafter. β-Blockers may need to be discontinued during intercurrent illnesses, but possible discontinuation should be discussed on an individual basis.

PREP Pearls
- β-Blockers are used in pediatrics in the context of hypertension, tachyarrhythmias, and hemangiomas as well as other less common indications.
- β-Blockers have side effects of bradycardia, hypotension, hypoglycemia, hypoglycemia-induced seizures, bronchospasm, and hyperkalemia.

ABP Content Specifications(s)
- Recognize the adverse effects associated with beta-blocking drugs

Suggested Readings
- Bayart CB, Brandling-Bennett HA. Beta-blockers for childhood vascular tumors. *Curr Opin Pediatr.* 2015;27(4):454–459. doi: http://dx.doi.org/10.1097/MOP.0000000000000238.
- Drolet BA, Frommelt PC, Chamlin SL, et al. Initiation and use of propranolol for infantile hemangioma: report of a consensus conference. *Pediatrics*. 2015;131(1):128–140. doi: http://dx.doi.org/10.1542/peds.2012-1691.

Question 121

A 14-month-old girl is brought to the emergency department in February with trouble breathing. She was in good health until 3 days ago when she developed low-grade fever and malaise. Yesterday, she had high fever, runny nose, mild cough, and a significant decrease in activity. The fever has persisted, and today she appears to have difficulty breathing. She has a temperature of 38.6°C, heart rate of 171 beats/min, respiratory rate of 50 breaths/min, blood pressure of 119/68 mm Hg, and oxygen saturation of 87% on room air. She is distressed and has nasal flaring and retractions. Bilateral rhonchi are heard on lung examination. Results of a rapid influenza test and a rapid respiratory syncytial virus test are negative. A chest radiograph shows increased perihilar markings with no focal consolidation.

Of the following, the BEST next step in management of this patient is to test for influenza with a

A. molecular assay and start oseltamivir before result is available
B. molecular assay and start oseltamivir if result is positive
C. rapid assay again and start oseltamivir if result is positive
D. viral culture and start oseltamivir before result is available
E. test for influenza with viral culture and start oseltamivir if result is positive

Correct Answer: A

The best next step in the management of the patient in this vignette is to test for influenza with a molecular assay and start oseltamivir treatment before the result is available.

Influenza virus has marked seasonality. In the United States, the largest number of cases usually occur between January and March, and the highest incidence occurs in school-aged children. Because the case in this vignette occurs in February, influenza infection should be considered. Children who are younger than 2 years or who have underlying chronic medical conditions are at risk of hospitalization and development of complications caused by influenza infection (**Item C121**).

C121. Individuals at High Risk for Complications from Influenza Infection.

- Children aged < 2 years

- Adults aged ≥ 65 years

- Persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), metabolic disorders (including diabetes mellitus), neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, seizure disorders, stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)

- Persons with immunosuppression, including that caused by medications or by human immunodeficiency virus infection

- Women who are pregnant or postpartum (within 2 weeks after delivery)

- Persons aged < 19 y who are receiving long-term aspirin therapy

- American Indian/Alaska Native persons

- Residents of nursing homes and other chronic care facilities

American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2016-2017. *Pediatrics*. 2016; 138 (4): e20162527.

Illness caused by influenza infection typically begins with sudden onset of nonspecific systemic symptoms including fever, malaise, and myalgias. These symptoms are followed by more prominent respiratory symptoms including congestion, rhinorrhea, and cough. Most individuals

recover within 1 week. Syndromes ascribed to influenza infection include croup, bronchiolitis, pneumonia, myositis, and encephalitis.

The sensitivity of molecular assays is quite high, ranging from 86% to 100%. In comparison, the sensitivity of rapid diagnostic assays ranges from 10% to 70%. Thus, as suggested in this vignette, a negative rapid influenza test result does not exclude influenza infection. Repeating the rapid test would not be of value. Although influenza can be cultured, culture results are often not available for 3 to 10 days. However, results from a molecular assay can be available in hours. The child in this vignette warrants treatment because she is younger than 2 years, which puts her at risk for developing complications from influenza infection, and because of the severity of her illness. Treatment for influenza infection should not be deferred until confirmatory test results are available because antiviral therapies are most efficacious when given within 48 hours of symptom onset. However, in individuals with severe or progressive influenza disease, antiviral therapy is recommended even when the duration of illness has been longer than 48 hours.

PREP Pearls
- Illness caused by influenza infection typically begins with sudden onset of nonspecific systemic symptoms including fever, malaise, and myalgias followed by more prominent respiratory symptoms including congestion, rhinorrhea, and cough.
- Children who are younger than 2 years or who have underlying chronic medical conditions are at risk of hospitalization and development of complications caused by influenza infection.
- The sensitivity of molecular assays for diagnosis of influenza is quite high, ranging from 86% to 100%.
- Treatment for influenza infection should not be deferred until confirmatory test results are available because antiviral therapies are most efficacious when given within 48 hours of symptom onset.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of influenza virus infection
- Understand the epidemiology of the influenza virus
- Recognize the clinical features associated with influenza virus infection

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, 2016-2017. *Pediatrics*. 2016;138(4):e20162527. doi: http://dx.doi.org/10.1542/peds.2016-2527.

Question 122

When you enter the room to perform a routine health supervision visit, a female child is sitting comfortably without support on her mother's lap. She exhibits mild anxiety and looks at her mother as you approach. After a few minutes of conversation with the child's mother, you successfully engage the patient in a game of peek-a-boo. The mother reports that her daughter is able to pull to stand and is beginning to cruise along furniture, but she is not standing alone or walking with her hands held. You witness her pick up a small object with a 3-finger grasp (first 2 fingers to thumb) and transfer that object between hands. When she awkwardly drops the object on the floor, she looks for it but does not point to it. As she becomes more comfortable with your presence, she vocalizes with polysyllabic babbling in response to you, and per her mother's report, the girl occasionally says "mama" nonspecifically.

Of the following, these milestones are MOST typical for a normally developing child whose age is

  A. 6 months
  B. 7 months
  C. 9 months
  D. 11 months
  E. 12 months

Correct Answer: C

The child described in this vignette exhibits the cognitive-behavioral and motor milestones typically attained by 9 months of age: sits without support; displays stranger anxiety; engages in back-and-forth play; pulls to stand and cruises along furniture; demonstrates a 3-finger grasp; and speaks with polysyllabic babbling plus nonspecific "mama."

Gross motor skills progress from the 6-month-old milestones of sitting with support and rolling over front-to-back and back-to-front to sitting without support by 9 months of age. At 9 months of age, a child should also be able to get into the sitting position from supine, crawl, and pull to a stand and cruise along furniture. By 11 months of age, children stand alone briefly and walk with hands held. Most 12 month olds are able take a few steps independently.

Social-emotional/behavioral development advances from the 6 month old who begins to show the basic emotions of happiness, sadness, fear, or anger to the 9 month old who exhibits stranger anxiety and attachment to the preferred caregiver. Enjoying back-and-forth play such as peek-a-boo is also typical of a 9 month old. By 11 months, a child will show or offer a toy to an adult, and at 12 months of age protoimperative pointing (pointing to an object to obtain it) emerges along with an awareness of object permanence.

The attainment of fine motor skills is exhibited through the progression of hand skills. The ability to transfer objects from hand to hand is usually present by 6 months of age. The 3-finger grasp or an immature pincer grasp is evident at 9 months of age and is refined to a mature pincer grasp by 12 months.

A 6-month-old child will combine consonant with vowel sounds in babbling, and by 9 months of age the babbling has become more sophisticated with many syllables and intonation. Although a 9 month old may say "mama," the term is not yet used specifically. At 12 months of age, the child's language should include at least one meaningful word in addition to saying "mama" and "dada" specifically.

An excellent table summarizing the normal developmental milestones from 1 month to 6 years of age is found in "Developmental Milestones: Motor Development" by Gerber and colleagues   (*Pediatr Rev.* 2010;31[7]:267-277.)

PREP Pearls
- Most 9-month-old infants will have attained the following milestones: sits without support; displays stranger anxiety; engages in back-and-forth play; pulls to stand and cruises along furniture; demonstrates a 3-finger grasp; and speaks with polysyllabic babbling plus nonspecific "mama."

ABP Content Specifications(s)
- Evaluate the cognitive and behavioral developmental progress/status of an infant at 9 months of age
- Evaluate the motor developmental progress/status of an infant at 9 months of age, including recognition of abnormalities

Suggested Readings
- Feigelman S. The first year. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Elsevier; 2016:65–70.
- Feigelman S. The second year. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier; 2016:70–76.
- Gerber RJ, Wilks T, Erdie-Lalena C. Developmental milestones 3: social-emotional development. *Pediatr Rev.* 2011;32(12):533–536. doi: http://dx.doi.org/10.1542/pir.32-12-533.
- 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.
- 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 123

An 8-year-old boy is brought to your office for an initial visit after moving to the area. He was born by normal vaginal delivery at full term following an uncomplicated pregnancy and was discharged home with his parents after 2 days. He had normal growth and development without any serious illnesses for the first 6 months after birth. Around 6 months of age, he began to experience recurrent episodes of otitis media that have persisted. Despite bilateral tympanostomy tube placement last year, he has continued to experience ear infections. At 18 months of age, he was hospitalized for 10 days for severe pneumonia. He has been treated with antibiotics for 2 other episodes of pneumonia since that time. He has also experienced frequent paronychial infections. His immunizations are up-to-date. He is not currently taking any medications, and he has no known allergies to medications.

He has 2 older sisters who are healthy and have had normal growth and development. Both of his parents are healthy and this is their first marriage. A male first cousin born to a maternal aunt died at 2 years of age from an infection.

The boy's temperature is 38.4oC, heart rate is 102 beats/min, and blood pressure is 96/68 mm Hg. He is at the 5th percentile for weight and the 10th percentile for height. He is thin, but otherwise appears well. His right tympanostomy tube is draining a purulent fluid. His tonsils are very small, and you confirm that he did not undergo a tonsillectomy. There is erythema, swelling, and a purulent discharge at the medial margin of the nail of his right great toe. The remainder of his examination results are unremarkable.

An initial laboratory evaluation reveals:

Laboratory Test	Result
White blood cell count	3,100/µL (3.1 x 10^9/L)
Hemoglobin	11.9 g/dL (119 g/L)
Platelet count	427 x 10^3/µL (427 x 10^9/L)
Neutrophils	60%
Lymphocytes	37%
Monocytes	3%

Of the following, this child's presentation is MOST consistent with

 A. congenital human immunodeficiency virus infection
 B. a humoral primary immunodeficiency
 C. an immunodeficiency secondary to malnutrition
 D. severe combined immunodeficiency
 E. severe congenital neutropenia

Correct Answer: B

The child described in this vignette has a history of multiple invasive bacterial infections that began at 6 months of age. The frequency and severity of the infections strongly suggest an underlying immune deficiency. Primary or congenital immune deficiencies can be caused by defects in the innate or adaptive immune systems. The innate immune system is nonspecific and comprised of physical barrier defenses (skin, hair, mucosal barriers) and cellular defenses (neutrophils, macrophages, natural killer cells). The adaptive immune system is highly specific and is comprised of humoral immunity (B cell–produced antibodies) and cellular immunity (T cells) (**Item C123**).
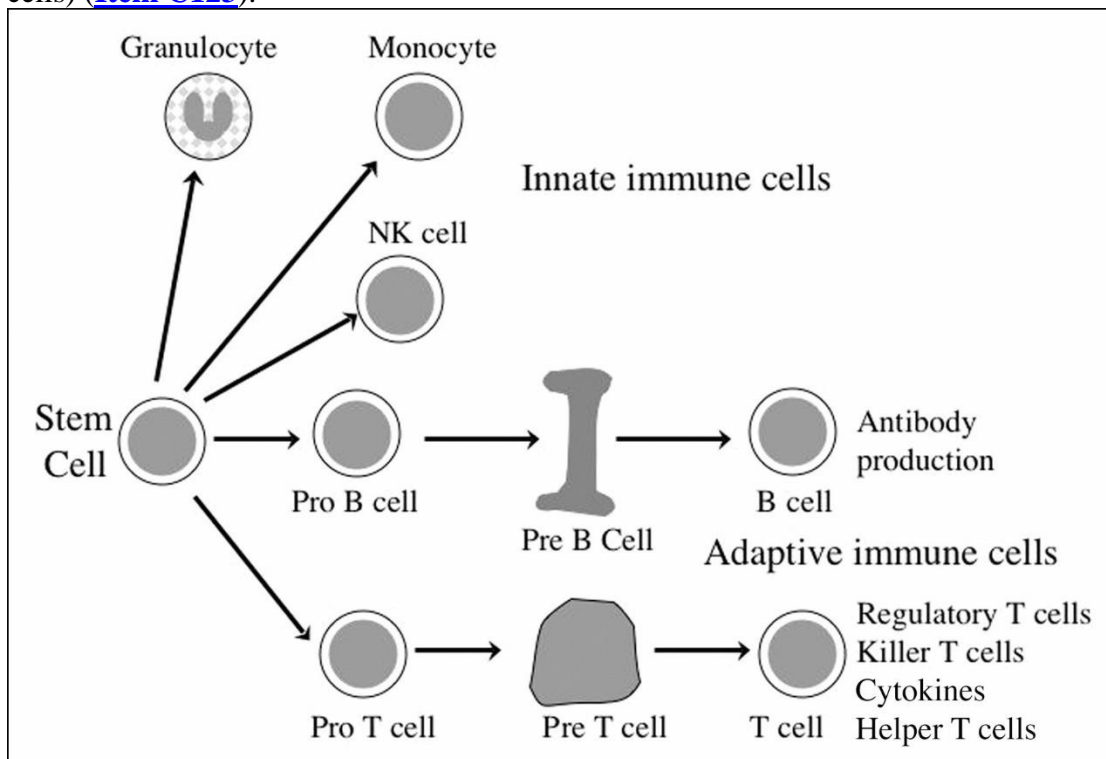
Item C123: Cells involved in the immune response.

Reprinted with permission from Fleisher TA. Back to basics: primary immune deficiencies: windows into the immune system. *Pediatr Rev*. 2006;27(10)363-372.

The constellation of infections starting at 6 months of age, an X-linked inheritance pattern, and small tonsils strongly suggest a diagnosis of hereditary agammaglobulinemia (also known as Bruton or X-linked agammaglobulinemia) for the boy in this vignette. Agammaglobulinemia is a genetic disease caused by mutations in *BTK* (the Bruton tyrosine kinase gene) on the X chromosome that cause a complete defect in B-cell production. As a result, the level of serum antibodies is profoundly reduced. Agammaglobulinemia can be diagnosed through flow cytometric measurement of the B-cell population and the quantitative assessment of serum antibody levels. B cells produce antibodies, which defend against bacterial infections. Newborns are protected from infection through the first few months after birth by maternal serum immunoglobulins passed through the placenta. As the maternal antibodies wane, the risk for infection increases, with infections occurring most commonly in the respiratory tract and skin.

The absence of normal B cells also precludes the formation of normal lymphoid and tonsillar tissues (thus the small tonsils noted for the boy in this vignette). Patients with agammaglobulinemia require intravenous or subcutaneous immunoglobulin replacement for life, unless they undergo a hematopoietic stem cell transplant.

Both human immunodeficiency virus (HIV) and severe combined immunodeficiency result in defects of cellular immunity, specifically T cells. Defects in T-cell function or number increase the risk of all infections but most prominently increase the risk of severe viral infections. Although congenital HIV and severe combined immunodeficiency could present with invasive bacterial infections early in life, congenital HIV would not have an X-linked pattern of inheritance, and neither congenital HIV nor severe combined immunodeficiency would cause small tonsils. The 6-month window of good health in the boy in this vignette also suggests a humoral immune defect rather than a cellular defect. The child's small size likely reflects growth failure secondary to recurrent infections rather than malnutrition as the cause of the immune defi openia.

PREP Pearls
- The innate immune system is comprised of nonspecific barrier defense (skin, hair, mucosal barrier) and cellular defense (neutrophils, macrophages, natural killer cells). The adaptive immune system is comprised of specific humoral immunity (B cells) and cellular immunity (T cells).
- Agammaglobulinemia is an X-linked genetic defect of the adaptive humoral immune system that presents with invasive bacterial infections in the first year after birth.
- Patients with agammaglobulinemia require treatment with replacement immunoglobulin subcutaneously or intravenously every 3 to 4 weeks for life, unless they undergo a hematopoietic stem cell transplant.

MOCA-Peds Objective
- Recognize patterns of opportunistic infection in an immunocompromised host

ABP Content Specifications(s)
- Presenting signs and symptoms of potential immunodeficiency
- Recognize the clinical characteristics of cellular immunodeficiency in the first few months after birth
- Recognize the clinical characteristics of antibody deficiency syndromes after 4 to 6 months of age

Suggested Readings

- Fleisher TA. Back to basics: 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.
- Lipstein EA, Vorono S, Browning MF, et al. Systematic evidence review of newborn screening and treatment of severe combined immunodeficiency. *Pediatrics.* 2010;125(5):e1226–e1235. doi: http://dx.doi.org/10.1542/peds.2009-1567.
- Reust CE. Evaluation of primary immunodeficiency disease in children. *Am Fam Physician.* 2013;87(11):773–778. http://www.aafp.org/afp/2013/0601/p773.html.

Question 124

A 16-year-old patient is brought to your office for a sick visit. She has a 2-day history of cough and fever, and you are concerned about pneumonia. She has a significant medical history of syncope and was recently diagnosed with long QT syndrome.

Of the following, the antibiotic that is MOST likely to worsen her cardiac condition is

A. amoxicillin
B. amoxicillin-clavulanate
C. azithromycin
D. cefazolin
E. penicillin

Correct Answer: C

Of amoxicillin, amoxicillin-clavulanate, azithromycin, cefazolin, and penicillin, only azithromycin will prolong the QT interval and should be avoided in patients with long QT syndrome.

Long QT syndrome is an abnormality of ventricular repolarization and is diagnosed by a prolonged corrected QT interval on electrocardiogram. Patients with long QT syndrome are at risk for ventricular arrhythmias (torsades de pointes) and sudden death. Five molecular genotypes have been described, and all 5 have mutations in ion channels. The disorder can be congenital or acquired. Medications are the most common cause of acquired long QT disorder. Long QT disorder can present with syncope, seizures, ventricular arrhythmias, aborted sudden death, and sudden death. Diagnosis can be difficult. One should obtain an electrocardiogram and correct the QT interval by using the Bazett formula (QTc = QT/[square root of the preceding RR interval]). Several types of T-wave abnormalities can also be present. Genetic testing is available and continues to be developed.

Long QT syndrome should be suspected in patients with a history of unexplained syncope, a family history of unexplained sudden death, unexplained near drowning, or frequent palpitations.

PREP Pearls
- Azithromycin can prolong the QT interval and should be avoided in patients with long QT syndrome.
- Prolonged QT interval can be congenital or acquired. It can cause torsades de pointes and sudden death.
- An electrocardiogram should be obtained and interpreted in the diagnosis of long QT interval.
- Long QT syndrome should be suspected in patients with a history of unexplained syncope or a family history of unexplained sudden death, unexplained near drowning, or frequent palpitations.

ABP Content Specifications(s)
- Understand the clinical significance of a prolonged corrected QT interval

Suggested Readings
- Ackerman M. Consultation with the specialist: the long QT syndrome. *Pediatr Rev.* 1998;19(7):232–238. doi: http://dx.doi.org/10.1542/pir.19-7-232.
- Friedman MJ, Mull CC, Sharieff GQ, Tsarouhas N. Prolonged QT syndrome in children: an uncommon but potentially fatal entity. *J Emerg Med.* 2003;24(2):173–179.
- Woosley RL, Heise CW, Romero KA. QTdrugs list. https://crediblemeds.org/ .

Question 125

A 9-month-old male infant is brought to your office by his parents for a new patient health supervision visit. The infant was diagnosed with bilateral sensorineural hearing loss shortly after birth and now uses hearing aids. His parents have questions about cochlear implants and whether their son would be a good candidate.

Of the following, the MOST accurate statement in response to the parents' questions about their son is that

A. this device will preserve his natural hearing, if any
B. even with good improvement in hearing and speech development with hearing aids, he would be a good candidate for this device
C. hearing assessment in infants is accurate and reliable, making the decision regarding the use of this device a straightforward one in this case
D. his social and educational outcomes would be optimized by implanting this device as early as possible
E. sound quality heard via this device is similar to that heard by people with normal hearing

Correct Answer: D

The most accurate statement in response to the parents' questions about a cochlear implant for their 9-month-old son is that his social and educational outcomes would be optimized by implanting this device as early as possible.

The prevalence of permanent hearing loss among infants in the United States is 1 to 3 per 1,000, and each year, approximately 4,000 US infants are born with bilateral severe to profound sensorineural hearing loss (SNHL). Universal screening for hearing loss is recommended for newborn infants, and in 2011, 97% of US infants completed this screening.

For most infants with bilateral severe to profound SNHL, cochlear implants (CI) placed at approximately 12 months of age are the best way to achieve optimal spoken language skills. However, CIs do not produce normal hearing, and it is important to note that implantation destroys the cochlear nerve, resulting in the loss of any residual hearing. Even with optimal auditory rehabilitation, many children do not achieve language skills equal to hearing peers. Some caregivers may opt to pursue manual communication (ie, sign language) only for a child with hearing impairment; however, many experts suggest that sign language communication combined with therapy to develop spoken language, supported by hearing aids or CI, is preferred because this approach offers more communication options for the child.

Healthy People 2010 goals recommend hearing screening by 1 month of age, audiology evaluation for abnormal results by 3 months of age, and enrollment into intervention services by age 6 months. A hearing-impaired infant's care team should include a primary care provider, audiologist, otolaryngologist, and a speech-language therapist. Hearing aids can be fitted as early as 3 months of age, and is the next step in management for those with confirmed hearing loss. Early intervention developmental services with a qualified speech therapist should commence as early as possible, and no later than 6 months of age.

Speech and language skills should be carefully monitored once hearing aids and speech therapy begin. Assessment of language development in infants younger than 12 months of age can be challenging, and involves specific tests administered by speech therapists using multiple modalities. If an infant meets age-appropriate language milestones, CIs are not indicated. However, most infants with bilateral severe to profound SNHL will not meet those milestones, and CIs would be recommended.

PREP Pearls
- Cochlear implants are a key component of therapy for children with severe to profound sensorineural hearing loss.
- Implantation of cochlear implants by 12 months of age achieves optimal language and educational outcomes; therefore, early identification and referral for evaluation and treatment are particularly important.

ABP Content Specifications(s)
- Understand the commonly used treatment for sensorineural hearing loss in children
- Understand the indications for the use of cochlear implants in children

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.
- Iseli C, Buchman CA. Management of children with severe, severe-profound, and profound sensorineural hearing loss. *Otolaryngol Clin North Am.* 2015;48(6):995–1010. doi: http://dx.doi.org/10.1016/j.otc.2015.06.004.

Question 126

A 7-year-old previously healthy boy is brought to your office for follow-up 1 week after an emergency department visit for a seizure. On the day of the event, he had walked into his parents' bedroom at 6:30 in the morning. He could not speak. They noted that his right cheek and eye were twitching, he was drooling, and his right arm had jerking movements. This lasted for 3 minutes and then stopped spontaneously. He was sleepy afterwards. His parents took him to the emergency department where a head computed tomography scan without contrast was normal. He was observed there for several hours and then discharged. Outpatient electroencephalography result states, "bilateral spikes in the perirolandic regions." The boy has an appointment with a pediatric neurologist in 2 weeks. In your office today, the boy's physical and neurologic examination findings are normal. You discuss seizures and epilepsy with his parents. They ask you if he will need to take anticonvulsants for the rest of his life.

Of the following, the BEST response is that

A. in this epileptic syndrome, anticonvulsants are often not needed
B. in this epileptic syndrome, anticonvulsants are usually required for life
C. in this epileptic syndrome, high-dose corticosteroids are often used as a first-line anticonvulsant
D. magnetic resonance imaging of the brain is needed to determine if anticonvulsants are needed
E. there is no identifiable epileptic syndrome, so it is not certain if anticonvulsants will be required for life

Correct Answer: A

The boy in the vignette has benign rolandic epilepsy (BRE), which is also known as childhood epilepsy with centrotemporal spikes. In this epileptic syndrome, anticonvulsants may not be needed at all, and certainly not for life.

Benign rolandic epilepsy is an epileptic syndrome that occurs in children generally starting at ages 5 to 10 years. The typical seizure is focal with rhythmic twitching of one side of the face and the ipsilateral arm. Drooling is prominent, and the child often cannot speak or has repetitive chewing or swallowing during the seizure. Seizures in BRE most often occur during sleep. In a typically developing child, the clinical presentation of a focal seizure of the face and arm that occurs early in the morning when the child is still asleep and is associated with expressive aphasia and drooling, is clinically suggestive of BRE. Electroencephalography results showing perirolandic (centrotemporal) spikes, either unilaterally or bilaterally, confirm the diagnosis. Magnetic resonance imaging of the brain is not necessary, especially when the electroencephalogram shows bilateral spikes. In cases in which unilateral spikes are seen, brain imaging can be obtained to rule out a structural brain abnormality, but in a typical clinical presentation, this is not always necessary. In BRE, seizures are usually infrequent, occur during sleep, and almost always resolve spontaneously by age 16 to 18 years. Therefore, in many cases, anticonvulsants are not needed. For the minority of children with BRE who have frequent seizures, focal seizures with secondary generalization into generalized tonic-clonic seizures, or seizures while awake, anticonvulsants can be considered. Anticonvulsants used to treat focal seizures in BRE include oxcarbazepine, levetiracetam, carbamazepine, valproate, and others. High-dose steroids are not used to treat this epileptic syndrome.

PREP Pearls
- In benign rolandic epilepsy (BRE), the typical seizure is focal with rhythmic twitching of one side of the face and the ipsilateral arm, with prominent drooling. The child often cannot speak or has repetitive chewing or swallowing during the seizure.
- In BRE, seizures are usually infrequent, occur during sleep, and almost always resolve spontaneously by 16 to 18 years of age. In many cases, anticonvulsants are not needed.

ABP Content Specifications(s)
- Recognize the clinical findings associated with rolandic epilepsy, and manage appropriately

Suggested Readings
- https://www.epilepsydiagnosis.org/syndrome/ects-overview .
- Sidhu R, Velayudam K, Barnes G. Pediatric seizures. *Pediatr Rev*. 2013;34(8):331–341. doi: http://pedsinreview.aappublications.org/content/34/8/333 .

Question 127

You are seeing a 10-year-old boy with a 3-day history of fever, nasal congestion, nonproductive cough, throat pain, and malaise. One day ago, he was evaluated at an urgent care center and was prescribed acetaminophen and a decongestant without any improvement. The boy's family is leaving on vacation soon. The mother is worried about the boy having a sinus infection and his illness getting worse while on vacation. She is requesting an antibiotic prescription. A review of a visit 3 months ago indicated that the boy had received a 14-day course of amoxicillin for a similar illness with complete resolution of symptoms.

The boy appears well and has a temperature of 39°C. He has bilateral yellow nasal discharge and pharyngeal erythema with no exudates. The rest of the physical examination findings are normal. A rapid streptococcal antigen test has negative results.

Of the following, the BEST next step in the management of his illness is

  A. amoxicillin-clavulanate treatment for 21 days
  B. amoxicillin treatment for 14 days
  C. amoxicillin treatment for 21 days
  D. azithromycin treatment for 5 days
  E. reassurance and observation

Correct Answer: E

The most likely cause of the symptoms and signs described for the boy in this vignette is a viral upper respiratory tract infection (URTI). Given the self-limited nature of most viral URTIs, reassurance and observation without the need for an antibiotic prescription despite parental request is the most appropriate next step in the management of this patient with recurrent URTI.

The emergence of global antimicrobial resistance is a major public health concern. In the United States more than 2 million individuals are infected with antimicrobial-resistant bacteria with an estimated 23,000 deaths each year. Antimicrobial-resistant infections are associated with a severe clinical course, longer hospital stays, increased mortality, excess direct health care costs, and increased use of alternative, unconventional agents with higher potential for adverse effects. The overprescription of antimicrobial agents, especially antibiotics in the absence of appropriate indications, is a key factor in the emergence of resistance.

Children with acute respiratory tract infections and other noninfectious respiratory conditions commonly visit primary care offices for evaluation. In the first few years after birth, infants and children will experience an average of 3 to 10 URTIs each year. In a recent study, acute respiratory tract infections accounted for more than 60% of ambulatory visits to primary care offices, and clinicians prescribed antibiotics in more than 20% of these visits. Broad-spectrum antibiotics accounted for 50% of the antibiotics prescribed. Children less than 6 years of age were prescribed broad-spectrum antibiotics more frequently than other age groups. Macrolides, especially azithromycin, were the most frequently prescribed broad-spectrum antibiotic agents; macrolides were often prescribed when no antibiotic therapy was indicated or in place of a narrow-spectrum alternative (eg, amoxicillin).

Adverse consequences of the unnecessary prescription of antibiotics include the continued threat of colonization and spread of antibiotic-resistant bacteria to close contacts, increased care-seeking behavior, excess economic burden, and increased risk of adverse effects.

Parental requests for an antibiotic prescription for self-limited illnesses such as viral URTIs are common, as described in this vignette. Studies have shown that decisions to inappropriately prescribe antibiotics are influenced by concerns of parental satisfaction with the clinic visit and the physician's perception of parent expectations. The uncertainty in diagnosing viral from bacterial URTIs and concerns of potential negative consequences of a missed diagnosis are other challenges that may influence physicians to overprescribe antibiotics.

The American Academy of Pediatrics, Centers for Disease Control and Prevention, and the Infectious Disease Society of America have published evidence-based clinical practice guidelines for the diagnosis and treatment of common outpatient acute respiratory tract infections such as acute otitis media and acute bacterial sinusitis. For example, the diagnosis of acute bacterial sinusitis is clinical, based on 1 of the following 3 findings: persistent symptoms such as nasal discharge or daytime cough for at least 10 days without improvement; ill-appearing child with fever of at least 39°C and associated purulent nasal discharge and facial pain lasting for at least 3 consecutive days; and worsening symptoms or fever after initial improvement. The well-

appearing boy described in this vignette with symptoms and signs of an URTI suggests a viral etiology and does not meet the clinical criteria for the diagnosis of acute bacterial sinusitis needed to warrant antibiotic therapy.

Clinical practice guidelines developed by professional societies are valuable educational tools for clinicians to promote rational antibiotic use and incorporate antibiotic stewardship practices in the ambulatory setting. Studies have shown that clinician education in conjunction with other strategies, such as provider audit and feedback and clinical decision support, can lead to appropriate antimicrobial use in ambulatory settings. Pediatricians must educate parents and patients about antibiotic resistance and implement principles of antimicrobial stewardship in their offices.

PREP Pearls
- The overprescription of antimicrobial agents, especially in the absence of appropriate indications, is a key factor in the emergence of global antimicrobial resistance.
- Unnecessary antibiotic use can lead to colonization and spread of antibiotic-resistant bacteria, excess economic burden, and increased risk of adverse effects.
- Clinical practice guidelines can help promote the rational prescription of antibiotics.
- Pediatricians must educate parents and patients about antibiotic resistance and implement principles of antimicrobial stewardship.

ABP Content Specifications(s)
- Recognize the effects of excessive antibiotic usage on the development of antibiotic resistance in the community
- Understand the diseases for which antibiotic therapy is inappropriate with regard to the development of antimicrobial resistance

Suggested Readings
- Hersh AL, Jackson MA, Hicks LA; Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics*. 2013;132(6):1146–1154. doi: http://dx.doi.org/10.1542/peds.2013-3260.
- Hersh AL, Shapiro DJ, Pavia AT, Shah SS. Antibiotic prescribing in ambulatory pediatrics in the United States. *Pediatrics*. 2011;128(6):1053–1061. doi: http://dx.doi.org/10.1542/peds.2011-1337.
- Wald EL, Applegate KE, Bordley C, et al; American Academy of Pediatrics. Clinical practice guidelines for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. *Pediatrics*. 2013;132(1):e262–e280. doi: http://dx.doi.org/10.1542/peds.2013-1071.

Question 128

A 2-year-old girl is brought to the emergency department after 24 hours of nausea, nonbloody, nonbilious emesis, and nonbloody diarrhea. Her parents report that she has vomited everything they have given her to eat in the past 24 hours.

The girl has a heart rate of 120 beats/min and a respiratory rate of 26 breaths/min, and she is afebrile. She is awake and fussy but consolable. Her abdomen has increased bowel sounds. She has no rashes. Her capillary refill time is 3 seconds.

Laboratory data are shown:

Laboratory Test	Result
Serum	
Sodium	148 mEq/L (148 mmol/L)
Potassium	4.8 mEq/L (4.8 mmol/L)
Carbon dioxide	17 mEq/L (17 mmol/L)
Blood urea nitrogen	29 mg/dL (10.4 mmol/L)
Creatinine	0.6 mg/dL (53 µmol/L)
Glucose	72 mg/dL (4 mmol/L)
Urine	
Specific gravity	1.025

Of the following, the treatment modality recommended for this child is

A. banana, rice, applesauce, toast (BRAT) diet
B. enteral rehydration with lactose-containing product
C. enteral rehydration with oral rehydration solution
D. metoclopramide
E. parenteral hydration

Correct Answer: C

The 2-year-old girl in this vignette has acute viral gastroenteritis with dehydration. Studies have demonstrated improved clinical outcomes with the use of enteral rehydration with oral rehydration solution. Oral rehydration solution takes advantage of the sodium-glucose cotransporter to increase water absorption and improve hydration. Rehydration with oral rehydration solution is associated with decreases in emergency department return visits, hospital admission, and mortality. Enteral hydration via nasogastric tube is preferred to parenteral hydration.

Once hydration is reestablished, early refeeding is recommended to promote mucosal health and gut integrity (including disaccharidase function). Early refeeding is associated with a shorter duration of diarrhea. Studies have not shown an increase in vomiting or diarrhea following early refeeding.

Lactose reduction has shown some benefit in reducing the duration of diarrhea in hospitalized patients; however, there is no data to support lactose reduction in children in the outpatient setting.

The banana, rice, applesauce, toast (BRAT) diet has not been studied and is not currently recommended.

Meta-analysis has shown no benefit for metoclopramide as a treatment for vomiting, and metoclopramide has no role in the treatment of acute viral gastroenteritis.

Intravenous hydration should be reserved for children with shock, altered levels of consciousness, severe acidosis, lack of improvement with enteral hydration, persistent vomiting despite enteral hydration, or significant abdominal distention or ileus.

PREP Pearls
- Oral rehydration solution is the treatment of choice for children with dehydration caused by acute viral gastroenteritis.
- Early refeeding is associated with improved outcomes.
- There is no data to support lactose reduction in the outpatient treatment of acute viral gastroenteritis.
- Intravenous hydration should be reserved for children with shock, altered levels of consciousness, severe acidosis, lack of improvement with enteral hydration, persistent vomiting despite enteral hydration, or significant abdominal distention or ileus.

ABP Content Specifications(s)
- Understand the importance of early refeeding in a child with gastroenteritis
- Plan dietary management for a patient with a gastrointestinal disorder

Suggested Readings
- Freedman SB, Thull-Freedman JD, Rumantir M, Atenafu EG, Stephens D. Emergency department revisits in children with gastroenteritis. *J Pediatr Gastroenterol Nutr.* 2013;57(5):612–618. doi: http://dx.doi.org/10.1097/MPG.0b013e3182a1dd93.
- Guarino A, Ashkenazi S, Gendrel D, et al. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014. *J Pediatr Gastroenterol Nutr.* 2014;59(1):132–152. doi: http://dx.doi.org/10.1097/MPG.0000000000000375.
- Lo Vecchio A, Dias JA, Berkley JA, et al. Comparison of recommendations in clinical practice guidelines for acute gastroenteritis in children. *J Pediatr Gastroenterol Nutr.* 2016;63(2):226–235. doi: http://dx.doi.org/10.1097/MPG.0000000000001133.
- Lo Vecchio A, Vandenplas Y, Benninga M, et al. An international consensus report on a new algorithm for the management of infant diarrhoea. *Acta Paediatr.* 2016;105(8):e384–e389. doi: http://dx.doi.org/10.1111/apa.13432.

Question 129

During his health supervision visit, you ask a 16-year-old boy about tobacco exposure. He reports that he first smoked cigarettes at age 14 years, now smokes about 25 cigarettes daily, with his first cigarette within 30 minutes of awakening. He has been disciplined for smoking on school grounds. He does this because he feels restless and unable to concentrate if he waits until after school to smoke. He states that he would like to quit smoking, but prior attempts to quit "cold turkey" have not worked. He is otherwise well and has normal physical examination findings.

Of the following, in addition to periodic follow-up, the MOST effective management for this adolescent would be to

A. prescribe nicotine gum for acute cravings
B. provide the phone number for the national smokers' quitline
C. provide written materials about smoking cessation
D. recommend transition to the use of electronic cigarettes
E. refer to a mobile phone–based quit program

Correct Answer: E

The adolescent in the vignette has symptoms of moderate nicotine addiction (smoking >20 cigarettes/day, smoking within 30 minutes of awakening, and difficulty refraining from smoking in a forbidden situation). A tobacco cessation plan should be developed with him, especially because the boy is expressing the desire to quit. Of the response choices offered, the most effective management would be referral to a mobile phone–based quit program. The data available on effective approaches to tobacco cessation for children and adolescents are limited.

The United States Preventive Services Task Force (USPSTF) found evidence of a small increase in successful cessation with school- and community-based behavioral counseling programs. Adolescents should be referred to this type of program when available; however, these programs may not be available in all communities. Alternative evidence-based approaches recommended by the USPSTF include mobile phone–based programs and proactive community-wide telephone support combined with patient education materials. Information about mobile phone–based programs can be found at www.aap.org/richmondcenter.

Proactive telephone support programs do not require the teen to make the first contact, but instead reach out to the adolescent (after a referral from health provider or other source) with information, counseling, and support over a period that often extends to months. Quit lines that require the adolescent to initiate contact may be less successful, but they may still be an important resource if other options are not available. Written materials by themselves have proven effective in preventing smoking, but they are not a good stand-alone approach to smoking cessation. USPSTF-recommended approaches to achieving cessation that are not directed at individuals, but rather are community-wide approaches, include increasing the price of tobacco products and mass media campaigns.

Currently, although there are no Food and Drug Administration–approved pharmacotherapy approaches to tobacco use cessation for adolescents and children, the American Academy of Pediatrics lists pharmaceutical treatment as an option for moderately to severely tobacco-dependent adolescents who express a desire to quit tobacco use. Studies of pharmaceutical treatment in this age group have not provided definitive evidence of effectiveness, but many of the studies suffer from short treatment duration and variable response measures.

Three pharmaceutical approaches are currently approved for adults, with similar effectiveness expected in adolescents. Nicotine replacement therapy (NRT) is the most frequently used approach. In the United States, nicotine patches, gum, and lozenges can be purchased over the counter, whereas nasal sprays and inhalers require a prescription. The alternatives to NRT are bupropion and varenicline (nicotine receptor agonist). The approach to treatment should mirror that of treatment for other chronic conditions, with long-acting medications such as nicotine patch or sustained-release bupropion prescribed as "controller" medications and short-acting medications (eg, nicotine gum) used as "rescue" medication. With any of these pharmaceutical treatments, frequent follow-up is necessary to monitor adherence, effectiveness, and side effects. The appropriate duration of treatment is unknown and should be tailored to the individual patient.

In the last decade, the use of e-cigarettes and other nonsmoking nicotine delivery systems have increased in popularity, and some have suggested their use to promote smoking cessation. However, evidence shows no decline in the cigarette smoking rate as the rate of e-cigarette use has increased. Studies have shown an increased likelihood of intention to use cigarettes among e-cigarette users. Some experts have suggested that e-cigarettes serve as a gateway to cigarette smoking and can promote nicotine addiction rather than treat it.

The long-term medical effects of smoking, such as lung cancer and increased cardiovascular related deaths, are well known. There are also many negative effects of tobacco use and exposure that occur during childhood and adolescence. Both prenatal and postnatal tobacco exposure have been associated with significant health effects, including harm to the fetus, increased infant mortality, and increased childhood morbidity. Tobacco use during pregnancy has been associated with orofacial clefts, increased risk of stillbirth, placenta-associated complications, preterm birth and reduced birth weight. Tobacco exposure during childhood increases the risk of asthma, wheezing exacerbations, adverse lung development, severity of bronchiolitis, frequency of pneumonia and cough, middle ear disease, and childhood obesity. The US surgeon general has concluded that evidence suggests a causal relationship between prenatal and postnatal secondhand smoke exposure and childhood cancer. Studies from several countries have detected increased carotid artery atherosclerotic changes in both children and adults who were exposed to tobacco smoking during childhood. Prenatal and postnatal exposure to tobacco may also affect behavior and development. Evidence suggests that exposure to parental, especially maternal, smoking during fetal development may be linked to subsequent disruptive behavior disorders, decreased academic performance, and attention-deficit/hyperactivity disorder. A study using data from the National Health and Nutrition Examination Survey III linked even low serum cotinine levels (a marker for tobacco smoke exposure) with lower scores for reading, math, and visuospatial skills in children.

PREP Pearls
- School and community programs, mobile phone–based programs and proactive phone outreach programs are recommended options for adolescent smoking cessation plans.
- Pharmacotherapy with nicotine replacement therapy, bupropion, or varenicline can be considered for treatment of adolescents with moderate to severe nicotine addiction.
- E-cigarettes are associated with increased rather than decreased tobacco use.
- There are numerous immediate and long-term health consequences of prenatal and postnatal tobacco smoke exposure.

ABP Content Specifications(s)
- Recognize the major behavioral consequences of tobacco use/abuse
- Identify the major physiologic consequences associated with smoking or chewing tobacco
- Plan the appropriate management to attain tobacco cessation

Suggested Readings
- Barrington-Trimis JL, Urman R, Leventhal AM, et al. E-cigarettes, cigarettes and the prevalence of adolescent tobacco use. *Pediatrics*. 2016;138:e20153983. http://pediatrics.aappublications.org/content/138/2/e20153983.
- Farber HJ, Groner J, Walley S, et al. Protecting children from tobacco, nicotine and tobacco smoke. *Pediatrics*. 2015;136:31439–31467. doi: http://dx.doi.org/10.1542/peds.2015-3110.
- Moyer VA. Primary care interventions to prevent tobacco use in children and adolescents: US Preventive Services Task Force recommendation statement. *Pediatrics*. 2013;132:560–565. doi: http://dx.doi.org/10.1542/peds.2013-2079.
- Pbert L, Farber H, Horn K, Lando HA, et al. State-of-the-art office-based interventions to eliminate youth tobacco use: the past decade. *Pediatrics*. 2015;135:734–747. doi: http://dx.doi.org/10.1542/peds.2014-2037.

Question 130

An otherwise healthy 6-year-old girl undergoes a craniotomy for decompression of a Chiari I malformation. Before surgery, she is in her usual state of good health. She does not have any drug allergies. Family history is significant for coronary artery disease and an aunt who suffered an unexpected and unexplained death during a routine surgery. At the beginning of the child's surgery, she is given a dose of intravenous midazolam, followed by propofol, and a dose of succinylcholine to facilitate induction of anesthesia and intubation. As is the surgeon's usual practice during Chiari I decompression, the child is given a dose of dexamethasone to reduce swelling and a prophylactic dose of cefazolin. During the surgery, she develops tachycardia, elevated end-tidal carbon dioxide, and hyperthermia. Vital signs are as follows: temperature, 40.2°C; heart rate, 170 beats/min; respiratory rate, 24 breaths/min (with the ventilator); and blood pressure, 130/80 mm Hg. Oxygen saturation by pulse oximetry is 100% on 40% oxygen through the ventilator. On physical examination, she has mottled skin coloring, warm extremities, and flash capillary refill. The heart is tachycardic with regular rhythm, with a II/VI systolic ejection murmur. She has bounding pulses. Lungs are clear to auscultation bilaterally. Arterial blood gas shows a pH of 7.10, partial pressure of carbon dioxide of 80 mm Hg (10.6 kPa), partial pressure of oxygen of 160 mm Hg (12.2 kPa), calculated bicarbonate level of 12 mEq/L (12 mmol/L), and lactate level of 10 mg/dL (1.1 mmol/L).

Of the following, the agent MOST likely responsible for the girl's deterioration is

  A. cefazolin
  B. dexamethasone
  C. midazolam
  D. propofol
  E. succinylcholine

Correct Answer: E

During surgery, the girl in the vignette had an episode of severe hyperthermia, elevated end-tidal carbon dioxide, tachycardia, and lactic acidosis. She has a family history of an unexplained death during surgery. This scenario is most indicative of malignant hyperthermia (MH). Of the response choices, the most likely causative agent is succinylcholine. The other drugs listed are not associated with MH.

Malignant hyperthermia is a rare, inherited, life-threatening condition caused by a defect in skeletal muscle calcium homeostasis. Under normal conditions, excitation-contraction coupling at the neuromuscular junction causes release of calcium from the sarcoplasmic reticulum, causing muscle contraction from the calcium-dependent cross-linking of myofilaments. Subsequently, calcium reuptake into the sarcoplasmic reticulum occurs. These processes are dependent on the opening and closing of the ryanodine receptor at the sarcoplasmic reticulum. In malignant hyperthermia, prolonged opening of the ryanodine receptor leads to an excess of cytosolic calcium, and thus prolonged muscle contraction. Oxygen consumption is thereby increased, leading to increased anaerobic metabolism, lactic acidosis, hypercarbia, hypoxia, and hyperthermia. A vicious cycle ensues, as the energy depletion in MH prevents calcium reuptake into the sarcoplasmic reticulum, an active, adenosine triphosphate–requiring process.

There are 2 genetic mutations associated with MH, both of which are inherited in an autosomal dominant fashion. Both mutations are in the gene encoding the ryanodine receptor, and lead to a higher predisposition to developing episodes of malignant hyperthermia. Almost all episodes of MH are triggered by a specific agent; volatile inhalational anesthetics such as halothane, isoflurane, and desflurane have been implicated in MH events, in addition to the depolarizing neuromuscular blocking agent succinylcholine. Some inhaled anesthetics such as nitrous oxide and xenon do not trigger MH, nor do other sedative/hypnotics such as propofol, benzodiazepines, or barbiturates. Cefazolin and dexamethasone also do not cause MH.

The incidence, morbidity, and mortality of MH have decreased in recent years, because of the knowledge of inheritance patterns and avoidance of trigger agents. Some causative agents, such as halothane and succinylcholine, are less frequently used than in the past. Use of anesthetics known to be safe in patients with a family history of MH should be planned. Early intraoperative recognition and treatment is important in attaining the best outcome in MH. Potentially causative agents should be discontinued, and dantrolene, a ryanodine receptor antagonist which prevents release of calcium from the sarcoplasmic reticulum, should be administered immediately. Supportive care for hypercarbia, hypoxia, hyperthermia, and acidosis may include ventilator strategies, temperature control, and sodium bicarbonate, as needed.

PREP Pearls
- Malignant hyperthermia (MH) is most often caused by an autosomal dominant inherited mutation in the ryanodine receptor, which regulates myocyte cytosolic calcium.
- MH is triggered by certain inhaled anesthetics such as halothane, isoflurane, and desflurane, and the depolarizing neuromuscular blocking agent succinylcholine.
- In MH, sustained muscle contraction leads to energy failure and increased metabolism. It is managed by discontinuing the triggering agent and administering the ryanodine receptor antagonist dantrolene.

ABP Content Specifications(s)
- Identify the conditions associated with malignant hyperthermia

Suggested Readings
- Larach MG, Gronert GA, Allen GC, Brandom BW, Lehman EB. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498–507. doi: http://dx.doi.org/10.1213/ANE.0b013e3181c6b9b2.
- Schneiderbanger D, Johannsen S, Roewer N, Schuster F. Management of malignant hyperthermia: diagnosis and treatment. *Ther Clin Risk Manag.* 2014;10:355–362. doi: http://dx.doi.org/10.2147/TCRM.S47632.
- Schuster F, Johannsen S, Schneiderbanger D, Roewer N. Evaluation of suspected malignant hyperthermia events during anesthesia. *BMC Anesthesiol.* 2013;13:24. doi: http://dx.doi.org/10.1186/1471-2253-13-24.

Question 131

You are called to the delivery room for the vaginal delivery of a 38-week-gestation neonate with a category 2 fetal monitor tracing. The mother is 27 years old with a history of depression, for which she takes citalopram. The mother was given a dose of morphine 30 minutes before delivery. A liveborn female neonate is delivered with poor tone, poor respiratory effort, and heart rate of 80 beats/min. There is no improvement in the heart rate after warming, drying, and stimulation. After initiating positive pressure ventilation with room air and a pressure of 20 cm H2O, you note minimal chest rise and a heart rate of 64 beats/min.

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

  A. begin chest compressions
  B. increase the fraction of inhaled oxygen to 100%
  C. increase positive pressure ventilation to 40 cm H2O
  D. intubate the neonate with a 3.5 endotracheal tube
  E. place a laryngeal mask for ventilation

Correct Answer: C

For the neonate in the vignette, because the heart rate remains below 100 beats/min with positive pressure ventilation (PPV), the best next step in management is to increase the positive pressure provided to 40 cm H_2O. For most neonates, the initial steps of warming, drying, and stimulating are sufficient to trigger first breaths. However, if the heart rate remains below 100 beats/min after these steps, PPV must be initiated. The initial pressure required to inflate neonatal lungs after delivery can be as high as 40 cm H_2O. Therefore, it is crucial to monitor chest rise as a marker of adequate lung expansion during resuscitation. At this time, it is not clear whether an inspiratory-to-expiratory ratio of 0.3 versus 0.5 is more effective during neonatal resuscitation. Based on the most recent Neonatal Resuscitation Program (NRP) guidelines, if the heart rate is less than 60 beats/min with adequate ventilation, the neonate should undergo endotracheal intubation, and chest compressions should be started. In neonates of more than 34 weeks' gestation, a laryngeal mask may be used in cases of a difficult airway or if ventilation is inadequate.

The optimal level of oxygen exposure for a neonate during resuscitation is not known. Data suggest an increased risk of mortality for neonates resuscitated with 100% fraction of inspired oxygen (FiO_2) compared with those resuscitated with 21% FiO_2. Neonates requiring PPV should have oxygen saturation monitored concurrently with pulse oximetry on the right hand. For neonates requiring chest compressions because their heart rate is less than 60 beats/min, NRP guidelines recommend resuscitation with an FiO_2 of 100%. In all other instances, the FiO_2 should be titrated to maintain oxygen saturation targets adjusted by postnatal age in minutes.

The current American College of Obstetrics and Gynecology nomenclature for describing fetal heart rate tracings is as follows:
- Category 1: Tracings are normal and require expectant management
- Category 2: Tracings are indeterminate and necessitate ongoing surveillance and monitoring
- Category 3: Tracings are not normal and warrant immediate intervention

PREP Pearls
- For neonates requiring resuscitation at birth, the initial steps of warming, drying, and stimulating are typically sufficient to trigger adequate respiration.
- Neonates requiring positive pressure ventilation should have oxygen saturation monitored concurrently with pulse oximetry on the right hand.
- The initial pressure required to inflate the lungs after birth may be as high as 40 mm Hg.

ABP Content Specifications(s)
- Understand the respiratory pattern in newborn infants, recognizing that increased pressure may be required for the first breath

Suggested Readings

- Carlo WA. Delivery room emergencies. In: Kliegman RM, Stanton BF, St Geme J, Schor NF eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016;chap 100:844–848e1.
- Kattwinkel J, Perlman JM, Aziz K, et al. Neonatal resuscitation: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Pediatrics*. 2010; 126(5):e1400–1413. doi: http://dx.doi.org/10.1542/peds.2010-2972E.
- Wyckoff MH, Aziz K, Escobedo MB, et al. Part 13: neonatal resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Pediatrics*. 2015;136:S196. doi: http://dx.doi.org/10.1542/peds.2015-3373G.

Question 132

A 3-year-old boy is brought to the emergency department for evaluation. His parents report that he has had a runny nose and cough for several days. Today, his symptoms rapidly worsened. They note that he has a fever and is breathing quickly. His voice and cry sound unusual to them, and he has been refusing to eat.

On physical examination, his temperature is 40°C, his heart rate is 125 beats/min, his respiratory rate is 45 breaths/min, and his oxygen saturation is 100% on room air. He appears ill. He has inspiratory stridor and subcostal retractions. He is holding his head midline and refuses to flex, extend, or rotate his neck. He is extremely resistant to examination of his oral cavity, and you cannot clearly visualize the posterior oropharynx. You obtain a lateral neck radiograph (Item Q132).

Item Q132: Lateral neck radiograph for the patient in the vignette
Reprinted with permission from Arcia, R., Batra, S., Bajwa, et al. Index of suspicion. *Pediatr Rev,* 2010:31(12), 519-524

Of the following, the MOST appropriate initial treatment for the boy's condition is

A. intravenous ceftriaxone
B. intravenous clindamycin
C. intravenous penicillin
D. oral amoxicillin
E. oral cefdinir

Correct Answer: B

The boy in this vignette has a retropharyngeal abscess. This infection occurs in the potential space anterior to the prevertebral fascia, which extends from the mediastinum to the skull base. Retropharyngeal abscesses are most common in children between 2 and 4 years of age and are often preceded by an upper respiratory infection. Common symptoms associated with retropharyngeal abscesses include:

- Fever
- Respiratory distress (tachypnea, stridor, or both)
- Difficulty swallowing, pain with swallowing, or drooling
- Voice changes ("hot potato" or muffled voice)
- Trismus
- Pain with neck movement, torticollis
- Neck swelling

Physical examination is often difficult because of trismus and pain. Tender anterior cervical lymphadenopathy is common, and if the posterior oropharynx can be visualized, an area of swelling can sometimes be appreciated. When epiglottitis cannot be ruled out, examination should be undertaken with care and with appropriate emergency equipment and trained personnel available.

Radiologic evaluation can include a lateral neck radiograph or computed tomography. On lateral neck radiograph, retropharyngeal abscesses appear as a thickened prevertebral space. A normal prevertebral space is thinner than the anterior-posterior diameter of the adjacent vertebral body. Computed tomography may be needed to differentiate between retropharyngeal cellulitis and abscess and can evaluate for extension of infection into the mediastinum.

Children with suspected retropharyngeal abscess and airway compromise require urgent surgical intervention. Initial management for children without severe respiratory distress should include a trial of broad-spectrum intravenous antibiotics. Deep neck infections are typically polymicrobial, including a mix of aerobic and anaerobic species. Empiric therapy should cover group A *Streptococcus*, *Staphylococcus aureus*, and respiratory anaerobes. Initial treatment may include intravenous ampicillin-sulbactam or intravenous clindamycin. For patients with severe infection, patients who do not respond to initial empiric treatment, or patients in settings with high local rates of methicillin-resistant *S aureus*, intravenous vancomycin or linezolid may be added to the empiric treatment. Oral therapy is not appropriate initially, but patients can be transitioned from intravenous to oral therapy after clinical improvement and should complete a 14-day course of antibiotic treatment.

Of the choices listed, the most appropriate initial therapy for the boy in this vignette is intravenous clindamycin. Neither intravenous ceftriaxone nor intravenous penicillin provide adequate antimicrobial coverage, and initial treatment should be with intravenous rather than oral antibiotics.

PREP Pearls
- Children with a retropharyngeal abscess are often febrile and appear ill; they may have torticollis, pain with neck movement, drooling, difficulty swallowing, trismus, respiratory distress, and/or muffled voice.
- A lateral neck radiograph showing a thickened prevertebral space is consistent with the diagnosis of retropharyngeal abscess.
- Children with suspected retropharyngeal abscess without airway compromise can be treated with empiric intravenous antibiotics. Infection is often polymicrobial; empiric therapy should cover group A *Streptococcus, Staphylococcus aureus,* and respiratory anaerobes.

ABP Content Specifications(s)
- Plan the appropriate management of retropharyngeal abscess
- Identify the pathogens commonly associated with retropharyngeal abscess
- Plan the appropriate diagnostic evaluation of retropharyngeal abscess

Suggested Readings
- Brook I. Microbiology and management of peritonsillar, retropharyngeal, and parapharyngeal abscesses. J *Oral Maxillofac Surg.* 2004;62(12):1545–1550. doi: http://dx.doi.org/10.1016/j.joms.2003.12.043 .
- Dudas R, Serwint JR. In brief: retropharyngeal abscess. *Pediatr Rev.* 2006;27(6):e45–e46. doi: http://dx.doi.org/10.1542/pir.27-6-e45.
- 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 133

An 8-year-old girl is brought to your office for a health supervision visit. She and her mother are concerned about her small size. She was born at 40 weeks' gestation, with a birthweight of 2.3 kg (small for gestational age), after an uncomplicated pregnancy. Her medical history is not significant, and she takes no medication. A comprehensive review of systems yields only picky eating habits. The girl performs well in school. Her mother is 165 cm tall and had menarche at age 12 years. Her father is 180 cm in height and had average timing of puberty. Her adjusted midparental height is at the 60th percentile. Physical examination reveals a temperature of 37°C, heart rate of 82 beats/min, blood pressure of 94/50 mm Hg, weight of 19 kg, height of 114 cm (2.5 standard deviations below the mean), and body mass index of 14.6 kg/m2 (22nd percentile). Her growth curve is shown in Item Q133. She has a high-arched palate. Her sexual maturity rating is 1 for breast development and pubic hair. The remainder of the girl's physical examination findings are within normal parameters. Her bone age is concordant with her chronologic age. Findings on her complete blood count, comprehensive metabolic panel, urinalysis, erythrocyte sedimentation rate, tissue transglutaminase antibody, thyroid function tests, insulin-like growth factor 1, and karyotype (46,XX) are normal.

Growth curve for the girl described in the vignette
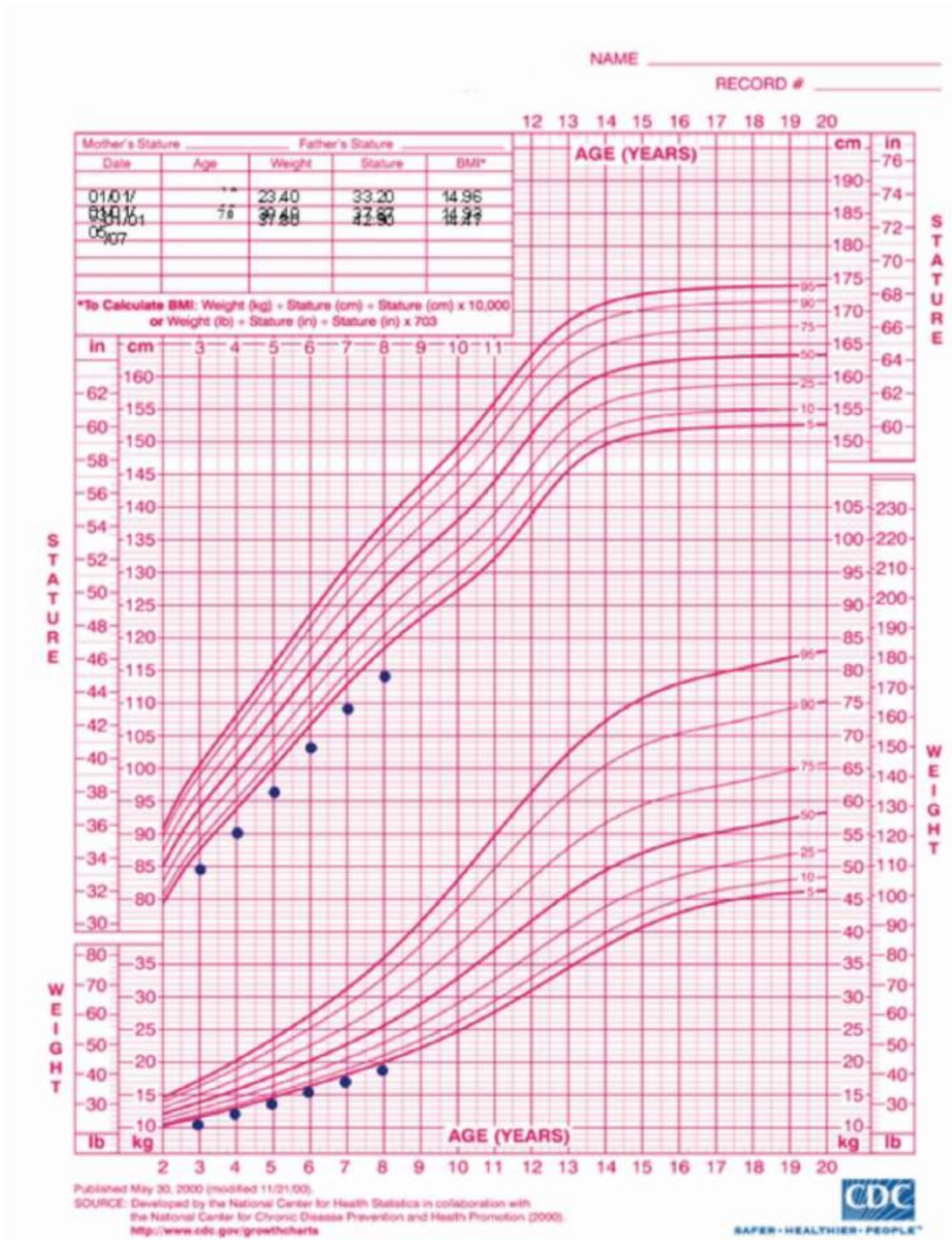
Courtesy of K. Vogt

Of the following, the BEST next management step for this girl is to

A. consult endocrinology for consideration of growth hormone therapy
B. consult gastroenterology to evaluate for a potential gastrointestinal disorder
C. consult a nutritionist to provide counseling for a higher calorie diet
D. order brain magnetic resonance imaging
E. order sweat chloride testing

Correct Answer: A

The girl in the vignette has significant short stature, at 2.5 standard deviations (SDs) below the mean, without an apparent etiology. She is growing at a normal height velocity, paralleling the bottom of the growth curve, and has a normal body mass index. The additional testing is unrevealing. The combination of her small-for–gestational age birthweight, high-arched palate, and concordant bone age is suggestive of an underlying genetic etiology.

This girl meets 2 of the indications approved by the US Food and Drug Administration (FDA) for growth hormone (GH) therapy:

1. She was born small for gestational age and did not catch up to a height of at least 2 SDs below the mean (about 2%) by age 2 years.
2. She has idiopathic short stature, with a height more than 2.25 SDs below the mean (<1%) without predicted catch-up.

Predicted adult height of less than 63 inches (160 cm) for boys and 59 inches (150 cm) for girls is considered a lack of catch-up growth. Based on her bone age and current height, this girl's predicted adult height is 4 feet 9 inches (145 cm).

Although GH treatment for idiopathic short stature is controversial, and many insurance companies do not cover GH therapy for this indication, the girl still warrants referral to pediatric endocrinology for evaluation for GH therapy. The decision about whether or not to use GH therapy should be made in consultation with a pediatric endocrinologist.

Use of GH for idiopathic short stature that is not associated with GH deficiency raises ethical issues. The average height gain with GH therapy for non–GH deficient children is 2 to 3 inches, and the financial cost is considerable. Whether GH administration would be considered treatment or enhancement should also be evaluated in each case. Short stature can be a significant disability in driving a car and other major life activities. Allen and Fost in 2004 proposed that decisions to treat with GH should be based on the expected effectiveness of therapy and degree of disability, rather than a particular diagnosis.

Framed using ethical principles, in this case:

- **beneficence** includes considerations of treatment efficacy and potential to lessen disability
- **nonmaleficence** consists of weighing the potential benefits of treatment versus the potential for adverse effects (eg, pseudotumor cerebri, risk for obstructive sleep apnea secondary to enlargement of tonsils and adenoids, worsening of scoliosis)
- **autonomy** requires assessment of the individual desires of the patient, family, and medical providers, which may be in conflict
- **justice** takes into consideration the high financial cost of therapy, disparities in treatment across socioeconomic status, and issues of health care resource allocation

The "small for gestational age with failure to catch up" indication for GH therapy is much less controversial, and likely captures many of those with genetic etiologies of short stature,

diagnosed or undiagnosed. However, GH effectiveness and degree of disability should also be considered for this group.

Gastrointestinal disorders, inadequate calorie intake, and cystic fibrosis can each cause poor growth. However, the girl in the vignette does not have signs or symptoms of an underlying chronic disease, has normal weight gain, and her body mass index is not low, making these conditions unlikely. Thus, consulting a gastroenterologist or nutritionist or ordering a sweat chloride test are not indicated. Brain magnetic resonance imaging is not indicated, because the girl does not have evidence of GH deficiency, other pituitary hormone deficiencies, or neurologic symptoms.

PREP Pearls
- Growth hormone (GH) therapy is approved by the US Food and Drug Administration for children with idiopathic short stature with a height more than 2.25 standard deviations below the mean (<1%) without predicted catch-up. GH therapy for this indication is controversial, and not covered by many insurance companies.
- Considerations for use of GH therapy for idiopathic short stature should include the expected effectiveness of therapy and the degree of disability.
- Decisions regarding GH treatment should be made in consultation with a pediatric endocrinologist.

ABP Content Specifications(s)
- Recognize and apply ethical principles involved in deciding when to use enhancement therapies
- Recognize and apply ethical principles involved in determining when the use of growth hormone therapy is appropriate (eg, in consultation with a pediatric endocrinologist)

Suggested Readings
- Allen DB, Fost N. hGH for short stature: ethical issues raised by expanded access. *J Pediatr.* 2004;144(5):648–652. doi: http://dx.doi.org/10.1016/j.jpeds.2004.02.028.
- Antiel RM, Jacobson RM, Fischer PR. Ethics for the pediatrician: a brave new pediatrics? Managing the desire for better children through biotechnological enhancement. *Pediatr Rev.* 2012;33(2):e13–e17. doi: http://dx.doi.org/10.1542/pir.33-2-e13.
- Grimberg A, DiVall SA, Polychronakos C, et al.; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. *Horm Res Paediatr.* 2016;86(6):361-397. doi: http://dx.doi.org/10.1159/000452150.
- Yates FD Jr. Ethics for the pediatrician: the persuasion of enhancements in pediatrics. *Pediatr Rev.* 2010;31(5):216–218. doi: http://dx.doi.org/10.1542/pir.31-5-216.

Question 134

A 10-year-old boy is brought to your office by his parents for concerns about learning. He started to struggle with his schoolwork last year, but received passing grades. This year, he has been saying that he is "stupid" and crying when his parents tell him it is time to leave for school. His parents requested and received an educational evaluation through his school. They have brought a copy of his school assessment to their appointment, and ask for your help in understanding the results, in preparation for their meeting at his school next week.

His aptitude test scores are as follows:
•verbal IQ = 85
•performance IQ = 78
•full-scale IQ = 83

His academic achievement scores are as follows:
•reading = 65
•math = 75
•writing = 68

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

Psychoeducational tests such as IQ tests and achievement tests generally have a mean of 100 and standard deviation (SD) of 15. The average range is within 1 SD of the mean (85–115). Verbal IQ measures language-based aptitude; performance IQ measures non–language-based aptitude. One definition of a learning disability is a meaningful discrepancy between intelligence (aptitude) scores and achievement scores. A discrepancy of at least 1 SD is significant. The boy in the vignette has a greater than 1 SD discrepancy between both his verbal IQ and his reading achievement, and his verbal IQ and his writing achievement. There is no significant discrepancy between his performance IQ and his math achievement. Therefore, this boy most likely has a learning disability in reading and in writing, but not in math. He does not meet the criteria for intellectual disability, which requires IQ scores that are 2 or more SDs below the mean.

Academic underachievement affects approximately 20% of school-aged children. Children with academic problems should be evaluated for learning or intellectual disability. Psychoeducational assessments should be requested through the school district, and typically include both measures of intelligence and achievement to help determine the etiology of academic underperformance. Intelligence includes the capacity to reason, plan, solve problems, think abstractly, learn, and use appropriate judgment. These cognitive abilities (aptitude) are measured using standardized IQ tests. 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]), Kaufman Assessment Battery for Children Second Edition (3–18 years), and Differential Ability Scales-II (2.5–17 years) are commonly used IQ tests. IQ tests can evaluate verbal and nonverbal abilities, and may include assessment of visuospatial abilities, working memory, knowledge, processing speed, and problem-solving skills.

Achievement, or academic proficiency, is measured using standardized tests that assess strengths and weaknesses in reading, math, written language, and oral language. Commonly used individually administered achievement tests include the Kaufman Test of Educational Achievement-II (Comprehensive Form 4.5–25 years; Brief Form 4.5–90 years), Wechsler Individual Achievement Test-III (4–50 years), Wide Range Achievement Test-4 (5–94 years), and the Woodcock-Johnson IV Tests of Achievement (2–90 years).

Standardized tests compare the individual's performance to that of same-age peers. Scores greater than 2 SD below the mean (<70) in both cognitive and adaptive measures are in the intellectually disabled range. Verbal IQ scores measure language-based aptitude and performance IQ scores measure non–language-based aptitude. Achievement scores are generally within 1 SD (15 points) of cognitive scores. Depending on the state, a discrepancy of at least 1 or 2 SD between IQ and achievement test scores meets the traditional educational definition of a learning disability. A learning disability may also be defined by low achievement in the setting of at least low average intelligence. In addition, the 2004 reauthorization of the Individuals with Disabilities Education Act (IDEA) allows learning disability to be defined by a student's failure to respond to evidence-based educational interventions.

Pediatricians who can interpret the results of psychoeducational tests can better understand the needs of their patients and more effectively guide families advocating for appropriate educational services. Early identification of and intervention for learning or intellectual disabilities improves the educational outcomes for these children.

PREP Pearls
- Psychoeducational tests, such as IQ tests and achievement tests, generally have a mean score of 100 and standard deviation (SD) of 15. The average range is within 1 SD of the mean (85–115).
- IQ test scores greater than 2 SD below the mean (<70) in both cognitive and adaptive measures are in the intellectually disabled range.
- A learning disability may be defined as a meaningful discrepancy between intelligence scores and achievement scores, low achievement in the setting of at least low average intelligence, or a student's failure to respond to evidence-based educational interventions.

ABP Content Specifications(s)
- Interpret the results of intelligence quotient tests, with emphasis on understanding the normal ranges
- Plan the appropriate diagnostic evaluation of achievement and intelligence

Suggested Readings
- Aylward GP. Psychoeducational testing. In: Voigt RG, Macias MM, Myers SM, eds. *Developmental and Behavioral Pediatrics.* Elk Grove Village, IL: American Academy of Pediatrics; 2011:293–311.
- Braaten EB, Norman D. Intelligence (IQ) testing. *Pediatr Rev.* 2006;27(11):403–408. doi: http://pedsinreview.aappublications.org/content/27/11/403 .
- 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 135

A 6-year-old girl is brought to the emergency department for a fracture of the right femur without a history of trauma. She reports that she has experienced recurrent bone pain in that region for several months. She has significant hepatosplenomegaly. No coarsening facial features are noted. A complete blood cell count shows mild thrombocytopenia, anemia, and leukopenia. You suspect a malignancy. A bone marrow examination reveals lipid-engorged macrophages, known as foam cells, with positive periodic acid-Schiff staining (Item Q135). A skeletal survey shows diffuse osteopenia and focal lytic lesions in varying regions.
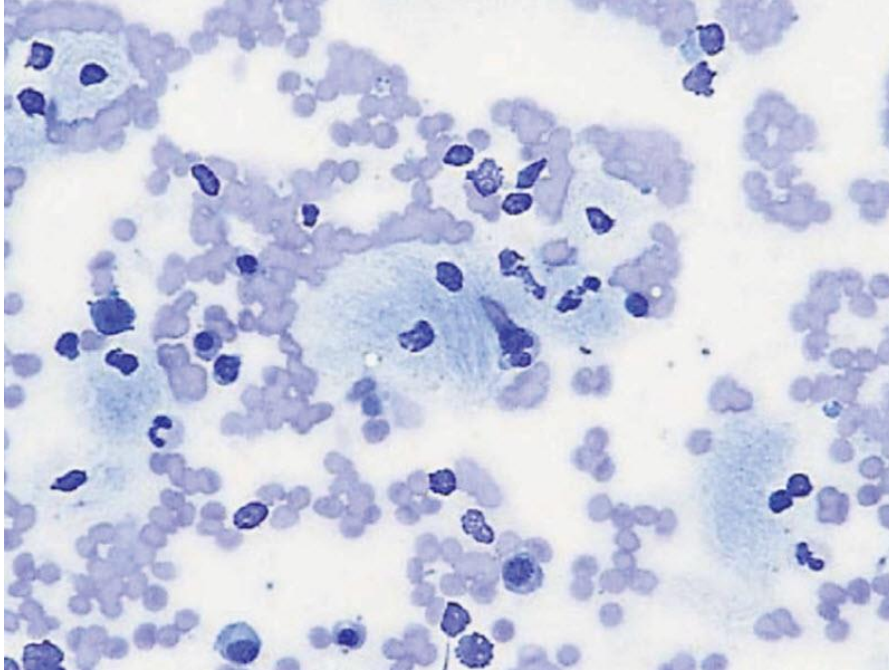
Item Q135: Foam cells seen on bone marrow examination.
Reprinted with permission from Mistry PK, Cappellini MD, Lukina E, et al. A reappraisal of Gaucher disease-diagnosis and disease management algorithms. *Am J Hematol*. 2011;86(1):110-115
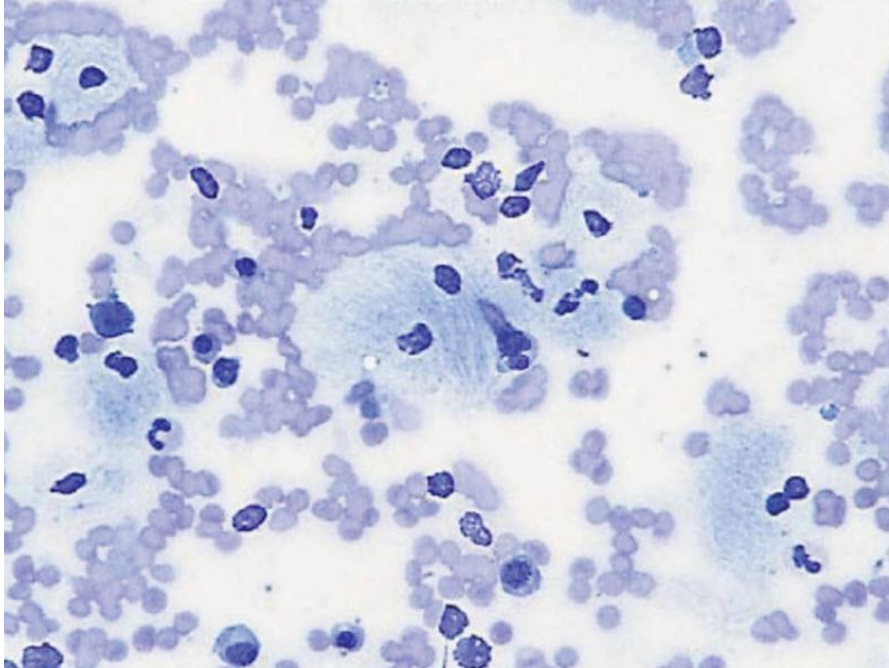
Of the following, the MOST likely diagnosis for this girl is

 A. Gaucher disease
 B. Hunter syndrome
 C. Langerhans cell histiocytosis
 D. Legg-Calvé-Perthes disease
 E. lymphoma

Correct Answer: A

The girl in this vignette has Gaucher disease type 1. Gaucher disease (GD) is an autosomal recessive disorder that has a continuum of clinical presentations. There are 3 major types of GD. Gaucher disease type 1 commonly presents with clinical and radiographic bone disease, including bone pain, pathologic fractures, subchondral joint collapse, osteopenia, focal sclerotic or lytic lesions, and osteonecrosis. Additionally, patients with GD type 1 typically exhibit hepatosplenomegaly, anemia, thrombocytopenia, and lung disease in the absence of the neurological findings that are more common in GD types 2 and 3. These findings include bulbar signs, pyramidal signs (opisthotonus, head retroflexion, spasticity, and trismus), cognitive impairment, oculomotor apraxia, seizures, and progressive myoclonic epilepsy. Gaucher disease type 2 typically has an onset prior to 2 years of age and has a rapidly progressive course that is generally fatal by 4 years of age. Neurologic findings in type 3 GD can occur before 2 years of age, but the disease course has slower progression with a patient lifespan into the second to fourth decade.

Clinical findings alone are not sufficient to confirm the diagnosis of GD. The physician should also measure the glucocerebrosidase enzyme activity in peripheral blood leukocytes. Affected individuals will have 0% to 15% of normal enzyme activity. Enzyme testing is not reliable to confirm carrier status because the enzyme levels of carriers and noncarriers can overlap. GBA is the only gene known to be associated with GD. Because GD is an autosomal recessive condition, 2 pathogenic mutations in GBA must be confirmed in the trans position (on separate chromosomes) to confirm the diagnosis. Bone marrow examination, often prompted by GD-related hepatosplenomegaly with anemia, thrombocytopenia, and leukopenia, reveals Gaucher cells, which are lipid-engorged macrophages (foam cells) (**Item C135**).

Item C135: Bone marrow smear from a child with Gaucher disease shows lipid-engorged macrophages (foam cells).

Treatment includes enzyme replacement therapy, substrate reduction therapy, partial or total splenectomy, blood transfusion for severe anemia or bleeding, analgesic medication for bone pain, joint replacement surgery, and oral bisphosphonates along with calcium and vitamin D. Hunter syndrome is an X-linked lysosomal storage disorder that presents with coarsening of facial features, progressive intellectual disability, progressive airway disease, cardiac disease, short stature, conductive and sensorineural hearing loss, and dysostosis multiplex on skeletal survey. Diagnosis can be established by abnormal urine glycosaminoglycans and a skeletal survey in combination with deficient iduronate 2-sulfate activity.

Langerhans cell histiocytosis is a multisystem disorder in which abnormal Langerhans cells proliferate in various tissues. Findings include granulomas and lytic lesions in the bones that can cause pathologic fractures, persistent skin rashes, and pituitary gland infiltration leading to diabetes insipidus and thyroid dysfunction. Langerhans cell histiocytosis can also affect the lungs, liver, and hematopoietic system. It is not an inherited condition, although familial clustering is sometimes noted.

Legg-Calvé-Perthes disease can present with osteonecrosis but would not have associated cytopenias and hepatosplenomegaly.

Lymphoma or leukemia could be suspected in this case, but the presence of lipid-engorged macrophages and lack of malignant cells in the bone marrow are not consistent with this diagnosis.

PREP Pearls
- Gaucher disease type 1 presents with hepatosplenomegaly, anemia, thrombocytopenia, bone pain, pathologic fractures, radiologic bone evidence of disease, and lung disease in the absence of the neurological findings commonly noted in Gaucher disease types 2 and 3.
- Neurologic findings in Gaucher disease types 2 and 3 include bulbar signs, pyramidal signs (opisthotonus, head retroflexion, spasticity, and trismus), cognitive impairment, oculomotor apraxia, seizures, and progressive myoclonic epilepsy.
- Treatment includes enzyme replacement therapy, substrate reduction therapy, partial or total splenectomy, blood transfusion for severe anemia or bleeding, medication for bone pain, joint replacement surgery, and oral bisphosphonates along with calcium and vitamin D.

ABP Content Specifications(s)
- Recognize the clinical features associated with Gaucher and other lipid storage diseases
- Plan the appropriate immediate and long-term management of lipid storage disease, including Gaucher disease, while considering the long-term prognosis

Suggested Readings
- Grabowski GA, Andria G, Baldellou A, et al. Pediatric non-neuronopathic Gaucher disease: presentation, diagnosis and assessment—consensus statements. *Eur J Pediatr.* 2004;163(2):58–66. doi: http://dx.doi.org/10.1007/s00431-003-1362-0.
- Pastores GM, Hughes DA. Gaucher disease. *GeneReviews*. 2015. http://www.ncbi.nlm.nih.gov/books/NBK1269/.

Question 136

The mother of a healthy 14-year-old patient calls to speak with you confidentially. She is concerned that her son may be abusing inhalants. He has seemed much more irritable and "moody" since he began high school 2 months ago, and he has been spending time with a new group of friends. Yesterday, while cleaning his room, the mother found an empty air-freshener aerosol container, 2 empty aerosol hairspray containers, and an empty aerosol spray paint can in her son's closet. She called her college-aged daughter, who told her that "some kids breathe the fumes from those cans to get high." The mother is very worried about her son, and has many questions about inhalant abuse. You discuss with her the risks of inhalant abuse, drug testing, and treatment.

Of the following, the MOST accurate statement you can make to this mother regarding the boy's substance abuse is that

 A. chronic abuse will likely lead to weight gain
 B. he should be treated with a neuroleptic medication
 C. he is at risk for sudden cardiac death
 D. he is at low risk for any significant health consequences
 E. urine drug screening will be useful in confirming his abuse

Correct Answer: C

The mother of the boy in the vignette has observed behaviors in her son which suggest he is abusing inhalants. The most accurate statement to make to her is that the boy is at risk for sudden cardiac death.

Inhalant abuse involves the intentional inhalation of vapors from a volatile substance to achieve an altered mental status, or "high." Inhalant abuse is often underrecognized, but may result in significant morbidity and even mortality in school-aged children and older adolescents. Although this disorder is more prevalent among geographically isolated and socioeconomically disadvantaged populations, it crosses all demographic, ethnic, and socioeconomic lines. Therefore, pediatricians must be prepared to recognize the clinical findings and risks of inhalant abuse, and to manage them appropriately.

A huge variety of volatile products, including glue, shoe polish, spray paint, hair spray, toluene, gasoline, paint thinner, and lighter fluid are commonly abused by both children and adults. These substances are easily accessible to children and adolescents, as they are inexpensive, legal, and generally can be purchased easily and kept without raising suspicion for substance abuse. Recent surveys indicate that inhalant abuse tends to start early among youth, with more than half of all users reporting their first use by the end of ninth grade. Important risk factors for inhalant abuse among middle and high school-aged children include low parental education levels and lack of intention to complete 4 years of college.

Although children may consider inhalant abuse to be a benign practice, it is associated with numerous negative health and psychosocial consequences, and may even result in death. Acutely, children who abuse inhalants display symptoms similar to those seen with alcohol intoxication: rapid onset of euphoria followed by sleepiness/stupor, dizziness, ataxia, slurred speech, slowed cognition and movement, blurred vision, and generalized weakness. Acute intoxication from inhalant abuse typically lasts only a few minutes, but the effects can be extended for hours by inhaling substances repeatedly. Mucous membrane irritation from inhalant abuse may cause rhinorrhea, sneezing, coughing, epistaxis, increased salivation, and conjunctival injection. Gastrointestinal symptoms such as nausea, vomiting, diarrhea, and abdominal cramps may also occur.

An extremely important health risk associated with inhalant abuse is the risk of "sudden sniffing death syndrome," which may occur in all users, including those experimenting with inhalant abuse for the first time. This syndrome is the leading cause of mortality due to inhalant abuse. In one study, more than one-fifth of victims of sudden sniffing death syndrome had no history of prior inhalant abuse. This syndrome is thought to arise from sensitization of myocardial cells to epinephrine. When epinephrine is produced by users in response to stimuli such as sudden stress or fright (which may arise from situations including being caught by or running from authority figures), a fatal cardiac arrhythmia may result. Death may also occur secondary to suffocation in the process of inhaling chemicals, aspiration, or traumatic injuries occurring when users are intoxicated.

Delayed health effects of inhalant abuse may include cardiomyopathy, central nervous system toxicity (including dementia, encephalopathy, and brain stem dysfunction), hepatocellular carcinoma, renal toxicity, pulmonary toxicity, aplastic anemia, and leukemia. Chronic users are at high risk for significant cognitive effects including memory loss, attention deficit, difficulty with learning and problem-solving, and mood disturbances.

The signs and symptoms of inhalant use are often subtle, so pediatricians must maintain a high index of suspicion for this disorder. Routine screening for inhalant abuse, in addition to other substance abuse and health risk behaviors, should be included as part of standard pediatric care. Inhalant abuse should be suspected when an individual is found to be storing "supplies" of products that can be abused, or when such products are found in unusual locations, such as in an adolescent's closet, vehicle, or under his or her bed. Behavioral changes (eg, apathy, anorexia, moodiness), a change in peer groups or activities, or declining school performance may also indicate inhalant abuse (as well as abuse of other substances). Chronic abusers may display poor hygiene and grooming, weight loss due to poor appetite, somnolence/fatigue, or signs of chronic mucous membrane irritation (eg, recurrent epistaxis, conjunctival injection, ulcerations of the oral and nasal mucosa). During or shortly after abuse of an inhalant, patients may exhibit signs of overt intoxication and have a detectable chemical odor on their breaths, skin, and/or clothing.

Treatment with a neuroleptic medication is not appropriate at this time. Little evidence is available to support the use of pharmacologic agents in the treatment of chronic inhalant abuse. Neuroleptics and other pharmacologic agents are generally not recommended for the treatment of inhalant abuse, except when used to treat comorbid psychiatric conditions.

It would not be accurate to state that this boy is at low risk for any significant health consequences. As described earlier, children and adolescents (as well as adults) who abuse inhalants are at risk for many significant acute and long-term health consequences, including sudden cardiac death.

Chronic inhalant abuse does not typically lead to weight gain. In fact, it is much more common for chronic inhalant abusers to experience weight loss due to poor appetite, resulting in inadequate caloric intake.

Urine drug screening is not useful for detecting inhalant use. Currently there are no widely available tests to detect inhalant exposure. Pediatric providers should not be falsely reassured that a patient is not abusing inhalants because of a negative urine drug screen result. Detection of this substance abuse disorder relies on consistently using screening questions as a routine component of a thorough history and physical examination.

PREP Pearls
- Inhalant abuse involves the intentional inhalation of vapors from a volatile substance to achieve an altered mental status or "high."
- An extremely important health risk associated with inhalant abuse is the risk of "sudden sniffing death syndrome," which results in cardiac arrest, and may occur in all users, including those experimenting with inhalant abuse for the first time.
- Delayed health effects of inhalant abuse may include cardiomyopathy, central nervous system toxicity (including dementia, encephalopathy, and brain stem dysfunction), hepatocellular carcinoma, renal toxicity, pulmonary toxicity, aplastic anemia, and leukemia.

ABP Content Specifications(s)
- Recognize the clinical findings and risks associated with an acute inhalant overdose, and manage appropriately

Suggested Readings
- Howard MO, Bowen SC, Garland EL, Perron BE, Vaughn MG. Inhalant use and inhalant use disorders in the United States. *Addiction Sci Clin Pract.* July 2011:18–31.
- Williams JF, Storck M; American Academy of Pediatrics Committee on Substance Abuse; American Academy of Pediatrics Committee on Native American Child Health. Inhalant abuse. *Pediatrics*. 2007;19(5):1009–1017. doi: http://dx.doi.org/10.1542/peds.2007-0470 .

Question 137

A 2-month-old infant with micrognathia is transferred to your hospital over the weekend for evaluation of poor feeding and consultation with a pediatric surgeon for possible gastrostomy tube placement. You order an upper gastrointestinal series to confirm normal anatomy. The next day, the radiologist calls to inform you that the results are unremarkable; he also informs you that the study was performed twice in error.

Of the following, from the family's perspective, the MOST important element to include when discussing this medical error is

A. a delay in disclosure until a root cause analysis is completed
B. a focus on the individuals responsible for the error
C. an apology for the error
D. a report of the error to hospital risk management before disclosure
E. the presence of the pediatric surgeon

Correct Answer: C

In 1999, the Institute of Medicine (IOM) published a report highlighting the prevalence of medical errors and their associated complications in the US health care system. They estimate 44,000 patients die annually as a result of preventable medical errors. In response, health care systems began examining their systems of practice in an effort to reduce medical errors. Medical errors can be classified as preventable and nonpreventable. Most preventable errors occur because of a combination of personal and systems factors. Nonpreventable errors are considered the baseline complication rate associated with a medical condition. By carefully examining systems of practice, health care organizations have significantly reduced medical errors.

In combination with the IOM report, there has been a change in practice regarding disclosure of medical errors to staff and families. Health care teams should openly discuss the event with patients (and their families as appropriate) as a mistake, and consider offering an apology. Currently, 36 states have legislation protecting providers who offer sympathetic statements during disclosure of a medical error. Offering an apology decreases the likelihood that patients will pursue legal recourse following a medical error. It is equally important, during disclosure, for the team to discuss potential harms that could result from this error, to highlight the steps being taken to understand the cause(s) of the mistake, and to adjust practice as needed to prevent a similar event in the future. Individual providers should not be singled out as responsible for the error. Disclosure should be timely, occurring as close in proximity to the event as possible. Disclosure should involve those directly involved in the event. Therefore, for the case in the vignette, there is no reason to delay discussion with the family for the arrival of the surgeon. Disclosure should not be postponed pending completion of a root cause analysis, nor should it be delayed until after a report to risk management can be made.

Investigation of medical error must be thoughtful and nonjudgmental, and should focus on systems issues. Despite the current emphasis on changing systems of care, providers involved in medical errors are often described as the second victims. Some institutions offer counseling for providers involved in medical errors.

PREP Pearls
- Discussion of a medical error should occur promptly after an event.
- When disclosing medical errors, providers should consider offering an apology.
- Counseling and support services should be offered to providers involved in a medical error.

ABP Content Specifications(s)
- Use appropriate methods of support for physicians and other health-care providers after an error producing medical harm occurs
- Apply appropriate methods of support for patients and their families after an error producing medical harm occurs
- Use appropriate means to disclose medical errors to patients

Suggested Readings

- Committee on medical liability and risk management; Council on quality improvement and patient safety. Disclosure of adverse events in pediatrics. *Pediatrics*. 2016;138(6):e20163215. doi: http://dx.doi.org/10.1542/peds.2016-3215.
- 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.
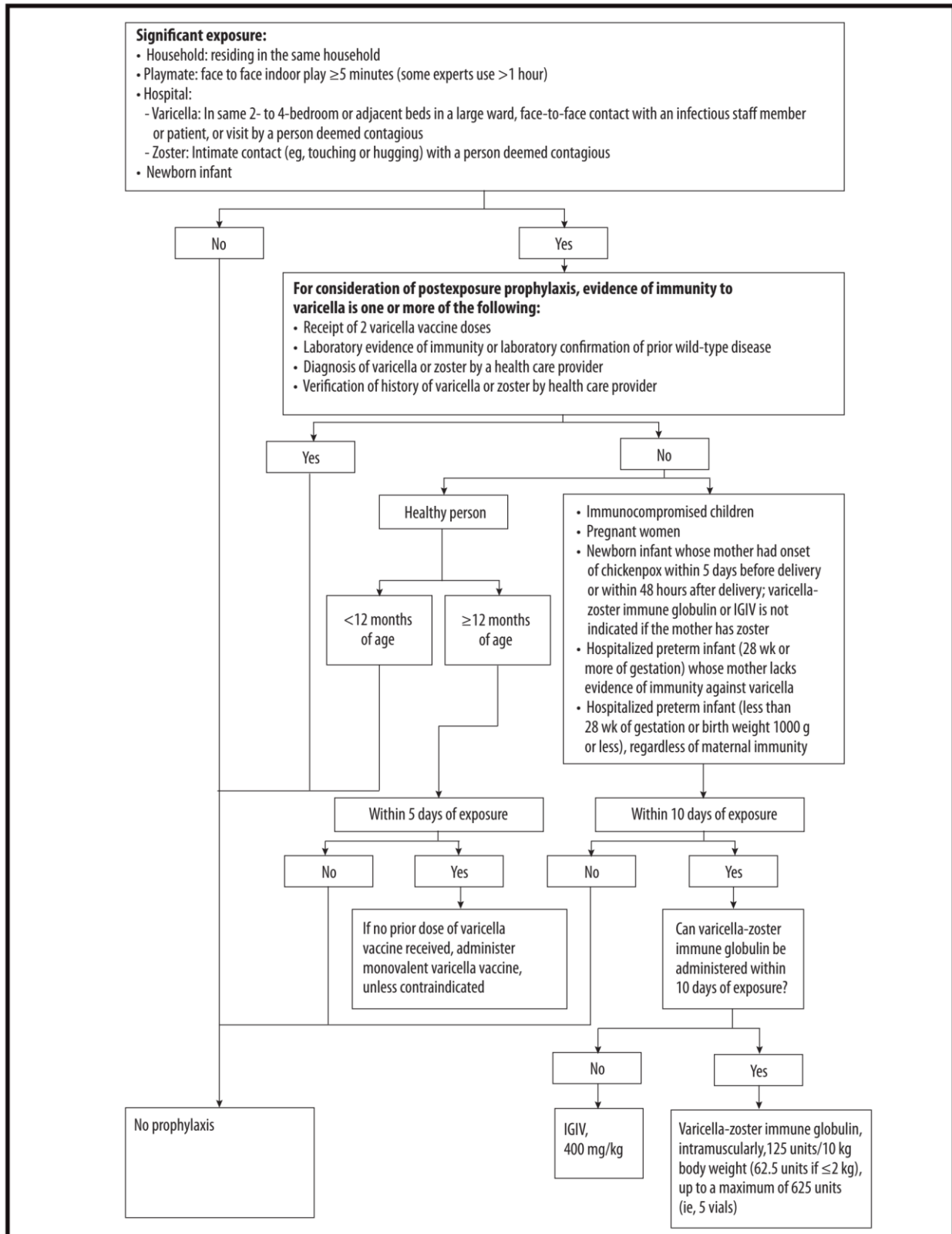
Question 138

The mother of a 12-month-old boy frantically calls your office for advice. Her son had been born prematurely at the estimated gestational age of 28 weeks. The entire family was together 2 days ago to celebrate her son's birthday, and his cousin now has chicken pox. The mother is concerned because her son has not yet had his 12-month-old health supervision visit. His vaccination status is up-to-date, except for the immunizations due at 1 year of age. Other than mild intermittent wheezing with viral respiratory illnesses, the child has been well and receives no daily medications. He is currently asymptomatic.

Of the following, the BEST recommendation is to give

A. acyclovir orally for 7 days
B. measles, mumps, rubella, varicella combined vaccine
C. varicella vaccine
D. varicella-zoster immune globulin

Correct Answer: C

This vignette highlights the importance of understanding the nuances of postexposure prophylaxis for varicella-zoster virus (VZV) infection. The immediate administration of varicella vaccine is the preferred method of prophylaxis for the boy in this vignette. Although primary VZV infection manifested as chickenpox is usually a self-limited and mild illness, it can cause significant morbidity and rarely mortality. Neonates, immunocompromised hosts, and pregnant women are at the greatest risk for complications. Susceptibility and potential risk for severe disease in the exposed individual if natural disease were to occur, along with the nature of the exposure, should be considered when assessing the need for postexposure prophylaxis (**Item C138**).

Significant exposure:
- Household: residing in the same household
- Playmate: face to face indoor play ≥5 minutes (some experts use >1 hour)
- Hospital:
  - Varicella: In same 2- to 4-bedroom or adjacent beds in a large ward, face-to-face contact with an infectious staff member or patient, or visit by a person deemed contagious
  - Zoster: Intimate contact (eg, touching or hugging) with a person deemed contagious
- Newborn infant

No   **Yes**

For consideration of postexposure prophylaxis, evidence of immunity to varicella is one or more of the following:
- Receipt of 2 varicella vaccine doses
- Laboratory evidence of immunity or laboratory confirmation of prior wild-type disease
- Diagnosis of varicella or zoster by a health care provider
- Verification of history of varicella or zoster by health care provider

Yes   **No**

Healthy person

- Immunocompromised children
- Pregnant women
- Newborn infant whose mother had onset of chickenpox within 5 days before delivery or within 48 hours after delivery; varicella-zoster immune globulin or IGIV is not indicated if the mother has zoster
- Hospitalized preterm infant (28 wk or more of gestation) whose mother lacks evidence of immunity against varicella
- Hospitalized preterm infant (less than 28 wk of gestation or birth weight 1000 g or less), regardless of maternal immunity

<12 months of age   **≥12 months of age**

Within 5 days of exposure   **Within 10 days of exposure**

No   **Yes**   **No**   **Yes**

If no prior dose of varicella vaccine received, administer monovalent varicella vaccine, unless contraindicated

Can varicella-zoster immune globulin be administered within 10 days of exposure?

No   **Yes**

No prophylaxis

IGIV, 400 mg/kg

Varicella-zoster immune globulin, intramuscularly, 125 units/10 kg body weight (62.5 units if ≤2 kg), up to a maximum of 625 units (ie, 5 vials)

ITEM C138: Management of exposures to varicella-zoster virus.

Individuals with primary VZV infection are considered contagious beginning 1 to 2 days before the onset of the rash. Varicella-zoster virus is highly communicable from cases of primary varicella, and transmission occurs via respiratory droplets or direct contact with vesicular fluid. Once the lesions of primary varicella or herpes zoster are fully crusted over, the index case is no longer considered contagious. Varicella vaccine is recommended within 3 to 5 days of exposure for healthy VZV-nonimmune individuals older than 12 months. Individuals with a history of only 1 prior dose of vaccine should receive the second dose if 3 months have elapsed since the first dose. Active immunization with varicella vaccine within this time frame prevents infection and lessens the severity of disease.

Varicella immunization is preferable to postexposure prophylaxis with acyclovir in healthy children and adults. Acyclovir may decrease the severity of disease but will not provide long-lasting protection.

Studies have been conducted of postexposure prophylaxis with the single-antigen varicella vaccine. There are limited data evaluating the effectiveness of the quadrivalent vaccine (measles, mumps, rubella, varicella); therefore, it is not the best recommendation for postexposure prophylaxis.

Passive immunoprophylaxis with varicella-zoster immune globulin is indicated for VZV-exposed patients who lack evidence of immunity to VZV and who are immunocompromised or not candidates to receive the live virus varicella vaccine. Passive immunization should be administered as soon as possible within 10 days after exposure. It is recommended that the following patients receive varicella-zoster immune globulin:
- Individuals with primary or acquired immunodeficiencies
- Individuals who take immunosuppressive therapies
- Newborns if their mother developed varicella 5 days before to 2 days after delivery
- Premature infants born after at least 28 weeks of gestation who are exposed during hospitalization and have nonimmune mothers
- Premature infants born at less than 28 weeks of gestation or who weigh 1,000 g or less at birth who are exposed during hospitalization, regardless of the mother's immunity status
- Pregnant women

Patients who receive varicella-zoster immune globulin should subsequently receive varicella vaccine, provided that no contraindications still exist, after at least 5 months have passed and they are 12 months of age or older. There is no indication to simultaneously administer varicella vaccine and varicella-zoster immune globulin. If varicella-zoster immune globulin is unavailable, immune globulin intravenous (IgIV) can be administered.

Although susceptible individuals can acquire VZV infection from exposure to persons with zoster, the transmission rates are much lower. If a VZV-nonimmune individual is closely exposed to open cutaneous zoster lesions, then postexposure prophylaxis should be considered. Routine active immunization with varicella vaccine is recommended by the Advisory Committee for Immunization Practices of the Centers for Disease Control and Prevention and the American

Academy of Pediatrics. The first dose is administered at 12 to 15 months of age, and the second dose is routinely administered at 4 to 6 years of age. Contraindications and minimal intervals should be respected when considering vaccine administration.

PREP Pearls
- Varicella vaccine is recommended within 3 to 5 days of exposure to varicella-zoster virus for healthy varicella-zoster virus–nonimmune individuals older than 12 months.
- Active immunization with varicella vaccine within 3 to 5 days of exposure prevents infection and lessens the severity of disease in individuals who become ill.
- Individuals with a history of only 1 prior dose of varicella vaccine should receive the second dose if 3 months have elapsed since the first dose.

ABP Content Specifications(s)
- Know the indications, contraindications, limitations, and schedule for varicella-zoster vaccine, including after exposure

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; 2015:846–859.
- Centers for Disease Control and Prevention (CDC). Updated recommendations for the use of VAriZIG - United States, 2013. MMWR Recomm Rep. 2013;62(28):574–576.
- Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP). Update: recommendations from the Advisory Committee on Immunization Practices (ACIP) regarding administration of combination MMRV vaccine. *MMWR Recomm Rep*. 2008;57(10):258–260.
- Marin M, Guris D, Chaves SS, et al. Prevention of varicella: recommendation of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2007;56(RR-4):1–40.

Question 139

You are discussing pubertal changes in boys with a group of medical students. You explain that there is a typical sequence in the development of secondary sexual characteristics.

Of the following, the sequence of events MOST often observed is

A. pubarche, testicular enlargement, spermarche, peak height velocity
B. pubarche, testicular enlargement, peak height velocity, spermarche
C. testicular enlargement, peak height velocity, pubarche, spermarche
D. testicular enlargement, pubarche, spermarche, peak height velocity
E. testicular enlargement, pubarche, peak height velocity, spermarche

Correct Answer: E

In most boys, the first physical changes of puberty occur between the ages of 9 and 14 years, in the following sequence: testicular enlargement, pubarche (the appearance of pubic hair), peak height velocity (PHV), and spermarche (the development of sperm). Testicular enlargement, sometimes called gonadarche, is present when the testicular volume is 4 mL or more or the long axis measures 2.5 cm or more.

Testicular enlargement (which defines Sexual Maturity Rating [SMR] genital [G] 2) occurs at a mean age of 10 years in non-Hispanic whites, 9 years in blacks, and 10 years in Hispanics. For the onset of pubic hair, the mean ages are 11.5, 10, and 11.5 years, respectively. The growth spurt begins at about 11.5 years of age, and the average boy reaches a PHV of 9.5 cm/year at 13.5 years of age, when he is in SMR G3 to G4.

Spermarche and ejaculation occur in G3, after boys achieve PHV, but fertility generally does not occur until SMR G4. Facial hair growth begins about 3 years after the appearance of pubic hair. The development of truncal hair may extend into adulthood. Although not a component of "normal" pubertal development, transient pubertal gynecomastia affects 40% to 60% of boys 1.2 years after reaching SMR G2 (peak age prevalence 14 years). Most cases resolve in 12 to 18 months.

Puberty in boys is usually complete in 3 years, with a range of 2 to 5 years. Evidence of puberty before the age of 9 years, or its absence by the age of 14 years, should prompt evaluation.

PREP Pearls
- In boys, puberty begins between the ages of 9 and 14 years. The first sign of puberty is testicular enlargement (>4 mL testicular volume, >2.5 cm in the long axis).
- Evidence of puberty in boys before the age of 9 years, or its absence by the age of 14 years, should prompt evaluation.

MOCA-Peds Objective
- Recognize normal variations in pubertal development

ABP Content Specifications(s)
- Distinguish normal from abnormal sexual development in males
- Understand the sequence of development of secondary sexual characteristics in boys

Suggested Readings
- Bordini B, Rosenfield RL. Normal pubertal development: part II—clinical aspects of puberty. *Pediatrics.* 2011;33:281-291. doi: http://dx.doi.org/10.1542/pir.32-7-281.
- Carswell JM, Stafford DEJ. Normal physical growth and development. In: Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.

- Gooding HC, DiVasta AD. Breast disorders and gynecomastia. In: Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.

Question 140

An 18-month-old girl is brought to your office for a health supervision visit. Her parents report that she has sucked her thumb since about 4 months of age. They note that she sucks her thumb at various times throughout the day and night, but she seems to engage in the behavior most frequently when she is tired, hungry, or scared. They ask about ways to help her break this habit.

Of the following, the BEST recommendation is to

A. consult with a dentist regarding placement of a dental device that will discourage thumb sucking
B. do nothing; most children will stop sucking their thumbs without any specific interventions
C. place gloves or socks on her hands during the times when she sucks her thumb most often
D. remind her verbally to stop sucking her thumb whenever they notice the behavior
E. start a sticker chart or other system of positive reinforcement for not engaging in the behavior

Correct Answer: B

Nonnutritive sucking habits like thumb and finger sucking or pacifier use are common soothing behaviors for many infants and young children. Finger and thumb sucking can be seen in utero after 29 weeks' gestation, and many newborns will suck their digits or hands while sleeping. By 1 year of age, 40% of children in the United States use a pacifier and 30% routinely suck their finger or thumb. By 4 years of age, this rate has decreased dramatically, with 4% of children still using a pacifier and 12% sucking their thumb or finger. Although these behaviors can be a beneficial part of self-soothing for many infants, there are associated risks. Infants or children who suck their thumbs or fingers are at increased risk for paronychia, irritant dermatitis, herpetic whitlow, and callouses. Children who continue the behavior after permanent dentition begins to erupt are also at increased risk for malocclusion and other orthodontic complications. Older children may be at risk of being teased or bullied by their peers.

Because most children will stop finger- or thumb-sucking behavior before 4 years of age without significant intervention, most clinicians do not advise that parents actively work to diminish this behavior until after 4 years of age. If sucking is contributing to orthodontic complications or is interfering socially, there are several techniques that may help the child stop the behavior. Small studies have shown that positive reinforcement for not engaging in the behavior (such as a sticker chart or non-food reward) can be beneficial. In contrast, punishment for thumb or finger sucking may reinforce the behavior as a way to gain caregiver attention. Aversive therapies such as placing socks or mittens on the child's hands or applying a bitter nail polish can be used as a reminder to the child not to suck, but these barriers are typically easily removed and may not contribute to long-term success without associated reinforcements. Older children can try to replace thumb or finger sucking with an alternative behavior or competitive response; for example, they can squeeze a small ball whenever they feel the urge to suck. When other techniques have not been successful, orthodontic devices can be used to assist the child with breaking the habit. Palatal arches and palatal cribs diminish sucking behaviors by serving as a persistent reminder to the child. Orthodontic devices should be used after permanent dentition begins to erupt.

In the absence of significant associated complications, the family in this vignette does not need to actively work to break their 18-month-old child's thumb-sucking habit. They should be advised that she will most likely outgrow the habit. Additionally, it is unlikely that behavioral techniques, such as placing gloves or socks on her hands, reminding her verbally when they notice the behavior, or using a sticker chart, would be successful at her age, because they require a more developmentally advanced child who can actively engage with her caregivers in the process of altering the habit. Orthodontic devices are not an appropriate option before permanent dentition has emerged.

PREP Pearls
- Thumb and finger sucking are common soothing behaviors in infants and young children. Most children will outgrow the habit.
- Infants and children who suck their fingers or thumbs are at increased risk for irritant dermatitis, paronychia, herpetic whitlow, and finger callouses. Children who continue the behavior after their permanent dentition has erupted are also at increased risk for malocclusion, and older children may be teased or bullied.
- Children who do not spontaneously outgrow thumb or finger sucking may benefit from intervention after 4 years of age, if complications are present. Positive reinforcement, aversive techniques, competitive responses, and orthodontic devices may be helpful in altering the habit.

ABP Content Specifications(s)
- Understand the natural history of thumb sucking, and manage appropriately

Suggested Readings
- Bishara SE, Warren JJ, Broffitt B, Levy SM. Changes in the prevalence of non-nutritive sucking patterns in the first 8 years of life. *Am J Orthod Dentofacial Orthop.* 2006;130(1):31–36. doi: http://dx.doi.org/10.1016/j.ajodo.2004.11.033.
- Borrie FR, Bearn DR, Innes NP, Iheozor-Ejiofor Z. Interventions for the cessation of non-nutritive sucking habits in children. *Cochrane Database Syst Rev.* 2015;3:CD008694. doi: http://dx.doi.org/10.1002/14651858.CD008694.pub2 .
- Davidson L. Thumb and finger sucking. *Pediatr Rev.* 2008;29(6):207–208. doi: http://dx.doi.org/10.1542/pir.29-6-207.

Question 141

A local preschool asks for your expertise in updating its inclusion and exclusion policy for head lice and nits. A healthy 4-year-old child who attends the center was recently found to have active head lice. They are concerned about how to respond to other parents regarding environmental control measures and criteria for the child's return.

Of the following, the BEST recommendation regarding this infestation is

A. all nits must be removed prior to the child's return
B. bagging items in plastic for 1 week is an effective decontamination technique
C. the child should be allowed to continue to come to school
D. exclusion is recommended until appropriate treatment followed by retreatment 1 week later
E. routine classroom screening for nits should be instituted

Correct Answer: C

When a school-aged child is found to have active head lice, he or she should be allowed to complete the school day. In 2015 the American Academy of Pediatrics' Council on School Health and the Committee on Infectious Diseases published a clinical revised report to clarify current diagnosis and treatment and provide guidance for the management of head lice in the school setting. The first key point from this report is: "No healthy child should be excluded from school or allowed to miss school time because of head lice or nits." (*Pediatrics.* 2015;135(5):e1355–1365.) The child should be allowed to remain in the classroom, but direct head-to-head contact with others should be discouraged. Confidential notification of the child's parents by telephone or written note should recommend prompt treatment.

Criteria for school attendance are outlined in this report. Head lice have low contagion within classrooms, and children with active infestations are likely to have been infested for some time. Therefore, a child with head lice should not be restricted from attending school, and no-nit policies should be abandoned. Exclusion from the classroom until appropriate treatment and retreatment has occurred is unnecessary and potentially harmful to the student's performance.

Environmental clean-up is an important feature of appropriate treatment. Household members should be checked for head lice and treated when live lice or nits are found within 1 cm of the scalp. Empiric treatment is recommended for all family members who share a bed with the affected child. Items that have been in contact with the head of the infested person within 48 hours prior to treatment should be considered contaminated and washed, vacuumed, or dried at a temperature greater than 54.4°C. Alternatively, placing items in a closed plastic bag for 2 weeks is an effective decontamination technique.

Routine screening for nits and live lice does not have a significant impact on the incidence of head lice in schools, and screening programs are not cost effective. However, it is prudent to check symptomatic children and children known to have direct head-to-head contact with the infested child.

Head lice is an example of the many conditions that may be transmitted in day care or school settings. Most minor illnesses do not warrant exclusion from these settings. In general, if the child is ill enough to limit participation in typical activities or if the child needs extra care that is beyond the capabilities of the staff, then it is advisable for the child to remain at home. In addition, most states have laws about isolation of individuals with specific communicable diseases. General recommendations (**Item C141A**) and disease- or condition-specific recommendations (**Item C141B**) from the American Academy of Pediatrics for the exclusion of children in out-of-home child care are summarized in Red Book Online (Section 2: Recommendations for Care of Children in Special Circumstances. Children in Out-of-Home Child Care). Pediatric health care providers should be familiar with these guidelines.

Item C141A. General Recommendations for Exclusion of Children in Out-of-Home Child Care.

Symptoms(s)	Management
Illness preventing participation in activities, as determined by child care staff	Exclusion until illness resolves and able to participate in activities
Illness that requires a need for care that is greater than staff can provide without compromising health and safety of others	Exclusion or placement in environment where appropriate care can be provided, without compromising care of others
Severe illness suggested by fever with behavior changes, lethargy, irritability, persistent crying, difficulty breathing, progressive rash with above symptoms	Medical evaluation and exclusion until symptoms have resolved
Persistent abdominal pain (2 hours or more) or intermittent abdominal pain associated with fever, dehydration, or other systemic signs and symptoms	Medical evaluation and exclusion until symptoms have resolved
Vomiting 2 or more times in preceding 24 hours	Exclusion until symptoms have resolved, unless vomiting is determined to be caused by a noncommunicable condition and child is able to remain hydrated and participate in activities
Diarrhea if stool not contained in diaper, or if fecal accidents occur in a child who is normally continent; if stool frequency is 2 or more stools above normal for that child or stools contain blood or mucus	Medical evaluation for stools with blood or mucus; exclusion until stools are contained in the diaper or when toilet-trained children no longer have accidents using the toilet and when stool frequency becomes less than 2 stools above that child's normal frequency/24 hours.
Oral lesions	Exclusion if unable to contain drool or if unable to participate because of other symptoms or until child or staff member is considered to be noninfectious (lesions smaller or resolved).
Skin lesions	Keep lesions on exposed skin surfaces covered with a waterproof dressing

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Item C141B. Disease-or Condition-Specific Recommendations for Exclusion of Children in Out-of-Home Child Care.

Condition	Management of Case	Management of Contacts
Hepatitis A virus (HAV) infection	Serologic testing to confirm HAV infection in suspected cases. Exclusion until 1 week after onset of illness.	In facilities with diapered children, if 1 or more cases confirmed in child or staff attendees or 2 or more cases in households of staff or attendees, HAV vaccine (HepA) or Immune Globulin (IG) should be administered within 14 days of exposure to all unimmunized staff and attendees. In centers without diapered children, HepA or IG should be given to unimmunized classroom contacts of index case. Asymptomatic IG recipients may return after receipt of IG.
Impetigo	Exclusion until 24 hours after treatment has been initiated. Lesions on exposed skin should be covered with waterproof dressing when possible.	No intervention unless additional lesions develop.
Measles	Exclusion until 4 days after beginning of rash and when the child is able to participate.	Immunize exposed children without evidence of immunity within 72 hours of exposure. Children who do not receive vaccine within 72 hours or who remain unimmunized after exposure should be excluded until at least 2 weeks after onset of rash in the last case of measles.
Mumps	Exclusion until 5 days after onset of parotid gland swelling.	In outbreak setting, people without documentation of immunity should be immunized or excluded. Immediate readmission may occur following immunization. Unimmunized people should be excluded for 26 or more days following onset of parotitis in last case.
Head lice infestation	Treatment at end of program day and readmission on completion of first treatment.	Household and close contacts should be examined and treated if infested. No exclusion necessary.
Pertussis	Exclusion until completion of 5 days of the recommended course of antimicrobial therapy if pertussis is suspected; untreated children and providers should be excluded until 21 days have elapsed from cough onset.	Immunization and chemoprophylaxis should be administered as recommended for household contacts. Symptomatic children and staff should be excluded until completion of 5 days of antimicrobial therapy. Untreated adults should be excluded until 21 days after onset of cough.
Rubella	Exclusion for 7 days after onset of rash for postnatal infection.	Pregnant contacts should be evaluated.
Infection with Salmonella serotypes Typhi or Paratyphi	Exclusion until diarrhea resolves and 3 consecutive stool cultures obtained at least 48 hours after cessation of antimicrobial therapy are negative.	When Salmonella serovar Typhi infection is identified in a child care staff member, local or state health departments may be consulted regarding regulations for length of exclusion and testing, which may vary by jurisdiction.
Infection with nontyphoidal Salmonella, Salmonella of unknown serotype, or Clostridium difficile	Exclusion until diarrhea resolves. Negative stool cultures results not required for non-serotype Typhi Salmonella species, and repeat testing should not be performed for asymptomatic children previously diagnosed with C difficile.	Symptomatic contacts should be excluded until symptoms resolve. Stool cultures are not required for asymptomatic contacts.
Scabies	Exclusion until after treatment given.	Close contacts with prolonged skin-to-skin contact should have prophylactic therapy. Bedding and clothing in contact with skin of infected people should be laundered.
Infection with Shiga toxin-producing Escherichia coli (STEC), including E coli O157:H7	Exclusion until diarrhea resolves and 2 stool cultures (obtained at least 48 hours after any antimicrobial therapy has been discontinued) are negative. Some state health departments have less stringent exclusion policies for children who have recovered from less virulent STEC infection.	Meticulous hand hygiene; stool cultures should be performed for any symptomatic contacts. In outbreak situations involving virulents STEC strains, stool cultures of asymptomatic contacts may aid controlling spread. Center(s) with causes should be closed to new admissions during STEC outbreak.
Shigellosis	Exclusion until 24 or more hours after diarrhea has ceased. State regulations may require one or more stool cultures to be negative for Shigella species before returning to care.	Meticulous hand hygiene; stool cultures should be performed for any symptomatic contacts.
Staphylococcus aureus skin infections	Exclusion only if skin lesions are draining and cannot be covered with a watertight dressing.	Meticulous hand hygiene; cultures of contacts are not recommended.
Streptococcal pharyngitis	Exclusion until 24 hours after treatment has been initiated.	Symptomatic contacts of documented cases of group A streptococcal infection should be tested and treated if test results are positive.
Tuberculosis	For active disease, exclusion until determined to be noninfectious by physician or health department authority. May return to activities after therapy is instituted, symptoms have diminished, and adherence to therapy is documented. No exclusion for latent tuberculosis infection.	Local health department personnel should be informed for contact investigation.
Varicella	Exclusion until all lesions have crusted or, in immunized people without crusts, until no new lesions appear within a 24-hour period.	For people without evidence of immunity, varicella vaccine should be administered within 3 days but up to 5 days after exposure, or when indicated, Varicella-Zoster IG should be administered up to 10 days after exposure.

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PREP Pearls
- No healthy child should be excluded from school or day care because of head lice or nits.
- The Committee on Infectious Diseases of the American Academy of Pediatrics has published recommendations for exclusion of a child from school or day care that should be referenced regarding head lice.
- Most minor illnesses do not warrant exclusion from school or day care.

ABP Content Specifications(s)
- Recommend appropriate measures to prevent transmission of pathogens to child-care center attendees and their families
- Understanding which illnesses require and do not require exclusion from child-care center attendance

Suggested Readings
- American Academy of Pediatrics. Children in out-of-home child care. 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; 2015:132–151.
- 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 142

A 24-month-old immunocompetent boy is brought to the pediatric clinic for a health supervision visit. Two months ago, he was hospitalized for Haemophilus influenzae type A meningitis. He experienced severe hearing loss as a result of this infection and underwent bilateral cochlear implant placement 3 weeks after completing treatment for meningitis. At the previous health supervision visit at 18 months of age, he received a second dose of hepatitis A vaccine, bringing his vaccination status up-to-date. He has not had any vaccinations since the 18-month-old visit.

Of the following, the MOST appropriate vaccination schedule for this patient is

  A. pneumococcal conjugate and polysaccharide vaccines now
  B. pneumococcal conjugate vaccine now and in 4 weeks
  C. pneumococcal conjugate vaccine now and polysaccharide vaccine in 4 weeks
  D. pneumococcal polysaccharide vaccine now and in 5 years
  E. pneumococcal polysaccharide vaccine now without further doses

Correct Answer: E

The 24-month-old boy in this vignette had meningitis caused by *Haemophilus influenzae* type A. As a result of the infection, he developed severe hearing loss, leading to the early placement of cochlear implants. The cochlear implants place him at risk of invasive pneumococcal infection. The vaccine indicated for this patient, who is fully vaccinated and is at risk of invasive pneumococcal infection, is 1 dose of pneumococcal polysaccharide vaccine.

There are over 90 serotypes of pneumococcus. Available vaccines target the serotypes most likely to cause invasive infections in humans. The 13-valent pneumococcal conjugate vaccine (PCV13) includes 13 serotypes whereas the 23-valent pneumococcal polysaccharide vaccine (PPSV23) includes 23 pneumococcal serotypes (12 serotypes included in PCV13 plus an additional 11 serotypes).

Conjugated pneumococcal vaccines are indicated in healthy infants and children between the ages of 2 and 59 months as part of a 4-dose series that is typically administered at 2, 4, 6, and 12 to 15 months of age. For children with chronic medical conditions that place them at risk of pneumococcal infection, catch-up immunization is recommended through 71 months of age. For at-risk individuals who are 6 to 18 years of age and have not previously received PCV13, one dose of PCV13 is recommended, followed by PPSV23.

The US Food and Drug Administration licensed PPSV23 for use in children who are 2 years of age or older, and PPSV23 is indicated for individuals at high risk of invasive pneumococcal infections. Individuals who are at risk but otherwise immunocompetent include individuals with chronic heart disease, chronic lung disease, diabetes mellitus, cerebrospinal fluid leaks, and cochlear implants. It is recommended that the at-risk immunocompetent group receives 1 lifetime dose of PPSV23. Individuals who have asplenia or other immunocompromising conditions including HIV should receive 2 doses of PPSV23. The interval between doses is 5 years, except for individuals with sickle cell anemia for whom the interval is 3 years. For at-risk individuals who are 6 to 18 years of age and have not previously received pneumococcal vaccination, PPSV23 should be administered 8 weeks after PCV13.

Because the patient in this vignette is up-to-date on vaccinations at 24 months of age, he has completed the 4-dose series of conjugated pneumococcal vaccine and does not require any further doses. For individuals at risk of invasive pneumococcal infections who are otherwise immunocompetent, only 1 dose of polysaccharide pneumococcal vaccine is recommended.

PREP Pearls
- There are over 90 serotypes of pneumococcus. The available vaccines, PCV13 and PPSV23, target the serotypes that are more likely to cause invasive infections in humans.
- Conjugated pneumococcal vaccines are indicated in healthy infants and children between the ages of 2 and 59 months as part of a 4-dose series that is typically administered at 2, 4, 6, and 12 to 15 months of age.

- Polysaccharide pneumococcal vaccination is recommended for individuals at high risk of invasive pneumococcal infections in either a 1- or 2-dose series, depending on the risk factor, starting at 2 years of age.
- Individuals who are at risk for invasive pneumococcal disease but are otherwise immunocompetent include individuals with chronic heart disease, chronic lung disease, diabetes mellitus, cerebrospinal fluid leaks, and cochlear implants.

ABP Content Specifications(s)
- Understand the composition of conjugated and unconjugated pneumococcal vaccines are multivalent
- Differentiate between appropriate use of conjugated versus unconjugated pneumococcal vaccine
- Know the indications and schedule for the pneumococcal vaccines

Suggested Readings
- American Academy of Pediatrics. Pneumococcal 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; 2015:626–638.
- Committee on Infectious Diseases. Immunization for *Streptococcus pneumoniae* infections in high-risk children. *Pediatrics*. 2014;134(6):1230–1233. doi: http://dx.doi.org/10.1542/peds.2014-2811 .

Question 143

A 2-year-old boy is brought to your office for evaluation. His medical history is significant for bilateral renal dysplasia diagnosed antenatally. He has a temperature of 37.2°C, respiratory rate of 20 breaths/min, heart rate of 95 beats/min, and blood pressure of 100/60 mm Hg. His physical examination findings are significant for a weight of 8 kg (less than fifth percentile), height of 77 cm (less than fifth percentile), and mild pallor.

The parents inform you that his nephrologist saw him last week and advised renal replacement therapy. You review the records from that visit and make note of a glomerular filtration rate of 20 mL/min/1.73 m2 and normal serum electrolyte levels. You discuss renal replacement therapy for treating chronic renal failure with the parents.

Of the following, you are MOST likely to inform the parents that

  A. choice of dialysis modality is solely decided by the physician
  B. chronic dialysis and renal transplant have similar mortality rates
  C. dietary restrictions are not indicated in patients on chronic dialysis
  D. hemodialysis has improved outcomes compared to peritoneal dialysis
  E. preemptive transplant is preferred over dialysis for renal replacement therapy

Correct Answer: E

In patients with deteriorating chronic renal failure, a discussion of treatment options for renal replacement therapy (RRT) should be initiated once the glomerular filtration rate declines to less than 30 mL/min/1.73 m^2 (onset of stage 4 chronic kidney disease [CKD]). Treatment options for RRT include hemodialysis, peritoneal dialysis, and renal transplant. Some form of RRT is needed when the glomerular filtration rate falls below 15 mL/min/1.73 m^2 (CKD stage 5). Fluid overload, uremia (vomiting, tiredness, excessive sleepiness), and uncontrolled hyperkalemia/hyperphosphatemia (with dietary restriction and medications) secondary to deteriorating glomerular filtration rate are usually observed at a glomerular filtration rate less than 15 mL/min/1.73 m^2.

Renal transplant is the treatment of choice for RRT in adults or children with renal failure. A preemptive transplant is a kidney transplant that occurs before dialysis, thereby allowing CKD patients to avoid dialysis. The benefits of a transplant compared to dialysis include lower mortality, improved growth and development, and better quality of life because dietary and fluid restrictions are not needed after the transplant. Moreover, the time not spent on dialysis (an average of 4 hours 3 times weekly for hemodialysis and 8-10 hours daily on peritoneal dialysis) translates into improved home, school, and social life.

As compared to adults, children with kidney failure are likely to survive longer and thereby are at increased risk for CKD-associated morbidity (especially cardiovascular). Preemptive renal transplant, or less time spent on dialysis, decreases the long-term morbidity associated with CKD. This approach also preserves vascular access and peritoneal membrane for future use if the renal transplant fails.

Dialysis is the removal of toxins, waste, and excess fluids by artificial filtering systems. In both hemodialysis and peritoneal dialysis, a specialized solution (dialysate) is used to remove wastes and fluids from the blood across a semipermeable membrane. In hemodialysis, this process occurs extracorporeally via a specialized filter in the dialysis machine. A central catheter (in the internal jugular vein) or an arteriovenous fistula/graft is used to remove and return the patient's blood after circulating through the hemodialysis circuit. In peritoneal dialysis, the peritoneal membrane acts as the semipermeable membrane, and the dialysate is added to the peritoneal cavity via a surgically placed catheter. In automated peritoneal dialysis, a machine is used to push fluid in and out of the abdomen. Gravity is used in ambulatory peritoneal dialysis. Dialysis provides only 10% to 15% of the function of a normal kidney; thus, patients on dialysis usually have dietary restrictions for phosphorus, potassium, and overall fluid intake.

Currently, there is no data showing a significant advantage for hemodialysis over peritoneal dialysis for RRT. The choice between hemodialysis and peritoneal dialysis for a patient with renal failure involves considerations for patient age, technical aspects, social factors, family preference, and compliance. Peritoneal dialysis at home is the preferred modality for chronic dialysis in newborns, infants, and young children. Vascular access for hemodialysis and absence of machines adapted for low extracorporeal neonatal blood volumes make hemodialysis technically difficult in neonates and small children. Another advantage of peritoneal dialysis is

the ability to perform dialysis at night while the patient is asleep in the comfort of home. However, hemodialysis is the preferred modality for patients who have poor living conditions or who lack a dedicated caregiver. Additionally, hemodialysis is preferred for patients with abdominal pathology that impairs the ability to perform peritoneal dialysis.

The United States Renal Data System (USRDS) reports that peritoneal dialysis is the most common initial dialysis modality for children aged 9 years and younger who weigh less than 20 kg, whereas hemodialysis is the most common initial dialysis modality for children aged 9.5 years and older who weigh more than 20 kg. Less than 40% of patients who need RRT receive a preemptive kidney transplant as the initial treatment modality. However, kidney transplant is the most prevalent RRT in children with kidney failure, and 80% of children aged 5 to 13 years needing RRT have a kidney transplant. According to USRDS data for children on RRT, the prevalence per million population for renal transplant is highest at 69.8, followed by 18.5 for hemodialysis, and 11.7 for peritoneal dialysis.

PREP Pearls
- Renal transplant is the treatment of choice for renal replacement therapy.
- A preemptive transplant is a kidney transplant that occurs before dialysis, thereby allowing a patient who needs renal replacement therapy to avoid dialysis.
- There is no significant advantage for hemodialysis over peritoneal dialysis for renal replacement therapy.
- The choice between hemodialysis and peritoneal dialysis for a patient with renal failure involves considerations for patient age, technical aspects, social factors, family preference, and compliance.

ABP Content Specifications(s)
- Plan the appropriate initial management of end-stage kidney disease

Suggested Readings
- National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Treatment methods for kidney failure in children. https://www.niddk.nih.gov/health-information/health-topics/kidney-disease/treatment-methods-for-kidney-failure-in-children/Pages/facts.aspx.
- United States Renal Data System. 2016 Annual Data Report: Chapter 8—ESRD among children, adolescents, and young adults. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2016. https://www.usrds.org/2016/view/v2_08.aspx.

Question 144

A 2-month-old female infant is brought to your office for a health supervision visit. She was born full-term without complications, is growing at the 50th percentile for length, weight, and head circumference, and is her parents' first child. She is smiling, cooing, and can lift her head up when placed prone. The girl's mother mentions that her niece has "terrible vision," which was not detected until elementary school, and she now wears "the thickest glasses I've ever seen." The infant's mother asks if she can have her daughter's vision tested.

Of the following, the BEST strategy for vision testing for this infant is to

A. advise the mother that vision in infants younger than 3 months cannot be reliably assessed
B. refer the infant to a pediatric ophthalmologist for formal testing
C. test the infant's ability to fixate on a small bright light, such as a pen light
D. test the infant's ability to fixate on a small, colorful toy
E. test the infant's ability to fixate on a human face

Correct Answer: E

Vision screening in primary care pediatrics is important for the early detection of vision problems, which maximizes the efficacy of treatment and accommodations for visual impairment. Although screening older children with standard eye charts (optotype-based screening) is fairly straightforward, assessment in preverbal infants requires age- and development-specific techniques.

For infants aged 6 months and younger, in addition to testing for the presence of a red reflex and pupillary reflex and examining the external aspects of the eyes, assessment of fixation and tracking is the best way to identify concerning vision problems. At age 2 months, infants should be able to fixate on a familiar caregiver's face. At age 3 months, infants begin to visually track moving objects, such as toys. Functional depth perception and the ability to reach for a visualized object develop by age 5 to 6 months.

It is important to routinely test children for ocular alignment, because abnormalities (strabismus) can lead to amblyopia. The corneal light reflex test and the cover test are used to test for strabismus, as well as to distinguish between true strabismus and pseudostrabismus, or the appearance of crossed eyes due to broad epicanthal folds. These tests should be administered starting at 6 months of age. Abnormalities should prompt referral to an ophthalmologist, because late diagnosis of amblyopia can result in permanent vision loss.

In recent years, instrument-based vision screening has been shown to be a superior method for identifying strabismus, high refractive error, and amblyopia in toddlers and children too young to cooperate with optotype-based (eye chart) screening. This type of screening can be performed in pediatric offices with children as young as 12 months. Several devices are commercially available, and have been extensively tested to ensure accuracy. This form of screening, which offers opportunities for even earlier identification and referral for vision problems, has been endorsed by the American Academy of Pediatrics and the US Preventive Services Task Force, and is often reimbursed separately by insurers.

Once a child can cooperate, optotype-based screening should be used to assess visual acuity. This occurs usually around 4 years of age, but sometimes earlier. Vision screening should be performed annually until children reach age 7 years, and biannually thereafter.

PREP Pearls
- Infant vision screening by assessing fixation on faces and moving objects can be used starting at age 2 months.
- Instrument-based screening is a more accurate way of assessing strabismus, amblyopia, and high refractive error in toddlers and children too young to cooperate with optotype-based (eye chart) screening.

ABP Content Specifications(s)
- Understand the importance of vision screening, including in newborn infants
- Plan the appropriate evaluation of vision in patients of various ages
- Understand which conditions can be detected by periodic ophthalmoscopic examinations

Suggested Readings
- Committee on Practice and Ambulatory Medicine, Section on Ophthalmology, American Association of Certified Orthoptists, American Association for Pediatric Ophthalmology and Strabismus, American Academy of Ophthalmology. Visual system assessment in infants, children, and young adults by pediatricians. *Pediatrics*. 2016;137(1):e20153596. doi: http://dx.doi.org/10.1542/peds.2015-3596.
- Donahue SP, Baker CN; Committee on Practice and Ambulatory Medicine, Section on Ophthalmology, American Association of Certified Orthoptists, American Association for Pediatric Ophthalmology and Strabismus, American Academy Of Ophthalmology. Procedures for the evaluation of the visual system by pediatricians. *Pediatrics*. 2016;137(1):e20153597. doi: http://dx.doi.org/10.1542/peds.2015-3597.

Question 145

A 17-year-old adolescent girl is brought to the emergency department after experiencing shortness of breath while practicing with her varsity soccer team. She reports a 2-month history of worsening exercise intolerance and a 1-week history of numbness in her feet and hands. She also reports feeling clumsy; specifically, she feels like she is going to fall over when taking her shirt off at night and when rinsing her hair while showering. Prior to the onset of this constellation of symptoms, she had been well.

Her past medical history is unremarkable. She has never been hospitalized and has never undergone surgery. Her only medication is a daily multivitamin. She reports that she does not use alcohol, tobacco, or illicit drugs and that she is not sexually active. She experienced menarche at 12 years of age, and has had regular monthly menses lasting 5 to 6 days for the last 3 years. She reports having a well-rounded, generally healthy diet. She lives at home with her parents and 2 younger siblings, and she is a straight "A" student.

Her family history is remarkable for her mother having autoimmune thyroiditis and a maternal aunt with system lupus erythematosus.

She has a temperature of 37.1°C, heart rate of 142 beats/min, and blood pressure of 116/76 mm Hg. She is at the 70th percentile for height and the 55th percentile for weight. She is pale and seems distraught, but she is awake, alert, and oriented and appropriately answers your questions. Her heart, lung, and abdominal examination results are unremarkable. Her neurological examination results are remarkable for a positive Romberg sign and a decreased sense of vibration and touch in her hands and feet. She successfully executes a tandem gait test.

A complete blood cell count reveals:

Laboratory Test	Result
White blood cell count	5,100/µL (5.1 x 10^9/L)
Hemoglobin	5.4 g/dL (54 g/L)
Platelet count	112 x 10^3/µL (112 x 10^9/L)
Mean corpuscular volume	118 fL
Neutrophils	48%
Lymphocytes	42%
Monocytes	10%

A urine toxicology screen and a urine pregnancy test have negative results.

Of the following, the MOST likely etiology of her presentation is

A. autoantibodies to gastric parietal cells
B. chronic alcohol abuse
C. compression of the spinal cord at the L3/L4 level
D. leukemic infiltration of the spinal cord
E. severe iron deficiency

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Correct Answer: A

The teenager in this vignette has new-onset exercise intolerance, abnormal neurological findings, and a severe macrocytic anemia. The differential diagnosis of macrocytic anemia in children includes vitamin B_{12} deficiency, folate deficiency, and bone marrow failure. Vitamin B_{12} deficiency caused by dietary deficiency is rare in children; instead, vitamin B_{12} deficiency is most often caused by a disruption of vitamin B_{12} absorption. Vitamin B_{12} absorption from the gastrointestinal tract occurs at the terminal ileum. Thus, a disruption of absorption can be caused by the absence of the terminal ileum (surgical or congenital) or by a deficiency of intrinsic factor. Intrinsic factor, a glycoprotein produced in the gastric parietal cells, is required to transport vitamin B_{12} from the lumen of the gastrointestinal tract through the terminal ileum into the body. Deficiency of intrinsic factor and subsequent vitamin B_{12} deficiency is called pernicious anemia. Congenital pernicious anemia occurs when there is a genetic defect resulting in hypofunctional or absent intrinsic factor. Pernicious anemia in adolescents typically results from gastric atrophy and achlorhydria caused by antibodies to the parietal cell and intrinsic factor. When vitamin B_{12} (also called cobalamin) is consumed, it attaches to haptocorrin and travels to the duodenum where it is hydrolyzed and released from the haptocorrin. The free vitamin B_{12} then binds to intrinsic factor and travels to the ileum. It is then absorbed in the ileum, enters the bloodstream, and binds to transcobalamin. Untreated vitamin B_{12} deficiency causes macrocytic anemia as well as neurologic symptoms, including paresthesias, ataxia, and gait abnormalities, as a result of posterior and lateral spinal column degeneration. Vitamin B_{12} deficiency can be treated with the parenteral administration of vitamin B_{12}.

The girl in this vignette has a family history remarkable for autoimmunity, suggesting that her macrocytic anemia has an autoimmune origin. Thus, it is likely that her macrocytic anemia is caused by autoimmune damage to the gastric parietal cells.

Chronic alcohol use results in vitamin B_{12} deficiency caused by the lack of dietary intake. Given the girl's normal growth and development and acute onset of symptoms, there is no indication that she chronically abuses alcohol. While compression of the spinal cord can result in neurological changes, it would not lead to anemia. Leukemia can lead to anemia and neurologic changes, but the white blood cell differential on the complete blood cell count in the vignette is normal. In addition, children with leukemia do not show macrocytic changes. Iron deficiency would result in a microcytic anemia, not a macrocytic anemia, and would not lead to the neurologic changes described in the vignette.

Folic acid deficiency can also lead to a macrocytic anemia. However, this deficiency is rare because many foods are supplemented with folic acid. The neurologic findings seen in the girl in this vignette are not seen in folic acid deficiency. The consumption of a diet high in goat milk, which is low in folic acid, and the presence of hemolytic anemia, which increases folic acid utilization because of rapid red blood cell turnover, are risk factors for folic acid deficiency. The offspring of pregnant women who have folate deficiency are at risk of neural tube defects.

PREP Pearls
- Vitamin B_{12} deficiency results in a macrocytic anemia and neurological changes caused by the degeneration of the posterior and lateral spinal columns.
- Intrinsic factor is produced in the gastric parietal cells and is necessary for the absorption of vitamin B_{12}.
- The most common cause of vitamin B_{12} deficiency in adolescents is autoimmune gastric atrophy and achlorhydria caused by autoantibody-mediated damage to the gastric parietal cells, resulting in a deficiency of intrinsic factor.
- Vitamin B_{12} is absorbed in the terminal ileum.

ABP Content Specifications(s)
- Recognize the signs, symptoms, and causes of vitamin B12 deficiency, and manage appropriately
- Recognize the signs, symptoms, and causes of folate deficiency, and manage appropriately

Suggested Readings
- Kaferle J, Strzoda CE. Evaluation of macrocytosis. *Am Fam Physician.* 2009;79(3):203–208.
- Sethuraman U. Vitamins. *Pediatr Rev.* 2006;27(2):44–55. doi: http://dx.doi.org/10.1542/pir.27-2-44.
- Stabler SP. Vitamin B12 deficiency. *N Engl J Med.* 2013;368(2):149–160. doi: http://dx.doi.org/10.1056/NEJMcp1113996.

Question 146

An 11-year-old boy is brought to the urgent care center for evaluation of worsening abdominal pain. The pain began last night and is described as an ache in the periumbilical region. The patient rates the pain as a 7 on a scale of 10. He reports nausea and nonbloody, nonbilious emesis that began several hours ago.

He has a temperature of 38°C, heart rate of 115 beats/min, respiratory rate of 25 breaths/min, and blood pressure of 115/84 mm Hg. He is curled in a ball on the examination table. His bowel sounds are hypoactive. His abdomen is diffusely tender to palpation with rebound and guarding. He has increased pain with coughing.

Of the following, the BEST next test to order is

 A. abdominal radiography
 B. barium enema
 C. computed tomography
 D. magnetic resonance imaging
 E. ultrasonography

Correct Answer: E

The boy in this vignette has acute appendicitis, which is best initially evaluated by ultrasonography. Ultrasonography of the appendix has a negative predictive value of 95.1%. Computed tomography has a positive predictive value of 96% and a negative predictive value of 95%; however, the patient incurs significant radiation exposure. In addition, computed tomography is more expensive and time-consuming than ultrasonography, which can be completed at the bedside. Magnetic resonance imaging requires significantly more time and resources, but it does not involve radiation exposure. Studies show no difference in appendicitis diagnosis rate for computed tomography as compared to ultrasonography with magnetic resonance imaging as needed. Abdominal radiographs are often normal in patients with acute appendicitis. Although a barium enema can be effective in the diagnosis of acute appendicitis, it can be limited by non-filling of the appendix and is therefore not used.

The boy in this vignette has referred pain caused by appendicitis. Referred pain is pain felt at a site other than the location of the stimulus and is caused by the activation of nerve fibers in cutaneous dermatomes entering the spinal cord at the same level. Typically, the 2 areas were developed from the same embryonic segment. Referred pain differs from visceral pain, which is caused by stimulation of nonmyelinated pain receptors located in the muscles, mucosa, mesentery, and serosal surfaces of the viscera. Visceral pain is not well localized and is usually described as dull, diffuse, or crampy. Finally, parietal pain is caused by myelinated pain receptors in the parietal peritoneum, muscle, and skin. This type of pain is localized and typically described as sharp. **Item C146** contains examples of the different types of pain.

Item C146. Referred Visceral and Parietal Abdominal Pain — Locations and Characteristics.

Source of Pain	Referred Location	Pain Mechanism
Liver/Gallbladder	Right scapula	Referred
Appendix	Periumbilical	Referred
Pancreatitis	Midback	Referred
Gastric or duodenal	Epigastric	Visceral
Cardiac	Left chest and arm	Referred
Appendicitis	Right lower quadrant	Parietal

Courtesy of C. Waasdorp Hurtado

PREP Pearls
- Referred pain is felt at a site different from the source of the pain and is caused by the stimulation of cutaneous dermatomes.
- Visceral pain is caused by stimulation of nonmyelinated pain receptors in the muscles, mucosa, mesentery, and serosal surfaces of the viscera, resulting in poorly localized pain.
- Parietal pain is caused by stimulation of myelinated pain receptors in the parietal peritoneum, muscle, and skin, resulting in well-localized pain.
- Studies show no difference in the appendicitis diagnosis rate for computerized tomography as compared to ultrasonography with magnetic resonance imaging as needed. Ultrasonography is the preferred initial imaging technique for suspected appendicitis.

ABP Content Specifications(s)
- Understand sources of referred abdominal pain and their associated pain patterns

Suggested Readings
- Aspelund G, Fingeret A, Gross E, et al. Ultrasonography/MRI versus CT for diagnosing appendicitis. *Pediatrics*. 2014;133(4):586–593. doi: http://dx.doi.org/10.1542/peds.2013-2128.
- Cervero F. Pathophysiology of visceral pain. *Revista Dor*. 2014;15(2):133–138. doi: http://dx.doi.org/10.5935/1806-0013.20140032.
- 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.

Question 147

A 3-month-old infant with chronic lung disease of prematurity is brought to your office for a health supervision visit. The infant was born at 28 weeks of gestation via normal vaginal delivery and weighed 1,000 g. According to the mother, the infant is doing well and gaining weight. He is currently on 0.5 L of oxygen by nasal cannula, feeds every 3 to 4 hours, and has 10 to 12 wet diapers per day. The infant's current medications include furosemide and thiazide.

Of the following, the MOST likely electrolyte abnormality associated with this infant's current therapy is

A. hyperchloremia
B. hypermagnesemia
C. hypernatremia
D. hyperuricemia
E. metabolic acidosis

Correct Answer: D

Diuretic therapy is commonly associated with hyperuricemia. In patients with diuretic-associated volume depletion, urate reabsorption is increased in the proximal tubule, leading to reduced urate excretion and hyperuricemia. Diuretic therapy–associated hyperuricemia is usually asymptomatic and does not lead to renal damage or gout arthritis. Volume repletion (by fluid intake or by stopping diuretics) removes the stimulus for urate absorption and corrects hyperuricemia.

Diuretics are frequently used to treat lung disease of prematurity because of the improvement in pulmonary function that occurs with negative fluid balance. Diuretics inhibit NaCl reabsorption in the nephron, leading to increased urine losses of sodium and water. Loop diuretics (furosemide, bumetanide) inhibit the Na^+-K^+-$2Cl^-$ channel in the thick ascending loop of Henle. Thiazide diuretics inhibit the Na^+-Cl^- cotransporter in the distal tubule and connecting segment. Hypokalemia is usually associated with diuretic therapy. Increased urinary potassium secretion is a consequence of increased delivery of sodium and water to the distal nephron segments. Secondary hyperaldosteronism can occur in response to volume depletion induced by diuretic therapy. Contraction metabolic alkalosis is usually seen with diuretic (loop or thiazide) therapy. Metabolic alkalosis is a result of extracellular volume depletion caused by loss of isotonic sodium chloride but little or no loss of HCO_3^- . Metabolic alkalosis is also caused by hypokalemia and secondary hyperaldosteronism, which lead to increased urinary H^+ ion secretion and net HCO_3^- reabsorption. Hypochloremia is usually associated with metabolic alkalosis because of the chloride loss associated with diuretic therapy.

Hypomagnesemia is associated with diuretic therapy. Magnesium is reabsorbed in the loop of Henle, and loop diuretics directly inhibit magnesium absorption leading to hypomagnesemia. Thiazide diuretics do not directly affect magnesium secretion in the urine, but hypokalemia associated with diuretic therapy may lead to hypomagnesemia. Hypokalemia inhibits magnesium uptake by the distal tubules, leading to increased urinary excretion of magnesium and hypomagnesemia.

Hyponatremia is usually present in volume-overload states such as heart failure that require chronic therapy with diuretics. Hyponatremia in the setting of volume overload may be especially worsened by thiazide diuretics. Antidiuretic hormone secretion is increased in response to effective circulatory volume depletion in patients with heart failure. This increased secretion of antidiuretic hormone leads to increased water reabsorption and lowered sodium concentration. Thiazide diuretic therapy adds to the decrease in effective circulatory volume, leading to the development or worsening of hyponatremia. By their inhibition of Na^+-K^+-$2Cl^-$ channels, loop diuretics (furosemide) also decrease the medullary concentration gradient important in the urinary concentration by antidiuretic hormone. In contrast, thiazide diuretics inhibit the distal Na^+-Cl^- cotransporter in the distal tubule and do not interfere with the urinary concentration response to antidiuretic hormone secretion. Therefore, development or worsening of hyponatremia in edematous patients with decreased effective circulatory volume is more commonly seen with thiazide diuretic therapy.

PREP Pearls
- Loop diuretics (furosemide, bumetanide) inhibit the Na+-K+-2Cl- channel in the thick ascending loop of Henle. Thiazide diuretics inhibit the Na+-Cl- cotransporter in the distal tubule and connecting segment.
- Volume contraction, hypokalemia, metabolic alkalosis, and hyperuricemia commonly occur with loop and thiazide diuretic therapy.

ABP Content Specifications(s)
- Recognize the adverse effects associated with diuretic therapy

Suggested Readings
- Rose BD, Post TW. *Clinical use of diuretics. In: Clinical Physiology of Acid-Base and Electrolyte Disorders.* 5th ed. New York, NY: McGraw Hill; 2001:447–477.

Question 148

A 10-year-old boy is brought to your office for evaluation of twitching. His parents believe it started about 1 month ago. His right eye and cheek briefly twitch, frequently throughout the day. He also repeatedly shrugs and rolls his right shoulder. There is no alteration in his mental status during these events. The boy reports that he can suppress these movements for a short time but then he feels he "has to" do them. His parents notice more twitching at the end of the day and sometimes the boy cannot fall asleep at night because of constant shoulder rolling. He is doing well at school. His teachers and classmates have not noticed these movements. The boy's father has attention-deficit/hyperactivity disorder and his younger brother had a febrile seizure at 1 year of age. In the clinic today, his physical examination findings are within normal parameters, with no evident twitching.

Of the following, the BEST next step is to

A. perform electrocardiography
B. perform magnetic resonance imaging of the brain
C. recommend comprehensive behavioral intervention for tics
D. recommend treatment with haloperidol
E. refer to neurology for electroencephalography

Correct Answer: C

The boy in the vignette has motor tics. The tics are interfering with his ability to fall asleep, so of the choices, the next best step is comprehensive behavioral intervention for tics (C-BIT). Tics are brief, stereotyped motor movements (motor tics) or sounds (phonic tics). They typically involve the face or upper extremities. Examples of simple motor tics include forceful eye blinking, mouth opening, facial twitching, or shoulder shrugging. Phonic tics include humming, coughing, or sniffing. Complex motor tics involve several muscle groups, for instance, hopping or jumping. Children with tics often describe a premonitory urge, a sense of needing to perform the tic, and then a sense of relief after. When present, this is helpful in distinguishing tics from other movement disorders. The diagnosis of tics is based on the history and physical examination findings. Video of the movements is helpful in making the diagnosis, especially when the tic is not present during the office visit. A family history of tics is sometimes present. When the clinical diagnosis is clear, no further diagnostic testing is needed.

Treatment for tics is reserved for situations when they significantly interfere with daily activities. Off-label use of medications such as clonidine or guanfacine can reduce tics, but typically does not stop them completely. Haloperidol and pimozide are approved by the US Food and Drug Administration to treat tics, but often have significant side effects, thus would not be the best next step for the boy in the vignette. C-BIT is a behavioral strategy that decreases or sometimes stops tics. The child learns how to substitute a "competing response" for the bothersome tic. For instance, instead of rolling his shoulder, the boy in the vignette could train himself to take in a slow, deep breath. This might allow him to fall asleep more easily.

Chorea is an irregular, quick jerking movement. Athetosis, a more fluid writhing movement, often occurs at the same time. Chorea does not have a premonitory urge, which is a useful distinction from tics. The most common cause of new-onset chorea in children in the United States is Sydenham chorea. Sydenham chorea occurs after a streptococcal infection, sometimes with a latency of months. Along with chorea, these children often experience behavior change, dysarthria, hypotonia, or gait instability. Sydenham chorea can occur as an element of acute rheumatic fever (ARF). ARF is another sequela of prior streptococcal infection. Diagnosis of ARF is made using the Jones criteria (**Item C148**). When a child presents with new-onset chorea, the diagnostic evaluation should include clinical evaluation for elements of the Jones criteria, laboratory studies looking for evidence of a prior streptococcal infection, and evaluation for carditis, with both electrocardiography and echocardiography. If results of all these tests are normal, magnetic resonance imaging of the brain or additional laboratory studies looking for other causes of chorea such as pregnancy or systemic lupus erythematosus may be considered. The boy in the vignette clearly has tics, not chorea, so none of these studies would be an appropriate choice.

Item C148. Jones Criteria for Diagnosis of Acute Rheumatic Fever[a].

Major Criteria	Minor Criteria	Supporting Evidence

Carditis
Polyarthritis
Chorea
Erythema marginatum
Subcutaneous nodules
	Clinical findings:
	  Fever, arthralgia[b]
	Laboratory findings:
	  Elevated acute phase reactants; prolonged PR interval
		Positive throat culture or rapid test for GAS antigen
		
		OR
		
		Elevated or rising streptococcal antibody test

GAS indicates group A streptococcal.
[a] Diagnosis requires 2 major criteria or 1 major and 2 minor criteria with supporting evidence of antecedent group A streptococcal infection.
[b] Arthralgia is not a minor criterion in a patient with arthritis as a major criterion.

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Focal seizures can present with rhythmic jerking of the face or arm. But, there is no premonitory urge in seizures, and focal seizures typically last several minutes or longer. It is very unlikely that the boy in the vignette is having focal seizures, so performing electroencephalography is not the best next step.

PREP Pearls
- Children with tics often describe a premonitory urge, a sense of needing to perform the tic, and then a sense of relief after. When present, this is helpful in distinguishing tics from other movement disorders.
- Tics are brief, stereotyped motor movements (motor tics) or sounds (phonic tics). They typically involve the face or upper extremities.

ABP Content Specifications(s)
- Distinguish among the findings associated with various movement disorders, and manage appropriately
- Identify the risk factors for various movement disorders

Suggested Readings
- http://tourette.org/.
- Kruer MC. Pediatric movement disorders. *Pediatr Rev.* 2015;36(3):104–116. doi: http://dx.doi.org/10.1542/pir.36-3-104.

Question 149

You are discussing medical errors with the residents on your rotation. They consider factors that may lead to medical errors in children, including the length of stay, complexity of care, percentage of weight change, and the developmental physiology of newborns, infants, and children.

Based on these factors, the area of the hospital MOST likely to put pediatric patients at risk for adverse events is

A. emergency department
B. neonatal intensive care unit
C. operating room
D. pediatric intensive care unit
E. urgent care unit

Correct Answer: B

Unfortunately, adverse events, most of which are preventable, are quite prevalent in hospitals across the country. In addition to contributing to the morbidity and mortality of patients, adverse events cost the health care system $37.6 billion yearly, with preventable events making up the majority of that cost.

Children are a high-risk population for errors and adverse drug events because of the more complicated dosing of medications by weight as opposed to a single drug dose used in adults. Dosing by weight results in different doses as well as the potential for error in dose calculation. Additionally, many children are cared for in adult-based settings in which the staff have less experience working with children.

Providing medical care for children becomes more complicated as their length of stay increases, their weight changes, and the complexity of their medical diagnoses increases. Premature infants have immature functioning of the hepatic and renal systems that increases the complexity of drug dosing. This increased complexity makes the neonatal intensive care unit a particularly error-prone setting.

Because of this vast problem, there have been many developments to mitigate medical errors. These developments include checklists, surgical site marking, patient identification methods, and electronic medical records. The electronic medical record offers a unique level of protection and intervention for prevention of medical errors. It offers legibility to order-writing with computer order entry, particularly in the context of medications, as well as dose-range checking, prescribing rules, corollary orders, and clinical decision support. Electronic medical records can also be queried to allow for data generation and reporting on specific events throughout a patient's hospitalization.

PREP Pearls
- Adverse events are preventable.
- Children are a high-risk population for errors and adverse drug events because of the more complicated dosing of medications by weight.
- Premature infants are particularly complex; they have immature functioning of the hepatic and renal systems that increases the complexity of drug dosing, as well as extended lengths of stay and continually changing weights. These factors, among others, make the neonatal intensive care unit a particularly error-prone setting.
- The electronic medical record is a tool frequently used in health care to mitigate adverse events from medical errors.

ABP Content Specifications(s)
- Recognize the common causes of adverse events in pediatric patients
- Understand the contribution of adverse events to the morbidity and mortality of pediatric patients
- Understand the contribution of adverse events to the cost of medical care
- Identify situations presenting high risk for adverse events in the management of pediatric patients

Suggested Readings
- Jacobs B. Electronic medical record, error detection, and error reduction: a pediatric critical care perspective. *Pediatr Crit Care Med*. 2007;8(2 suppl):S17–S20. doi: http://dx.doi.org/10.1097/01.PCC.0000257484.86356.39.
- 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.

Question 150

A 14-year-old adolescent boy is brought to your office for concerns about an itchy rash on his right foot that has been present for several weeks. He is in good health and takes no medications. He is afebrile and has normal growth parameters. The physical examination findings are remarkable only for the skin of the right foot (Item Q150).

Item Q150: Cutaneous findings for the boy described in the vignette.
Kimberlin DW, et al. *Red Book Online.* Elk Grove Village, IL. American Academy of Pediatrics 2015.

Of the following, the MOST appropriate therapy is topical

 A. aluminum chloride
 B. clobetasol
 C. clotrimazole
 D. erythromycin
 E. petrolatum

Correct Answer: C

The boy in this vignette has a pruritic eruption involving the foot that is characterized by scaling and erosions in the interdigital spaces. These findings are consistent with the interdigital form of tinea pedis, and treatment with a topical antifungal preparation like clotrimazole is indicated. Interdigital involvement with scaling, fissuring, and maceration is the most common form of tinea pedis. It is caused by infection with the dermatophytes *Trichophyton rubrum* and *Epidermophyton floccosum*. Less common forms of infection include the moccasin type (infection with *T rubrum* causes widespread scaling of the plantar surface of the foot) and the inflammatory type (*Trichophyton mentagrophytes* infection produces erythematous papules and vesicles on the instep of the foot, **Item C150A**). The diagnosis of tinea pedis is usually made clinically but can be confirmed with a potassium hydroxide preparation or fungal culture. First-line treatment is a fungistatic topical imidazole (eg, clotrimazole, miconazole nitrate, econazole) applied twice daily until the eruption resolves (usually 2 to 4 weeks). If this treatment is ineffective, a fungicidal topical agent like terbinafine or naftifine should be used. For widespread or resistant infections, an oral agent such as griseofulvin, terbinafine, itraconazole, or fluconazole may be used. If there is concomitant nail infection that requires treatment, oral terbinafine or itraconazole will be required.

Item C150A: Inflammatory tinea pedis on the instep of the foot.
Reprinted with permission from Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide.* 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016

Disorders that involve the feet and may mimic tinea pedis include pitted keratolysis, atopic dermatitis, and juvenile plantar dermatosis.

- Pitted keratolysis is caused by infection with *Kytococcus sedentarius, Dermatophilus congolensis,* or *Corynebacterium* species. The organisms produce proteases that degrade keratin in the stratum corneum, resulting in small shallow craters that may coalesce to form large superficial erosions located on the plantar surface of the foot (**Item C150B**). Infection usually occurs in the setting of excessive foot moisture. In addition to the skin changes, patients often report foot odor (the result of the production of sulfur-containing compounds). Treatment includes topical aluminum chloride (to reduce moisture) and a topical antibiotic (such as erythromycin, clindamycin, or mupirocin).
- Atopic dermatitis may involve the feet, especially in adolescents and young adults (**Item C150C**). Treatment may require a potent topical corticosteroid like clobetasol (class I) or fluocinonide (class II).
- Juvenile plantar dermatosis ("sweaty sock" syndrome) is caused by friction from footwear and excessive moisture. Cycles of foot moisture (due to sweating and occlusion by socks and shoes) and evaporative drying (when footwear is removed) likely contribute. Physical findings include scaling and erythema of the forefeet and toes with sparing of the interdigital spaces (**Item C150D**). Deep and painful fissures may occur. In addition to wearing absorbent socks, avoiding occlusive footwear, and sprinkling absorbent powder in shoes, an emollient (like petrolatum) should be applied after socks and shoes have been removed at the end of the day.

Item C150B: Pitted keratolysis on the plantar surface of the foot.
Courtesy of D. Krowchuk

Item C150C: Atopic dermatitis involving the feet.
Reprinted with permission from Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide.* 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016

Item C150D: Juvenile plantar dermatosis.
Reprinted with permission from Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide.* 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016

PREP Pearls
- Tinea pedis commonly presents as a pruritic eruption that involves the interdigital spaces with scaling and fissuring.
- Although atopic dermatitis, juvenile plantar dermatosis, and pitted keratolysis may mimic tinea pedis, these conditions are characterized by unique physical findings and lack interdigital involvement.

ABP Content Specifications(s)
- Recognize the clinical features associated with factitious dermatitis

Suggested Readings
- Section on Dermatology, American Academy of Pediatrics. Atopic dermatitis. In: Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide.* 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016:31–44 .
- Section on Dermatology, American Academy of Pediatrics. Tinea pedis. In: Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide.* 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016:273–276 .

Question 151

A 15-year-old, previously healthy adolescent boy visits your office with an 8-day history of fever, sore throat, malaise, and fatigue. He is febrile (39°C) and has pharyngeal erythema; exudative tonsillitis; palatal petechiae; bilateral, tender posterior cervical lymphadenopathy; and splenomegaly. Results of a rapid group A streptococcal antigen test are positive. Treatment with amoxicillin is initiated. Two days later, the boy develops a rash with worsening of symptoms (Item Q151).

Item Q151: Rash seen on the adolescent described in this vignette.
Reprinted with permission from Kimberlin DW, et al. Red Book Online. Elk Grove Village, IL. American Academy of Pediatrics; 2015.

Of the following, the BEST next step in the diagnostic evaluation is

  A. blood culture
  B. complete blood cell count
  C. Epstein-Barr virus antibody titers
  D. respiratory virus panel for adenovirus
  E. skin testing for penicillin allergy

Correct Answer: C

The adolescent boy in this vignette exhibits a clinical syndrome consistent with a diagnosis of infectious mononucleosis (IM), which is most frequently associated with primary Epstein-Barr virus (EBV) infection. Epstein-Barr virus is a ubiquitous human γ-herpesvirus that infects more than 95% of the global population by adulthood. B lymphocytes are the primary cellular target of EBV. Individuals between the ages of 15 and 24 years are at highest risk of developing IM, with an overall incidence of approximately 500 cases per 100,000 persons annually in the United States. In adolescents, transmission occurs via exposure to infected saliva and rarely via a sexual route. In preadolescents, the mode of transmission is unknown.

Primary EBV infections among young children are often asymptomatic. In adolescents and young adults, primary EBV infections frequently manifest as IM, which is characterized by fever, malaise or fatigue, pharyngitis (**Item C151A**), and cervical lymphadenopathy (**Item C151B**). An enlarged spleen may be palpable in 15% to 65% of cases during the first 3 weeks of illness. Uncommon manifestations include palatal petechiae (**Item C151C**), bilateral upper eyelid edema, and rash (3% to 15% of cases). The classic morbilliform rash associated with acute IM is noted during the first days of illness. It primarily involves the trunk and spares the extremities, and resolution occurs within 1 to 6 days of illness. The rash can also be macular, petechial, scarlatiniform, urticarial, or erythema multiforme.

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Item C151A: Exudative pharyngitis and tonsillitis associated with EBV infectious mononucleosis
Reprinted with permisison from Brien J and Kimberlin DW, et al. *Red Book Online.* Epstein-Barr virus infections. Elk Grove Village, IL. American Academy of Pediatrics 2015.
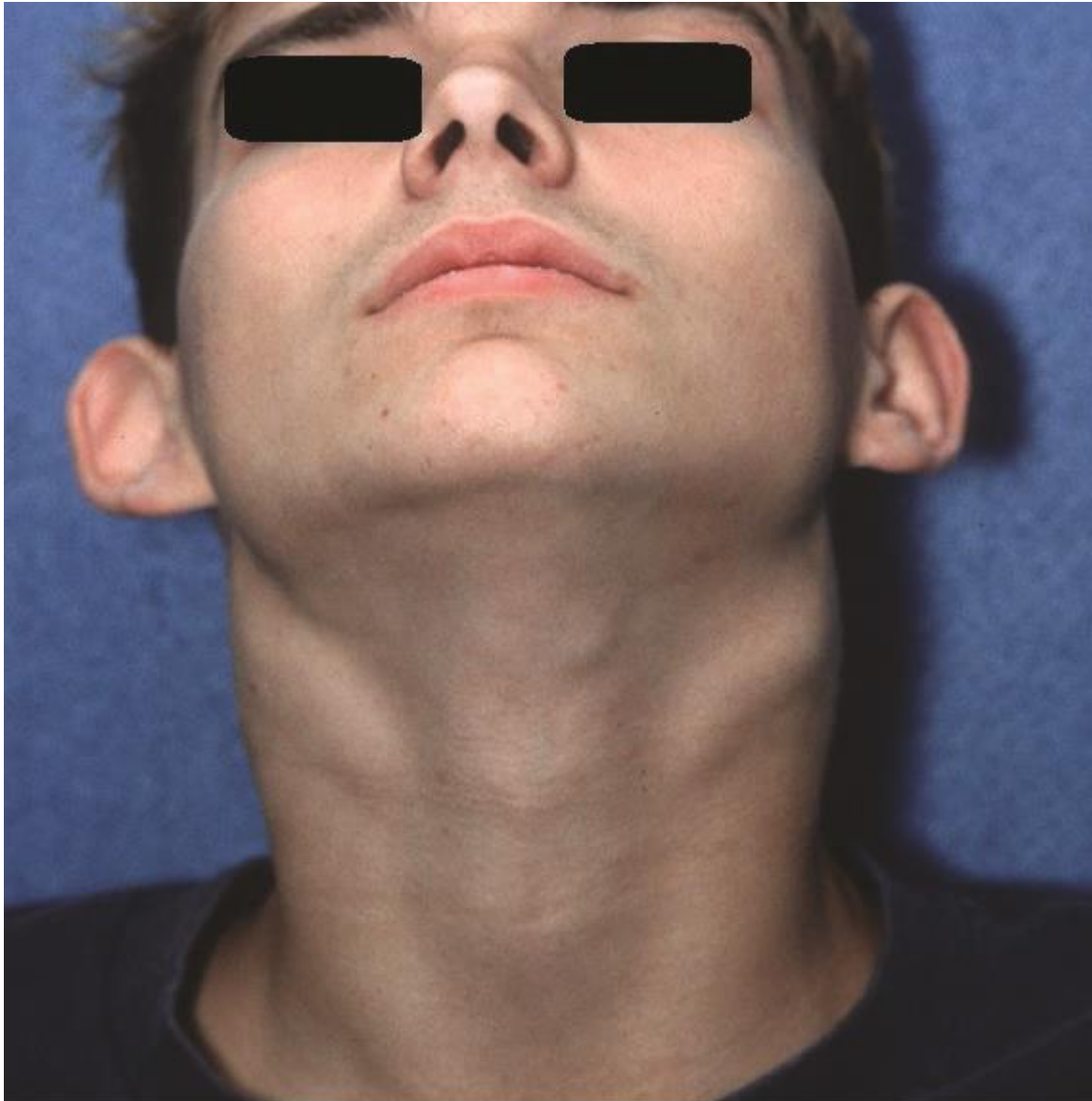
Item C151B: Bilateral cervical lymphadenopathy associated with EBV infectious mononucleosis
Courtesy of J. Brien.

Item C151C: Palatal petechiae associated with EBV infectious mononucleosis
Reprinted with permission from Kimberlin DW, et al. AAP RedBook Online. Epstein-Barr virus infections. Elk Grove Gillage, IL. American Academy of Pediatrics. 2015.

Patients with IM who are treated with antibiotics, especially amoxicillin or ampicillin, can develop a distinct morbilliform rash (**Item C151D**), like the adolescent boy in this vignette. Ampicillin-induced rash in acute IM was initially reported during the 1960s with an incidence of 80% to 100%. Similar eruptions have been reported after administration of cephalexin, erythromycin, levofloxacin, and tetracycline. A recent report has suggested a much lower incidence (approximately 30%) of antibiotic-induced rash following EBV-related acute IM. Compared to the spontaneous EBV exanthem, ampicillin-induced rash in individuals with EBV IM typically occurs within 1 week of treatment initiation and is more severe and generalized, involving the face, neck, trunk, extremities, and sometimes the palms and soles. The pathogenesis of aminopenicillin-induced rash is unclear. Various mechanisms have been postulated, including an allergic reaction, transient EBV-induced immunostimulation, or circulating complement-fixing immune complexes. However, studies have found no association with antibiotic dosing, treatment duration, history of atopy, or prior exposure to penicillin.
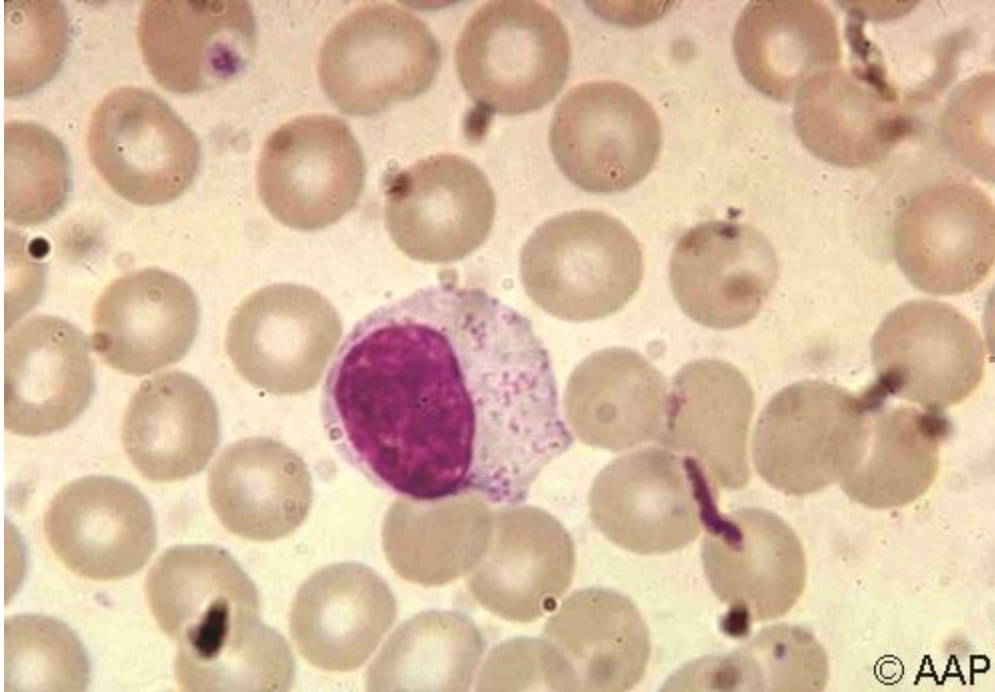
Item C151D: Ampicillin-induced generalized rash in a patient with EBV infectious mononucleosis
Reprinted with permission from Kimberlin DW, et al. *AAP RedBook Online*. Epstein-Barr virus infections. Elk Grove Village, IL. American Academy of Pediatrics. 2015.

The laboratory diagnosis of acute EBV infection is based on serology. Heterophile antibody tests (eg, Paul-Bunnell test or slide agglutination reaction test) primarily detect IgM and are sensitive (approximately 85%) in the diagnosis of IM in older children and adolescents during the first 2 weeks of illness. Heterophile antibodies are often absent in children younger than 4 years. A complete blood cell count may show marked lymphocytosis with an elevated number of atypical lymphocytes during the second week of illness. In a patient with symptoms and signs consistent with a diagnosis of acute IM, the detection of greater than 10% atypical lymphocytes on a peripheral blood smear (**Item C151E**) in conjunction with a positive heterophile antibody test result is diagnostic of acute EBV infection. Measurement of EBV-specific antibody titers is recommended for definitive diagnosis of EBV IM, especially in young children with suspected acute EBV infection or patients with heterophile antibody–negative IM. The detection of IgM

antibody against viral capsid antigen in the absence of antibodies against Epstein-Barr nuclear antigen confirms the diagnosis of recent acute EBV infection (**Item C151F**).

Item C151E: Atypical lymphocyte in a peripheral blood smear in a patient with EBV infectious mononucleosis

Reprinted with permission from Kimberlin DW, et al. AAP RedBook Online. Epstein-Barr virus infections. Elk Grove Village, IL. American Academy of Pediatrics. 2015.
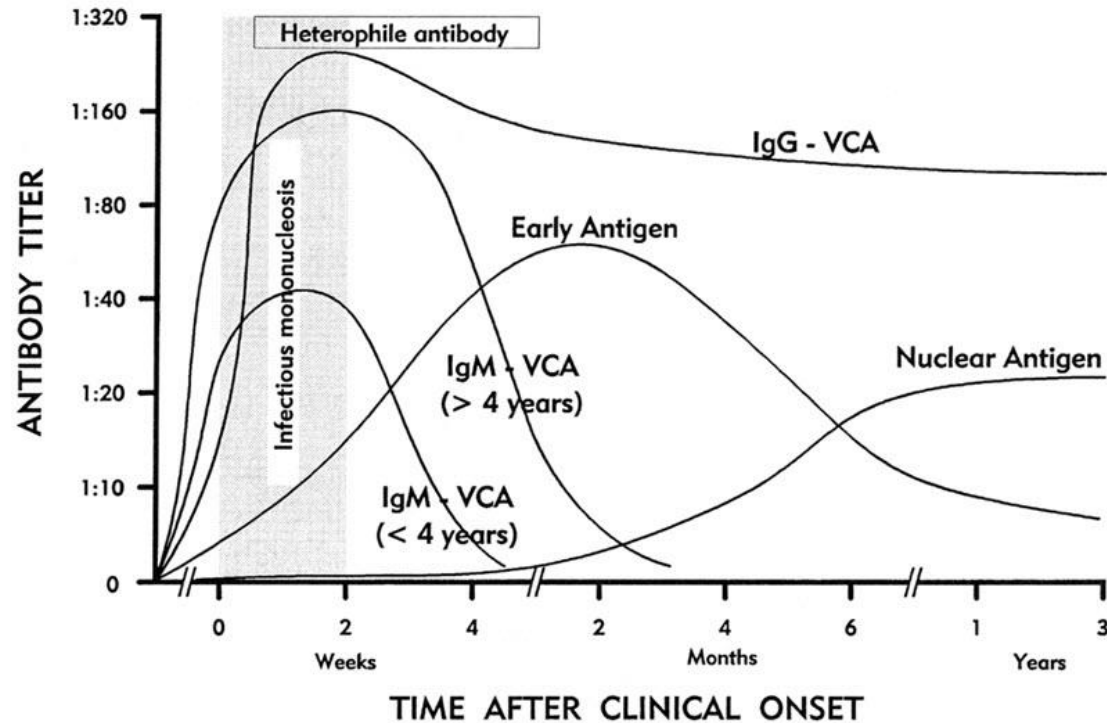
Item C151F: VCA, viral capsid antigen. EBV-specific serologic responses in infectious mononucleosis
Jenson HB. Epstein-Barr virus. In: Detrick B, Hamilton RG, Folds JD, eds. *Manual of Molecular and Clinical Laboratory Immunology.* 7th ed. Washington, DC: American Society for Microbiology; 2006:637–647

The natural history of EBV IM in most patients is characterized by recovery without sequelae. However, severe complications affecting a variety of organ systems can occur. Hematologic complications include hemolytic anemia, thrombocytopenia, aplastic anemia, disseminated intravascular coagulation, and hemophagocytic lymphohistiocytosis. Neurologic complications include aseptic meningitis, encephalitis, optic neuritis, facial nerve palsy, transverse myelitis, and Guillain-Barré syndromes. Other unusual but potentially life-threatening complications include splenic rupture, upper airway obstruction caused by severe tonsillar enlargement, and myocarditis. Epstein-Barr virus has been associated with solid tumors (eg, Burkitt lymphoma, nasopharyngeal carcinoma) and distinct lymphoproliferative disorders in immunocompromised patients (eg, transplant recipients, patients with HIV). Severe or fatal infectious mononucleosis can occur in male individuals with X-linked lymphoproliferative syndrome.

In addition to primary EBV infection, IM can also be caused by primary HIV, human herpesvirus 6, cytomegalovirus, or *Toxoplasma gondii* infection. The differential diagnosis of exudative pharyngitis also includes group A *Streptococcus* and other viral enanthems such as adenovirus and enterovirus. Given the classic presentation of IM and the severe rash following initiation of amoxicillin therapy, testing for EBV-specific antibody titers is the preferred test to confirm the diagnosis of primary EBV infection in the adolescent described in this vignette. The

clinical presentation makes a bacterial infection unlikely. The positive group A streptococcal antigen test likely represents colonization (reported in approximately 30% of patients with IM). The absence of conjunctivitis in the setting of exudative pharyngitis makes the diagnosis of adenovirus less likely. Finally, studies have demonstrated that re-challenge with ampicillin after resolution of EBV illness does not cause recurrence of rash, arguing against an IgE-mediated allergic reaction.

PREP Pearls

- Epstein-Barr virus is an ubiquitous human γ-herpesvirus that infects greater than 95% of the global population by adulthood. Adolescents and young adults with primary Epstein-Barr virus infections frequently exhibit infectious mononucleosis characterized by fever, malaise or fatigue, pharyngitis, and cervical lymphadenopathy.
- Patients with infectious mononucleosis treated with antibiotics, especially amoxicillin or ampicillin, can develop a distinct morbilliform rash.
- In a patient with infectious mononucleosis, the detection of greater than 10% atypical lymphocytes on a peripheral blood smear in conjunction with a positive heterophile antibody test result is diagnostic of acute Epstein-Barr virus infection.
- The presence of IgM antibody against viral capsid antigen in the absence of antibodies against Epstein-Barr nuclear antigen confirms the diagnosis of acute Epstein-Barr virus infection.

ABP Content Specifications(s)

- Recognize the potential complications of Epstein-Barr virus infection in normal and immunocompromised children of various ages
- Understand the significance of a rash following ampicillin therapy in patients with infectious mononucleosis

Suggested Readings

- American Academy of Pediatrics. Epstein-Barr virus infections (infectious mononucleosis). 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; 2015:336–339.
- Chovel-Sella A, Ben Tov A, Lahav E, et al. Incidence of rash after amoxicillin treatment in children with infectious mononucleosis. *Pediatrics.* 2013;131(5):e1424–e1427. doi: http://dx.doi.org/10.1542/peds.2012-1575.
- Jenson HB. Epstein-Barr virus. *Pediatr Rev.* 2011;32(9):375–384. doi: http://dx.doi.org/10.1542/pir.32-9-375.
- Pinninti S, Hough-Telford C, Pati S, Boppana S. Cytomegalovirus and Epstein-Barr virus infections. *Pediatr Rev.* 2016;37(6) 223–234. doi: http://dx.doi.org/10.1542/pir.2015-0072.

Question 152

You are seeing a 10-year-old boy in your office who was stung by a flying insect about 36 hours ago. Shortly after the sting he developed local itching and a red raised bump at the site of the sting. He has been taking diphenhydramine every 6 to 8 hours and applying cold packs, but the swelling has continued to increase. He has had no other rash, difficulty breathing, dizziness, or fever. His examination findings, including vital signs, are normal except for a red, raised, warm, mildly tender 12-cm area on his right lower leg.

Of the following, the MOST appropriate next step in management for this boy is to

A. continue oral diphenhydramine and application of cold packs
B. obtain serum specific immunoglobulin E antibodies to bee and wasp venom
C. prescribe clindamycin for developing cellulitis
D. prescribe an epinephrine injector to be used in the case of future stings
E. refer him to an allergist for venom immunotherapy

Correct Answer: A

The boy in the vignette has a large (>10 cm) local reaction to an insect sting. This type of reaction is characterized by erythema and swelling at the bite site, increasing in size for the first 24 to 48 hours, and often accompanied by itching or pain. While this is likely an immunoglobulin E–mediated event, it is not life threatening, and the child has no more than a 5% to 10% chance of developing a systemic response (anaphylaxis) to a subsequent insect sting. Treatment is symptomatic, with cool packs for swelling and antihistamines or topical corticosteroids for itching; therefore, treatment for this child would be to continue the current symptomatic care. Although there are no controlled studies to determine efficacy, many providers also recommend a short course of oral corticosteroids for large local reactions to shorten the duration of symptoms.

Local reactions can be confused with cellulitis because of the redness and swelling, but infection is unlikely to occur in the first 48 hours after a sting and generally would be accompanied by fever, systemic signs of illness, and a greater degree of tenderness at the site. Therefore, clindamycin would not be an appropriate treatment for this child.

While local reactions are much more common, in children, potentially life-threatening systemic reactions occur with 0.4% to 0.8% of insect stings; the incidence in adults is 3%. The offending insects belong to the order Hymenoptera, which includes bees, wasps, and ants. Systemic reactions can range from isolated cutaneous to potentially life-threatening multisystem involvement. Anaphylaxis involves 2 or more organ systems, one of which is typically the skin. Cutaneous reactions include hives, flushing, and angioedema. Respiratory symptoms can include throat tightening, cough, and wheezing; laryngeal edema is the most common respiratory cause of death in cases of anaphylaxis. Cardiovascular symptoms include dizziness, hypotension, bradycardia, and shock. Additional organ systems may be affected, including gastrointestinal (vomiting, diarrhea) and genital (uterine cramping). Symptoms can progress rapidly and lead to death.

Treatment for insect sting–induced anaphylaxis is the same as for other forms of anaphylaxis: immediate administration of intramuscular epinephrine. Epinephrine administration should not be delayed while antihistamines or corticosteroids are administered, because the latter 2 medications require several hours to produce benefits. More than 1 dose of epinephrine may be needed to reverse anaphylaxis. Additional supportive measures such as oxygen, airway management, intravenous fluids to reverse shock, and albuterol for wheezing may be needed as part of emergency department care, but should never take precedence over the administration of epinephrine. If the patient responds well and symptoms resolve quickly, he/she should still be observed in the emergency setting for at least 4 to 6 hours because of the small, but clinically significant, risk of a delayed anaphylactic reaction.

Appropriate care for a child who has had an anaphylactic reaction includes (1) education on insect avoidance; (2) a prescription for 1 to 2 epinephrine auto-injector(s), and (3) referral to an allergist for skin testing and probable venom immunotherapy. Skin testing is preferred over serum specific immunoglobulin E or the radioallergosorbent test, in part because studies

demonstrate that many adults who were stung, but had no systemic response, tested positive for sensitivity on serum tests. Serum testing is sometimes used in patients who have a clear history of an anaphylactic event, but have negative results on skin testing. Identification of the specific Hymenoptera that induced the event guides the type of venom immunotherapy that will be given. Skin testing and immunotherapy are not recommended for children and adolescents who had a purely cutaneous systemic reaction (hives, angioedema), because their risk for anaphylaxis with subsequent sting is quite low. No skin testing, immunotherapy, or epinephrine auto-injector is recommended for patients such as the child in the vignette, who have had only local reactions (**Item C152**).

Item C152. Algorithim for Treating Insect Stings.
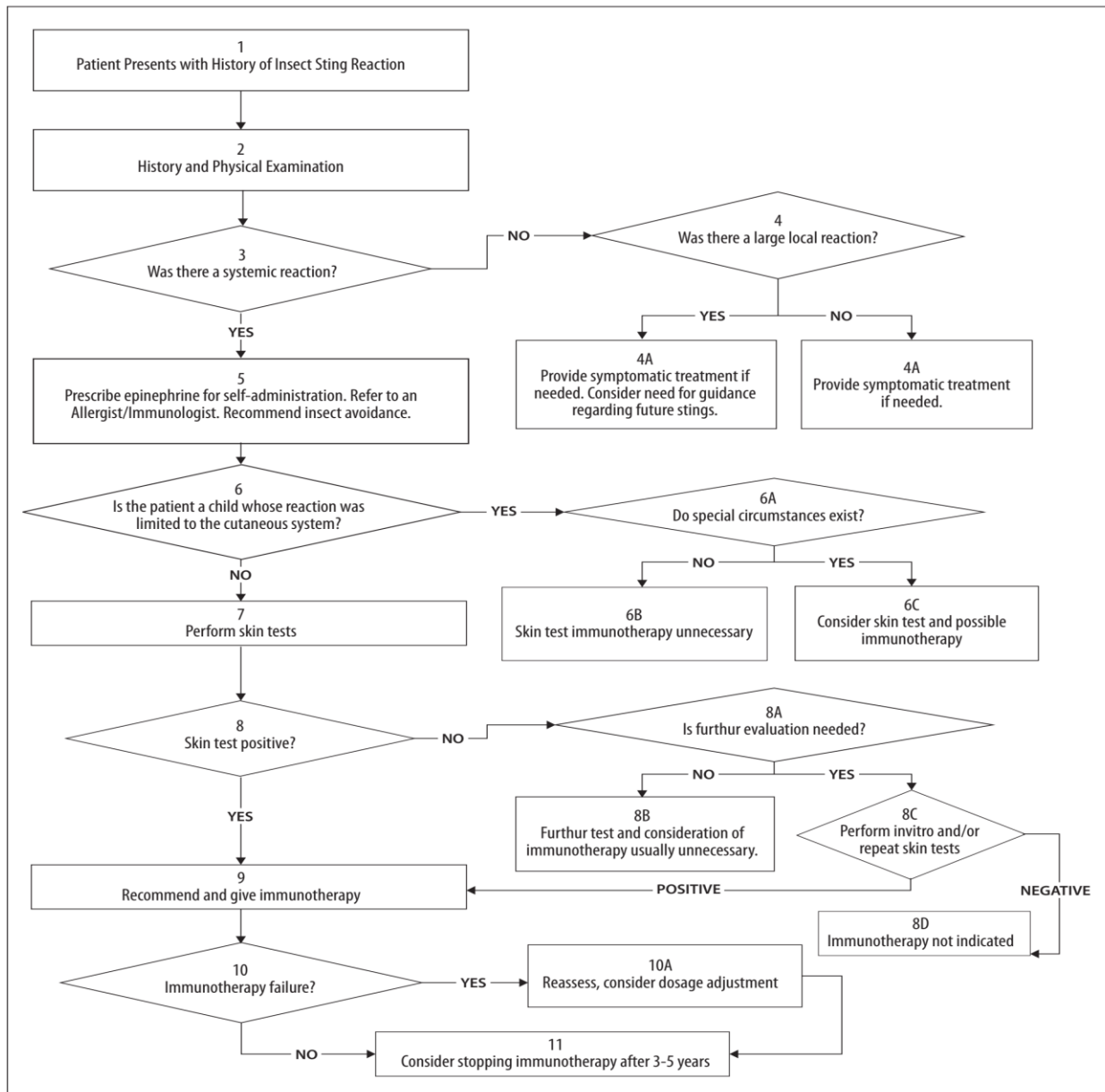
Reprinted with permission from Moffitt JE et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol*. 2004;114:869-886.

PREP Pearls
- The treatment of anaphylaxis due to insect sting is the immediate administration of intramuscular epinephrine.
- Local reactions to insect stings are treated with cool compresses, antihistamines, and topical corticosteroids as needed.
- Skin testing, immunotherapy, and epinephrine auto-injectors are not recommended for children who have had local reactions to insect stings.

ABP Content Specifications(s)
- Instruct families regarding the acute management of sting anaphylaxis at home

Suggested Readings
- Lieberman P, Nicklas RA, Randolph C, Oppenheimer J, et al. Anaphylaxis: a practice parameter update 2015. *Ann Allergy Asthma Immunol*. 2015;115:341–384.
- Moffitt JE, Golden DB, Reisman RE, et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol.* 2004;114:869–886. doi: http://dx.doi.org/10.1016/j.jaci.2004.07.046.
- Zimgibl G, Burrows HL. Hymenoptera stings. *Pediatr Rev.* 2013;33:534–535.

Question 153

A father brings his 8-year-old child to your office for a health supervision visit. He reports that he was recently diagnosed with Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer syndrome, after being diagnosed with colon cancer at 33 years of age. His mother died of metastatic uterine cancer in her 40s. He is concerned that his child is at risk for the disorder and would like your advice on when to test the child for the disorder.

Of the following, the BEST advice to offer regarding genetic testing for this child is

A. no testing is necessary
B. test the child after 18 years of age when the child can make an independent and informed decision
C. test the child at 33 years of age (his father's age at the time of the colorectal cancer diagnosis)
D. test the child now, but do not relay the result to the child, just the parents
E. test the child when pubertal signs develop

Correct Answer: B

The father and paternal grandmother of the child in this vignette have Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer syndrome. This adult-onset autosomal dominant hereditary cancer syndrome is associated with increased risks for colon, endometrial, ovarian, stomach, small intestine, hepatobiliary tract, urinary tract, and brain cancers as well as for sebaceous neoplasms (a subtype of skin cancer). Lifetime risks for types of cancer with Lynch syndrome vs the general population are noted in **Item C153** . The most common cancers encountered in a family history with Lynch syndrome are colon and uterine cancer. Lynch syndrome is caused by a germline pathogenic mutation in *MSH2, MSH6, MLH1, PMS2,* or *EPCAM*. To optimize outcomes based on specific cancer risks, the National Comprehensive Cancer Network developed guidelines for surveillance and management of Lynch syndrome.

Item C153. Cancer Risks in Individuals with Lynch Syndrome Age ≤ 70 Years Compared to the General Population.

Cancer Type	General Population Risk	Lynch Syndrome (*MLH1* and *MSH2* heterozygotes)	
		Risk	Mean Age of Onset
Colon	4.8%	52%-82%	44-61 years
Endometrium	2.7%	25%-60%	48-62 years
Stomach	<1%	6%-13%	56 years
Ovary	1.4%	4%-12%	42.5 years
Hepatobiliary tract	<1%	1.4%-4%	Not reported
Urinary tract	<1%	1%-4%	~55 years
Small bowel	<1%	3%-6%	49 years
Brain/central nervous system	<1%	1%-3%	~50 years
Sebaceous neoplasms	<1%	1%-9%	Not reported

Reprinted with permission from Kohlmann W, Gruber SB. Lynch syndrome. *GeneReviews*. 2014.

The malignancy risk in Lynch syndrome occurs during adulthood, making this an adult-onset genetic disorder. The Committee on Bioethics of the American Academy of Pediatrics (AAP) has advised against the predictive genetic testing of children for adult-onset genetic disorders until the child reaches adulthood or, rarely, in adolescence if the child has mature decision-making capacity. "Ethical and Policy Issues in Genetic Testing and Screening of Children" is a policy statement published by the AAP in 2013. The American College of Medical Genetics (ACMG) has also issued a similar policy statement. Both the AAP and the ACMG advocate that

the child's best interest should be the guiding principle in deciding who is offered testing and screening for genetic disorders. The ACMG and AAP both advocate for mandatory newborn screening for disorders that have implications during childhood where delayed intervention could lead to a less than optimal outcome or even death. Most genetic testing in childhood involves a diagnosis of inborn errors of metabolism, autism spectrum disorder, multiple congenital anomalies, or intellectual disability for potential diagnostic etiologies. Testing for adult-onset genetic disorders is discouraged unless an intervention in childhood would decrease morbidity and mortality. Because of ethical and legal reasons, a health care provider should be very cautious about ordering predictive genetic testing for minors without parental consent. This type of testing can have serious psychological, social, and medical ramifications to the minor and other family members. When a child is at risk for a childhood-onset genetic disorder, testing can be performed with appropriate parental consent and, if possible, the child's assent as well.

Adult-onset inherited disorders that a pediatrician may encounter in a family history include Huntington disease and hereditary breast and ovarian cancer syndrome caused by *BRCA* mutations; childhood screening of these disorders is discouraged. Several hereditary cancer syndromes, including familial adenomatous polyposis coli caused by *APC* mutations and Li Fraumeni syndrome caused by *TP53* mutations, have childhood management implications that warrant testing. This testing should be performed in the context of a formal genetic counseling visit with informed consent.

Genetic testing for hereditary adult-onset disorders during childhood is not recommended. Once the child becomes at least 18 years of age, he or she may pursue genetic testing but only in the setting of a formal genetic counseling session. Genetic testing should be considered before the age that the specific diagnosis would impact the management and surveillance of the individual. For the child in this vignette, no testing would be an incorrect choice because the child is at 50% risk to inherit Lynch syndrome; but, the testing should occur in adulthood rather than childhood. Although the child could wait until reaching 33 years of age to be tested, earlier testing should be encouraged because annual colonoscopies to screen for colorectal cancer would typically begin in the mid-20s, the age at which the child's management would vary from the general population.

PREP Pearls
- The American Academy of Pediatrics and the American College of Medical Genetics advise against predictive genetic testing of children for adult-onset genetic disorders until the child reaches adulthood or, rarely, adolescence if the child has mature decision-making capacity and only with appropriate informed consent and genetic counseling.
- Because of ethical and legal reasons, a health care provider should be very cautious about ordering predictive genetic testing for minors without parental consent, as this testing can have serious psychological, social, and medical ramifications for the minor and other family members.
- Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer syndrome, is an adult-onset autosomal dominant hereditary cancer syndrome associated with increased

risks for colon, endometrial, ovarian, stomach, small intestine, hepatobiliary tract, urinary tract, and brain cancers as well as sebaceous neoplasms, a subtype of skin cancers.

MOCA-Peds Objective
- Recognize and apply ethical principles regarding minors as decision makers

ABP Content Specifications(s)
- Recognize and apply ethical principles involved in use of technology for genetic studies in genetics counseling

Suggested Readings
- Caga-anan ECF, Smith L, Sharp RR, Lantos JD. Testing children for adult-onset genetic diseases. *Pediatrics*. 2012;129(1):163–167. doi: http://dx.doi.org/10.1542/peds.2010-3743.
- Committee on Bioethics; Committee on Genetics; American College of Medical Genetics and Genomics, Social, Ethical, and Legal Issues Committee. Policy statement: ethical and policy issues in genetic testing and screening of children. *Pediatrics*. 2013;131(3):620–622. doi: http://dx.doi.org/10.1542/peds.2012-3680.
- Kohlmann W, Gruber SB. Lynch syndrome. *GeneReviews*. 2014. https://www.ncbi.nlm.nih.gov/books/NBK1211/.
- Ross LF, Saal HM, David KL, Anderson RR; American Academy of Pediatrics; American College of Medical Genetics and Genomics. Technical report: ethical and policy issues in genetic testing and screening of children. *Genet Med.* 2013;15(3):234–245. doi: http://dx.doi.org/10.1038/gim.2012.176.

Question 154

A 9-month-old infant is brought to your office for evaluation of persistent watery diarrhea. You evaluated her 3 weeks ago for an episode of low-grade fever, vomiting, and diarrhea that was diagnosed as viral gastroenteritis. The mother reports that the fever and vomiting resolved after 3 to 4 days. Although the volume and frequency of diarrhea have improved, the infant's stools continue to be watery and more frequent than usual. In addition, the mother states that the infant is gassier and her stools are more malodorous than prior to this recent illness. There is no blood or mucus in her stools, and she continues to feed well. She eats a variety of puréed foods, in addition to breastfeeding. She is a well-developed, well-nourished infant with normal vital signs and weight gain. Her abdomen is nontender, but slightly distended with active bowel sounds. The remainder of the examination findings are unremarkable. A stool sample is negative for occult blood and has a pH of 5.0.

Of the following, the MOST likely etiology for the infant's symptoms is

  A. congenital lactase deficiency
  B. developmental lactase deficiency
  C. IgE-mediated milk protein allergy
  D. non-IgE–mediated milk protein allergy
  E. secondary lactase deficiency

Correct Answer: E

The persisting symptoms of frequent watery stools, flatulence, and malodorous stools in the infant in this vignette suggest malabsorption. The occurrence of these symptoms following an episode of viral gastroenteritis, plus the absence of blood and mucus in the stools or other systemic complaints in a well-nourished patient, supports the diagnosis of secondary lactase deficiency as the most likely etiology.

Lactose is the primary carbohydrate in mammalian milk. Lactose absorption requires lactase to hydrolyze the disaccharide into glucose and galactose in the small intestine. These monosaccharides can then be transported across the intestinal membrane. Lactose that escapes digestion and absorption by the small intestine passes into the colon where it is fermented by enteric bacteria. The byproducts of fermentation lower the stool pH to less than 6.0. The stools may also have positive test results for reducing substances. The fermentation products and the unfermented lactose cause the symptoms of lactose intolerance. The gases cause bloating, flatulence, and pain; the lactose causes osmotic diarrhea. The symptoms of lactose intolerance usually occur within a few hours of ingesting lactose, and the severity is determined by the amount consumed and the degree of lactase deficiency. Because lactase is located distally on the small intestinal villi, it is the most common disaccharidase to be affected by mucosal injury from infection or inflammation.

Lactose malabsorption may occur secondary to conditions that cause flattening of the villi or damage to the epithelium of the small intestine, resulting in decreased lactase levels or decreased transport across the intestinal mucosal wall. Small bowel bacterial overgrowth may also be associated with secondary lactose intolerance because of increased fermentation of ingested lactose. Acute gastroenteritis that is severe enough to cause intestinal injury (often due to rotavirus infection) is a common cause of transient lactose intolerance in young children. The symptoms are often not clinically relevant. Treatment of the underlying condition is the first step in treating secondary lactase deficiency and lactose malabsorption. If the child is symptomatic, one may consider prescribing supplemental lactase or probiotics, or recommending the temporary elimination of lactose from the diet.

Primary lactose malabsorption may be caused by congenital lactase deficiency, which is a rare autosomal recessive disorder that presents with intractable diarrhea soon after birth. Primary lactase deficiency more typically presents in childhood or adolescence and is caused by a genetically regulated reduction in lactase activity or availability. Developmental lactase deficiency is observed in premature infants born at less than 34 weeks of gestation. Lactase levels and activity increase as the gut matures.

Cow milk protein allergy is the most common food allergy in young children and may be IgE mediated, mixed, or related to non-IgE reactions. Exclusive breastfeeding during the first 4 to 6 months after birth reduces the risk for cow milk protein allergy. The clinical manifestations usually appear in the first few weeks to months after birth. The IgE-mediated reactions generally occur within minutes to 2 hours after ingestion and vary in severity from mild to life-threatening

anaphylaxis. Mixed or non-IgE–mediated reactions may present with acute or chronic conditions and usually have a delayed onset.

Cow milk protein allergy may be associated with respiratory, cutaneous, and gastrointestinal reactions. Milk protein allergy that is IgE mediated may present with wheezing, stridor, otitis media with effusion, urticaria, angioedema, atopic dermatitis, vomiting, diarrhea, colic, or anaphylactic shock. Pulmonary hemosiderosis, contact or atopic dermatitis, gastroesophageal reflux, colic, constipation, failure to thrive, food protein–induced enterocolitis syndrome, eosinophilic gastrointestinal disorders, and protein-losing enteropathy are the range of clinical presentations of non-IgE–mediated milk protein allergy. Individuals with cow milk protein allergy often have stools that contain mucus and occult or frank blood, which helps to differentiate them from individuals with lactose intolerance.

PREP Pearls
- Frequent, watery, nonbloody, acidic, and malodorous stools, mild abdominal distention, and flatulence are characteristic symptoms of lactose intolerance.
- Lactose malabsorption may occur secondary to conditions that cause flattening of the villi or damage to the epithelium of the small intestine.
- Acute gastroenteritis is a common cause of secondary lactose intolerance that is transient in young infants and children.
- Individuals with cow milk protein allergy often have stools that contain mucous and occult or frank blood and may experience a range of respiratory, cutaneous, and gastrointestinal reactions.

ABP Content Specifications(s)
- Differentiate milk protein allergy from lactose intolerance

Suggested Readings
- American Academy of Pediatrics Committee on Nutrition. Carbohydrate and dietary fiber. In: Kleinman RE, Greer FR, eds. *Pediatric Nutrition.* 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:387–406.
- American Academy of Pediatrics Committee on Nutrition. Food allergy. In: Kleinman RE, Greer FR, eds. *Pediatric Nutrition.* 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:845–862.
- Heyman MB. Lactose intolerance in infants, children, and adolescents. *Pediatrics*. 2006;118(3):1279–1286. doi: http://dx.doi.org/10.1542/peds.2006-1721.
- Vandenplas Y, Koletzko S, Isolauri E, et al. Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Arch Dis Child*. 2007;92(10):902–908.

Question 155

You are examining a 2-week-old neonate in your office. She was born at 38 weeks of gestation weighing 2.6 kg. She is breast and bottle feeding well, and has lost 7% of her birthweight. Her mother reports 2 to 3 bowel movements daily. On physical examination, you note jaundice, mild hypertelorism, and a 2/6 systolic ejection murmur radiating to the back. The remainder of her physical examination findings are unremarkable. The neonate's total bilirubin level is 7.8 mg/dL (133.4 µmol/L) and conjugated bilirubin level is 5.6 mg/dL (95.8 µmol/L).

Of the following, the MOST likely diagnosis in this neonate is

A. Alagille syndrome
B. congenital cytomegalovirus infection
C. galactosemia
D. urinary tract infection
E. Wilson disease

Correct Answer: A

The neonate in the vignette has a normal unconjugated bilirubin and an elevated conjugated bilirubin level. Although she has not regained birthweight by 2 weeks of age, her number of bowel movements suggests adequate milk intake. Her elevated conjugated bilirubin level, in combination with findings of hypertelorism and a murmur of peripheral pulmonic stenosis, suggest the diagnosis of Alagille syndrome.

Hyperbilirubinemia in a neonate can be characterized as physiologic jaundice, breastfeeding jaundice, or pathologic jaundice. Many neonates have physiologic jaundice, with an elevated unconjugated bilirubin because of decreased activity of glucuronyl transferase and increased enterohepatic circulation. Significant hyperbilirubinemia is concerning in the first days after birth because neonates have increased permeability of the blood-brain barrier. Bilirubin can pass into the brain and cause permanent neuronal damage, resulting in the clinical syndrome of acute bilirubin encephalopathy. Typically, these neonates present with fever, high-pitched shrill cry, opisthotonos, and retrocollis posturing.

Cholestasis is defined as a conjugated bilirubin concentration greater than 2 mg/dL (34.2 μmol/L) or greater than 20% of the total bilirubin level. All neonates who are more than 14 days old with jaundice should be evaluated with a total and conjugated bilirubin level. The differential diagnosis for conjugated hyperbilirubinemia includes urinary tract infection; genetic syndromes such as Alagille syndrome, galactosemia, total parenteral nutrition–associated cholestasis, α_1-antitrypsin deficiency, medication side effect; and congenital anomalies such as biliary atresia.

Evaluation of a neonate with cholestasis should include transaminase levels, a γ-glutamyltransferase level, and urinalysis. Because the Kasai procedure to surgically correct biliary atresia is most successful in the first 2 months after birth, any neonate with evidence of cholestasis must undergo gallbladder ultrasonography to confirm the absence of biliary atresia. The newborn screening results should also be reviewed for galactosemia. Urinalysis can screen for both a urinary tract infection and reducing substances suggestive of galactosemia.

Alagille syndrome is the most common form of familial intrahepatic cholestasis. Clinical characteristics include cardiac defects (peripheral pulmonic stenosis is the most common), short stature, vertebral anomalies, and cholestatic liver disease because of a paucity of bile ducts. Characteristic facial features include a prominent forehead, pointed chin, hypertelorism, deep-set eyes (**Item C155**). Affected children may also have posterior embryotoxon, an opaque ring around the cornea, due to thickening of the ring of Schwalbe. Alagille syndrome has an autosomal dominant inheritance pattern with variable penetrance because of mutations primarily in the *JAG1* gene.

Item C155: Boy with facial features characteristic of Alagille syndrome.
Courtesy of M. Rimsza

Mild cholestasis is seen with congenital cytomegalovirus infection, but typically there are no associated cardiac defects. Neonates with galactosemia present with feeding intolerance, failure to thrive, and possibly cataracts. A neonate with cholestasis due to a urinary tract infection likely would show signs of poor feeding and would not have hypertelorism or a cardiac defect. Wilson disease, a disorder of copper excretion in the biliary system, causes cholestasis in older children

and adolescents. Of note, in older children with Wilson disease, copper deposition causes a Kayser Fleischer ring around the cornea visualized with slit lamp examination.

PREP Pearls
- In a neonate, Alagille syndrome may present with cholestasis, cardiac murmur, and vertebral anomalies.
- Alagille syndrome results from mutations in the *JAG1* gene.
- Neonates with cholestasis, defined as a conjugated bilirubin level greater than 20% of the total bilirubin, should undergo prompt abdominal ultrasonography to evaluate for biliary atresia.

MOCA-Peds Objective
- Evaluate a patient with jaundice beyond the neonatal period.

ABP Content Specifications(s)
- Understand strategies to prevent the development of severe hyperbilirubinemia in newborn infants
- Recognize metabolic diseases that can produce conjugated hyperbilirubinemia in neonates
- Recognize disorders associated with conjugated hyperbilirubinemia in neonates

Suggested Readings
- American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114:297. doi: http://dx.doi.org/10.1542/peds.114.1.297.
- Brumbaugh D, Mack C. Conjugated hyperbilirubinemia in children. *Pediatr Rev*. 2012;33:291. doi: http://dx.doi.org/10.1542/pir.33-7-291.
- Setia S, Villaveces A, Dhillon P, et al. Neonatal jaundice in Asian, white, and mixed-race infants. *Arch Pediatr Adolesc Med*. 2002;156(3):276–279. doi: http://dx.doi.org/10.1001/archpedi.156.3.276.

Question 156

During the initial health supervision visit, the mother of a newborn girl tells you that she is having a difficult time adjusting to life as the parent of 2 children. She tells you she is exhausted from the demands of feeding and caring for her newborn, and has been having a difficult time with her 2-year-old son who has been having more frequent tantrums. She is a single parent whose family lives in another state. The mother asks you where she can get help.

Of the following, the BEST next step in this situation is to refer this mother to

  A. a breastfeeding support group
  B. an early intervention program
  C. a Head Start program
  D. a home visiting program
  E. The Women, Infants, and Children Program

Correct Answer: D

The single mother described in the vignette is in need of psychological support, and could benefit from parenting guidance and additional support. A home visiting program could provide these services for this mother facing the challenge of raising 2 young children on her own.

Home visiting programs improve physical and mental health outcomes for parents and children, as well as children's developmental outcomes. Home visits by skilled professionals (eg, nurses, social workers, early childhood educators) empower parents by building parenting skills and knowledge. Administered by the Health Resources and Services Administration (HRSA), the nationwide Maternal, Infant, and Early Childhood Home Visiting Program or Federal Home Visiting Program was established to implement evidence-based home visiting models (eg, Early Head Start–Home Based Option, Healthy Families America, Nurse-Family Partnership, Parents as Teachers) to improve maternal and child health. States receive funding to establish programs to serve at-risk expectant parents and families with children from birth to kindergarten entry. These programs may include developmental and behavioral screening, maternal mental health screening, case management with linkage to medical services, social programs, educational programs, family support services, parenting skills training, and counseling on healthy habits.

Other resources for maternal and family support during prenatal, perinatal, and early infancy periods include federally funded health centers for low-cost health care and services, and faith-based services through religious entities such as churches, synagogues, or temples. A call to the 2-1-1 resource and information helpline may identify community-based services that cover a range of essential needs including food, housing, health care, disaster services, and employment.

A breastfeeding support group can help the mother in the vignette with any breastfeeding difficulties and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) can provide nutritional information, healthy supplemental food, and linkage with health care resources. However, these programs do not provide the variety of supports at the level needed by the mother in the vignette. An early intervention program provides services for children birth to 3 years of age who exhibit developmental delays, but there is no indication that her 2-year-old boy would qualify for the program. His frequent tantrums are likely in response to the change in the family's constellation.

The children in this family are too young for the Head Start program, which serves preschool-aged children. However, Early Head Start programs do provide child development, health and mental health, and family support services for low-income pregnant women and children younger than 3 years. Services are federally funded and community based and would be appropriate for supporting the health, development, and functioning of the family in the vignette. The Early Head Start-Home Based Option is an evidence-based home visiting model.

Pediatricians can effectively support families in the prenatal and perinatal periods and early infancy by knowing the resources available. Home visiting programs are an important evidence-based intervention for these families.

PREP Pearls
- Home visiting programs improve physical and mental health outcomes for parents and children, as well as improve children's developmental outcomes.
- The 2-1-1 resource and information helpline may identify community-based services that cover a range of essential needs including food, housing, health care, disaster services, and employment.
- Early Head Start provides child development, health and mental health, and family support services for low-income pregnant women and children younger than 3 years.

MOCA-Peds Objective
- Manage breast-feeding difficulties

ABP Content Specifications(s)
- Identify resources for maternal/familial support during the prenatal and perinatal periods and early infancy

Suggested Readings
- Adirim T, Supplee L. Overview of the federal home visiting program. *Pediatrics*. 2013;132(S2):S59–S64. doi: http://dx.doi.org/10.1542/peds.2013-1021C.
- Avellar SA, Supplee LH. Effectiveness of home visiting in improving child health and reducing child maltreatment. *Pediatrics*. 2013;132(S2):S91–S99. http://pediatrics.aappublications.org/content/132/Supplement_2/S90.

Question 157

After you introduce yourself during a routine health supervision visit, your male patient is able to clearly tell you his first and last name, but not his phone number. You offer him some crayons and paper while you visit with his parents. They do not report any health concerns. He likes to dress himself, but needs some help with tying his shoes. He can brush his teeth fairly well and is toilet trained. He tells you he likes to play with blocks and can build a house. His mother adds that he will play simple board games that involve matching colors, but gets angered by games that involve a lot of rules, especially if others win. He is very inquisitive and asks a lot of "why" questions. He is a well-developed, well-nourished child who is able to hop on 1 foot 7 times, but is not able to skip. He tells you he is good at riding his tricycle and catching a ball. You note that he is able to copy a square, but not a triangle.

Of the following, these findings are MOST typical for a child whose age is

A. 30 months
B. 36 months
C. 48 months
D. 60 months
E. 72 months

Correct Answer: C

The child described in this vignette exhibits the cognitive-behavioral and motor milestones typically attained by 4 years of age. These milestones include:

- Language: clearly states first and last name, speaks in paragraphs using past and present tense, is 100% intelligible to family and strangers, identifies 5 or 6 colors, asks many "why" questions
- Social-emotional: dresses self but not yet able to tie shoelaces, brushes teeth and uses toilet independently, plays simple interactive board games, voices frustration about rules, displays curiosity, begins to understand the feelings of others, shows increased cooperative play
- Gross motor: hops on 1 foot several times, catches a large ball, performs a standing broad jump
- Fine motor: builds a house with blocks, copies a cross and square, holds a crayon well, cuts with scissors on a line

A younger child would have less advanced language skills. The ability to tell a story about an experience that includes past and present tense plus the ability to relate some emotion and the perspective of others is not typical until 4 years of age. Most 4 year olds will not be able to recite their telephone number, which is a skill more typical of a child entering kindergarten at 5 years of age. By 60 months of age and beyond, a child's language will have grown to more than 2,000 words; they form sentences with 6 to 8 words and are able to answer "why" questions. A 6-year-old child is able to read words by site recognition and exhibits beginning phonemic awareness.

Social-emotional development progresses from the imitative and pretend parallel play found at 30 months of age to simple imaginative play and cooperative sharing with a peer at 36 months of age. Four-year-old children are usually able to distinguish between real and imaginary; they can play in groups of 3 or 4; and their imaginative play is becoming more complex. At 60 months of age and beyond, children are acquiring the social skills demanded in larger structured group settings, such as school. Self-help skills of dressing, toileting, and brushing teeth need more assistance in the younger child. The 4-year-old child is able to accomplish most of these tasks independently, but the dexterity to tie shoelaces is usually not present until 5 years of age. The ability to play games with more involved rules emerges at 6 years (72 months) of age.

For gross motor skills, a 30-month-old child is able to jump in place, and a 36-month-old child is learning to pedal a tricycle and hop a few times on 1 foot. A 5 year old is able to skip, hop on 1 foot more than 10 times, and perform a running broad jump. Coordination, balance, and speed continue to show improvement in the 6-year-old child.

Fine motor skills are demonstrated through building blocks. At 30 months of age, a tower of 8 cubes can be built. This skill progresses to a 3-block bridge at 36 months and to a 5-block gate or simple house at 48 months. Early literacy skills such as drawing and cutting can also be used to assess fine motor skills. Vertical and circular strokes will begin to form in the scribbling of a 24 month old. By 36 months of age a child can copy a circle. Copying a cross or square is typical for the 4 year old, copying a triangle is present at 5 years, and copying a diamond can be

demonstrated by a 6 year old. A 3 year old can cut paper with child-safe scissors, but is not able to cut on a line until 4 years of age or to cut more refined shapes well until 60 months or older. A comprehensive summary of developmental milestones can be found in Table 1 of "Developmental Milestones: Motor Development" (*Pediatr Rev*. 2010;31[7]:267-277).

PREP Pearls
- Language milestones attained by 4 years of age include: clearly states first and last name, speaks in paragraphs using past and present tense, is 100% intelligible to family and strangers, identifies 5 or 6 colors, asks many "why" questions.
- Social-emotional milestones attained by 4 years of age include: dresses self but not yet able to tie shoelaces, brushes teeth and uses toilet independently, plays simple interactive board games, voices frustration about rules and displays curiosity, begins to understand the feelings of others, shows increased cooperative play.
- Gross motor milestones attained by 4 years of age include: hops on 1 foot several times, catches a large ball, performs a standing broad jump.
- Fine motor milestones attained by 4 years of age include: builds a house with blocks, copies a cross and square, holds a crayon well, cuts with scissors on the line.

ABP Content Specifications(s)
- Evaluate the motor developmental progress/status of a child at 4 years of age
- Evaluate the cognitive and behavioral developmental progress/status of a child at 4 years of age

Suggested Readings
- Feigelman S. Middle childhood. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics*. Philadelphia, PA: Elsevier; 2016:79–84.
- Feigelman S. The preschool years. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics*. Philadelphia, PA: Elsevier; 2016:76–79.
- Gerber RJ, Wilks T, Erdie-Lalena C. Developmental milestones 3: social-emotional development. *Pediatr Rev*. 2011;32(12):533–536. doi: http://dx.doi.org/10.1542/pir.32-12-533.
- 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.
- 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 158

You are seeing a 30-month-old boy for a health supervision visit. His mother reports that the child typically walks on his toes. The child is otherwise healthy. He was born at 37 weeks of gestation and has been meeting all developmental milestones appropriately. On physical examination, the boy has normal tone and reflexes. His hip range of motion is full and symmetric. He has 10 degrees of ankle dorsiflexion with the knees extended bilaterally. When the child is standing still, his heels are on the ground. However, while you are observing his gait, he consistently walks on his toes.

Of the following, the BEST next management step for this child is

A. observation with reevaluation in 6 months
B. referral for serial casting to stretch the calf muscles
C. referral for surgical lengthening of the Achilles tendon
D. use of custom ankle foot orthoses during the day
E. use of shoe inserts with an arch support

Correct Answer: A

The boy in the vignette consistently walks on his toes, but has no history of abnormal development or functional limitations. Toe-walking is a normal variant in children younger than 3 years of age and no treatment is warranted for this boy.

Idiopathic toe-walking is common in young children, with an incidence of about 5%. Toe-walking resolves in more than half of children by 5.5 years of age. In children with developmental disorders, such as autism, toe-walking occurs much more frequently and has a lower rate of spontaneous improvement. While toe-walking does not appear to result in any serious sequelae (eg, arthritis), affected children and adults may have an increased risk of ankle sprains and lower extremity pain. In addition, toe-walking leads to higher energy expenditure than walking with a heel-toe gait; for this reason, individuals with toe-walking may have decreased exercise tolerance.

Children with idiopathic toe-walking typically present to medical attention between the ages of 2 and 4 years. Parents often note that toe-walking has been present since their children began walking. When evaluating these children, physicians should ask about functional limitations, history of prematurity, abnormal development (especially gross motor, social, and language), and family history. Idiopathic toe-walking is often familial.

Physical examination of affected children should include assessment of tone, strength, and reflexes. Most children with idiopathic toe-walking are able to stand with their heels in contact with the ground. Toddlers and preschool age children with toe-walking typically have good ankle flexibility. Calf muscle contractures often develop when toe-walking persists into school age. The differential diagnosis for idiopathic toe-walking includes cerebral palsy, muscular dystrophy, and spinal cord abnormalities (eg, tethered cord). Idiopathic toe-walking should be bilateral and symmetric. Unilateral toe-walking should always be evaluated further, because it could indicate the presence of hemiplegia, developmental dysplasia of the hip, or leg-length discrepancy.

The approach to treatment of idiopathic toe-walking is controversial given the lack of data from high-quality studies. Physical therapy may be useful for both muscle lengthening and teaching parents to provide postural cues about gait. Use of ankle foot orthoses (AFOs) at night allows children to maintain calf muscle flexibility but does not directly change the toe-walking motor pattern. Children appear to be more likely to have heel strike during gait when wearing rigid shoe inserts or AFOs; however, toe-walking typically recurs when these orthoses are discontinued. Serial casting is thought to improve flexibility and "train" children to use a normal heel-toe gait, though there are no prospective, controlled studies demonstrating efficacy. Surgery to lengthen the Achilles tendon can compromise gastrocnemius and soleus strength, and should be considered as a last resort for children with functional limitations and chronic pain.

PREP Pearls
- Toe-walking is a normal variant in children younger than 3 years and no treatment is warranted in this age range.
- Unilateral toe-walking should always be evaluated further, because it may indicate the presence of hemiplegia, developmental dysplasia of the hip, or leg-length discrepancy.
- The approach to treatment of idiopathic toe-walking is controversial given the lack of data from high-quality studies.

ABP Content Specifications(s)
- Understand the significance of toe-walking in patients of various ages

Suggested Readings
- Engstrom P, Tedroff K. The prevalence and course of idiopathic toe-walking in 5-year-old children. *Pediatrics*. 2012;130(2):279–284. doi: http://dx.doi.org/10.1542/peds.2012-0225.
- Ruzbarsky JJ, Scher D, Dodwell E. Toe walking: causes, epidemiology, assessment, and treatment. *Curr Opin Pediatr.* 2016;28(1):40–46. doi: http://dx.doi.org/10.1097/MOP.0000000000000302.
- Schoeneker P, Rich M, Gordon JE. The lower extremity. In: Weinstein SL, Flynn HM, eds. *Lovell & Winter's Pediatric Orthopaedics.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:chap 27:1261–1340.

Question 159

A 6-year-old girl is brought to your office for evaluation of nonspecific periumbilical abdominal pain and loose stools. The mother reports that the girl has previously had intermittent transient abdominal pain, but the frequency of pain has increased. She has been soiling her underwear with small amounts of nonbloody loose stool for 2 weeks. Her previous stooling pattern was reported as 1 small stool every day or every other day. When the girl had a urinary tract infection at 4 years of age, a doctor recommended a stool softener, but the mother discontinued the medication after 1 month. The girl has always been a picky eater, refusing most fruits and vegetables, but her appetite is now decreased. She is voiding normally and is otherwise well.

She has normal growth parameters and velocity; normoactive bowel sounds; an abdomen that is soft and nontender with a sausage-shaped mass palpable in the left lower quadrant; and deep tendon reflexes that are normal. Rectal examination reveals a normal anal wink, slight dilation of the rectal vault, and the presence of a hard stool mass.

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

A. begin an oral stimulant laxative
B. encourage increased dietary fiber
C. perform a mineral oil enema
D. recommend behavioral therapy
E. try a gluten-free diet

Correct Answer: C

The girl in this vignette exhibits many of the clinical features associated with fecal overflow incontinence. Given the hard stool mass present in a dilated rectal vault, the best initial step in management is to remove the fecal impaction by performing an enema.

Encopresis is the repetitive involuntary passage of feces into inappropriate places after the age of 4 years when most children have attained continence. The most common cause of functional encopresis is chronic constipation leading to overflow incontinence. Children may not respond to the urge to defecate for a variety of reasons: fear of pain associated with prior episodes of passing large dry stools or the presence of anal fissures; fear related to prior negative or punishing parenting practices of toilet training; unsubstantiated fears related to sitting upon or flushing the toilet; timidness about stooling in a public restroom; and being too busy or distracted by enjoyable activities. When the urge to defecate is ignored, the rectal vault stretches to accommodate a greater volume. Repeated withholding causes further stretching and the retained stool becomes larger, drier, and harder. Passage of stool becomes increasingly more difficult, which leads to further avoidance of defecation, and eventually a large impacted fecal mass is formed. The pressure of this mass on the anosphincter complex makes voluntary closure of the external anal sphincter more difficult. Eventually semi-formed and liquid stool leaks around this mass. The child is often unaware of the fecal soiling because the chronic dilation impairs sensation, decreases rectal tone, and leads to pelvic floor dysfunction.

The clinical features of the girl in this vignette that are typical of chronic constipation and may be associated with fecal overflow incontinence or functional encopresis include:
- Intermittent transient nonspecific or lower left quadrant abdominal pain that is increasing in frequency
- Involuntary, and perhaps unrecognized, soiling of underwear with small amounts of nonbloody loose stool in the context of a prior stooling pattern of small or infrequent stools
- History of stool softener or laxative use
- Previous episode of urinary tract infection or enuresis
- Decreased appetite because of early satiety
- A diet with limited intake of natural fiber
- Normal growth parameters
- The presence of a fecal mass in the left lower quadrant, dilation of the rectal vault, and fecal impaction

External indirect pressure of the fecal mass on the urethra and bladder, plus increased intra-abdominal pressure may lead to enuresis, incomplete voiding, or rectal prolapse. Dysfunctional voiding, in combination with increased urethral exposure to enteric pathogens from soiling in the underwear, leads to the greater prevalence of recurrent urinary tract infections, especially in female patients.

The management of encopresis has 4 key components: disimpaction, maintenance pharmacotherapy, behavioral modification, and education of the patient and

family. Disimpaction may be performed manually. Enemas, suppositories, oral polyethylene glycol, or magnesium citrate may also be used. After disimpaction, the use of an oral stimulant laxative, stool softeners/lubricants, or osmotic laxatives is necessary to maintain regular stooling. If these treatments are initiated without prior disimpaction, the patient may experience discomfort from abdominal cramping and additional overflow incontinence. Maintenance therapy should continue until 1 or 2 soft bowel movements are passed daily, the rectal vault has returned to normal capacity, and normal sensation and anal sphincter functionality have resumed. Dietary and behavioral modifications are integral to the successful management of functional constipation. Celiac disease or gluten sensitivity may present with a range of gastrointestinal problems including constipation and diarrhea; this etiology should be given consideration in patients who do not respond to the routine management of encopresis. Family education must emphasize that fecal overflow incontinence is not intentional, relapses are common, and the corrective process is long.

PREP Pearls
- Encopresis is the repetitive involuntary passage of feces into inappropriate places after the age of 4 years when most children have attained continence.
- The most common cause of functional encopresis is chronic constipation leading to overflow incontinence.
- The management of encopresis has 4 components: initial disimpaction, maintenance pharmacotherapy, behavioral modification, and education of the patient and family.

ABP Content Specifications(s)
- Understand the physiologic effects of stool retention
- Recognize the clinical features associated with fecal overflow incontinence
- Recognize co-morbidities commonly associated with encopresis
- Plan the appropriate management of encopresis of various etiologies

Suggested Readings
- Biggs WS, Dery WH. Evaluation and treatment of constipation in infants and children. *Am Fam Physician.* 2006;73(3):469–477.
- Colombo JM, Wassom MC, Rosen JM. Constipation and encopresis in childhood. *Pediatr Rev.* 2015;36(9):392–402. doi: http://dx.doi.org/10.1542/pir.36-9-392.
- Har AF, Croffie JM. Encopresis. *Pediatr Rev.* 2010;31(9):368–374. doi: http://dx.doi.org/10.1542/pir.31-9-368.

Question 160

You are caring for a child who is eligible for a randomized and blinded study to evaluate a new medication compared to standard therapy. The family has declined enrollment in the study and asks that you give the standard medication. The residents on your rotation ask how many patients need to be enrolled in the study to get valid results. You discuss the need for appropriate sample size as an important component needed to obtain meaningful results of valid research.

Of the following, this component of research design has a direct effect on

A. choice of statistical test
B. consent process
C. funding
D. methodology
E. power

Correct Answer: E

One of many challenges to conducting good research is determining, recruiting, and maintaining the needed sample size. A researcher does not ethically want to impose the research on more children than necessary; yet, there needs to be enough participants for the results to be meaningful. Therefore, researchers often use power calculations to determine the necessary number of participants or sample size. The power of a study is the probability that the difference between 2 variables in a study are true differences that did not occur by chance. These power calculations are based on assumptions from prior research or clinical problems.

There are 3 concepts that standard power calculations are based on:
- A researcher needs to know the targeted difference between the possible outcomes of the study.
- A researcher needs to pre-identify a level of risk they are willing to take in determining if any difference identified between the 2 variables in a study is by chance alone (type 1 error rate [chance of finding a difference where none exists] or α, which is conventionally 5% or a *P* value of .05).
- A researcher must specify the probability that the difference between the variables is a true difference (this is the statistical power, conventionally 80%-90%, which relates to the type 2 error [chance of not detecting a difference when one exists] or β; power = 1 – β).

The needed sample size increases with a smaller probability of type 1 error, a larger power, or a smaller relevant difference between study groups. **Item C160** depicts an approach to sample size relative to power. Choice of statistical test, consent process, funding, and methodology are necessary considerations for a research project, but they are not affected by sample size.

Item C160. Determining Adequate Sample Size.

Estimating Nuisance Parameters

Is information available from previous studies for a reliable estimate of the clinically meaningful difference in the primary outcome?

— YES →

Scenario 1: Options

A standard sample size calculation can be made using mathematical formulas or readily available software.

↓ NO

Is reliable information available from either other pediatric (eg., older children) or adult populations? Is reliable information available from a similar condition?

— YES →

Scenario 2: Options

- Make the sample size calculation using the estimated nuisance parameters from the similar studies.
- Use Bayesian methods to incorporate prior information and/or expert opinion as "pseudo-information" in your new trial.

↓ NO

Scenario 3: Options

- Do an "internal pilot" with small sample and use its resultant nuisance parameters to estimate sample size needed for entire trial.
- Compute a sample size based on effect size.

→

Recruitment Problems

Once you have computed your sample size, is there going to be problems in recruiting the required number of participants (eg, rate disease, limited recruitment potential, ethical issues)?

NO

YES ↓

Proceed with trial.

Scenario 4: Options

- Use an alternative study design such as cross-over or repeated measures.
- Perform a meta-analysis of N of 1 trials.
- Use a sequential design.
- Perform a prospective meta-analysis.
- Perform a trial using an adaptive design.

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PREP Pearls
- The needed sample size increases with a smaller probability of type 1 error (finding an effect where none exists, false positive), a larger power, or a smaller relevant difference between study groups.
- The power of a study is the likelihood of finding a true effect vs an effect caused by chance. The larger the power of the study, the larger the sample size needed.

MOCA-Peds Objective
- Understand the principles and application of study design

ABP Content Specifications(s)
- Understand how sample size affects the power of a study

Suggested Readings
- Jennings JM, Sibinga E. Demystifying type I and type II errors. *Pediatr Rev*. 2010;31(5):209–210. doi: http://dx.doi.org/10.1542/pir.31-5-209.
- Van der Tweel I, Askie L, Vandermeer B, et al. Standard 4: determining adequate sample sizes. *Pediatrics*. 2012;129(S3):S138–S145. doi: http://dx.doi.org/10.1542/peds.2012-0055G.

Question 161

A 16-year-old boy is brought to your office for a health supervision visit in August. He reports good overall health and states that he has been working 2 jobs over the summer—one at a fast food restaurant and the other with his parents' moving company. His height is 173 cm (45th percentile) and weight is 73 kg (83rd percentile). His body mass index is 24.5 kg/m2 (86th percentile). The adolescent states that he knows he has gained weight recently, which he attributes to both increased fast food consumption and "building muscle," lifting heavy boxes as part of his employment experience. He asks you if he is "too fat."

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

  A. he is at risk for being overweight
  B. he is obese
  C. he is overweight
  D. his growth is normal
  E. his growth parameters cannot be interpreted because he is physically active

Correct Answer: C

The adolescent in the vignette, who has increased his physical activity level but also his intake of non-nutritive, high-density foods, can accurately be diagnosed as overweight. Identification of children and adolescents with obesity, overweight, and risk for obesity is recommended as part of pediatric preventive care. Doing so offers opportunities for tailored prevention and treatment of this common chronic condition. Body mass index (BMI), based on weight and height, and adjusted for age and gender, is widely used to diagnose overweight and obesity. A BMI at the 95th percentile or greater indicates obesity and at or above the 85th percentile designates a child as overweight. BMI is an imprecise measure of adiposity; skinfold and abdominal girth are better measures. Extremely fit individuals, such as professional athletes, can have a high BMI, but little body fat.

Even among children with a normal BMI, the trend over time can be a starting point for preventive measures against overweight and obesity. It has been suggested that the degree of change in BMI from childhood to adulthood could be a marker for those at risk for more severe morbidity from obesity. It is important to note that even small decreases in BMI can have significant positive effects on blood pressure and lipid measurements.

Management of overweight and obese children should focus on education and behavior change for the whole family. The home environment should support healthy eating and increased physical activity. This includes having less unhealthy food brought into the home, greater availability of more nutritious foods, and less opportunity for sedentary behaviors. This environment can be bolstered by community and school-level interventions. Most successful interventions for obesity management have some degree of goal-setting and self-monitoring. Better communication strategies among household members (eg, children and their parents) can help facilitate changes at home. Motivational interviewing techniques, to assess desire for and barriers to change, can be helpful.

PREP Pearls
- A body mass index (BMI) at or above the 95th percentile indicates obesity and at or above the 85th percentile designates a child as overweight.
- Management of overweight and obese children should focus on education and behavior change for the whole family.
- Most successful interventions for obesity management have some degree of goal-setting and self-monitoring.

ABP Content Specifications(s)
- Understand the uses and limitations of the various anthropometric techniques available to assess growth and/or nutritional status

Suggested Readings

- Daniels SR, Hassink SG, Committee on Nutrition. The role of the pediatrician in primary prevention of obesity. *Pediatrics*. 2015;136(1):e275–e292. doi: http://dx.doi.org/10.1542/peds.2015-1558.
- Rome ES. Obesity prevention and treatment. *Pediatr Rev*. 2011;32(9):363–373. doi: http://dx.doi.org/10.1542/pir.32-9-363.

Question 162

A 7-year-old girl presents to your office with fever and sore throat. She had a temperature of 38.3°C on the previous day, and has had a sore throat for 2 days. Last night she developed nasal congestion and cough. Her eyes are itchy and she has been rubbing them. Her appetite is mildly decreased. She denies headache or abdominal pain. Her mother states that 2 of the girl's siblings have had symptoms of runny nose and cough, but with a less pronounced sore throat. A classmate recently had "Strep throat." On physical examination, the girl is afebrile. She has mild bilateral conjunctival erythema. Her posterior pharynx is erythematous with tonsillar exudate. She has small, palpable anterior cervical lymph nodes. Her lungs are clear to auscultation and her abdomen is nontender, with no organomegaly.

Of the following, the MOST appropriate strategy to use in the diagnosis and management of this girl is

  A. a heterophile antibody test
  B. antihistamine prescription
  C. a rapid antigen detection test for group A Streptococcus
  D. a rapid antigen detection test for group A Streptococcus, and, if negative, a throat culture
  E. supportive care

Correct Answer: E

The most appropriate strategy to use in the diagnosis and management of the girl in the vignette is supportive care. A sore throat with fever in children and adolescents prompts many pediatric primary care visits. The most common infectious causes of pharyngitis are respiratory viruses (eg, adenovirus); group A *Streptococcus* (GAS); and coxsackie, herpes, and Epstein Barr viruses.

Distinguishing between GAS and viral causes of pharyngitis guides treatment. For patients presenting with overt viral symptoms (eg, cough, rhinorrhea, and conjunctivitis), and lacking symptoms common in GAS (eg, headache, abdominal pain, palatal petechiae, and enlarged anterior cervical lymph nodes), testing for GAS is not necessary. For children without viral symptoms or with overlapping symptoms (eg, cough and abdominal pain), rapid antigen *Streptococcus* testing (RAST) should be performed on pharyngeal secretions obtained by swabbing the tonsillar arches and posterior pharynx. In children (but not adults), if the result of RAST is negative, a second sample should be sent for GAS culture because RAST is only about 90% sensitive. Alternatively, the clinician can obtain a sample for culture only (ie, no RAST) if results are expected to return within 48 hours and the family can be readily contacted to start antibiotics if needed.

Prescribing antibiotics for presumed GAS without testing is not appropriate. Multiple studies have demonstrated that even experienced clinicians overdiagnose GAS in patients with fever and sore throat. Even for those with classic symptoms, GAS is the cause only about 50% of the time.

For the girl in the vignette, adenovirus is the most likely cause of her symptoms. Adenovirus commonly presents with pharyngoconjunctival fever, and the appropriate management is supportive care. Testing for adenovirus is not usually needed unless other conditions (eg, Kawasaki disease) are being considered. Although topical antihistamines can provide some relief for the symptoms of conjunctivitis, these can sometimes irritate the eyes further. Oral antihistamines are not helpful to treat pharyngoconjunctivitis.

Epstein-Barr virus is a common cause of pharyngitis, which is more severe in older children and adolescents. Heterophile antibodies are often not present in young children, thus, for the 7-year-old child in the vignette, serologic testing would be required to make this diagnosis.
There are several potentially serious causes of pharyngitis that require urgent evaluation and intervention. These include peritonsillar abscess, characterized by a unilaterally enlarged tonsil; and if the child is ill-appearing, a retropharyngeal abscess, epiglottitis, or Lemierre syndrome should be suspected.

PREP Pearls

- Children presenting with pharyngitis along with overt viral symptoms do not need testing for group A *Streptococcus* (GAS).
- Rapid antigen *Streptococcus* testing (RAST) or culture should be performed before prescribing antibiotics for streptococcal pharyngitis.
- In children with suspected GAS pharyngitis with a negative rapid antigen test result, a second sample should be sent for GAS culture, because RAST is only about 90% sensitive.

ABP Content Specifications(s)

- Formulate a differential diagnosis of exudative tonsillitis/pharyngitis
- Plan the appropriate diagnostic evaluation of tonsillitis/pharyngitis

Suggested Readings

- Bhumbra N, Wroblewski ME. Adenovirus. *Pediatr Rev.* 2010;31(4):173–174. doi: http://dx.doi.org/10.1542/pir.31-4-173.
- Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012 Nov 15;55(10):1279–82. doi: http://dx.doi.org/10.1093/cid/cis847.

Question 163

A 12-year-old boy is brought to your office for a health supervision visit. His body mass index has dropped from the 50th to the 20th percentile. His mother reports that he has developed anxiety around eating and is not eating as much as he used to following an episode of food impaction several months ago. He was able to clear the impaction prior to evaluation in the emergency department. He reports no dysphagia, odynophagia, or emesis. He now takes longer than the entire family to eat and is drinking large volumes of water with meals. His medical history is positive for eczema and asthma.

He has normal vital signs. He appears to be thin and is in no distress. He has no oral lesions. His abdomen is soft, nontender to palpation, and without mass.

Of the following, the MOST likely diagnosis is

A. achalasia
B. eosinophilic esophagitis
C. esophageal stricture
D. gastroesophageal reflux disease
E. nutcracker esophagus

Correct Answer: B

The boy in this vignette has eosinophilic esophagitis. This diagnosis is based on his history of food impaction, slow eating with excessive chewing and flushing his food down with large volumes of liquids, and atopy (asthma and eczema). He reports no dysphagia or odynophagia, which would be expected with esophageal stricture, achalasia, and nutcracker esophagus. Children with gastroesophageal reflux are not likely to experience food impactions. Eosinophilic esophagitis is an allergy/immune condition in which large numbers of eosinophils are found in the esophagus. This chronic condition is summarized in **Item C163**.

Item C163. Summary of Eosinophilic Esophagitis.

Epidemiology	• Prevalence: 4.3 per 10,000 • Boy to girl ratio: 3 to 1
Diagnostic findings	• Endoscopy findings: longitudinal furrows, white exudates, edema, friability • Histology findings: > 15 eosinophils per high power field
Short-term complications	• Food impactions • Esophageal candidiasis

Long-term complications	• Stricture formation:
	  – 5% prevalence in children
	  – 71% prevalence after 20 years of untreated disease

Differential diagnosis	• Esophagitis–peptic, infectious • Esophageal stricture • Esophageal stenosis • Esophageal dysmotility including achalasia

Courtesy of C. Waasdorp Hurtado

Presentation can vary significantly but may include the following:
- Gastroesophageal reflux that is unresponsive to acid blockade
- Food refusal in infants and toddlers
- Odynophagia
- Chronic abdominal pain and vomiting in school-aged children
- Dysphagia with food impactions in adolescents and adults
- Prolonged chewing and food lubrication (excessive sauce use or liquid consumption with eating)
- A history of asthma, food allergies, eczema, chronic rhinitis, or familial atopy in two-thirds of patients

Eosinophilic esophagitis can be a challenging diagnosis because of the broad differential diagnosis and overlap of symptoms. The gold standard for diagnosis is evaluation of esophageal biopsies. Untreated gastroesophageal reflux can appear very similar to eosinophilic esophagitis with eosinophils on biopsy. Therefore, children should be placed on proton pump inhibitors for a minimum of 6 weeks prior to endoscopy. In children with eosinophilic esophagitis, the esophagus often demonstrates longitudinal furrows, white plaques, and pallor. Biopsies should include both distal and proximal esophagus. Eosinophilic esophagitis is diagnosed if there are more than 15 eosinophils per high power field while on a proton pump inhibitor.

PREP Pearls
- Eosinophilic esophagitis is an allergy/immune condition in which large numbers of eosinophils are found in the esophagus.
- Eosinophilic esophagitis typically presents in infants and toddlers with food refusal and in school-aged children with chronic abdominal pain and vomiting.
- The prevalence of stricture in children with eosinophilic esophagitis is 5%.

ABP Content Specifications(s)
- Recognize the clinical features associated with eosinophilic or allergic esophagitis

Suggested Readings

- Beausoleil JL, Brown-Whitehorn T. Allergic and atopic features of children with eosinophilic esophagitis. In: Liacouras CA, Markowitz JE, eds. *Eosinophilic Esophagitis.* New York, NY: Humana Press; 2012:239–252.
- Markowitz JE, Liacouras CA. Eosinophilic esophagitis: treatment approach in children. In: Liacouras CA, Markowitz JE, eds. *Eosinophilic Esophagitis.* New York, NY: Humana Press; 2012:409–418.
- Papadopoulou A, Koletzko S, Heuschkel R, et al. Management guidelines of eosinophilic esophagitis in childhood. *J Pediatr Gastroenterol Nutr.* 2014;58(1):107–118. doi: http://dx.doi.org/10.1097/MPG.0b013e3182a80be1.
- Sorser SA, Barawi M, Hagglund K, Almojaned M, Lyons H. Eosinophilic esophagitis in children and adolescents: epidemiology, clinical presentation and seasonal variation. *J Gastroenterol.* 2013;48(1):81–85. doi: http://dx.doi.org/10.1007/s00535-012-0608-x.
- Sutton AG, Mir M, Steiner MJ. Esophagitis: allergic and eosinophilic. *Pediatr Rev.* 2015;36(8):375–376. doi: http://dx.doi.org/10.1542/pir.36-8-375.

Question 164

An 8-year-old boy is brought to the emergency department for multiple episodes of vomiting since awakening this morning. His mother reports a 2-week history of polyuria, polydipsia, and nocturnal enuresis after being dry at night for the past 4 years. A review of systems is significant for recent fatigue and weight loss. His medical history is not significant, and he takes no medications. On physical examination, the boy's temperature is 37°C, heart rate is 120 beats/minute, blood pressure is 98/64 mm Hg, respiratory rate is 30 breaths/minute, and weight is 20.4 kg (10th percentile). He is tired-appearing, but interactive. He has deep respirations, and his capillary refill is 3 seconds. The remainder of his physical examination findings are within normal parameters.

Laboratory investigation reveals the following:
•Sodium, 130 mEq/L (130 mmol/L)
•Potassium, 5.2 mEq/L (5.2 mmol/L)
•Chloride, 91 mEq/L (91 mmol/L)
•Bicarbonate, 8 mEq/L (8 mmol/L)
•Blood urea nitrogen, 26 mg/dL (9.3 mmol/L)
•Creatinine, 1.0 mg/dL (88.4 µmol/L)
•Glucose, 620 mg/dL (34.4 mmol/L)
•Venous pH, 7.0
•Serum ketones, high
•Urinalysis, large glucose, large ketones

Of the following, the BEST initial management step for this boy is to

 A. administer intravenous half-normal saline with potassium at twice-maintenance rate
 B. give 2 mEq/kg of intravenous sodium bicarbonate over 1 hour
 C. give 10 mL/kg of intravenous normal saline over 1 hour
 D. give a 0.1 unit/kg bolus of intravenous insulin
 E. start an insulin drip at 0.1 unit/kg per hour

Correct Answer: C

The boy described in the vignette meets the diagnostic criteria for diabetic ketoacidosis (DKA): blood glucose greater than 200 mg/dL (11.1 mmol/L), venous pH less than 7.3 or bicarbonate less than 15 mmol/L, and ketonemia plus ketonuria. He also has evidence of significant volume depletion with tachycardia, prolonged capillary refill time, and elevated blood urea nitrogen and creatinine. Although care should be taken to not give excessive fluids, current consensus guidelines recommend initiation of fluid therapy before starting insulin. For those with volume depletion, 0.9% saline is recommended at 10 to 20 mL/kg over 1 to 2 hours, repeated as needed to restore adequate tissue perfusion. Hence, giving 10 mL/kg of intravenous normal saline over 1 hour is the most appropriate initial management step for this boy.

Subsequent fluid administration should provide daily maintenance requirements plus the estimated fluid deficit given evenly over 48 hours. This rate usually does not exceed 1.5 to 2 times maintenance. Isotonic fluid should be continued for at least the first 4 to 6 hours, and thereafter, fluid should be administered with 0.45% or greater saline plus potassium at a concentration of at least 40 mEq/L (due to total body potassium depletion). Administration of intravenous half-normal saline with potassium at twice-maintenance rate is appropriate after the first 4 to 6 hours, but is not the best initial management step.

Guidelines recommend insulin administration at 0.05 to 0.1 unit/kg per hour after 1 to 2 hours of fluid therapy. Starting insulin within the first hour of fluid therapy is associated with an increased risk of cerebral edema. Thus, starting intravenous insulin is not the best initial management step for the boy in the vignette nor is a bolus of intravenous insulin, which can also worsen hypokalemia.

Insulin is required to correct the acidosis and clear the ketones. The glucose level corrects before the acidosis, and it is important to avoid hypoglycemia. Therefore, until the acidosis corrects, as the glucose level falls, dextrose should be added to the fluids rather than decreasing the insulin infusion rate. Sodium bicarbonate should not be given to children with DKA, because it is associated with an increased risk of cerebral edema.

Cerebral edema is the major complication of DKA. Fortunately it is rare, but it can cause significant morbidity and mortality. Cerebral edema has been associated with greater dehydration and acidosis at presentation, greater volumes of fluid given in the first 4 hours, and insulin administration during the first hour of fluid administration. Its cause is unclear. A proposed mechanism is that cerebral hypoperfusion before treatment causes cytotoxic injury, predisposing the brain to reperfusion injury and subsequent edema during treatment. Rapid overhydration should be avoided to prevent reperfusion injury; however, underhydration or delayed hydration carries the risk of worsening the cerebral cytotoxic injury caused by dehydration and acidosis. Diabetic ketoacidosis may occur as the initial presentation of diabetes or with existing diabetes. Common presenting symptoms include polyuria, polydipsia, fatigue, weight loss, nausea, vomiting, abdominal pain, and rapid breathing. Symptoms can mimic gastroenteritis, viral syndromes (eg, influenza), acute abdomen, pneumonia, or asthma. Thus, a high index of suspicion for diabetes is necessary to avoid delayed diagnosis. The nausea, vomiting, and

abdominal pain occur secondary to elevated ketone bodies, as does a fruity or acetone (similar to nail polish remover) breath odor. Deep, sighing (Kussmaul) respirations may occur secondary to acidosis. Physical examination findings may be significant for signs of dehydration and altered mental status. In addition to the biochemical criteria of DKA described, the white blood cell count is increased secondary to stress and a left shift is common. Serum sodium will be low because of hyperglycemia, and should be assessed after correction for the plasma glucose level. The serum potassium may be low, normal, or elevated; however, total body potassium depletion is characteristic in DKA. Potassium should be replaced regardless of the serum potassium level.

PREP Pearls
- Common presenting symptoms of diabetic ketoacidosis (DKA) include polyuria, polydipsia, fatigue, weight loss, nausea, vomiting, abdominal pain, and rapid breathing.
- Symptoms of DKA can mimic other common conditions, so a high index of suspicion for diabetes is necessary.
- Consensus guidelines for management of DKA recommend initiation of fluid therapy before starting insulin. For those with volume depletion, 0.9% saline is recommended at 10 to 20 mL/kg over 1 to 2 hours, repeated as needed to restore adequate tissue perfusion.
- Cerebral edema is a major complication of DKA. It is associated with greater dehydration and acidosis at presentation, greater volumes of fluid given in the first 4 hours, insulin administration in the first hour of fluid treatment, and bicarbonate administration.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Recognize the risks associated with fluid and electrolyte therapy in a patient with diabetic ketoacidosis
- Plan the appropriate management of diabetic ketoacidosis
- Recognize the clinical and laboratory features associated with diabetic ketoacidosis

Suggested Readings
- Cooke DW, Plotnick L. Management of diabetic ketoacidosis in children and adolescents. *Pediatr Rev.* 2008;29(12):431-5; quiz 436. doi: http://dx.doi.org/10.1542/pir.29-12-431.
- Gregory JM, Moore DJ, Simmons JH. Type 1 diabetes mellitus. *Pediatr Rev.* 2013;34(5):203-15. doi: http://dx.doi.org/10.1542/pir.34-5-203.
- Watts W, Edge JA. How can cerebral edema during treatment of diabetic ketoacidosis be avoided? *Pediatr Diabetes.* 2014 Jun;15(4):271-276.
- Wolfsdorf JI, Allgrove J, Craig ME, et al; International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes.* 2014;15(suppl 20):154–179. doi: http://dx.doi.org/10.1111/pedi.12165.

Question 165

A 4-month-old, 26-week-gestation male infant develops a runny nose, cough, and poor feeding. He is brought to the hospital because of progressive difficulty breathing. He undergoes intubation and mechanical ventilation because of hypoxic and hypercapnic respiratory failure. Over the next 3 days, he requires high ventilator settings to maintain gas exchange. His temperature is 37°C, heart rate is 130 beats/min, blood pressure is 90/50 mm Hg, respiratory rate is 30 breaths/min, and oxygen saturation is 93% on 50% oxygen from the ventilator. On physical examination, the boy is sedated and in no apparent distress. His heart sounds are regular without murmurs. He is warm and well-perfused. Breath sounds are decreased bilaterally, with mid- to end-expiratory wheezes, crackles, and rhonchi evenly scattered throughout all lung fields. Arterial blood gas analysis reveals a pH of 7.20, partial pressure of carbon dioxide of 72 mm Hg, and partial pressure of oxygen of 70 mm Hg.

Of the following, this infant's compensatory mechanism over the next several days will MOST likely include increased

  A. alveolar dead space
  B. alveolar diffusion of carbon dioxide
  C. renal absorption of bicarbonate
  D. renal absorption of chloride
  E. renal excretion of sodium

Correct Answer: C

The boy in the vignette has acute-on-chronic lung disease due to his prematurity and superimposed intercurrent illness. As a result, he has primary respiratory acidosis. The most likely consequence of this respiratory acidosis, over the next several days, is renal compensation with increased renal absorption of bicarbonate.

The acid-base balance in the blood is largely controlled through the equilibrium of the carbonic anhydrase reaction:

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

In acute respiratory acidosis, there is initially a small increase in bicarbonate concentration, because the rise in CO_2 shifts this equilibrium to the right. In the red blood cell, the hydrogen ion that is produced is buffered by intracellular proteins, further driving the reaction to the right and producing bicarbonate. The bicarbonate is then exchanged with chloride at the erythrocyte cell membrane, which increases the serum bicarbonate level. This acute compensation only raises the serum bicarbonate level by 1 mmol/L for every 10 mm Hg of increased partial pressure of carbon dioxide (Pco_2).

When respiratory acidosis continues for several days, increased absorption of bicarbonate then occurs at the level of the nephron. Increased arterial Pco_2 causes the diffusion of carbon dioxide into proximal tubule cells where, because of the equilibrium of the carbonic anhydrase reaction, hydrogen ion is produced. As opposed to the mechanism in the erythrocyte, in the nephron, pH and electroneutrality are achieved by the increased secretion of hydrogen ion into the tubular lumen and urine. This increases bicarbonate (HCO_3^-) production which enters the circulation, increases sodium reabsorption, decreases chloride reabsorption (leading to hypochloremic metabolic acidosis), and increases ammonium chloride excretion. The consequence of this renal compensation for chronic respiratory acidosis is generally a rise in serum bicarbonate of 3.5 mEq/L (3.5 mmol/L) for every 10 mm Hg of Pco_2. The expected changes in pH for the acute and chronic phases of respiratory acidosis would be:

Acute respiratory acidosis: delta pH = $0.008 \times (40 - Paco_2)$
Chronic respiratory acidosis: delta pH = $0.003 \times (40 - Paco_2)$

For the boy in the vignette, alveolar dead space (the lung units participating in ventilation but not perfusion), may increase during his acute illness, but the mechanism is not compensatory. Although tachypnea, increased alveolar ventilation, and increased Pco_2 diffusion can occur in response to an acute illness, the boy in the vignette demonstrates impaired alveolar ventilation as evidenced by his rise in Pco_2. As described before, renal absorption of chloride and excretion of sodium would both be decreased in this situation because of the increased level of intraluminal hydrogen ion.

PREP Pearls
- In the acute phase of respiratory acidosis, serum bicarbonate rises slightly (approximately 1 mmol/L for every 10 mm Hg of increased partial pressure of carbon dioxide [Pco_2]) due to buffering by intracellular proteins.
- In the chronic phase of respiratory acidosis, over days or longer, serum bicarbonate rises approximately 3.5 mmol/L for every 10 mm Hg of increased Pco_2, because of the increased reabsorption of bicarbonate at the renal tubular level.

ABP Content Specifications(s)
- Identify the renal compensatory changes associated with primary respiratory acidosis

Suggested Readings
- Kellum JA. Determinants of plasma acid-base balance. *Crit Care Clin.* 2005;21(2):329–346.
- Martinu T, Menzies D, Dial S. Re-evaluation of acid-base prediction rules in patients with chronic respiratory acidosis. *Can Respir J.* 2003;10(6):311–315.

Question 166

A 15-year-old boy is seen with a complaint of hip pain that developed acutely the previous day while he was sprinting during track practice. He felt a pop in the front of his right hip and had immediate onset of pain. On physical examination, the boy has tenderness to palpation over his anterior inferior iliac spine. He exhibits pain and weakness with resisted hip flexion, and pain with passive extension of the hip. You obtain radiographs of the hips (Item Q166).

Item Q166: Radiograph for the adolescent described in the vignette.
Courtesy R Carl

Of the following, the MOST accurate statement is that this boy's hip condition

 A. has an infectious cause that was aggravated by running
 B. involves tearing of the hip extensor muscles
 C. is due to immaturity of the pediatric skeleton
 D. is likely to require surgery
 E. is more likely to occur in obese adolescents

Correct Answer: C

The adolescent in the vignette has sustained an anterior inferior iliac spine (AIIS) apophyseal avulsion injury. This type of injury occurs due to the relative weakness at the apophysis, a cartilaginous area of bone growth.

An apophysis is a "minor" growth plate, an area of bone growth that does not contribute to lengthening of a long bone. Most apophyses are sites at which muscles attach to bones via tendons. An apophyseal avulsion occurs when a strong muscle contraction causes a piece of bone to pull away from the skeleton at the relatively weak apophysis. The most common sites of apophyseal injuries around the pelvis are the anterior superior iliac spine (ASIS), AIIS, ischial tuberosity, and iliac crest.

Athletes who experience avulsion of a pelvic apophysis typically describe feeling a "pop" associated with sudden pain while performing dynamic activities such as sprinting or kicking. These injuries typically occur during early to mid-adolescence. On physical examination, affected teens generally have tenderness at the site of avulsion and pain with contraction and stretch of the muscle group attached to the affected apophysis. Radiography will show widening of the apophysis or an avulsed bony fragment at the site of injury. Treatment involves rest and protected weight-bearing. Once affected individuals are pain-free, they can begin range-of-motion exercises, followed by light strengthening exercises. Sports activities should be advanced slowly with dynamic, explosive activities, such as sprinting, added last. Athletes typically return to full activity 6 to 12 weeks after injury, depending on the site of avulsion and degree of injury. Surgical treatment is indicated in rare cases in which the avulsed fragment is more than 2 cm from the pelvis, or in cases in which the avulsion injury does not heal or chronically recurs.

Pelvic avulsion injuries are not caused by infection. These injuries typically involve only bone, though there may be some tearing of muscle fibers. The athlete in the vignette had an injury to the AIIS, the site of attachment of the hip flexors, so he would not have tearing of the hip extensors. Obesity is not a risk factor for pelvic apophyseal injuries. Teens with apophyseal injuries are unlikely to require surgery.

PREP Pearls
- An apophyseal avulsion occurs when a strong muscle contraction causes a piece of bone to pull away from the skeleton at the relatively weak apophysis.
- Treatment of apophyseal avulsion injuries involves rest and protected weight-bearing; surgery is rarely indicated.

ABP Content Specifications(s)
- Recognize the preventable causes of trauma in juvenile athletes and the physiology associated with increased trauma risk

Suggested Readings
- Sanders TG, Zlatkin MB. Avulsion injuries of the pelvis. *Semin Musculoskeletal Radiol.* 2008;12(1):42-53.
- Sarwark JF, LaBella CR, eds. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014..

Question 167

You are seeing a 20-year-old college student at the cam-pus health clinic with a complaint of left scrotal pain that started yesterday. The patient tells you that he was "feeling fine" until yesterday morning, when he had gradual onset of pain and swelling in his left testicle. He has been "feeling bad" in general over the past day, with intermittent dysuria and subjective fever, but denies any cough, congestion, diffi-culty breathing, sore throat, or pain or swelling in his glands. He has had no vomiting or diarrhea, and denies any history of traumatic injury.

The patient has no significant medical history, takes no medications, and has no medication allergies. His immuni-zations are up to date. He denies use of any illicit or over-the-counter drugs or smoking. He has been sexually active with 2 female partners over the past year. He has had no recent travel outside the United States.

The patient's temperature is 38.9°C, heart rate is 80 beats/min, respiratory rate is 16 breaths/min, blood pres-sure is 120/82 mm Hg, and pulse oximetry is 99% on room air. He is non–toxic appearing and in no acute distress. His physical examination is remarkable only for moderate swell-ing, tenderness, and erythema of his left testicle, with warmth of the overlying skin. His cremasteric reflexes are intact bilat-erally. He notes that his pain improves with elevation of the left testicle. There is no urethral discharge.

Scrotal ultrasonography reveals enlargement of the left tes-ticle as well as the left epididymis, with associated hypoecho-genicity and hypervascularity of both structures. There is no evidence of testicular torsion. Urinalysis reveals the presence of leukocyte esterase but is otherwise negative, and a urine culture is pending. You recommend scrotal support and an oral analgesic.

Of the following, the MOST effective additional treatment regimen for this patient would be

  A. intramuscular ceftriaxone and oral doxycycline
  B. intravenous ciprofloxacin and metronidazole
  C. no additional medications
  D. oral acyclovir
  E. oral prednisone

Correct Answer: A

The young man in the vignette presents with symptoms and clinical findings that are consistent with the diagnosis of epididymo-orchitis affecting his left epididymis and testicle. In addition to scrotal support and an oral analgesic, the most appropriate treatment regimen for him would be intramuscular ceftriaxone and oral doxycycline.

Orchitis is an infectious or inflammatory disorder involving the testis, which may occur due to extension of epididymitis, hematogenous spread of a systemic bacterial infection, or as the sequela of a viral infection (including mumps, Epstein-Barr virus, adenovirus, coxsackievirus, and parvovirus). In sexually active adolescents and young adults, epididymo-orchitis is commonly associated with sexually transmitted organisms, including *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Escherichia coli*, mycobacterial, and viral infections are other important causes in healthy men.

Key clinical features of orchitis include testicular pain and swelling, typically gradual in onset, which may be unilateral or bilateral. There may be associated fever, dysuria, urethral discharge, nausea, vomiting, and increased urinary frequency. Physical examination findings often include redness and swelling over the affected hemiscrotum. The affected testicle should lie normally, and cremasteric reflexes should be present. In cases of orchitis due to spread from epididymitis, patients generally have tenderness and swelling of the epididymis as well. Doppler ultrasonography will typically demonstrate testicular enlargement and hypervascularity.

Intravenous ciprofloxacin and metronidazole would not be the appropriate first-line antibiotic agent for treating this young man's presumed bacterial epididymo-orchitis. Although common urinary tract pathogens, including *Escherichia coli*, can cause bacterial orchitis in young children, chlamydiaand gonorrhea are much more likely to cause orchitis in a healthy young sexually active man with no prior history of urinary tract infection or genitourinary pathology.

Viral infections may certainly lead to cases of orchitis, and supportive management would be the treatment strategy of choice for these cases. However, epididymo-orchitis secondary to a sexually transmitted infection is more likely in this patient, given his acute fever, lack of concurrent viral symptoms, and findings of both epididymal and testicular infection.

Oral acyclovir would not be useful for the patient in the vignette, because infection with herpes simplex virus is not a typical cause of orchitis. Oral prednisone is generally not indicated for patients with orchitis, regardless of underlying etiology.

PREP Pearls
- Orchitis is an infectious or inflammatory disorder involving the testis, which may occur due to extension of epididymitis, hematogenous spread of a systemic bacterial infection, or the sequelae of a viral infection.
- In sexually active adolescents and young adults, epididymo-orchitis is commonly associated with sexually transmitted organisms including *Chlamydia trachomatis* and *Neisseria gonorrhoeae.*
- Key clinical features of orchitis include testicular pain and swelling, typically gradual in onset. There may be associated fever, dysuria, urethral discharge, nausea, vomiting, and increased urinary frequency. Physical examination findings often include redness and swelling over the affected testicle.

MOCA-Peds Objective
- Provide appropriate treatment for a sexually transmitted infection in an adolescent

ABP Content Specifications(s)
- Recognize the clinical findings associated with orchitis
- Identify common causes of orchitis

Suggested Readings
- Gatti JM, Murphy JP. Acute testicular disorders. *Pediatr Rev*. 2008;29(7):235. doi: http://dx.doi.org/10.1542/pir.29-7-235.
- Perron CR, Bin SS. Pain: scrotal. In: Shaw KN, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Wolters Kluwer; 2016;chap 56.

Question 168

A 6-month-old female infant exhibits failure to thrive, loose stools, and recurrent respiratory problems. The infant has had 2 positive sweat chloride test results (> 60 mEq/L). She has 1 full sibling who is healthy. The parents inquire about the recurrence risk to future siblings.

You explain that the estimated chance for the parents to have another child with this diagnosis is

A. 0%
B. 25%
C. 33%
D. 50%
E. 75%

Correct Answer: B

The child in this vignette has cystic fibrosis, an autosomal recessive condition characterized by chronic sinopulmonary disease, failure to thrive, loose stools, malabsorption/pancreatic insufficiency, fat-soluble vitamin deficiencies, chronic hepatobiliary disease, obstructive azoospermia, and salt loss. It is diagnosed when a patient has at least 1 characteristic clinical feature of cystic fibrosis and 1 of the following: 2 pathogenic variants of *CFTR*, 2 abnormal sweat chloride test results (> 60 mEq/L), or a nasal potential difference in transepithelial measurements. The child's clinical symptomatology and 2 positive sweat chloride test results fulfill the criteria of a cystic fibrosis diagnosis.

To develop an autosomal recessive disorder, an individual must inherit 2 abnormal copies of a gene, 1 from each parent. With an autosomal recessive condition, the full siblings of the affected individual have a 25% chance of being affected, a 50% chance of being an unaffected carrier, and a 25% chance of being neither a carrier nor affected. **Item C168** denotes autosomal recessive inheritance recurrence risk for a couple who are both carriers of a disorder to have another affected child (1 in 4 risk). In addition to cystic fibrosis, other types of autosomal recessive conditions commonly encountered in pediatrics include sickle cell disease, phenylketonuria, galactosemia, and other inborn errors of metabolism.

The remaining answer choices (0%, 33%, 50%, 75%) would be incorrect with regards to recurrence risk for a future sibling given 2 presumed carrier parents. If a child had an autosomal dominant condition, such as Marfan syndrome, inherited from an affected parent, the risk would be 50% for the child's future siblings as well as for the child's offspring later in life.

PREP Pearls
- To develop an autosomal recessive disorder, an individual must inherit 2 abnormal copies of a gene, 1 from each parent.
- With an autosomal recessive condition, the full siblings of the affected individual have a 25% chance of being affected, a 50% chance of being an unaffected carrier, and a 25% chance of being neither a carrier nor affected.
- Autosomal recessive conditions commonly encountered in pediatrics include cystic fibrosis, sickle cell disease, phenylketonuria, galactosemia, and other inborn errors of metabolism.

ABP Content Specifications(s)
- Recognize the inheritance pattern associated with an autosomal recessive disorder

Suggested Readings

- Ong T, Marshall SG, Karczeski BA, Sternen DL, Cheng E, Cutting GR. Cystic fibrosis and congenital absence of the vas deferens. *GeneReviews*. 2017. https://www.ncbi.nlm.nih.gov/books/NBK1250/.
- US National Library of Medicine, National Institutes of Health. What are the different ways in which a genetic condition can be inherited? Genetics Home Reference website. https://ghr.nlm.nih.gov/primer/inheritance/inheritancepatterns.
- Watson MS, Cutting GR, Desnick RJ, et al. Cystic fibrosis population carrier screening: 2004 revision of American College of Medical Genetics mutation panel. *Genet Med*. 2004;6(5):387–391.

Question 169

A medical student rotating in your office is about to see a 13-year-old boy for a health maintenance visit. Preparing for the encounter, you briefly review pubertal growth and development in boys and its assessment.

Of the following, the statement that you are MOST likely to include in your discussion is that

A. boys who experience early pubertal development have lower peak height velocities than those who mature later
B. delayed puberty and growth most often are the result of primary (hypergonadotropic) hypogonadism
C. early (precocious) puberty may compromise final adult height
D. in boys, puberty usually begins between the ages of 8 and 13 years
E. the first event of puberty in most boys is the appearance of pubic hair

Correct Answer: C

In boys, puberty begins between the ages of 9 and 14 years. The earliest sign of puberty in 98% of boys is an increase in testicular volume to 4 mL or more, or 2.5 cm or more in the long axis (this event defines sexual maturity rating (SMR) genital [G] 2). The average age at which testicular enlargement (gonadarche) begins is 10 years in non-Hispanic white boys, 9 years in black boys, and 10 years in Hispanic boys, respectively. The onset of pubic hair for these same groups occurs at mean ages of 11.5, 10, and 11.5 years, respectively.

Boys experience initiation of growth spurt (IGS) at about 11.5 years of age, and reach an average peak height velocity (PHV) of 9.5 cm/year at the age of 13.5 years (when most are in SMR G3-G4). Those who mature early develop higher PHVs than those who mature later. An earlier IGS means earlier cessation of growth that may result in shorter adult height. In contrast, later IGS is associated with later cessation of growth and a final height percentile that often exceeds that observed before puberty.

Unlike in girls, precocious puberty is rare in boys and may be due to a pathologic cause that requires evaluation. When it occurs very early or is rapidly progressive, treatment is recommended to preserve adult height and address psychosocial concerns. In boys, pubertal and growth delay typically do not have a serious cause. Most are due to constitutional delay of puberty and growth.

PREP Pearls
- Adolescent boys who mature early develop higher peak height velocities than those who mature later.
- Precocious puberty (ie, before the age of 9 years) occurs rarely in boys but merits evaluation because it may be due to a pathologic cause and may compromise final adult height.

MOCA-Peds Objective
- Recognize normal variations in pubertal development

ABP Content Specifications(s)
- Understand the relationship between the timing of onset of puberty and final adult height

Suggested Readings
- Bordini B, Rosenfield RL. Normal pubertal development: part II: Clinical aspects of puberty. *Pediatrics*. 2011;33:281-291. doi: http://dx.doi.org/10.1542/pir.32-7-281.
- Carswell JM, Stafford DEJ. Normal physical growth and development. In: Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine.* 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.
- Long D. Precocious puberty. *Pediatr Rev 2*015;36:319-321. doi: http://dx.doi.org/10.1542/pir.36-7-319.

Question 170

A 6-year-old boy is brought to your office by his mother for a health supervision visit. He had tympanostomy (pressure-equalizing) tubes placed by an otolaryngologist when he was 18 months of age because of chronic middle ear effusion with hearing loss. Since that time, he has had 2 discrete episodes of acute otitis media. Results of the postsurgical audiologic examination were normal. Today, you clearly visualize a blue tympanostomy tube in his left tympanic membrane. His right tympanic membrane appears normal with no tympanostomy tube and no evidence of perforation.

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

A. examine yearly and refer to an otolaryngologist for removal if the tympanostomy tube remains in place after 8 years of age
B. irrigate his left ear with warm water to induce extrusion of the tympanostomy tube
C. prescribe corticosteroid otic drops to induce extrusion of the tympanostomy tube
D. refer to an otolaryngologist for removal of the remaining tympanostomy tube
E. refer to an otolaryngologist for replacement of the extruded tympanostomy tube

Correct Answer: D

Tympanostomy tube insertion is a common childhood surgery. It is recommended in situations where ventilation of the middle ear would be beneficial, including specific cases of otitis media with effusion (OME) and recurrent acute otitis media (AOM). Indications for tympanostomy tube insertion include:

- Bilateral OME lasting at least 3 months together with conductive hearing loss
- Bilateral or unilateral OME lasting at least 3 months together with risk factors for speech, language, or learning problems (eg, neurodevelopmental disabilities, craniofacial anomalies)
- Bilateral or unilateral OME lasting at least 3 months together with symptoms or conditions such as pain, vestibular problems, tympanic membrane damage, or middle ear damage
- Recurrent AOM with OME at the time of assessment

Tympanostomy tube insertion is not appropriate for patients with OME lasting less than 3 months or for recurrent AOM without the presence of OME at the time of assessment. Patients with prolonged OME who do not have conductive hearing loss or other symptoms should be monitored until their OME resolves or until they develop an indication for tympanostomy tube insertion.

The risks of tympanostomy tube insertion include anesthesia-related risks and tympanic membrane damage, including otorrhea, tympanosclerosis, focal atrophy, or persistent perforation.

Tympanocentesis (puncture of the tympanic membrane to aspirate fluid from the middle ear) and myringotomy (surgical incision of the tympanic membrane to allow drainage of fluid from the middle ear) are not routinely recommended for the treatment of OME or AOM. Tympanocentesis is rarely used to obtain a culture in cases of severe refractory AOM.

Most tympanostomy tubes placed in the United States are designed to remain in place for a short time, typically 12 to 18 months. Over time, as the epithelial layer of the tympanic membrane turns over, most tubes are spontaneously extruded. A small percentage (5%-10%) of tympanostomy tubes must be surgically removed. Tympanostomy tubes that remain in place for longer than 3 years are unlikely to spontaneously extrude; they are more likely to lead to chronic tympanic membrane perforation. Indications for surgical tympanostomy tube removal include:

- Failure of the tube to extrude more than 3 years after insertion
- Migration of the tube into the middle ear
- Tube-associated granulation tissue that does not respond to treatment
- Chronic otorrhea that does not respond to treatment
- Resolution of the condition that prompted insertion (eg, repair of cleft palate), especially in an older child

The boy in this vignette had tympanostomy tubes placed more than 4 years ago. The remaining tube should be surgically removed. The patient does not have any indications for tube

replacement. Yearly examinations are not appropriate because the remaining tube is unlikely to spontaneously extrude. Neither irrigation of the ear canal nor corticosteroid otic drops induce extrusion.

PREP Pearls
- Tympanostomy tubes are indicated for children with otitis media with effusion that lasts longer than 3 months and is accompanied by hearing loss, pain, damage to the middle ear or tympanic membrane, neurodevelopmental disabilities, or craniofacial anomalies. They are also indicated for children with recurrent acute otitis media who have middle ear effusion at the time of assessment.
- Tympanostomy tubes should be surgically removed if they remain in place more than 3 years after insertion, migrate into the middle ear, or are associated with chronic otorrhea or granulation tissue that does not respond to treatment.
- Tympanostomy tubes that remain in place longer than 3 years are not likely to spontaneously extrude; they are more likely to lead to chronic perforation of the tympanic membrane.

ABP Content Specifications(s)
- Understand the indications for tympanostomy tube insertion
- Recognize potential complications associated with tympanocentesis, tympanostomy tubes, and myringotomy

Suggested Readings
- Lentsch EJ, Goudy S, Ganzel TM, Goldman JL, Nissen AJ. Rate of persistent perforation after elective tympanostomy tube removal in pediatric patients. *Int J Pediatr Otorhinolaryngol.* 2000;54(2–3):143–148.
- Rosenfeld RM, Schwartz SR, Pynnonen MA, et al. Clinical practice guideline: tympanostomy tubes in children. *Otolaryngol Head Neck Surg.* 2013;149(1 suppl):S1–S35. doi: http://dx.doi.org/10.1177/0194599813487302.
- Rosenfeld RM, Shin JJ, Schwartz SR, et al. Clinical practice guideline: otitis media with effusion (update). *Otolaryngol Head Neck Surg*. 2016;154(1 suppl):S1–S41. doi: http://dx.doi.org/10.1177/0194599815623467.

Question 171

A 12-year-old girl with a history of tetralogy of Fallot with pulmonary atresia and major aortopulmonary collaterals is brought to your office by her mother for evaluation of slurred speech. She has undergone multiple palliative cardiac surgical procedures, and her cardiac care team has communicated to you that there is no other procedure or intervention that can be performed. She is also followed by a palliative care team. Today, you note facial drooping and dysarthria. You refer her to the emergency department for further evaluation and management of a presumed cerebrovascular accident.

Of the following, the predisposing factor MOST likely to be the etiology of her current symptoms is

A. heart failure
B. iron deficiency anemia
C. polycythemia
D. pulmonary overcirculation
E. viral illness

Correct Answer: C

The girl in this vignette with cyanotic congenital heart disease has symptoms of a cerebrovascular accident. Among heart failure, iron deficiency anemia, polycythemia, pulmonary overcirculation, and viral illness, the most likely predisposing factor is the polycythemia seen in patients with chronic cyanosis.

Patients with congenital heart disease are more likely to survive and live longer than ever before. Many therapies, procedures, and operations for congenital heart disease are palliative (not curative). Complications are relatively common and increase in prevalence and severity as patients age. It is important to understand the associated long-term effects and complications of congenital heart disease.

Complications, such as heart failure caused by systolic dysfunction, diastolic dysfunction, valve regurgitation, and stenosis, can lead to symptoms such as fatigue, exercise intolerance, shortness of breath, anorexia, and vomiting. Arrhythmias are common and can result in symptoms of heart failure as well as the perception of a fast or slow heartbeat, dizziness, palpitations, or syncope. Pulmonary hypertension can lead to pulmonary hemorrhage, syncope, and heart failure. Patients are also at risk for other organ injury such as hepatic and renal disease. Neurologic problems are common and include cognitive delay, attention-deficit disorder, and cerebrovascular accidents, as described for the patient in this vignette. Thromboembolic events outside of the neurologic system are also common. One reason for these thromboembolic events is the polycythemia that occurs in chronically cyanotic patients, such as the patient in this vignette. Iron deficiency anemia and viral illness are not described in this vignette and are not specifically associated with congenital heart disease. Pulmonary over circulation and heart failure can occur in congenital heart disease but are unlikely to cause the neurologic symptoms seen in the patient in this vignette. Polycythemia in the setting of chronic cyanosis increases the risk of a thromboembolic event. Many patients with cyanotic congenital heart disease are treated prophylactically with aspirin, warfarin, or other anticoagulants to help prevent thromboembolic events.

PREP Pearls
- Patients with congenital heart disease are more likely to survive and live longer than ever before.
- Polycythemia increases the chance of thromboembolic events in patients with cyanotic congenital heart disease.
- Heart failure, arrhythmias, pulmonary hypertension, and neurologic, hepatic, and renal dysfunction are complications of cyanotic congenital heart disease.

ABP Content Specifications(s)
- Recognize complications associated with cyanotic congenital heart disease

Suggested Readings

- Ntiloudi G, Giannakoulas G, Parcharidou D, Panagiotidis T, Gatzoulis MA, Karvounis H. Adult congenital heart disease: a paradigm of epidemiological change. *Int J Cardiol.* 2016;218:269–274. doi: http://dx.doi.org/10.1016/j.ijcard.2016.05.046.
- Strong WB. Consultation with the specialist: complications of polycythemia in patients who have cyanotic congenital heart disease. *Pediatr Rev.* 1992;13(10):379–380. doi: http://dx.doi.org/10.1542/pir.13-10-379.

Question 172

A 12-year-old girl who has had cola-colored urine for 3 days is brought to your office. She has a temperature of 37.7°C, respiratory rate of 26 breaths/min, heart rate of 110 beats/min, and blood pressure of 140/90 mm Hg. Her physical examination findings are only significant for mild edema. She has normal growth parameters. Results of a urine test strip analysis are shown:

Laboratory Test	Result
Specific gravity	1.025
pH	6.6
Blood	3+
Leukocyte esterase	2+
Protein	1+
Nitrites	Negative

Urine microscopy shows greater than 100 red blood cells, 10 to 20 white blood cells, and 2 to 3 granular casts per high-power field. Based on your findings, you suspect acute postinfectious glomerulonephritis as the underlying cause of the patient's symptoms.

Of the following, the laboratory findings MOST likely to be seen in this patient's disorder include

 A. low C3 level and low C4 level
 B. low C3 level and normal C4 level
 C. low C3 level and normal CH50 level
 D. normal C3 level and normal CH50 level
 E. normal C3 level and normal C4 level

Correct Answer: B

Glomerulonephritis (GN) refers to the immune-mediated (noninfectious) inflammation of the renal parenchyma. The girl in this vignette has clinical features of acute GN (cola-colored urine, microscopic hematuria, and hypertension). Further classification of acute GN requires measurement of complement components C3 and C4. Determining whether the patient has hypocomplementemic (associated with a low C3 level) or normocomplementemic (associated with a normal C3 level) GN helps in differentiating various types of GN (**Item C172**). Postinfectious glomerulonephritis, membranoproliferative GN (MPGN), and systemic lupus erythematosus–related nephritis are the most frequently identified types of hypocomplementemic GN in children. The combination of a low C3 level and a normal C4 level indicates activation of the alternative pathway of complement and occurs in postinfectious GN or MPGN. In patients with systemic lupus erythematosus–related nephritis, there is immune-mediated activation of the classical pathway of complement associated with reductions in both C3 and C4 levels. The level of total complement activity (CH50) is decreased in patients with hypocomplementemic GN and normal in patients with normocomplementemic GN.

Item C172. Complement Levels Associated with Different Causes of Acute Nephritis.

Low C3 GN	Normal C3 GN
Postinfectious/Poststreptococcal	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)

Abbreviations: ANCA, antineutrophil cytoplasmic antibodies; GN, glomerulonephritis

Courtesy of G. Kapur

Postinfectious GN is characterized by immune complex–mediated nephritis developing after an infectious process. Poststreptococcal GN exclusively relates to a group A, β-hemolytic streptococcal infection. The terms postinfectious GN and poststreptococcal GN are often used interchangeably because poststreptococcal GN is the most common cause of acute nephritis in

children worldwide. Elevated titers of antibodies to streptococcal antigens are present only in patients in whom postinfectious GN is associated with streptococcal infection. However, in postinfectious GN secondary to nonstreptococcal infections, streptococcal antibody titers will be normal.

Membranoproliferative GN, similar to postinfectious GN, can follow a viral illness. It is difficult to differentiate MPGN from postinfectious GN, especially in patients with no clear history of preceding infection or in patients with a short duration between infection and onset of nephritis. Hypocomplementemia usually resolves by 6 to 8 weeks in most cases of postinfectious GN. Persistently decreased C3 levels (beyond 6 to 8 weeks) and nephrotic syndrome are more frequently seen in patients with MPGN as compared to postinfectious GN.

Systemic lupus erythematosus is a chronic inflammatory disease with multisystem involvement that may include skin, joints, kidneys, lungs, nervous system, serosal membranes, or other organs. Systemic lupus erythematosus in children may present with renal involvement alone. The renal involvement may manifest as hematuria and proteinuria identified on routine examination, nephrotic syndrome (proteinuria, edema, and hypoalbuminemia), or acute nephritis (acute renal failure, hematuria, and hypertension). In this situation, levels of C3 and C4 can distinguish systemic lupus erythematosus–related nephritis from poststreptococcal GN and MPGN .

PREP Pearls
- Acute glomerulonephritis is characterized by the triad of cola-colored urine, hypertension, and azotemia.
- A low C3 level in acute glomerulonephritis indicates activation of the alternative pathway of complement (postinfectious or membranoproliferative glomerulonephritis), and decreased C3 and C4 levels indicate activation of the classical pathway (systemic lupus erythematosus nephritis).
- Poststreptococcal glomerulonephritis related to group A, β-hemolytic streptococcal infection is the most common acute nephritis in children worldwide.

ABP Content Specifications(s)
- Understand the natural history of acute post-streptococcal glomerulonephritis
- Plan the appropriate diagnostic evaluation of acute post-streptococcal glomerulonephritis, with attention to the timing of resolution of abnormal findings
- Plan the appropriate initial management of post-streptococcal glomerulonephritis

Suggested Readings
- VanDeVoorde RG. 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, Kamat DM, Kelleher KJ, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* Elk Grove Village, IL: American Academy of Pediatrics; 2009:2286–2296.

Question 173

You are seeing a 12-year-old girl in the emergency department for injuries to her head, face, and mouth, sustained 30 minutes earlier when she lost control of her bicycle. She ran head-on into a brick wall and then fell from her bicycle onto the sidewalk. She was not wearing a helmet. The girl's friends report that she lost consciousness briefly (<1 minute) after hitting the wall, but then was crying and asking them to call her mother. She has had no episodes of vomiting. Both of her upper central incisors were "knocked out" when she hit the wall. Paramedics found the avulsed teeth on the sidewalk at the scene of the accident, which they transported to the emergency department in a plastic bag.

On arrival to the emergency department, the girl is awake and crying. She seems uncomfortable, but is answering questions appropriately and following directions. Her vital signs are normal for her age. The girl's airway is intact, and she is breathing easily with equal breath sounds. Her extremities are warm and well-perfused. She has a 5-cm hematoma in the center of her forehead, with abrasion of the overlying skin and multiple abrasions to her face. There is dried blood in both of her nares, but no deformity of her nasal bridge and there is no septal hematoma. The girl's cervical spine, chest, abdomen, pelvis, and extremities are nontender to palpation. There is a 1-cm laceration to the inner surface of her lower lip, which appears fairly deep but does not cross the vermilion border. Both of her upper central incisors are missing, with small blood clots at both tooth sockets. You identify no step-offs or crepitus on palpation of the girl's facial bones. Her neurologic function is fully intact.

Of the following, based on your clinical findings, the BEST next management step for this patient is to

 A. arrange for evaluation by a pediatric dentist within 12 hours
 B. cleanse the recovered teeth thoroughly using a chlorhexidine solution and sterile gauze
 C. perform computed tomography of the brain and facial bones
 D. place sutures in her lower lip laceration to achieve approximation of the edges
 E. reimplant the teeth that were recovered by the paramedics

Correct Answer: E

The 12-year-old girl in the vignette presents with multiple injuries to her head, face, and mouth (including avulsion of 2 teeth) after crashing her bicycle into a wall. Her airway, breathing, circulation, and neurologic function are fully intact. The best next management step is to reimplant her avulsed teeth.

All pediatric providers should be familiar with the appropriate management of an avulsed tooth. An avulsed tooth is one that has been displaced completely from its socket. Avulsed permanent teeth should be immediately reimplanted, as the prognosis is best when reimplantation is completed within 15 to 30 minutes of avulsion. Patients/parents/bystanders should be encouraged to replace an avulsed tooth into its socket as soon as possible. Children can bite on a cloth/handkerchief to hold the tooth in position until they can access dental care. Avulsed primary teeth are generally *not* reimplanted, because reimplantation of an avulsed primary tooth may actually damage the developing permanent tooth.

Avulsed permanent teeth should be carefully handled by the crown, not the root, to avoid damage to the delicate root structure. Before reimplantation, teeth should be rinsed very briefly (10 seconds) and gently under cold, running water or saline. Teeth that cannot be replaced into the socket immediately after avulsion can be transported in a specific storage media for avulsed teeth (Hanks solution), a glass of milk, or even in the patient's mouth (held inside the cheek, provided that the child is old enough not to choke on or swallow it). Saline can be used as a transport medium, if neither Hanks solution nor milk is available. Families/prehospital providers should avoid storing avulsed teeth in water, as it may damage the root structure.

If an avulsed tooth has not already been replaced into its socket when a child presents for care, pediatric providers should hold the tooth by its crown and gently but firmly replace it directly into its socket. Emergent dental consultation should then be obtained, or the child should be immediately referred to a dentist for radiography, final alignment, placement of a dental splint, and close follow-up.

Referring the child for evaluation by a pediatric dentist within 12 hours would not be the most appropriate next step in management. As mentioned before, avulsed teeth should be reimplanted as soon as possible—within 15 to 30 minutes after avulsion—to achieve the best possible outcome.

Cleansing the recovered tooth thoroughly with chlorhexidine solution and sterile gauze would not be recommended because aggressive cleaning/scrubbing of an avulsed tooth can damage its delicate root structure.

Computed tomography of this patient's brain and facial bones would not be the most appropriate next step for the girl in the vignette. Based on her clinical presentation, she is at very low risk for intracranial injury and facial bone fractures. Given that she is awake and alert and her neurologic status is fully intact, reimplanting her avulsed teeth should be addressed before obtaining any radiographs.

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Placing sutures in the girl's lower lip to approximate the edges of her laceration is not the most immediate priority for this child. Replacing the avulsed teeth is a time-sensitive issue, therefore, this step should be completed before proceeding to the next steps in management (given that her airway, breathing, circulation, and neurologic function are intact and stable).

PREP Pearls
- Avulsed permanent teeth should be immediately reimplanted. Prognosis is best when reimplantation is completed within 15 to 30 minutes of avulsion.
- Avulsed primary teeth are generally *not* reimplanted, as this may actually damage the developing permanent tooth.
- If an avulsed tooth has not already been replaced into its socket when a child presents for care, providers should hold the tooth by its crown and gently but firmly replace it directly into its socket.
- Teeth that cannot be replaced into the socket immediately after avulsion can be transported in a specific storage media for avulsed teeth (Hanks solution), a glass of milk, or even held against the cheek inside the patient's mouth.

ABP Content Specifications(s)
- Plan the appropriate management of an avulsed tooth

Suggested Readings
- Fida Z, Nelson LP, Needleman HL, Padwa BL. Dental trauma. In: Shaw K, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine.* Philadelphia, PA: Wolters Kluwer; 2016;chap 113:1134.
- The International Association of Dental Traumatology. Online Dental Trauma Guide. www.dentaltraumaguide.org .

Question 174

You are seeing a 15-year-old girl for a health supervision visit. You note that her body mass index is 32 kg/m2, greater than the 95th percentile. She would like to lose weight and tries to eat a healthy diet, but because of her busy schedule, she has had difficulty establishing an exercise routine. Her medical history is unremarkable, and she takes no medication. A review of systems is significant for fatigue and irregular, infrequent menses since menarche at age 12 years. Her mother has a history of hyperlipidemia requiring medication, and her maternal uncle had a myocardial infarction at age 38 years. Her father has type 2 diabetes, diagnosed at age 40 years, and hypertension. Her paternal grandmother also has type 2 diabetes and hypertension. Physical examination reveals a temperature of 37°C, blood pressure of 130/88 mm Hg, heart rate of 102 beats/min, weight of 89 kg (greater than 95th percentile), and height of 167 cm (75th percentile). She appears overweight. She has acanthosis nigricans over the nape of her neck and in both axillae, and mild hirsutism over her upper lip, chin, and lower abdomen. The remainder of her physical examination findings are within normal parameters.

You assist her in developing strategies to make healthy lifestyle changes and order a fasting lipid profile. Of the following, the BEST additional laboratory test to order is

A. 17-hydroxyprogesterone level
B. cortisol level
C. fasting glucose level
D. fasting insulin level
E. thyroid-stimulating hormone level

Correct Answer: C

The girl in the vignette likely has metabolic syndrome. Metabolic syndrome is a constellation of risk factors for cardiovascular disease and type 2 diabetes mellitus. Components include obesity, hypertension, dyslipidemia, and glucose intolerance.

The girl's body mass index, blood pressure, and lipid levels have been measured, but she has not been screened for glucose intolerance or type 2 diabetes. Thus, a fasting glucose level is indicated. A level of 100 mg/dL (5.6 mmol/L) or greater is classified by the American Diabetes Association as impaired fasting glucose, and a level of 125 mg/dL (6.9 mmol/L) or greater is diagnostic for diabetes mellitus.

Other options for glucose intolerance and diabetes screening include a:
2-hour plasma glucose level obtained during a 75-g oral glucose tolerance test
≥140 mg/dL or 7.8 mmol/L is impaired glucose tolerance
≥200 mg/dL or 11.1 mmol/L is diagnostic for diabetes
OR
hemoglobin A1c
≥5.7% or 39 is classified as prediabetes
≥6.5% or 48 is diagnostic for diabetes

Although there is no consensus on the definition of metabolic syndrome in pediatrics, attempts have been made to modify the adult criteria reflecting pediatric measurements. Adults meet criteria for metabolic syndrome when 3 of the following are present:
- High waist circumference
- High fasting triglycerides (≥150 mg/dL [1.7 mmol/L])
- Low high-density lipoprotein (HDL) cholesterol (<40 mg/dL [1.0 mmol/L] in men, <50 mg/dL [1.29 mmol/L] in women)
- High blood pressure (≥130 mm Hg systolic and/or ≥85 mm Hg diastolic)
- High fasting glucose (≥100 mg/dL [5.6 mmol/L])

Obesity and insulin resistance play key roles in the pathogenesis of metabolic syndrome. The girl in the vignette has obesity, elevated blood pressure, and a high-risk family history (hyperlipidemia, hypertension, cardiovascular disease, and type 2 diabetes). Her acanthosis nigricans is a marker of insulin resistance. Her hirsutism and irregular menses suggest polycystic ovarian syndrome, which is also associated with insulin resistance. The girl's tachycardia may be a marker of poor fitness, and may also be a marker of insulin resistance. A fasting insulin level would most likely be elevated in this case, but would not add additional diagnostic information.

For children with obesity (body mass index [BMI] ≥95th percentile), an expert committee in 2007 recommended the following laboratory screening: lipid panel, fasting glucose, aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Elevated AST and ALT levels can be markers of nonalcoholic fatty liver disease, which is also associated with obesity and insulin resistance. The expert committee recommended against screening for hypothyroidism unless otherwise indicated, and recommended against obtaining a fasting insulin level.

A 17-hydroxyprogesterone level would be useful if nonclassic congenital adrenal hyperplasia (CAH) were suspected. Although CAH is in the differential diagnosis of polycystic ovarian syndrome, this would be a lower priority than screening for glucose intolerance. A cortisol level would help evaluate for Cushing syndrome, but is not a priority in a child presenting with obesity without other indications, and is not a preferred screening test for Cushing syndrome unless tested as a midnight salivary cortisol. Cushing syndrome is an extremely rare cause of pediatric obesity unless caused by exogenous steroids. A thyroid-stimulating hormone (TSH) level would test for thyroid disorders, but this girl's clinical picture is not suggestive of a thyroid disorder. The girl's fatigue is most likely secondary to obstructive sleep apnea, which is commonly associated with obesity.

The primary treatment for metabolic syndrome is to make healthy lifestyle changes that promote weight loss. Even a small decrease in BMI can lead to significant improvement in metabolic risk. The 9-5-2-1-0 principle provides a framework for counseling:
- 9 hours of sleep per night
- 5 servings of fruits and vegetables per day
- Less than 2 hours of screen time per day (television, computer, electronic devices)
- 1 hour of physical activity per day
- 0 sugary drinks (soda, juice)

PREP Pearls
- Metabolic syndrome is a constellation of risk factors for cardiovascular disease and type 2 diabetes mellitus. Components include obesity, hypertension, dyslipidemia, and glucose intolerance.
- The primary treatment for metabolic syndrome is to make healthy lifestyle changes that promote weight loss. Even a small decrease in body mass index can lead to significant improvement in metabolic risk.

ABP Content Specifications(s)
- Recognize the clinical features associated with metabolic syndrome
- Plan an appropriate screening evaluation for metabolic syndrome, considering risk factors that necessitate such screening
- Plan appropriate initial management of a patient with metabolic syndrome

Suggested Readings
- American Diabetes Association. 2: Classification and diagnosis of diabetes. *Diabetes Care.* 2017;40(suppl 1):S11-S24.
- Barlow SE; Expert Committee. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics.* 2007;120(suppl 4):S164–S192. doi: http://dx.doi.org/10.1542/peds.2007-2329C.

- Styne DM, Arslanian SA, Connor EL, et al. Pediatric obesity — assessment, treatment, and prevention: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2017:102(3):709-757. doi: http://dx.doi.org/10.1210/jc.2016-2573 .
- Wittcopp C, Conroy R. Metabolic syndrome in children and adolescents. *Pediatr Rev.* 2016 May;37(5):193-202. doi: http://dx.doi.org/10.1542/pir.2014-0095.

Question 175

You are seeing a 4-year-old previously healthy boy for follow-up 1 week after discharge following hospitalization for meningitis. His hospital records show that he presented to the emergency department after a generalized tonic-clonic seizure at home that lasted for 2 minutes. In the emergency department, he was minimally arousable. He had a temperature of 39.4°C and nuchal rigidity. Computed tomography of the head showed normal findings. A lumbar puncture was performed, blood cultures were obtained, and he was started on antibiotics.

Cerebrospinal fluid results were as follows:

Laboratory Test	Results
Protein	300mg/dL (3,000 mg/L)
Glucose	15 mg/dL (0.83 mmol/L)
White blood cell count	13,000/µL (13,×10^9/L)
Differential	92% neutrophils, 6% lymphocytes, 2% monocytes
Gram stain	gram-positive diplococci

The boy had 1 generalized tonic-clonic seizure on hospital day 5, but no other acute complications. He completed a 2-week course of intravenous antibiotics during his hospital stay which included 12 days of inpatient rehabilitation. He passed a hearing test just before his discharge. In your office, his physical and neurologic examination results are normal.

Of the following, the BEST next management step for this boy would be to

 A. advise the parents that he is at risk for intellectual disability
 B. delay any required immunizations for 3 months
 C. perform a lumbar puncture for follow-up cerebrospinal fluid studies
 D. refer him to a neurologist for electroencephalography
 E. refer him to an audiologist for repeat hearing testing in 1 month

Correct Answer: A

The boy in the vignette had pneumococcal meningitis. Long-term neurologic complications of bacterial meningitis in children include intellectual disability, hearing impairment, epilepsy, spasticity, and hemiparesis. Of the response choices, the best next management step is to discuss possible long-term complications with the parents, including the risk of intellectual disability.

Acute complications of bacterial meningitis include seizures, empyema, cerebral edema, hydrocephalus, cerebral vasculitis, cerebral hemorrhage or infarction, septic arthritis, and pericarditis. The boy's decreased level of consciousness at presentation increases his overall risk for long-term neurologic sequelae or death.

Follow-up care after bacterial meningitis includes close monitoring of the child's development. Immunizations do not need to be delayed. Hearing testing should be performed before hospital discharge or soon after. Because this child's hearing was normal at hospital discharge, repeat testing is not needed. He has fully recovered from the acute illness and is not febrile, therefore, he does not need to have repeat cerebrospinal fluid studies. He is not having seizures, thus electroencephalography is not needed.

PREP Pearls
- In children with bacterial meningitis, a decreased level of consciousness at presentation increases the risk for long-term neurologic sequelae or death.
- Long-term neurologic complications of bacterial meningitis in children include developmental delay, intellectual disability, hearing impairment, epilepsy, spasticity, and hemiparesis.

ABP Content Specifications(s)
- Recognize the acute and long-term complications associated with meningitis

Suggested Readings
- Prober CG, Srinivas NS, Mathew R. Central nervous system infections. In: Kliegman RM, MD, Stanton BMD, St. *Geme J, Schor NF, eds. Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Elsevier; 2015;chap 603:2936–2948.
- Swanson D. Meningitis. *Pediatr Rev.* 2015;36(12):514–526. doi: http://dx.doi.org/10.1542/pir.36-12-514.

Question 176

You are called to the newborn nursery to evaluate a 7-hour-old male newborn who has a petechial rash. He was born at 37 weeks of gestation following an uncomplicated pregnancy. His Apgar scores were 9 at 1 minute and 9 at 5 minutes. His parents have a healthy 5-year-old girl and a healthy 2-year-old boy. His mother has not been taking any medications other than a prenatal vitamin and has been healthy with an unremarkable medical history. Her complete blood cell count was normal 2 days prior to delivery.

The couple's first child had no complications after delivery, but their second child had a very low platelet count that was discovered when he had excessive bleeding following a heel stick. The low platelet count improved over the first few months after birth, and he has been healthy with normal growth and development since that time.

This newborn appears well. His physical examination results were normal except for a petechial rash on the face, chest, back, thighs, and upper arms.

A complete blood cell count reveals:

Laboratory Test	Result
White blood cell count	4,100/µL (4.1 x 10^9/L)
Hemoglobin	15.9 g/dL (159 g/L)
Platelet count	18 x 10^3/µL (18 x 10^9/L)

A medical student making rounds with you asks about this newborn's thrombocytopenia.

Of the following, you are MOST likely to tell the medical student that

A. future girls born to this couple will not be at increased risk for severe thrombocytopenia
B. initial management of the thrombocytopenia should include immunosuppression with corticosteroids
C. initial management of the thrombocytopenia should include a platelet transfusion with paternal platelets
D. the thrombocytopenia is caused by a maternal alloantibody to an antigen on the father's platelets and the newborn's platelets
E. the thrombocytopenia is caused by a maternal autoantibody to an antigen on the mother's platelets and the newborn's platelets

Correct Answer: D

The family history is critical to understanding the pathophysiology of the thrombocytopenia in this neonate. Neonatal thrombocytopenia can result from either the decreased production or the increased destruction of platelets. This neonate's sibling had transient thrombocytopenia, but his mother has no history of thrombocytopenia. This family history strongly suggests that the cause of the neonate's thrombocytopenia is platelet destruction caused by a maternal antibody to an antigen on the neonate's platelets that is absent on the maternal platelets. This condition is called neonatal alloimmune thrombocytopenia and is the platelet equivalent to Rh incompatibility of the red cells. The fetal platelets express a paternally inherited antigen, most commonly HPA-1a (Pl^{A1}), that is foreign to the mother. The mother produces antibodies to that antigen that 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 following birth. If the neonatal thrombocytopenia is severe, it should be treated by a transfusion of maternal platelets collected via apheresis. The maternal platelets will not express the responsible antigen and will therefore not be destroyed by the circulating antibody.

Most platelet antigens are encoded on chromosome 17. Thus, the sex of future children will not influence their risk for developing neonatal alloimmune thrombocytopenia. Each subsequent child born to this couple is at risk for neonatal alloimmune thrombocytopenia. Because the mother has been immunologically sensitized to the paternal platelet antigen, it is possible that each subsequent pregnancy will result in a higher antibody titer and more severe thrombocytopenia. Transfusion of paternal platelets would not help with the thrombocytopenia because these platelets would express the responsible antigen. Neonatal alloimmune thrombocytopenia is not an autoimmune phenomenon, meaning that the neonate is not producing the responsible antibodies; rather, these antibodies have passively transferred through the placenta. Treatment with immune suppression, such as corticosteroids, would not be indicated.

PREP Pearls
- Family history is critical to determining the etiology of neonatal thrombocytopenia.
- Neonatal alloimmune thrombocytopenia results from maternal antibody production to an antigen expressed on fetal platelets that is not expressed on maternal platelets. If severe, it is treated with a transfusion of maternal platelets because they do not express the responsible antigen.
- Subsequent children born to parents of a neonate with neonatal alloimmune thrombocytopenia are at risk to develop this condition.

ABP Content Specifications(s)
- Understand the significance of neonatal thrombocytopenia in multiple siblings

Suggested Readings

- Buchanan GR. Thrombocytopenia during childhood: what the pediatrician needs to know. *Pediatr Rev.* 2005;26(11):401–409. doi: http://pedsinreview.aappublications.org/content/26/11/401 .
- Roberts IA, 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.

Question 177

A 9-year-old boy is brought to your office for a health supervision visit. He is accompanied by his mother and 7-year-old-brother. While his mother is telling you about the boy's extracurricular activities, his younger brother interjects with comments about his brother's poor performance at his most recent sports event. The 9-year-old punches his brother on the arm. Their mother yells at them to stop and tells the 9-year-old that he should know better. She asks you what she should do to improve her family's dynamics.

Of the following, the BEST recommendation is for this mother to

A. ignore her children's behaviors
B. set aside time to spend individually with each child
C. settle her children's arguments
D. take away privileges from the child who starts the fight
E. treat each child the same

Correct Answer: B

Setting aside special time with each child can not only improve parent-child relationships, but can also decrease sibling rivalry. The desire of each child for their parent's love and attention can underlie sibling rivalry. Children can be jealous of the attention received by their siblings and respond by competing or fighting. Children need to feel that they are listened to and valued by their parents. Receiving their parent's undivided attention, even for short periods, validates their uniqueness and importance, and helps children feel secure of their place in their parents' hearts. Pediatricians can guide parents in considering the children's individual developmental needs, and to develop appropriate expectations for their children. Older siblings may have different privileges according to their age. Younger siblings may need to be shown how to request positive attention from their older siblings. Each child needs time for his/her own friends and interests. Each child's space and property should be respected.

Sibling rivalry is common. It is normal for siblings to compete with each other and to have some degree of conflict. Children may argue, pester, or physically fight with their siblings, and compete for the attention of their parents. Healthy competition helps children learn resilience and compromise, and develop skills for effective communication, negotiation, and positive interactions with others.

Sibling conflicts are more likely to arise when there is a change in family membership or structure (eg, divorce of parents; addition of other siblings via birth, adoption, or blending of families). Changes in caregivers or in the health of family members may also trigger increased rivalry. An important strategy in preventing significant rivalry is to provide the support needed for each child to feel special and secure. Upcoming changes should be discussed with the child, who should be encouraged to express his/her feelings while the parent listens attentively. The child should be reassured that despite the changes, he/she will always be important and loved.

Parents need to supervise their children, set limits (eg, no hurting), and ensure open lines of communication between family members. Whenever possible, parents should encourage and allow the children to resolve their own conflicts. Parents may unintentionally reinforce behaviors when they intervene. When rivalry requires parental intervention, parents should acknowledge the children's anger, listen to each side, and express confidence in the children's ability to figure out a solution. Parents can help facilitate communication between the children; they should guide their children to listen to each other, instead of focusing on who was in the right. If needed, the parent can offer suggestions, but should allow the children to determine which option to use. When children are physically hurting each other, they should be separated and told that violence is not allowed. The focus of attention should be on the injured child. Behaviors that are persistently aggressive should be investigated.

Parents can help their children learn to express anger in ways other than attacking their sibling. They should acknowledge, and not dismiss, their children's negative feelings. They can guide their children to verbalize feelings or to draw or write about them. Parents can also support children in standing up for themselves. Each child's behavior should be addressed individually. Parental favoritism, real or perceived, can have a negative impact on sibling relationships.

Parents should avoid comparing children to each other, even when the comparison is favorable. This helps each child to believe that the parent loves and values him/her uniquely. Instead of treating each child equally, parents should focus on meeting the individual needs of each child, giving each one the time and attention needed. At times one child may have more need than the other(s).

While the mother in the vignette may ignore her children's normal low-level bickering, their ongoing rivalry behaviors will likely persist without her intervention. The mother should not settle her children's arguments but instead encourage them to communicate their feelings, consider their options, and decide on a mutually agreeable solution. The mother should refrain from attempting to determine who started a particular fight. Two are needed to fight, and the consequences should apply to both children. For example, if the children are fighting over a toy, the toy could be placed in time out. Taking away privileges from the child who ostensibly started the fight may inadvertently reinforce the other child's behaviors. Finally, each child should be treated uniquely, according to their individual needs, and not the same.

PREP Pearls
- Instead of treating each child equally, parents should focus on meeting the individual needs of each child, giving each the time and attention needed.
- Providing each child with one-on-one time and focused attention, even for short periods, can not only improve parent-child relationships but also decrease the children's need to compete with each other for their parents' consideration.
- Sibling conflicts are more likely to arise when there is a change in family membership or structure (eg, divorce of parents; addition of other siblings via birth, adoption, or blending of families).
- Whenever possible, parents should encourage and allow the children to resolve their own conflicts.

ABP Content Specifications(s)
- Provide appropriate anticipatory guidance and counseling with regard to sibling rivalry

Suggested Readings
- Faber A, Mazlish E. *Siblings Without Rivalry: How to Help your Children Live Together So You Can Live Too.* New York, NY: WW Norton & Co; 2012.
- Needlman R. Sibling rivalry. 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 & Wilkins; 2011:476–478.

Question 178

A female neonate was born at 26 weeks of gestation via cesarean delivery. The mother received a dose of betamethasone 2 hours before the delivery. Cord clamping was performed 30 seconds after birth. The neonate was resuscitated in the delivery room using continuous positive airway pressure with a positive end-expiratory pressure of +5 mm Hg and fraction of inspired oxygen equal to 30%. On day 1 after birth, she underwent intubation due to poor respiratory effort, and developed a pneumothorax that required chest tube placement. Ultrasonography of the head performed 1 week after birth shows a right grade 3 intraventricular hemorrhage. Her mother asks what caused this bleeding.

Of the following, the risk factor MOST likely to be associated with this complication is

A. delayed cord clamping
B. female sex
C. intubation
D. pneumothorax
E. prenatal betamethasone

Correct Answer: D

Pneumothorax requiring chest tube placement is associated with increased risk of intraventricular hemorrhage (IVH) in premature neonates. Intraventricular hemorrhage is primarily a disease of premature neonates born before 32 weeks of gestation, and occurs due to a combination of developmental factors and postnatal exposures. The germinal matrix is a structure present in the periventricular region of the developing fetus. This highly vascularized region, with limited perivascular support, typically involutes by term. After birth, premature neonates have impaired autoregulation of their cerebral vasculature, unlike term neonates, whose cerebral perfusion is maintained at a constant value as systemic blood pressure varies. Therefore, in premature neonates, fluctuations in systemic blood pressure can cause acute increases and decreases in cerebral perfusion that increase the risk of bleeding into the vascularized germinal matrix, resulting in IVH.

The risk of IVH is highest in the first few hours after birth. Clinically, most neonates with IVH are asymptomatic. Rarely, a premature neonate will present with an acute drop in blood pressure, decrease in activity, and associated increased fullness of the anterior fontanelle. Screening head ultrasonography at 1 week of age will identify approximately 90% of cases of IVH. IVH is characterized by the extent of hemorrhage as follows:
- Grade 1: Involves only the germinal matrix
- Grade 2: Involves the ventricle without ventricular dilation
- Grade 3: Involves at least 50% of the ventricle with associated dilation
- Grade 4: Involves periventricular brain parenchyma

Clinical factors associated with increased risk of IVH include lower gestational age, pneumothorax, male sex, and bolus administration of normal saline or sodium bicarbonate. Protective factors include prenatal administration of betamethasone and delaying cord clamping until 30 to 60 seconds after birth.

Among neonates weighing less than 1,500 g at birth, 30% will develop IVH, most often grade 1 or 2. The risk of long-term neurologic impairment is higher for those with grade 3 or 4 IVH. However, those with grade 1 or 2 IVH typically have worse neurodevelopmental outcomes than neonates without IVH.

PREP Pearls
- Intraventricular hemorrhage (IVH) is primarily a disease of premature neonates born before 32 weeks of gestation.
- Most neonates with IVH are clinically asymptomatic.
- Pneumothorax is associated with increased risk of IVH in premature neonates.
- Antenatal corticosteroid administration and delayed cord clamping reduce the risk of IVH among premature neonates.

ABP Content Specifications(s)
- Recognize the clinical and laboratory features associated with intracranial hemorrhage in a neonate, and manage appropriately

Suggested Readings
- Carlo WA, Ambalavanan N. Nervous system disorders. In: Kliegman RM, Stanton BF, St Geme J, Schor NF eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016;chap 99:834–844.
- Mercer JS, Vohr BR, McGrath MM, et al. Delayed cord clamping in very preterm infants reduces the incidence of intraventricular hemorrhage and late-onset sepsis: a randomized, controlled trial. *Pediatrics*. 2006;117(4):1235–1242. doi: http://dx.doi.org/10.1542/peds.2005-1706.
- Volpe JJ. Intraventricular hemorrhage in premature infants. *Pediatr Rev*. 1980;2:145-153. doi: http://dx.doi.org/10.1542/pir.2-5-145 .

Question 179

A local news program is running a series on burns in young children, and several families have commented on the reports during health supervision visits in your office today. The mother of a 3-year-old child seeks further information about the risks for her child.

Of the following, the most accurate information to provide this mother about children this age is that

A. electrical burns are more common than thermal burns
B. microwave oven–related burns occur frequently
C. most burns are the result of child abuse
D. they are less likely to be affected than school age (6- to 10-year-old) children
E. the trunk is the most common site for burns

Correct Answer: B

Burn injuries are common events leading to approximately 120,000 emergency department visits annually for individuals younger than 21 years of age. Among burns requiring medical attention, thermal events far outpace electrical, chemical, and radiation (including sunburn) burns in all pediatric age groups. Children younger than 6 years of age are the most frequently affected by burns. The most common mechanism is scalding, either from tap water or heated food and liquids. Overall, the most common location for burns in children is the hand and finger (36.0%), followed by the head and face (21.1%), lower arm (10.5%), upper arm and trunk (9.6%), lower trunk and upper leg (6.0%), and the foot and toe (5.4%).

In a study of children younger than 61 months who were cared for in a burn unit over a 2-year period, most non–tap water scalds occurred in the kitchen/dining area, involved hot food or beverages, and happened during food preparation or the interval between preparation and consumption. The most frequent events involved a child pulling over a container of hot substance, causing the contents to spill onto him or herself; a number occurred when someone else (eg, an older sibling) spilled hot material onto the child or while carrying the child. Approximately 9% of scalds occurred when a toddler or preschooler opened a microwave oven and removed a heated substance. Only 2% of burns occurred from eating a substance that was too hot. In slightly more than 16% of cases, the mechanism of the burn was unknown.

In recent years, burn prevention has focused on advising families regarding important topics such as installing smoke alarms, covering electrical outlets, using sun block, and setting hot water heater thermostats to 120°F or less. Data suggest that additional attention to kitchen safety is warranted. In particular, young children should not be left in the kitchen unsupervised, and, whenever possible, should not play in the kitchen during meal preparation. The handles of cookware (eg, pots and pans) should be turned toward the back of the stove where toddlers are less able to reach them. Given that a substantial number of burns occur while 7- to 14-year-old siblings are caring for infants and toddlers, older siblings should be cautioned to take care while heating foods around young children. All caregivers should be advised to avoid carrying a child while also carrying a hot substance. Microwave ovens should be placed so that they are difficult for toddlers and preschoolers to reach. Ideally, families should have the option to purchase microwave ovens with child safety locks. Children should not be allowed to independently operate a microwave oven or other appliances that generate heat until they are able to read instructions or around 7 years of age.

PREP Pearls
- Burns are common events, and children younger than 6 years old are the most frequently affected.
- The kitchen and dining area, especially during meal preparation, are areas in the home where pediatric burns occur frequently.
- Nearly 10% of kitchen-related burns among children younger than 6 years of age occur when a toddler opens a microwave oven and handles heated foods.

ABP Content Specifications(s)
- Counsel parents regarding prevention of burns (eg, matches, electrical burns, fireworks, hot water heater settings)

Suggested Readings
- D'Souza AL, Nelson NG, McKenzie LB. Pediatric burn injuries treated in US emergency departments between 1990 and 2006. *Pediatrics*. 2009;124:1424-1430. doi: http://dx.doi.org/10.1542/peds.2008-2802.
- Gardner HG and the Committee on Injury, Violence, and Poison Prevention. Office-based counseling for unintentional injury prevention. *Pediatrics*. 2007;119:202-206. doi: http://dx.doi.org/10.1542/peds.2006-2899.
- Lowell G, Quinlan K, Gottlieb LJ. Preventing unintentional scald burns: moving beyond tap water. *Pediatrics*. 2008;122:799-804. doi: http://dx.doi.org/10.1542/peds.2007-2979.
- Thambiraj DF, Chounthirath T, Smith GA. Microwave oven-related injuries treated in hospital EDs in the United States, 1990 to 2010. *Am J Emerg Med*. 2013;31(6):958–963. doi: http://dx.doi.org/10.1016/j.ajem.2013.03.023.

Question 180

A previously healthy 2-year-old girl is seen in the emergency department in October with a 3-day history of clear nasal drainage, a 1-day history of respiratory distress, and a barking cough. The parents report that some of the girl's classmates have had a similar illness in the past few weeks. The girl is febrile (38°C) with a heart rate of 131 beats/min, respiratory rate of 24 breaths/min, and oxygen saturation of 92% on room air. She has clear nasal drainage and inspiratory stridor. The rest of the physical examination findings are normal. A neck radiograph is shown in Item Q180.
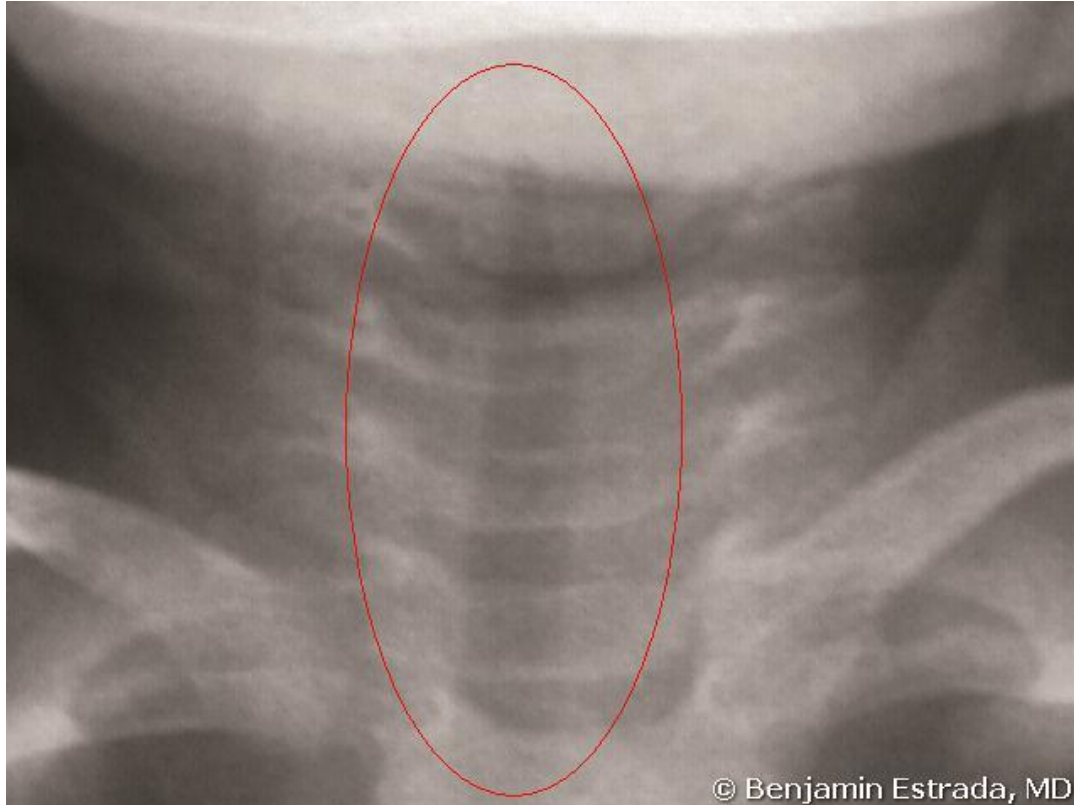
Item Q180: Neck radiograph for the girl described in the vignette
Reprinted with permission from Estrada B and Kimberlin DW, et al. *Red Book Online.* Elk Grove Village, IL. American Academy of Pediatrics 2015

Of the following, the MOST likely pathogen causing her illness is

 A. human metapneumovirus
 B. influenza virus
 C. parainfluenza virus
 D. respiratory syncytial virus
 E. rhinovirus

Correct Answer: C

The history and physical examination of the girl in this vignette, with an antecedent upper respiratory tract infection, fever, barking cough, inspiratory stridor, and respiratory distress with radiographic evidence of subglottic narrowing of the trachea (steeple sign) (**Item C180A**) is consistent with the diagnosis of croup. Croup (laryngotracheitis) is a common inflammatory illness of the larynx and trachea in infants and preschool-aged children. Croup affects up to 5% of children during the second year after birth, with a peak incidence between the ages of 6 months and 3 years. Croup affects 1.5 times as many boys as girls. Although croup is caused by many community respiratory viruses, human parainfluenza virus (HPIV) accounts for 75% of all cases. Influenza A and B, respiratory syncytial virus, human metapneumovirus, adenovirus, measles, coronavirus, and rhinovirus can also cause croup. *Mycoplasma pneumoniae* has also been rarely implicated.
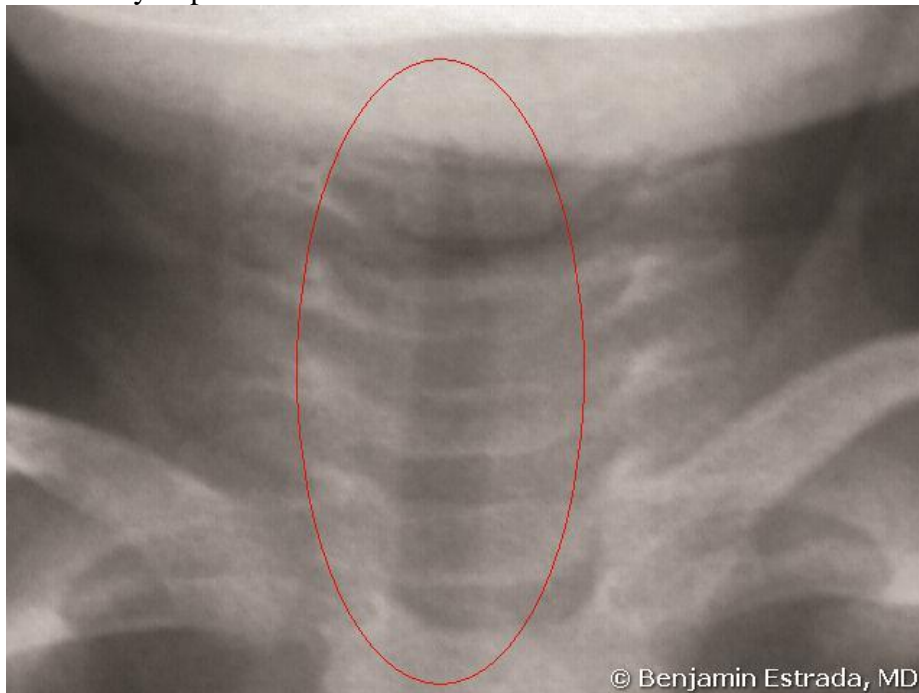
© Benjamin Estrada, MD

Item C180A: Steeple sign in a child with croup.
Reprinted with permission from Estrada B and Kimberlin DW, et al. Parainfluenza viral infections. Red Book Online. Elk Grove Village, IL. American Academy of Pediatrics 2015

Seasonal HPIV infection is an important cause of acute respiratory tract infections among infants and children younger than 5 years in the United States; seasonal HPIV infection accounts for 4% of all respiratory tract infections and 6% to 11% of hospital admissions for lower respiratory tract infections in this age group, second only to respiratory syncytial virus. Infants younger than 6 months are at highest risk for hospitalizations due to HPIV infections with an estimated rate of 3 per 1,000 infants younger than 6 months. Among children aged 2 to 6 years, croup due to HPIV1 is the primary cause of hospitalization. Coinfections with other community respiratory viruses during the same illness are a frequent occurrence among young children, with reported rates as high as 40%. Most children acquire primary infection with multiple HPIV types by 5

years of age. Immunity resulting from HPIV infection in childhood is incomplete; reinfection with HPIV of all serotypes can occur at any age and usually causes a mild upper respiratory tract infection.

Human parainfluenza viruses are single-stranded, enveloped, medium-sized RNA viruses of the *Paramyxoviridae* family that are classified into 4 genetically and antigenically distinct serotypes, each with unique age- and season-specific cyclic outbreak patterns in temperate climates (**Item C180B**). Type 1 is the most common serotype, typically causing large well-defined biennial mid-autumn outbreaks of croup. Type 2 also causes autumn outbreaks, often following HPIV1 outbreaks. Compared to HPIV1 outbreaks, type 2 outbreaks are mild, rare, and less predictable. Type 3 outbreaks occur most frequently during the spring, summer, and fall in odd-numbered years and last longer than outbreaks of types 1 and 2. Young infants are at highest risk for developing severe HPIV3 infection, primarily bronchiolitis and pneumonia. There are few studies describing the epidemiology of HPIV4, which can cause lower respiratory tract infection and affects all age groups; some infections may be severe and require hospitalization.
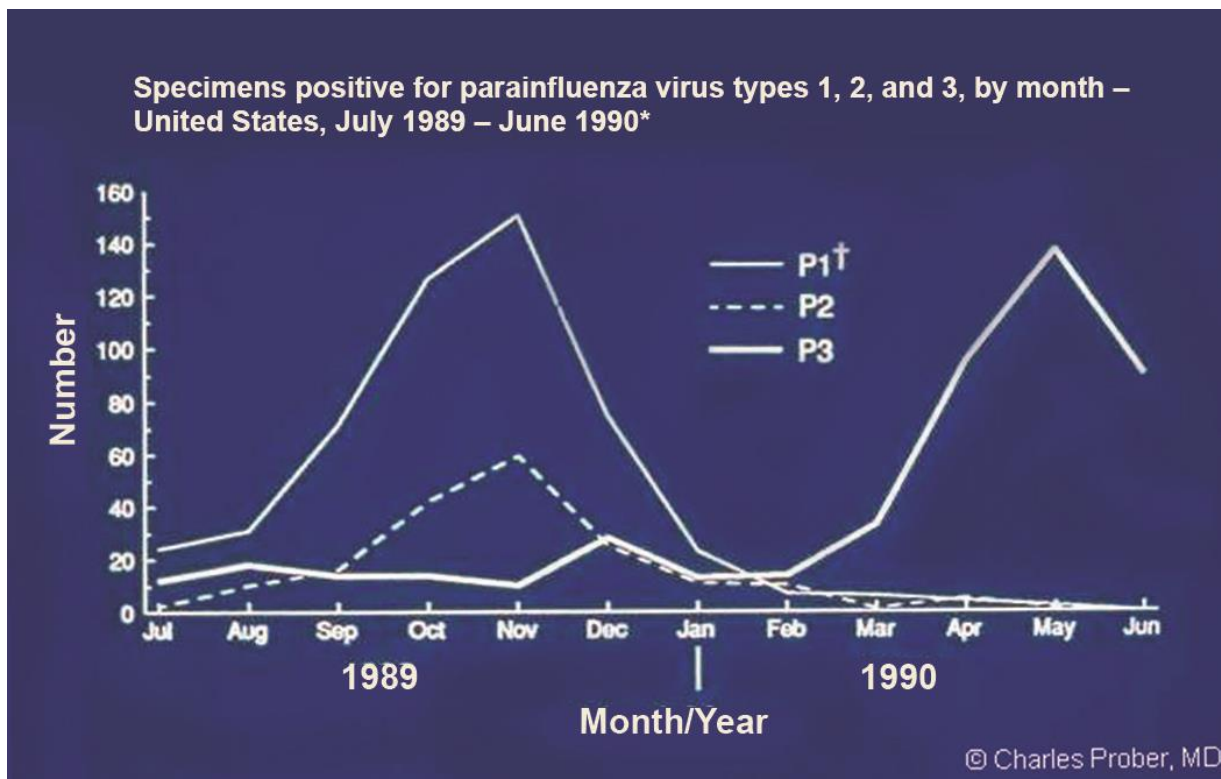
Item C180B: Seasonal pattern of human parainfluenza virus infections type 1-3
Reprinted with permission from Prober C and Kimberlin DW, et al. Parainfluenza viral infections. *Red Book Online.* Elk Grove Village, IL. American Academy of Pediatrics 2015

Transmission of HPIV occurs through direct contact and exposure to upper respiratory tract secretions via droplets and fomites. After an incubation period of 2 to 6 days, HPIV replicates in the ciliated nasopharyngeal epithelial cells, followed 1 to 3 days later by spread to the lower

respiratory tract. In immunocompetent hosts, the onset of viral shedding occurs approximately 1 week before symptom onset and may last up to 3 weeks depending on the serotype.

Human parainfluenza viruses commonly cause lower respiratory tract infections in children. Croup is the most notable clinical manifestation of HPIV (especially type 1), and 75% of croup cases are caused by HPIV. Other manifestations of HPIV are bronchiolitis (5%-15%) and pneumonia (7%), similar to the manifestations of respiratory syncytial virus. Upper respiratory tract infection due to HPIV is complicated by otitis media in 30% to 50% of cases. Uncommon clinical manifestations associated with HPIV3 include parotitis, aseptic meningitis, and encephalitis. Human parainfluenza viruses often cause a mild upper respiratory tract infection in adults, but elderly populations may experience severe illness. Infection with HPIV may aggravate symptoms of asthma or chronic lung disease. Similar to respiratory syncytial virus, HPIVs are potential opportunistic pathogens among immunocompromised patients, especially recipients of hematopoietic stem cell transplants; in this setting, HPIV can cause severe lower respiratory tract infection complicated by respiratory failure, disseminated disease, and death.

Most patients with croup experience improvement of symptoms within 48 hours. Rarely, severe upper airway obstruction can result in respiratory failure and arrest. The differential diagnosis of croup with associated upper airway obstruction includes bacterial tracheitis, retropharyngeal abscess, epiglottitis, inhaled foreign body, or spasmodic croup (**Item C180C**). Children with spasmodic croup are afebrile and generally have transient symptoms with a history of recurrence and absence of antecedent upper respiratory tract infection.

Item C180C. Differential Diagnosis of Acute Upper Airway Obstruction in Infants and Children.

Variable	Laryngomalacia	Supraglottitis (Epiglottitis)	Laryngotracheitis (Croup)	Bacterial Tracheitis
Affected site	Supraglottis	Supraglottis	Subglottis	Trachea
Common ages	2-4 weeks, resolves around 18 months	2-6 years	6-36 months	3 months to 6 years
Onset	Slow	Rapid	Slow	Rapid
Stridor	Inspiratory	Inspiratory, biphasic	Biphasic	Biphasic
Toxic appearance	Uncommon	Yes	Uncommon	Yes
Drooling	No	Yes	No	No
Hoarseness	No	Uncommon	Yes	Possible
Cough	No	Possible	Yes	Yes
Microbiology	None	Bacterial: *Haemophilus influenzae, Streptococcus pneumoniae,* β-hemolytic streptococci, *Staphylococcus aureus*	Viral: parainfluenza	Bacterial: *S aureus, S pneumoniae, H influenzae, Moraxella catarrhalis*

Reprinted with permission from Virbalas J, Smith L. Upper airway obstruction. *Pediatr Rev.* 2015;36(2):62-73.

The laboratory diagnosis of HPIV infection is made by sensitive and specific reverse-transcriptase multiplex polymerase chain reaction assays that can rapidly detect community respiratory viruses including HPIV in nasopharyngeal specimens. Rapid antigen detection methods such as immunofluorescent assays and enzyme immunoassays can also detect the virus in nasopharyngeal specimens, but the utility of these assays is limited by variable sensitivity.

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Other diagnostic techniques, such as viral isolation by culture and serology, are rarely used except for research purposes or in outbreaks. Treatment for HPIV infection is supportive, except for croup, in which the administration of oral, nebulized, or parenteral corticosteroids is effective. For outpatients with mild croup, a single dose of oral dexamethasone is beneficial. For children with moderate to severe croup, oral or intramuscular dexamethasone, nebulized epinephrine, and nebulised budesonide are associated with clinically significant reductions of symptoms as compared to placebo. Contact precautions (in addition to standard precautions) are recommended for hospitalized patients with HPIV infection for the duration of illness.

PREP Pearls
- Human parainfluenza virus is an important cause of acute respiratory tract infections among infants and children younger than 5 years.
- Human parainfluenza virus type 1 is the most common serotype, typically causing large well-defined biennial mid-autumn outbreaks of croup.
- Croup (laryngotracheitis) is the most notable clinical manifestation of human parainfluenza virus, followed by bronchiolitis and pneumonia.
- For outpatients with mild croup, a single dose of oral dexamethasone is beneficial. For children with moderate to severe croup, oral or intramuscular dexamethasone, nebulized epinephrine, and nebulized budesonide are associated with clinically significant reductions of symptoms as compared to placebo.

ABP Content Specifications(s)
- Understand the epidemiology of parainfluenza virus
- Recognize the clinical features associated with parainfluenza virus infection

Suggested Readings
- American Academy of Pediatrics. Parainfluenza viral 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; 2015:586–588.
- Fox TG, Christenson JC. Influenza and parainfluenza viral infections in children. *Pediatr Rev.* 2014;35(6):217–228. doi: http://dx.doi.org/10.1542/pir.35-6-217.
- Virbalas J, Smith L. Upper airway obstruction. *Pediatr Rev.* 2015;36(2):62–73. doi: http://dx.doi.org/10.1542/pir.36-2-62.

Question 181

You are seeing a 3-year-old boy with vomiting and decreased oral intake in the urgent care center. He has vomited 8 times over the past 2 days. His mother states that he is now taking very little fluid, "only a couple of sips in the last 2 hours." She cannot report on his urine output because he had been staying at his father's house.

On physical examination, the child is lying on the examining table and appears somewhat listless, but is able to select a video on his tablet computer. His heart rate is mildly elevated and blood pressure is normal. His eyes are sunken, mucous membranes are dry, and skin is cool to the touch with mildly reduced turgor.

Of the following, the MOST accurate statement regarding the child's degree of dehydration is that

A. determination of dehydration level requires measurement of serum electrolytes and blood urea nitrogen
B. determination of dehydration level requires measurement of urine specific gravity
C. he has mild dehydration ($\leq$5%)
D. he has moderate dehydration (6%–9%)
E. has severe dehydration ($\geq$10%)

Correct Answer: D

Based on his history and physical examination, the boy in the vignette has moderate dehydration. Dehydration occurs when fluid is lost from the extracellular space faster than it is replaced. This is a common presenting complaint at visits to the pediatrician, and is a leading cause of mortality in children worldwide. Gastrointestinal illness with volume losses through vomiting and diarrhea, combined with decreased fluid intake, is the most common cause of dehydration in children. When dehydration occurs, the body shifts fluid from the intracellular to the extracellular space, and conserves fluid by decreasing urine output via release of antidiuretic hormone.

The mainstay of treatment for dehydration, aside from addressing the primary cause, is intravenous or oral fluid replacement. The degree of dehydration should guide the type and amount of fluid needed. To assess the degree of volume loss, the child's weight can be compared to baseline, if available. Other clinical signs and symptoms used to assess the degree of dehydration are found in **Item C181**. Laboratory data can be useful to further clarify the degree and type of dehydration in children with moderate to severe dehydration.

Item C181. Clinical Signs and Symptoms of Dehydration*

Clinical Signs	Mild (3%-5%)	Moderate (6%-9%)	Severe (≥10%)
Systemic signs	Increased thirst	Irritable	Lethargic
Urine output	Decreased	Decreased (<1 mL/kg/h)	Decreased (oliguria/anuria)
Mucous membranes	Tacky	Dry	Parched
Skin turgor[†]	Normal	Reduced	Tenting
Capillary refill[†]	Normal	Mildly delayed	Markedly delayed
Skin temperature	Normal	Cool	Cool, mottled
Anterior fontanelle	Normal	Sunken	Markedly sunken
Heart rate	Normal	Increased	Markedly increased or ominously low
Blood pressure	Normal	Normal to low	Low
Respirations[†]	Normal	Deep rate, may be increased	Deep rate, may be increased or decreased to absent

* These findings for isonatremic dehydration. They may overestimate the degree of dehydration with hyponatremia and underestimate the degree of dehydration with hypernatremia.

[†] Best predictors of dehydration.

Powers KS. Dehydration: Isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev*. 2015;36(7):274-285.

Children with mild dehydration have an essentially normal presentation, except for decreased urine output and tacky mucous membranes. They are unlikely to have abnormal laboratory findings, and thus this testing is not indicated.

For children with hypo- or hypernatremic dehydration, estimation of dehydration based on clinical signs and symptoms can be inaccurate. In hyponatremic dehydration, the degree of dehydration can be overestimated because of the tendency for fluid to shift from the extracellular to the intracellular spaces, thus causing more severe symptoms; the opposite is true for hypernatremic dehydration. Therefore, children who appear to have moderate dehydration should be continually assessed during attempts at oral rehydration.

If oral rehydration is successful, laboratory testing is generally not helpful. However, if intravenous fluids are indicated, obtaining a serum sodium level can be helpful. If abnormal (<130 or >150 mEq/L), this information can be used to adjust the estimated degree of dehydration, as well as guide changes in the type of fluid needed to restore water and sodium balance. Other laboratory values, such as serum bicarbonate, blood urea nitrogen, and urine specific gravity, may change based on the degree of dehydration, but are nonspecific and do not substitute for estimation of hydration status based on clinical signs and symptoms.

PREP Pearls
- A child's degree of dehydration can usually be estimated correctly based on clinical signs and symptoms.
- In cases of hypo- and hypernatremic dehydration, estimates based on clinical signs and symptoms may be inaccurate.

ABP Content Specifications(s)
- Identify early and late clinical signs of dehydration
- Understand the role of changes in extracellular fluid volume in the development of dehydration

Suggested Readings
- Moritz ML, Ayus JC. Misconceptions in the treatment of dehydration in children. *Pediatr Rev*. 2016;37(7):e29–e31. doi: http://dx.doi.org/10.1542/pir.2016-003.
- Powers KS. Dehydration: Isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev*. 2015;36(7):274–285. doi: http://dx.doi.org/10.1542/pir.36-7-274.

Question 182

An 8-year-old boy is brought to your office for evaluation of a gradually enlarging area of hair loss first noticed 3 weeks ago. The boy is otherwise well and is taking no medications. His vital signs and growth parameters are normal. The only notable physical findings are an area of hair loss near the vertex and several erosions (Item Q182).


Item Q182: Alopecia and erosions as described in the vignette.
Courtesy of D. Krowchuk

Of the following, the MOST appropriate treatment is

A. cephalexin orally
B. fluocinonide topically
C. griseofulvin orally
D. minoxidil topically
E. zinc pyrithione-containing shampoo

Correct Answer: C

The boy in this vignette has a well-defined acquired patch of alopecia that contains "black-dot" hairs, the remnants of broken hairs within follicles (**Item C182A**). The presence of crusted erosions suggests that pustules, present as part of an inflammatory response, have ruptured. These findings suggest the diagnosis of tinea capitis, and treatment with oral griseofulvin is indicated.
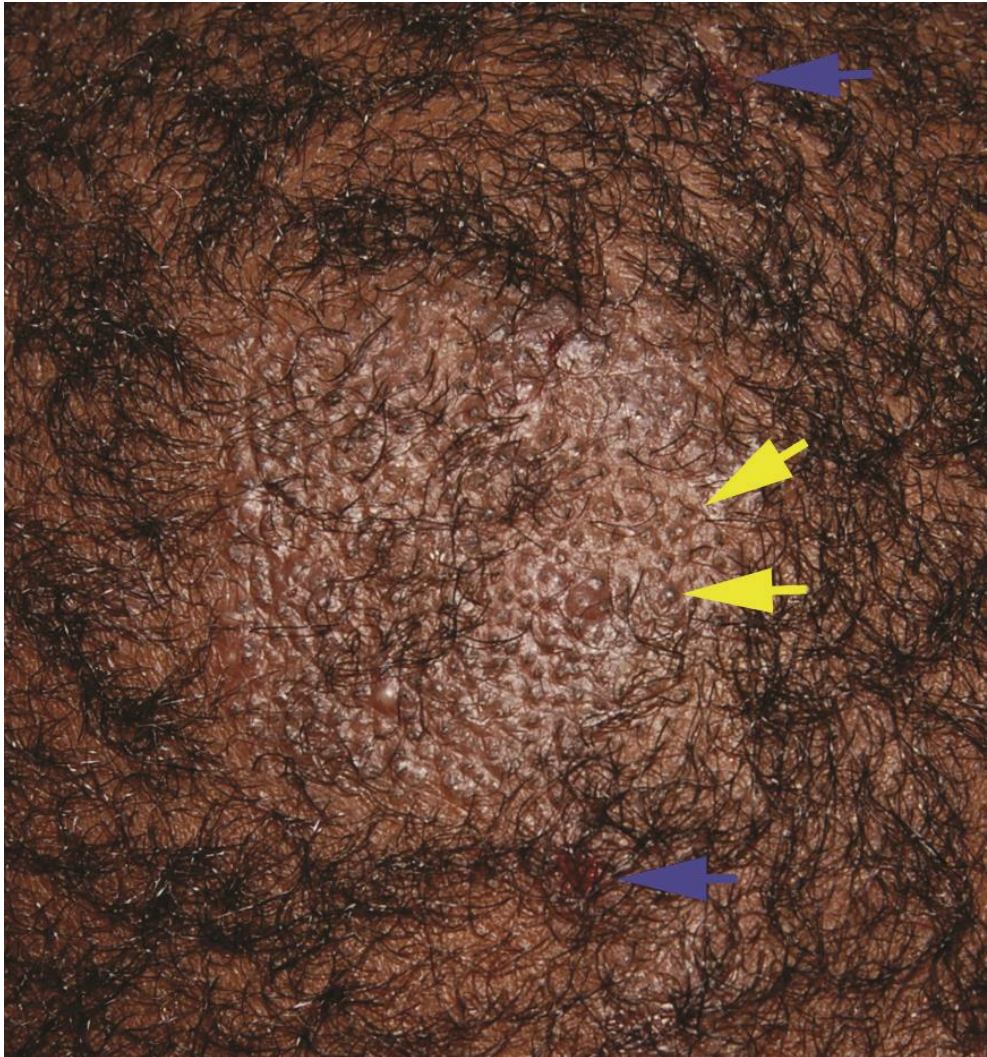
Item C182A: Tinea capitis with "black-dot" hairs (yellow arrows) and crusted erosions (blue arrow). Courtesy of D. Krowchuk

Traction on hairs, often the result of tight braiding, may produce folliculitis and ultimately alopecia (**Item C182B**). In severe cases, therapy with an oral antibiotic, like cephalexin, may be required. Alopecia areata is characterized by well-defined areas of hair loss, but the scalp appears normal and black-dot hairs are not present. If treatment is warranted, a potent topical corticosteroid (eg, fluocinonide) is recommended, often in conjunction with topical minoxidil.

Item C182B: Erythematous follicular papules or pustules (arrows) due to traction on hairs. Courtesy of D. Krowchuk

Seborrheic dermatitis of the scalp results in scaling but not localized alopecia. First-line treatment is an anti-seborrheic shampoo containing zinc pyrithione or selenium sulfide.

Tinea capitis is a common cause of acquired, localized hair loss in children. For reasons that are unclear, African American children are disproportionately affected. In the United States, more than 90% of infections are caused by *Trichophyton tonsurans* (transmitted person to person); the remainder are caused by *Microsporum canis* (transmitted to humans by cats or dogs).Three patterns of infection are recognized:

- Alopecia: one or more well-defined patches of hair loss with associated scale. Infection with *T tonsurans* causes hairs to break at the scalp, resulting in black-dot hairs and complete alopecia (**Item C182A**). *Microsporum canis* causes hair to break further from the scalp. As a result, black-dot hairs are absent and hair loss is incomplete.
- Seborrheic: some patients infected with *T tonsurans* develop patchy or diffuse scaling of the scalp with subtle alopecia.
- Inflammatory: when there is an immune response to the fungus, patients may develop pustules and crusting (**Item C182A**) or a tender, boggy mass called a kerion (**Item C182C**). Suboccipital or posterior cervical lymphadenopathy may be present in all forms of tinea capitis but especially in the inflammatory forms. Although complete hair re-growth usually occurs following kerion resolution, some degree of permanent alopecia occasionally occurs.

Item C182C: Kerion. Courtesy of D. Krowchuk

The diagnosis of tinea capitis is usually made clinically. The presence of alopecia and regional lymphadenopathy is highly predictive. If uncertainty exists, a potassium hydroxide preparation may be performed, although expertise is required for accurate interpretation. Culture in dermatophyte test medium or another suitable medium is the most sensitive diagnostic technique. If dermatophyte test medium is available in the clinical setting, it may be inoculated by using a specimen collected with a moistened cotton-tipped applicator, sterile toothbrush, or cytobrush. If it is not available, a collection kit containing a swab, tube, and transport medium should be used and sent to a reference laboratory.

Treating tinea capitis requires oral therapy. Food and Drug Administration (FDA)–approved options include the following treatments:

- Griseofulvin (20-25 mg/kg/d of the microsize preparation or 10-15 mg/kg/d of the ultramicrosize preparation) is generally considered the first-line choice. Patients should be treated for 6 to 8 weeks, and laboratory monitoring is unnecessary.
- Terbinafine tablets (10-20 kg, 62.5 mg/d; 21-40 kg, 125 mg/d; > 40 kg, 250 mg/d) have become first-line therapy for some clinicians because of the shorter treatment course (4-6

weeks) and favorable cost profile. A granule formulation is available but may not be covered by insurance.
- Fluconazole (6 mg/kg/d for 3-6 weeks) is the only FDA-approved agent for children younger than 2 years, although other agents are used "off label."

Ancillary issues:
- Using an antifungal shampoo containing selenium sulfide (1% or 2.5%) or ketoconazole (2%) twice weekly for 2 weeks may reduce the likelihood of spread of infection to others. Some experts recommend antifungal shampoo use by asymptomatic family members, but the efficacy of this strategy is unknown.
- For children who have severe inflammatory tinea capitis, a 1- to 3-week course of prednisone may be considered.
- Although *Staphylococcus aureus* can often be cultured from the scalp of children who have tinea capitis, antibiotic therapy rarely is necessary.
- Children should not be excluded from school once treatment is begun.
- Patients should be seen for follow-up in 1 month to assess response to therapy.

PREP Pearls
- Tinea capitis most often presents as an acquired patch of alopecia that contains black-dot hairs or scale.
- The treatment of tinea capitis requires oral therapy with griseofulvin, terbinafine, or fluconazole.

ABP Content Specifications(s)
- Understand the etiology and complications of kerions
- Recognize the clinical findings associated with tinea capitis, and manage appropriately

Suggested Readings
- Moriarty B, Hay R, Morris-Jones R. The diagnosis and management of tinea. *BMJ*. 2012;345:e4380. doi: http://dx.doi.org/10.1136/bmj.e4380.
- Section on Dermatology, American Academy of Pediatrics. Tinea capitis. In: Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016:255–262.

Question 183

A medical student observes a health supervision visit for a 4-month-old boy who is new to your practice. He is accompanied by his mother. During the visit, you screen the patient's mother for intimate partner violence, as you do for all families. After the visit, the medical student asks why you routinely screen your patients' parents for intimate partner violence.

Of the following, the MOST accurate reason to screen for this condition is that

A. children exposed to intimate partner violence are at increased risk of maltreatment
B. children exposed to intimate partner violence are less likely to experience violent relationships as teenagers
C. if intimate partner violence were revealed, you would be required to file a police report
D. if intimate partner violence were revealed, you would immediately place the child into foster care
E. infants exposed to intimate partner violence are more likely to overeat and become obese

Correct Answer: A

Intimate partner violence (IPV) is defined as psychological, physical, or sexual harm or threats of harm from a current or previous partner. It occurs in individuals of all ages, races, socioeconomic groups, gender identities, and sexual orientations. Risk factors for IPV include younger age, female gender, lower socioeconomic status, and family or personal history of violence. Pregnancy and the immediate postpartum period are times of particularly high risk for women. Intimate partner violence is underreported because victims may conceal the abuse and symptoms can be subtle. Factors that should raise suspicion for IPV include:

- Inconsistent explanations for injuries
- Delays in seeking care, missed appointments, or noncompliance with medical recommendations
- Overutilization of emergency department services
- Inappropriate affect, extreme discomfort with sensitive portions of the examination, or unwillingness to undress
- An overly attentive or verbally abusive partner

Children are affected by IPV in a variety of ways. Teens are at particularly high risk for IPV, and adolescent dating violence may be more likely to involve stalking or electronic threats. Child abuse and neglect are more likely in families where IPV is also present, and children may be accidental victims of violence between their parents. Children who witness violence are at higher risk for physical, behavioral, and mental health problems and are more likely to have poor health outcomes as adults, including obesity, physical inactivity, and depression.

Although there is no current recommendation that pediatricians screen all families for IPV, pediatricians should be aware of risk factors, signs, and symptoms. The primary reason that a pediatrician might screen for IPV is that children exposed to IPV are at increased risk of maltreatment. Children exposed to IPV are also more likely to experience violent relationships as teenagers. Laws regarding child protective service reporting for IPV that occurs in a home with children vary by state, but clinicians are not required to file a police report and would not immediately place a child exposed to IPV into foster care. Infants exposed to IPV are more likely to be underweight, not overweight.

PREP Pearls
- Intimate partner violence occurs across all demographic groups, and risk factors include young age, lower scioeconomic status, female gender, and personal or family history of violence. Teens and pregnant women are at particularly high risk for intimate partner violence.
- Children exposed to intimate partner violence are at increased risk for medical, behavioral, and mental health problems and are more likely to be abused or neglected.

ABP Content Specifications(s)
- Identify the important precipitants of intimate partner violence
- Recognize common characteristics that may indicate intimate partner violence, and the effects of such violence on children

Suggested Readings
- Centers for Disease Control and Prevention. Intimate partner violence. https://www.cdc.gov/violenceprevention/intimatepartnerviolence/index.html.
- Nelson HD, Bougatsos C, Blazina I. Screening women for intimate partner violence: a systematic review to update the U.S. Preventive Services Task Force recommendation. *Ann Intern Med*. 2012;156(11):796–808. doi: http://dx.doi.org/10.7326/0003-4819-156-11-201206050-00447.
- Thackeray JD, Hibbard R, Dowd MD. Intimate partner violence: the role of the pediatrician. *Pediatrics*. 2010;125(5):1094–1100. doi: http://dx.doi.org/10.1542/peds.2010-0451.

Question 184

A 10-year-old obese girl is brought to your office for an urgent appointment for evaluation of elevated liver function tests identified during a recent emergency department visit for acute gastroenteritis (fever, nausea, and vomiting). Her mother reports that her school performance has been declining over the past 6 to 12 months. She has been fatigued despite increasing sleep. She continues to have a good appetite. They report no recent medication, alcohol, or cannabinoid use.

Her heart rate is 87 beats/min, respiratory rate is 18 breaths/min, and blood pressure is 115/69 mm Hg. She is tracking on her growth curve at the 25th percentile for height and 98th percentile for weight. Her physical examination is remarkable for a soft abdomen without hepatosplenomegaly. Her neurologic examination demonstrates grossly normal cranial nerves, although a slight tremor is noted in both hands. The patient's right eye is shown in Item Q184.
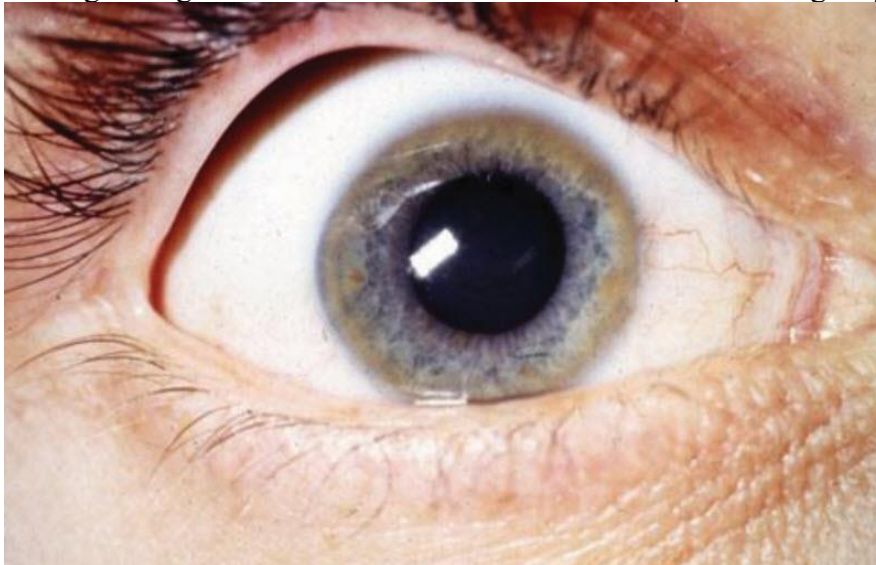
Item Q184: Ocular findings for the girl described in the vignette.
Courtesy of T.Koch

Laboratory data are shown:

Laboratory Test	Result
Complete blood cell count	Normal
Aspartate aminotransferase	142 U/L
Alanine aminotransferase	98 U/L
γ-Glutamyltransferase	50 U/L
Total bilirubin	4 mg/dL (68.4 µmol/L)
Direct bilirubin	2.8 mg/dL (47.9 µmol/L)

Of the following, the MOST likely diagnosis is

A. autoimmune hepatitis
B. Gilbert disease
C. hepatitis B
D. progressive familial intrahepatic cholestasis
E. Wilson disease

Correct Answer: E

The girl in this vignette has Wilson disease. Wilson disease should be suspected because of the elevated liver function test results, including conjugated hyperbilirubinemia, in a child with decreasing school performance, worsening fatigue, and tremor. The eye examination showing a Kayser-Fleischer ring, which is due to copper accumulation around the cornea, supports this diagnosis. Kayser-Fleischer rings are seen in 97% of patients with Wilson disease who have neurologic manifestations.

The differential diagnosis for conjugated hyperbilirubinemia (**Item C184A**) is extensive for neonates, older children, and adults. Conjugated hyperbilirubinemia is rare outside of infancy. Presentation can vary based on the underlying etiology. Symptoms can include scleral icterus, jaundice, pruritus, abdominal pain, nausea, and fatigue. The evaluation of conjugated hyperbilirubinemia involves a complete history and physical examination. The examination should focus on the abdomen to assess the size and texture of the liver, along with an evaluation for stigmata of portal hypertension and cirrhosis (splenomegaly, ascites, palmar erythema, caput medusae, and spider angioma).

Item C184A. Differential Diagnosis for Conjugated Hyperbilirubinemia by Age.

Neonate	Child or Adult
Acquired infections	**Acute infections**
• Urinary tract infection	• Adenovirus
• Sepsis	• Cytomegalovirus
Cholestatic syndromes	• Hepatitis A, B, C, D, and E viruses
• Alagille syndrome	• Epstein-Barr virus
• Progressive familial intrahepatic cholestasis	• Influenza virus
Congenital infections	**Cholestatic syndromes**
• Cytomegalovirus	• Crigler-Najjar
• Herpes simplex virus	• Dubin-Johnson
• Human immuno-deficiency virus	• Gilbert
• Rubella	• Rotor
• Syphilis	• Progressive familial intrahepatic cholestasis
• Toxoplasmosis	**Drug and toxin induced**
Drug and toxin induced	• Drugs (antibiotics, azathioprine, bupropion, cetirizine, cyclosporine, isoniazid, gabapentin, risperidone)
• Parenteral nutrition	• Environmental toxins
• Drugs (antibiotics, azathioprine, cyclosporine, isoniazid, gabapentin)	• Parenteral nutrition
Endocrinopathy	**Immunologic**
• Hypothyroidism	• Autoimmune hepatitis
• Hypopituitarism	• Primary sclerosing cholangitis
Metabolic	**Metabolic**
• α1-Antitrypsin deficiency	• α1-antitrypsin deficiency
• Cystic fibrosis	• Cystic fibrosis
• Defects in bile acid synthesis	• Glycogen storage disease (types 1 and 4)
• Galactosemia	• Lipid storage disease
• Inborn error of carbohydrate, fat, protein metabolism	• Mitochondrial disorders
• Tyrosinemia	• Nonalcoholic fatty liver disease
Obstructive	• Peroxisomal disorders
• Biliary atresia	• Storage disorders
• Choledochal cyst	• Wilson disease
• Inspissated bile syndrome	**Obstructive**
• Spontaneous perforation of the bile duct	• Autosomal recessive polycystic kidney disease
Systemic disorders	• Caroli disease
• Congenital heart disease/heart failure	• Choledochal cyst
• Shock	• Cholelithiasis
	Vascular
	• Hepatic outflow obstruction (Budd-Chiari syndrome)
	• Portal vein thrombosis
	• Veno-occlusive disease associated with chemotherapy

Courtesy of C. Waasdorp Hurtado
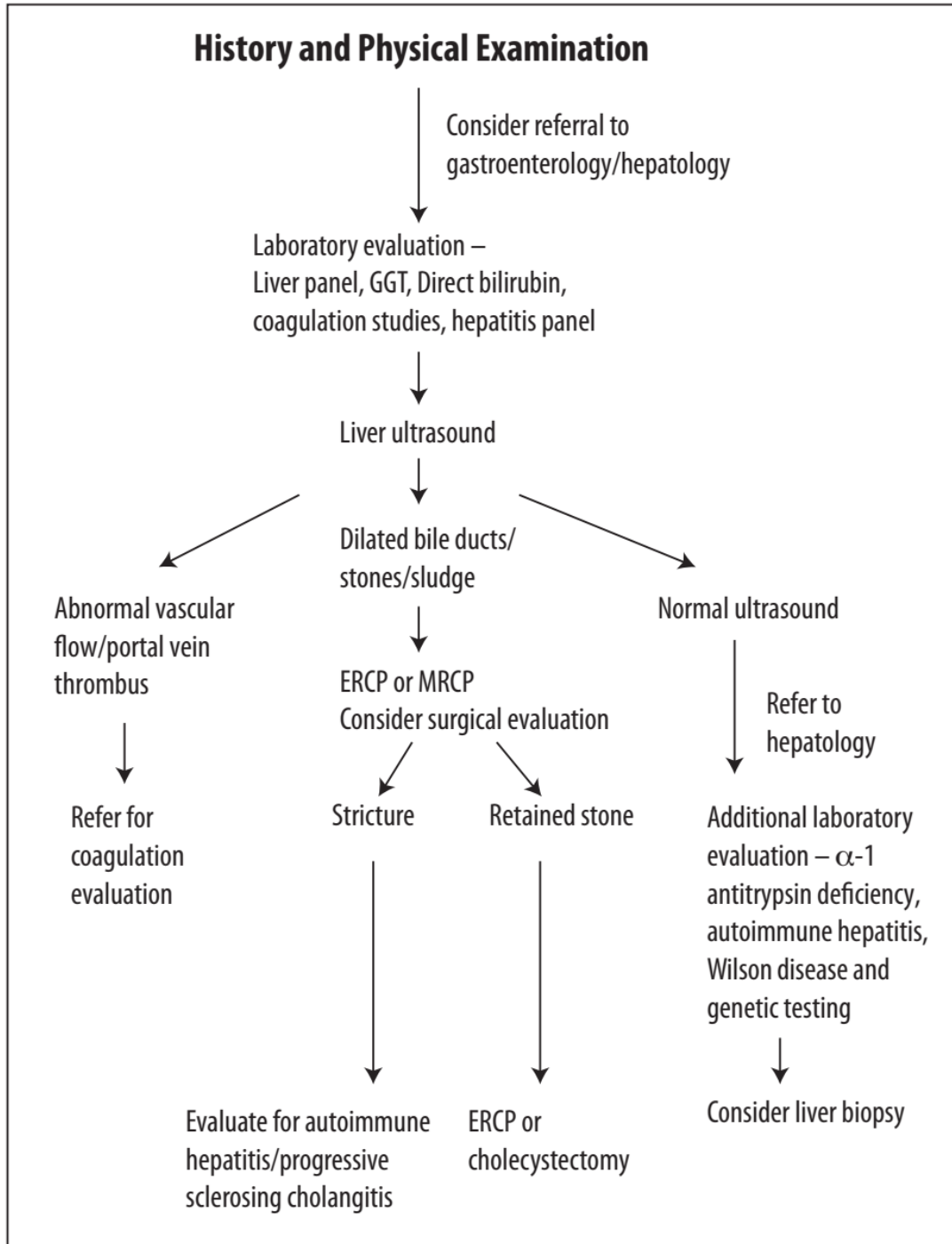
Following the history and physical examination, additional laboratory studies should be obtained (**Item C184B**). Abdominal ultrasonography is needed to assess for obstruction and evaluate anatomy. If there are concerns for cholelithiasis with obstruction or additional questions about biliary anatomy, an endoscopic retrograde cholangiopancreatography is the evaluation of choice because it allows for both visualization and treatment. Magnetic resonance cholangiopancreatography can be used for anatomic evaluation, but it does not allow for therapeutic intervention. **Item C184C** demonstrates the recommended algorithm for evaluation.

Item C184B. Laboratory Studies for Evaluation of Conjugated Hyperbilirubinemia.

Laboratory Test	Indication
Serum aminotransferases (aspartate aminotransferase, alanine aminotransferase, γ-glutamyltransferase, and bilirubin)	Assess for hepatitis/ acute or chronic liver injury
Coagulation studies (prothrombin time, partial thromboplastin time, and international normalized ratio)	Assess liver synthetic function
Infectious evaluation with titers	Screen for acute infection
α1-antitrypsin phenotype	Screen for α1-antitrypsin deficiency
Antinuclear antibody, anti-smooth muscle antibody, anti-liver antibody, kidney microsomal antibody	Screen for autoimmune hepatitis
Serum ceruloplasmin, urine copper, and slit-lamp examination for Kayser-Fleischer rings	Screen for Wilson disease

Courtesy of C. Waasdorp Hurtado

Item C184C. Algorithm for Evaluation of Conjugated Hyperbilirubinemia in a Child and Adult.

History and Physical Examination

Consider referral to gastroenterology/hepatology

Laboratory evaluation –
Liver panel, GGT, Direct bilirubin,
coagulation studies, hepatitis panel

Liver ultrasound

Dilated bile ducts/
stones/sludge

Abnormal vascular flow/portal vein thrombus

Normal ultrasound

ERCP or MRCP
Consider surgical evaluation

Refer to hepatology

Refer for coagulation evaluation

Stricture   Retained stone

Additional laboratory evaluation – α-1 antitrypsin deficiency, autoimmune hepatitis, Wilson disease and genetic testing

Evaluate for autoimmune hepatitis/progressive sclerosing cholangitis

ERCP or cholecystectomy

Consider liver biopsy

Abbreviations: ERCP, endoscopic retrograde cholangiopancreatography; GGT, γ-glutamyltransferase; MRCP, magnetic resonance cholangiopancreatography

Courtesy of C. Waasdorp Hurtado

The child in this vignette does not have autoimmune hepatitis. Autoimmune hepatitis can present as acute hepatitis with malaise, nausea, and vomiting with or without jaundice, or it can present insidiously with few symptoms. At the time of presentation, laboratory data show significant elevation in serum transaminases, elevated bilirubin (direct and indirect), and the presence of autoantibodies. People with autoimmune hepatitis do not have Kayser-Fleischer rings and have normal neurologic examination results.

The child does not have Gilbert disease, which is a defect in the bilirubin conjugation enzyme resulting in unconjugated hyperbilirubinemia.

Hepatitis B can present as a congenital infection caused by vertical transmission, or it can present later as an acute infection. Children with hepatitis B do not have Kayser-Fleischer rings and have normal neurologic examination results.

Finally, this child does not have progressive familial intrahepatic cholestasis, which is a heterogenous group of autosomal recessive disorders that presents in infancy.

PREP Pearls
- Conjugated hyperbilirubinemia is uncommon outside of infancy.
- The differential diagnosis of conjugated hyperbilirubinemia is extensive and can be grouped into infections, obstruction, metabolic, vascular, immunologic, and cholestatic disorders.
- History, physical examination, and laboratory studies (liver function tests, coagulation studies, infectious evaluation) are the initial steps in the evaluation of conjugated hyperbilirubinemia.

MOCA-Peds Objective
- Evaluate a patient with jaundice beyond the neonatal period.

ABP Content Specifications(s)
- Plan the appropriate evaluation of a child with conjugated hyperbilirubinemia

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.
- 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.
- Levy C. Advances in cholestatic liver diseases. *Clin Liver Dis.* 2016;20(1):xiii–xiv. doi: http://dx.doi.org/10.1016/j.cld.2015.10.013.

Question 185

As part of their routine health supervision, you obtain blood lead levels in 1- and 2-year-old siblings. The results are as follows: 7 µg/dL (0.3 µmol/L) for the 1 year old and 9 µg/dL (0.4 µmol/L) for the 2 year old. This was the first assessment for the younger child, and last year the 2 year old had a blood lead level that was not detectable. An environmental review with the parents only reveals that they live in an older apartment building that is undergoing renovation.

Of the following, the MOST appropriate management for these children is to

  A. arrange an intensive professional cleaning of their apartment
  B. educate the parents in appropriate home cleaning techniques
  C. prescribe oral chelation therapy
  D. relocate the family during renovations
  E. repeat the blood test in 6 months

Correct Answer: D

The children in the vignette live in a home that is undergoing renovation. Renovation may release lead-containing dust, and is a risk factor for increased blood lead levels (BLL). In one study, home renovation was associated with 12% higher mean BLLs. Lead safe work practices during renovation help protect against these elevations. These include: (1) relocating families during work, when necessary; (2) minimizing dust creation; (3) dust containment; (4) thorough clean up; (5) safe waste disposal; and (6) clearance testing (ie, testing dust for residual lead levels at the completion of the work).

Both children in the vignette have lead levels above the current reference value for acceptable levels of lead (5 μg/dL [0.2 μmol/L]), but there is no threshold value below which blood levels are safe. The older child demonstrates a measurable increase in lead level compared with levels before renovation. Therefore, the safest intervention for this family would be to relocate the children until the work is completed and clearance testing has been done. Unfortunately, this can be costly, but alternative approaches have not proved to be effective. Education strategies that focus on home cleanliness and lead toxicity awareness have not resulted in significant decreases in mean BLLs, even when cleaning supplies were provided or the education was intensive and prolonged. A single intensive professional cleaning can effectively decrease BLLs in homes without carpeting, but the contaminated dust reaccumulates within 3 to 6 months.

Because there is no safe threshold for lead exposure, management of environmental lead exposure focuses on primary prevention. Lead safe work practices; lead remediation in housing built before 1978 (particularly focusing on homes built before 1960); appropriate corrosion control and water line replacement of lead pipes; and monitoring for and banning lead-containing consumer products such as herbal medicines, toys, and other household items are important management steps.

Most children with elevated BLLs are asymptomatic, therefore surveillance is important to detect those at risk. Current Medicaid guidelines require lead screening at ages 12 and 24 months for all children enrolled in the program. Repeat monitoring, generally within 1 to 3 months, is recommended for children with levels between 5 and 10 μg/dL (0.2–0.5 μmol/L) especially when their history indicates likely lead exposure; more frequent monitoring is necessary for children with higher BLLs. Chelation therapy does not reverse the neurologic and behavioral effects of elevated lead levels, and is recommended only for children with BLLs higher than 44 μg/dL (2.1 μmol/L). The primary care provider should consider consulting with a toxicology specialist regarding treatment for children with levels higher than 20 μg/dL (1.0 μmol/L). Affected families should receive dietary counseling to encourage adequate iron and calcium intake (both of which compete with lead for absorption). Although there is no specific developmental pattern or abnormality associated with lead toxicity, children with elevated BLLs are at risk for future neurobehavioral problems. Therefore, pediatricians should perform, or refer such children for, periodic neurodevelopmental screening. Most importantly, parents should be supported in providing a developmentally rich home environment and encouraged to have their children participate in early enrichment programs. These developmental interventions may ameliorate some of the cognitive impact of lower level elevations in BLLs.

PREP Pearls
- The current reference value for blood lead levels in the United States is 5 µg/dL (0.2 µmol/L), but there is no threshold value below which blood lead levels are safe.
- Because there is no effective treatment to reverse the effects of lead on cognition and behavior, primary prevention is the most important approach to managing lead toxicity.
- Home renovation is a risk factor for increased blood lead levels in children but can be mitigated by: (1) relocating families during renovation work when appropriate; (2) minimizing dust creation; (3) dust containment; (4) thorough clean up; (5) safe waste disposal; and (6) clearance testing.

ABP Content Specifications(s)
- Plan appropriate management of an increased blood lead concentration

Suggested Readings
- American Academy of Pediatrics Council on Environmental Health. Prevention of childhood lead toxicity. *Pediatrics*. 2016;138(1):e20161493. doi: http://dx.doi.org/10.1542/peds.2016-1493.
- Binns HF, Campbell C, Brown MJ, Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning Prevention. Interpreting and managing blood lead levels of less than 10 µg/dL in children and reducing childhood exposure to lead: recommendations of the Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning Prevention. *Pediatrics*. 2007;120:e1285–e1298. doi: http://dx.doi.org/10.1542/peds.2005-1770.
- Chandran L, Cataldo R. Lead poisoning: basics and new developments. *Pediatr Rev.* 2010;31:399–405. doi: http://dx.doi.org/10.1542/pir.31-10-399.

Question 186

You are seeing a 6-month-old male infant who was brought to the emergency department because of progressive poor feeding and listlessness over the past 2 weeks. He previously took 5 oz of formula every 3 hours and was gaining weight well, but is now taking only 2 oz per feed. Each feed now requires 30 minutes, and is accompanied by occasional coughing and sputtering. He has had no fever or vomiting, and had no sick contacts. His bowel movements are becoming less frequent. His sleep habits have not changed. He is less active. He had recently learned to sit up, but over the past 2 weeks, he has been falling over quickly.

The boy's vital signs include a temperature of 37.0°C, heart rate of 120 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 80/45 mm Hg. His oxygen saturation is 100% on room air. On physical examination, he is awake and alert. He has bilateral ptosis, his pupils are equal and reactive, and his mucous membranes are dry. His cough and gag reflexes are weak. He has decreased head control and mild weakness of all extremities. His upper and lower extremity deep tendon reflexes are present, but diminished. He is breathing comfortably, with clear lung fields. His heart has a regular rate and rhythm, without rubs, murmurs, or gallops, and he has strong peripheral pulses. His abdomen is soft, nontender, and nondistended, with no organomegaly.

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

A. Duchenne muscular dystrophy
B. Guillain-Barré syndrome
C. infant botulism
D. myasthenia gravis
E. spinal muscular atrophy

Correct Answer: C

The 6-month-old boy in this vignette has constipation and physical examination findings of muscular weakness affecting his facial and oropharyngeal muscles more than his limbs. The most likely diagnosis is infant botulism.

Infant botulism is caused by the gram-positive, spore-forming anaerobic bacillus *Clostridium botulinum*, which can be found in soil. It most commonly occurs in infants between 2 and 6 months of age. Ingestion of contaminated food products such as honey and corn syrup, has been implicated, but many cases are presumably acquired through breathing in and then swallowing the spores. Spores from the bacteria ingested by the infant germinate in the colon and release the botulinum neurotoxin, which binds irreversibly to postsynaptic acetylcholine receptors. This results in inhibition of neurotransmission at the neuromuscular junction synapses, parasympathetic synapses, and postganglionic synapses.

The clinical presentation of infant botulism often starts with constipation, then weakness develops, which progresses in a rostrocaudal fashion. Early involvement of muscles innervated by the cranial nerves leads to a weak cry, difficulty swallowing, facial droop, ptosis, and diminished cough, gag, swallow, and pupillary reflexes. Later, decreased power in the large muscles can cause poor head control, limb weakness, diminished deep tendon reflexes, and truncal instability. Impaired gag reflex and decreased respiratory effort are life-threatening manifestations of infant botulism. Involvement of the parasympathetic nervous system is manifested by dry mucous membranes, constipation, blood pressure instability, and urinary retention. It is very important to note that respiratory failure can occur without respiratory distress. Clinicians often depend on signs of accessory breathing muscles (substernal, intercostal, and supraclavicular retractions) to make the diagnosis of respiratory failure, but these may be absent in infant botulism and other causes of neuromuscular weakness.

Treatment of infant botulism is supportive, with consideration of administration of intravenous botulism immune globulin within 3 days of hospital admission. This has been shown to shorten hospital course and decrease illness severity. Affected infants with impaired cough or gag reflexes should be monitored for aspiration. Tube feedings may be necessary for infants who are too weak to take adequate oral feeds. Those with weak respiratory effort may require admission to the intensive care unit, and in some cases may require noninvasive or invasive mechanical ventilation. The gold standard method for diagnosing infant botulism is the detection of *Clostridium botulinum* spores or toxin in the feces.

The differential diagnosis for neuromuscular weakness in this age group includes inborn errors of metabolism, hypothyroidism, tick paralysis, myasthenia gravis, Guillain-Barré syndrome, and spinal muscular atrophy. Duchenne muscular dystrophy is not a likely diagnosis for the boy in this vignette, because it usually presents in the preschool age group, not in infants, and the initial signs usually involve large muscle weakness as opposed to bulbar weakness. Guillain-Barré syndrome can cause bulbar signs and neuromuscular weakness, but the weakness is usually ascending, there is often sensory involvement, and it is extremely rare in infancy. Myasthenia gravis is unlikely, because it is not common in this infant's age group and there is no history of

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waxing and waning symptoms. Lastly, type 1 spinal muscular atrophy can also cause life-threatening weakness in infancy, but the weakness spares the face, and is slowly progressive over months, compared with the days to weeks-long time course of infant botulism.

PREP Pearls
- Infant botulism can result from ingestion of honey, corn syrup, or more commonly, presumed inhalation of *Clostridium botulinum* spores.
- Treatment for infant botulism is supportive, focusing on nutrition and monitoring for aspiration and respiratory failure.
- Intravenous botulism immune globulin, especially if given within 3 days of hospital admission, has been shown to decrease length of hospital stay and severity of illness.
- In patients with neuromuscular weakness, respiratory failure can occur without signs of respiratory distress.

ABP Content Specifications(s)
- Plan appropriate diagnostic evaluation of botulism
- Understand the epidemiology of Clostridium botulinum infection
- Recognize the clinical features associated with botulism
- Plan appropriate management for a patient with botulism

Suggested Readings
- Arnon SS, Schechter R, Maslanka SE, Jewell NP, Hatheway CL. Human botulism immune globulin for the treatment of infant botulism. *N Engl J Med.* 2006;354:462–471. doi: http://dx.doi.org/10.1056/NEJMoa051926.
- Cherington M. Clinical spectrum of botulism. *Muscle Nerve.* 1998;21(6):701–710.
- From the Centers for Disease Control and Prevention: infant botulism—New York City, 2001-2002. *JAMA*. 2003;289(7):834–836.
- Ringe H, Schuelke M, Weber S. Infant botulism: is there an association with thiamine deficiency? *Pediatrics*. 2014;134:e1436. doi: http://dx.doi.org/10.1542/peds.2013-3378.

Question 187

A 2-month-old male infant is brought to the emergency department for evaluation of jitteriness and muscle twitching that has been worsening over the past 2 days. He is otherwise behaving normally and is breastfeeding well with no change in feeding pattern. The boy was born at term. Soon after birth, a heart murmur was noted, and he was diagnosed with Tetralogy of Fallot. He has had no hypercyanotic spells. Surgical repair is planned for when he reaches 6 months of age. He takes no medication and no vitamins. Physical examination reveals a temperature of 37°C, heart rate of 140 beats/min, respiratory rate of 22 breaths/min, and oxygen saturation of 93% on room air. The boy appears jittery. His skin color is pink. He has a small chin and his ear helices are overfolded. A 3/6 harsh systolic murmur is heard best at the left upper sternal border.

Laboratory investigation reveals the following:
•Plasma glucose, 82 mg/dL (4.6 mmol/L)
•Serum calcium, 7.1 mg/dL (1.77 mmol/L) (reference range 9–11 mg/dL [2.25–2.75 mmol/L])
•Serum albumin, 4.0 g/dL (40 g/L) (reference range, 2.2–4.8 g/dL [22–48 g/L])
•Serum phosphorus, 8.0 mg/dL (2.58 mmol/L) (reference range 4.0–6.5 mg/dL [1.29–2.10 mmol/L])

Of the following, the MOST likely cause of this infant's hypocalcemia is

  A. hypoparathyroidism
  B. inadequate calcium intake
  C. maternal diabetes
  D. phosphorous load
  E. vitamin D deficiency

Correct Answer: A

The infant in the vignette has 22q11.2 deletion syndrome with hypocalcemia due to associated hypoparathyroidism. Some manifestations of the 22q11.2 deletion syndrome result from abnormal development of the third and fourth pharyngeal pouches, which form the thymus and parathyroid glands. Abnormal development of the parathyroid glands results in hypoparathyroidism, which manifests as hypocalcemia in about half of all infants with 22q11.2 deletion syndrome. The hypocalcemia is often transient, but may recur during times of stress with increased calcium needs, such as postoperatively or during puberty.

Jitteriness and muscle twitching are common symptoms of hypocalcemia. Seizures can also occur. The boy's normal plasma glucose level rules out hypoglycemia, which can cause similar symptoms.

Other features of 22q11.2 deletion syndrome exhibited by the infant in the vignette include congenital heart disease (tetralogy of Fallot) and classic facial features (small chin, overfolded ear helices). Associated heart anomalies are most often conotruncal malformations; interrupted aortic arch is especially common. Other common findings include palatal abnormalities (eg, velopharyngeal insufficiency), immune deficiency (associated with abnormal thymus development), and developmental delay.

Biochemically, hypoparathyroidism manifests as low serum calcium, low parathyroid hormone (PTH), and high phosphorous levels. Although the PTH level is not given for the infant in the vignette, if measured, it would be low. In addition to maintaining normal serum calcium levels, PTH also causes phosphate excretion in the kidney. Thus, this infant's high phosphorous level indicates a lack of PTH effect. The normal serum albumin suggests true hypocalcemia. If the serum albumin were low, the serum calcium should be corrected for the albumin level. An ionized calcium level, although not measured for this infant, would reflect the free, active form of calcium.

Hypoparathyroidism can also occur in familial forms (eg, activating mutations of the calcium sensing receptor), as part of the autoimmune polyendocrine syndrome type 1, as part of the HDR syndrome (hypoparathyroidism, sensorineural deafness, and renal anomaly; GATA3 mutations), and in association with mitochondrial disorders (eg, Kearns-Sayre syndrome, MELAS).

Vitamin D deficiency is a relatively common cause of hypocalcemia in infants. It is associated with high PTH levels, thus the phosphorous level would not be as high as seen in this infant. In extreme cases, inadequate calcium intake can cause hypocalcemia, but the resulting high PTH levels usually compensate to maintain a normal serum calcium level, and the phosphorous level would not be as high as in this case. This infant is breastfed, therefore he should have adequate calcium intake. A phosphorous load (eg, phosphate-based laxative administration) can cause hypocalcemia by binding available calcium. However, this infant does not have a history suggestive of a phosphorous load. Children born to mothers with diabetes mellitus are at increased risk for neonatal hypocalcemia. The mechanism is unclear, but is associated with an

exaggeration of the physiologic calcium and PTH nadir during the first 1 to 3 days after birth. The boy in the vignette is beyond the age for this condition to present.

Hyperparathyroidism is rare in children. The most common causes are parathyroid adenomas, and parathyroid hyperplasia that may be associated with multiple endocrine neoplasia type 1. Laboratory features consistent with hyperparathyroidism include high levels of serum calcium, PTH, and urine calcium. Serum phosphorous levels are low due to renal phosphate wasting secondary to the high PTH levels. Hyperparathyroidism should be distinguished from familial hypocalciuric hypercalcemia (FHH), a benign condition due to inactivating mutations in the calcium sensing receptor. In FHH, the serum calcium level is mildly elevated, the urine calcium level is low, and PTH levels are inappropriately normal for the calcium level.

PREP Pearls
- The 22q11.2 deletion syndrome is associated with hypoparathyroidism that is secondary to abnormal development of the parathyroid glands.
- Biochemically, hypoparathyroidism manifests as hypocalcemia, low parathyroid hormone (PTH), and high phosphorous levels. Phosphorous levels are high because, in addition to maintaining normal serum calcium levels, PTH also causes phosphate excretion in the kidney.
- Features of the 22q11.2 deletion syndrome include congenital heart disease (conotruncal malformations, eg, interrupted aortic arch), palatal abnormalities (eg, velopharyngeal insufficiency), immune deficiency (associated with abnormal thymus development), and developmental delay.

ABP Content Specifications(s)
- Recognize the typical laboratory features associated with hypo- and hyperparathyroidism
- Understand the association of hypoparathyroidism with other disorders

Suggested Readings
- Markowitz ME, Underland L, Gensure R. Parathyroid disorders. *Pediatr Rev*. 2016;37(12):524-535. http://dx.doi.org/10.1542/pir.2015-0076.
- McDonald-McGinn DM, Emanuel BS, Zackai EH. 22q11.2 Deletion syndrome. *GeneReviews* [Internet]. http://www.ncbi.nlm.nih.gov/books/NBK1523/. .
- Pereira E, Marion R. Chromosome 22q11.2 deletion syndrome. *Pediatr Rev*. 2015;36(6):270–272; discussion 272. doi: http://dx.doi.org/10.1542/pir.36-6-270.
- Zhou P, Markowitz M. Hypocalcemia in infants and children. *Pediatr Rev*. 2009;30(5):190–192. doi: http://dx.doi.org/10.1542/pir.30-5-190.

Question 188

A 3-month-old infant with shortness of breath, poor feeding, and lethargy is brought to the emergency department. The mother states that he has had 2 prior episodes of low blood sugar, 1 in the newborn period and the other at 1 month of age. He is nondysmorphic with low tone, hepatomegaly, poor peripheral perfusion, tachypnea, rales in both lung fields, grunting with retractions, and nasal flaring. There is no jaundice present. An echocardiogram shows dilated cardiomyopathy with pericardial effusions. Laboratory data are shown:

Laboratory Test	Result
Serum	
Blood glucose	42 mg/dL (2.3 mmol/L)
Aspartate aminotransferase	85 U/L
Alanine aminotransferase	70 U/L
Creatine kinase	200 U/L
Ammonia	200 µg/dL (143 µmol/L)
α-Fetoprotein	12 ng/mL (12 µg/L)
Arterial blood gas	
pH	7.22
Bicarbonate	10 mEq/L (10 mmol/L)
Anion gap	23 mEq/L (23 mmol/L)
Urine	
Ketones	Negative
Organic acids	C6-C14 dicarboxylic acids

The parents had a prior child that died of cardiac failure in early infancy.

You suspect an inborn error of metabolism.

Of the following, the MOST likely metabolic disorder is

  A. fatty acid oxidation disorder
  B. galactosemia
  C. hereditary hemochromatosis
  D. hereditary tyrosinemia type 1
  E. lysosomal storage disorder

Correct Answer: A

The infant in this vignette likely has very long-chain acyl-CoA dehydrogenase deficiency, which is a fatty acid oxidation disorder with a severe early onset presentation of hypoketotic hypoglycemia, cardiomyopathy, hepatomegaly, and hypotonia. Laboratory abnormalities include metabolic acidosis and mild to moderate elevations in creatine kinase levels, liver function test results, and ammonia levels. Further metabolic testing should include an acylcarnitine panel which, in this case, would reveal elevations of C16:1, C14:2, C14:1, and C18:1 during acute illness. This disease is an autosomal recessive condition in which both parents would be carriers of an *ACADVL* mutation, thus yielding a 25% risk of having an affected child with each pregnancy. Treatment involves intravenous glucose, hydration, evaluation and treatment for cardiac rhythm disturbance, and management of rhabdomyolysis. The cardiac component of this disorder is reversible with treatment and intensive supportive care. Infants should be placed on a low-fat formula with supplemental medium-chain triglycerides as well as a schedule of frequent feeding to avoid hypoglycemia.

Hypoglycemia is defined as a blood glucose level of less than 45 mg/dL (2.6 mmol/L). Hypoglycemia should be evaluated and treated promptly to avoid permanent brain damage and other adverse consequences. Clinical management of hypoglycemia should first involve consideration of the timing of the hypoglycemia, liver size, presence of lactic acidosis, and the presence of hyperketosis or hypoketosis. The clinician should also note evidence of cardiomyopathy, myopathy, encephalopathy, short stature, hyperpigmentation, small genitals, or dehydration. Classic forms of hypoglycemia involving endocrine disorders and liver disease should be considered in the initial evaluation.

Laboratory investigations during an episode of symptomatic hypoglycemia should include the following:
- General evaluation: arterial blood gas, complete blood cell count, C-reactive protein, electrolytes, liver/renal function tests, creatine kinase, uric acid, triglycerides, phosphate, and urinary ketones, glucose, and nonglucose reducing substances
- Endocrinologic studies: insulin, growth hormone, and cortisol levels
- Metabolic studies: serum lactate, free fatty acids plus 3-hydroxybutyrate, acylcarnitine panel, carnitine panel, urine organic acids, serum ammonia, and serum amino acids
- Consideration of toxicologic investigations

Hypoglycemia secondary to metabolic disorders can be divided into 2 major groups based on liver size: hypoglycemia without permanent hepatomegaly and hypoglycemia with permanent hepatomegaly.

If a patient develops hypoglycemia without ketosis and permanent hepatomegaly after a 2- to 6-hour fast, growth hormone deficiency or hyperinsulinism should be considered. Most episodes of hypoglycemia secondary to metabolic disorders and not accompanied by permanent hepatomegaly present after at least 8 hours of fasting. In this scenario, and without evidence of ketosis (as in the infant in this vignette), a fatty acid oxidation disorder must be strongly considered. If ketoacidosis is present, the clinician should suspect organic acidurias, ketolytic

defects, late-onset maple syrup urine disease, or glycerol kinase deficiency. Adrenal insufficiency, hypopituitarism, and congenital adrenal hyperplasia must also be included in the differential diagnosis. Another more common entity is recurrent functional ketotic hypoglycemia that presents in early childhood (1-2 years of age) with fasting hypoglycemia with ketosis, especially in the morning, without evidence of metabolic acidosis. This condition tends to resolve by 6 to 8 years of age.

If a patient has hypoglycemia and permanent hepatomegaly, the clinician should strongly consider a metabolic disorder. If liver insufficiency is not present in association with the increased size, glycogen storage diseases and defects in gluconeogenesis should be suspected, including glucose-6-phosphate deficiency, fructose bisphosphatase deficiency, and glycogenosis type III. If liver insufficiency is present with hepatic fibrosis and cirrhosis, hereditary tyrosinemia type 1, hereditary fructose intolerance, respiratory chain disorders, and congenital disorders of glycosylation should be considered.

The evaluation of hypoglycemia in a suspected metabolic disorder is best managed in consultation with a metabolic specialist and an endocrinologist to reach a specific diagnosis and implement the optimal treatment in an expedient manner to improve outcomes.

Galactosemia presents in the first week after birth (after implementation of milk feedings) with life-threatening complications including liver failure, feeding problems, failure to thrive, bleeding, jaundice, cataracts, and *Escherichia coli* sepsis. These complications will quickly resolve with aggressive management of the liver failure and *E coli* sepsis as well as immediate implementation of a lactose-restricted diet. Despite dietary restrictions, many patients will still have learning disabilities, speech delays, and, in female individuals, premature ovarian insufficiency. Hypoglycemia will be noted in association with the profound liver failure. This disorder is detected by newborn screening.

Hereditary hemochromatosis causes excessive storage of iron in the liver, skin, pancreas, heart, joints, and testes and manifests as abdominal pain, lethargy, weakness, and weight loss. If the ferritin level is greater than 1,000 ng/mL, a patient will likely begin to experience congestive heart failure, cardiac arrhythmias, diabetes mellitus, hyperpigmentation to the skin, arthritis, and hypogonadism. These symptoms typically present in adulthood, not childhood. Many women never experience symptoms because of the loss of iron through monthly menses. Hypoglycemia is not a presenting symptom.

Hereditary tyrosinemia type 1 is detected from newborn screening and typically presents in early infancy with profound liver failure. It can present in later infancy or early childhood with renal tubular dysfunction, rickets, and neurologic crises. Blood and urine succinylacetone levels are increased. An evaluation of serum amino acids will reveal elevated levels of methionine, tyrosine, and phenylalanine, and an evaluation of urine organic acids will reveal elevated levels of tyrosine metabolites. α-Fetoprotein levels will be significantly elevated. Hypoglycemia can present in association with profound liver failure.

A lysosomal storage disorder typically presents with coarse facies, developmental regression, skeletal dysostosis multiplex, frequent upper respiratory infections, umbilical/inguinal hernia, hepatosplenomegaly, and short stature in the absence of hypoglycemia, liver failure, or metabolic acidosis.

PREP Pearls
- Very long-chain acyl-CoA dehydrogenase deficiency is a fatty acid oxidation disorder with a severe early onset presentation of hypoketotic hypoglycemia, cardiomyopathy, hepatomegaly, and hypotonia. Laboratory abnormalities include metabolic acidosis and mild to moderate elevation of creatine kinase, liver function test results, and ammonia levels as well as C16:1, C14:2, C14:1, and C18:1 acylcarnitine.
- Very long-chain acyl-CoA dehydrogenase deficiency treatment involves high-dose intravenous glucose, hydration, evaluation and treatment for cardiac rhythm disturbance, and management of rhabdomyolysis during an acute episode.
- Clinical management of hypoglycemia should first involve consideration of the timing of the hypoglycemia, liver size, presence of lactic acidosis, and presence of hyperketosis or hypoketosis.
- The evaluation of hypoglycemia in a suspected metabolic disorder is best managed in consultation with a metabolic specialist and an endocrinologist to reach a specific diagnosis and implement the optimal treatment in an expedient manner to improve outcomes.

MOCA-Peds Objective
- Recognize and evaluate an infant with an inborn error of metabolism

ABP Content Specifications(s)
- Plan the evaluation of a patient with suspected metabolic disease who has hypoglycemia, and manage appropriately

Suggested Readings
- American Academy of Pediatrics. Quick reference: hypoglycemia. Pediatric Care Online website. https://pediatriccare.solutions.aap.org/content.aspx?resultClick=24&gbosid=165598.
- Greene CL. Metabolic disorders beyond the newborn period. 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; 2017:2315–2331.
- Leslie ND, Valencia CA, Strauss AW, Connor JA, Zhang K. Very long-chain acyl-coenzyme a dehydrogenase deficiency. *GeneReviews*. 2014. https://www.ncbi.nlm.nih.gov/books/NBK6816/.
- Rios A, Adams DJ. Specific congenital metabolic diseases. 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; 2017:938–962.

- Zschocke J, Kölker S. Function tests. In: Hoffmann GF, Zschocke J, Nyhan WL, eds. *Inherited Metabolic Diseases: A Clinical Approach.* 2nd ed. Berlin, Germany: Springer; 2017:505–520.

Question 189

You are seeing a 17-year-old girl in the emergency department for abdominal pain. She has a 3-day history of lower abdominal pain and a 1-week history of abnormal vaginal discharge; there has been no vomiting or diarrhea. The girl reports 4 lifetime male sexual partners and reports inconsistent condom use. She has an etonogestrel implant for contraception. On physical examination, she is afebrile with normal vital signs. She has lower abdominal tenderness to palpation. The remainder of the physical examination findings are normal. You are concerned that she may have pelvic inflammatory disease.

Of the following, the MINIMUM criterion needed to make this diagnosis is

A. cervical infection with Chlamydia trachomatis
B. cervical motion tenderness
C. cervical mucopurulent discharge
D. elevated erythrocyte sedimentation rate
E. oral temperature greater than 38.3°C

Correct Answer: B

The girl in the vignette has symptoms and signs concerning for pelvic inflammatory disease (PID). Abdominal or pelvic pain that is constant, with cramping, and exacerbated by ambulation or sexual intercourse is typical in PID. Abnormal vaginal discharge or bleeding are reported by up to 50% of patients. Anorexia, nausea, vomiting, dysuria, or urinary frequency may be present. The Centers for Disease Control and Prevention (CDC) minimal diagnostic criteria for PID include pelvic examination findings of cervical motion tenderness, *or* uterine tenderness, *or* adnexal tenderness. Thus, in young women presenting with abdominal or pelvic pain, any one of these findings is sufficient to prompt treatment provided that other diagnoses have been excluded.

Criteria that are not diagnostic, but *support* the diagnosis of PID include:
- Oral temperature higher than 38.3°C; however, fever may be present in as few as 14% of patients
- Mucopurulent cervical discharge (yellow-green in color)
- Excessive numbers of white blood cells (WBC) on microscopy of vaginal secretions (>1 WBC per epithelial cell)
- Elevated erythrocyte sedimentation rate
- Elevated C-reactive protein
- Proven cervical infection with *Chlamydia trachomatis* or *Neisseria gonorrhoeae*

A definitive diagnosis can be provided, if necessary, by endometrial biopsy, transvaginal ultrasonography, or laparoscopy.

Because PID is a polymicrobial infection that may involve *C trachomatis*, *N gonorrhoeae*, genital mycoplasmas, and aerobic and anaerobic bacteria, broad-spectrum coverage is needed. Some experts recommend routine inclusion of anaerobic coverage. If the patient is to be treated in the ambulatory setting, the following combined intramuscular and oral regimen is recommended by the CDC:
- Ceftriaxone 250 mg intramuscularly (IM) × 1 dose (or cefoxitin 2 g IM and probenecid 1 g orally × 1 dose administered concurrently)

PLUS
- Doxycycline 100 mg orally twice daily for 14 days

WITH OR WITHOUT
- Metronidazole 500 mg orally twice daily for 14 days (for anaerobic coverage)

Few patients require hospitalization. However, if a surgical emergency such as appendicitis cannot be excluded, a tubo-ovarian abscess is suspected; if the patient is pregnant, has severe illness, cannot follow an oral regimen, or fails to respond to an oral regimen, the CDC recommends inpatient management. For such individuals, several recommended parenteral regimens exist, and are available at http://www.cdc.gov/std/tg2015/default.htm.

Although more than 90% of those treated for PID respond to treatment, the long-term consequences can be significant. In 1 study, following a single episode of mild-to-moderate PID,

18% of women reported infertility, 29% had chronic pelvic pain, and 15% had recurrent PID. A single episode of PID increases the risk of ectopic pregnancy by 6- to 10-fold.

PREP Pearls
- The minimum diagnostic criteria for pelvic inflammatory disease (PID) are pelvic examination findings of cervical motion tenderness, *or* uterine tenderness, *or* adnexal tenderness. In young women presenting with abdominal or pelvic pain, any 1 of these findings is sufficient to prompt treatment for PID provided other diagnoses have been excluded.
- The long-term consequences of PID can include infertility, chronic pelvic pain, recurrent PID, and an increased risk of ectopic pregnancy.

MOCA-Peds Objective
- Provide appropriate treatment for a sexually transmitted infection in an adolescent

ABP Content Specifications(s)
- Understand the complications associated with pelvic inflammatory disease
- Plan the appropriate management of pelvic inflammatory disease
- Recognize the clinical and laboratory findings associated with pelvic inflammatory disease, and manage appropriately

Suggested Readings
- Brunham RC, Gottlieb SL, Paavonen J. Pelvic inflammatory disease. *New Engl J Med*. 2015;372:2039–2048. doi: http://dx.doi.org/10.1056/NEJMra1411426.
- Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2015. *MMWR Recomm Rep*. 2015;64(No. RR-3):1–137.
- Shrier LA. Pelvic inflammatory disease. In: Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.

Question 190

A 12-year-old girl with a history of inflammatory bowel disease is brought to your office for evaluation of increasing symptoms. She has been taking drug A for years. The girl's mother mentions that she has learned of the release of a new drug (drug B) for adults with inflammatory bowel disease that is boasted to have superior outcomes. You explain that the new drug is not approved for use in children and that further studies are needed before it can be used in children.

Of the following, the study design that would BEST determine if drug B produces superior outcomes in children is

A. an administrative database review
B. a case-control study
C. a cohort study
D. a cross-sectional study
E. a randomized controlled trial

Correct Answer: E

Data obtained using large sample sizes, collected free from bias, and analyzed in a statistically appropriate fashion will help a clinician in the decision-making process. However, such large studies are impractical, expensive, and sometimes impossible for rare diseases. Knowing the limitations and benefits of different study designs and data sources will aid in the interpretation of study data and the evaluation of its validity.

In this vignette, the physician and the patient's mother discuss a current medication (drug A) compared to a new medication (drug B). A randomized controlled trial is the best way to minimize bias and make a comparison of these 2 drugs with minimal confounders, if the groups are formed in a truly randomized manner.

Administrative database review is helpful to provide data regarding hospitalizations and mortality in a large population over a long time. This approach is not helpful in determining the comparative efficacy of 2 drugs.

Case-control studies would be useful to study individuals with a disease compared to individuals without the disease to evaluate risk factors and outcomes for the disease. As these studies are mostly retrospective analyses, data must be considered in the context of the important bias that is inherent in this design. Participants with the disease may be more likely to look for risk factors and associations as compared to participants without the disease (recall bias). Case-controlled studies are not designed to compare different treatments of a disease.

Cohort studies follow a population of patients with a disease over time. This approach is likely to yield important information about the natural history of a disease and associated manifestations and complications. A cohort study is not an appropriate study for the clinical question posed in the vignette.

A cross-sectional study would be more appropriate in the context of comparing a new diagnostic test to the gold standard. Compared in the same population, this study could illuminate the differences in the 2 tests, and the classic 2×2 table could organize the data in a way to establish the sensitivity and specificity of each test.

PREP Pearls
- A randomized controlled study is the optimal way to evaluate the effect of 2 different treatments for a disease.
- Case-control studies would be useful to study individuals with a disease compared to individuals without the disease to evaluate risk factors and outcomes for the disease.
- Cohort studies follow a population of patients with a disease over time. This approach is likely to yield important information about the natural history of a disease

MOCA-Peds Objective
- Understand the principles and application of study design

ABP Content Specifications(s)
- Assess how the data source (eg, diaries, billing data, discharge diagnostic code) may affect study results

Suggested Readings
- Palaia A. 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. 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 191

A 2-month-old infant is brought to the emergency department for diarrhea and decreased oral intake. The infant has been having intermittent diarrhea for the last month. The infant was born to a 30-year-old primigravida woman at 39 weeks of gestation via normal vaginal delivery. The mother mentions that her pediatrician had expressed concern about the infant's lack of weight gain at her last visit 2 weeks ago. The infant's weight (3.7 kg) and length (54 cm) are both below the fifth percentile. She has a temperature of 37.5°C, heart rate of 132 beats/min, respiratory rate of 35 breaths/min, and a blood pressure of 72/58 mm Hg.

Laboratory results show:

Laboratory Test	Result
Sodium	135 mEq/L (135 mmol/L)
Potassium	1.9 mEq/L (1.9 mmol/L)
Chloride	110 mEq/L (110 mmol/L)
Bicarbonate	14 mEq/L (14 mmol/L)
Blood urea nitrogen	40 mg/dL (14.3 mmol/L)
Creatinine	0.3 mg/dL (26.5 µmol/L)
Urinary sodium	100 mEq/L (100 mmol/L)
Urinary anion gap	-44 mEq/L (-44 mmol/L)

You discuss chronic diarrhea vs renal tubular acidosis as the underlying etiology for this patient with the medical student rotating with you.

You inform the student that the test MOST likely to distinguish chronic diarrhea from renal tubular acidosis in this patient is

 A. serum anion gap
 B. serum creatinine
 C. serum electrolytes
 D. urinary anion gap
 E. urinary sodium

Correct Answer: D

The infant in this vignette has failure to thrive (weight and height less than third percentile) and serum chemistry results significant for acidosis and hypokalemia. The presence of diarrhea and absence of respiratory symptoms indicate metabolic acidosis as the etiology of the patient's serum chemistry profile. A negative urine anion gap indicates chronic diarrhea as the underlying etiology for normal anion gap acidosis in this patient.

Further characterization of metabolic acidosis involves the identification of a normal (12 ± 4 mEq/L) or elevated serum anion gap ($Na^+ - [Cl^- + HCO_3^-]$) (**Item C191A**). The concentration of potassium in the blood is relatively low compared to the concentrations of sodium, chloride, and bicarbonate; therefore, potassium is usually omitted from the serum anion gap calculation. The reference range for anion gap will vary in health care laboratories depending upon the method and calibration for electrolyte measurement. Knowledge of the normal reference range for an individual laboratory is critical for the accurate interpretation of serum anion gap changes.

Item C191A. Causes of Metabolic Acidosis.

Normal Anion Gap
- Gastrointestinal loss of bicarbonate
  – Diarrhea
  – Pancreatic fistula
  – Ureteroenterostomy
  – Ureterosigmoidostomy
- Drugs
  – Acidifying agents
  – Cholestyramine
  – Magnesium chloride
  – Sulfamylon
- Hyperalimentation
- Rapid intravenous hydration with 0.9% NaCl
- Renal loss of bicarbonate
  – Renal tubular acidosis
  – Carbonic anhydrase inhibitor
  – Hyperparathyroidism
- Posthypocapnea
- Hypoaldosteronism

Elevated Anion Gap
- Renal failure
- Ketoacidosis
  – Starvation or fasting
  – Diabetic ketoacidosis
  – Ethanol intoxication
- Lactic acidosis
  – Tissue hypoxia
  – Muscular exercise
  – Ethanol ingestion
  – Systemic diseases
  – Inborn errors of metabolism
- Toxins
  – Methanol
  – Ethylene glycol
  – Salicylates
  – Paraldehyde

Reprinted with permission from Schwaderer AL, Schwartz GJ. *Pediatr Rev*. Oct 2004, 25 (10) 351.

Unmeasured anions and cations also influence serum anion gap:

$Na^+ + \text{Unmeasured Cations} = Cl^- + HCO_3^- + \text{Unmeasured Anions}$

$Na^+ - (Cl^- + HCO_3^-) = \text{Unmeasured Anions} - \text{Unmeasured Cations (Serum Anion Gap)}$

Increased unmeasured anions (lactate, toxins) or a reduction in unmeasured cations (magnesium, ionized calcium) can increase the serum anion gap, whereas a reduction in unmeasured anions (albumin) or an increase in unmeasured cations can lower the serum anion gap.

The infant in this vignette has normal anion gap acidosis (11 mEq /L). In the absence of renal failure, normal anion gap metabolic acidosis is caused by the loss of HCO_3^- (diarrhea, enteric fistula, enterostomies) or impaired renal excretion of H^+ (renal tubular acidosis). Diarrhea is the most common cause of normal anion gap acidosis in children. However, patients with hypoperfusion associated with severe diarrhea develop lactic acidosis and may exhibit elevated anion gap metabolic acidosis (unmeasured lactate anions).

Renal tubular acidosis (RTA) is an inherited or acquired defect in the ability of the kidneys to reabsorb filtered bicarbonate or excrete ammonia. Renal tubular acidosis is characterized by normal anion gap metabolic acidosis. The 4 forms of RTA are distal (type 1), proximal (type 2), mixed (type 3; features of both type 1 and 2), and hypoaldosteronism (type 4).

Kidneys maintain acid-base balance by absorption of filtered bicarbonate (**Item C191B**) and regeneration of new bicarbonate used in buffering acid generated from routine metabolism (2-3 mEq/kg/d) or diet. For every new bicarbonate returned to systemic circulation, an H^+ ion is secreted into the tubular lumen (**Item C191C**). Urinary ammonia (NH_3) and monohydrogen phosphate (HPO_4^{-2}) are the 2 principal buffers that bind these H^+ ions. Increased urinary ammonia excretion is the main adaptive response to normal or increased acid excretion because urinary phosphate excretion is fixed; urinary ammonia excretion can be increased by up to 10 fold. Therefore, all forms of RTA are associated with metabolic acidosis (low plasma HCO_3^-) and decreased renal ammonium (NH_4^+) excretion.

PROXIMAL TUBULE CELL
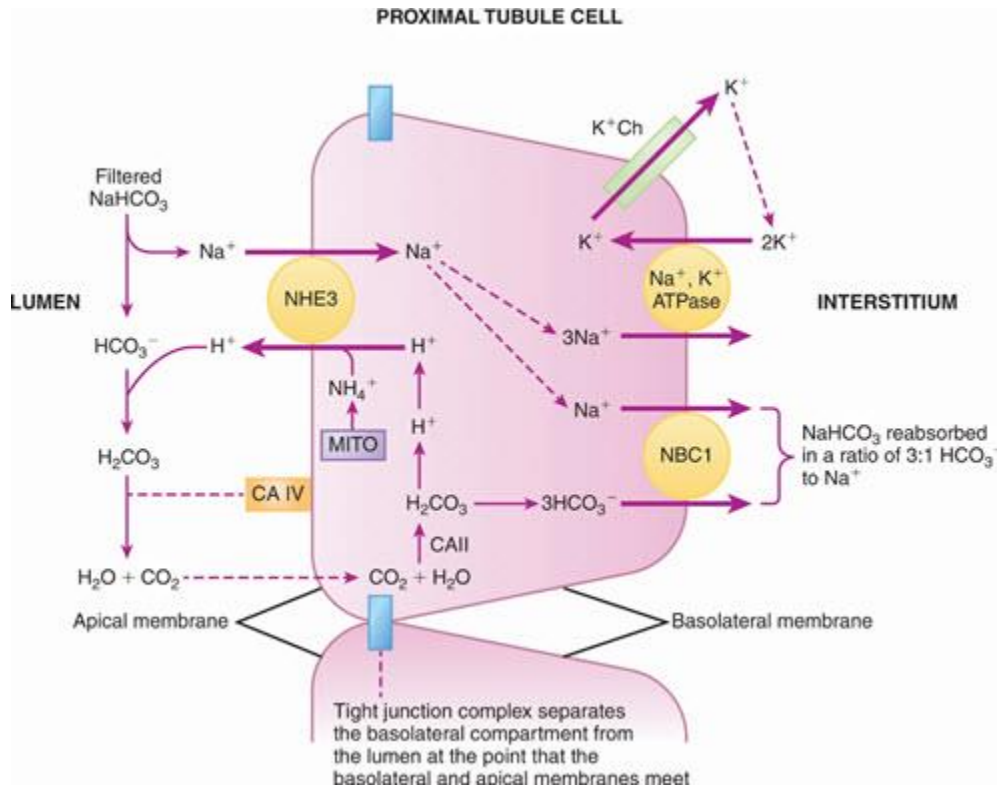
Item C191B: Approximately 80% to 90% of the bicarbonate is reabsorbed in the proximal tubule. The proximal tubule reclaims the filtered HCO_3^-, as the HCO_3^- molecule returned to circulation is not the same as the molecule that is filtered. Increased ammonia generation in response to metabolic acidosis occurs primarily in the proximal tubule.

Reprinted with permssion from Kallen R. 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: 2557.
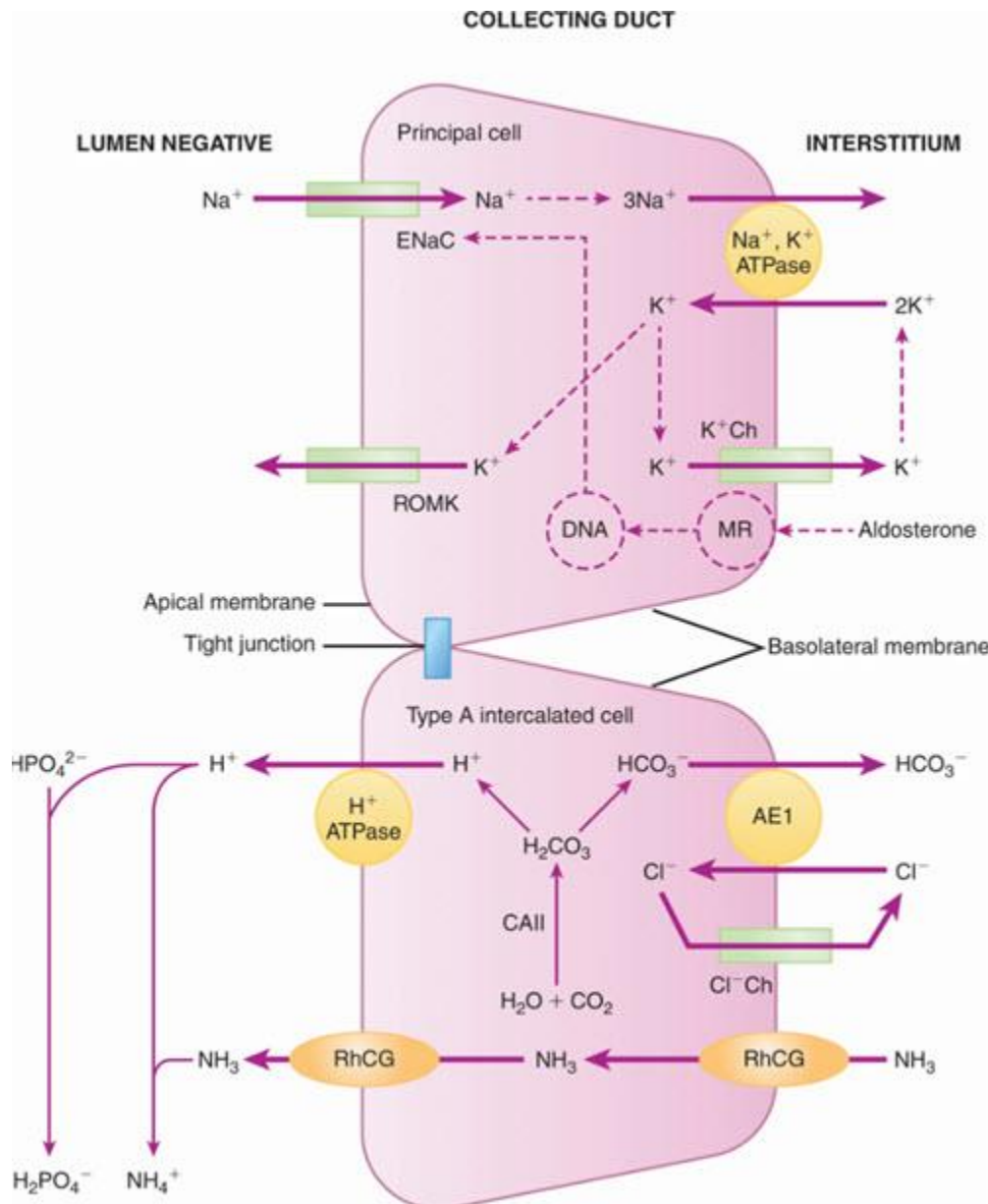
COLLECTING DUCT

Item C191C: Cortical collecting ducts replenish HCO_3^- lost in buffering endogenous H^+ produced from metabolism. Negative lumen potential in the cortical collecting ducts is secondary to Na^+ movement across the aldosterone-stimulated ENaC channel. The negative transepithelial potential facilitates H^+ ion secretion by the intercalated cells (type A) and the addition of a new HCO_3^- to the circulation. The newly generated H^+ ion is excreted along with NH_3. Renal response to metabolic acidosis is increased NH_4^+ excretion and is maintained in patients with chronic diarrhea, leading to a negative urinary anion gap.

Reprinted with permssion from Kallen R. 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: 2558.

The urinary anion gap ($Na^+ + K^+ - Cl^-$) acts as a surrogate marker for urinary ammonium excretion. In metabolic acidosis associated with normal renal tubular ammonia (NH_3) production (as in diarrhea), the renal excretion of hydrogen ion excess is increased by ammonia production and excretion as ammonium chloride (NH_4Cl). This increased urinary chloride leads to a negative urinary anion gap, indicating normal ammonia production by the renal tubules. Patients with type 1, type 3, or type 4 RTA have a positive urinary anion gap (**Item C191D**). Impaired regeneration of new HCO_3^- is indicative of a decreased rate of NH_4^+ ammonium (predominant urinary buffer) secretion by the kidney. Impaired H^+ ion secretion by the cortical collecting duct leads to type 1 (distal) RTA, which is associated with failure to thrive, polyuria, hypokalemia, and medullary nephrocalcinosis (caused by hypercalciuria and hypocitraturia). Type 4 RTA most frequently occurs in patients with chronic renal failure associated with renal parenchymal injury and scarring. Mineralocorticoid deficiency is caused by genetic or acquired factors (eg, tubular scarring) that lead to decreased production or receptor insensitivity. Mineralocorticoid deficiency causes hyperkalemia, which impairs ammonia generation and leads to type 4 RTA.

Item C191D. Findings in Patients With Diarrhea and Renal Tubular Acidosis.

	Diarrhea	Type 2 (Proximal) RTA	Type 1 (Distal) RTA	Type 4 RTA
Urine pH	< 5.5	Variable[a]	> 5.5	> 5.5
Urine anion gap	Negative	Positive or negative[a]	Positive	Positive
Serum potassium level	Normal or decreased	Decreased	Normal or decreased	Elevated
Fanconi syndrome	Absent	Present	Absent	Absent
Alkali dose, mEq/kg/d	Individualized to patient	10-20	5-8 for infants 3-4 for children	5-8 for infants 3-4 for children

RTA, renal tubular acidosis.

[a] In proximal RTA, when the serum bicarbonate drops to 12 to 15 mEq/L, the urine may be appropriately acidified, leading to a urine pH less than 5.5 and a negative urine anion gap.

Courtesy of G. Kapur

Proximal (type 2) RTA is a defect in the ability of the proximal renal tubules to reclaim filtered HCO_3^- from the tubular fluid. Reclamation, rather than reabsorption, is the appropriate term to describe the processes of the proximal tubule because the HCO_3^- molecule returning to the circulation is different from the filtered HCO_3^- molecule. In children, type 2 RTA is usually associated with a generalized proximal tubular defect (Fanconi syndrome) in absorbing glucose, amino acids, and phosphate. Fanconi syndrome is associated with cystinosis, galactosemia, tyrosinemia, oculocerebrorenal (Lowe) syndrome, and hereditary fructose intolerance. In proximal RTA once the serum bicarbonate has dropped to a level (12-15 mEq/L) wherein the distal renal tubules can absorb the filtered bicarbonate load, the urine can be appropriately acidified, leading to a negative urinary anion gap and a urine pH of less than 5.5. As the proximal tubules reabsorb 80% to 90% of the filtered bicarbonate, the alkali dose is higher for

type 2 RTA (10-20 mEq/kg/d) as compared to types 1, 3, or 4 RTA (5-8 mEq/kg/d). Type 3 RTA is rare and associated with marble bone disease. It has findings of both type 1 and type 2 RTA. A normal serum creatinine level, as seen in the infant in this vignette, is usually noticed in chronic diarrhea and RTA. The serum potassium level may be normal or decreased in patients with diarrhea and type 1 or type 2 RTA. Patients with type 4 RTA have elevated serum potassium levels (**Item C191D**). The urine sodium concentration is an indicator of intravascular volume status. The normal renal response to a decreased effective circulating volume (dehydration) is to increase salt and water reabsorption, thereby increasing the effective circulatory volume and leading to a low urine sodium concentration ($< 20\text{-}25$ mEq/L). The urine sodium concentration is not a good indicator of effective circulatory volume in patients with underlying renal disease (eg, renal dysplasia, acute glomerulonephritis) or patients receiving diuretic therapy.

PREP Pearls
- Diarrhea is the most common cause of normal serum anion gap acidosis in children.
- Urinary anion gap (Na+ + K+ − Cl-) acts as a surrogate marker for urinary ammonium excretion.
- In metabolic acidosis, renal excretion of hydrogen ion excess is associated with increased ammonia production and excretion as ammonium chloride (NH_4Cl). This increased urinary chloride leads to negative urinary anion gap and indicates normal ammonia production by the renal tubules.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Formulate a differential diagnosis of renal tubular acidosis
- Understand the clinical and laboratory findings associated with renal tubular acidosis

Suggested Readings
- Chan JCM, Scheinman JI, Roth KS. Consultation with the specialist: renal tubular acidosis. *Pediatr Rev.* 2001;22(8):277–287. doi: http://dx.doi.org/10.1542/pir.22-8-277.
- Kallen R. 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. doi: http://dx.doi.org/10.1542/pir.25-10-350.

Question 192

You are asked by a community group to share your knowledge as a pediatrician. A parent in the audience raises concerns about his perception of an increase in gun-related injuries in the neighborhood. You share statistical information and emphasize that safe storage and handling of guns and ammunition is key to decreasing gun violence and gun-related injuries.

Regarding gun-related injuries in 0- to 19-year-old individuals, the evidence BEST supports the statement that

  A. intentional fatal injuries occur equally across ethnicities
  B. intentional nonfatal injuries increase significantly with age
  C. teenagers are 5 times more likely to experience gun-related violence than other age groups
  D. unintentional fatal injuries are greatest in the 10- to 14-year-old age group
  E. unintentional nonfatal injuries are most common in the 5- to 9-year-old age group

Correct Answer: B

The incidence of intentional and unintentional injuries and deaths related to firearms increases with age. Firearm-related injury to children and adolescents continues to be a significant cause of morbidity and mortality in the United States. Gun ownership is common in homes with children; therefore, child health care providers should be comfortable in counseling parents and adolescents about firearm safety in the home. Counseling parents about safe storage of guns (recommending guns be unloaded, locked, and stored separately from ammunition) reduces children's risk of injury, but educational programs directed to children have not been effective.

Pediatric health care providers can be guided by policy statements on firearm-related injuries and the role of the pediatrician in violence prevention that were created by the Council on Injury, Violence, and Poison Prevention of the American Academy of Pediatrics.

The following statements summarize important data that can be used in counseling or intervention strategies:
- Firearm-related injuries are often fatal; primary prevention is essential.
- Safer storage of guns and ammunition reduces injuries.
- Access to a gun increases the likelihood that intentional injuries to oneself or others is lethal.
- Access to a gun and unsafe storage practices create risk of serious unintentional injury and death.
- There are ethnic and racial disparities in the frequency of gun violence and injury. White children experience the least gun violence and injury, and black children experience the most.
- Youth 15 to 19 years of age incur firearm-related injuries about 2.5 times more frequently than the general population.
- Children 0 to 4 years of age have the highest proportion of unintentional firearm-related deaths.
- The incidence of unintentional injuries from guns increases with age.
- Guns are the leading mechanism of intentional deaths for children aged 5 years and older.
- Access to guns increases the mortality rate from suicide attempts to 90%.
- For children and adolescents, most firearm-related injuries and deaths involve a handgun; however, in rural areas, a large number of unintentional injuries and suicides involve long guns.

PREP Pearls
- Firearm-related injury is a significant cause of morbidity and mortality in children and adolescents.
- Preventive strategies include decreasing access to guns and encouraging safer storage and handling of firearms and ammunition.
- Counseling parents about the safe storage of guns (recommending guns be unloaded, locked, and stored separately from ammunition) reduces children's risk of injury, but educational programs that are directed to children have not been effective.

ABP Content Specifications(s)
- Counsel parents and adolescents regarding firearm safety in the home

Suggested Readings
- Committee on Injury, Violence, and Poison Prevention. Policy statement: role of the pediatrician in youth violence prevention. *Pediatrics*. 2009;124(1):393–402. doi: http://dx.doi.org/10.1542/peds.2009-0943.
- Council on Injury, Violence, and Poison Prevention Executive Committee, American Academy of Pediatrics. Policy statement: firearm-related injuries affecting the pediatric population. *Pediatrics*. 2012;130(5):e1416–e1423. doi: http://dx.doi.org/10.1542/peds.2012-2481.
- Crossen EJ, Lewis B, Hoffman BD. Preventing gun injuries in children. *Pediatr Rev*. 2015;36(2):43–50. doi: http://dx.doi.org/10.1542/pir.36-2-43.
- Guralnick S. Firearms. *Pediatr Rev*. 2007;28(10):396–397. doi: http://dx.doi.org/10.1542/pir.28-10-396.

Question 193

A 24-month-old boy is brought to your office for a health supervision visit. His mother tells you that he is a challenging child. He is very active and has frequent tantrums. He becomes upset by small changes in his routine. He follows directions "when he wants to" and often does not acknowledge his parents when they call his name. He speaks using only single words and cannot tolerate loud noises. He avoids other children if they approach him because he will not share his favorite toy with anyone. The boy is a picky eater. Aside from several episodes of otitis media and mild intermittent asthma, he has been a healthy child. During the visit, the boy is preoccupied with waving a small drumstick back and forth in front of his eyes. His paternal uncle had similar behaviors as a child.

Of the following, the MOST likely cause of this child's behaviors is

 A. autism spectrum disorder
 B. difficult temperament
 C. fragile X syndrome
 D. global developmental delay
 E. speech and language delay

Correct Answer: A

The 24-month-old boy in the vignette is not yet combining 2 words as expected for age, and therefore has language delay. In addition, he exhibits deficits in social communication and social interaction as demonstrated by his failure to initiate or respond to social interactions and absence of interest in peers. He has a preoccupation and visual fascination with the movement of an object. The boy also shows some behavioral rigidity, as well as sensory sensitivity to noise and possibly food textures. These symptoms are consistent with an autism spectrum disorder (ASD).

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria for the diagnosis of ASD include deficits in social communication and interactions along with restricted, repetitive patterns of behavior, interests, or activities. Social challenges include difficulty understanding and navigating social situations, verbal and nonverbal communication, and friendships and other relationships. Conversational skills are impaired and affected individuals have difficulty starting and sustaining verbal exchanges. The child with ASD may speak in an unusual tone or with atypical voice inflection. Eye contact and gesture use may be impaired, and the child may have difficulty understanding another person's facial expressions, body language, or point of view. There is a lack of shared attention in activities with others (joint attention). In addition, the child may exhibit repetitive speech (echolalia) or repetitive or stereotypic motor movements, such as hand flapping, rocking, or spinning of self or objects. The child with ASD may have behavioral rigidity, with significant problems tolerating changes in routine or their environment. They may seek out or avoid sensory stimuli such as noises, odors, food textures, and lights. Interests may be abnormal in topic or intensity, and play may be ritualistic (eg, lining things up) or with unusual objects.

Assessment of a child presenting with language delay should determine if the language delay is isolated, or if it is present in the context of an ASD. The child with isolated language delay typically has a strong interest in engaging socially and will effectively use nonverbal communication (eg, eye contact, gestures, facial expressions, body language). Pretend play and joint attention develop appropriately. A specialist in the diagnosis of autism (eg, developmental-behavioral pediatrician, neurologist, psychologist, psychiatrist) can be helpful in clarifying or confirming the diagnosis.

Although a difficult temperament may explain some of the boy's behaviors (eg, activity level, tendency to throw tantrums, and difficulty with changes in routine), it does not account for the language delay, lack of social engagement, or unusual repetitive behaviors. Children with fragile X syndrome often have autism or autistic behaviors. Because fragile X is an X-linked disorder, the boy in the vignette would have inherited his condition through his mother, but the only family member noted to have similar behaviors is a paternal uncle. Genetic or chromosomal disorders account for about 10% of ASDs. A 24-month-old child with global developmental delay can have language delay and may have some stereotypic behaviors; however, similar to the child with isolated language delay, the child's social interest and reciprocity, joint attention, play skills, and nonverbal communication would be appropriate for the child's developmental level.

This child with language delay should be referred for an evaluation by an audiologist and speech pathologist. A full evaluation of the child's other developmental delays is indicated, particularly given clinical signs consistent with an ASD. By understanding the distinction between isolated language delay and ASDs, the pediatrician is better equipped to provide appropriate guidance, direction, and support for children with developmental differences.

PREP Pearls
- The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria for a diagnosis of autism spectrum disorder includes deficits in social communication and interactions, along with restricted, repetitive patterns of behavior, interests, or activities.
- The child with isolated language delay typically has a strong interest in engaging socially and will effectively use nonverbal communication (eg, eye contact, gestures, facial expressions, body language). Pretend play and joint attention remain intact.
- A child with global developmental delay will have language delay and may have some stereotypic behaviors; however, the child's social interest and reciprocity, joint attention, play skills, and nonverbal communication would be appropriate for the child's developmental level.

MOCA-Peds Objective
- Evaluate and manage the behavioral complications of autism spectrum disorder

ABP Content Specifications(s)
- Identify the clinical findings, including developmental parameters, associated with autism spectrum disorders
- Distinguish findings associated autism spectrum disorder from those of isolated speech and language delay

Suggested Readings
- 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.
- Simms MD, Jin XM. Autism, language disorder, and social (pragmatic) communication disorder: DSM-V and differential diagnosis. *Pediatr Rev*. 2015:36(8):355–363. doi: http://dx.doi.org/10.1542/pir.36-8-355.
- Zwaigenbaum L, Bauman ML, Choueiri R, et al. Early intervention for children with autism spectrum disorder under 3 years of age: recommendations for practice and research. *Pediatrics*. 2015;136(S1):S60–S81. doi: http://dx.doi.org/10.1542/peds.2014-3667E.

Question 194

The mother of a 17-year-old boy calls for guidance. The boy's family is currently on a beach vacation on the mid-Atlantic coast of the United States. Approximately 10 minutes ago, the boy stepped on a jellyfish with his right foot. He rinsed off the foot with a pail of sea water and took a dose of acetaminophen. However, the boy has been in severe pain since stepping on the jellyfish.

The boy's mother tells you that he is not having any respiratory symptoms, and she has not noted any swelling of his lips, tongue, or face. She reports that the boy has a "red streak" on the sole of his right foot, but she does not see any other rash on the rest of his body. The mother asks what she should do to help relieve her son's pain.

Of the following, the MOST effective treatment for relieving his pain would be to

 A. apply a meat tenderizer paste to the right foot
 B. soak the right foot in a diluted ammonia solution
 C. soak the right foot in hot water
 D. soak the right foot in ice water
 E. soak the right foot in isopropyl alcohol solution

Correct Answer: C

The boy in the vignette has severe pain in his right foot after being stung by a jellyfish while visiting the mid-Atlantic coast of the United States. The most effective management for relieving his pain would be to soak the affected foot in hot water.

All pediatric providers should be able to plan the appropriate management of a jellyfish sting. Jellyfish stings are common occurrences in temperate coastal regions. Jellyfish tentacles have specialized organelles called nematocysts, which are used to catch, handle, and envenomate prey. These nematocysts fire and release toxins when they make contact with an object (or person). Signs and symptoms of jellyfish envenomation vary according to the species of jellyfish involved, number of nematocysts discharged, and the underlying health of the victim. Common symptoms that develop after jellyfish stings include burning pain and skin changes such as redness or urticaria at the sting site; these symptoms arise because of the release of inflammatory mediators, including serotonin, histamine, or histamine-related agents, present in the nematocyst venom. Systemic symptoms including abdominal/back/chest pain, tachycardia, hypertension, sweating, agitation, piloerection, and even cardiac complications can occur.

Treatment of jellyfish stings consists of deactivating any nematocysts remaining on the skin, neutralizing the toxin released by activated nematocysts, providing therapies to alleviate symptoms (such as pain), and supportive care. Many strategies have been proposed for treating jellyfish stings, but little evidence is available regarding which treatments are effective. Treatment recommendations for jellyfish stings also vary in different parts of the world (ie, nontropical versus tropical areas).

A 2013 Cochrane review found that the application of hot water was effective in relieving the pain arising specifically from stings of the *Physalia* (Blue Bottle) jellyfish species. Another systematic review examining outcomes of various treatments for jellyfish envenomation in North America and Hawaii support hot water and topical lidocaine as the preferred treatment modalities for jellyfish stings in North America and Hawaii, based on available evidence. Treatment recommendations for jellyfish stings occurring in different areas of the world, such as in tropical Australia, vary from those occurring in the United States. For instance, the International Life Saving Federation recommends application of ice packs and topical acetic acid for the treatment of box jellyfish stings, which occur most commonly in the tropical waters of Australia. The Australian Resuscitation Council recommends the application of vinegar as the first-line treatment for jellyfish stings occurring in tropical Australia; however, the council recommends using hot water to treat stings occurring in nontropical regions and for those known to have been caused by the Blue Bottle species of jellyfish.

Currently available published trials and systematic reviews do not support the benefits of applying meat tenderizer paste, diluted ammonia solution, or isopropyl alcohol to relieve pain associated with jellyfish stings. In fact, application of these remedies may promote nematocyst activation and *worsen* sting-related pain. Furthermore, currently available evidence does not support the use of ice water to relieve pain caused by jellyfish stings.

It is important to understand that clinical trial data supporting the current recommendations for treating jellyfish stings are scarce. Further studies need to be completed, and recommendations may change as additional evidence becomes available.

PREP Pearls
- The most common symptoms that develop after jellyfish stings include burning pain and skin changes (eg, redness or urticaria) at the sting site because of the release of inflammatory mediators. Systemic symptoms including abdominal/back/chest pain, tachycardia, hypertension, sweating, agitation, piloerection, and even cardiac complications can also occur.
- Application of hot water and topical lidocaine appears to be the most beneficial strategy for alleviating pain due to jellyfish stings in North America and Hawaii.

ABP Content Specifications(s)
- Plan the appropriate management of a jellyfish sting

Suggested Readings
- Li L, McGee RG, Isbister GK, Webster AC. Interventions for the symptoms and signs resulting from jellyfish stings (review). *Cochrane Database Syst Rev.* 2013;(12):CD009688.
- Ostermayer DG, Koyfman A. What is the most effective treatment for relieving the pain of a jellyfish sting? *Ann Emerg Med.* 2015;65(4):432–433. doi: http://dx.doi.org/10.1016/j.annemergmed.2014.09.009.
- Ward NT, Darracq MA, Tomaszewski C, Clark R. Evidence-based treatment of jellyfish stings in North America and Hawaii. *Ann Emerg Med*. 2012;60(4):399–414. doi: http://dx.doi.org/10.1016/j.annemergmed.2012.04.010.

Question 195

A 10-year-old boy is brought to the cardiology clinic for a follow-up appointment. He was born with hypoplastic left heart syndrome and received a heart transplant 4 months ago after developing refractory heart failure. His current immunosuppressive regimen consists of prednisolone and tacrolimus. At today's visit, his mother reports that he has developed pain when he swallows. Vital signs show a temperature of 37.4°C, heart rate of 85 beats/min, respiratory rate of 22 breaths/min, and blood pressure of 110/72 mm Hg. On physical examination, he appears uncomfortable. White plaques are present in the buccal mucosa and the posterior pharynx, which is also friable.

Of the following, the antifungal medication MOST likely to increase the risk for arrhythmia in this patient is

  A. amphotericin
  B. caspofungin
  C. fluconazole
  D. micafungin
  E. nystatin

Correct Answer: C

The immunocompromised patient in this vignette has an extensive oral candidal infection as evidenced by the description of pain with swallowing and the white friable plaques on the buccal mucosa and posterior pharynx. Fluconazole is the antifungal medication most likely to increase the patient's risk for arrhythmia because it can increase the concentration of tacrolimus, which raises the risk of prolongation of the Q-T interval.

The triazole class of antifungals includes fluconazole, itraconazole, voriconazole, and posaconazole. The use of triazoles is limited by their interaction with phase I/II metabolic enzymes. Fluconazole increases the levels of tacrolimus and other calcineurin inhibitors by inhibiting their first-pass metabolism. All azoles can cause gastrointestinal tract symptoms. With the exception of posaconazole, azoles can also potentially cause hepatotoxicity. Cytopenias can develop with the use of triazoles other than fluconazole. Voriconazole, but not other triazoles, can cause visual disturbances and hallucinations.

Amphotericin is a polyene antifungal medication. Adverse effects ascribed to the original formulation, amphotericin B deoxycholate, include infusion-related reactions (rigors and fever colloquially referred to as "shake and bake"), nephrotoxicity, and electrolyte abnormalities including hypokalemia and hypomagnesemia. Modification of the original formulation via a liposomal carrier or lipid complex reduces the risk of nephrotoxicity.

Caspofungin and micafungin are in the echinocandin class of antifungals. Adverse effects include gastrointestinal tract symptoms, elevated hepatic enzyme levels, and headache. Infusion-related events including phlebitis and fever can occur and are more common with caspofungin than with the other echinocandins. Histamine-associated infusion reactions, including pruritus, bronchospasm, angioedema, and hypotension, have been reported.

Adverse effects of nystatin are principally limited to gastrointestinal tract symptoms, including abdominal pain, nausea, emesis, and diarrhea.

PREP Pearls
- Fluconazole is in the triazole class of antifungals, which can have drug-drug interactions that limit their use.
- Adverse effects ascribed to amphotericin B deoxycholate include infusion-related reactions, nephrotoxicity, and electrolyte abnormalities including hypokalemia and hypomagnesemia.
- Adverse effects described for the echinocandins (eg, micafungin) include gastrointestinal tract symptoms, elevated hepatic enzyme levels, headache, and infusion-related reactions.

ABP Content Specifications(s)
- Recognize the adverse effects associated with the use of various antifungal drugs

Suggested Readings
- American Academy of Pediatrics. Recommended doses of parenteral and oral antifungal drugs. 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; 2015:909–912.
- Stockmann C, Constance J, Roberts J, et al. Pharmacokinetics and pharmacodynamics of antifungals in children and their clinical implications. *Clin Pharmacokinet.* 2014;53(5):429–454. doi: http://dx.doi.org/10.1007/s40262-014-0139-0.

Question 196

You are seeing a 3-year-old girl in your office the day after she was seen in the emergency department for refusal to walk. Her parents report that the girl would not bear any weight on her left leg when she awoke the previous morning. There is no history of trauma, but the girl had been at the playground with a babysitter for several hours on the previous day. She has not had fever, rash, or joint swelling. She has not seemed irritable, except when her parents try to coax her to walk. On physical examination, the girl is well appearing. Her temperature is 37.1°C, heart rate is 102 beats/min, blood pressure is 100/68 mm Hg, and respiratory rate is 24 breaths/min. She refuses to bear weight on her left leg. The girl has no tenderness to palpation over the spine or lower extremities. She resists passive range of motion of the left hip.

Her hip range of motion is as follows: abduction, 30 degrees on the left, 45 degrees on the right; internal rotation, 40 degrees on the left, 55 degrees on the right; and external rotation, 50 degrees bilaterally. Hip radiography and laboratory studies performed at the emergency department, including complete blood cell count and C-reactive protein, were normal.

Of the following, the MOST likely diagnosis for the girl in the vignette is

  A. juvenile idiopathic arthritis
  B. occult fracture
  C. septic arthritis
  D. Legg-Calvé -Perthes disease
  E. transient synovitis

Correct Answer: E

The girl in the vignette presents with refusal to walk in the absence of a history of trauma. She does not have systemic symptoms or fever. Her physical examination reveals slightly limited left hip motion. She most likely has transient synovitis. Although transient synovitis is often referred to as "toxic" synovitis, this condition is self-limited and does not lead to serious sequelae.

Transient synovitis typically affects preschool-aged children, with the average age at presentation being 4 years. While the exact etiology is unknown, this condition is thought to be related to a viral infection or postviral reaction. However, many children lack the classic history of antecedent viral infection. Affected children often present with a limp or refusal to bear weight. On physical examination, hip range of motion is typically decreased.

The differential diagnosis for transient synovitis is broad and includes septic arthritis, juvenile idiopathic arthritis (JIA), Legg-Calvé-Perthes disease (avascular necrosis of the femoral head), trauma, and neoplastic disease. Kocher described 4 criteria that support the diagnosis of septic arthritis: refusal to bear weight, elevated erythrocyte sedimentation rate, elevated white blood cell count, and fever. The child in the vignette meets only 1 of these criteria, making septic arthritis unlikely. However, the child should be followed closely and her parents should be educated about signs and symptoms, such as fever, increased pain, or systemic symptoms that would warrant urgent reevaluation.

In addition to laboratory studies, radiographic studies may be useful for ruling out serious conditions in a child with suspected transient synovitis. Plain radiography of the hip may show evidence of other conditions, such as Legg-Calvé-Perthes disease or may demonstrate increased medial joint space, a nonspecific finding. Hip ultrasonography can be used to demonstrate increased hip joint fluid, as seen in JIA, transient synovitis, or septic arthritis, and can be used to guide hip aspiration in a child with suspected septic arthritis.

Nonsteroidal anti-inflammatory medications and relative rest are the mainstays of treatment for transient synovitis. Symptoms generally last about 1 week, but tend to be especially severe in the first 2 to 3 days. Parents should be counseled that recurrence is common.

Although Legg-Calvé-Perthes, septic arthritis, and JIA are in the differential diagnosis for refusal to bear weight, this girl's presentation is most consistent with transient synovitis; transient synovitis is also the most common diagnosis. Occult fracture is unlikely in the absence of focal tenderness and would not explain the girl's limited range of motion of the hip.

PREP Pearls
- Transient synovitis typically causes a limp or refusal to bear weight in an otherwise well-appearing preschool-aged child.
- Four criteria that support the diagnosis of septic arthritis include refusal to bear weight, elevated erythrocyte sedimentation rate, elevated white blood cell count, and fever. The more of these criteria a child exhibits, the more likely it is that he or she has septic arthritis.

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- Nonsteroidal anti-inflammatory medications and relative rest are the mainstays of treatment for transient synovitis.

ABP Content Specifications(s)
- Formulate a differential diagnosis of a painful hip

Suggested Readings
- Herman MJ, Martinek M. The limping child. *Pediatr Rev.* 2015;36(5):184–195. doi: http://dx.doi.org/10.1542/pir.36-5-184.
- Kocher MS, Zurakowski D, Kasser JR. Differentiating between septic arthritis and transient synovitis of the hip in children: an evidence-based clinical prediction algorithm. *J Bone Joint Surg.* 1999;81(12):1662–1670.
- Nouri A, Walmsley D, Pruszczynski B, Synder M. Transient synovitis of the hip: a comprehensive review. *J Pediatr Orthop B.* 2014;23(1):32–36. doi: http://dx.doi.org/10.1097/BPB.0b013e328363b5a3.

Question 197

You are called to the room of a term neonate who is now 12 hours old. He was delivered via cesarean delivery at 38 weeks of gestation to a 28-year-old, gravida 1 para 1 woman with a history of obesity and poorly controlled gestational diabetes. The delivery was scheduled because of concerns for fetal macrosomia. Prenatal test results for group B Streptococcus were negative. The maternal blood type is O+. The nurse reports that the neonate has had trouble latching to the breast. He has had several capillary blood glucose measurements because of his mother's history of gestational diabetes; these levels have all been greater than 60 mg/dL (3.3 mmol/L). The resident caring for the neonate was concerned that he appeared ruddy and jittery and ordered a hematocrit with the most recent capillary blood glucose test, and the result was 73% (0.73). The resident asks what he should do next.

Of the following, the MOST appropriate next step in management is to order a(n)

A. intravenous infusion of normal saline
B. partial exchange transfusion
C. repeat heel stick to confirm the hematocrit
D. type and screen with direct antiglobulin (Coombs) test
E. venous blood draw to confirm the hematocrit

Correct Answer: E

The most appropriate next step in management for the neonate in this vignette is to determine the hematocrit from a peripheral venous blood sample. Neonatal polycythemia is defined as a venous hematocrit of at least 65% (0.65). A hematocrit from a venous sample can be up to 15% lower than a hematocrit measured from capillary sampling, and a hematocrit drawn centrally (eg, through an umbilical venous catheter in a neonate) tends to be even lower.

Neonatal polycythemia is concerning because an elevated hematocrit contributes to increased plasma viscosity, which can lead to vascular stasis and poor perfusion. Possible outcomes include stroke, pulmonary hypertension, or other end-organ damage. Risk factors for neonatal polycythemia include maternal diabetes, intrauterine growth restriction, small or large for gestational age, placental insufficiency, cyanotic congenital heart disease, in utero tobacco exposure, in utero exposure to propranolol and other medications, maternal-fetal transfusion, or twin-twin transfusion. Although most neonates with polycythemia are asymptomatic, signs and symptoms can include plethora, lethargy, hypotonia, poor suck, hypoglycemia, tremulousness, and jaundice. Because only half of neonates with polycythemia have evidence of hyperviscosity, treatment with intravenous fluid administration or with partial exchange transfusion is somewhat controversial, especially at lower hematocrits and for asymptomatic infants.

The newborn in this vignette has risk factors and symptoms concerning for polycythemia. However, his elevated hematocrit was drawn via capillary sampling, so it would not be appropriate to initiate intravenous fluids or partial exchange transfusion at this time. A repeat capillary (heel-stick) sample or a blood type and direct antiglobulin (Coombs) test would not be helpful for diagnosis. The most appropriate next step is a venous blood draw to measure the hematocrit.

PREP Pearls
- Neonatal polycythemia is defined as a peripheral venous hematocrit of at least 65% (0.65).
- Hematocrits vary by collection method. Hematocrits obtained via peripheral venous collection can be up to 15% lower than levels from capillary draws, and results from central sampling tend to be even lower.

MOCA-Peds Objective
- Evaluate and manage a neonate born to a diabetic mother

ABP Content Specifications(s)
- Understand the potential differences between the hematocrit of a centrally or peripherally obtained blood sample

Suggested Readings

- Ramamurthy RS, Brans YW. Neonatal polycythemia: I, criteria for diagnosis and treatment. *Pediatrics*. 1981;68(2):168–174.
- Kato GJ, Casella JF, Seidel HM. Hematology. In: Seidel HM, Rosenstein BJ, Pathak AA, McKay WH, eds. *Primary Care of the Newborn*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2006: 276–279.
- Ramamurthy RS, Brans YW. Neonatal polycythemia: I, criteria for diagnosis and treatment. *Pediatrics*. 1981;68(2):168–174.

Question 198

You are seeing a 2-year-old boy with hemoglobin SS disease for routine health care in your primary care practice. His mother is 7 months pregnant with the couple's second child. They know that there is a risk that the newborn will also have sickle cell disease, but they declined prenatal diagnostic procedures because of the risk to the fetus. They ask how soon after birth the diagnosis of sickle cell disease can be made.

Of the following, the MOST appropriate answer to their question is

 A. at birth
 B. by 1 month of age
 C. by 3 months of age
 D. by 6 months of age
 E. by 12 months of age

Correct Answer: A

Hemoglobin SS disease is an autosomal recessive disorder that occurs when both β-globin genes, located on chromosomal band 11p15.5, contain a point mutation resulting in the replacement of glutamic acid with valine at position 6. In this vignette, a sibling to the unborn child has hemoglobin SS disease, suggesting that both parents carry the sickle cell trait. Therefore, there is a 25% chance that the fetus also has hemoglobin SS disease. Screening for this disorder can be performed by hemoglobin isoelectric focusing or high-performance liquid chromatography to determine the relative quantities of hemoglobin variants in a newborn blood spot.

Normal adult hemoglobin (hemoglobin A) consists of tetramers of 2 α-globin chains and 2 β-globin chains. Fetuses require hemoglobin with a higher oxygen affinity given the relatively hypoxic in utero environment. Fetal hemoglobin (hemoglobin F) consists of 2 α-globin chains and 2 γ-globin chains. Newborns with normal globin genes have a predominance of hemoglobin F and a minority component of hemoglobin A. This combination is reported in the newborn screening results as FA. Newborns with hemoglobin SS disease also have a predominance of hemoglobin F, but they express hemoglobin S instead of hemoglobin A (newborn screening result, FS). Newborns with sickle cell trait have a predominance of hemoglobin F with minority components of both hemoglobin A, expressed from the normal globin gene, and hemoglobin S, expressed from the mutated globin gene (newborn screening result, FAS). Although sickle cell disease can certainly be diagnosed at 1, 3, 6, or 12 months of age, the earliest and most frequent time for the diagnosis in the United States is at birth. Newborn screening for sickle cell disease is mandated in all 50 states and the District of Columbia.

Given the high proportion of hemoglobin F at birth, the complications of sickle cell disease do not typically manifest in the first few months after birth. As a child with sickle cell disease ages, the relative amount of hemoglobin S increases, and the amount of hemoglobin F decreases. The qualitatively defective hemoglobin molecule in hemoglobin S is prone to polymerization, which results in deformation of the red blood cell membrane (sickling). This deformation leads to an abbreviated red blood cell lifespan, chronic hemolysis, and frequent small vessel occlusion resulting in end-organ damage. This damage leads to a multitude of acute and chronic illnesses, as well as a shortened life span. Early diagnosis of sickle cell disease allows for the early implementation of counseling, screening, and prophylaxis that can help maintain health in this complex population.

PREP Pearls

- Newborns have a predominance of hemoglobin F (fetal hemoglobin, $\alpha_2\gamma_2$) at birth and a minor expression of hemoglobin A (adult hemoglobin, $\alpha_2\beta_2$).
- Abnormal hemoglobin can be detected from a neonatal blood spot, thus sickle cell disease can be diagnosed in the newborn.
- All 50 states and the District of Columbia have mandated newborn screening for sickle cell disease.
- Newborn screening results are reported as FA for newborns with normal hemoglobins, FS for newborns with hemoglobin SS disease, and FAS for newborns with sickle cell trait.

ABP Content Specifications(s)
- Recognize the clinical findings associated with sickle cell disease in children of various ages
- Understand that sickle cell disease can be diagnosed at birth

Suggested Readings
- Driscoll MC. Sickle cell disease. *Pediatr Rev.* 2007;28(7):259–268. doi: http://dx.doi.org/10.1542/pir.28-7-259.
- Gonzales JL. Ethics for the pediatrician: genetic testing and newborn screening. *Pediatr Rev.* 2011;32(11):490–493. doi: http://dx.doi.org/10.1542/pir.32-11-490.
- McCavit TL. Sickle cell disease. *Pediatr Rev.* 2012;33(5):195–206. doi: http://dx.doi.org/10.1542/pir.33-5-195.

Question 199

A 5-year-old boy is brought to your office by his mother with concerns of progressive muscular weakness. He has been falling frequently and has increasing difficulty with climbing stairs, running, jumping, and rising from a squatting position. On review of his developmental milestones, the mother noted that he sat at 10 months and walked at 18 months, but his verbal and cognitive skills were acquired normally. The maternal uncle has a disorder that began similarly and has required him to use a wheelchair since his early teens.

You note a waddling gait, toe-walking, and bilateral calf hypertrophy. The boy's creatine kinase level is greater than 10 times the normal level.

Of the following, the MOST likely diagnosis is

 A. arthrogryposis
 B. Duchenne muscular dystrophy
 C. limb girdle muscular dystrophy
 D. myasthenia gravis
 E. spinal muscular atrophy

Correct Answer: B

The boy in this vignette has Duchenne muscular dystrophy (DMD), an X-linked recessive disorder, which is a childhood-onset form of muscular dystrophy. It is a rapidly progressive skeletal muscle disease that presents in boys during early childhood with delayed motor milestones and proximal symmetric muscle weakness accompanied by calf hypertrophy. Children will have a waddling gait and problems climbing, eventually becoming wheelchair dependent by 13 years of age. No cognitive deficits are noted. Cardiomyopathy will manifest by late childhood or the early 20s. Most patients will not survive beyond the third decade, dying from a combination of cardiomyopathy and respiratory difficulties. The creatine kinase level is greater than 10 times the normal level in DMD. *DMD* is the only gene known to be associated with Duchenne and Becker muscular dystrophy. Molecular testing can establish the diagnosis in children with suspected DMD and Becker muscular dystrophy without the need for a muscle biopsy in many cases. Because this is an X-linked recessive condition, male individuals are more severely affected than female individuals. Female heterozygous carriers of a *DMD* mutation are at higher risk for dilated cardiomyopathy but often times will not have the skeletal muscle weakness, rapid decline, and shortened lifespan seen in male individuals.

Becker muscular dystrophy presents with later onset proximal skeletal muscle weakness than DMD due to partial dystrophin function. Most patients will maintain ambulatory capabilities into their 20s. Despite the milder skeletal muscle presentation, most patients will die from dilated cardiomyopathy in their 40s.

Arthrogryposis is a general term describing the clinical presentation of nonprogressive contractures affecting at least 1 region of the body at the time of birth. Arthrogryposis multiplex congenita affects at least 2 areas of the body, typically the joints of the arms or legs, but it can also affect the shoulders, elbows, wrists, knees, ankles, and digits.

There are many genetic subtypes of limb girdle muscular dystrophies, which can present in childhood or adulthood with proximal skeletal muscle weakness and wasting. There is sparing of the bulbar musculature. Limb girdle muscular dystrophies can affect male and female individuals equally because there are autosomal dominant and autosomal recessive forms. The creatine kinase level is elevated. Most individuals will have undergone an evaluation for DMD and Becker muscular dystrophy to formally exclude the more commonly recognized X-linked form of dystrophinopathy. A muscle biopsy is usually required to make the diagnosis, although molecular genetic panels for limb girdle muscular dystrophies are available.

Myasthenia gravis is an autoimmune neuromuscular disease characterized by muscular weakness that increases with activity and improves after a period of rest. The predominant involvement of facial and eye muscles causes lid lag (ptosis) and impaired extraocular eye movement, facial expression, talking, and swallowing. Weakness is rarely generalized and is caused by antibodies against acetylcholine nicotinic postsynaptic receptors at the neuromuscular junction.

Spinal muscular atrophy, an autosomal recessive disorder, presents with progressive muscle weakness caused by degeneration of the anterior horn cells of the spinal cord and brainstem. The clinical onset of spinal muscular atrophy ranges from birth to adolescence to adulthood. Clinical manifestations include muscular weakness, finger trembling, tongue fasciculations, absent deep tendon reflexes, intact intellectual skills, and alert appearance. The presence of fasciculations, a very common finding in spinal muscular atrophy, would exclude a dystrophinopathy diagnosis.

PREP Pearls

- Duchenne muscular dystrophy, an X-linked recessive disorder, is a childhood-onset form of muscular dystrophy that leads to rapidly progressive skeletal muscle disease clinically manifesting as delayed motor milestones and proximal symmetric muscle weakness accompanied by calf hypertrophy in boys during early childhood. boys during early childhood.
- *DMD* is the only gene associated Duchenne muscular dystrophy, an X-linked recessive disorder, is a childhood-onset form of muscular dystrophy that leads to rapidly progressive skeletal muscle disease clinically manifesting as delayed motor milestones and proximal symmetric muscle weakness accompanied by calf hypertrophy in boys during early childhood.
- Female heterozygous carriers of a DMD mutation are at higher risk for dilated cardiomyopathy but often will not have the skeletal muscle weakness, rapid decline, and shortened lifespan seen in male individuals.

ABP Content Specifications(s)

- Recognize the clinical findings associated with proximal muscle weakness
- Recognize the clinical findings associated with dystrophinopathy (eg, Duchenne/Becker muscular dystrophy)

Suggested Readings

- American Academy of Pediatrics Section on Cardiology and Cardiac Surgery. Cardiovascular health supervision for individuals affected by Duchenne or Becker muscular dystrophy. *Pediatrics*. 2005;116(6):1569–1573. doi: http://dx.doi.org/10.1542/peds.2005-2448.
- Bushby K, Finkel R, Birnkrant DJ, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis and pharmacological and psychosocial management. *Lancet Neurol.* 2010;9(1):77–93. doi: http://dx.doi.org/10.1016/S1474-4422(09)70271-6.
- Bushby K, Finkel R, Birnkrant DJ, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. *Lancet Neurol*. 2010;9(2):177–189. doi: http://dx.doi.org/10.1016/S1474-4422(09)70272-8.
- Darras BT, Miller DT, Urion DK. Dystrophinopathies. *GeneReviews*. 2014. https://www.ncbi.nlm.nih.gov/books/NBK1119/.
- Pegoraro E, Hoffman EP. Limb-girdle muscular dystrophy overview. *GeneReviews*. 2012. https://www.ncbi.nlm.nih.gov/books/NBK1408/.

Question 200

A 15-year-old boy who has recently emigrated from Mexico is brought to the emergency department because of an episode of shaking movements of his left arm and leg associated with eye deviation to the left, headache, and emesis. The episode lasted approximately 5 minutes and ended abruptly. He had a similar episode 2 months ago. There are no sick contacts, no pets at home, and no history of exposure to tuberculosis contacts. His immunizations are up-to-date.

He is afebrile and alert with normal vital signs. No focal neurologic deficit is noted. The rest of the physical examination findings are normal. Magnetic resonance imaging of the brain reveals a ring-enhancing lesion in his cerebral cortex (Item Q200). He is admitted to the hospital for further evaluation.
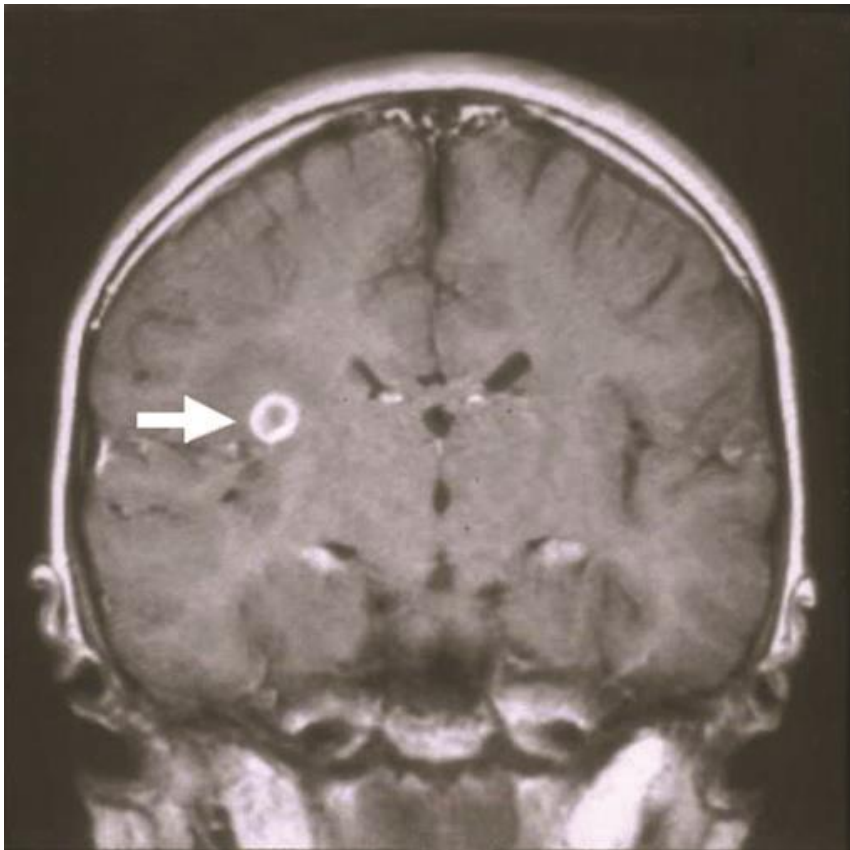
Item Q200: Magnetic resonance imaging of the brain for the boy described in the vignette revealed a ring-like lesion.
Reprinted with permission from Jantausch BA and Kimberlin DW, et al. Red Book Online. Elk Grove Village, IL. American Academy of Pediatrics 2015

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

A. biopsy of the brain lesion
B. cerebrospinal fluid culture
C. interferon-γ release assay
D. serum antibody assay for larval Taenia solium
E. stool examination for ova and parasites

Correct Answer: D

Human cysticercosis is a tropical parasitic disease caused by 1 or more cysticerci (larvae) of the pork tapeworm *Taenia solium* (cysticercosis cellulosae) (**Item C200A**). *Taenia solium* is prevalent worldwide, especially in Mexico, most of Latin America, parts of Central and South America, China, Indonesia, India, and sub-Saharan Africa. The highest prevalence of *T solium* infection is found in low- and middle-income countries where pigs are raised and fed in areas with poor sanitation and contamination with human feces.
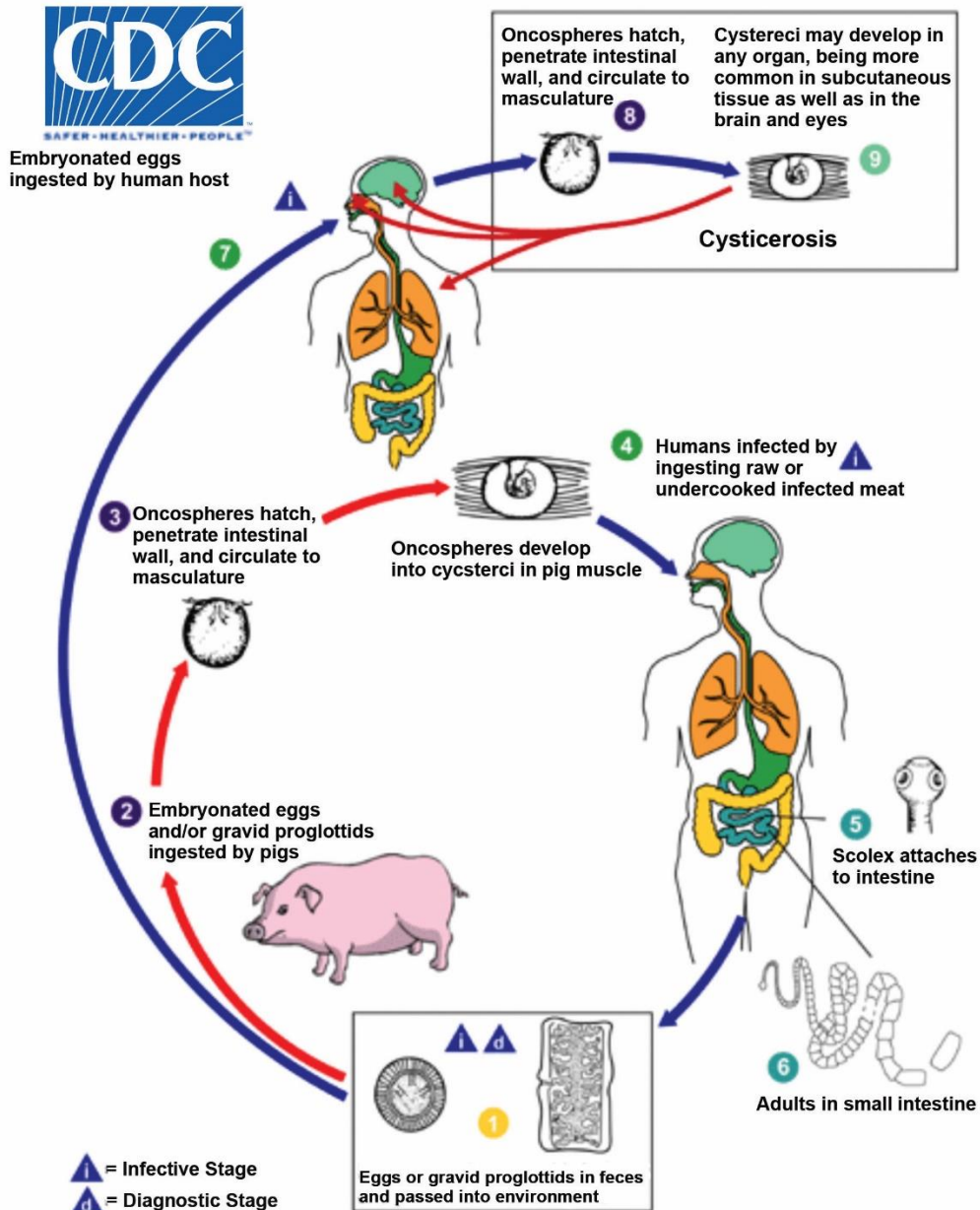
Item C200A: Life cycle of *Taenia Solium*
Reprinted with permission from the Centers for Disease Control and Prevention.

The life cycle of *T solium* is depicted in **Item C200B**. Humans are the obligate definitive host. Individuals acquire infection by fecal-oral contact by accidentally ingesting the eggs of *T solium* shed in human feces by a household carrier of the adult tapeworm or through consumption of fecally contaminated food. Once ingested, the embryonated eggs of *T solium* release oncospheres that penetrate the small intestinal wall, enter the bloodstream, and lodge in tissues, especially the brain parenchyma, where they develop into cysticerci. The intraparenchymal cysts can remain quiescent for a period of months to years. Infections caused by adult tapeworms are usually asymptomatic, although infected individuals may develop a mild gastrointestinal illness. In contrast, infections caused by the encysted larvae of *T solium* can cause severe disease, depending on the organ involved and the host immune response.
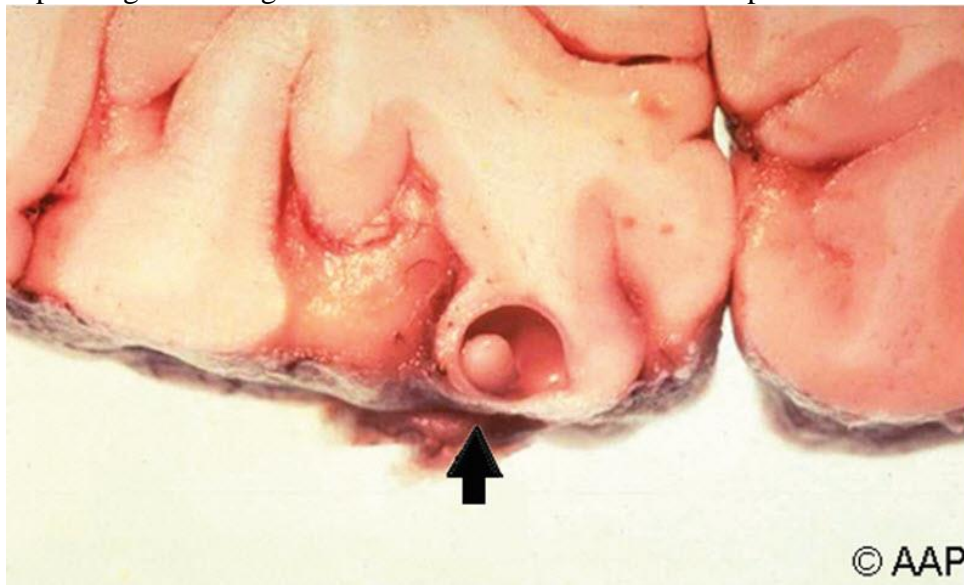
Item C200B: Cross-section of the brain at autopsy showing cysticeri
Reprinted with permission from Kimberlin DW, et al. Tapeworm Diseases. Red Book Online. Elk Grove Village, IL. American Academy of Pediatrics 2015

Neurocysticercosis (NCC) is the most common clinical manifestation of cysticercosis and results in substantial morbidity and excess social and economic burden. Neurocysticercosis is a major cause of adult-onset epilepsy in low and middle income countries that are disease endemic, accounting for 30% of epilepsy cases. The global disease burden attributed to NCC is estimated at 1.4 million cases of epilepsy and 0.5 million disability-adjusted life years (ie, the number of life years lost either from premature death or disability). Increased migration and travel has resulted in increased recognition of NCC in high income countries. In the United States, most cases of NCC are reported among immigrants from Latin America or Asia. Frequently, a family member in the home of a patient is the carrier of *T solium*.

The clinical manifestations of NCC are protean and vary from asymptomatic disease to a severe complicated course, depending on the number, size, and location of the cysticerci and the host immune response. Seizures are the most common clinical manifestation of intracranial NCC, as

seen in the patient in this vignette, and often result from acute or chronic host inflammation of degenerating *T solium* brain cysts. Extraparenchymal localizations of the cysticerci include the subarachnoid space, ventricular system, or spinal cord. Other manifestations may include focal neurologic deficits, increased intracranial pressure, obstructive hydrocephalus, behavioral disturbances, or cognitive decline. Rare manifestations may include chronic meningitis and encephalitis. Spinal cord involvement may result in progressive paraplegia. Ocular cysticercosis is characterized by cysts in the subretinal area or the vitreous humor and can cause visual impairment or blindness.

The diagnosis of NCC can be made by neuroimaging studies in conjunction with *T solium* antibody tests. Computed tomography scan or magnetic resonance imaging can detect cysts, calcifications, intraventricular lesions, or cisternal cysts. Magnetic resonance imaging is preferred to computed tomography for visualization of posterior fossa and spinal lesions, whereas computed tomography is superior for visualization of calcifications. In general, the neuroimaging findings of NCC are nonspecific. However, in the appropriate clinical context, the presence of cystic lesions on computed tomography or magnetic resonance imaging revealing the scolex as an eccentric nodule is considered diagnostic of NCC. Antibody assays to *T solium* are more sensitive in serum than in cerebrospinal fluid. Serum antibody test results are often negative with minimal disease (a solitary cyst) but positive in patients with multiple lesions.

The clinical presentation of the adolescent boy in this vignette with a focal seizure (especially with a history of previous seizures), recent immigration from Mexico, and magnetic resonance imaging findings of a solitary ring-enhancing lesion in the brain parenchyma is highly suggestive of NCC. The most appropriate next step to confirm the diagnosis of NCC is to obtain a serum antibody assay for larval *T solium*. Stool examination for ova and parasites for diagnosis of taeniasis (adult tapeworm infection) is not sensitive and not indicated for evaluation of suspected NCC. The differential diagnosis of intracranial space-occupying lesions must also include tuberculosis, pyogenic brain abscess, toxoplasmosis, and rarely neoplastic disease. The clinical presentation with no history of exposure to tuberculosis contacts makes the diagnosis of central nervous system tuberculosis unlikely. Similarly, pyogenic brain abscess or a brain tumor is an unlikely possibility.

Antiparasitic treatment decisions for NCC are complex and depend on the stage of the disease and the presence of solitary or multiple cysts. Available anthelmintic drugs with cysticercidal activity include albendazole and praziquantel. A single ring-enhancing inflamed lesion may resolve spontaneously without antiparasitic therapy, although emerging data suggest benefit from treating solitary enhancing cysts with albendazole, resulting in more rapid resolution of the lesions and reduced seizure relapses. In contrast, for multiple cysts or cysts without ring enhancement, treatment with albendazole or praziquantel is recommended. The frequency of drug-drug interactions with anticonvulsants is less with albendazole than with praziquantel. A recent study has shown that combination therapy with albendazole and praziquantel is more effective in destroying viable intraparenchymal brain cysticercosis cysts than albendazole alone. Many experts recommend combination therapy with albendazole and praziquantel for treatment of NCC with more than 2 cystic lesions.

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Corticosteroid administration during anthelmintic therapy is indicated to reduce the local inflammatory response when additional cysts are destroyed. An ophthalmologic evaluation should be performed before initiating anthelmintic treatment to exclude ocular cysticerci. Symptomatic treatment of NCC includes the administration of anticonvulsants for seizures. Consultation with a pediatric neurologist is recommended for management of epilepsy. Neurosurgical intervention may be necessary to manage complicated disease and could include endoscopic surgical excision of intraventricular cysts and shunt placement for hydrocephalus. Control and prevention of *T solium* transmission must remain a global health priority to reduce the substantial health care and economic burdens caused by NCC and taeniasis.

PREP Pearls
- Neurocysticercosis is a neglected tropical parasitic disease caused by 1 or more cysticerci (larvae) of the pork tapeworm *Taenia solium.*
- In the United States, most patients with neurocysticercosis are immigrants from Latin America or Asia.
- Seizures are the most common clinical manifestation of intracranial neurocysticercosis and often result from acute or chronic host inflammation of degenerating *Taenia solium* brain cysts.
- Antibody assays to *Taenia solium* are more sensitive in serum than in cerebrospinal fluid.

ABP Content Specifications(s)
- Recognize the clinical features associated with cysticercosis
- Understand the epidemiology of cysticercosis

Suggested Readings
- Garcia HH, Lescano AG, Gonzales I, et al. Cysticidal efficacy of combined treatment with praziquantel and albendazole for parenchymal brain cysticercosis. *Clin Infect Dis.* 2016;62(11):1375–1379. doi: http://dx.doi.org/10.1093/cid/ciw134.
- Weatherhead JE, Hotez PJ. Worm infection in children. *Pediatr Rev.* 2015;36(8):341–354. doi: http://dx.doi.org/10.1542/pir.36-8-341.
- Webb CM, White AC Jr. Update on the diagnosis and management of neurocysticercosis. *Curr Infect Dis Rep.* 2016;18(12):44. doi: http://dx.doi.org/10.1007/s11908-016-0547-4.

Question 201

A 4-year-old boy is brought by his mother to your office for evaluation of cough and fever. His mother reports that the boy has had rhinorrhea for 3 days, cough for 2 days, and a fever of 39.4°C yesterday. He is taking adequate fluids but is eating little solid food. His energy has been decreased overall, but he is playing with a puzzle in the examining room. He denies ear pain. He has no significant past medical history.

On physical examination, the boy is cooperative and answers questions appropriately. He is afebrile. There is visible fluid behind his left tympanic membrane, with impaired movement on pneumatic otoscopy. No erythema is noted. His right tympanic membrane appears normal. The boy has visible clear rhinorrhea and a mildly inflamed oropharynx. His lungs are clear to auscultation.

On review of his chart, you see that the boy was treated for left acute otitis media 6 weeks ago with high-dose amoxicillin (90 mg/kg per day). He is otherwise healthy.

Of the following, the MOST appropriate next management step for this boy is

 A. amoxicillin-clavulanate for 10 days
 B. high-dose amoxicillin for 10 days
 C. reevaluation of the left tympanic membrane in 6 weeks
 D. referral to audiology for evaluation of his hearing
 E. referral to otolaryngology for tympanostomy tube placement

Correct Answer: C

The boy in the vignette has otitis media with effusion (OME), which is defined as inflammation and liquid collection in the middle ear, without signs and symptoms of acute infection, such as an erythematous and bulging tympanic membrane and otalgia. The most appropriate next management step for this boy is reevaluation of the left tympanic membrane in 6 weeks (12 weeks after the infection). OME can be a consequence of acute otitis media (AOM), and can predispose patients to recurrent AOM. Distinguishing between AOM and OME is important because the recommended approaches to management are different.

In OME, the contour of the tympanic membrane can be either retracted or slightly full. The membrane usually appears opaque, and is white to amber in color. Pneumatoscopy is a very helpful tool for making the diagnosis of OME, because the movement of the tympanic membrane in response to positive and/or negative pressure is diminished in OME compared with that of a healthy tympanic membrane. Tympanometry, which tests the compliance of the tympanic membrane, can provide similar information about mobility, but without visualization of the membrane, it is less specific for a diagnosis of OME.

Otitis media with effusion is a common complication of AOM. After AOM, 10% of children will have persistent OME at 12 weeks. Of these, 30% will experience spontaneous resolution by 12 months after the episode of AOM. Therefore, the mainstay of treatment for most children with OME, including the boy in the vignette, is watchful waiting with follow-up examinations at 12-week intervals. The presence of OME can cause conductive hearing loss, and caregivers should be cautioned that a child's behavior can be affected accordingly. Reduced hearing during this short period does not appear to affect long-term language development.

However, longer periods of conductive hearing loss can contribute to speech and language delays. Children with bilateral OME at 12 weeks, or unilateral OME at 6 months, after an episode of AOM should undergo a hearing evaluation. If a 30-dB hearing loss in the speech range (500–2,000 Hz) is found, referral to otolaryngology for tympanostomy tube placement should be considered. Children with, or at risk for, speech and language delay due to other conditions (eg, cerebral palsy, cognitive impairment) may benefit from earlier evaluation for hearing loss and referral for surgical treatment, to minimize the impact of OME-associated conductive hearing loss on development. Persistent OME can also lead to anatomical damage to the middle ear. If retraction pockets, persistent perforation with discharge, or cholesteatoma is seen, prompt referral to otolaryngology is needed. Because children with craniofacial abnormalities are less likely to experience spontaneous resolution of OME, observation for several months before otolaryngology referral may not be appropriate in this population.

Effective medications to treat OME remain elusive. Antibiotic treatment has been shown to be of only temporary benefit, and is not recommended when spontaneous resolution is likely. Antihistamines and decongestants are ineffective in OME. No alternative treatments for OME have been found to be helpful.

PREP Pearls
- Watchful waiting is the appropriate management approach for most children with otitis media with effusion (OME), given the high likelihood of spontaneous resolution.
- Referral to otolaryngology for surgical management is appropriate for children with hearing loss due to OME who have, or are at risk for, speech and language delay.

ABP Content Specifications(s)
- Understand the natural history of otitis media with effusion in patients of various ages
- Recognize potential physical, behavioral, and developmental complications 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/pediatrics/113/5/1412.full.pdf?download=true.
- 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 202

A family who previously declined to vaccinate has now agreed to immunize their child because there is a measles outbreak in their community. During a clinic visit, the mother mentions that she was not fully immunized as a child. She asks whether she should receive the measles-mumps-rubella (MMR) vaccine now because she is currently trying to conceive.

Of the following, the MOST accurate information you can give to this child's mother regarding her question is that

A. all reproductive-age women should undergo a pregnancy test before receiving this vaccine
B. if this vaccine was given during early pregnancy, it is an indication to consider pregnancy termination
C. if given during pregnancy, this vaccine has been associated with symptomatic congenital disease
D. this vaccine has not been associated with teratogenic effects
E. this vaccine should be delayed until 1 month after delivery to prevent transmission to the newborn

Correct Answer: D

While the component diseases, particularly rubella, can have profound effects on the fetus if the mother acquires infection during pregnancy, the mumps-measles-rubella (MMR) vaccine does not carry a similar risk. Although it is a live virus vaccine, and fetal seroconversion has been seen to occur when MMR was given during pregnancy, to date there has been no association between the vaccine and symptomatic congenital disease. Neither has there been any evidence that the vaccine is teratogenic. Even so, because of the theoretical risk of maternal-to-fetal transmission and subsequent infection from a live virus vaccine, MMR should not be given during pregnancy. Ideally, MMR should be given to nonimmune women at least 1 month before conceiving; however, a pregnancy test is not recommended or required before vaccine administration to a woman of childbearing age. Neither does pregnancy termination need to be considered if MMR is inadvertently given to a pregnant woman. MMR should be administered soon after delivery, usually before discharge from the hospital, to any woman who is nonimmune or has indeterminate immunity. The Centers for Disease Control and Prevention list no precautions related to breastfeeding and MMR administration.

PREP Pearls
- It is recommended that the mumps-measles-rubella vaccine (MMR) be given to nonimmune women at least 1 month before conceiving. It is not recommended during pregnancy.
- MMR should be given to nonimmune mothers after delivery but before discharge from the hospital.
- There has been no evidence to date of teratogenicity or congenital rubella syndrome in neonates born to mothers who received MMR during pregnancy.

ABP Content Specifications(s)
- Advise a pregnant woman regarding receipt of MMR vaccine

Suggested Readings
- Glatman-Freedman A. Rubella vaccine. *Pediatr Rev.* 2002;23:106–107. http://pedsinreview.aappublications.org/content/23/3/106.
- Global Advisory Committee on Vaccine Safety. Safety of immunization during pregnancy: a review of the evidence. Geneva, Switzerland: World Health Organization; 2014. http://www.who.int/vaccine_safety/publications/safety_immunization_pregnancy/en/. Accessed August 9, 2016.
- Pickering LK. 6 cases of congenital rubella syndrome identified in U.S. since 2004. *AAP News.* 2013;34:11.

Question 203

A 15-year-old adolescent girl goes to the emergency department with her mother for evaluation of red-colored urine and a 1-day history of fever. She also reports increased frequency, pain, and a burning sensation on micturition since this morning. She has no prior history of urinary tract infections, red urine, or flank pain. She reports that she is not sexually active. Her urinalysis shows a bright red urine specimen with blood clots. She has a temperature of 38.9°C, respiratory rate of 16 breaths/min, heart rate of 90 beats/min, and blood pressure of 110/74 mm Hg. Her physical examination findings are significant only for mild suprapubic tenderness. Results of a urine test strip analysis are shown:

Laboratory Data	Result
Specific gravity	1.025
pH	6.0
Blood	3+
Leukocyte esterase	3+
Nitrites	Positive
Protein	Negative

Of the following, the MOST likely risk factor predisposing to this adolescent's symptoms is

  A. congenital renal anomaly
  B. renal stones
  C. sexual activity
  D. vesicoureteral reflux
  E. voiding dysfunction

Correct Answer: C

Bright red hematuria usually indicates lower urinary tract bleeding. Glomerular hematuria (as in nephritis) is usually described as cola-, tea-, or brown-colored. An underlying etiology is more frequently identified in patients presenting with gross hematuria. A detailed history, physical examination, and urinalysis usually provide clues to the underlying cause of gross hematuria.

The presence of blood clots associated with dysuria, fever, and suprapubic tenderness in the adolescent in this vignette indicates cystitis. Cystitis, or inflammation of the urinary bladder, may occur alone (uncomplicated cystitis) or in association with pyelonephritis (complicated cystitis). One of the most important risk factors for the development of acute cystitis, especially in female individuals, is sexual intercourse. Acute cystitis in the adolescent girl in this vignette should prompt suspicion for sexual activity. Therefore, the patient should be questioned about her sexual history after requesting that the parents step out of the room. Consideration should also be made for evaluation for sexually transmitted disease and counselling about safe sex and personal hygiene after sexual intercourse. The patient should also be counseled about contraception and encouraged to discuss contraception with her parents.

Bacteria, fungi, viruses, and parasites from the intestinal tract that are present in the periurethral area and urinary tract are the etiological agents for cystitis. Gram-negative bacteria, such as *Escherichia coli*, account for nearly 90% of cases of uncomplicated cystitis and would be the most likely pathogen for the girl in this vignette. Uncomplicated hemorrhagic cystitis, reported with adenovirus infection, is not common in children.

Risk factors for cystitis with pyelonephritis include anatomic or physiologic abnormalities associated with incomplete bladder emptying, urinary catheters, and associated diagnoses such as malignancy or diabetes. Congenital anomalies of the kidney and urinary tract are usually diagnosed on antenatal ultrasound and represent 20% to 30% of all antenatal anomalies and 60% of pediatric chronic kidney disease (including cystic renal disease). Renal abnormalities identified on antenatal ultrasound (eg, hydronephrosis; kidney size, number, and position; abnormal renal parenchyma) must be confirmed with postnatal ultrasounds. Further imaging studies in these patients include voiding cystourethrography, diuretic renal scan, and serial ultrasonography to identify and characterize congenital anomalies of the kidney and urinary tract and minimize long-term injury and other associated side effects (urinary tract infections, bladder dysfunction). Tubulointerstitial injury associated with congenital anomalies of the kidney and urinary tract leads to reduced urinary concentration (acquired nephrogenic diabetes insipidus). Patients whose congenital anomalies are missed in the antenatal period usually exhibit associated complications such as recurrent urinary tract infections, polyuria with or without enuresis, growth retardation, and pallor; these findings are not seen in the girl in this vignette. Vesicoureteral reflux is the retrograde passage of urine from the bladder to the kidneys. Vesicoureteral reflux may present antenatally as hydronephrosis on antenatal ultrasonography screening or be diagnosed in children after an episode of urinary tract infection (usually before 6-7 years of age). Patients with antenatally diagnosed vesicoureteral reflux are usually male individuals and have increased risk for other congenital abnormalities of the kidney, such as renal hypoplasia or dysplasia. Vesicoureteral reflux is associated with increased risk for

pyelonephritis. In the absence of prior urinary tract infections and given the age of the patient in this vignette, vesicoureteral reflux is unlikely to be a risk factor for her cystitis.

Symptoms of bladder dysfunction (associated with underlying small bladder capacity, overactive bladder, or dysfunctional voiding) include urinary frequency, urgency, and urge incontinence. Incontinence in such patients may present with daytime or nocturnal enuresis. Constipation is a commonly associated symptom in patients with bladder dysfunction. The adolescent girl in this vignette has no symptoms of voiding dysfunction. Examination of the spine is vital in any patient presenting with abnormal voiding patterns. Skin abnormalities of the spine such as tufts of hair, vascular lesions (hemangioma), or discoloration of the overlying skin are suggestive of an underlying vertebral or spinal lesion. Very low sacral lesions associated with normal lower extremity function are also associated with bladder dysfunction because bladder control is below the level for lower extremity function in the spinal cord. Bladder function is evaluated with renal and bladder ultrasonography, voiding cystourethrogram, and urodynamic studies to determine intravesical pressures and the volume of urine during filling, storage, and voiding.

Nephrolithiasis presents with varying degrees of flank pain or discomfort; severe colicky pain radiating to the flank is more commonly seen with large and or obstructing calculi. Such patients may have dysuria with associated infection or hypercalciuria. 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.

PREP Pearls
- Bright red hematuria is usually indicative of lower urinary tract bleeding. Glomerular hematuria (as in nephritis) is usually described as cola-, tea-, or brown-colored.
- Presence of blood clots with dysuria, fever, and suprapubic tenderness indicates underlying cystitis.
- One of the most important risk factors for the development of acute cystitis, especially in female individuals, is sexual intercourse.

ABP Content Specifications(s)
- Plan the appropriate clinical evaluation of cystitis
- Plan the appropriate initial and long-term management of cystitis
- Recognize the clinical and laboratory findings associated with cystitis

Suggested Readings
- Azzarone G, Liewehr S, Connor K. Cystitis. *Pediatr Rev.* 2007;28(12):474–476. doi: http://dx.doi.org/10.1542/pir.28-12-474.
- Reidy KJ, Del Rio MD. Hematuria. In: McInerny TK, Adam HM, Campbell DE, Kamat DM, Kelleher KJ, eds. *American Academy of Pediatrics Textbook of Pediatric Care*. Elk Grove Village, IL: American Academy of Pediatrics; 2009:1566–1570.

Question 204

A 26-month-old boy is brought to the emergency department by emergency medical services (EMS) after a seizure at home. His mother reports that he had a temperature of 37.7°C that morning and was fussy. He had been sitting on the couch watching television when his mother heard a sudden cry and found him having convulsions. His face was white and his lips were blue. This event lasted about 2 minutes and then stopped spontaneously. The mother called 911 and when EMS arrived, he was slightly arousable, with a glucose level of 98 mg/dL (5.4 mmol/L). He was transported to the emergency department, where his vital signs included a temperature of 39.4°C, heart rate of 130 beats/min, and respiratory rate of 28 breaths/min. He is sleeping, but arouses during your physical examination. His right tympanic membrane is bulging, red, and opacified with decreased mobility. The remainder of his examination findings are normal. By the end of the emergency department visit, he is awake and eating a popsicle. His mother reports no chronic medical problems or developmental concerns, and there is no family history of seizures.

Of the following, the next BEST step in the boy's evaluation and management is to

  A. admit the boy to the hospital for observation
  B. advise the parents there is a 30% risk of recurrence of this kind of seizure
  C. advise the parents that the boy has a 10% risk of developing epilepsy
  D. obtain serum electrolyte and calcium level measurements
  E. perform outpatient electroencephalography

Correct Answer: B

The boy in the vignette had a simple febrile seizure and was found to have acute otitis media. He is recovering as expected. In this clinical setting, no further diagnostic testing is needed. The recurrence risk after a first simple febrile seizure in children older than 12 months of age is approximately 30%. The risk of developing epilepsy in children with simple febrile seizures is approximately 2%.

Simple febrile seizures occur in children from 6 to 60 months of age in the setting of a temperature greater than or equal to 38°C. The seizure is a generalized tonic-clonic seizure lasting less than 15 minutes and does not recur within 24 hours. Simple febrile seizures can be diagnosed clinically in children with typical growth and development who do not have epilepsy. Evaluation in the acute setting should be directed at finding the source of the fever.
For the boy in the vignette, who was found to have acute otitis media, laboratory studies, electroencephalography, and brain imaging are not needed. As long as he is recovering as expected, he does not require admission for observation.

A complex febrile seizure has the same clinical characteristics as a simple febrile seizure except that the seizure lasts longer than 15 minutes, recurs within 24 hours, or has a focal onset. Further evaluation with electroencephalography or brain imaging is often done for complex febrile seizures, especially if the seizure has a focal onset. Children with epilepsy can have seizures triggered by fever, but for those who already have a diagnosis of epilepsy, these seizures are not referred to as febrile seizures.

PREP Pearls
- After a first simple febrile seizure in children older than 12 months, the recurrence risk is approximately 30%.
- The risk of developing epilepsy in children with simple febrile seizures is approximately 2%.
- Simple febrile seizures can be diagnosed clinically in children with typical growth and development who do not have epilepsy.
- In the case of a simple febrile seizure, diagnostic testing should be performed only if needed to identify the underlying source of the fever.

ABP Content Specifications(s)
- Plan the appropriate evaluation and management of a febrile seizure

Suggested Readings
- Mikati MA, Hani AJ. Seizures in childhood. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Elsevier; 2016:2823–2857.
- Subcommittee on Febrile Seizures. Febrile seizures: guideline for the neurodiagnostic evaluation of the child with a simple febrile seizure. *Pediatrics*. 2011;127(2):389–394. doi: http://dx.doi.org/10.1542/peds.2010-3318.

Question 205

A 3-year-old girl is brought to the emergency department for a 2-day history of fever, nausea, vomiting, and diarrhea. She has been unable to keep any fluids down for the past 24 hours and has decreased urine output. She appears ill with sunken eyes and decreased skin turgor. Her heart rate is 130 beats/min, respiratory rate is 28 breaths/min, and blood pressure is 85/55 mm Hg. She has tachycardia without murmur, clear breath sounds, and a soft, nontender abdomen with hyperactive bowel sounds and no masses. The resident seeing her would like to give her an intravenous fluid infusion and an antiemetic, ondansetron, and asks you to review the mechanism of action of this medication.

Of the following, the mechanism of action is BEST described as a receptor antagonist of

  A. 5-hydroxytryptamine
  B. cannabinoids
  C. dopamine
  D. H1
  E. muscarinic

Correct Answer: A

Ondansetron is a 5-hydroxytryptamine (5-HT3, serotonin) receptor antagonist. Although the mechanism of action is not completely understood, it is known that 5-HT3 receptors are present in the vagal nerve and, more importantly, in the chemoreceptor trigger zone of the area postrema. Thus, ondansetron may work peripherally or centrally.

Vomiting can be a defense against a gastrointestinal pathogen or an associated symptom of a systemic illness. The differential diagnosis of vomiting is extensive and reviewed in **Item C205** . Many factors may induce vomiting, including stimulation of vagal nerves in the gastrointestinal tract, stimulation of H_1 and M receptors in the area postrema of the chemoreceptor trigger zone, stimulation of the vestibular nuclei in response to motion, and stimulation of cerebral cortex.

Item C205. Differential Diagnosis of Vomiting.

System	Differential diagnosis
Cardiac	Congestive heart failure
	Vascular ring
Infectious	Acute viral gastroenteritis
	Hepatitis
	Meningitis
	Otitis media
	Pneumonia
	Sepsis
	Urinary tract infection
Gastrointestinal	Allergy
	Celiac disease
	Cyclic vomiting
	Cholecystitis/choledocholithiasis
	Eosinophilic gastrointestinal disease
	Food protein-induced enterocolitis syndrome
	Gastritis
	Gastroparesis
	Gastroesophageal reflux disease
	Infection: bacterial, viral, parasitic
	Inflammatory bowel disease
	Malrotation
	Pancreatitis
	Pyloric stenosis
	Regurgitation
	Toxic/medication ingestions
Neurologic	Brain tumor
	Chiari syndrome
	Concussion
	Hydrocephalus
	Migraines
	Pseudotumor cerebri
	Seizure
	Subdural hemorrhage
Metabolic/Endocrine	Amino and organic acidemia
	Congenital adrenal hyperplasia
	Diabetes mellitus
	Galactosemia
	Hereditary fructose intolerance
	Urea cycle defects
Renal	Obstructive uropathy
	Renal insufficiency
	Pyelonephritis
	Renal tubular acidosis
Psychiatric	Eating disorder
	Medical child abuse
	Rumination
	Self-induced

Courtesy of C. Waasdorp Hurtado

Antiemetic medications work by a variety of mechanisms. Ondansetron is a 5-HT3 receptor antagonist. Promethazine (antihistamine) is an H_1-antagonist and has limited dopaminergic (D_2) effects, resulting in antiemetic effects with sedative properties. It also has anticholinergic effects. Hyoscine (antimuscarinic) is a muscarinic M_1 receptor antagonist used to treat motion sickness. Metoclopramide is a dopamine receptor antagonist (D_2) that inhibits stimulation of the chemoreceptor trigger zone. It also has some 5-HT3 receptor antagonist effects. Metoclopramide has significant promotility effects and can increase gastric emptying; it's main role is to prevent vomiting secondary to medications and operations. Cannabinoids are increasingly used, however their mechanisms of action and efficacy are unknown. They are thought to act by inhibition of cortical activity and some inhibition of 5-HT3 receptors.

PREP Pearls
- Ondansetron is a 5-hydroxytryptamine (serotonin) receptor antagonist.
- Promethazine (antihistamine) is an H_1-antagonist and has limited dopaminergic (D_2) effects.
- Hyoscine (antimuscarinic) is a muscarinic M_1 receptor antagonist.
- Metoclopramide is a dopamine receptor antagonist (D_2) that inhibits stimulation of the chemoreceptor trigger zone.
- The differential diagnosis for vomiting is broad.

ABP Content Specifications(s)
- Understand the role of serotonin receptor antagonists in the prevention and treatment of vomiting
- Recognize the role of vomiting in the clinical presentation of acute gastroenteritis
- Recognize the association of vomiting with a systemic illness

Suggested Readings
- Navari RM, Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. *N Engl J Med.* 2016;374(14):1356–1367. doi: http://dx.doi.org/10.1056/NEJMra1515442.
- Parashette KR, Croffie J. Vomiting. *Pediatr Rev.* 2013;34(7):307–321. doi: http://dx.doi.org/10.1542/pir.34-7-307.
- Phillips RS, Friend AJ, Gibson F, et al. Antiemetic medication for prevention and treatment of chemotherapy-induced nausea and vomiting in childhood. *Cochrane Database Syst Rev.* 2016;2:CD007786. doi: http://dx.doi.org/10.1002/14651858.CD007786.pub3.

Question 206

You are seeing a 7-year-old girl in your office who is brought in for "pink eye." She has had a fever for 2 days, with temperatures of up to 38.8°C, cloudy rhinorrhea, mild cough, and headache. Today she developed left eye redness with watery drainage. She denies any trauma to her eye. On physical examination, you find a mildly ill appearing, febrile child. She has pharyngeal redness with scant exudates, a palpable left preauricular lymph node, and edematous nasal mucosa. Her left eye conjunctiva is hyperemic and there is profuse tearing. On close inspection, tiny follicles are present on the inner lower lid. No foreign body is seen. The remainder of the examination findings are within normal parameters.

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

  A. ciprofloxacin drops to the eye
  B. intravenous immunoglobulin
  C. oral prednisone
  D. symptomatic treatment
  E. trifluridine drops to the eye

Correct Answer: D

The girl in the vignette has signs and symptoms of pharyngoconjunctival fever, a common syndrome caused by adenovirus types 3, 4, 5, or 7. This syndrome typically occurs in young children and presents with fever, pharyngitis, cervical and preauricular lymphadenopathy, and follicular conjunctivitis (**Item C206A**). Transmission may occur through water (eg, swimming pools) which may lead to community outbreaks. This self-limited condition typically resolves within 10 days without treatment. The appropriate management for this child is symptomatic care including cool compresses to the eyes, lubrication, analgesics, rest, and fluids. Antibiotic ophthalmic drops would not be an appropriate treatment.
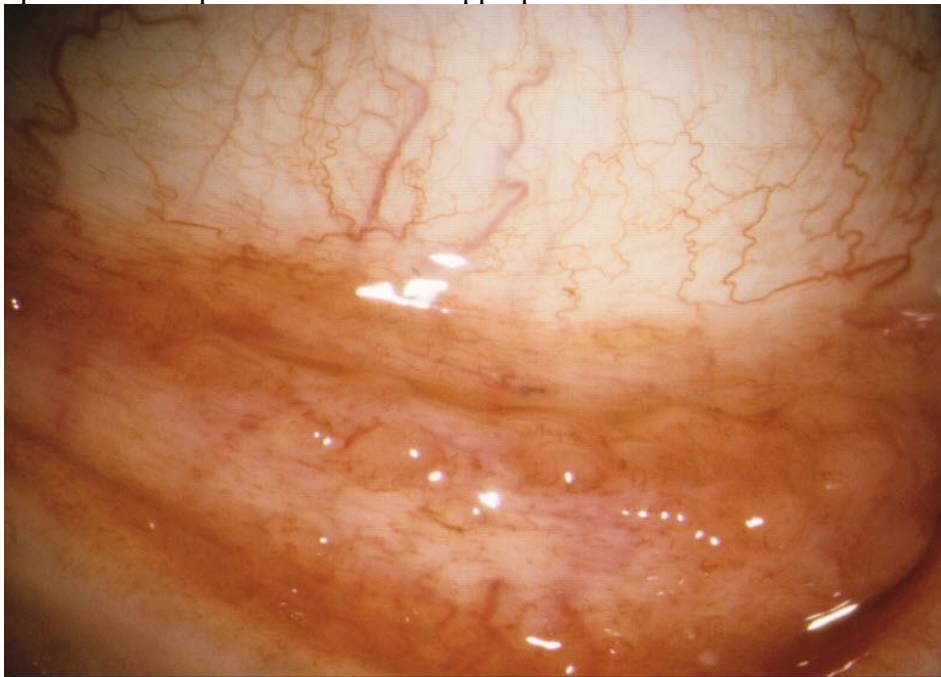
Item C206A: Follicular conjunctivitis.
Reprinted with permission from Richards A, Guzman-Cottrill JA. Conjunctivitis. *Pediatr Rev*. 2010;31:197.

Conjunctivitis is common among pediatric patients, and may be infectious, allergic, chemical, or mechanical in nature (**Item C206B**). Most cases in otherwise healthy children are infectious, with more than half caused by bacteria. Typical organisms seen include nontypeable *Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis, and Staphylococcus aureus*. Studies indicate that the presence of mucopurulent discharge and/or a history of glued/matted eyelids is suggestive of bacterial etiology. Children with bacterial conjunctivitis do not usually complain of itching or foreign body sensation. Although most cases of bacterial conjunctivitis are self-limited, and will resolve without treatment within 8 days, topical antibiotics hasten resolution and decrease transmission. Either topical fluoroquinolone or polymyxin B-trimethoprim are appropriate antibiotic choices, and have equivalent efficacy.

Item C206B. Differential Diagnosis for Red Eye.

- Infectious conjunctivitis (bacterial, viral, parasitic)
- Allergic or vernal (seasonal) conjunctivitis
- Drug, toxin, or chemical exposure
- Trichiasis (inward turning of eyelashes irritating the eye)
- Nasolacrimal duct obstruction
- Congenital glaucoma
- Preseptal or orbital cellulitis
- Blepharitis (inflammation of the eyelids, especially the margins)
- Iritis/uveitis
- Episcleritis or scleritis
- Foreign body
- Trauma (corneal abrasion/infection, subconjunctival hemorrhage)

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By contrast, viral conjunctivitis is most often characterized by itchy red eyes with watery discharge and ipsilateral preauricular lymphadenopathy. Often, the child has a concurrent upper respiratory infection. On physical examination, follicles may be seen on the inferior palpebral conjunctiva. Adenovirus is the most common viral etiology. Picornaviruses (enterovirus, rhinovirus), Zika virus, and herpes simplex virus (HSV) can also cause conjunctivitis. Adenovirus 8, 19, and 37 cause epidemic keratoconjunctivitis, a highly contagious form of the condition, in which inflammation lasts 2 to 3 weeks and is often associated with subconjunctival hemorrhage and subepithelial corneal infiltrates. Treatment of viral conjunctivitis is symptomatic. If the symptoms are persistent, chronic, or associated with decreased visual acuity or severe photophobia, evaluation by an ophthalmologist is indicated.

Conjunctivitis may be part of a systemic syndrome, or require systemic treatment because of severity or associated pathology. Pharyngoconjunctival fever may at times be confused with Kawasaki disease. Treatment for Kawasaki disease includes intravenous immunoglobulin infusion and high-dose aspirin. In the past, and rarely now for resistant cases, systemic

corticosteroids have been used. The girl in the vignette does not meet the criteria for a diagnosis of Kawasaki disease, so neither of these treatments would be appropriate.

Parinaud oculoglandular syndrome is an uncommon systemic condition that includes unilateral granulomatous conjunctivitis with preauricular and submandibular lymphadenopathy. The most common causative organism is *Bartonella henselae,* which can also cause neuroretinitis in association with cat-scratch disease. Additional causes of Parinaud oculoglandular syndrome include *Chlamydia, Francisella, Mycobacterium tuberculosis, Sporothrix, Coccidioides, Actinomyces, and Treponema pallidum.*

Chlamydia, gonorrhea, and herpes simplex virus (HSV) can all cause conjunctivitis, and all require systemic treatment. Ophthalmia neonatorum occurs within the first 4 weeks after birth, and in the United States is most frequently associated with *Chlamydia trachomatis.* Chlamydial conjunctivitis presents at about 1 week of age with unilateral or bilateral purulent discharge. More than 50% of affected neonates have colonization or infection of the nasopharynx, genitalia, or lungs. The diagnosis should be confirmed with nucleic acid amplification testing (NAAT, such as polymerase chain reaction) and, if positive, the neonate should be treated orally with erythromycin or azithromycin. *Neisseria gonorrhoeae* ophthalmia neonatorum is much less frequent in the United States. Most infections are prevented with eye prophylaxis at birth. Infected neonates present with a markedly swollen eye with profuse purulent discharge. Diagnosis is confirmed with NAAT. Affected neonates should be admitted to the hospital for parenteral antibiotics, eye lavage, and ophthalmology evaluation. Untreated, *N gonorrhoeae* infection may penetrate the corneal epithelium, leading to permanent vision impairment. Conjunctivitis may also be the initial presentation of neonatal skin, eye, and mouth HSV. In this case, the neonate should be admitted to the hospital for antiviral therapy and investigation for disseminated or central nervous system involvement.

In older children and adolescents, some sexually (and occasionally nonsexually) transmitted infections can lead to conjunctivitis requiring systemic treatment. Because of the risk of corneal perforation, *N gonorrhoeae or N meningitidis* conjunctivitis should be treated with parenteral antibiotics, whereas sexually transmitted chlamydial conjunctivitis requires oral antibiotic treatment. Suspected HSV eye infections should be evaluated by ophthalmology because of the high risk of corneal involvement. HSV treatment is usually with the topical antiviral trifluridine in combination with topical corticosteroid. Corticosteroids should never be used as single drug therapy for HSV, because they may worsen the infection when used alone. The patient in the vignette does not have the typical vesicular eruption seen with HSV, therefore, trifluridine is not a recommended treatment.

PREP Pearls

- Findings that characterize bacterial conjunctivitis include the presence of mucopurulent discharge, glued/matted eyelids, and absence of itching or foreign body sensation.
- Adenovirus is the most common cause of viral conjunctivitis. It is characterized by itchy red eyes with watery discharge, preauricular lymphadenopathy, and follicles in the lower lid conjunctiva.
- Some forms of conjunctivitis require systemic treatment including ophthalmia neonatorum, and conjunctivitis caused by herpes simplex virus, Chlamydia *trachomatis,* or *Neisseria gonorrhoeae.*

MOCA-Peds Objective

- Evaluate and manage a patient with eye redness

ABP Content Specifications(s)

- Recognize the clinical findings associated with conjunctivitis in patients of various ages
- Recognize the association between conjunctivitis and systemic disease

Suggested Readings

- Bhumbra N, Wroblewski ME. Adenovirus. *Pediatr Rev*. 2010;31:173–174. doi: http://dx.doi.org/10.1542/pir.31-4-173.
- Patel PB, Diaz MC, Bennett JE, Attia MW. Clinical features of bacterial conjunctivitis in children. *Acad Emerg Med.* 2007;14:1–5.
- Richards A, Guzman-Cottrill JA. Conjunctivitis. *Pediatr Rev*. 2010;31:196–207. doi: http://dx.doi.org/10.1542/pir.31-5-196 .
- Tarabishy AB, Jeng BH. Bacterial conjunctivitis: a review for internists. *Cleve Clin J Med.* 2008;75:507–512.

Question 207

You are called to see a 21-day-old neonate born at 28 weeks of gestation. She is lethargic, tachycardic, and apneic. She requires intubation to maintain adequate ventilation. She is found to have a hemoglobin of 5 g/dL (50 g/L). The medical team would like to give her a transfusion of packed red blood cells because of her severe, symptomatic anemia. Her parents are Jehovah's witnesses, therefore they refuse to sign a consent for red blood cell transfusion. The hospital liaison from their Jehovah's Witness Kingdom Hall is not available. Therefore, the medical team consults the hospital's institutional ethics committee.

Of the following, the ethical principle MOST likely to be illustrated through consultation with the institutional ethics committee in this case is

A. beneficence
B. capacity
C. justice
D. nonmaleficence
E. respect for autonomy

Correct Answer: A

Beneficence, or acting in the best interest of the patient, is the ethical principle most likely to be used by the ethics committee to justify ordering a blood transfusion for the neonate in this vignette. Beneficence refers to the choice that provides maximal benefit to the patient. Capacity describes the ability of patients to participate in medical decision making based on their comprehension of the potential risks, benefits, and alternatives to their choices. Because neonates and children do not have capacity, decision making for major decisions is dependent on the capacity of their parents or legal guardians. Children and adolescents should be allowed to participate in their medical care commensurate with their developmental abilities.

Justice requires that medical care be provided in a similar manner to all patients regardless of race, gender, class, or disability. For example, ensuring access to medical care with federally sponsored child health insurance is an attempt at justice in pediatric health care.

The ethical principle of nonmaleficence entails avoiding harm. Though there is potential risk with any medical decision, the benefit of any decision should outweigh possible harm. For example, in well-appearing children with trivial head injuries, the possible harm of ionizing radiation outweighs the benefits of computed tomography.

For those who have the capacity to make decisions, the principle of autonomy involves respecting the decisions made by an individual. Among adults with the mental capacity to make their own medical decisions, autonomy carries more weight than beneficence. Parents have the authority to make medical decisions for their children. However, parents do not have complete autonomy over their children, as illustrated in this vignette. Because this neonate will clearly benefit from a transfusion, in this case, parental authority is not as important as beneficence.

Clinicians should make every effort to work with families to find mutually acceptable decisions for the medical care of their children. In rare cases, when disagreements persist between families and the medical team, consultation with the institutional ethics committee may be helpful. Institutional ethics teams may facilitate communication and provide a framework for discussing ethical issues. This approach is not without controversy. Although most children's hospitals have pediatric ethics teams, critics have argued that they lack uniform guidelines and may introduce bias in their discussions with families.

PREP Pearls

- Parents do not have complete autonomy over their children. In cases in which there is clear benefit to the child, beneficence may override parental autonomy.
- Because pediatric patients lack complete autonomy and capacity, they are dependent on their parents or guardians for major medical decisions.
- Institutional ethics committees may facilitate discussion and provide an ethical framework when medical care teams disagree with families.

MOCA-Peds Objective
- Recognize and apply ethical principles regarding religious or cultural exemptions for medical treatment

ABP Content Specifications(s)
- Recognize and apply ethical principles regarding institutional ethics committees

Suggested Readings
- Cummings CL, Mercurio MR. Ethics for the pediatrician: autonomy, beneficence, and rights. *Pediatr Revi* 2010;31:252. doi: http://dx.doi.org/10.1542/pir.31-6-252.
- Myers D, Lantos J. The slow, steady development of pediatric ethics committees, 1975-2013. *Pediatr Revi* 2014;35:e15. doi: http://dx.doi.org/10.1542/pir.35-3-e15.

Question 208

A 15-year-old girl is brought to your office for a sports preparticipation physical examination. The girl participates in cheerleading in the fall and soccer in the spring. Her parents express concern about her risk of concussion; they have seen numerous media reports about the negative effects of repeated concussions in professional athletes. At age 2 years, the girl had a computed tomography (CT) scan of the brain after she fell down a flight of stairs. She sustained a documented concussion at age 12 years during physical education class.

Of the following, the MOST accurate statement regarding this girl's concussion risk is that

A. her risk of concussion during soccer is lower than that of a male soccer player
B. her risk of concussion is greater during soccer than during cheerleading
C. she should stop playing contact sports if she sustains another concussion
D. the concussion rate is higher during practice than during competition
E. using headgear during soccer will reduce her risk of concussion

Correct Answer: B

The girl in the vignette participates in soccer and cheerleading. A large study demonstrated that among high school sports, concussion rates were the highest in football, boys' hockey, boys' lacrosse, and girls' soccer. The rate of concussions is over twice as high in girls' soccer as in cheerleading.

Sports concussion has been an increasingly common diagnosis over the past 2 decades, and now represents about 10% of high school sports injuries. The incidence of concussion has risen with increasing awareness of this entity and since the criteria for sports-related concussion diagnosis became less strict, with loss-of-consciousness no longer required. In addition, child and adolescent participation in contact and collision sports has increased, particularly among girls. Although sports participation conveys many health benefits, the number of injuries has risen with increasing sports involvement.

The rate of concussion is higher during sports competition than during practice. However, because athletes typically spend more time practicing than in competition, the absolute number of concussions is often higher in the practice setting. For most high school sports offered for both girls and boys, girls have a higher rate of sports concussion. An exception to this is boys' lacrosse, which has a higher concussion rate but also has different rules governing player contact than does girls' lacrosse.

Implementation of rules that limit player-to-player contact during practice and competition appears to be a successful strategy for reducing sports concussion. Protective headgear, mouthguards, and helmets with increased padding have not proven effective in preventing concussions.

The girl in the vignette has a history of 1 prior sports concussion and a head injury as a young child. There are no absolute rules about how many mild closed head injuries can occur before a physician should withhold contact sports clearance. An increasing frequency of concussions, injuries that occur with seemingly low forces, and long symptom duration following concussions are concerning features that should lead physicians to consider recommending retirement from sports with high contact risk.

PREP Pearls

- Among high school sports injuries, concussion rates are highest in football, boys' hockey, boys' lacrosse, and girls' soccer.
- For most high school sports offered for both girls and boys, girls have a higher rate of sports concussion than boys.
- An increasing frequency of concussions, injuries that occur with seemingly low forces, and long symptom duration following concussions are concerning features that should lead physicians to consider recommending retirement from sports with high contact risk.

ABP Content Specifications(s)
- Identify the sports in which a head injury most commonly occurs

Suggested Readings
- Marar M, McIlvain NM, Fields SK, Comstock RD. Epidemiology of concussions among United States high school athletes in 20 sports. *Am J Sports Med.* 2012;40(4):747–755. doi: http://dx.doi.org/10.1177/0363546511435626.
- McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med.* 2013;47(5):250–258. doi: http://dx.doi.org/10.1136/bjsports-2013-092313.
- Schneider DK, Grandhi RK, Bansal P, et al. Current state of concussion prevention strategies: a systematic review and meta-analysis of prospective, controlled studies. *Br J Sports Med.* doi: http://dx.doi.org/10.1136/bjsports-2015-095645.

Question 209

A 7-day-old neonate has been hospitalized since birth. He was born at 39 weeks' gestation without complications. One day after birth, he developed temperature instability. He was admitted to the neonatal intensive care unit, where he was diagnosed with meningitis due to Citrobacter koseri and was treated appropriately with antibiotics. Today, he had a 4-minute long episode of facial twitching and rhythmic arm jerking. His physical examination findings are within normal parameters.

Of the following, the test or procedure MOST likely to yield the underlying diagnosis is

  A. electroencephalography
  B. human leukocyte antigen (HLA) haplotype
  C. magnetic resonance imaging of the brain
  D. occipital frontal circumference measurement
  E. serum electrolytes

Correct Answer: C

The neonate in the vignette, who has *Citrobacter koseri* meningitis and had a seizure 6 days after starting appropriate antibiotic therapy, most likely has a brain abscess. Magnetic resonance imaging (MRI) of the brain, with and without contrast, is the best test to yield the underlying diagnosis. In neonates with meningitis, persistent fever or new focal neurologic symptoms, such as seizure, occurring more than 3 days after starting antibiotics should raise suspicion for a new neurologic process. Certain bacteria, such as *Citrobacter species* including *C koseri, Serratia marcescens, Proteus mirabilis, and Cronobacter sakazakii* are particularly associated with brain abscesses. Thus, the clinical picture for the neonate in the vignette with a focal seizure 6 days after starting antibiotics, is particularly concerning for brain abscess.

Electroencephalography may show focal findings that suggest an underlying brain lesion, but MRI of the brain is a better test to diagnose an abscess. HLA haplotype would not be helpful in diagnosing an abscess. Although occipital frontal head circumference measurement should be monitored in neonates with meningitis, in the setting of an excessive increase suggesting a new abnormality such as abscess, empyema, or hydrocephalus, brain imaging is the best test to determine the specific diagnosis. Although serum electrolyte abnormalities can cause focal seizures, for the infant in the vignette, brain abscess is more likely and brain imaging is the test most likely to yield this diagnosis.

PREP Pearls
- In a neonate with meningitis who has been receiving appropriate antibiotic therapy for 3 days or more, persistent fever, or new focal neurologic findings including seizure, is suggestive of a new neurologic process.
- Certain bacteria such as *Citrobacter species* including *C koseri*, *Serratia marcescen*s, *Proteus mirabilis*, and *Cronobacter sakazakii* are particularly associated with brain abscesses.

ABP Content Specifications(s)
- Understand the risk factors associated with a brain abscess

Suggested Readings
- Kim KS. Neonatal bacterial meningitis. *NeoReviews*. 2015;16(9):e535–e543. doi: http://dx.doi.org/10.1542/neo.16-9-e535.
- Swanson D. Meningitis. *Pediatr Rev*. 2015;36(12):514-526. http://pedsinreview.aappublications.org/content/36/12/514.

Question 210

A 14-year-old adolescent boy is brought to the emergency department by his parents for evaluation of a painful red eye. While woodworking 2 hours earlier, he sensed something fly into his right eye. He applied saline eye drops and experienced some improvement in his discomfort, but the eye has become increasingly red and more painful since the episode. He is reluctant to open the right eye because of the pain. He reports photophobia and exhibits increased tearing. There is no other evident discharge and no trauma to the eyelid.

Of the following, the MOST important initial step in evaluation is to

A. assess visual acuity
B. conduct a fluorescein examination
C. evert the eyelid to look for foreign body
D. examine the pupil and anterior chamber
E. instill a topical anesthetic

Correct Answer: D

The most important initial step in the clinical evaluation of the boy in this vignette is to exclude penetrating trauma as a cause for his painful red eye. The history of sudden onset of worsening pain and erythema, photophobia, and tearing in the setting of woodworking should prompt the medical provider to be highly suspicious for penetrating trauma of the eye, even when no obvious external damage is seen. Therefore, careful examination of the pupil and anterior chamber must be performed first.

A stepwise approach to the full examination of a painful and erythematous eye is recommended:

1. Examine the pupil and anterior chamber. While avoiding pressure on the globe, the lids can be lifted or gently separated. The pupil should appear round and centralized; the anterior chamber should be clear, deep, and normally contoured. Reactive miosis is often evident in cases of corneal abrasion. A large nonreactive pupil, an irregularly shaped pupil, or hyphema warrant prompt ophthalmologic consultation. Any patient with corneal opacification or pus in the anterior chamber should be evaluated by an ophthalmologist the same day.
2. Assess visual acuity. Ophthalmologic consultation is warranted if the visual acuity is significantly affected.
3. Instill topical anesthetic. After penlight examination reveals no evidence of penetrating trauma and visual acuity is measured, topical anesthetic may be instilled to relieve discomfort and facilitate the remainder of the examination. However, animal studies suggest that topical anesthetics may be toxic to the epithelium and potentially retard healing and lead to increased scarring. When possible, it may be best to perform the examination without anesthesia.
4. Perform fundoscopic examination and assess eye motility. Confirmation of the presence of symmetric red reflexes and a full range of motion is a necessity, even if full visualization of the fundus is difficult to obtain. Abnormalities revealed by the examination warrant ophthalmologic consultation.
5. Perform fluorescein examination. If the working diagnosis based on the history and physical examination findings is corneal abrasion, then the instillation of fluorescein dye and visualization with cobalt blue light will confirm the diagnosis. Earlier instillation of the dye may interfere with previous steps.
6. Evert the eyelid. The clinician should evert the upper lid to look for a retained foreign body in cases of corneal abrasion noted on examination or with ongoing reports of a foreign body sensation or discomfort with blinking.

PREP Pearls
- A stepwise approach to the full examination of a painful and erythematous eye is recommended.
- The initial step in evaluation is careful examination of the pupil and anterior chamber to exclude penetrating trauma.
- Next steps include: (1) assess visual acuity; (2) instill topical anesthetic if necessary; (3) perform fundoscopic examination and assess eye motility; (4) perform fluorescein examination; and (5) evert the eyelid.

MOCA-Peds Objective
- Evaluate and manage a patient with eye redness

ABP Content Specifications(s)
- Plan the appropriate clinical evaluation of a painful erythematous eye

Suggested Readings
- Browner EA. Corneal abrasions. *Pediatr Rev.* 2012;33(6):285–286. doi: http://dx.doi.org/10.1542/pir.33-6-285.
- Calhoun JH. Consultation with the specialist: eye examinations in infants and children. *Pediatr Rev.* 1997;18(1):28–31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4274336/.
- 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 211

You are seeing a 14-year-old boy for a preparticipation physical examination before the start of the school soccer season. He has a history of type 1 diabetes, diagnosed at age 11 years, with no known complications. His insulin regimen consists of insulin glargine 26 units at bedtime, and prandial aspart 1 unit for every 10 g of carbohydrate plus 1 unit for every 40 mg/dL (2.2 mmol/L) increase in his premeal blood glucose level above 120 mg/dL (6.6 mmol/L). His most recent hemoglobin A1c is 11%. A review of his glucometer data shows an average of 1 to 2 blood glucose checks per day, which range from 50 to 490 mg/dL (2.7–27.2 mmol/L). He states that he often forgets to take insulin because of his busy schedule, and when he does remember, he often takes his insulin after he eats. His physical examination findings are normal. His weight is 50 kg.

Of the following, the action MOST likely to help this adolescent achieve better glycemic control is to

A. counsel him on the long-term consequences of poor diabetes control
B. increase his glargine dose to 28 units at bedtime with follow-up in 1 week
C. instruct him to check and record at least 4 glucose levels per day with follow-up in 1 week
D. refer him to a nutritionist for instruction regarding low-carbohydrate snacks
E. switch his insulin administration to an insulin pump

Correct Answer: C

The adolescent described in the vignette has uncontrolled type 1 diabetes and is not effectively integrating diabetes self-care into his daily routine. He checks his blood glucose only 1 to 2 times per day, often omits insulin doses, and frequently takes insulin after meals. These habits are not conducive to good glycemic control. The action most likely to help him achieve better glycemic control is to instruct him to check and record at least 4 glucose levels per day, and conduct a follow-up review of his glucose log in 1 week. Studies have shown a direct correlation between frequency of blood glucose monitoring and better glycemic control. Checking blood glucose more frequently will help him establish a better diabetes self-care routine, and allow for more opportunities to respond to blood glucose levels that are not in the goal range. Follow-up review of his glucose log will help his physician determine if insulin dose changes are needed or if he needs other assistance with diabetes management. It also provides the opportunity to further educate the boy on interpreting his blood glucose patterns.

For those on multiple-dose insulin regimens, as is this boy, the American Diabetes Association (ADA) recommends blood glucose measurement before meals and snacks, at bedtime, before exercise, for suspected hypoglycemia, and before driving. Prandial insulin should be taken before meals to best match the onset of insulin action with rising blood glucose.

The ADA-recommended hemoglobin A1c goal is less than 7.5% for all pediatric age groups. Achieving good glycemic control is important in preventing long-term complications. These complications include macrovascular and microvascular disease, manifested as nephropathy, retinopathy, and neuropathy. Although the boy in the vignette needs to understand the importance of good glycemic control, research shows that behavior change is unlikely in response to solely counseling him on the long-term consequences of poor diabetes control.

The boy may require adjustments in his insulin regimen, but at this office visit, not enough good-quality glucose data are available to make an informed adjustment. Thus, increasing his glargine dose to 28 units at bedtime is not the best action to take. Similarly, switching his insulin administration to an insulin pump would change the insulin delivery mechanism, but would not address the need to integrate basic diabetes self-care into the boy's daily routine.

Carbohydrate counting, avoiding simple sugars, and eating a well-balanced diet are also important contributors to good glycemic control. Although eating low- or non-carbohydrate snacks can obviate the need for an insulin injection to cover the snack, referring the boy in the vignette to a nutritionist for instruction on low-carbohydrate snacks is of lower priority than the need for more frequent glucose monitoring.

PREP Pearls
- In those with diabetes, achieving good glycemic control is important in preventing long-term complications, including nephropathy, retinopathy, neuropathy, and macrovascular disease.
- The American Diabetes Association recommends a hemoglobin A1c goal of <7.5% for all pediatric age-groups.
- In children with type 1 diabetes there is a direct correlation between the frequency of blood glucose monitoring and better glycemic control.

ABP Content Specifications(s)
- Counsel patients regarding self-management of type 1 diabetes
- Plan the appropriate management of type 1 diabetes to effectively achieve good control and to avoid long-term complications

Suggested Readings
- American Diabetes Association. Standards of medical care in diabetes: 12, children and adolescents. *Diabetes Care.* 2017;40(suppl 1):S105-S113.
- American Diabetes Association. Standards of medical care in diabetes: 6, glycemic targets. *Diabetes Care.* 2017;40(suppl 1):S48-S56.
- Gregory JM, Moore DJ, Simmons JH. Type 1 diabetes mellitus. *Pediatr Rev.* 2013;34(5):203–215. doi: http://dx.doi.org/10.1542/pir.34-5-203.

Question 212

You are seeing a 16-year-old girl in the emergency department. She was referred by her primary care provider for concerns of dehydration. Her father reports that the girl has had poor oral intake for the last 3 months, over which time she has lost 16 kg. During an interview with the girl alone, she discloses that she was very upset about her weight and placed herself on a 500 kcal/day diet 3 months ago. The girl reports that she often feels fat and bloated. She uses an over-the-counter diuretic 3 or 4 times per day. On physical examination, the girl's body mass index is at the second percentile for age. Her heart rate is 49 beats/min and her blood pressure is 90/55 mm Hg. She has lanugo hair on her chest and marked diffuse muscle wasting.

Of the following, a diagnostic criterion for this patient's suspected condition is

 A. amenorrhea
 B. excessive exercise
 C. intense fear of gaining weight
 D. self-induced vomiting
 E. use of medication to prevent weight gain

Correct Answer: C

The girl described in this vignette has anorexia nervosa (AN). Diagnostic criteria for AN, as defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-V include:
1. Restriction of energy intake resulting in significantly low body weight
2. Intense fear of gaining weight
3. Severe body image distortion with denial of the seriousness of the illness

Amenorrhea was removed as a criterion for diagnosis in the DSM-5. There are 2 subtypes of AN: restrictive, marked by severe restriction of caloric intake, and binge-eating/purging, characterized by caloric restriction along with regular binge-eating episodes or purging behaviors such as self-induced vomiting and/or diuretic use.

The prevalence of AN in the United States has been reported to be between 1% and 2% of females of all ages, and approximately 0.5% among adolescent girls. The prevalence and incidence of AN has been increasing. While the etiology of AN is unclear, it is likely multifactorial. There are biological, psychological, environmental/cultural, and sociological risk factors. Recent studies of physiology, genetics, epigenetics, and brain imaging suggest that AN may be due to an abnormality of reward pathways or an attempt to preserve mental homeostasis.

The differential diagnosis for AN includes medical conditions that may cause weight loss such as thyroid disease, inflammatory bowel disease, and chronic infection. However, many of these conditions can be excluded with a thorough history and physical examination.

Medical complications of AN include dehydration, electrolyte disturbance, menstrual irregularities, impaired gastric motility, dysrhythmias, cardiomyopathy, and cognitive deficits. Collaborative interdisciplinary and interprofessional care is necessary for the management of AN and includes medical stabilization, nutritional rehabilitation, and psychotherapy.

PREP Pearls
- Diagnostic criteria for anorexia nervosa (AN) include:
    1. Restriction of energy intake resulting in significantly low body weight
    2. Intense fear of gaining weight
    3. Severe body image distortion with denial of the seriousness of the illness
- Amenorrhea is no longer a criterion for the diagnosis of AN.

ABP Content Specifications(s)
- Recognize the clinical findings associated with anorexia nervosa and the criteria for diagnosis
- Recognize the clinical findings associated with bulimia and the criteria for diagnosis
- Plan the appropriate management of bulimia
- Plan the appropriate management of anorexia nervosa

Suggested Readings

- Gorwood P, Blanchet-Collet C, Chartrel N, et al. New insights in anorexia nervosa. *Front Neurosci.* 2016;10:256. doi: http://dx.doi.org/10.3389/fnins.2016.00256.
- Lock J, La Via MC; American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of children and adolescents with eating disorders. *J Am Acad Child Adolesc Psychiatry.* 2015;54(5):412–425. doi: http://dx.doi.org/10.1016/j.jaac.2015.01.018.
- Rosen DS; Committee on Adolescence. Clinical report: identification and management of eating disorders in children and adolescents. *Pediatrics*. 2010;126(6):1240–1253. doi: http://dx.doi.org/10.1542/peds.2010-2821.

Question 213

You are seeing a 30-month-old previously healthy, fully immunized girl in the urgent care center (UCC) for intermittent tactile fevers over the last 36 hours. Her mother states that her daughter has had less energy overall and is more irritable than usual, but she is playful for brief periods after receiving antipyretics. She has a decreased appetite, but is taking fluids normally. She has had a normal number of wet diapers. She has not had cough, rhinorrhea, vomiting, diarrhea, or rash, and does not seem to be in pain. In the UCC, her temperature is 39.5°C, heart rate is 90 beats/min, and respiratory rate is 25 breaths/min. She received ibuprofen shortly after arrival. When examined 30 minutes later, she is comfortable in her mother's lap and quietly playing with stickers and a stuffed toy. Her physical examination findings are within normal parameters.

Of the following, the MOST appropriate next step in this girl's evaluation is to order

 A. a complete blood cell count with differential; blood culture; and urinalysis and urine culture obtained by bladder catheterization
 B. a urinalysis and urine culture obtained by catheterization
 C. a urinalysis obtained using a sterile urine collection bag
 D. chest radiography
 E. no diagnostic tests at this time

Correct Answer: E

The most appropriate next step in evaluating the girl in the vignette is to order no diagnostic tests at this time, and to provide supportive care. Approximately one-third of pediatric office visits involve evaluation for fever. Self-limited viral infections and bacterial infections with localizing symptoms or physical examination findings account for the vast majority of these cases. Fever without localizing signs in well-appearing children, as seen in the girl in the vignette, is particularly challenging. Considerable effort has been expended to investigate the optimal diagnostic approach to identify which of those children has a serious bacterial illness (eg, occult bacteremia or urinary tract infection) requiring urgent treatment.

The implementation of routine vaccination against *Haemophilus influenzae* type B and pneumococcus has changed the approach to diagnosis and management of children with fever without localizing signs. Well-appearing children 6 to 36 months of age who are immunized with at least the 3-vaccine primary series for *H influenzae* and either PCV7 or PCV13 are at particularly low risk for occult bacteremia (<1% likelihood), and no testing for bacteremia is needed.

For children 3 to 6 months of age and those who have received fewer than 3 HiB and/or 3 PCV7 or PCV13 vaccines, the risk of occult bacteremia is higher. For these children, a complete blood cell count with differential should be obtained, and if the white blood cell (WBC) count is higher than 15,000/µL (15×10^9/L), a blood specimen should be sent for culture. It is also reasonable to perform chest radiography in children with no history of respiratory symptoms if the WBC is greater than 20,000/µL (20×10^9/L) and a reliable respiratory examination cannot be performed to assess for pneumonia.

The most common bacterial cause for fever without localizing signs in children aged 3 to 36 months is a urinary tract infection (UTI). In children older than 24 months, signs and symptoms of a UTI can often be elicited (eg, dysuria, abdominal pain, incontinence). In addition, UTI is unlikely in uncircumcised boys older than 12 months of age and circumcised male infants older than 6 months of age who have not had a prior UTI. Therefore, in girls older than 24 months without symptoms of UTI, uncircumcised boys older than 12 months, and circumcised boys older than 6 months with fever for less than 48 hours, it is reasonable to defer testing for a UTI. In younger children, or if the child has been febrile for more than 48 hours, or if social factors preclude reliable follow-up, a urine sample obtained by sterile catheterization should be used for urinalysis and culture. If the result of urinalysis is abnormal, the child should be treated empirically with antibiotics pending culture results.

For neonates younger than 30 days of age with temperatures of 38.0°C or greater, the likelihood of a serious bacterial infection is around 10% to 15%, and a thorough evaluation for a cause should be performed. This includes cultures of blood, urine, and spinal fluid, as well as WBC counts with differential for blood and spinal fluid. A urinalysis should also be performed, but is less sensitive for detecting a UTI in this age group. Following specimen collection, empiric antibiotics should be administered intravenously or intramuscularly until cultures determine the presence or absence of a serious bacterial infection.

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Infants aged 30 to 90 days with temperatures of 100.4°F (38.0°C) or greater should be promptly evaluated as well; however, the likelihood of occult bacteremia in these patients is relatively low. Urine specimens obtained via sterile catheterization should be sent for urinalysis and culture to assess for UTI. Further diagnostic workup should be guided by a number of factors, including age and degree of fever. For infants aged 30 to 60 days, obtaining a complete blood cell count with differential should be strongly considered. If WBC count is less than 5,000/µL (5×10^9/L) or greater than 15,000/µL (15×10^9/L), blood and cerebrospinal fluid cultures should be performed, and empiric intravenous or intramuscular antibiotics should be administered. If the child appears well and the results of laboratory testing are not concerning, supportive care and close monitoring may be appropriate. Additional factors, such as a high degree of fever, incomplete immunization status, or recent antibiotic administration, may warrant more conservative treatment. Because serious bacterial infection (SBI) is uncommon in infants with enterovirus, respiratory syncytial virus, or influenza virus infections, some experts recommend performing a viral polymerase chain reaction test when assessing for risk of SBI, if the result can be obtained quickly.

PREP Pearls
- Occult bacteremia is now rare in immunized older infants and children (since the implementation of routine *Haemophilus influenzae* type b and pneumococcal vaccination), limiting the usefulness of a diagnostic workup.
- Infants younger than 90 days of age with a temperature greater than 38°C should be promptly evaluated.

ABP Content Specifications(s)
- Plan the appropriate evaluation and management of fever without source in patients of various ages
- Formulate a differential diagnosis of fever without localizing signs in patients of various ages

Suggested Readings
- Byington CL, Reynolds CC, Korgenski K, et al. Costs and infant outcomes after implementation of a care process model for febrile infants. *Pediatrics*. 2012;130(1):e16–24. doi: http://dx.doi.org/10.1542/peds.2012-0127.
- Cioffredi LA, Jhaveri R. Evaluation and management of febrile children: a review. *JAMA Pediatr.* 20161;170(8):794–800. doi: http://dx.doi.org/10.1001/jamapediatrics.2016.0596.
- 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/10.1542/peds.2011-1330.

Question 214

A 2-year-old girl presents to your office for evaluation 2 hours after she awoke from a nap, screaming in pain and holding her chest and anterior neck. Since the onset of these symptoms, the girl has had 2 episodes of bloody emesis. She has refused to swallow any of the water her mother has been encouraging her to drink.

The girl was born full-term and has been healthy, with normal growth and development. However, 6 days ago, she required admission to a local hospital after her family discovered that she had swallowed a button battery. The battery was endoscopically removed from the girl's esophagus within 2 hours of ingestion. She was observed in the hospital for 48 hours, with no apparent complications. She was discharged after she began drinking fluids without difficulty. Her mother reports that she had been doing very well at home since then, until she woke up from her nap this afternoon.

In your office, the girl is screaming loudly and clutching her chest and anterior neck. Her temperature is 37.9°C, heart rate is 155 beats/min, respiratory rate is 40 breaths/min, blood pressure is 70/50 mm Hg, and pulse oximetry is 94% on room air. On physical examination, the girl is drooling. There is faint scattered wheezing on lung examination, as well as subcutaneous crepitus noted on palpation of her anterior neck and upper chest wall. She has tachypnea, with intermittent subcostal retractions. Her abdomen is soft, with no focal tenderness or peritoneal signs. As you are finishing your physical examination, the girl has another episode of vomiting, and you note that the emesis is mixed with bright red blood.

Of the following, the MOST likely explanation for this girl's symptoms is

  A. aspiration pneumonia
  B. bacterial tracheitis
  C. esophageal perforation
  D. Mallory-Weiss tear

Correct Answer: C

The young girl in the vignette presents with symptoms of pain in her anterior neck and chest, hematemesis, dysphagia, and drooling, which manifested acutely 6 days after endoscopic removal of an ingested button battery from her esophagus. The most likely explanation for her symptoms is esophageal perforation.

Esophageal perforation is rare in children, and may be difficult to identify when it does occur. It is crucial that all pediatric providers recognize the clinical features associated with esophageal injury, because delayed diagnosis may result in devastating consequences, including mediastinitis, sepsis, multisystem organ failure, and even death. In children, esophageal perforation results most frequently from iatrogenic causes, but may also be caused by penetrating and blunt trauma. Spontaneous esophageal perforation is rare, but may occur. Esophageal injury may also occur as a complication of foreign bodies or caustic ingestions. In children with a history of button battery ingestion, ongoing progression of esophageal injury, even after the operative removal of the battery, has been reported. Progression of esophageal injury has been reported days to weeks after removal of esophageal button batteries, resulting in serious sequelae, including esophageal perforation and aortoesophageal fistula formation.

Clinical features of esophageal perforation may include neck pain and/or stiffness, chest pain, epigastric pain, abdominal guarding, hematemesis, odynophagia, drooling, or dyspnea. Symptoms may vary depending on the portion of the esophagus that is injured. Physical examination findings may include crepitus noted on palpation of the neck and/or chest wall, asymmetric breath sounds (which may indicate a concurrent pneumothorax), coarse lung sounds, wheezing, tachycardia, tachypnea, or signs of respiratory distress.

Aspiration pneumonia is an infection of the lung parenchyma that develops as a sequela of inhaling foreign material, often due to oropharyngeal bacteria. Signs and symptoms include fever, cough, tachypnea, respiratory difficulty, and hypoxia; symptoms typically develop within 1 hour of an aspiration event. The girl in the vignette has had no recent history of choking, aspiration, or recent fevers. She is complaining of pain in her anterior neck, which is not a typical symptom of aspiration pneumonia.

Bacterial tracheitis is an exudative bacterial infection involving the soft tissues of the trachea. Affected children may present with pain or difficulty with swallowing, fever, stridor, anterior neck pain, cough, drooling, signs of respiratory distress, or a toxic clinical appearance. Bacterial tracheitis may arise as a complication of viral croup, and should be suspected in children who significantly worsen over the clinical course of a croup infection. Although some of the symptoms displayed by the girl in the vignette may be seen in children with bacterial tracheitis, bloody emesis and the presence of subcutaneous crepitus over the anterior chest wall and neck would not be explained by this diagnosis.

A Mallory-Weiss tear, or syndrome, is part of the differential diagnosis for children presenting with hematemesis. Hematemesis due to Mallory-Weiss syndrome typically occurs in children with a history of repeated vomiting and/or forceful retching, which causes tears in the mucosa of

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the distal esophagus and proximal stomach. The girl in the vignette had acute onset of hematemesis that was *not* preceded by repeated vomiting and/or forceful retching; this is inconsistent with the clinical picture of Mallory-Weiss syndrome. In addition, the findings of drooling, neck/chest wall crepitus, wheezing, and respiratory distress in this patient cannot be explained by a diagnosis of Mallory-Weiss syndrome.

Manifestations of spontaneous pneumothorax include the sudden onset of chest pain and shortness of breath. Physical examination findings include unilateral decreased breath sounds, decreased chest wall movement, and hyperresonance to percussion over the affected lung. Depending on the degree of the pneumothorax (and the presence or absence of tension pneumothorax), affected patients may present with respiratory distress, tachycardia, hypotension, or cyanosis. Spontaneous pneumothorax most commonly affects adolescents and adult men with a tall, thin body habitus. The girl in the vignette has no known risk factors for spontaneous pneumothorax, and her lung examination findings are not consistent with that expected in patients with pneumothorax.

PREP Pearls
- In children, esophageal perforation results most frequently from iatrogenic causes, but may also be caused by penetrating or blunt trauma. Cases of spontaneous esophageal perforation are rare, but may occur.
- Esophageal injury may also occur as a complication of esophageal foreign bodies or caustic ingestions.
- Clinical features of esophageal perforation may include neck pain and/or stiffness, chest pain, epigastric pain, abdominal guarding, hematemesis, odynophagia, drooling, and dyspnea.
- In children with a history of button battery ingestions, ongoing progression of esophageal injury, even after operative removal of the battery, has been reported.

ABP Content Specifications(s)
- Recognize the clinical features associated with esophageal trauma

Suggested Readings
- Eisenberg M, Mooney DP. Thoracic trauma. In: Shaw KN, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia, PA: Wolters Kluwer; 2016;1297-1312.
- Garey CL, Laituri CA, Kaye AJ, et al. Esophageal perforation in children: a review of one institution's experience. *J Surg Res.* 2010;164:13–17. doi: http://dx.doi.org/10.1016/j.jss.2010.05.049 .
- Leinwand K, Brumbaugh DE, Kramer RE. Button battery ingestion in children: a paradigm for management of severe pediatric foreign body ingestions. *Gastrointest Endosc Clin North Am.* 2016;26(1):99–118. doi: http://dx.doi.org/10.1016/j.giec.2015.08.003.

Question 215

You are seeing a 10-year-old girl in your office for her annual health supervision visit. She has a complex medical history consisting of cyanotic congenital heart disease as a newborn, leading to a heart transplant when she was 2 years old. She is growing well, performing well in school, and has an active summer planned. She has a temperature of 36.5°C, heart rate of 70 beats/min, blood pressure of 120/80 mm Hg, and respiratory rate of 12 breaths/min. Her physical examination findings are unremarkable aside from a well-healed median sternotomy scar. You repeat her blood pressure manually and obtain a comparable result.

In reviewing her medications, the drug MOST likely to be causing her hypertension is

A. enalapril
B. mycophenolate mofetil
C. nystatin
D. sulfamethoxazole/trimethoprim
E. tacrolimus

Correct Answer: E

Tacrolimus is a calcineurin inhibitor and thus an inhibitor of T-cell signal transduction and interleukin-2. Calcineurin inhibitors are commonly used in transplant recipients to prevent rejection. Unfortunately, they have several important side effects, including hypertension.

Many other medications cause hypertension. Current and recent medications need to be considered when monitoring a patient and considering the etiology of hypertension. Drugs frequently associated with hypertension include corticosteroids, decongestants, nonsteroidal anti-inflammatory medications, herbal supplements, β-adrenergic agonists, erythropoietin, cyclosporine, tacrolimus, and stimulants (attention-deficit disorder medications). Recent discontinuation of antihypertensive medications can also cause hypertension. Enalapril, mycophenolate mofetil, nystatin, and sulfamethoxazole/trimethoprim do not cause hypertension.

PREP Pearls
- Tacrolimus and other calcineurin inhibitors can cause hypertension.
- Drugs that cause hypertension include corticosteroids, decongestants, nonsteroidal anti-inflammatory medications, herbal supplements, β-adrenergic agonists, erythropoietin, cyclosporine, tacrolimus, and stimulants (attention-deficit disorder medications).
- Discontinuation of antihypertensive medications can cause hypertension.

ABP Content Specifications(s)
- Understand the effects of certain drugs on the development of hypertension in children of various ages

Suggested Readings
- Brady TM. Hypertension. *Pediatr Rev*. 2012;33(12):541–552. doi: http://dx.doi.org/10.1542/pir.33-12-541.
- Luft FC. How calcineurin inhibitors cause hypertension. *Nephrol Dial Transplant*. 2012;27(2):473–475. doi: http://dx.doi.org/10.1093/ndt/gfr679.

Question 216

A 6-year-old boy with autism has been hospitalized for apparent leg pain, weakness, and refusal to walk. His diet consists exclusively of "white foods," notably mashed potatoes, chicken nuggets, and plain macaroni. Water is his only beverage.

His physical examination shows an afebrile nonverbal child with diffuse extremity tenderness, without swelling or deformity. He has inflamed gums with mild bleeding, several bruises on his legs, and a hemorrhagic follicular rash on his buttocks. The remainder of his examination findings are within normal parameters. Laboratory findings include normal prothrombin and partial thromboplastin times; a mild microcytic anemia but an otherwise normal complete blood count; normal liver and renal functions; and normal alkaline phosphatase, calcium, and phosphorus levels. Radiography shows osteopenia and a distal femur metaphyseal fracture.

Of the following, the laboratory test MOST likely to help determine the cause of this child's symptoms is

A. 1,25 dihydroxy-vitamin D level
B. antinuclear antibody and rheumatoid factor
C. creatine kinase level
D. leukocyte ascorbic acid concentration
E. nasopharyngeal viral cultures

Correct Answer: D

The child in the vignette has signs and symptoms characteristic of vitamin C deficiency, including bone pain, inflamed gums, perifollicular hemorrhage, and osteopenia. The most appropriate test to assess the boy's body stores of vitamin C is a leukocyte ascorbic acid level; a serum ascorbic acid level would assess recent intake rather than stores, and so is less useful. Once the diagnosis is confirmed, treatment consists of 100 mg of ascorbic acid (orally, intramuscularly, or intravenously) 3 times per day for 1 week, followed by 100 mg daily for several weeks until symptoms resolve and body stores are repleted.

Hypovitaminosis C is rarely seen in developed countries today, though patients with severely restricted diets remain at risk. It has been seen most often in children with neurologic or neurobehavioral conditions such as cerebral palsy and autism. Adolescents with eating disorders, children undergoing dialysis (which removes vitamin C), children with inflammatory bowel disease, and patients receiving unsupplemented parenteral nutrition are also at risk. Vitamin C is involved in collagen synthesis, bone formation, iron absorption, folate metabolism, and neurotransmitter synthesis, among other functions. Affected children often present initially with fatigue and lethargy, but then develop corkscrew hairs and perifollicular keratosis that progresses to perifollicular hemorrhage. Other dermatologic findings include petechiae and ecchymoses. Affected children may also develop diarrhea, ocular hemorrhages, as well as anemia due to poor iron absorption, bleeding, and other nutritional deficiencies. Gum involvement, with inflammation and hemorrhage is a classic finding (**Item C216A**). Children are particularly vulnerable to scurvy, which includes bone pain, subperiosteal hemorrhage, joint hemorrhage, arthropathy, and disordered bone matrix development. Wimberger and Frankel lines, white lines around the metaphysis and epiphysis, respectively, are rarely seen today but are specific to scurvy (**Item C216B**).

Item C216A: Gum inflammation and hemorrhage seen in hypovitaminosis C.
Reprinted with permission from Weinstein M, Babyn P, Zlotkin S. An orange a day keeps the
doctor away: scurvy in the year 2000. *Pediatrics*; 2001; 108:e55

Item C216B: Radiographic findings in scurvy.
Reprinted with permission from Weinstein M, Babyn P, Zlotkin S. An orange a day keeps the doctor away: scurvy in the year 2000. *Pediatrics*; 2001; 108:e55

Hypovitaminosis C may coexist with other nutritional deficiencies, thus affected patients require a thorough nutritional evaluation. In the 19th century, scurvy in infants was felt to be an acute form of rickets and only later was recognized as a separate entity. Both conditions involve bone development, and it is reasonable to consider vitamin D deficiency in such patients. However, the child in the vignette has a normal alkaline phosphatase, calcium, and phosphorus, as well as physical examination findings such as gum inflammation that are characteristic of vitamin C deficiency. Therefore a vitamin D level is not likely to provide an explanation for this child's symptoms. In addition, the most appropriate test to assess vitamin D deficiency is a 25-hydroxyvitamin D level. Given the characteristic symptoms of vitamin C deficiency and the concerning nutritional history, as well as the normal inflammatory markers, rheumatologic studies such as antinuclear antibody and rheumatoid factor are also unlikely to be helpful. Viral infections can cause oral inflammation, myalgias, arthralgias, weakness, and lethargy, but the chronicity of symptoms, the patient's diet history, and the classic findings of scurvy make viral infection less likely as the primary cause of this patient's symptoms. Creatine kinase levels may be elevated with muscle damage but would not be diagnostic for the symptoms seen in the child in the vignette.

PREP Pearls

- Although infrequent in the developed world, children with severely restricted diets such as those with neurobehavioral conditions, eating disorders, malabsorption, undergoing dialysis, or receiving unsupplemented parenteral nutrition may develop vitamin C deficiency.
- Symptoms of vitamin C deficiency include fatigue, lethargy, corkscrew hairs, perifollicular keratosis that progresses to perifollicular hemorrhage, petechiae, ecchymoses, diarrhea, ocular hemorrhages, anemia, gum inflammation and hemorrhage, bone pain, subperiosteal hemorrhage, joint hemorrhage, arthropathy, and disordered bone matrix development.
- The most appropriate test to assess body stores of vitamin C is a leukocyte ascorbic acid level.

ABP Content Specifications(s)

- Recognize the signs, symptoms, and causes of vitamin C deficiency, and manage appropriately

Suggested Readings

- Duvall MG, Pikman Y, Kantor DB, et al. Pulmonary hypertension associated with scurvy and vitamin deficiencies in an autistic child. *Pediatrics*. 2013;132:31699–31703. doi: http://dx.doi.org/10.1542/peds.2012-3054.
- Lauer B, Spector N. Vitamins. *Pediatr Rev.* 2012;33:339–351. doi: http://dx.doi.org/10.1542/pir.33-8-339.
- Vitoria I, López B, Gómez J, et al. Improper Use of a Plant-Based Vitamin C–Deficient Beverage Causes Scurvy in an Infant. *Pediatrics*. 2016;137(2):e20152781. https://www.ncbi.nlm.nih.gov/pubmed/26783325.
- Weinstein M, Babyn P, Zlotkin S. An orange a day keeps the doctor away: scurvy in the year 2000. *Pediatrics*. 2001;108:e55. doi: http://dx.doi.org/10.1542/peds.108.3.e55.

Question 217

An 8-month-old male infant is brought to the emergency department for evaluation of left eyelid swelling and redness after a recent bug bite. There are no sick contacts. His immunizations are up-to-date. He is alert with a temperature of 38.9°C. Eye examination reveals left periorbital erythema and swelling (**Item Q217**). Extraocular movement is normal, and there is no chemosis. The remainder of the examination findings are normal.

Item Q217: Infant with left eyelid swelling and redness.
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Of the following, the MOST likely pathogen causing this infant's illness is

 A. Haemophilus influenzae nontypeable
 B. Haemophilus influenzae type b
 C. Staphylococcus aureus
 D. Streptococcus anginosus
 E. Streptococcus pneumoniae

Correct Answer: C

The infant in this vignette exhibited fever, unilateral periorbital swelling, and redness with normal extraocular movements and absence of conjunctival chemosis following a bug bite. These findings and the patient history are consistent with a diagnosis of periorbital (preseptal) cellulitis. Periorbital cellulitis is an infection of the eyelid and surrounding skin and soft tissue anterior to the orbital septum. The orbital septum is a protective fibrous connective tissue of the periosteum extending to the upper and lower eyelids.

Periorbital cellulitis occurs commonly in preschool children and is typically caused by local skin trauma (eg, an insect bite). In this setting, the most common etiologic agents include *Staphylococcus aureus* (including methicillin-resistant *S aureus*) and group A *Streptococcus*. In the era of *Haemophilus influenzae* type b vaccination and pneumococcal conjugate vaccination, bacteremic periorbital cellulitis is very unusual in clinical practice.

The clinical manifestations of preseptal cellulitis are eyelid erythema, induration, and tenderness without proptosis, ophthalmoplegia, or loss of vision. Patients with periorbital cellulitis related to trauma are usually nontoxic appearing. Culture of the wound exudate (if present) may reveal the microorganism. In cases with evidence of bacteremia, a lumbar puncture may be indicated to exclude meningitis. Treatment of uncomplicated posttraumatic periorbital cellulitis usually consists of oral antimicrobial agents (eg, clindamycin or trimethoprim-sulfamethoxazole in combination with amoxicillin or linezolid) that treat *S aureus* (including methicillin-resistant *S aureus*) and group A *Streptococcus*. A 10-day course of antibiotic therapy generally results in a successful outcome. In severe cases, a short duration of parenteral antibiotic therapy may be necessary.

Distinguishing periorbital cellulitis from orbital cellulitis is critical to avoid potentially serious complications including vision loss and intracranial infection. The microbiology, pathogenesis, diagnostic evaluation, and management of periorbital cellulitis and orbital cellulitis are very different. Orbital cellulitis is a serious infection of the orbital tissue posterior to the orbital septum usually complicating sinusitis (especially ethmoid sinus). The ethmoid sinus is separated from the orbit by a thin medial orbital wall (lamina papyracea). The microbiology of orbital cellulitis includes organisms associated with acute or chronic sinusitis including *Streptococcus anginosus*, *S aureus, Streptococcus pneumoniae*, *Moraxella catarrhalis*, nontypeable *H influenzae*, and upper respiratory tract anaerobes.

The clinical manifestations of orbital cellulitis are proptosis, conjunctival chemosis, ophthalmoplegia, or pain with eye movement (**Item C217A**). In patients with marked eye swelling, it may be difficult to distinguish periorbital cellulitis from orbital cellulitis by physical examination alone because of difficulties in assessing visual acuity or extraocular movements. All patients with a suspected diagnosis of orbital cellulitis should undergo orbital computed tomography with contrast to confirm the diagnosis and exclude orbital complications including subperiosteal abscess and orbital abscess (**Item C217B**).

Management of orbital cellulitis warrants a multidisciplinary approach with consultations from pediatric infectious disease, otolaryngology, and ophthalmology. Empiric antimicrobial therapy of orbital cellulitis may be initiated with ampicillin-sulbactam and vancomycin to treat methicillin-resistant *S aureus* and other microorganisms associated with sinusitis. A 5- to 7-day course of parenteral antibiotic therapy (until the eye examination results are greatly improved), followed by 3 weeks of oral therapy is a reasonable approach. Surgery may be indicated in patients with subperiosteal abscess or orbital abscess.
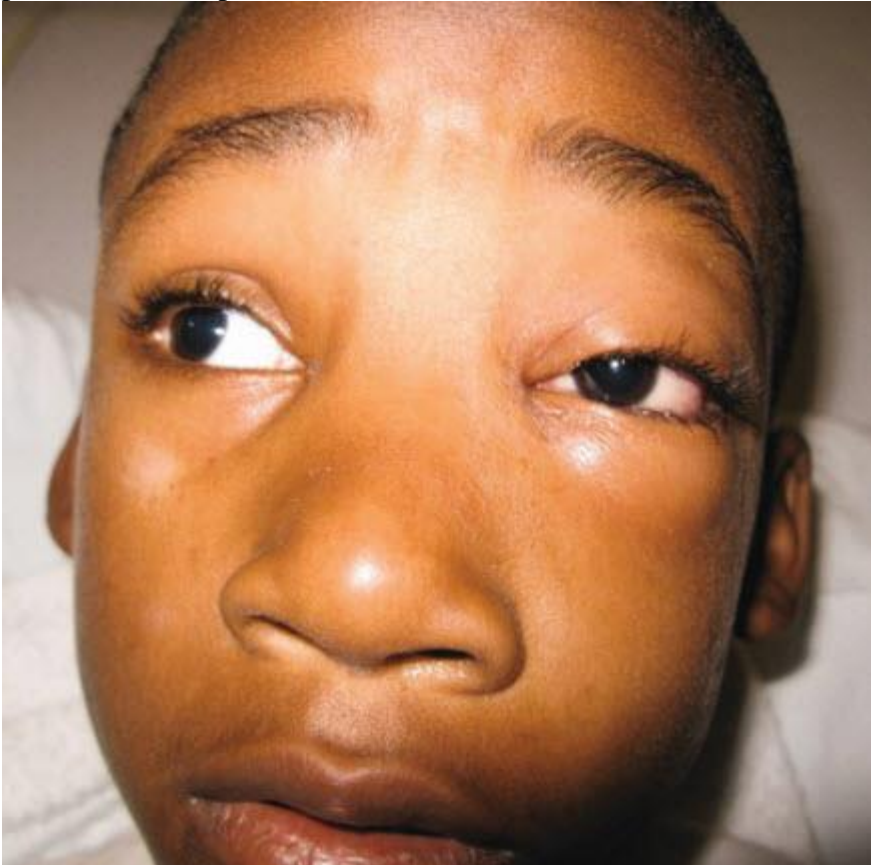
Item C217A: Proptosis, chemosis, and limitations of extraocular movements seen in orbital cellulits. Reprinted with permission from Hauser A, Fogarasi S. *Pediatr Rev.* 2010;31:244.
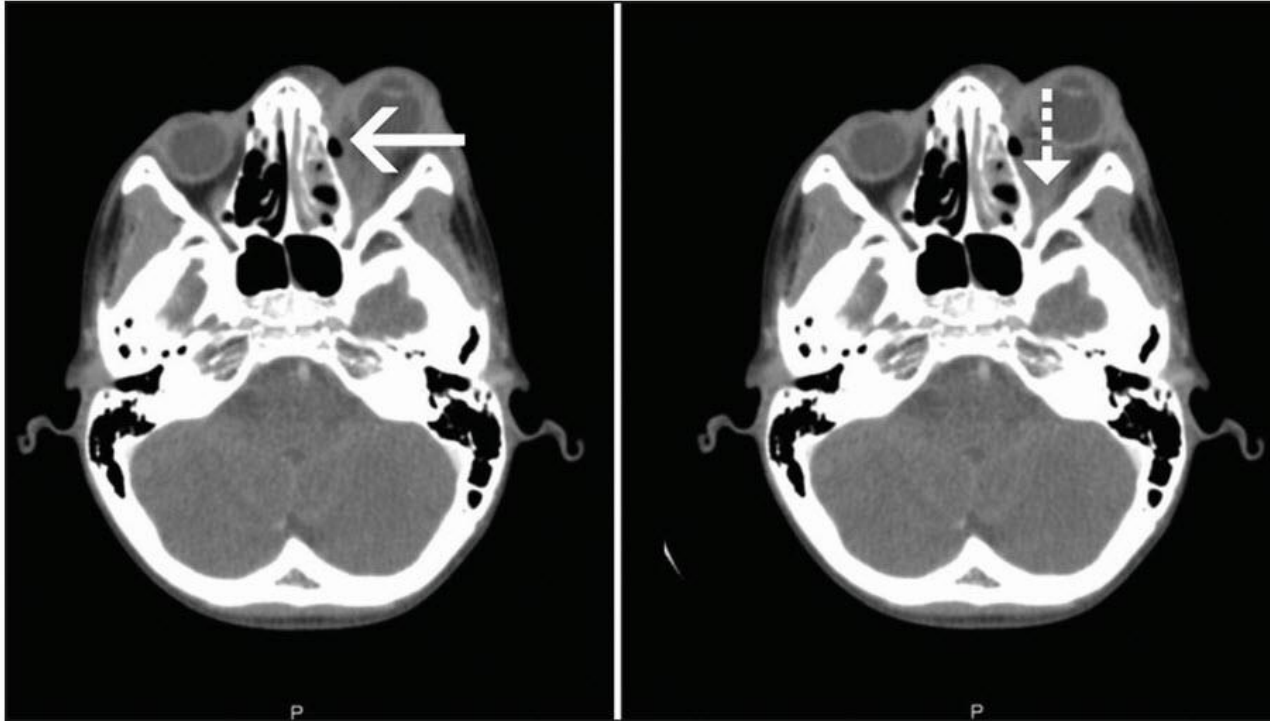
Item C217B: CT scan of the orbit with contrast showing orbital cellulitis. Left: (proptosis; phlegmon formation; left paranasal sinus opacification; intraorbital free air (solid arrow), stranding of the intraconal fat along the orbital floor (dotted arrow).
Reprinted with permission from Hauser A, Fogarasi S. *Pediatr Rev.* 2010;31:247.

Staphylococcus aureus is most likely to cause periorbital cellulitis in the infant described in this vignette following local skin trauma after a bug bite. Although *H influenzae* type b and *S pneumoniae* can cause bacteremic periorbital cellulitis, this entity is very rare in the era of the *H influenzae* type b vaccine and pneumococcal conjugate vaccine. In patients with orbital cellulitis, *S aureus*, *S anginosus, S pneumoniae*,and nontypeable *H influenzae* can be identified from the polymicrobial aerobic and anaerobic microorganisms isolated from infected sinuses or subperiosteal abscess.

PREP Pearls
- Periorbital cellulitis is an infection of the eyelid and surrounding skin and soft tissue anterior to the orbital septum. It commonly affects preschool children and is typically caused by local skin trauma (such as insect bite).
- The most common etiologic agents of traumatic periorbital cellulitis include *Staphylococcus aureus* (including methicillin-resistant *S aureus*) and group A *Streptococcus*; in the era of *Haemophilus influenzae* type b and pneumococcal conjugate vaccination, bacteremic periorbital cellulitis is very unusual.
- The clinical manifestations of periorbital cellulitis are eyelid erythema, induration, and tenderness without proptosis, ophthalmoplegia, or loss of vision.

- Treatment of uncomplicated post-traumatic periorbital cellulitis usually consists of oral antimicrobial agents that treat *Staphylococcus aureus* (including methicillin-resistant *S aureus)* and group A *Streptococcus*.

ABP Content Specifications(s)
- Plan the appropriate diagnostic evaluation of periorbital (preseptal) cellulitis
- Plan the appropriate management of periorbital (preseptal) cellulitis
- Recognize pathogens commonly associated with periorbital (preseptal) cellulitis

Suggested Readings
- Givner LB. Periorbital versus orbital cellulitis. *Pediatr Infect Dis J.* 2002;21(12):1157–1158.
- Hauser A, Fogarasi S. Periorbital and orbital cellulitis. *Pediatr Rev.* 2010;31(6):242–249. doi: http://dx.doi.org/10.1542/pir.31-6-242.
- Seltz LB, Smith J, Durairaj VD, Enzenauer R, Todd J. Microbiology and antibiotic management of orbital cellulitis. *Pediatrics*. 2011;127(3):e566–e572. doi: http://dx.doi.org/10.1542/peds.2010-2117.

Question 218

A mother comes to your office with her newborn for a new patient visit. The newborn was recently discharged from the neonatal intensive care unit where she was hospitalized because of an open neural tube defect necessitating surgical closure and management. The mother is concerned about the risk for her and her husband to have another child with a neural tube defect.

Of the following, the recurrence risk for this couple is CLOSEST to

A. less than 1%
B. 5%
C. 25%
D. 33%
E. 50%

Correct Answer: B

A neural tube defect (NTD) is an isolated congenital malformation that can recur in families, is not part of a specific syndrome, and is commonly due to multifactorial inheritance. Anencephaly and spina bifida are both types of NTDs. The recurrence risk in this situation for a future pregnancy with 1 sibling affected and neither parent affected is closest to 5%. If 2 siblings were affected, the recurrence risk would be higher, approaching 10% to 12% (**Item C218**).

Item C218. Recurrence Risks (%) For Multifactorial Inheritance—Spina Bifida and Anacephaly

	Parents							
	Neither Affected		Father Affected		Mother Affected		Both Affected	
	Pat	Mat	Pat	Mat	Pat	Mat	Pat	Mat
No Sibs	0·3		4·9		4·3		32·7	
1 sib U	0·3		4·5		4·0		29·8	
1 M sib A	4·2		13·9		13·0		39·3	
1 F sib A	3·6		12·8		11·9		38·4	
1 F sib A + 1 sib U	3·4		11·6		10·8		35·4	
2 M sibs A	11·5		23·0		22·4		44·5	
1 M + 1 F sibs A	10·6		21·8		21·1		43·7	
2 F sibs A	9·8		20·6		19·9		43·0	
2 F sibs A + 1 sib U	9·0		18·8		18·1		39·9	
1 2nd-degree relative A	1·2	1·2	6·3	14·0	12·9	5·6	37·5	37·8
1 M sib + 1 2nd A	7·4	7·2	15·9	23·7	22·7	15·2	43·4	43·8
1 F sib + 1 2nd A	6·6	6·5	14·7	22·5	21·4	14·0	42·5	42·9
1 F sib + 1 2nd A + 1 sib U	6·1	5·9	13·2	20·4	19·4	12·5	39·3	39·6
2 sibs +1 2nd A	14·4	14·2	23·5	30·1	29·4	23·1	47·1	47·6
2 sibs + 1 2nd A + 1 sib U	13·2	13·0	21·4	27·6	26·9	20·9	43·8	44·2
1 3rd-degree relative A	0·6	0·6	5·8	8·7	7·8	5·1	35·8	35·9
1 M sib + 1 3rd A	5·9	5·8	15·2	18·8	17·9	14·4	42·0	42·2
1 F sib +1 3rd A	5·2	5·1	14·1	17·5	16·6	13·3	41·1	41·3
1 M sib + 1 pat 2nd + 1 3rd A	9·1	10·2	17·2	21·3	27·2	24·9	45·9	46·3
1 M sib + 1 mat 2nd + 1 3rd A	10·1	8·7	25·8	28·2	20·6	16·5	46·6	46·6
1 F sib + 1 pat 2nd + 1 3rd A	8·2	9·2	15·9	20·0	26·0	23·5	45·1	45·5
1 F sib + 1 mat 2nd + 1 3rd A	9·1	7·9	24·5	26·9	19·2	15·3	45·8	45·8
1 F sib + 1 3rd A + 1 sib U	4·8	4·7	12·7	15·8	14·9	11·9	37·9	38·1
2 sibs + 1 3rd A	12·8	12·6	22·9	26·1	25·5	22·3	45·9	46·2
2 sibs + 1 3rd A + 1 sib U	11·7	11·6	20·8	23·8	23·1	20·2	42·7	42·8
2 sibs + 1 pat 2nd + 1 3rd A + 1 sib U	15·0	16·0	22·5	26·0	30·6	28·8	46·0	46·4
2 sibs + 1 mat 2nd + 1 3rd A + 1 sib U	16·0	14·6	29·4	31·3	25·6	22·1	46·6	46·7

M, male; F, female; A, affected; U, unaffected; pat, paternal; mat, maternal.

Reprinted with permission from Risk Tables for genetic counselling in some common congenital malformations Bonaiti-Pellie, C and Smith C. *Journal of Medical Genetics* 1974,11: 377.

Neural tube defects are a major cause of stillbirth, early infantile deaths, and disability in surviving children. The incidence in the Unites States is less than 0.2%. The frequency can vary based on socioeconomic factors, seasonality, maternal intake of antiepileptic medications, and the presence or absence of folate deficiency. Maternal serum folic acid levels during pregnancy are inversely correlated with NTD risk. Below a threshold of 200 µg/L, the risk for NTD rises substantially. Additionally, elevated homocysteine levels can also play a role, suggesting that a biochemical abnormality in the recycling of tetrahydrofolate to methylate homocysteine to methionine plays a role in NTD risk. The discovery of folic acid deficiency contributing to NTD

risk led to a public health initiative to supplement all women preconceptually for 1 month and postconceptually for at least 3 months with 400 to 800 µg/d of folic acid, which led to a greater than 75% reduction in the incidence of NTDs. If a parent has had a child with NTD, it is recommended that the mother receive a supplement with 4,000 µg (4 mg)/d of folic acid beginning 1 month prior to planning to become pregnant and continuing through the first 3 months of pregnancy. Neural tube defects during a pregnancy are commonly detected by elevations of the maternal α-fetoprotein level or by prenatal ultrasonography.

Many diseases "run in families" as demonstrated by recurrence in relatives of an affected individual at a rate higher than in the general population. The inheritance in many cases does not follow a Mendelian pattern, as seen with a well-defined single-gene disorder. Familial clustering of a disorder that does not follow Mendelian inheritance patterns is likely a reflection of complex interactions between genetic and environmental factors known as multifactorial inheritance. Most relatives share similar gene-gene and gene-environment interactions. These shared interactions could trigger, accelerate, reduce, or protect against a specific disease. Some examples of disorders that display multifactorial inheritance include cleft lip/palate, Alzheimer disease, infantile pyloric stenosis, congenital dislocation of the hip, congenital heart disease, diabetes, and mental health disorders.

Among the remaining answer choices, less than 1% would be a correct answer if the question was about the general population risk for NTD. Twenty-five percent would be correct if the condition was an autosomal recessive disorder, such as sickle cell disease or cystic fibrosis. Fifty percent would be correct if the condition was an autosomal dominant condition, such as Marfan syndrome or neurofibromatosis type 1. Thirty-three percent is a much greater percentage than would be seen in a multifactorial disorder with only 1 affected first-degree relative.

PREP Pearls
- A neural tube defect, such as anencephaly or spina bifida, is an isolated congenital malformation that can recur in families, is not a part of a specific syndrome, and is caused by multifactorial inheritance.
- The recurrence risk for neural tube defect in a future pregnancy with 1 sibling affected and neither parent affected is closest to 5%. If 2 siblings were affected, the recurrence risk would approach 10% to 12%.
- The contribution of folic acid deficiency to neural tube defects led to a public health recommendation to supplement all women preconceptually for 1 month and postconceptually for at least 3 months with 400 to 800 µg/d of folic acid.
- Familial clustering of a disorder that does not follow Mendelian inheritance patterns is likely a reflection of complex interactions between genetic and environmental factors impacting risk known as multifactorial inheritance. Common examples include cleft lip/palate, neural tube defect, Alzheimer disease, congenital hip dysplasia, and diabetes.

ABP Content Specifications(s)
- Understand the role of multifactorial inheritance in genetic disorders

Suggested Readings
- Centers for Disease Control and Prevention. Facts about cleft lip and cleft palate. 2015. http://www.cdc.gov/ncbddd/birthdefects/CleftLip.html.
- Centers for Disease Control and Prevention. Folic acid: recommendations. 2016. http://www.cdc.gov/NCBDDD/folicacid/recommendations.html.
- Centers for Disease Control and Prevention. Use of folic acid for prevention of spina bifida and other neural tube defects–1983-1991. *MMWR Morb Mortal Wkly Rep*. 1991;40(30):513–516. http://www.cdc.gov/mmwr/preview/mmwrhtml/00014915.htm.
- National Library of Medicine, National Institutes of Health. What are complex or multifactorial disorders? 2017. https://ghr.nlm.nih.gov/primer/mutationsanddisorders/complexdisorders.
- US Preventive Service Task Force. Folic acid to prevent neural tube defects: preventive medication. 2013. https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/folic-acid-to-prevent-neural-tube-defects-preventive-medication.

Question 219

A 6-year-old boy is brought to your office for an annual health supervision visit. He has a complex medical history of myocarditis as an infant with subsequent heart transplantation months later. His vital signs and physical examination findings are unremarkable. He is feeling well and thriving in school. His cardiologist recently performed a series of tests. Remarkable findings include: an echocardiogram with normal biventricular function, normal function of all 4 valves, and no pericardial effusion; an electrocardiogram with normal sinus rhythm; and a metabolic panel with a blood urea nitrogen level of 20 mg/dL (7.1 mmol/L) and a creatinine level of 1 mg/dL (88.4 µmol/L).

Of the following, the MOST likely etiology for this patient's kidney injury is

  A. antibody-mediated rejection
  B. chronic tacrolimus use
  C. ingestion
  D. poor cardiac function
  E. supraventricular tachycardia

Correct Answer: B

Although posttransplant survival continues to improve, the adverse effects of the medications linked to this success can cause chronic morbidity. Immune suppression is an important adjunct to prevent organ rejection in solid organ transplant and to prevent graft-vs-host disease in stem cell (bone marrow) transplant. Calcineurin inhibitors are commonly used after transplant, and an important adverse effect of these medications is renal dysfunction. The rate of posttransplant renal injury in pediatric solid organ transplants ranges from 15% to 30%. These medications cause glomerular vascular constriction, interstitial fibrosis, and arterial hyalinosis. Routine testing to monitor renal function is warranted in all patients who receive calcineurin inhibitors.

There are many classes of immunosuppressive agents used in transplant recipients and patients with autoimmune disorders. These agents include calcineurin inhibitors, corticosteroids, mammalian target of rapamycin inhibitors (eg, sirolimus, everolimus), antimetabolites (eg, 6-mercaptopurine, azathioprine), and newer biologic agents (eg, infliximab, rituximab, adalimumab). All of these agents can have adverse short- and long-term side effects, and pediatricians caring for children on these medications must be aware of the risks.

Calcineurin inhibitors can cause hypertension, associated left ventricular hypertrophy, and metabolic syndrome. Corticosteroids can cause metabolic syndrome, hyperglycemia, and diabetes mellitus. Antimetabolites can cause cytopenia and hepatic dysfunction. Mammalian target of rapamycin inhibitors can cause hypomagnesemia and abnormal serum lipid levels. The complications of biologic agents depend on the biologic pathways inhibited in addition to immune suppression. Given the effects on the immune system, patients on immunosuppressive agents remain at risk for infection as well as malignancy. In the setting of solid organ or bone marrow transplant, posttransplant lymphoproliferative disorder is a risk of chronic immune suppression.

The patient in this vignette is feeling well with normal vital signs and normal cardiac function by echocardiogram, making the renal dysfunction unlikely related to supraventricular tachycardia, antibody-mediated rejection, or poor cardiac function. There is no history or physical examination findings suggestive of ingestion.

PREP Pearls
- Calcineurin inhibitors cause renal dysfunction over time in a meaningful percentage of transplant recipients because of vascular construction and fibrosis.
- Immunosuppressive agents (corticosteroids and calcineurin inhibitors) can cause hypertension, metabolic syndrome, and diabetes mellitus. They also increase the risks of infection and posttransplant lymphoproliferative disorder.
- Many classes of immunosuppressive agents are used by transplant recipients and patients with autoimmune disorders. These agents include calcineurin inhibitors, corticosteroids, mammalian targets of rapamycin inhibitors (eg, sirolimus, everolimus), antimetabolites (eg, 6-mercaptopurine, azathioprine), and newer biologic agents (eg, infliximab, rituximab, adalimumab).

ABP Content Specifications(s)
- Recognize the long-term risks associated with immunosuppressive drug therapy

Suggested Readings
- Kim JJ, Marks SD. Long-term outcomes of children after solid organ transplantation. *Clinics*. 2014;69(S1):28–38.
- Kim S, Webster AC, Craig JC. Current trends in immunosuppression following organ transplantation in children. *Curr Opin Organ Transplant.* 2013;18(5):537–542. doi: http://dx.doi.org/10.1097/MOT.0b013e3283651b35.
- Schnepp E, Kaminski D. Chronic immunosuppression. *Pediatr Rev.* 2012;33(10):481–482. doi: http://dx.doi.org/10.1542/pir.33-10-481.

Question 220

A 3-year-old boy is brought to your office for a health supervision visit. He is a new patient to your practice. Six months ago, he was diagnosed with autism by a developmental pediatrician after he was referred for evaluation of expressive language delay, repetitive stereotyped movements, and abnormal social development. He currently uses less than 10 words. His parents report that he is extremely sensitive to being touched. You are unable to perform a thorough physical examination because he screams and cries when you attempt to touch his body. The boy's previous pediatrician recommended that he have his hearing tested to determine if a hearing deficit is contributing to his developmental delays. His family moved before he was able to have this testing completed, and they are interested in testing at this time.

Of the following, the MOST appropriate initial test for this patient is

 A. auditory brainstem response testing
 B. pure-tone audiometry
 C. speech audiometry
 D. tympanometry
 E. visual reinforcement audiometry

Correct Answer: E

Although the child in this vignette is 3 years old, he has autism, very limited verbal skills, and is resistant to examination and physical contact with others. The best initial hearing test for him would be visual reinforcement audiometry. He would likely need to be sedated to undergo auditory brainstem response testing, making this an inappropriate first test. With his limited communication and cooperation, pure-tone and speech audiometry would not be feasible. Tympanometry is not appropriate because it is not a hearing test.

Pediatric hearing loss is a common and often under-recognized issue. Early identification and prompt intervention are associated with improved language and developmental outcomes. All states have universal newborn hearing screening programs, which aim to identify children with permanent congenital hearing loss by 3 months of age and begin interventions by 6 months of age. Universal newborn hearing screening programs use either otoacoustic emission (OAE) or auditory brainstem response testing.

During OAE testing, a speaker is placed in the ear canal. Sound triggers the cochlea to respond; this response can be sensed by a recorder within the ear canal insert. The OAEs serve as a surrogate marker for a normally functioning cochlea. This test is quick, inexpensive, and does not require the infant to be cooperative or sedated. Results can be affected by cerumen, fluid, or debris in the external ear canal or the middle ear. Auditory neuropathies or other neuronal problems are missed by OAE testing because the function of the auditory nerve is not measured. Auditory brainstem response testing measures electrical activity along the auditory nerve. Electrodes are placed on the scalp to record the electrical activity as speakers in the ear canal emit clicks or tones. Results can be affected by movement; newborns are best tested when sleeping, and older children may require sedation for an accurate test. Results can also be affected by outer or middle ear conditions, although less so than in OAE testing.

Both OAE and auditory brainstem response testing evaluate portions of the auditory pathway but are not true tests of hearing. Hearing cannot definitively be considered normal until a reliable audiogram can be obtained. Audiometry evaluates hearing thresholds at a variety of frequencies and can determine the degree and type of hearing loss. Ears can be tested separately and simultaneously. Various types of audiometric testing can be used with patients of different ages (**Item C220A**).

Item C220A. Types of Audiometric Testing.

Type of Audiometric Testing	Description of Test	Age Range	Potential Drawbacks
Visual reinforcement/ behavioral audiometry	Child is conditioned to associate sound with a specific stimuli (eg, lighted toy); examiner observes behavioral responses	Infants as young as 6-9 mo, older children with developmental delays	Requires highly trained testing staff and calibrated, sound-treated room
Play audiometry	Child is conditioned to perform a task (eg, drop a toy in a box) in response to sound	Children as young as 2.5 y	Child's attention span may limit testing
Conventional audiometry • Pure-tone • Speech	Patient is instructed to raise her hand in response to sound (either pure tones or speech)	Children > 4 y, adolescents and adults	Requires patient understanding and cooperation

Courtesy of I. Larson

Although not a hearing test per se, tympanometry can be used to assess the function of the outer and middle ear. During this test, a small probe is inserted into the ear canal, forming a seal. This probe measures pressure and can identify normal middle ear pressure, decreased tympanic membrane mobility, or tympanic membrane retraction caused by eustachian tube dysfunction. Beyond the newborn period, children with risk factors for hearing loss should have ongoing screening as well as a formal diagnostic audiology assessment by 24 to 30 months of age. All

children should have periodic hearing screening, and any parental concern for hearing loss should be taken seriously. Risk factors for hearing loss are shown in **Item C220B**.

Item C220B. Risk Factors for Hearing Loss in Children.

Birth to Age 28 Days:

- Family history of congenital or early-onset hearing loss
- Congenital infection known to be associated with hearing loss (eg, cytomegalovirus, rubella, herpes, syphilis, toxoplasmosis, varicella)
- Craniofacial abnormality
- Birth weight < 1,500 g
- Hyperbilirubinemia requiring exchange transfusion
- Exposure to ototoxic medications
- Bacterial meningitis
- Low Apgar scores at birth (< 3 at 5 minutes and < 6 at 10 minutes)
- Prolonged mechanical ventilation (> 10 days)
- Findings consistent with a syndrome with known hearing loss

Age 29 days to 2 years:

- Concern about hearing, speech, language, or other developmental delay
- Bacterial meningitis
- Neonatal risk factors associated with hearing loss
- Head trauma, especially temporal bone fracture
- Findings of syndrome associated with sensorineural hearing loss
- Exposure to ototoxic medications (eg, aminoglycosides, loop diuretics, cisplatin)
- Neurodegenerative disorders
- Infectious diseases associated with hearing loss

Reprinted with permission from Grindle CR. Pediatric hearing loss. *Pediatr Rev.* 2014;35(11):459.

PREP Pearls

- Universal newborn hearing screening is performed with otoacoustic emission testing, which measures a response from the cochlea, or auditory brainstem response testing, which measures electrical activity along the acoustic nerve.
- Otoacoustic emission testing and auditory brainstem response testing evaluate portions of the auditory pathway but are not true tests of hearing.
- Visual reinforcement/behavioral audiometry, play audiometry, and conventional audiometry evaluate hearing thresholds at various frequencies and can determine the degree and type of hearing loss.

MOCA-Peds Objective

- Evaluate and manage the behavioral complications of autism spectrum disorder

ABP Content Specifications(s)

- Understand the indications for and limitations of standard audiology tests (including acoustic emissions, tympanometry, auditory brainstem response, and behavioral audiometry) and be able to interpret their results
- Plan the age-appropriate initial and follow-up evaluation of hearing loss of various etiologies

Suggested Readings

- Grindle CR. Pediatric hearing loss. *Pediatr Rev.* 2014;35(11):456–463. doi: http://dx.doi.org/10.1542/pir.35-11-456.
- Harlor AD Jr, Bower C; Committee on Practice and Ambulatory Medicine; 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.

Question 221

A 18-month-old girl presents to the emergency department with diarrhea and vomiting. Over the past several days, she has vomited approximately 5 times per day, and has had 8 to 10 stools per day. She refuses to eat solids, but has been drinking fluids adequately, including milk, juice, and water. She continues to urinate approximately 5 times per day. Her vital signs are as follows: temperature, 37.8°C; heart rate, 150 beats/min; respiratory rate, 40 breaths/min; and blood pressure, 90/50 mm Hg. On physical examination, she is awake and alert, and has slightly dry mucous membranes. She is warm and well-perfused, with a capillary refill time of 2 seconds. She is breathing slightly rapidly and deeply. Her lungs are clear to auscultation bilaterally.

Laboratory results are as follows:

Sodium	130 mEq/L (130 mmol/L)
Potassium	5.0 mEq/L (5.0 mmol/L)
Chloride	108 mEq/L (108 mmol/L)
Bicarbonate	14 mEq/L (14 mmol/L)
Serum urea nitrogen	20 mg/dL (7.1 mmol/L)
Creatinine	0.3 mg/dL (27 µmol/L)
Glucose	80 mg/dL (4.4 mmol/L)
Capillary blood gas pH	7.25
Partial pressure of carbon dioxide	28 mm Hg (3.7 kPa)

Of the following, the MOST likely contributor to this girl's acidemia is

A. decreased renal excretion of hydrogen ion
B. end-organ production of lactic acid
C. gastric production of hydrochloric acid
D. intestinal losses of bicarbonate
E. respiratory accumulation of carbon dioxide

Correct Answer: D

The girl in the vignette has metabolic acidosis caused by acute gastroenteritis with appropriate respiratory compensation. Evidenced by a normal anion gap, the most important contributor to her acidemia is intestinal losses of bicarbonate.

Acute gastroenteritis is a very common cause of emergency department visits for children. Denuding of epithelium and dysfunction of small intestinal villi can result in malabsorption, and if severe, can impair intestinal absorption of bicarbonate causing metabolic acidosis. Electrolyte and serum bicarbonate levels can provide useful information about the severity of illness and guide management. Children with bicarbonate levels higher than 15 mEq/L (15 mmol/L) are unlikely to be more than 10% dehydrated, and those with bicarbonate levels less than 14 mEq/L (14 mmol/L) are less likely to tolerate an oral fluid challenge. Other electrolyte disturbances seen in acute gastroenteritis can include hypernatremia, hyponatremia, and hypokalemia.

Blood gas analysis can provide helpful information in cases of severe gastroenteritis and other causes of acid-base imbalances. It is important to characterize both the respiratory and metabolic contributions to acidosis or alkalosis, if present. This can be accomplished by evaluating the PH, Pco_2, and the calculated bicarbonate level from blood gas data. The normal serum bicarbonate level is 22 to 26 mEq/L (22–26 mmol/L); a value below or above this range constitutes metabolic acidosis or alkalosis, respectively. In cases of metabolic acidosis, such as with the girl in this vignette, it is important to determine whether the anion gap is increased or normal. The anion gap is the mathematical difference between serum values of the predominantly measured cations (sodium and potassium) and the predominantly measured anions (chloride and bicarbonate). The normal anion gap is between 3 and 11 mEq/L. Because serum is electroneutral, an elevated anion gap indicates the presence of unmeasured anions in the serum. The possibilities for the identity of these unmeasured anions comprise the differential diagnosis of an elevated anion gap metabolic acidosis, which is represented by the mnemonic "MUDPILES": methanol, uremia, diabetic ketoacidosis, paraldehyde, iron/isoniazid, lactate, ethanol/ethylene glycol, and salicylates. A more broad differential diagnosis includes toxic ingestions, lactic acidosis, renal failure, and ketoacidosis. In contrast, normal anion gap metabolic acidosis is not caused by unmeasured anions. Rather, it is caused by the loss of bicarbonate, either from the urine or the gastrointestinal tract, most commonly because of renal tubular acidosis or gastroenteritis.

In cases of metabolic acidosis, it is important to recognize whether there is a concomitant respiratory alkalosis or acidosis. Appropriate respiratory compensation for a metabolic acidosis can be assessed by using the Winters formula:

Expected $Pco_2 = 1.5 \times$ (Serum bicarbonate) $+ 8 \pm 2$

If the Pco_2 is above or below the expected level, there is a concomitant respiratory acidosis or alkalosis, respectively. It should be noted that appropriate respiratory compensation does not usually restore the PH to the normal level, and mathematically, the Pco_2 can be lower than the reference range but still be classified as respiratory acidosis (ie, inadequate compensation).

The girl in the vignette has a normal anion gap metabolic acidosis with appropriate respiratory compensation, therefore respiratory accumulation of carbon dioxide is not the correct answer. The etiology of her acidosis is intestinal losses of bicarbonate, not increased gastric production of hydrochloric acid. Although lactic acidosis can occur with hypovolemic shock from severe gastroenteritis, it usually presents with an elevated anion gap. In response to acidosis, there is increased reabsorption of bicarbonate by the kidneys as opposed to decreased renal excretion of hydrogen ion.

PREP Pearls
- The anion gap is the mathematical difference between serum values of the predominantly measured cations (sodium and potassium) and the predominantly measured anions (chloride and bicarbonate).
- Normal anion gap metabolic acidosis is caused by the loss of bicarbonate from the urine or stool.
- Elevated anion gap acidosis is caused by lactic acidosis, toxic ingestions, ketoacidosis, or renal failure.

MOCA-Peds Objective
- Evaluate and manage a patient with metabolic acidosis

ABP Content Specifications(s)
- Formulate a differential diagnosis of acidosis associated with various anion gap values
- Identify the arterial blood gas abnormalities associated with an acid-base imbalance

Suggested Readings
- Kappy MS, Morrow G. A diagnostic approach to metabolic acidosis in children. *Pediatrics*. 1980;65(2):351–356. http://pediatrics.aappublications.org/content/65/2/351.
- Nagler J, Wright RO, Krauss B. End-tidal carbon dioxide as a measure of acidosis among children with gastroenteritis. *Pediatrics*. 2006;118:260–267. doi: http://dx.doi.org/10.1542/peds.2005-2723.
- Schwaderer AL, Schwartz GJ. Back to basics: acidosis and alkalosis. *Pediatr Rev*. 2004;25:350. http://pedsinreview.aappublications.org/content/25/10/350.

Question 222

You are evaluating a newborn in the nursery. The baby was born to a 32-year-old primigravida mother via normal vaginal delivery. The mother's prenatal history was significant for oligohydramnios. The neonate's temperature is 38°C, respiratory rate is 60 breaths/min, heart rate is 120 beats/min, blood pressure is 80/46 mm Hg, and oxygen saturation is 97% (on 2 L oxygen by nasal cannula). The neonate is tachypneic, and the skin of the anterior abdominal wall is wrinkled (**Item Q222**).

Item Q222: Neonate described in the vignette Courtesy of M Rimsza

You discuss the patient's clinical symptoms with the medical student rotating with you.

Of the following, you are MOST likely to inform the student that this newborn's condition

  A. affects the abdominal muscles and genitourinary tract only
  B. is confirmed by genetic testing
  C. is frequently associated with undescended testes
  D. more commonly affects female neonates
  E. rarely progresses to chronic kidney disease

Correct Answer: C

The wrinkled appearance of the abdominal wall in the newborn in this vignette is a characteristic feature of prune-belly (Eagle-Barrett) syndrome. Partial or complete absence of the abdominal wall muscles leads to a wrinkled abdominal wall described as a "prune belly." In addition to the abnormalities of the abdominal wall muscles and the genitourinary tract, multisystem involvement is frequently associated with prune-belly syndrome; this involvement includes anomalies of the musculoskeletal, gastrointestinal, and cardiopulmonary systems.

Abnormal intermediate and lateral plate mesoderm affecting abdominal wall development, mesonephric ducts, and genitourinary organs has been suggested as the underlying defect in prune-belly syndrome. Another hypothesis proposes intrauterine bladder outlet obstruction resulting in bilateral hydronephrosis leading to abnormal development of the abdominal wall and descent of the testes. A definite genetic defect has not been identified in prune-belly syndrome.

Prune-belly syndrome has an estimated incidence of nearly 4 per 100,000 live births and occurs almost exclusively in male individuals. Patients are diagnosed clinically by the characteristic abdominal wall appearance, undescended testes, and urinary tract abnormalities. Associated urinary tract abnormalities and clinical findings include:
- Bilateral hydroureteronephrosis caused by replacement of ureteral smooth muscle with collagen leading to ineffective peristalsis and recurrent infections
- Enlarged bladder with thick walls (collagen deposits) and abnormal bladder pressures leading to low voiding pressures and urinary retention, lateral placement of ureteral ostia, and increased risk for reflux
- Varying degrees of renal dysplasia; nearly 30% of patients with prune-belly syndrome develop end-stage renal disease requiring renal replacement therapy with dialysis or renal transplant.
- Hypoplastic or dysplastic prostate

Gastrointestinal malformations secondary to the absence of abdominal wall muscles include malrotation, elongated colon, volvulus, and anorectal malformations. Skeletal abnormalities in prune-belly syndrome are in part related to oligohydramnios and include clubfoot, kyphoscoliosis, torticollis, and pectus excavatum. Pulmonary hypoplasia secondary to oligohydramnios is an important determinant of neonatal mortality and long-term outcome. Additionally, patients are at increased risk for recurrent chest infections because of restricted respiratory movement secondary to chest wall deformities and paradoxical abdominal movement during breathing. Cardiac abnormalities, although rare, have been reported with prune-belly syndrome.

PREP Pearls
- Patients with prune-belly syndrome are diagnosed clinically by the characteristic wrinkled abdominal wall, undescended testes, and urinary tract abnormalities.
- Multisystem involvement is seen in association with prune-belly syndrome.
- The severity of renal dysplasia and associated pulmonary hypoplasia are important determinants of neonatal mortality and long-term outcome in prune-belly syndrome.

- Nearly 30% of patients with prune-belly syndrome develop end-stage renal disease requiring renal replacement therapy with dialysis or transplant.

ABP Content Specifications(s)
- Recognize the clinical findings associated with prune belly (Eagle-Barrett) syndrome

Suggested Readings
- Prune belly syndrome. NORD (National Organization for Rare Disorders) website. https://rarediseases.org/rare-diseases/prune-belly-syndrome/.
- Prune belly syndrome. Orphanet website. www.orpha.net/static/GB/prune_belly_syndrome.html .

Question 223

A 6-year-old boy with nasal discharge is brought to the pediatric clinic. He has a history of allergic rhinitis that is controlled with cetirizine in the spring and fall. He was in his usual state of health until 2 weeks ago when he developed fever and malaise. His maximum temperature was 38.4°C, and the fever lasted for 2 days. He has had a runny nose since the onset of this illness, which worsened after about 1 week as the discharge changed in color from clear to white and became thicker. He has a temperature of 37.3°C, heart rate of 80 beats/min, respiratory rate of 22 breaths/min, and blood pressure of 105/70 mm Hg. He has audible nasal congestion, white discharge in the right nare, and swelling of the nasal turbinates in the left nare.

Of the following, the feature in this patient that would MOST support a diagnosis of acute bacterial sinusitis is

  A. duration of symptoms
  B. fever characterization
  C. predisposing condition
  D. quality of discharge
  E. turbinate appearance

Correct Answer: A

For the patient in this vignette, a diagnosis of acute bacterial sinusitis would be most supported by the symptom duration of 2 weeks. According to the "Clinical Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years" published by the American Academy of Pediatrics in 2013, the persistence of nasal discharge for 10 or more days without improvement meets criteria for acute bacterial sinusitis (**Item C223A**).

Item C223A. Criteria for the Diagnosis of Acute Bacterial Sinusitis.

Persistent symptoms

- Nasal discharge/congestion and/or cough for ≥10 days without improvement

Severe symptoms

- Temperature ≥38.5℃ with purulent rhinorrhea for at least 3 days

Worsening symptoms

- Worsening of nasal congestion or rhinorrhea, cough, and fever after a 3- to 4-day period of improved symptoms

Reprinted with permission of DeMuri G, Wald E. Acute bacterial sinusitis in children. *Pediatr Rev.* 2013; 34 (10):432.

Only 5% to 10% of upper respiratory infections are complicated by bacterial infection of the sinuses. To provide appropriate guidance to patients and families and avoid unnecessary antibiotic prescriptions, it is critical for pediatricians to distinguish viral upper respiratory infections from bacterial processes. Based on the 2013 guideline, criteria for acute bacterial sinusitis can be met with 1 of the 3 following patterns: persistent symptoms, severe symptoms, or worsening symptoms (**Item C223A**).

Item C223B. Major Complications of Sinusitis.

Intracranial
- Meningitis
- Subdural empyema
- Epidural empyema
- Brain abscess
- Venous sinus thrombosis

Orbital
- Optic neuritis
- Orbital cellulitis
- Orbital abscess
- Subperiosteal abscess
- Inflammatory edema (periorbital cellulitis)

Osteitis
- Maxillary
- Frontal (Pott puffy tumor)

Reprinted with permission of DeMuri G, Wald E. Acute bacterial sinusitis in children. *Pediatr Rev.* 2013; 34 (10):433.

The fever pattern for the patient in this vignette, fever at the onset of illness that resolves within 1 to 2 days, is typical of most viral processes. If the temperature had been higher ($\geq$ 38.5°C), had lasted for at least 3 days, and had been associated with purulent rhinorrhea, the patient in this vignette would have met criteria for acute bacterial sinusitis based on fever characteristics.

Allergies can predispose an individual to sinusitis. Approximately 20% of cases of acute bacterial sinusitis are thought to result from allergic inflammation of nasal mucosa. However, underlying conditions are not used to fulfill criteria for acute bacterial sinusitis.

In viral infections, including infections that do not progress to bacterial infection, there is a natural progression from clear watery discharge to thick purulent discharge caused by an influx of neutrophils. Purulent discharge is not independently predictive of a bacterial process and must be associated with other symptomatology to meet criteria for a bacterial infection. Additionally, the physical examination findings, including the appearance of the turbinates, do not distinguish between viral and bacterial upper respiratory infections.

The diagnostic criteria for simple acute bacterial sinusitis rely on information from the patient history and do not utilize culture or radiologic data. The nasal mucosa is heavily colonized with

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bacteria, and nasopharyngeal swabs or endoscopic samples from the middle meatus do not accurately reflect the microbiology of the sinuses. Imaging studies, similar to the physical examination, do not distinguish between viral and bacterial inflammation of sinus mucosa. Therefore, imaging is not necessary to confirm the diagnosis. Imaging is warranted only when complications of bacterial sinusitis are suspected (**Item C223B**).

Appropriate management of acute bacterial sinusitis includes antibiotics for children that meet clinical criteria. First-line antibiotics are amoxicillin or amoxicillin-clavulanate for a minimum of 10 days or for 7 days after the patient becomes symptom-free. Patients with suspected complications require parenteral therapy in addition to further investigation including imaging studies and potential surgical intervention.

PREP Pearls
- Only 5% to 10% of upper respiratory infections are complicated by bacterial infection of the sinuses.
- Criteria for acute bacterial sinusitis can be met with 1 of the 3 following patterns: persistent symptoms, severe symptoms, or worsening symptoms.
- Physical examination findings and radiologic imaging studies do not distinguish viral from bacterial inflammation of sinus mucosa.

ABP Content Specifications(s)
- Plan the appropriate management of acute sinusitis
- Plan the appropriate diagnostic evaluation of acute sinusitis while recognizing the limitations of some modalities
- Recognize complications associated with acute sinusitis

Suggested Readings
- DeMuri G, Wald E. Acute bacterial sinusitis in children. *Pediatr Rev.* 2013;34(10):429–437. doi: http://dx.doi.org/10.1542/pir.34-10-429.
- Wald E, Applegate K, Bordley C, et al. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. *Pediatrics.* 2013;132(1):e262–e280. doi: http://dx.doi.org/10.1542/peds.2013-1071.

Question 224

A 10-year-old girl is brought to your office for a new patient health supervision visit. Her family moved into the area a few months ago. When you ask the girl how she likes school, she tells you that it is "okay," except for a group of girls in her class who encourage others to exclude her from activities. They also frequently make fun of her accent and lack of athletic ability. She attempts to avoid these girls, but they follow her around on the playground. The girl's mother asks you if there is anything that can be done at school to address the situation.

Of the following, the BEST intervention you can recommend for implementation at the girl's school is to

A. allow the girl to stay in her classroom at recess
B. assign the involved girls to different classrooms
C. increase adult supervision of the school grounds
D. implement an anti-bullying intervention in the girl's class
E. suspend the students who are bullying

Correct Answer: C

Increasing adult supervision of school grounds (eg, playgrounds, restrooms, hallways) helps to make the environment safer for all students, and serves as a deterrent to bullies. As is typical, the problematic behaviors seen in this vignette are occurring outside the classroom.

During normal development, children may exhibit limited periods of aggressive behaviors such as hitting, biting, pushing, and making threats. Typical aggressive behaviors may present in children as tantrums in toddlers or defiance in adolescents. When aggressive behaviors persist, escalate, impair functioning, and/or are accompanied by delinquent acts (eg, vandalism, theft, assault), a child may meet criteria for a mental health condition such as oppositional defiant disorder or conduct disorder. Children with conditions such as attention-deficit/hyperactivity disorder (ADHD) or anxiety disorder may demonstrate aggressive behaviors in response to stressors. Standardized rating scales (eg, Child Behavior Checklist, Behavior Assessment System for Children) can help determine if a child's behaviors are outside the normal range for age.

Bullying is defined as repeated aggression (eg, verbal harassment, physical harm or threats, social exclusion) toward an apparently less powerful peer. Cyberbullying involves the use of electronic devices (eg, cell phones, computers) to threaten or harass peers. Bullying is common in children, with a prevalence rate between 15% and 50%. Bullying most commonly occurs at school, particularly during less supervised activities (eg, breaks, recess, lunch) and in less supervised settings (eg, playground, hallways).

Parents can teach their children appropriate social behaviors by role modeling, talking to them about empathy and compassion, and by avoiding the use of physical discipline. They can help their children understand that aggressive behaviors are not acceptable, and coach them on preferred approaches. Children should be encouraged to form positive relationships with their peers, and to use nonviolent means to resolve disagreements. They should be praised when demonstrating appropriate social behaviors. For toddlers demonstrating aggressive behavior, a simple statement (eg, "No hitting") followed by distraction or redirection can be effective. Older children and adolescents having difficulty with conflict resolution may benefit from social skills and/or anger management training. When behavioral strategies are not sufficiently effective in managing an aggressive child with ADHD or anxiety, psychopharmacologic agents (eg, stimulants or alpha-agonists for ADHD; selective serotonin reuptake inhibitors for anxiety) can be helpful.

Victims of bullying can be taught strategies to avoid situations in which they are vulnerable. These include avoidance of less supervised areas of the school, participation in structured activities during break times, and remaining near friends at school. They should be taught that reporting a student's inappropriate behavior to seek help is different from tattling to get that person in trouble. Because children who appear insecure are more likely to be bullied, these children can be taught how to look confident through role-modeling or participation in drama clubs. Activities that build self-esteem (eg, athletics, clubs) should be encouraged.

Effective interventions to address bullying are typically school-based and work to improve the school environment. They often include antiviolence or conflict resolution curricula. Successful programs aim to change the school culture with participation by the entire school, rather than a single classroom. Effective programs incorporate improved student supervision, school-wide rules and antibullying policies, parent training, and collaboration between schools and families. Zero-tolerance policies are ineffective in decreasing bullying; removing the bully from school (eg, suspension, expulsion) can unintentionally reward and thereby reinforce bullying behavior.

Allowing the girl in the vignette to stay in her classroom at recess does not address the problem, and isolating her decreases her opportunities for developing healthy relationships and friendships with her classmates. Assigning the girls to different classrooms does not address the behaviors that are occurring on the playground. The pediatrician can assist families dealing with aggressive behaviors in children by validating their concerns, providing strategies and resources for managing these behaviors, and advocating for violence prevention. Helpful antibullying resources include the American Academy of Pediatrics Connected Kids program (Connected Kids Clinical Guide) and www.stopbullying.gov.

PREP Pearls
- Bullying most commonly occurs at school and in less supervised settings (eg, playground, hallways).
- Effective antibullying programs incorporate improved student supervision, school-wide rules and antibullying policies, parent training, and collaboration between schools and families.
- Zero-tolerance policies are ineffective in decreasing bullying; removing the bully from school (eg, suspension, expulsion) can unintentionally reward and thereby reinforce bullying behavior.

ABP Content Specifications(s)
- Plan the appropriate management of aggressive or intimidating (bullying) behavior in patients of various ages, including those who are victims of such behavior
- Differentiate the findings associated with aggressive behavior from those of normal variants

Suggested Readings
- Glew GM, Frey KS, Walker WO. Bullying update: are we making any progress? *Pediatr Rev.* 2010;31(9):e68–e74. doi: http://dx.doi.org/10.1542/pir.31-9-e68.
- Shetgiri R. Bullying and victimization among children. *Adv Pediatr.* 2013;60(1):33–51. doi: http://dx.doi.org/10.1016/j.yapd.2013.04.004.
- Zahrt DM, Melzer-Lange MD. Aggressive behavior in children and adolescents. *Pediatr Rev.* 2011;32(8):325–331. doi: http://dx.doi.org/10.1542/pir.32-8-325.

Question 225

A 17-year-old adolescent boy is brought to the emergency department by emergency medical services. His parents arrive shortly afterwards. They report that he was found unconscious in his bathroom surrounded by a large volume of bright red blood vomitus. They found a vodka bottle in his room.

He is arousable but intoxicated. He continues to have intermittent hematemesis. He appears pale. He has a heart rate of 190 beats/min, respiratory rate of 32 breaths/min, and blood pressure of 80/52 mm Hg. He has a soft abdomen that is tender to palpation in the epigastric area with hypoactive bowel sounds and no mass. His skin is without rash.

Laboratory testing shows:
•Hemoglobin, 7.3 g/dL (73 g/L)
•Hematocrit, 25% (0.25)

The remainder of the laboratory results are pending.

Of the following, the MOST important next step is to

 A. obtain abdominal radiography
 B. perform a hemoccult of the stool
 C. perform upper gastrointestinal endoscopy
 D. start a proton pump inhibitor
 E. type and crossmatch for packed red blood cells

Correct Answer: E

For the adolescent boy in this vignette with significant hematemesis, sending a type and crossmatch for packed red blood cells is the most appropriate next step in management. It is likely that he has a gastric ulcer, gastritis, or both caused by excessive alcohol consumption. His blood loss has resulted in tachycardia and low blood pressure and requires intervention. Alcohol-induced gastritis is caused by a direct toxic effect of alcohol that leads to gastric inflammation and eventual ulceration. Alcohol also decreases gastric motility, increasing contact time and thus worsening the injury. The effect of alcohol on the gastric mucosa is dose dependent. However, the mechanisms leading to the inflammation are not fully understood. *Helicobacter pylori* infection and nonsteroidal anti-inflammatory drug use may also play roles in the inflammation and injury. Patients present with abdominal pain, heartburn, nausea, vomiting, and hematemesis.

The entire stomach is typically involved with alcoholic gastropathy with some worsening in the antral area. Ulcerations are typically small and heal quickly with discontinued exposure. Treatment is based on hemodynamic stabilization followed by use of proton pump inhibitors or H$_2$ receptor antagonists as well as discontinuation of exposure.

The differential diagnosis for hematemesis varies with age and is reviewed in **Item C225** .

Item C225. Differential Diagnosis of Hematemesis by Age Group.

Neonate	Infant	Child	Adolescent
Coagulopathy: congenital or vitamin K deficient	Esophagitis	Caustic ingestion	Caustic ingestion
Esophagitis	Gastrointestinal duplication	Esophagitis	Esophagitis
Gastrointestinal duplication	Gastric or esophageal varices	Foreign body	Foreign body
Milk or soy protein intolerance	Mallory-Weiss tear	Gastrointestinal duplication: Meckel diverticulum	Gastritis
Swallowed maternal blood	Milk or soy protein intolerance	Gastric or esophageal varices	Gastric or esophageal varices
Stress gastritis	Peptic injury	Hemolytic uremic syndrome	Inflammatory bowel disease
Trauma: orogastric or nasogastric tube placement	Stress gastritis	Mallory-Weiss tear	Mallory-Weiss tear
Vascular anomaly: hemangioma, telangiectasia, arteriovenous malformation, etc.	Vascular anomaly: hemangioma, telangiectasia, arteriovenous malformation, etc.	Nonsteroidal anti-inflammatory drug use	Nonsteroidal anti-inflammatory drug use
		Obstruction	Obstruction
		Peptic injury	Peptic injury: ulcers
		-	Pill esophagitis
		Stress gastritis	Stress gastritis
		Vascular anomaly: dieulafoy lesion, hemangioma, telangiectasia, arteriovenous malformation, etc.	Vascular anomaly: dieulafoy lesion, hemangioma, telangiectasia, arteriovenous malformation, etc.
		Vasculitis: Henoch-Schönlein purpura	Vasculitis: Henoch-Schönlein purpura

Courtesy of C. Waasdorp Hurtado

Presentation of upper gastrointestinal bleeding can vary significantly from bright red blood to coffee ground emesis. Point of care testing for occult blood can be used to confirm the presence of blood, because foods such as beets, red drinks, and red sauce can appear to be blood if vomited. Sudden onset of massive bleeding is concerning for a vascular etiology, while vomiting preceding hematemesis suggests a Mallory-Weiss tear, esophagitis, or gastritis. Epigastric pain suggests gastritis, esophagitis, or ulceration. Odynophagia should raise concern for infectious or chronic esophagitis, foreign body, caustic ingestion, and pill esophagitis. Consideration of underlying chronic disease, such as liver disease or coagulopathy, can help determine the etiology for upper gastrointestinal bleeding.

Assessment of upper gastrointestinal bleeding should start with evaluating the hemodynamic stability of the patient, placement of intravenous access, and resuscitation as indicated. These steps are concurrent with obtaining additional history and completing an extensive physical examination for stigmata of disease such as caput medusae associated with portal hypertension or a rash consistent with Henoch-Schönlein purpura. Significant bleeding is typically associated with large volume hematemesis and dropping hemoglobin levels.

Laboratory studies should include coagulation studies, complete blood cell count, liver function tests, and pancreatic enzymes. In a patient with significant gastrointestinal bleeding, type and crossmatch for packed red blood cells should be sent.

Abdominal radiography is useful to evaluate for a foreign body, obstruction, or perforation, but would not be the first step in the evaluation of the adolescent in this vignette. An upper gastrointestinal series is not recommended in acute bleeds as it can interfere with endoscopy and visualization of the bleeding source. Upper endoscopy should be performed in children who are clinically stable with clinical concern for continued bleeding or if there is a foreign body or caustic ingestion. The endoscopy can be diagnostic and therapeutic. Acid suppression is recommended in children with upper gastrointestinal bleeding, with intravenous medication used in children with severe bleeding. Studies of acid reduction in adults with gastrointestinal bleeding have shown decreases in hospital stay, re-bleeding, and transfusion; however, there are limited confirmatory studies in children.

PREP Pearls
- Assessment of hemodynamic stability is the first step in evaluation of any child with active gastrointestinal bleeding.
- The differential diagnosis for upper gastrointestinal bleeding is broad and varies by age.
- Endoscopy is used in children with significant or persistent upper gastrointestinal bleeding and can be both diagnostic and therapeutic.
- Proton pump inhibitors are recommended for treatment of upper gastrointestinal bleeding and may reduce hospital stay, re-bleeding, and the need for transfusion.

ABP Content Specifications(s)
- Formulate a differential diagnosis for vomitus that tests positive for occult blood
- Formulate a differential diagnosis for coffee-ground material in vomitus
- Formulate an age-appropriate differential diagnosis for vomiting bright red blood
- Recognize the clinical features associated with upper gastrointestinal bleeding
- Recognize the clinical features associated with alcohol-induced gastritis, and manage appropriately

Suggested Readings
- Chawla S, Seth D, Mahajan P, Kamat D. Upper gastrointestinal bleeding in children. *Clin Pediatr (Phila).* 2007;46(1):16–21. doi: http://dx.doi.org/10.1177/1084713806297151.
- Hizal G, Ozen H. Gastrointestinal bleeding in children. *J Pediatr Sci.* 2011;3(4):e100.
- Neidich GA, Cole SR. Gastrointestinal bleeding. *Pediatr Rev.* 2014;35(6):243–254. doi: http://dx.doi.org/10.1542/pir.35-6-243.
- Owensby S, Taylor K, Wilkins T. Diagnosis and management of upper gastrointestinal bleeding in children. J Am Board Fam Med. 2015;28(1)134–145. doi: http://dx.doi.org/10.3122/jabfm.2015.01.140153.

Question 226

You are seeing a 3-year-old boy in your office for a routine health supervision visit. He has been healthy, and his growth and development have been normal. The boy's mother tells you that over the past few months, he has become particularly interested in cars and trucks. He has a number of toy vehicles to play with, but he frequently insists on climbing into and out of real parked vehicles, pretending that he is repairing, cleaning, and driving them, while his father (who is self-employed as a mechanic) works on them in their driveway. The mother is concerned about her son's risk of getting injured as a result of these behaviors.

Of the following, you tell the mother that, based on national statistics, the type of injury her son is most likely to incur as a result of playing around and in parked vehicles is a

A. crush injury to his fingers
B. fall-related injury
C. heat-related injury
D. strangulation injury
E. thermal burn injury

Correct Answer: A

The type of injury the boy in the vignette is most likely to incur as a result of playing around and in parked vehicles is a crush injury to his fingers. Based on data published by the National Highway Traffic Safety Administration (NHTSA), it is estimated that more than 90,000 injuries resulting from noncrash automobile accidents affect children 14 years of age and younger in the United States each year. Most of these injuries occurred at the children's homes.

Among children, the most commonly reported noncrash automobile injuries are sustained from closing automobile doors and involve the extremities (most often the fingers and hands). These injuries account for approximately half of all reported noncrash automobile injuries affecting children, based on recent national statistics. Falls occurring while entering or exiting a vehicle, or from the exterior of a vehicle (such as the tailgate or bed of a pickup), are the next most commonly reported types of noncrash automobile injuries affecting children.

Other noncrash automobile injuries that are fairly common in children include lacerations caused by a vehicle part (eg, a license plate or bumper), injuries sustained from striking a stationary vehicle, and injuries resulting from being struck by a moving vehicle part (eg, an opening car door or pick-up truck tailgate).

Heat-related injuries are certainly a risk for children who are automobile passengers, as well as for those who play in or around vehicles. Heat stroke/hyperthermia has been the cause of most noncrash automobile-related *fatalities* involving children in recent years, but not the most common cause of injury. Since 1998, an average of 37 children have died each year because of vehicular-related heat stroke.

Children who play in cars are at risk of becoming strangled by seat belts or child safety seat straps, resulting in a small number of child fatalities.

Thermal burns secondary to contact with hot surfaces, on both the exterior and interior of automobiles, is a potential risk to children who are both in and around vehicles. These types of noncrash automobile accidents are less common than hand/finger crush injuries.

Parents and other caregivers should be advised not to let children play in or around cars, and to supervise children at all times when they are in and around vehicles. Parents should keep automobile doors and trunks locked at all times, when their vehicle is parked, to help protect their children from becoming victims of noncrash automobile accidents. Parents should also be cautioned to keep car keys and remote entry devices out of the sight and reach of children. A wealth of useful safety information related to protecting children from automobile-related injuries can be found at www.safercar.gov/parents, a website sponsored by the National Highway and Transportation Safety Administration (NHTSA).

PREP Pearls
- The most common type of noncrash automobile injury sustained by children involves the extremities (most commonly the fingers and hands) being crushed in closing automobile doors.
- Fall-related injuries are the second most common type of injury affecting children involved in noncrash automobile accidents.
- Heat stroke/hyperthermia is the cause of the majority of noncrash automobile-related fatalities involving children in recent years.
- Parents and other caregivers should be advised not to let children play in or around cars, and to supervise children at all times when they are in and around vehicles

ABP Content Specifications(s)
- Understand the effects of non-crash automobile accidents in young children

Suggested Readings
- Automobile-related safety tips for parents. Available online at https://www.nhtsa.gov/parents-and-caregivers Website maintained by the National Highway and Traffic Safety Administration .
- United States Department of Transportation, National Highway Traffic Safety Administration. Not-in-traffic surveillance: non-crash fatalities and injuries. Traffic Safety Facts. March 2015. http://noheatstroke.org/NHTSA2015.pdf.
- US Department of Transportation, National Highway Traffic Safety Administration. NHTSA studies vehicle safety and driving behavior to reduce vehicle crashes. https://www.nhtsa.gov/research-data.

Question 227

You are seeing a 9-month-old female infant for her routine health supervision visit. She has been healthy, but her mother raises concerns about the infant's behavior. Her mother reminds you that the infant was "colicky" until about 5 months of age and that she took extra time off work to stay at home as the primary caregiver. Now the mother would like to resume her career, but she is worried that her daughter is very attached to her. The infant does not adapt well to new environments and cries if left with a babysitter. The mother describes the baby as usually quiet and content, but easily upset around new people. After she gets to know them, she is less fussy and becomes more friendly. She sleeps well with an established sleep routine. She has been growing at a normal velocity, but the mother reports she does not easily accept new foods as they are introduced into her diet, so she eats a limited number of puréed vegetables. You discuss the infant's temperament with the mother to help her understand how best to plan for the upcoming change in daytime caregivers.

Of the following, the category of temperament that BEST describes this infant is

A. difficult
B. easy
C. overanxious
D. routine regulated
E. slow to warm

Correct Answer: E

The infant in this vignette best fits the temperament category of slow to warm. Although she is fussy when presented with new environments or caregivers, she eventually calms and becomes friendly. She has an established sleep routine, and she accepts new foods slowly. She would most likely initially withdraw from new situations or observe hesitantly before entering into a new activity, but her negative response is moderate and she gradually warms up to the setting.

Temperament is defined as the way one behaves or responds to the environment. Temperament is influenced by genetics, environmental factors, and physical condition. Temperament is most often classified into the categories of difficult, easy, or slow to warm. Overanxious and routine regulated are not categories of temperament as described in the literature. The 9 attributes of temperament are: activity level, rhythmicity or regularity, initial approach/withdrawal, adaptability, intensity, mood, persistence/attention span, distractibility, and sensory threshold. Children with difficult temperaments have more intense emotional reactions, adapt poorly to new situations, are unpredictable, have a lower sensory threshold, and are viewed as moody and negative. Children with easy temperaments are adaptable, have regular sleeping and eating patterns, tend to be less demanding, and are cheerful.

Temperament traits are real, and it is helpful for parents to understand how these traits may impact interactions with their child. Parenting styles and techniques are most successful when they accommodate for temperament differences rather than attempting to change them, especially in young children. When a child's temperament fits poorly with parental expectations, the child may exhibit reactive behavioral problems and parents may report a great deal of distress or poor self-efficacy. Pediatric health care providers should help parents and caregivers identify normal behavior differences, disallow misperceptions, discourage the placement of blame, and offer guidance on parenting techniques or discipline based on the child's temperament. Also, encouragement may be given that as children grow older, they can learn to moderate their own temperamental reactions.

PREP Pearls
- Temperament is most often classified as difficult, easy, or slow to warm.
- Attributes related to temperament are: activity level, rhythmicity or regularity, initial approach/withdrawal, adaptability, intensity, mood, persistence/attention span, distractibility, and sensory threshold.
- Variation in temperament traits is real, and it is important for parents to understand how these traits may impact interactions with their child.

ABP Content Specifications(s)
- Understand the variations in temperament in infants, and counsel parents appropriately

Suggested Readings

- Balck R, Glass P. Temperament and school performance. *Pediatr Rev.* 1998;19(5):177. doi: http://dx.doi.org/10.1542/pir.19-5-177.
- Carey WB. Teaching parents about infant temperament. *Pediatrics*. 1998;102(5 suppl E):1311–1316. http://pediatrics.aappublications.org/content/102/Supplement_E1/1311.
- Weissbluth M. Healthy Sleep Habits, *Happy Child*. 3rd ed. New York, NY: Random House; 2009.

Question 228

You are a member of the hospital safety committee. You have been asked to the review and make recommendations regarding a serious patient safety event. A 6-month-old male infant was admitted for a right inguinal hernia repair. The surgical procedure was performed on the left side.

Of the following the MOST appropriate next step in this situation is

A. mental health counseling for the operating physician
B. remedial training of the operating room staff
C. review of operating room procedures
D. review of risk management reporting protocols
E. termination of employment of the operating physician

Correct Answer: C

Of the answer choices, the most appropriate next step is to review the operating room procedures. Disclosure to the family would also be an important early step in the response to this event. Mental health counseling for the operating physician, remedial training of the operating room staff, review of the risk management reporting protocols, and termination of employment of the operating physician may also be appropriate consequences of this event, but would not be the most appropriate next step.

Patient safety has been defined by the Institute of Medicine as the prevention of patient harm and freedom from accidental injury in healthcare settings. To ensure patient safety, the American Academy of Pediatrics recommends thorough processes for identifying and reporting of medical errors and adverse events. A medical error is defined as an act of either commission or omission that increases risk of an unfavorable patient outcome. An adverse event, patient harm resulting from medical care, may result from a medical error.

While the incidence of pediatric adverse events is unclear, these events are typically preventable. The costs of adverse events are estimated to account for 18% to 45% of health care expenditures in the United States.

The American Academy of Pediatrics Committee on Medical Liability and Risk Management, Council on Quality Improvement and Patient Safety issued the following recommendations:
- Pediatric health care providers and institutions should develop and implement their own policies and procedures for identifying and disclosing adverse events to patients and families in an honest and empathetic manner as part of a nonpunitive culture of medical error reporting.
- Pediatric institutions and practices should develop policies and procedures to provide emotional support for clinicians involved in adverse events.
- Pediatric medical educators should develop and implement educational programs regarding identification and prevention of medical errors and communication about adverse events with patients and their families as part of a comprehensive patient safety curriculum.

The Joint Commission Sentinel Event Policy provides guidance regarding the investigation of patient safety events. Recommendations include:
- A formalized team response that stabilizes the patient, discloses the event to the patient and family, and provides support for the family and staff involved
- Notification of organizational leadership
- Prompt investigation
- Completion of a comprehensive systematic analysis to identify any causal and contributory factors
- Corrective actions to address causal and contributory factors
- Action plan and timeline for implementation of corrective actions
- Systemic improvement

American academy of pediatrics   791

PREP Pearls

- The American Academy of Pediatrics Committee on Medical Liability and Risk Management, Council on Quality Improvement and Patient Safety issued the following recommendations.
    1. Pediatric health care providers and institutions should develop and implement their own policies and procedures for identifying and disclosing adverse events to patients and families.
    2. Pediatric institutions and practices should develop policies and procedures to provide emotional support for clinicians involved in adverse events.
    3. Pediatric medical educators should develop and implement educational programs regarding identification and prevention of medical errors and communication about adverse events.

ABP Content Specifications(s)

- Understand the relationship between the detection of a medical error and the ability to discover and effect improvements

Suggested Readings

- Committee on Medical Liability and Risk Management, Council on Quality Improvement and Patient Safety. Disclosure of adverse events in pediatrics. *Pediatrics*. 2016;138(6):e20163215. doi: http://dx.doi.org/10.1542/peds.2016-3215.
- The Joint Commission. Sentinel event policy and procedures. https://www.jointcommission.org/sentinel_event_policy_and_procedures/. Accessed March 28, 2017.

Question 229

A 7-month-old male infant is brought to the emergency department by ambulance for vomiting and lethargy. His parents report that he was sitting on the front step of the house earlier in the day when he fell over and hit the right side of his head on the driveway. The fall was approximately 4 in (10 cm) from the step to the driveway. Both surfaces are cement. He cried immediately and was consoled, but 3 hours later he started vomiting. His parents noticed that he was not easily arousable and called 911.

He was born full term following an uncomplicated pregnancy, although his postnatal course was complicated by prolonged bleeding from a circumcision. He has had normal growth and development and has never been hospitalized or had surgery.

On physical examination, he is poorly responsive. There is a large palpable ecchymosis and superficial abrasions on the right side of his head. There is also nonpalpable bruising on his knees and elbows.

You perform a laboratory evaluation that reveals:

Laboratory Test	Result
White blood cell count	8,100/µL (8.1 x 10^9/L)
Hemoglobin	11.1 g/dL (111 g/L)
Platelet count	342 x 10^3/µL (342 x 10^9/L)
Mean corpuscular volume	73 fL
Prothrombin time	12.1 s (normal, 10.8-13.9 s)
Partial thromboplastin time	53 s (normal, 26.6-30.3 s)
Mixing studies	Correction of partial thromboplastin time

Head computed tomography reveals a large subdural hemorrhage on the right side.

Of the following, the MOST likely cause of the infant's intracranial bleed is

A. child abuse
B. factor VII deficiency
C. factor IX deficiency
D. factor X deficiency
E. an inherited disorder of platelet function

Correct Answer: C

The infant in this vignette has a large intracranial bleed after a minor trauma. He also has a history of excessive bleeding from a circumcision and has an abnormal partial thromboplastin time (PTT). This constellation of signs, symptoms, and laboratory values should raise concern for a bleeding disorder. Mixing studies can determine whether abnormal coagulation values are caused by interfering antibodies or factor deficiency by taking advantage of the fact that 50% of a normal factor level will result in a normal prothrombin time (PT) and PTT. If a patient's plasma has 0% of a given factor, mixing equal amounts of patient plasma and normal plasma, which has 100% of the given factor, results in a mixture that has 50% of the given factor, which is sufficient to correct the PT and PTT. Correction suggests a factor deficiency because the addition of normal plasma has provided a sufficient amount of the deficient factor to normalize the results. A lack of correction suggests the presence of an interfering antibody because the addition of normal plasma with all of the coagulation factors present does not correct the result. Thus, the correction of the PTT in a mixing study means that the infant in this vignette has a decreased or absent coagulation factor.

The fact that the PTT is prolonged but the PT is normal means that the factor must reside in the intrinsic coagulation factor pathway (**Item C229**). Factor IX is the only factor among the list of possible answers that is in the intrinsic pathway. Factor IX deficiency (also called hemophilia B or Christmas disease) is an X-linked bleeding disorder with the affected gene located at Xq27.1-q27.2. Although it is most commonly inherited from a carrier mother, one-third of cases of factor IX deficiency are the result of a spontaneous mutation in the factor IX gene. Thus, the absence of a family history of hemophilia should not change the index of suspicion for a boy who has abnormal bleeding. The severity of the bleeding disorder is defined by the plasma level of circulating factor IX:
- Severe factor IX deficiency (factor levels < 1%) accounts for 60% of cases
- Moderate factor IX deficiency (factor levels of 1%-5%) accounts for 15% of cases
- Mild factor IX deficiency (factor levels of 6%-30%) accounts for 25% of cases
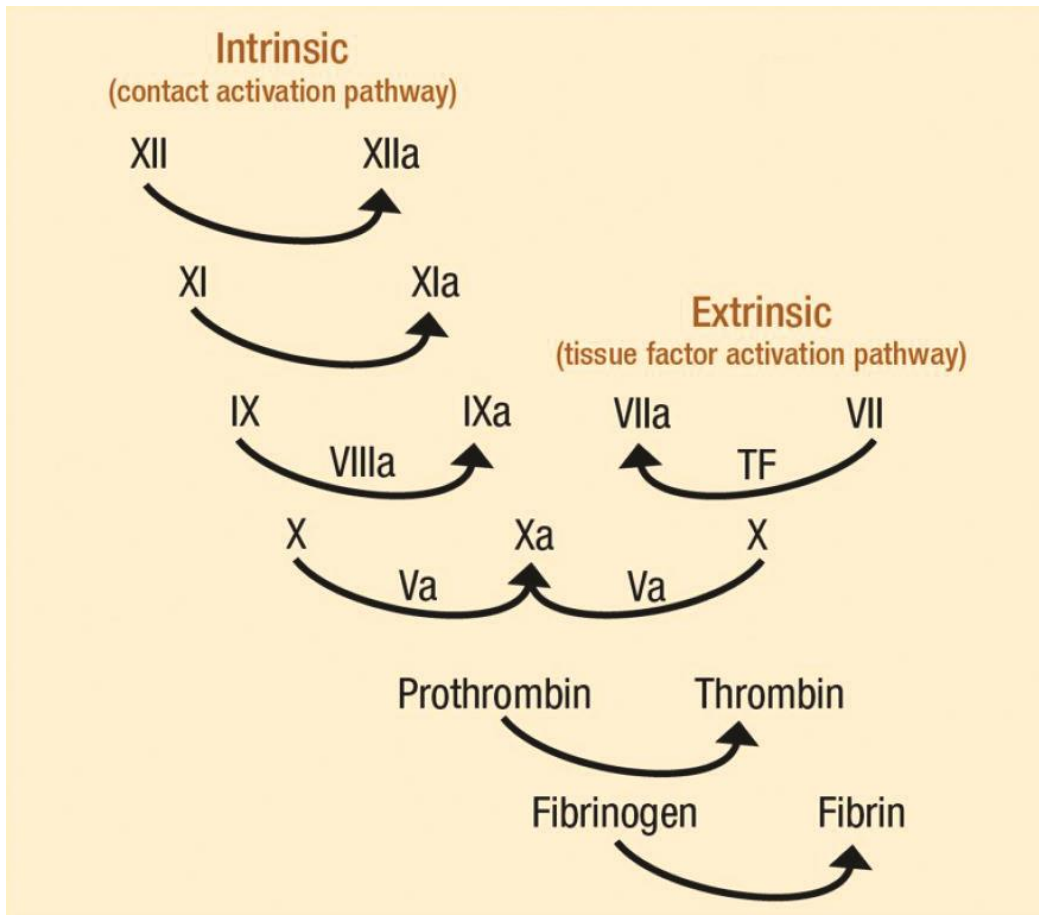
Item C229: Coagulation Pathways.   Reprinted with permission from the Mayo Clinic Foundation for Medical Education and Research. All rights reserved.

Factor IX deficiency (hemophilia B) accounts for 20% to 25% of hemophilia cases. Factor VIII deficiency (hemophilia A), which is also X-linked, is the most common form of hemophilia, accounting for 75% to 80% of hemophilia cases. Treatment for hemophilia A or B includes intravenous infusion of recombinant replacement factors.

Factor VII is in the extrinsic pathway, thus a low factor VII level would result in an isolated prolonged PT and a normal PTT. Factor X is in the common pathway, so a low factor X level would result in both a prolonged PT and PTT. The patient's history is very concerning for a bleeding disorder, and the prolonged PTT makes child abuse extremely unlikely. Although inherited disorders of platelet function could lead to severe bleeding and can present with a normal platelet count, they would not present with a prolonged PTT.

PREP Pearls
- A mixing study is performed by mixing patient plasma with normal plasma in a 1:1 ratio and then repeating the prothrombin time and partial thromboplastin time at specified time intervals. If there is an absent or low level of a coagulation factor in the patient plasma, the prothrombin time and partial thromboplastin time will correct with the addition of normal plasma.
- Factor IX deficiency is an X-linked bleeding disorder, although one-third of cases are sporadic.

ABP Content Specifications(s)
- Recognize clinical findings associated with intracranial bleeding, and manage appropriately
- Recognize the clinical manifestations and complications associated with hemophilia, and manage appropriately

Suggested Readings
- Acharya SA. Rare bleeding disorders in children: identification and primary care management. *Pediatrics*. 2013;132(5):882–892. doi: http://dx.doi.org/10.1542/peds.2012-3662.
- Rodriguez V, Warad D. Pediatric coagulation disorders. *Pediatr Rev*. 2016;37(7):279–291. doi: http://dx.doi.org/10.1542/pir.2015-0062.
- Zimmerman B, Valentino LA. Hemophilia: in review. *Pediatr Rev*. 2013;34(7):289–294. doi: http://dx.doi.org/10.1542/pir.34-7-289.

Question 230

A 7-year-old previously healthy girl is brought to the infectious diseases clinic for evaluation of fever of unknown origin. The illness began 10 days ago, and she has had daily fever with a maximum temperature of 40°C. She has had headaches, and 6 days ago she developed a rash involving her face, thorax, and extremities. She has not had eye redness, lip cracking, or extremity swelling. She has a temperature of 36.9°C, heart rate of 129 beats/min, respiratory rate of 24 breaths/min, and blood pressure of 102/62 mm Hg. She has mild pallor and faint red macules over the thorax and extremities. The liver edge is palpable 2 cm below the costal margin, and the spleen tip is palpable. Laboratory data are shown:

Laboratory Test	Result
White blood cell count	7,700/µL (7.7 x 10^9/L)
Hemoglobin	11.5 g/dL (115 g/L)
Platelet count	123 x 10^3/µL (123 x 10^9/L)
Neutrophils	73%
Lymphocytes	22%
Monocytes	5%
Mononucleosis screen	Negative
Epstein-Barr viral capsid antigen IgM	≤ 0.90
Epstein-Barr virus IgG	2.96 (positive, ≥ 1.10)
Epstein-Barr virus nuclear antigen IgG	4.42 (positive, ≥ 1.10)

Of the following, the BEST interpretation of this patient's laboratory data is that an Epstein-Barr virus infection

A. has not occurred
B. is active
C. is reactivated
D. occurred at least 4 months ago
E. occurred within the last 2 months

Correct Answer: D

The best interpretation of this patient's laboratory data is that an Epstein-Barr virus (EBV) infection occurred at least 4 months ago. The serologic findings were negative for EBV IgM and positive for EBV IgG and EBV nuclear antigen (EBNA) IgG. As noted in **Item C230**, IgG against EBNA becomes detectable 1 to 2 months after infection but overlaps with IgM against viral capsid antigen (VCA) until about 3 to 4 months after infection.
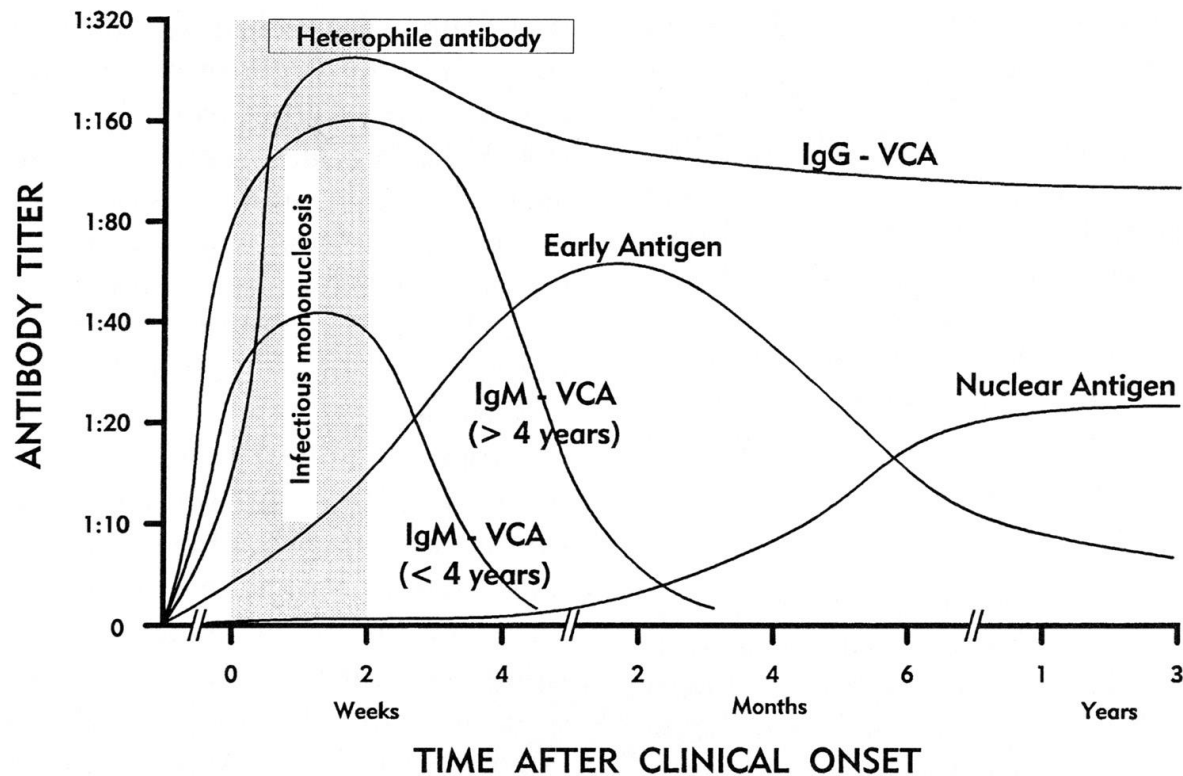
Item C230: VCA, viral capsid antigen. EBV-specific serologic responses in infectious mononucleosis
Jenson HB. Epstein-Barr virus. In: Detrick B, Hamilton RG, Folds JD, eds. *Manual of Molecular and Clinical Laboratory Immunology*. 7th ed. Washington, DC: American Society for Microbiology; 2006:637–647

In the setting of an acute infection, serologic findings for both IgM and IgG against VCA are expected to be positive. The IgG against VCA persists for life. The IgM against VCA declines in the weeks to months that follow an acute infection and is replaced with IgG against EBNA. Acute or recent infection is suggested by the presence of IgM against VCA and the absence of IgG against EBNA. A past infection is suggested by the absence of EBV IgM and the presence of IgG against EBNA. The patient in this vignette could have had acute primary infection in the preceding months or years.

If infection had not previously occurred, the serologic results for all EBV antibodies would be expected to be negative. In an active infection, the presence of antibodies against EBNA would not be expected. Two months from the start of infection, IgM against VCA could still be present.

Lastly, reactivation could have the serologic pattern observed in the patient in this vignette; however, reactivation would be best supported by a high level of antibody against early antigen, which was not provided in this vignette.

Infection with EBV can manifest purely as a febrile illness. Infectious mononucleosis is characterized by fever, pharyngitis, lymphadenopathy (especially cervical), and hepatosplenomegaly. Periorbital edema and palatal petechiae can be present. Infectious mononucleosis is noted in adolescents and adults whereas infection in young children is often not recognized. Up to 10% of patients with infectious mononucleosis experience fatigue for months to years following infection. In patients with primary immune deficiencies and in patients that have received organ or stem cell transplants, EBV can be associated with a lymphoproliferative disorder. Infection with EBV has been associated with lymphomas and carcinomas including Burkitt lymphoma, Hodgkin lymphoma, and nasopharyngeal carcinoma.

PREP Pearls
- Acute or recent Epstein-Barr virus infection is suggested by serological results that are positive for IgM against viral capsid antigen and negative for IgG against Epstein-Barr virus nuclear antigen.
- A past Epstein-Barr virus infection is suggested by serological results negative for Epstein-Barr virus IgM and positive for IgG against Epstein-Barr virus nuclear antigen.
- A past Epstein-Barr virus infection is suggested by serological results negative for Epstein-Barr virus IgM and positive for IgG against Epstein-Barr virus nuclear antigen.
- Lymphoproliferative disorders associated with Epstein-Barr virus infection can occur in immunocompromised individuals.

ABP Content Specifications(s)
- Identify the clinical features associated with Epstein-Barr virus infection in normal and immunocompromised children of various ages
- Assess the results of laboratory evaluation of a patient in whom Epstein-Barr virus infection is suspected, including the ability to distinguish between acute and past infection

Suggested Readings
- American Academy of Pediatrics. Epstein-Barr 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; 2015:336–340.
- Jenson HB. Epstein-Barr virus. *Pediatr Rev*. 2011;32(9):375–384. doi: http://dx.doi.org/10.1542/pir.32-9-375.
- Pinninti S, Hough-Telford C, Pati S, Boppana S. Cytomegalovirus and Epstein-Barr virus infections. *Pediatr Rev*. 2016;37(6):223–234. doi: http://dx.doi.org/10.1542/pir.2015-0072.

Question 231

A 4-week-old male infant born at 40 weeks of gestation is brought to your office for a health supervision visit. His mother is concerned that his face is "uneven." His birth history was significant for prolonged labor of 30 hours with vacuum-assisted delivery, and his birthweight was 4.1 kg. In the office today, he weighs 4.5 kg. On physical examination, he has mild right forehead flattening, his left eye appears slightly smaller than the right eye, and the left jaw line is tilted. Passive lateral flexion of the neck to the right is limited, and there is a firm, well-circumscribed mass palpable on the left inferolateral aspect of the neck.

Of the following, the MOST likely etiology of this infant's findings is

A. benign paroxysmal torticollis of infancy
B. congenital vertebral anomaly
C. fracture of the clavicle
D. trauma to the sternocleidomastoid muscle
E. weakness of the superior oblique muscle

Correct Answer: D

The infant in the vignette has congenital muscular torticollis (CMT), likely secondary to trauma to the sternocleidomastoid muscle. Congenital muscular torticollis is the most common cause of torticollis in infants. The etiology of the muscular trauma is uncertain, but experts theorize that it results from positioning during fetal head descent or abnormal intrauterine positioning. Others suggest that it is due to direct trauma to the muscle during difficult deliveries. It is a prominent cause of positional plagiocephaly, and prompt treatment early in infancy can prevent this deformity.

In infants with congenital muscular torticollis, the head is usually tilted toward the side of the injured muscle. There may be skull and facial asymmetry, including jaw asymmetry, and the ear and eye ipsilateral to the injured side can appear smaller. The contralateral occipital and ipsilateral frontal areas are flattened. A cephalocaudal view of the infant can highlight the asymmetry on physical examination (**Item C231**).

Right frontal flattening

Left ear anteriorly shifted
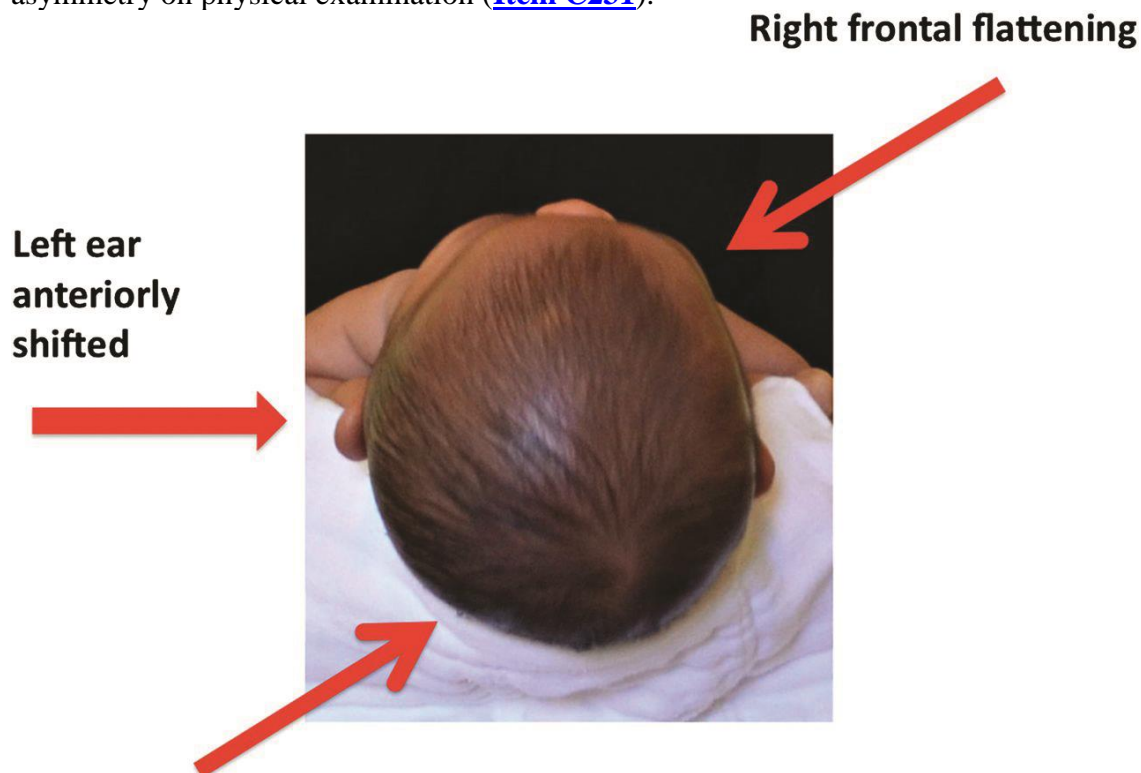
Left parietal flattening

Item C231: Features of asymmetry related to plagiocephaly in a 4-month-old infant
Reprinted with permission from Kuo AA, Tritasavit S, Graham JM. Congenital muscular torticollis and positional plagiocephaly. *Pediatr Rev*. 2014;35(2):81

There is an association between CMT and developmental delays. Congenital muscular torticollis can affect postural and gross motor development, because persistence of head tilt affects the

infant's balance and perception of the environment. Hypotonia can also worsen the effects of CMT, because the infant is less likely to self-correct the abnormality.

A physical examination, with attention to the neck's range of motion, can be helpful in confirming the diagnosis. In infants, full passive range of motion in rotation is 100 degrees to 110 degrees, and full cervical passive range of motion in lateral flexion is between 65 degrees and 75 degrees. It is important to note that CMT can be bilateral, which is particularly challenging to diagnose. Early diagnosis is key, because CMT can be corrected with timely treatment. Most infants respond to a home exercise program, which can be taught to caregivers by pediatricians or physical therapists. Prone positioning while awake (tummy time) may decrease the risk of positional plagiocephaly.

Benign paroxysmal torticollis of infancy (BPTI) is another cause of head tilt, which presents in the first several months after birth. Symptoms may also include vomiting, irritability, and increased drowsiness. The etiology of BPTI is not known, but is thought to be related to migraine physiology. It is self-limited, but can be recurring. Episodes usually last a few hours, and occasionally for several days.

Congenital vertebral anomalies can cause CMT, but is a much rarer cause than sternocleidomastoid muscle trauma. Clavicular fracture is a known complication of difficult deliveries. Affected infants commonly exhibit fussiness with movement of the arm on the involved side. The fracture is self-resolving, but can be associated with brachial plexus injury. Clavicular fracture does not cause the symptoms described in the vignette. Congenital fourth cranial nerve palsy can affect the superior oblique muscle. Affected infants commonly develop head tilt in an attempt to improve vision; however, a sternocleidomastoid muscle mass is not associated with this condition.

PREP Pearls
- Congenital muscular torticollis (CMT) is the most common cause of torticollis in infancy.
- Congenital muscular torticollis presents with asymmetric craniofacial physical examination findings, including jaw asymmetry and the appearance that the ear and eye ipsilateral to the injured side are smaller.
- Early treatment of congenital muscular torticollis can prevent the positional plagiocephaly that commonly results from this condition.

ABP Content Specifications(s)
- Differentiate the clinical findings associated with congenital torticollis from those of paroxysmal torticollis
- Identify the etiology of torticollis

Suggested Readings

- Kuo AA, Tritasavit S, Graham JM. Congenital muscular torticollis and positional plagiocephaly. *Pediatr Rev.* 2014;35(2):79–87. doi: http://dx.doi.org/10.1542/pir.35-2-79.
- Yaghin O, Badihian N, Badihian S. The efficacy of topiramate in benign paroxysmal torticollis of infancy: report of four cases. *Pediatrics.* 2016;137(4):e20150868. doi: http://dx.doi.org/10.1542/peds.2015-0868.

Question 232

You are evaluating a 2-day-old term male newborn. The 4.0-kg newborn was born to a 35-year-old primigravida mother by emergent cesarean delivery because of bradycardia and umbilical cord prolapse. Maternal history is significant for type 2 diabetes diagnosed at 33 years of age. Gestational history is only significant for polyhydramnios. The newborn required resuscitation with positive pressure ventilation in the delivery room. The Apgar scores were 1, 3, and 5 at 1, 5, and 10 minutes, respectively.

The newborn has a current weight of 3.8 kg, temperature of 37°C, heart rate of 158 beats/min, respiratory rate of 44 breaths/min, blood pressure of 110/76 mm Hg, and pulse oximetry of 96% on 2 L oxygen by nasal cannula. He has warm, pink extremities with capillary refill time of 3 seconds, clear and equal lung sounds bilaterally, and a right flank mass.

Ultrasonographic examination is significant for an enlarged right kidney with loss of corticomedullary differentiation. The left kidney is normal. No hydronephrosis or bladder abnormality is noticed.

Laboratory studies indicate:

Laboratory Test	Result
Serum	
White blood cell count	25,000/µL (25 x 10^9/L)
Hemoglobin	20.1 g/dL (201 g/L)
Platelet count	90 x 10^3/µL (90 x 10^9/L)
Blood urea nitrogen	40 mg/dL (14.3 mmol/L)
Creatinine	2.1 mg/dL (186 µmol/L)
Urine (Test Strip and Microscopy)	
Specific gravity	1.010
Blood	3+
Protein	2+
Red blood cells	> 100 per high-power field

Of the following, the MOST likely cause of the patient's findings is

A. multicystic dysplastic kidney
B. posterior urethral valves
C. renal dysplasia
D. renal vein thrombosis
E. ureteropelvic junction obstruction

Correct Answer: D

Neonatal serum creatinine concentration (usually < 1.0 mg/dL [88.4 µmol/L]) is reflective of maternal serum creatinine concentration. In a full-term neonate, the serum creatinine concentration normalizes in 7 to 10 days, whereas in a preterm infant, it may take up to 1 month to normalize. A serum creatinine concentration higher than 1.5 mg/dL (133 µmol/L) usually indicates acute kidney injury (also known as acute renal failure), as seen in the newborn in this vignette. The recent neonatal acute kidney injury KDIGO (Kidney Disease: Improving Global Outcomes) definition proposes risk stratification for acute kidney injury in newborns based on serum creatinine levels and urine output (**Item C232**). For management of neonatal acute kidney injury, it is important to evaluate the urine output. Placement of a urinary catheter is useful in evaluating neonates with oliguria/anuria as the catheter bypasses the urethral/bladder outlet obstruction (eg, posterior urethral valves in boys) and also provides an accurate estimate of urine output. Initial evaluation in an infant with acute renal failure should include a detailed history and physical examination. The obstetric history should focus on presence or absence of oligohydramnios, polyhydramnios, renal anomalies on antenatal ultrasonography, drug exposure, and family history of renal failure. Physical examination should evaluate genitalia, abdomen (flank mass or palpable bladder), and signs of oligohydramnios/Potter sequence. Initial laboratory evaluation will include electrolytes, serum urea nitrogen, creatinine, complete blood cell count, and urinalysis. Renal ultrasonography allows diagnosis of congenital anomalies of the kidney and urinary tract, urinary obstruction (hydronephrosis, hydroureter, enlarged bladder), or abnormal renal blood flow (arterial or venous) as the underlying etiology for acute renal failure.

Item C232. Neonatal Acute Kidney Injury KDIGO Classification.

Stage	Serum Creatinine	Urine Output
0	No change in SCr or rise <0.3 mg/dL	≥ 0.5 mL/kg/h
1	SCr rise ≥0.3 mg/dL within 48 h or SCr rise ≥1.5 - 1.9 x reference SCr[a] within 7 d	< 0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥2.0 – 2.9 x reference SCr[a]	< 0.5 mL/kg/h for ≥12 h
3	SCr rise ≥3 x reference SCr[a] or SCr ≥2.5 mg/dL[b] or Receipt of dialysis	< 0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

KDIGO, Kidney Disease: Improving Global Outcomes; SCr, Serum Creatinine

Differences between the proposed neonatal acute kidney injury definition and KDIGO include the following:

[a] Reference SCr will be defined as the lowest previous SCr value

[b] SCr value if 2.5 mg/dL represents <10 mL/min/1.73m²

Reprinted with permission from Selewski DT, Charlton JR, Jetton JG, et al. Neonatal acute kidney injury. *Pediatrics*. 2015;136(2):e465.

In the neonatal period, asphyxia, hypovolemia, sepsis, and vascular thrombosis are risk factors for acute kidney injury. Renal vein thrombosis is the most common cause of noncatheter-associated thrombosis in the newborn and is the most likely cause of the findings in the newborn described in this vignette. Prematurity, perinatal asphyxia, shock, dehydration, sepsis, polycythemia, cyanotic congenital heart disease, and maternal diabetes have all been associated with an increased risk for renal vein thrombosis. Flank mass, thrombocytopenia, and hematuria (as present in this patient) are the classic features associated with renal vein thrombosis. Renal vein thrombosis may also be associated with elevated blood pressure, laboratory features of disseminated intravascular coagulation, and leukocytosis. Ultrasonography of the kidney is the imaging modality of choice for diagnosing renal vein thrombosis in a newborn. In the early stages of thrombosis, the kidneys appear swollen and echogenic. The subsequent loss of

corticomedullary differentiation followed by scarring and decreased renal size occurs gradually. Color Doppler examination on renal ultrasonography will show absent intrarenal and renal venous flow in the early stages of thrombosis.

Renal dysplasia is one of the disorders of renal development categorized under the broader category of congenital anomalies of the kidney and urinary tract. Congenital anomalies of the kidney and urinary tract and and cystic kidney diseases (nonglomerular) account for nearly 60% of pediatric chronic kidney disease. Patients with congenital anomalies of the kidney and urinary tract may develop acute renal failure in the presence of severe bilateral hypoplasia or dysplasia, risk factors of neonatal acute renal failure (perinatal asphyxia, hypovolemia, sepsis, and vascular thrombosis), or urinary obstruction.

Abnormal renal development may lead to the following disorders:
- Hypoplasia is characterised by a lower number of normal nephrons with no evidence of abnormal renal parenchyma. Hypoplasia is usually diagnosed by a kidney size 2 standard deviations below the mean for age or by the presence of renal scarring on DMSA (^{99m}Tc-dimercaptosuccinic acid) radionuclide scan in the absence of secondary causes of scarring or reduced renal mass (urinary tract infection, surgery).
- Dysplasia is confirmed only by histology with demonstration of disorganized nephrons (tubules and glomerular), abnormal differentiation of mesenchymal and epithelial elements, and a decreased number of nephrons. Dysplastic kidneys are usually small because of the reduced number of nephrons, resulting in renal hypodysplasia.
- Abnormal ascent of the kidneys from the pelvis, renal ectopy (eg, pelvic kidney), and fusion anomalies (horseshoe kidney)
- Abnormalities in development of the urinary collecting system, as seen in duplicated collecting systems, posterior urethral valves (PUV), and ureteropelvic junction (UPJ) obstruction

Abnormal renal development is multifactorial and may be caused by genetic and environmental etiologies (teratogens). Renal dysplasia is often diagnosed during routine antenatal ultrasonography screening or postnatal ultrasonography performed in a dysmorphic infant. Renal dysplasia on ultrasonography is characterized by increased echogenicity, poor corticomedullary differentiation, and parenchymal cysts. Neonates with oligohydramnios and bilateral dysplasia are more likely to be identified earlier. Patients with unilateral renal dysplasia with a normal contralateral kidney showing compensatory growth have excellent outcomes with decreased risk for chronic kidney disease. This contrasts to increased risk for chronic kidney disease in patients with suboptimal compensatory hypertrophy of the contralateral kidney. Chronic kidney disease in such patients may lead to elevated blood pressure, growth retardation (height less than the fifth percentile), and pallor. Tubulointerstitial injury associated with congenital anomalies of the kidney and urinary tract leads to reduced urinary concentration (acquired nephrogenic diabetes insipidus). These patients usually develop polyuria with or without enuresis. Blood pressure, urinalysis results, and serum creatinine levels should be initially monitored yearly and subsequently monitored more frequently depending on the stage of chronic kidney disease.

Patients with multicystic dysplastic kidney are usually asymptomatic. Multicystic dysplastic kidney is suspected based on renal abnormalities detected on antenatal ultrasonography or in neonates with an abdominal mass detected by physical examination. Classic findings on renal ultrasonography include multiple noncommunicating cysts with intervening dysplastic renal tissue. The contralateral normal kidney has increased risk for congenital renal anomalies such as vesicoureteral reflux.

Posterior urethral valves are identified by antenatal ultrasonography in most cases. Lack of prenatal care can lead to patients with PUV exhibiting symptoms later in childhood with urinary tract (more common) or respiratory (less common) problems. Postnatally, patients with PUV may develop urinary tract infection, failure to thrive, abdominal distension (from enlarged bladder), and poor urinary stream or voiding difficulty. Older boys may develop urinary tract infections or voiding dysfunction (urinary frequency, daytime and nocturnal enuresis, and poor urinary stream). Some of these patients may exhibit respiratory distress in the neonatal period. Neonates with PUV can have oligohydramnios caused by decreased fetal urinary excretion associated with severe bladder outlet obstruction. This condition would lead to pulmonary hypoplasia because normal amniotic fluid levels between 16 and 28 weeks of gestation are required for normal lung development. The outcome for neonates with lung hypoplasia caused by severe PUV is poor. Ultrasonographic findings of bilateral hydronephrosis, dilated bladder, thickened bladder wall, and a dilated posterior urethra in male patients are highly suggestive of underlying PUV. Bilateral hydronephrosis in PUV is caused by urinary tract obstruction distal to the urinary bladder in the prostatic urethra from persistent and obstructing urogenital membrane.

Congenital ureteropelvic junction obstruction is most commonly diagnosed upon postnatal evaluation of antenatal hydronephrosis detected on maternal ultrasonography screening. In the absence of antenatal screening, UPJ obstruction in newborns usually presents with a palpable abdominal mass caused by an enlarged obstructed kidney. Other less common presentations include urinary tract infection, hematuria, or failure to thrive. Ureteropelvic junction obstruction rarely presents as renal failure; renal failure may occur in patients with a single obstructed kidney or with bilateral UPJ obstruction. Ureteropelvic junction obstruction in older children presents with episodes of flank or abdominal pain (Dietl crisis) accompanied by nausea and vomiting. Therefore, painful episodes secondary to UPJ obstruction may be confused with episodes of gastritis and managed as such; these patients may return to the emergency department with recurrent episodes of flank or abdominal pain. Children may also rarely exhibit renal injury to the enlarged obstructed kidney after minor trauma, hematuria, renal calculi, or hypertension. In older patients, findings of hydronephrosis on ultrasonography are the clue to the possibility of UPJ obstruction as the underlying cause of symptoms. It is important to perform ultrasonography during episodes of acute pain because the ultrasonography results may be normal once the pain subsides.

PREP Pearls
- Renal vein thrombosis is the most common cause of noncatheter-associated thrombosis in the newborn.
- Flank mass, thrombocytopenia, and hematuria are the classic features associated with renal vein thrombosis.
- In the neonatal period, perinatal asphyxia, hypovolemia, sepsis, and vascular thrombosis are risk factors for acute kidney injury.
- Congenital anomalies of the kidney and urinary tract are the most common cause of pediatric chronic kidney disease.

MOCA-Peds Objective
- Evaluate and manage a neonate born to a diabetic mother

ABP Content Specifications(s)
- Recognize complications associated with acute renal failure
- Identify the etiology of acute renal failure in patients of various ages

Suggested Readings
- Chua AN, Sarwal MM. Acute renal failure management in the neonate. *Neoreviews.* 2005;6(8):e369–e376. doi: http://dx.doi.org/10.1542/neo.6-8-e369 .
- Schlomer BJ, Copp HL. Antenatal hydronephrosis: assessment and management. *NeoReviews.* 2013;14(11):e551–e561. doi: http://dx.doi.org/10.1542/neo.14-11-e551.
- Selewski DT, Charlton JR, Jetton JG, et al. Neonatal acute kidney injury. *Pediatrics.* 2015;136(2):e463–e473. doi: http://dx.doi.org/10.1542/peds.2014-3819.

Question 233

You are teaching a group of residents about the pattern of pubertal changes. The residents ask about the respective heights of girls and boys at the onset of their growth spurts.

Of the following, you are MOST likely to respond that on average

A. girls and boys have the same height
B. girls are 5 cm shorter than boys
C. girls are 5 cm taller than boys
D. girls are 10 cm shorter than boys
E. girls are 10 cm taller than boys

Correct Answer: D

Rapid growth due to sex-steroid stimulation of growth hormone and insulinlike growth factors is one of the most notable features of adolescence. In girls, initiation of the growth spurt (IGS) typically occurs around age 9.5 years, with a peak height velocity of 8.3 cm/year achieved at age 11.5 years when most girls are at sexual maturity rating (SMR) 3. Boys have IGS at 11.5 years of age, and reach a peak height velocity of 9.5 cm/year 2 years later when they are in genital SMR 3 to 4. Boys' growth rates then gradually decline, with 99% of growth complete at a bone age of 17 years.

When compared with girls, boys experience an additional 2 years of growth (at a rate of about 5 cm/year) before growth spurt initiation (**Item C233**). As a result, girls are about 10 cm shorter than boys at IGS, which is the primary explanation for the observed 13-cm mean difference in heights of adult women and men. A greater growth velocity in boys explains much of the remaining 3 cm difference.

Girls Pubertal Development and Growth Velocity

Boys Pubertal Development and Growth Velocity
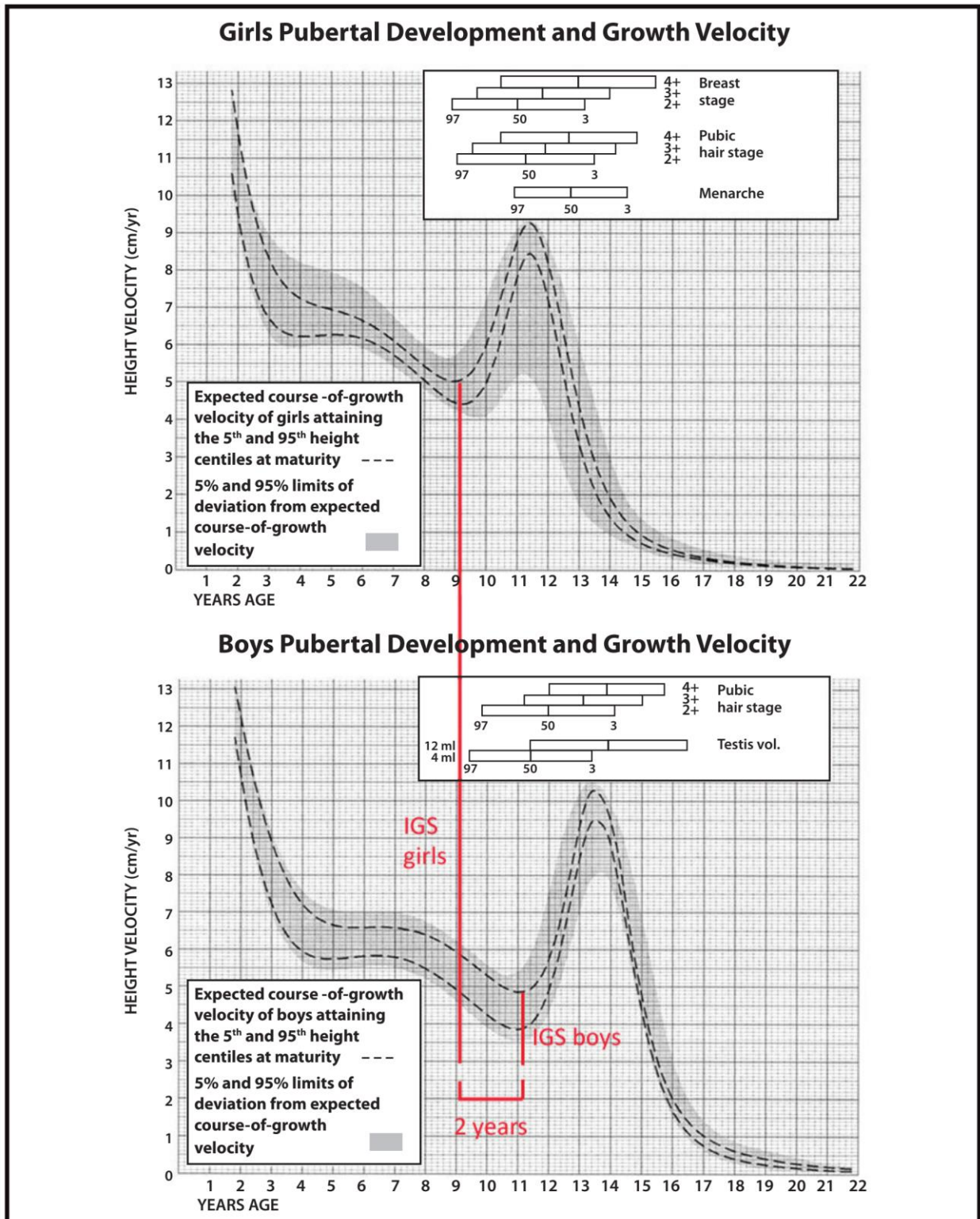
Adapted and reprinted with permission from Bordini B, Rosenfield RL. Normal pubertal development: part II—clinical aspects of puberty. *Pediatr Rev.* 2011;32:286.

ITEM C233: Growth velocity curves for girls (top) and boys (bottom). As shown by the red lines, in girls, growth spurts are initiated about 2 years before boys.

PREP Pearls
- Girls have initiation of the growth spurt 2 years earlier than boys.
- At the initiation of the growth spurt, boys are on average 10 cm taller than girls.

MOCA-Peds Objective
- Recognize normal variations in pubertal development

ABP Content Specifications(s)
- Understand the timing, duration, and normal range of peak height velocity in male and female adolescents

Suggested Readings
- Bordini B, Rosenfield RL. Normal pubertal development: part II—clinical aspects of puberty. *Pediatr Rev*. 2011;32:281–291. doi: http://dx.doi.org/10.1542/pir.32-7-281.
- Carswell JM, Stafford DEJ. Normal physical growth and development. In Neinstein LS, Katzman DK, Callahan ST, Gordon CM, Joffe A, Rickert VI, eds. *Neinstein's Adolescent and Young Adult Medicine*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2016.

Question 234

You are reviewing discharge plans for a 2-day-old neonate born at 35 weeks of gestation with a birthweight of 2.62 kg. His mother, a recent immigrant from Sri Lanka, has blood type O positive. The neonate's blood type is O positive. He has been breastfeeding well, with 4 wet diapers and 2 stools in the past 24 hours. He received 1 feeding of formula. On physical examination, his weight is 2.58 kg and he has mild facial jaundice. His total bilirubin is 10.2 mg/dL (174.5 μmol/L) at 48 hours of age. Using the Bhutani nomogram, the pediatric resident labeled his bilirubin risk level as low intermediate with no recommendation for a repeat bilirubin level on discharge.

Of the following, the factor that places this neonate at INCREASED risk of hyperbilirubinemia is

   A. east Asian race
   B. excess weight loss
   C. hemolytic disease
   D. jaundice
   E. prematurity

Correct Answer: E

For the neonate in the vignette, prematurity is the risk factor that places him at increased risk for hyperbilirubinemia. As a result, a repeat serum bilirubin level should be performed after discharge. All neonates have physiologic jaundice in the first days after birth because of a relatively high bilirubin load, decreased uptake of bilirubin in the liver, increased enterohepatic circulation, and lower activity of uridine diphosphoglucuronosyl transferase. In addition, immediately after birth, the blood-brain barrier is relatively permeable, allowing passage of bilirubin into the brain where it can damage neurons. The blood-brain barrier strengthens quickly, allowing neonates to tolerate increasingly higher serum bilirubin levels over the first few days after birth. It is recommended that providers use hour- and risk factor–specific total serum bilirubin level nomograms to estimate a neonate's risk of bilirubin-associated neurologic damage (**Item C234**). Serum bilirubin level may be accurately predicted with transcutaneous measurement. All neonates should be screened for pathologic jaundice with total bilirubin measurement (serum or transcutaneous) prior to discharge.
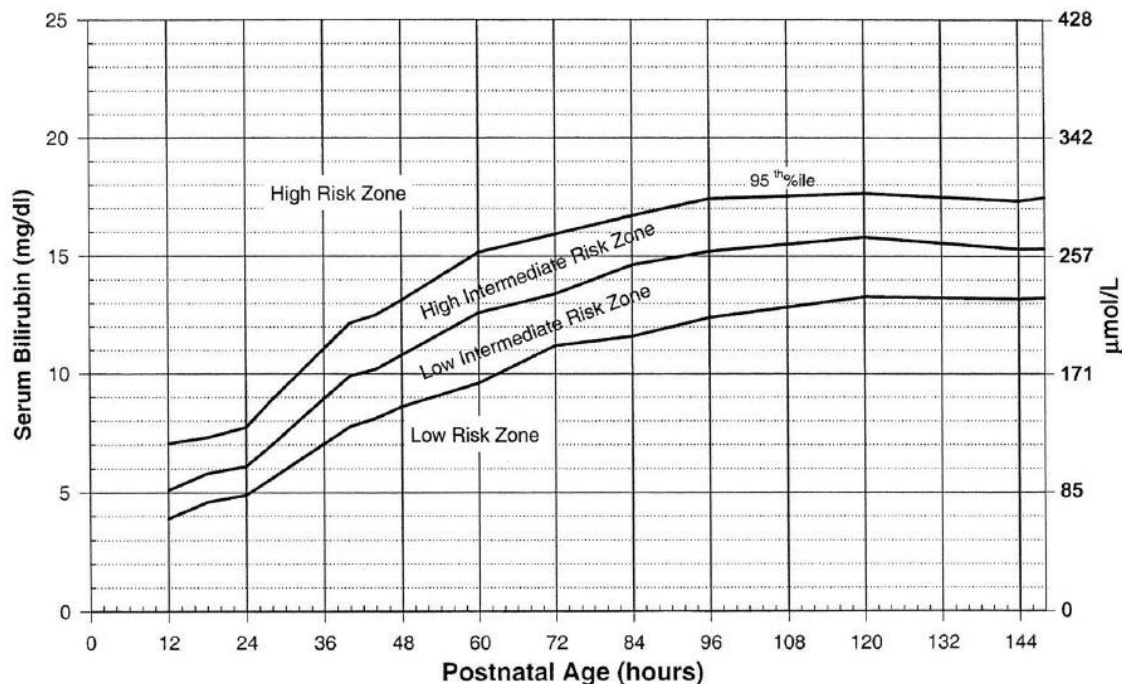
Item C234: Nomogram for designation of risk in 2840 well newborns at 36 weeks' gestational age with birth weight of 2000 g or 35 weeks' gestational age and birth weight of 2500 g based on the hour-specific serum bilirubin values.
Reproduced with permission from Bhutani VK, Johnson L, Sivieri EM. *Pediatrics*. 1999;103[1]:6 –14.

Premature neonates, born at less than 37 weeks of gestation, are at risk for acute bilirubin encephalopathy at lower bilirubin levels than term neonates. They have relatively slower clearance of bilirubin. The risk is even greater if enteral feeds cannot be started immediately after

birth because of respiratory distress, leading to increased enterohepatic circulation. East Asian race is associated with an increased risk of pathologic jaundice. Those at highest risk include those born to Chinese, Japanese, or Filipino parents.

Exclusively breastfed neonates who have lost more than 10% of their birthweight within the first 3 days after birth are at higher risk for jaundice, presumably due to increased enterohepatic circulation. This likely occurs because the mother's milk supply takes time to be established. The increased risk of jaundice in exclusively breastfed neonates is called "breastfeeding jaundice." The 2-day-old neonate in the vignette has lost only 2% of his birthweight, and has had 4 wet diapers in the past 24 hours, suggesting adequate enteral intake. Therefore, excess weight loss is not a risk factor for pathologic jaundice for this neonate.

Hemolytic disease in neonates may occur due to Rh or ABO isoimmunization. In the United States, the use of Rho (D) immune globulin for mothers who are negative for the Rh antigen has markedly decreased the incidence of Rh isoimmunization. ABO isoimmunization occurs when a mother with type O blood delivers a neonate with type A, B, or AB blood. Mothers with type O blood have anti-A and anti-B antibodies because of environmental exposure to these epitopes. However, in this vignette, both the mother and neonate are blood type O positive.

Typically, jaundice moves from the face to the thorax and downward, as bilirubin levels increase. Visibly yellow skin can be used as an initial screen for pathologic jaundice. However, it has been shown that clinicians are not able to reliably diagnose pathologic jaundice based solely on visual appearance, particularly in neonates with darker skin pigmentation. In addition, jaundice is visible on the skin at levels that may not be pathologic, therefore, jaundice alone does not necessitate a repeat bilirubin test.

PREP Pearls
- Serum bilirubin levels in neonates should be monitored based on hour- and risk factor–specific nomograms.
- Neonates born before 37 weeks of gestation are at increased risk for acute bilirubin encephalopathy.
- All neonates should be screened for pathologic jaundice with a total serum bilirubin or transcutaneous bilirubin level prior to discharge.

MOCA-Peds Objective
- Manage breast-feeding difficulties

ABP Content Specifications(s)
- Understand the mechanism of breast-milk jaundice and manage appropriately
- Plan the appropriate diagnostic evaluation of jaundice in a full-term infant
- Recognize the association between breast-feeding and physiologic jaundice in the neonatal period
- Understand the differences between physiologic jaundice in pre-term and full-term infants

Suggested Readings

- Lauer BJ, Spector ND. Hyperbilirubinemia in the newborn. *Pediatr Rev.* 2011;32:341. doi: http://dx.doi.org/10.1542/pir.32-8-341.
- Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR. Hyperbilirubinemia in the newborn infant =35 weeks' gestation: an update with clarifications. *Pediatrics.* 2009;124;1193; originally published online September 28, 2009. doi: http://dx.doi.org/10.1542/peds.2009-0329.

Question 235

A 6-year-old-boy presents to the emergency department with status asthmaticus. Since arriving in the ED 2 hours ago, he has received a dose of intramuscular epinephrine, intravenous (IV) methylprednisolone, and 2 nebulized treatments of ipratropium bromide. He also immediately started receiving an IV infusion of terbutaline and continuous nebulized albuterol. His current vital signs include a temperature of 37.0°C, heart rate of 150 beats/min, respiratory rate of 50 breaths/min, and blood pressure of 100/60 mm Hg. His oxygen saturation is 90% on 100% oxygen by nonrebreather face mask. On physical examination, the boy's consciousness is moderately impaired; he responds intermittently to questions with 1-word answers. He is in severe respiratory distress and appears anxious, holding onto the side rails of the bed. He has severe intercostal retractions. On auscultation, his lungs have decreased air entry throughout, with soft end-expiratory wheezing and a prolonged expiratory phase. His pulses are strong, and his capillary refill time is 2 seconds. Capillary blood gas analysis shows a pH of 7.10 and a partial pressure of carbon dioxide of 72 mm Hg (9.5 kPa).

Of the following, the BEST next management step for this boy is to

　A.　administer nebulized racemic epinephrine
　B.　perform intubation and ventilation
　C.　start helium-oxygen mixture
　D.　start inhaled nitric oxide
　E.　start intravenous isoproterenol

Correct Answer: B

The boy in this vignette has status asthmaticus, and has been treated with several therapies including inhaled and parenteral beta-agonists, intravenous steroids, and inhaled anticholinergics. Despite this high therapeutic intensity, he has respiratory failure evidenced by anxiety, air hunger, hypercapnia, and hypoxia. Thus, the best next management step is endotracheal intubation.

The decision to intubate a child with status asthmaticus should not be taken lightly, because further respiratory and hemodynamic collapse could ensue. Asthmatics who present in extremis are usually intravascularly depleted because of poor oral intake and increased insensible losses from tachypnea. Intense beta-agonist therapy can decrease cardiac preload because of peripheral vasodilation, diastolic hypotension, and tachycardia. If lower airway obstruction and hyperinflation are severe, cardiac tamponade physiology could be present, which can further decrease preload. When the child is intubated and positive pressure ventilation is implemented, systemic hypotension may occur. Thus, intravascular fluid expansion and therapies to minimize hyperinflation should be undertaken if considering intubation. The clinician must also critically consider whether mechanical ventilation is likely to improve respiratory mechanics compared with spontaneous breathing. In severe lower airway obstruction, the patient's accessory respiratory muscles aid expiration by forcibly creating positive intrathoracic pressure to overcome the obstruction. If the patient can sustain this effort, it may be more effective than passive exhalation on the ventilator.

Clinicians tend to perform bag-mask ventilation at too fast a rate, especially in a high-stress situation such as respiratory failure and intubation. This can be harmful in status asthmaticus. The time required for airflow during both inhalation and exhalation is increased when there is bronchoconstriction. It is important for bag-valve mask ventilation and mechanical ventilation of an asthmatic to occur at a low rate, with sufficiently long expiratory and inspiratory times. High inspiratory pressures, which can exceed 40 or 50 cm H_2O in severe asthmatics, are often required to bypass the airway obstruction. This can cause concern for the risk of a pneumothorax. However, the *plateau pressure*, the pressure seen by the alveoli under the equilibrium condition of no airflow, is significantly lower than the peak inspiratory pressure in severe dynamic airway obstruction. Thus, it is important that enough inspiratory pressure be given to adequately move the chest. Pneumothorax is more likely to be caused by hyperinflation, air trapping, and breath stacking from inappropriately high respiratory rates than high inspiratory pressures.

Despite the potential hemodynamic complications in status asthmaticus, positive pressure ventilation does have some benefit. Applied intraluminal pressure can stent airways open, which can relieve obstruction. If tolerated, noninvasive positive pressure ventilation with continuous positive airway pressure or bilevel positive airway pressure can be beneficial. This can be particularly effective if concomitant hypoxia from atelectasis, pneumonia, or ventilation-perfusion mismatch is present. Given the potential complications of intubation in status asthmaticus, the clinician should reserve it for patients whose spontaneous respiratory efforts are ineffective. Signs of this condition include obtundation, fatigue, air hunger, and anxiety, which

are all present in the boy in this vignette. If any of these signs are present despite high therapeutic intensity, either invasive or noninvasive mechanical ventilation should be considered.

Racemic epinephrine can ameliorate upper airway obstruction due to laryngeal edema, but is not helpful in status asthmaticus.The best choices for beta-agonist therapy include intramuscular epinephrine, inhaled albuterol, and terbutaline. Isoproterenol is a potent $beta_1$- and $beta_2$-agonist that can be effective in status asthmaticus. It is rarely used because of its side effect profile, which includes tachycardia and diastolic hypotension. It is not the best choice for the boy in the vignette because terbutaline, also a potent intravenous $beta_2$-agonist, has not been effective. Helium-oxygen mixture (heliox), less dense than 100% oxygen or a nitrogen-oxygen mixture, has a lower coefficient of friction for gas moving through the airways, and has been shown to improve ventilation and the delivery of albuterol to the small airways. However, the effect of heliox diminishes when the fraction of helium is less than 50%. Because the boy in the vignette requires 100% oxygen to achieve an oxygen saturation of 90%, heliox administration would make him hypoxic. Although inhaled nitric oxide causes pulmonary vasodilation, and in some cases, improves ventilation-perfusion matching, improving lower airway obstruction and the work of breathing is more important in this instance.

PREP Pearls
- Anxiety is a sign of impending respiratory failure. Along with obtundation, it can be an indication for intubation in status asthmaticus.
- Bag-valve mask ventilation, intubation, and mechanical ventilation in children with status asthmaticus each carry significant risks. Therefore, a high threshold for use of these therapies should be maintained.
- Helium-oxygen mixture (heliox) can improve ventilation in status asthmaticus, but loses its effectiveness when less than 50% helium can be given because of hypoxia.

ABP Content Specifications(s)
- Plan appropriate management for respiratory failure of various etiologies

Suggested Readings
- Gluckman TJ, Corbridge T. Management of respiratory failure in patients with asthma. *Curr Opin Pulm Med*. 2000;6(1):79–85.
- Sarnaik AA, Sarnaik AP. Noninvasive ventilation in pediatric status asthmaticus: sound physiologic rationale but is it really safe, effective, and cost-efficient?" *Pediatr Crit Care Med.* 2012;13(4):484–485. doi: http://dx.doi.org/10.1097/PCC.0b013e31823db1ff.
- Vo P, Kharasch VS. Respiratory failure. *Pediatr Rev.* 2014;35:476–484. doi: http://dx.doi.org/10.1542/pir.35-11-476.

Question 236

An 8-year-old boy with hereditary spherocytosis has had persistent anemia with a baseline hemoglobin level of 9 g/dL (90 g/L) and a baseline reticulocyte count of 10%. His hematologist has recommended that he undergo splenectomy. The family asks you for recommendations on how to reduce the risk of postsplenectomy infection.

You counsel the family that the BEST approach would be

A. prophylaxis with amoxicillin 80 mg/kg once 30 to 60 minutes prior to splenectomy
B. prophylaxis with trimethoprim/sulfamethoxazole twice daily on Mondays and Thursdays after splenectomy
C. vaccination against pneumococcus immediately after splenectomy
D. vaccination against pneumococcus prior to splenectomy
E. vaccination against varicella-zoster virus prior to splenectomy

Correct Answer: D

The spleen plays an important immunologic role in protecting patients from infections with encapsulated bacteria. After a splenectomy, patients are at a markedly higher risk for pneumococcal infection, *Haemophilus influenzae* type b infection, and meningococcal sepsis. Therefore, it is imperative that an elective splenectomy be preceded by vaccinations that boost immunity to these organisms.

Hereditary spherocytosis is a genetic disease resulting in fragile red blood cell membranes and a shortened red blood cell lifespan. Multiple genetic lesions cause hereditary spherocytosis with a range of clinical severities. The boy in this vignette has a severe phenotype of hereditary spherocytosis that includes chronic anemia (hemoglobin < 11 g/dL) and an elevated reticulocyte count. Patients with hereditary spherocytosis with these characteristics are at higher risk for complications, and splenectomy is recommended. The child in this vignette will undergo an elective splenectomy and should be vaccinated against pneumococcus prior to the splenectomy. If the patient has not previously been vaccinated with an age-appropriate regimen, the patient should receive the 13-valent pneumococcal conjugate vaccine (PCV13) followed by a dose of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) after 8 weeks (and at least 2 weeks before splenectomy) and a second dose of PPSV23 after 5 years. In addition, the patient should receive a single dose of *H influenzae* type b conjugate vaccine (if he has not previously been vaccinated with a complete vaccination regimen), a single dose of the quadrivalent meningococcal conjugate vaccine (if not previously administered), and the annual influenza vaccine. In addition to this pre-splenectomy preparation, patients who undergo splenectomy must be counseled to seek medical attention for all fevers; if the patient's temperature is greater than 38°C, a blood culture should be immediately performed and broad spectrum antibiotics should be initiated.

Preoperative prophylaxis with amoxicillin or postoperative prophylaxis with trimethoprim/sulfamethoxazole is not effective in reducing the risk of postsplenectomy bacteremia. Although vaccination against pneumococcus is recommended, it should be performed prior to an elective splenectomy rather than after the procedure. Splenectomized patients are not at higher risk for infection with varicella-zoster virus.

PREP Pearls
- Splenectomy should be recommended for patients with severe hereditary spherocytosis (hemoglobin level chronically < 11 g/dL).
- Splenectomized patients are at higher risk for bacteremia with encapsulated organisms, including pneumococcus, meningococcus, and *Haemophilus influenzae* type b.
- Patients undergoing elective splenectomy should be vaccinated against encapsulated organisms prior to the splenectomy.

ABP Content Specifications(s)
- Plan appropriate pre- and postoperative prophylaxis for a patient who has hereditary spherocytosis or another erythrocyte membrane disorder

Suggested Readings
- Christensen RD, Yaish HM, Gallagher PG. A pediatrician's practical guide to diagnosing and treating hereditary spherocytosis in neonates. *Pediatrics*. 2015;135(6):1107–1114. doi: http://dx.doi.org/10.1542/peds.2014-3516.
- Rubin LG, Schaffner W. Clinical practice: care of the asplenic patient. *N Engl J Med*. 2014;371(4):349–356. doi: http://dx.doi.org/10.1056/NEJMcp1314291.
- Shah S, Vega R. Hereditary spherocytosis. *Pediatr Rev*. 2004;25(5):168–172. doi: http://dx.doi.org/10.1542/pir.25-5-168.

Question 237

A 4-year-old, previously healthy boy is brought to your office in July for evaluation of a 7-day history of fever, anorexia, malaise, and rash. In June, the family vacationed in New Hampshire where they participated in camping and hiking activities. There are no sick contacts. His mother did not recall any exposure to mosquitoes or ticks on the child. His immunizations are up to date.

He appears well. He has a temperature of 38.2°C and a rash on his right shoulder (Item Q237). The remainder of the examination findings are normal. Laboratory data are shown:

Laboratory Test	Result
White blood cell count	11,000/µL (11 x 10^9/L)
Neutrophils	43%
Lymphocytes	51%
Monocytes	5%
Eosinophils	1%

Item Q237: Annular, erythematous rash on right shoulder of the patient described in this vignette. Jacobs R and Kimberlin DW, et al

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

 A. amoxicillin therapy
 B. doxycycline therapy
 C. serology for Borrelia burgdorferi infection
 D. skin scraping from lesion for Trichophyton species infection
 E. topical clotrimazole

Correct Answer: A

Lyme disease is the most common vector-borne disease in the United States, accounting for an estimated 30,000 cases annually. The disease is endemic in the temperate regions of the Northern Hemisphere, Europe, and Asia. Lyme disease is caused by the spirochete *Borrelia burgdorferi* sensu stricto and transmitted to humans by the bite of the infected *Ixodes* (deer) tick vectors, *Ixodes scapularis* (Eastern United States), commonly known as the blacklegged tick (**Item C237A**), and *Ixodes pacificus* (Western United States). Small rodents are the natural vertebrate reservoir host. The risk of human infection is influenced by the geographic distribution of hard tick vectors, ecologic changes that affect tick infection rates, and human behaviors that promote tick bites.In recent years, there has been a rise in the deer population and the *Ixodes* species tick vector population in the United States, leading to a substantial increase in the incidence and geographic distribution of Lyme disease.

**Item C237A:** Ixodes Scapularis (Blacklegged tick)
Courtesy of Levin M and the Centers for Disease Control and Prevention.

Most reported cases of Lyme disease occur in New England, the Eastern mid-Atlantic, the upper Midwest, and (less frequently) the West Coast, primarily northern California (**Item C237B**). Ten states (Connecticut, Delaware, Massachusetts, Maryland, Minnesota, New Jersey, New York, Pennsylvania, Rhode Island, and Wisconsin) account for more than 90% of reported cases. Rates of infection are highest among children aged 5 to 9 years and adults aged 55 to 59 years; more than 50% of reported cases occur in male individuals. Early Lyme disease cases are most common in the spring and summer (especially June and July). The clinical manifestations of

Lyme disease are diverse and may involve the skin and other organ systems, depending on the stage of the illness. Lyme disease presents in 3 stages: early localized disease (70%); early disseminated disease (20%), which includes multiple erythema migrans (EM), meningitis, cranial nerve palsies, and carditis; and late disease (mainly arthritis).

LYME DISEASE. Incidence* of reported confirmed cases, by county — United States, 2012

| | 1.01–10.00 | | 10.01–100.00 | | ≥100.01 |
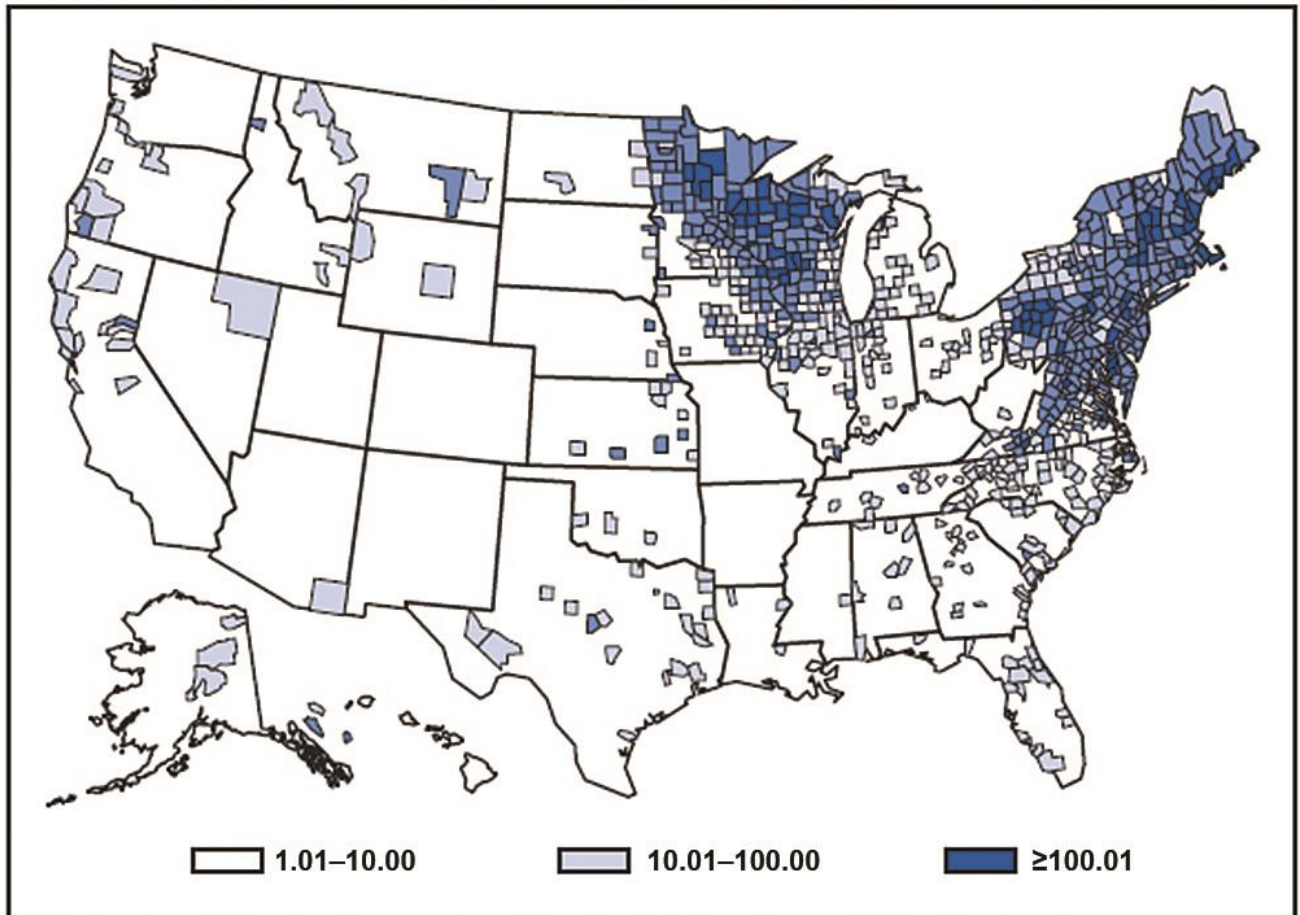
* Per 100,000 population.

Approximately 955 of confirmed Lyme disease cases were reported from states Northeast, mid-Atlantic and upper Midwest. A rash that can be confused with early Lyme disease sometimes occurs following bites of the lone star tick (*Amblyomma americanum*). These ticks, which do not transmit the Lyme disease bacterium, are common human-biting ticks in the southern and southeastern United States.

Item C237B: Geographic distribution of Lyme disease in the U.S.
Red Book reference to Courtesy of Morbidity and Mortality Weekly Report. 2012

Early localized infection typically manifests as a highly distinctive, characteristic expanding annular rash, EM, about 1 to 4 weeks after the tick bite. Erythema migrans begins as an erythematous macule or papule that gradually expands centrifugally over days to weeks to form an erythematous, annular lesion (≥ 5 cm in diameter) with partial central clearing. Erythema

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migrans is most common at the location of the tick bite; these lesions are nonpruritic and often painless. Erythema migrans may present with varying morphology, without central clearing or with central purpura or vesicles. Early disseminated disease is characterized by multiple EM lesions (**Item C237C**), seventh cranial nerve palsy (**Item C237D**), aseptic meningitis, and carditis (usually heart block). Early localized disease and early disseminated disease may be accompanied by fever, malaise, headache, myalgia, or arthralgia. Late manifestations of Lyme disease occur months after the tick bite and include monoarticular arthritis, primarily involving the knee joint (**Item C237E**).

Item C237C: Multiple erythema migrans lesions
Reprinted with permission from Jantausch M. and Kimberlin DW, et al. Red Book Online. Lyme disease. Elk Grove Village, IL. American Academy of Pediatrics 2015.

Item C237D: Left facial nerve palsy due to Lyme disease
Reprinted with permisison from Rajnik M and Kimberlin DW, et al. Red Book Online. Lyme Disease. Elk Grove Village, IL. American Academy of Pediatrics 2015.

Item C237E: Right Knee Arthritis due to Lyme disease
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As illustrated by the case in this vignette, early localized Lyme disease is diagnosed clinically based on the characteristic EM and plausible epidemiologic risk in the absence of serologic testing. Antibodies to *B burgdorferi* are not detectable in the majority of patients for 1 to 2 weeks after the tick bite. Thus, serologic testing for *B burgdorferi* infection in patients with EM often yields false-negative results and is not recommended for the diagnosis of EM. Serology may be a useful adjunct in the diagnosis of early, disseminated, or late disease in the clinical and epidemiologic context. The Centers for Disease Control and Prevention recommends a 2-tiered serologic testing protocol consisting of an enzyme-linked immunoassay or immunofluorescence assay that is followed by reflexive western blot if the first-tier assay result is positive. Sensitivity of 2-tiered testing is low (30%-40%) during early infection when the antibody response is developing (the window period). For disseminated Lyme disease, sensitivity of 2-tiered testing is 70% to 100%. Specificity is high (> 95%) during all stages of disease. Physicians must recognize the limitations of serologic testing for Lyme disease and order these tests judiciously because of the likelihood of false-positive results in low endemic regions and incorrect diagnosis in patients with only nonspecific symptoms such as fatigue or arthralgia. Serologic testing must be limited to patients with objective signs and symptoms compatible with Lyme disease (eg, facial nerve palsy, arthritis) who have a history of potential exposure to ticks from endemic regions. The role of other diagnostic tests for Lyme disease (eg, polymerase chain reaction for *Borrelia*-specific DNA in joint fluid) is limited.

Early clinical diagnosis of EM is crucial because treatment with appropriate oral antibiotic therapy results in cure rates greater than 90% and prevents late disease and sequelae. The Infectious Diseases Society of America has published clinical practice guidelines for treatment of Lyme disease in children (**Item C237F**) and adults. Oral amoxicillin (or cefuroxime) for 14 days is recommended for the treatment of EM in children younger than 8 years. For children 8 years old or older, oral doxycycline is the drug of choice for EM.

Item C237F. Recommended Treatment of Lyme Disease in Children.

Disease Category	Drug(s) and Dose[a]
Early localized disease[a]	
8 y or older	Doxycycline, 4 mg/kg per day, orally, divided into 2 doses (maximum 200 mg/day) for 14 days[b]
Younger than 8 y or unable to tolerate doxycycline[b]	Amoxicillin, 50 mg/kg per day, orally, divided into 3 doses (maximum 1.5 g/day) for 14 days
	OR
	Cefuroxime, 30 mg/kg per day in 2 divided doses (maximum 1000 mg/day or 1 g/day) for 14 days
Early disseminated and late disease	
Multiple erythema migrans	Same oral regimen as for early localized disease, for 14 days
Isolated facial palsy	Same oral regimen as for early localized disease, for 14 days (range 14-21 days)[c,d]
Arthritis	Same oral regimen as for early localized disease, for 28 days
Recurrent arthritis	Same oral regimen as for first-episode arthritis, for 28 days
	OR
	Preferred parenteral regimen:
	Ceftriaxone sodium, 50-75 mg/kg, IV, once a day (maximum 2 g/day) for 14 days (range 14-28 days)
	Alternative parenteral regimen:
	Penicillin, 200,000-400,000 U/kg per day, IV, given in divided doses every 4 h (maximum 18-24 million U/day) for 14 days (range 14-28 days)
	OR
	Cefotaxime 150-200 mg/kg per day, IV, divided into 3 or 4 doses (maximum 6 g/day) for 14 days (range 14-28 days)
Antibiotic-refractory/persistent arthritis[e]	Symptomatic therapy
Atrioventricular heart block or carditis	Oral regimen as for early disease if asymptomatic[f] or not hospitalized, for 14 days (range 14-21 days)
	OR
	Parenteral regimen initially for hospitalized patients, dosing as for recurrent arthritis, for 14 days (range 14-21 days); oral therapy can be substituted to complete the 14-21 day course
Meningitis	Ceftriaxone[g] or alternatives of cefotaxime or penicillin[g]: dosing as for recurrent arthritis, for 14 days (range 10-21 days)
	OR
	Doxycycline, 4-8 mg/kg per day, orally, divided into 2 doses (maximum 100-200 mg for 14 days (range 14-21 days)[b]
Encephalitis or other late neurologic disease[h]	Ceftriaxone[g] or alternatives of cefotaxime or penicillin[g]: dosing as for recurrent arthritis, for 14 days (range 14-28 days)

IV indicates intravenously.

[a] For patients who are allergic to penicillin, alternatives are cefuroxime, azithromycin, and erythromycin.

[b] Tetracycline-based antimicrobial agents, including doxycycline, may cause permanent tooth discoloration for children younger than 8 years if used for repeated treatment courses. However, doxycycline binds less readily to calcium compared with older tetracyclines, and in some studies, doxycycline was not associated with visible teeth staining in younger children.

[c] Corticosteroids should not be given.

[d] Treatment has no effect on the resolution of facial nerve palsy; its purpose is to prevent late disease.

[e] Arthritis is not considered persistent unless objective evidence of synovitis exists at least 2 months after completion of a course of parenteral therapy or of two 28-day courses of oral therapy. Some experts administer a second course of an oral agent before using an IV-administered antimicrobial agent.

[f] Symptoms for heart block or carditis include syncope, dyspnea, or chest pain.

[g] For treatment of meningitis or encephalitis with ceftriaxone, cefotaxime or penicillin, drug should be administered IV.

[h] Other late neurologic manifestations include peripheral neuropathy or encephalopathy.

Reprinted with permission from American Academy of Pediatrics. Lyme disease. 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; 2015:516-525.

Erythema migrans may be mistaken for other conditions that cause annular skin rashes, including cellulitis, tinea corporis, contact dermatitis, fixed drug reaction, granuloma annulare, an insect or spider bite reaction, and southern tick-associated rash illness (STARI). The bite of the lone star tick (*Amblyomma americanum*), which is prevalent in the southeast and south-central states, causes STARI. The etiologic agent of STARI is unknown. The rash associated with STARI is smaller, more circular, more likely to have central clearing, and more likely to be singular as compared to EM. Given the similarity to EM, antibiotics are often administered to patients with STARI. The rash of tinea corporis (caused by *Trichophyton* species) is typically a well-demarcated, erythematous plaque with raised, scaly borders. Topical imidazoles, such as clotrimazole, are often effective in treating localized tinea corporis. The boy in this vignette has EM consistent with Lyme disease; therefore, a potassium hydroxide mount of a skin scraping to detect *Trichophyton* fungi is not indicated.

PREP Pearls
- Lyme disease is caused by the spirochete *Borrelia burgdorferi* and transmitted to humans by the bite of the infected Ixodes (deer) tick vectors, *Ixodes* species.
- Lyme disease is the most common vector-borne disease in the United States with most cases reported in New England, the Eastern mid-Atlantic, and the upper Midwest.
- Early localized Lyme disease is diagnosed clinically based on the characteristic erythema migrans and plausible epidemiologic risk in the absence of serologic testing.
- Oral amoxicillin (or cefuroxime) for 14 days is recommended for the treatment of erythema migrans in children younger than 8 years; for children 8 years old or older, oral doxycycline is the drug of choice.

MOCA-Peds Objective
- Evaluate and manage a child with possible tick-borne illness

ABP Content Specifications(s)
- Recognize the clinical features associated with Borrelia burgdorferi infection
- Plan the appropriate laboratory evaluation for Borrelia burgdorferi infection
- Plan appropriate management for a patient with Borrelia burgdorferi infection
- Understand the epidemiology of Borrelia burgdorferi

Suggested Readings
- American Academy of Pediatrics. Lyme disease. 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; 2015:516–525.
- Shapiro ED. Borrelia burgdorferi (Lyme disease). *Pediatric Rev.* 2014;35(12):500–509. doi: http://dx.doi.org/10.1542/pir.35-12-500.
- Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis.* 2006;43(9):1089–1134. doi: http://dx.doi.org/10.1086/508667.

Question 238

During a prenatal visit, a pregnant woman with phenylketonuria is noted to have been nonadherent with her phenylalanine-restricted diet. Her plasma phenylalanine concentrations were consistently greater than 900 µmol/L (recommended range, 120 to 360 µmol/L) during the first and second trimester. She finally attained improved control in the third trimester.

Of the following, her newborn will be at highest risk for

A. cardiomyopathy
B. hepatic failure
C. intellectual disability
D. intrauterine growth restriction
E. normal outcome

Correct Answer: C

The newborn of the woman described in this vignette would be at highest risk for intellectual disability (> 90%). There is an inverse relationship between cognitive function and maternal phenylalanine levels greater than 360 µmol/L during the pregnancy of a woman with phenylketonuria (PKU) (phenylalanine hydroxylase deficiency) that is poorly controlled. Another common manifestation of poor control of PKU during pregnancy is microcephaly. The risk for microcephaly is 5% to 18% if the maternal phenylalanine level is not controlled prior to 10 weeks' gestation and increases to 67% if the maternal phenylalanine levels are not optimized prior to 30 weeks' gestation. Other associated findings include poor behavioral outcomes, congenital heart defects (8%-12%), and intrauterine growth restriction. Intrauterine growth restriction frequency is similar to that of the general population if the maternal phenylalanine levels are controlled by 10 weeks of gestation; however, the risk of intrauterine growth restriction increases if the maternal phenylalanine levels are not controlled until later in the pregnancy. Cardiomyopathy and hepatic failure are not common complications associated with poorly controlled maternal PKU.

A woman with PKU should maintain a phenylalanine-restricted diet for several months prior to conception and continuing through the pregnancy, with preferred phenylalanine levels between 120 and 360 µmol/L (2-6 mg/dL) to reduce the potential for teratogenic effects of elevated phenylalanine. Once a woman has become pregnant, continuous nutritional management and weekly or biweekly measurements of plasma phenylalanine levels should be monitored to ensure an adequate diet with the recommended proportions of protein, fat, and carbohydrates. A metabolic team and a maternal-fetal medicine specialist should be involved in the medical management of a pregnant woman with PKU, which should include high-risk ultrasonography and fetal echocardiography during the pregnancy to look for associated anomalies. In the situation in this vignette with maternal phenylalanine levels consistently greater than 900 µmol/L until sometime in the third trimester, a normal outcome would be less likely.

Phenylalanine hydroxylase deficiency is an autosomal recessive condition. For a woman with phenylketonuria caused by biallelic *PAH* mutations, each of her children will be obligate carriers of PKU. The partner of a patient with PKU should be screened for carrier status to formally assess the risk of having a child with PKU. If her partner is a carrier, the risk for having a child with PKU would be 50%.

Phenylalanine hydroxylase deficiency causes an intolerance to dietary ingestion of phenylalanine due to impaired enzymatic function of phenylalanine hydroxylase, resulting in excess phenylalanine levels and low tyrosine levels. Without treatment in the early months after birth, most patients with classic PKU will develop severe intellectual disability, highlighting the importance of PKU's inclusion in newborn screening protocols.

PREP Pearls
- A woman with phenylketonuria that is poorly controlled (phenylalanine levels consistently > 360 µmol/L) during pregnancy will be at highest risk for having a child with intellectual disability, microcephaly, or both. Other associated findings include poor behavioral outcomes, congenital heart defects (8%-12%), and intrauterine growth restriction.
- A woman with phenylalanine hydroxylase deficiency should closely maintain a phenylalanine-restricted diet for several months prior to conception and then continuing throughout the pregnancy. Phenylalanine levels should be between 120 and 360 µmol/L (2-6 mg/dL) to reduce the potential for teratogenic effects.

ABP Content Specifications(s)
- Understand the long-term prognosis for patients who have phenylketonuria, including the importance of dietary adherence
- Understand the risks for a neonate of a nonadherent mother with phenylketonuria

Suggested Readings
- American College of Obstetricians and Gynecologists. Committee opinion: management of women with phenylketonuria—number 636. *Obstet Gynecol.* 2015;125(6):1548–1550.
- Regier DS, Greene CL. Phenylalanine hydroxylase deficiency. *GeneReviews*. 2017.
- Singh RH, Rohr F, Frazier D, et al. Recommendations for the nutrition management of phenylalanine hydroxylase deficiency. *Genet Med.* 2014;16(2):121–131. doi: http://dx.doi.org/10.1038/gim.2013.179.
- Vockley J, Andersson HC, Antshel KM, et al; American College of Medical Genetics and Genomics Therapeutics Committee. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med*. 2014;16(2):188–200. doi: http://dx.doi.org/10.1038/gim.2013.157.

Question 239

A 6-year-old previously healthy girl presents to the rural emergency department where you work, after she was bitten by an unknown dog during a family camping trip. Approximately 90 minutes ago, the girl and her siblings were playing close to their family's campsite when a stray dog appeared, barking and growling at them. The children ran back toward the family campsite; however, the dog ran after them and attacked the girl, biting her multiple times in her right axillary region, upper back, shoulder, and upper arm before running away into the woods. The girl's parents immediately took her to the park ranger who applied direct pressure to her bites with gauze and called emergency medical services. The ranger attempted but was unable to locate the dog.

On arrival to the emergency department, the girl is alert and oriented, but crying in pain. Her temperature is 36.7°C, heart rate is 120 beats/min, respiratory rate is 16 breaths/min, and blood pressure is 110/70 mm Hg. On physical examination, she has no respiratory distress, and her extremities are well perfused. You note multiple (>20) puncture wounds over her right shoulder and upper arm, a 3×4–cm gaping wound in her right axillary region, and a 6×8–cm deep wound to her right upper back with exposed muscle. There is a slight bleeding from the deep wound on the girl's back.

The girl's medical and surgical history are not significant, she takes no medications, has no known drug allergies, and is up to date on all recommended immunizations. A nurse places a peripheral intravenous catheter, and you order an analgesic for her pain. Because of the number and complexity of the girl's wounds, you request an emergent surgical consultation for evaluation and management of the girl's wounds.

Of the following, the MOST appropriate treatment plan for this girl includes

A. rabies immunoglobulin and intravenous clindamycin
B. rabies vaccine and intravenous ampicillin-sulbactam
C. rabies vaccine, rabies immunoglobulin, and intravenous ampicillin-sulbactam
D. rabies vaccine, rabies immunoglobulin, and intravenous doxycycline
E. rabies vaccine, rabies immunoglobulin, tetanus immunoglobulin, and intravenous clindamycin

Correct Answer: C

The girl in the vignette presents for management of multiple wounds after being attacked by a stray dog that cannot be located for further observation. The most appropriate treatment regimen includes administration of the rabies vaccine, rabies immunoglobulin, and intravenous ampicillin-sulbactam.

Nearly 5 million dog bites occur in the United States each year. In most cases (85%–90%), the dog's owner can be identified, but cases involving stray dogs with unknown ownership and immunization status certainly occur. Because of the significant pressure dogs can generate in their bites, dog bites can cause crush injuries, leaving behind devitalized tissue that is prone to infection. The estimated rate of wound infections after dog bites is thought to be in the range of 10% to 18%. Careful assessment and meticulous wound management are essential to preventing infection and other significant complications in children presenting with dog bite wounds.

Injuries resulting from dog bite wounds may range from superficial scratches, to simple lacerations, to major traumatic injuries including depressed skull fractures and penetration of vital organs, leading to life-threatening blood loss. Bites involving penetration of joint spaces, tendons, vascular structures, bones, the hand, and facial compartments, as well as large wounds (>3 cm), and those resulting in devitalized tissue are particularly at risk for infection. The bacterial organisms most commonly involved in wound infections arising from dog bites are *Staphylococcus aureus* and *Pasteurella* species. Other causative organisms include streptococci, coagulase-negative staphylococci, and anaerobic bacteria.

The American Academy of Pediatrics Committee on Infectious Diseases recommends that for children presenting with dog bite wounds, prophylactic antibiotic therapy should be routinely initiated in those with:
- moderate or severe bite wounds (especially if edema or crush injury is present)
- puncture wounds (especially when penetration of bone(s), tendon sheath(s), or joint(s) have occurred)
- deep or surgically closed facial wounds
- wounds involving the hands and/or feet, wounds affecting the genital area
- wounds sustained by immunocompromised and/or asplenic patients or wounds with signs of infection.

Amoxicillin-clavulanic acid is the recommended first-line oral agent for children requiring antibiotic therapy after sustaining a dog bite wound. This agent is effective for treating infections caused by the range of organisms frequently isolated from dog bites, including *Pasteurella* species, *Staphylococcus aureus* (methicillin-susceptible), streptococci, *Corynebacterium* species, *Moraxella* species, and oral anaerobes. For children requiring intravenous antibiotic therapy, ampicillin-sulbactam is the recommended first-line antibiotic agent. An extended-spectrum cephalosporin or trimethoprim-sulfamethoxazole *plus* clindamycin is the recommended alternative regimen for children who are allergic to penicillin. It is essential for providers to recognize that early, meticulous local wound care is more effective than

prophylactic antibiotics in preventing infection. All significant dog bite wounds should be reevaluated within 24 to 48 hours after initial presentation.

The risk for systemic infections, particularly rabies and tetanus, must be considered in all children presenting with dog bite wounds. Tetanus status should be reviewed, and appropriate tetanus prophylaxis should be administered. Although the rabies virus is not frequently transmitted to humans through dog bites in the United States, the risk for rabies must be considered in every case, and postexposure prophylaxis should be administered whenever indicated.

Infection with the rabies virus results in an acute illness that causes rapidly progressive central nervous system manifestations and almost universally results in death. Wild animals, including bats, raccoons, skunks, foxes, coyotes, and bobcats, are the most important sources for rabies infection in the United States, but other animals including dogs, cats, and ferrets can become infected. Humans who have contact with a rabid animal can become exposed to the virus through a bite from the infected animal, or via inoculation of scratches, abrasions, or mucous membranes with saliva or other infectious material from the animal.

Postexposure rabies prophylaxis includes infiltration of human rabies immune globulin into and around the patient's wound(s) and initiation of the rabies vaccine series (in previously unimmunized patients). Treatment should be administered as soon as possible to all patients bitten by wild mammalian carnivores, bats, or domestic animals that are suspected to have rabies, unless laboratory tests can prove that the offending animal does not have the disease. Rabies postexposure prophylaxis should also be given to patients with potential contamination of an open wound, scratch, or mucous membranes with saliva or other infectious material from a rabid animal.

Any dog, cat, or ferret that has bitten a human and is suspected of having rabies should be captured, confined, euthanized, and tested for the virus, or should be observed by a veterinarian for a period of at least 10 days. For patients who sustain bites from dogs that appear healthy and can be observed for 10 days, rabies postexposure prophylaxis is indicated only if the dog develops signs of rabies during the observation period. In situations in which it is unclear whether rabies postexposure prophylaxis is indicated, providers should contact their local public health agency or the United States Centers for Disease Control and Prevention (1-800-CDC-INFO).

Administration of rabies immunoglobulin and intravenous clindamycin would not be the recommended treatment for the girl in the vignette. Given that she has no history of a penicillin allergy, oral amoxicillin-clavulanate (or intravenous ampicillin-sulbactam) would be the recommended first-line antibiotic agent. In addition, the rabies vaccine series should be initiated in this case, in addition to rabies immune globulin.

Although it would be appropriate for the girl in the vignette to receive both the rabies vaccine and intravenous ampicillin-sulbactam, she should also be given human rabies immunoglobulin

because she has been bitten by a stray dog that cannot be observed and could potentially be rabid.

A regimen consisting of the rabies vaccine, rabies immunoglobulin, and intravenous doxycycline would not be the most appropriate treatment for this girl; intravenous doxycycline is not a recommended antimicrobial agent for patients with dog bite wounds.

Finally, a regimen including the rabies vaccine, rabies immunoglobulin, tetanus immunoglobulin, and intravenous clindamycin would not be the most appropriate treatment for the girl. Her tetanus status is up to date, so tetanus immunoglobulin is not indicated. Furthermore, intravenous clindamycin should be combined with either an extended-spectrum cephalosporin or trimethoprim-sulfamethoxazole in treating dog bites that are infected or at risk for becoming infected.

PREP Pearls
- The bacterial organisms most commonly involved in wound infections arising from dog bites are *Staphylococcus aureus* and *Pasteurella* species. Other causative bacteria may include streptococci, coagulase-negative staphylococci, and anaerobic bacteria.
- Amoxicillin-clavulanic acid is the recommended first-line oral agent for children requiring antibiotic therapy after sustaining dog bite wounds.
- For children requiring intravenous antibiotic therapy after sustaining dog bite wounds, ampicillin-sulbactam is the recommended first-line antibiotic agent. An extended-spectrum cephalosporin or trimethoprim-sulfamethoxazole *plus* clindamycin is the recommended alternative regimen for children who are allergic to penicillin.
- Any dog, cat, or ferret that has bitten a human and is suspected of having rabies should be captured, confined, euthanized, and tested for the virus or should be observed by a veterinarian for period of at least 10 days.
- For patients bitten by dogs that appear healthy and can be observed for 10 days, rabies postexposure prophylaxis is indicated only if the dog develops signs of rabies during the observation period. Patients bitten by dogs that are known or suspected to be rabid should receive postexposure prophylaxis as soon as possible.

ABP Content Specifications(s)
- Understand the appropriate steps to take with regard to an animal that has bitten a patient
- Plan the appropriate antimicrobial management of a dog or cat bite

Suggested Readings

- Black KD, Cico SJ, Caglar D. Wound management. *Pediatr Rev*. 2015;36(5):207–216. doi: http://dx.doi.org/10.1542/pir.36-5-207.
- Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Bite wounds. In: *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.
- Seeyave DM, Brown KM. Environmental emergencies, radiological emergencies, bites and stings. In: Shaw KN, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Wolters Kluwer; 2016;chap 98:718–760.

Question 240

A previously healthy 9-year-old girl is brought to your office for a 3-month history of headache, nausea, and worsening vision. Her fluid intake has also increased significantly, and she wakes up several times at night to urinate. Vital signs reveal a temperature of 37°C, blood pressure of 125/88 mm Hg, heart rate of 96 beats/min, weight of 26 kg (25th percentile), and height of 133 cm (50th percentile). Her visual acuity is 20/100 bilaterally. Physical examination is significant for bilateral peripheral visual field deficits, and is otherwise unremarkable. Head computed tomography scan shows a 4-cm mostly cystic, suprasellar mass with calcifications, consistent with craniopharyngioma.

Of the following, the hormone MOST likely to be deficient in this girl is

A. adrenocorticotropic hormone
B. antidiuretic hormone
C. insulin
D. prolactin
E. thyroid-stimulating hormone

Correct Answer: B

The girl in the vignette has polyuria and polydipsia in the context of a craniopharyngioma, a scenario consistent with diabetes insipidus (DI). DI occurs when there is a deficiency of antidiuretic hormone from the posterior pituitary. DI can be present at the time of diagnosis of craniopharyngioma and is very common after resection. Growth hormone deficiency is the most common anterior pituitary hormone deficiency at the time of diagnosis of craniopharyngioma, and other anterior pituitary hormone deficiencies, especially gonadotropin, may also be present. Thus, growth problems, pubertal delay or arrest, and weight gain are common findings at the time of diagnosis of craniopharyngioma.

Although adrenocorticotropic and thyroid-stimulating hormone deficiencies can occur due to craniopharyngioma, the girl in the vignette shows no signs or symptoms suggestive of these. Insulin deficiency also causes polyuria and polydipsia and occurs in diabetes mellitus, but this is not associated with craniopharyngioma. Because prolactin is under inhibitory control from the hypothalamus, if affected, levels are likely to be elevated with craniopharyngioma because of compression of the pituitary stalk.

Craniopharyngioma is the most common suprasellar tumor seen in childhood. Although it is a benign tumor originating from the remnants of the Rathke pouch, it can cause significant problems because of its location and mass effect. The computed tomography (CT) description in the vignette of a cystic mass with intratumoral calcifications is characteristic. However, magnetic resonance imaging with and without contrast is the standard imaging modality. Calcifications are only seen on CT, and can help refine the differential diagnosis. Symptoms of increased intracranial pressure (eg, headache, nausea, vomiting) and vision problems, because of mass effect on the optic chiasm, are common at presentation. The peak incidence in childhood is between 5 and 14 years of age. Treatment is associated with significant morbidity, specifically panhypopituitarism, diabetes insipidus, hypothalamic obesity, and vision loss.

Diabetes insipidus results from a deficiency of antidiuretic hormone (central DI) in the posterior pituitary, or resistance to antidiuretic hormone (nephrogenic DI) in the kidneys, resulting in their inability to reabsorb free water. In either form of DI, polyuria and polydipsia with a craving for cold water occur, and if free water is not adequately replaced, hypernatremic dehydration develops. Hypernatremia, hyperosmolality, and dilute urine are characteristic. Other laboratory findings consistent with dehydration may be seen. The diagnosis of DI is made if the serum osmolality is greater than 300 mOsm/kg when the urine osmolality is less than 300 mOsm/kg. A water deprivation test may be required to make the diagnosis. The response to vasopressin differentiates central from nephrogenic DI. DI can be differentiated from other causes of hypernatremic dehydration by the presence of dilute urine; concentrated urine is expected in cases of hypernatremic dehydration with a normal antidiuretic hormone response.

PREP Pearls

- Craniopharyngiomas can cause growth hormone deficiency, gonadotropin deficiency, and diabetes insipidus. Symptoms suggestive of this tumor include growth restriction, pubertal delay or arrest, and polyuria/polydipsia.
- Diabetes insipidus results from a deficiency of, or resistance to, antidiuretic hormone. Polyuria and polydipsia, hypernatremia, hyperosmolality, and dilute urine are characteristic findings.
- Diabetes insipidus can be differentiated from other causes of hypernatremic dehydration by the presence of dilute urine; concentrated urine is expected in cases of hypernatremic dehydration with a normal antidiuretic hormone response.

ABP Content Specifications(s)

- Differentiate diabetes insipidus from other causes of hypernatremic dehydration
- Recognize the clinical and laboratory features associated with diabetes insipidus
- Recognize the clinical features associated with pituitary disorders caused by craniopharyngioma

Suggested Readings

- Breault DT, Majzoub JA. Diabetes Insipidus. In: Kliegman RM, Stanton BF, St. Geme JW, Schor NF, eds. *Nelson Textbook of Pediatrics. 20th ed.* Philadelphia, PA: Elsevier; 2016: 2644-2646..
- Daubenbüchel AM, Müller HL. Neuroendocrine disorders in pediatric craniopharyngioma patients. *J Clin Med*. 2015;4(3):389-413.
- Saborio P, Tipton GA, Chan JC. Diabetes insipidus. *Pediatr Rev*. 2000;21(4):122-9; quiz 129. http://pedsinreview.aappublications.org/content/21/4/122.

Question 241

A 4-week-old infant is brought to your office for evaluation. He was born with a vascular lesion on the right side of the face that has not changed since birth. The infant has normal vital signs and growth parameters. The physical examination is remarkable only for the lesion shown in Item Q241.

Item Q241: Lesion described for the girl in the vignette.
Reprinted with permission from Mancini AJ, Krowchuk DP, eds. Pediatric Dermatology. *A Quick Reference Guide*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016.

Of the following, the infant is MOST at risk for

A. arterial abnormalities and posterior fossa malformations
B. arteriovenous malformations and tissue (bone and soft tissue) overgrowth
C. no associated abnormalities
D. seizures and glaucoma
E. venous varicosities and tissue (bone and soft tissue) overgrowth

Correct Answer: D

The infant in this vignette has a port-wine stain (PWS, also known as a nevus flammeus) that involves the first branch of the distribution of the trigeminal nerve. As a result, he is at risk of Sturge-Weber syndrome (SWS) that may be associated with seizures and glaucoma. A PWS located on an extremity most often is an isolated cutaneous finding. However, occasionally it may be associated with underlying arteriovenous malformations and bone and soft tissue overgrowth (Parkes Weber syndrome) or venous varicosities accompanied by bone and soft tissue hypertrophy (Klippel-Trenaunay syndrome). A large segmental facial hemangioma may be a clue to the presence of PHACE association (**P**osterior fossa abnormalities, **H**emangiomas, **A**rterial anomalies, **C**ardiovascular abnormalities, and **E**ye abnormalities).

Port-wine stains are permanent vascular (capillary) malformations that occur in approximately 0.3% of newborns. They appear as flat pink to dark red patches that are present at birth and may become darker and somewhat elevated over time. In contrast, a hemangioma usually is not present at birth (typically appears by 4 weeks of age), proliferates during the first months after birth (growth is usually complete by 5 months of age), and begins to involute by 6 to 12 months of age.

Port-wine stains may involve any area of the body. When present on the face, a PWS raises concern for SWS and may be disfiguring. Sturge-Weber syndrome is a sporadic neurocutaneous disorder caused by a mutation in *GNAQ* that results in abnormal cell proliferation. In SWS, vascular malformations may involve the skin (PWS), brain (leptomeningeal angiomatosis that may cause seizures, stroke, and intellectual disability), and eyes (glaucoma). The diagnosis of SWS is clinical and requires involvement in at least 2 of these 3 areas.
Concern about SWS is greatest when the PWS involves the distribution of V1, especially the upper eyelid; involves V1 along with V2 and/or V3; or is bilateral.

In a study of 259 children and adolescents younger than 16 years with facial PWS, 15 (5.8%) had SWS. The risk of SWS was 14% if the upper lid was involved, 18% if the PWS was bilateral, and 41% if V1, V2, and V3 were involved. All individuals with SWS had involvement of V1. Recent evidence indicates that the location of the PWS and the risk of SWS has less to do with neuronal innervation than the common embryologic origin of the forehead, cerebral cortex, and eye. This observation suggests that SWS is caused by a single mutation affecting neural crest cells emanating from the forebrain region.

Infants who have a facial PWS concerning for possible SWS should undergo ophthalmologic consultation to assess intraocular pressure. Glaucoma occurs in 30% to 70% of individuals who have SWS. Glaucoma is especially likely if both the upper and lower lids are affected. Neurologic consultation is also warranted to determine the timing of brain magnetic resonance imaging. It may be performed before symptom onset but sometimes is delayed until after the age of 1 year because of the possibility of false-negative results in young infants, the need for sedation, and the large number of infants who have facial PWS but not SWS. Pulsed dye laser is the gold standard for treating potentially disfiguring PWS. Most patients require several

treatments at 4- to 8-week intervals. Lightening by 40% to 55% can be anticipated but complete clearance is rarely achieved, and lesions may become darker over time requiring additional treatment. Pulsed dye laser therapy often is begun in infancy or toddlerhood before the child develops self-awareness. Some studies have shown improved treatment responses in children younger than 1 year of age, but other studies have not. Lesions involving the middle area of the face respond less well than lesions on the forehead and lateral cheeks.

PREP Pearls
- Port-wine stains are vascular malformations that are present at birth and remain throughout life. Unlike hemangiomas, they do not proliferate.
- Concern for Sturge-Weber syndrome exists when a facial port-wine stain involves the distribution of V1, especially the upper eyelid; involves V1 along with V2 and/or V3; or is bilateral.

ABP Content Specifications(s)
- Recognize the clinical findings associated with Sturge-Weber syndrome
- Plan the appropriate management of a port wine stain
- Recognize the importance of the distribution of a port wine stain

Suggested Readings
- Comi A. Current therapeutic options in Sturge-Weber syndrome. *Sem Pediatr Neurol.* 2015;22(4):295–301. doi: http://dx.doi.org/10.1016/j.spen.2015.10.005.
- Faux BM, Suhr AW, Hsieh DT. Newborn with a facial vascular birthmark. *Pediatr Rev.* 2015;36(9):e30–e34. doi: http://dx.doi.org/10.1542/pir.36-9-e30.
- Mann JA. Update on pediatric dermatologic surgery from tots to teens. *Curr Opin Pediatr.* 2014;26(4):452–459. doi: http://dx.doi.org/10.1097/MOP.0000000000000123 .
- Piram M, Lorette G, Sirinelli D, Herbreteau D, Giraudeau B, Maruani A. Sturge-Weber syndrome in patients with facial port-wine stain. *Pediatr Dermatol.* 2012;29(1):32–37. doi: http://dx.doi.org/10.1111/j.1525-1470.2011.01485.x.
- Waelchli R, Aylett SE, Robinson K, Chong WK, Martinez AE, Kinsler VA. New vascular classification of port-wine stains: improving prediction of Sturge-Weber risk. *Br J Dermatol.* 2014;171(4):861–867. doi: http://dx.doi.org/10.1111/bjd.13203.

Question 242

A 10-year-old girl is brought to the emergency department because of difficulty walking. Her symptoms started 2 days ago when her parents noticed that she was tripping frequently. Over the past day, she has had difficulty getting up from a chair and has had to use her hands to pull herself up the stairs. She does not have pain in her back, hips, or legs, and has had no fever or recent illnesses. The girl returned from a camping trip 1 week ago. On physical examination, her vital signs are normal, and she is afebrile. Her face and arms have normal strength. She can wiggle her feet and toes, but cannot lift her legs off the bed. Her deep tendon reflexes are present in the upper extremities, but absent in her patellae and ankles. Her toes do not respond to plantar stroking. You order forced vital capacity and negative inspiratory force measurements immediately, and arrange for her to be admitted to the pediatric intensive care unit.

Of the following, the BEST next step in identifying the cause of this girl's symptoms is

A. detailed examination of the skin
B. electromyography and nerve conduction study
C. magnetic resonance imaging of the brain
D. recent food ingestion history
E. serum creatine kinase level

Correct Answer: A

The girl in the vignette has ascending paralysis with absent reflexes. Although this is a common presentation of Guillain-Barré syndrome, her history of a recent camping trip suggests that she could have tick paralysis. A detailed skin examination should be performed, especially in the scalp, to search for ticks. In patients with tick paralysis, once the tick is removed, the weakness will rapidly resolve.

Tick paralysis can be caused by several species of ticks, including *Dermacentor andersoni*, the Rocky Mountain wood tick. Symptoms begin 4 to 7 days after the tick starts feeding. Restlessness or lethargy can be noted early on, followed by ascending paralysis. This can rapidly progress to involve the respiratory and bulbar muscles. Removal of the tick results in improvement of symptoms within hours. It is thought that a toxin in the tick's saliva blocks transmission across the neuromuscular junction, which results in paralysis.

Electromyography/nerve conduction study (EMG/NCS) should be ordered when ascending paralysis is diagnosed. But when tick paralysis is suspected, a detailed skin examination can be performed more quickly and should not be delayed until after the EMG/NCS. Magnetic resonance imaging of the brain is unlikely to show a cause for ascending paralysis with areflexia, so this is not the best answer. A food ingestion history would be very important if botulism were suspected, which in a 10-year-old girl, would most likely be foodborne. Symptoms of botulism include descending paralysis, beginning with symptoms such as ptosis, mydriasis, and facial weakness. The girl does not have symptoms of botulism, so obtaining a food ingestion history is not the next best step. Serum creatine kinase would be elevated in muscle disorders such as rhabdomyolysis, dermatomyositis, or muscular dystrophies. Because the girl in the vignette does not have symptoms of these conditions, this test would not be helpful.

PREP Pearls
- Tick paralysis can mimic the presentation of Guillain-Barré syndrome.
- Removal of the tick results in improvement in symptoms of tick paralysis within hours.

MOCA-Peds Objective
- Evaluate and manage a child with possible tick-borne illness

ABP Content Specifications(s)
- Recognize the clinical findings associated with tick paralysis

Suggested Readings
- McCarthy Dj, Tuite RJ, Conners GP. Index of suspicion. *Pediatr Rev*. 1995;16(6):223–225. doi: http://dx.doi.org/10.1542/pir.16-6-223.
- Rosen BA. Guillain-Barré syndrome. *Pediatr Rev*. 2012;33(4):164–171. doi: http://dx.doi.org/10.1542/pir.33-4-164.

Question 243

A 2-year-old previously healthy girl is brought to the otolaryngology clinic for evaluation of cervical lymphadenitis. For the last 2 months, she has had swelling on the left side of her neck. She has received a 2-week course of trimethoprim-sulfamethoxazole and then clindamycin without improvement. She has had progressive neck swelling and recently the skin overlying the swelling has developed a purple hue (Item Q243). She has not had any sick contacts or contact with animals. She has a temperature of 36.7°C, heart rate of 123 beats/min, respiratory rate of 26 breaths/min, and blood pressure of 118/62 mm Hg. She has a right submandibular node measuring 2 cm in length with overlying violaceous discoloration. The remainder of the physical examination findings are normal. Diagnostic evaluation shows:

•Tuberculin skin test, 12 mm
•Chest radiograph results, within normal limits

Item Q243: Findings for the girl described in the vignette.
Reprinted with permission from Frenkel L. and Kimberlin DW, et al. Red Book Online. Lyme disease. Elk Grove Village, IL. American Academy of Pediatrics 2015.

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

  A. Mycobacterium abscessus
  B. Mycobacterium avium complex
  C. Mycobacterium chelonae
  D. Mycobacterium kansasii
  E. Mycobacterium tuberculosis

Correct Answer: B

The most likely cause of the illness for the girl in this vignette is *Mycobacterium avium* complex. Approximately 70% of cases of nontuberculous mycobacteria (NTM) lymphadenitis are caused by *M avium* complex.

The species of NTM can be categorized by their growth rate in culture. Rapid-growing NTM, including *M abscessus, M chelonae*, and *M fortuitum*, can be identified in the laboratory within 3 to 7 days. Rapid-growing NTM account for a large portion of hospital-acquired infections in immunocompromised patients or patients with indwelling devices. Slow-growing NTM can cause infections in immunocompetent and immunocompromised individuals. In the United States, *M kansasii* is typically a cause of pulmonary infections in patients with cystic fibrosis and skeletal infections.

The history and physical examination findings for the girl in this vignette do not support *M tuberculosis* as the etiology of the illness. The girl appears well overall, except for the localized abnormalities, and her chest radiograph findings are within normal limits. Her tuberculin skin-test results are positive, which occurs in about half of patients with NTM lymphadenitis. In otherwise healthy children, the most common manifestation of NTM infections is lymphadenitis followed by skin and soft-tissue infections. Typically, NTM lymphadenitis occurs in the cervicofacial region of young children and is unilateral. Skin and soft-tissue infections can be caused by *M ulcerans* (the cause of Buruli ulcer in tropical regions), *M marinum* (with exposure to pools or fish tanks), and rapid-growing NTM (with trauma or as a nosocomial infection).

The optimal management of NTM lymphadenitis is complete excision of the involved nodes. Surgery without antimicrobial therapy has a success rate of 95% when performed early in the course of illness. However, depending on the anatomic location, surgical intervention has the potential of causing facial nerve damage; therefore, the decision to resect nodes has to be evaluated for each patient. Incision and drainage is not recommended because of the possible subsequent formation of sinus tracts, which can lead to chronic drainage. Antibiotics (azithromycin or clarithromycin in combination with rifampin, rifabutin, or ethambutol) can be offered to patients with sinus tracts or patients who are not candidates for surgery. For other disease processes, debridement and extended courses of combination antibiotic therapy are recommended. For nosocomial infections, removal of any potentially infected device is recommended.

PREP Pearls
- Cervicofacial lymphadenitis is the most common manifestation of nontuberculous mycobacterial infection in healthy children.
- Rapid-growing nontuberculous mycobacteria, including *Mycobacterium abscessus*, *M chelonae*, and *M fortuitum*, account for a large portion of hospital-acquired infections.
- Complete excision of the involved nodes, without antimicrobial treatment, has a success rate of 95% when performed early in the course of illness.

MOCA-Peds Objective
- Recognize patterns of opportunistic infection in an immunocompromised host

ABP Content Specifications(s)
- Recognize the major clinical features associated with a nontuberculous mycobacterial infection in immunocompetent children
- Plan the appropriate management of the complications of nontuberculous mycobacteria infection

Suggested Readings
- American Academy of Pediatrics. Diseases caused by nontuberculous mycobacteria. 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; 2015:831–839.
- Chesney P. Nontuberculous mycobacteria. *Pediatr Rev.* 2002;23(9):300–309. doi: http://dx.doi.org/10.1542/pir.23-9-300.

Question 244

An 18-month-old girl is brought to your office for evaluation of fever and fussiness. She developed congestion and cough 4 days ago and fever 2 days ago. She has decreased appetite and is not sleeping well. She has no significant prior medical history and her immunizations are up-to-date. She has a temperature of 39.4°C, heart rate of 100 beats/min, respiratory rate of 30 breaths/min, and oxygen saturation of 100% on room air. She appears ill but not in acute distress. Both tympanic membranes have a similar appearance (Item Q244).
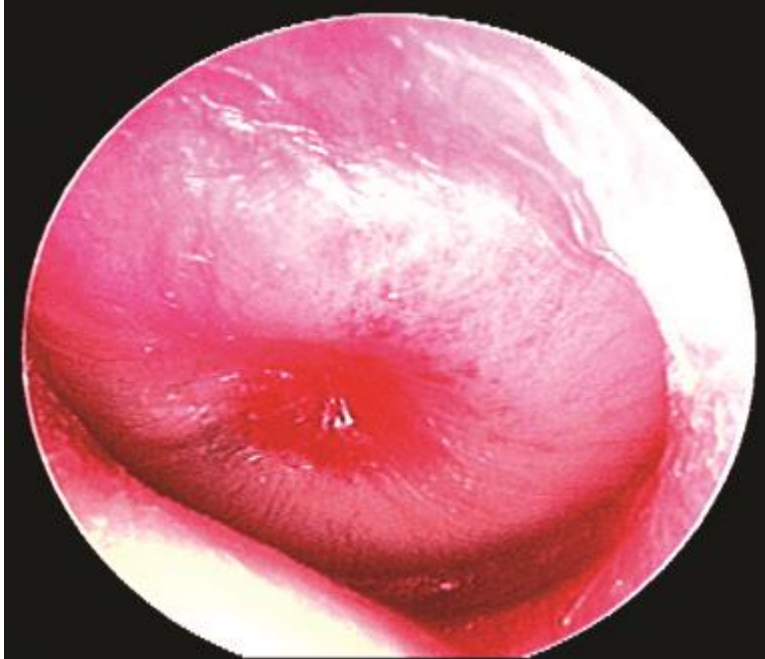
Item Q244: Tympanic membrane of the girl described in the vignette.
Reprinted with permission from Mccormick D. Siegel RM, Bien JP. *Pediatr Rev.* 2004;25:187–193

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

 A. amoxicillin, high dose (90 mg/kg/d)
 B. amoxicillin, low dose (40 mg/kg/d)
 C. amoxicillin-clavulanate, high dose (90 mg/kg/d)
 D. amoxicillin-clavulanate, low dose (40 mg/kg/d)
 E. ibuprofen

Correct Answer: A

The 18-month-old patient in this vignette has acute otitis media (AOM), an inflammatory process in the middle ear that complicates a noninflammatory middle ear effusion. Effusions occur when the eustachian tube cannot drain properly, typically because of edema triggered by a viral process. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are the most common bacterial pathogens in AOM.

Children with AOM typically have acute onset of fever, ear discomfort, fussiness, or difficulty sleeping. They often have signs of an upper respiratory tract infection, including rhinorrhea, congestion, and cough.

When considering treatment options, the age of the child and severity of disease must be considered. Clinical practice guidelines from the American Academy of Pediatrics recommend observation and pain control (without antimicrobial drugs) for children between 6 and 24 months of age with unilateral nonsevere disease and for children older than 24 months with either unilateral or bilateral nonsevere disease. Antimicrobial drugs should be considered for infants younger than 6 months, children younger than 24 months with bilateral AOM, and children of all ages with severe AOM. Large studies have demonstrated that most children with AOM will improve without antimicrobial treatment, and withholding antibiotics decreases the rates of antibiotic-associated side effects and bacterial resistance.

If antimicrobial treatment is appropriate, the first-line medication for most children is amoxicillin 90 mg/kg/d divided into twice daily doses. This higher dose of amoxicillin ensures better penetration of the middle ear and can overcome resistance due to penicillin-binding proteins expressed by some *S pneumoniae* strains. If a child has been treated for AOM within the last 30 days or has concurrent purulent conjunctivitis (a clinical indicator of *H influenzae* infection), amoxicillin-clavulanate 90 mg/kg/d divided into twice daily doses would be the best option. Children with penicillin allergies can be treated with a second or third generation cephalosporin. Children younger than 2 years should be treated for 10 days, children aged 2 to 5 years should be treated for 7 days, and children 6 years old and older should be treated for 5 to 7 days.

The child in this vignette is younger than 24 months and has bilateral severe AOM. Therefore, the most appropriate treatment would be high-dose amoxicillin, 90 mg/kg/d. Ibuprofen alone would not be appropriate. Low-dose amoxicillin and amoxicillin-clavulanate (40 mg/kg/d) are never recommended for the treatment AOM. This patient does not have a history of a recent AOM or concurrent purulent conjunctivitis, so she would not need treatment with high-dose amoxicillin-clavulanate.

PREP Pearls
- Not all children with acute otitis media need to be treated with antibiotics; many will improve with observation and pain control alone. Antimicrobial drugs should be considered for infants younger than 6 months, children younger than 24 months with bilateral acute otitis media, and children of all ages with severe disease.
- *Streptococcus pneumoniae, Haemophilus influenzae*, and *Moraxella catarrhalis* are the most common bacterial pathogens in acute otitis media.
- The most appropriate first-line antimicrobial treatment for the majority of children with acute otitis media is amoxicillin 90 mg/kg/d. If a child has been treated for acute otitis media within the last 30 days or has concurrent purulent conjunctivitis (a clinical indicator of *Haemophilus influenzae* infection), amoxicillin-clavulanate 90 mg/kg/d would be the best option.

ABP Content Specifications(s)
- Recognize pathogens commonly associated with acute otitis media in patients of various ages
- Recognize the clinical findings associated with acute otitis media
- Understand the natural history of acute otitis media in patients of various ages

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 .
- 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):480–486. doi: http://dx.doi.org/10.1542/pir.36-11-480.

Question 245

A 15-month-old girl who was recently adopted from Vietnam is brought to your office for the first time. Her adoptive parents provide you with the laboratory results they were given at the orphanage. You recommend additional screening. You are concerned about possible chronic hepatitis B infection.

Of the following laboratory test results, the ones MOST likely to confirm your suspicion are

(Abbreviations: anti-HBc, antibody to hepatitis B core antigen; anti-HBs, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; IgM anti-HBc, IgM to hepatitis B core antigen.)

    A. HBsAg -ve   Anti-HBc -ve Anti-HBs -ve IgM Anti-HBc -ve
    B. HBsAg -ve   Anti-HBc +ve Anti-HBs -ve IgM Anti-HBc -ve
    C. HBsAg +ve   Anti-HBc -ve Anti-HBs -ve IgM Anti-HBc -ve
    D. HBsAg +ve   Anti-HBc +ve Anti-HBs -ve IgM Anti-HBc -ve
    E. HBsAg +ve   Anti-HBc +ve Anti-HBs -ve IgM Anti-HBc +ve

Correct Answer: D

The adopted child in this vignette has chronic hepatitis B infection, identified by the presence of both hepatitis B surface antigen and antibody to hepatitis B core antigen in the absence of antibody to hepatitis B surface antigen and IgM to hepatitis B core antigen. **Item C245A** shows the serology results for different states of hepatitis B exposure and infection.

Item C245A. Serology Results for Different States of Hepatitis B Exposure and Infection.

Exposure status	HBsAg	Anti-HBc	Anti-HBs	IgM anti-HBc
No exposure	-	-	-	-
Immunized	-	-	+	-
Immune due to infection	-	+	+	-
Acute infection	+	+	-	+
Chronic infection	+	+	-	-
Resolving infection[a]	-	+	-	-

[a] This may also represent a false positive anti-HBc or a low level chronic infection.

Abbreviations: anti-HBc, antibody to hepatitis B core antigen; anti-HBs, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; IgM anti-HBc, IgM to hepatitis B core antigen

The presence of hepatitis B e antigen identifies active viral infection with high levels of infectivity.

Individuals acutely infected with hepatitis B may be symptomatic or asymptomatic. The likelihood of having symptoms increases with age from less than 1% in infancy to 30% to 50% in children older than 5 years. Symptoms are often nonspecific and include fever, anorexia, malaise, nausea, and arthritis. Patients can also present with jaundice and hepatitis. Fulminant hepatic failure, which is caused by a massive immune-mediated lysis of infected hepatocytes, is rare with acute infection (< 0.5% of patients). Extrahepatic manifestations of hepatitis B include rash, polyarteritis nodosa, thrombocytopenia, cryoglobulinemia, acute pericarditis, arthritis,

arthralgia. and papular acrodermatitis. Symptoms cannot be used to differentiate the different etiologies of hepatitis.

Chronic hepatitis B infection is identified by persistence of hepatitis B surface antigen for more than 6 months. Infants are the most likely group to develop chronic infection, with 90% of infected infants becoming chronically infected. Vaccination of newborns in conjunction with administration of hepatitis B immune globulin is effective in preventing vertical transmission in 85% to 95% of at-risk infants. Of patients 5 years and older, only 5% to 10% will have a chronic infection. Chronic infection rates decrease with increasing ages at acute infection. Children with chronic infection are at risk (15%-40%) for hepatocellular carcinoma and cirrhosis during their lifetime. One quarter of these children die from the complications of chronic infection. Chronically infected patients are also at risk for development of non-Hodgkin lymphoma. **Item C245B** shows the hepatitis B infection status for the response choices given in the vignette.

Item C245B. Serology Results and Hepatitis B Infection Status for Response Choices.

HBsAg	Anti-HBc	Anti-HBs	IgM anti-HBc	Hepatitis B status
-	-	-	-	No exposure (at risk)
-	+	-	-	Resolving infection or false positive
+	-	-	-	Unclear
+	+	-	-	Chronic infection
+	+	-	+	Acute infection

Abbreviations: anti-HBc, antibody to hepatitis B core antigen; anti-HBs, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; IgM anti-HBc, IgM to hepatitis B core antigen

PREP Pearls
- Children with hepatitis B infection are often asymptomatic. The likelihood of symptoms increases with age.
- Children with chronic infection are at risk (15%-40%) for hepatocellular carcinoma and cirrhosis in their lifetime.
- Fulminant hepatic failure is rare with acute infection and is seen in less than 0.5% of patients.
- Approximately 90% of vertically infected infants will develop chronic infection.

ABP Content Specifications(s)
- Identify the immediate and long-term complications of hepatitis
- Recognize the age-related clinical features associated with chronic hepatitis
- Plan the appropriate diagnostic evaluation of hepatitis

Suggested Readings
- Christenson JC, Manaloor JJ. Hepatitis A, B, and C. *Pediatr Rev.* 2016;37(10):426–438. doi: http://dx.doi.org/10.1542/pir.2015-0075.
- Clemente MG, Schwarz K. Hepatitis: general principles. *Pediatr Rev.* 2011;32(8):333–340. doi: http://dx.doi.org/10.1542/pir.32-8-333.
- Paganelli M, Xavier S, Sokal EM. Chronic hepatitis B in children and adolescents. *J Hepatol.* 2012;57(4):885–896. doi: http://dx.doi.org/10.1016/j.jhep.2012.03.036.

Question 246

You are seeing a 17-year-old girl for a health maintenance visit. During the interview, she reports that she has been sexually active with 2 lifetime male partners and engages only in vaginal intercourse. She is taking an oral contraceptive but uses condoms inconsistently. The girl reports no abnormal vaginal discharge, dysuria, or genital lesions.

Of the following, you are MOST likely to recommend that the girl undergo screening for

 A. cervical cancer
 B. chlamydia
 C. herpes simplex virus infection
 D. syphilis
 E. trichomoniasis

Correct Answer: B

Of the response choices, the girl in the vignette should undergo screening for chlamydia.
In the United States, the rates of many sexually transmitted infections (STIs) are highest among adolescents and young adults. One recommended control strategy is screening for infection. The Centers for Disease Control and Prevention (CDC) recommend screening for the following adolescent groups. (Note that testing for human immunodeficiency virus [HIV] should be offered to all adolescents and repeated every 3 to 5 years. For those at very high risk of infection [young men who have sex with men, injection drug users] repeat testing may be performed annually.)

Sexually active young women younger than 25 years:
- Annual testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using a urine or vaginal swab specimen for nucleic acid amplification testing (NAAT)
- Cervical cancer screening by cervical cytology (ie, the Papanicolaou test) is recommended beginning at age 21 years with repeat testing every 3 years until age 29 years.
- Routine screening for herpes simplex virus infection, syphilis, trichomoniasis, bacterial vaginosis, hepatitis A, and hepatitis B is *not* advised.

Heterosexual adolescent men:
- Evidence does not support routine screening for *C trachomatis* and *N gonorrhoeae* (in part because the prevalence of asymptomatic infection is low)
- In settings where the prevalence of infection is higher (eg, adolescent clinics, correctional facilities, STI clinics) screening for *C trachomatis* and *N gonorrhoeae* may be offered.

Young men who have sex with men:
- Annual Screening for human immunodeficiency virus and syphilis
- Annual screening for *C trachomatis* and *N gonorrhoea*
  - If practicing insertive anal intercourse: urine NAAT for both organisms
  - If practicing receptive anal intercourse: rectal swab NAAT for both organisms
  - If practicing receptive oral intercourse: pharyngeal swab NAAT for *N gonorrhoeae* only (testing for pharyngeal infection with *C trachomatis* is not recommended)

Young women who have sex with women:
- Limited information exists regarding STI transmission between women, but the risk likely is related to the type of sexual practice and the STI itself. Therefore, effective screening requires a candid discussion about sexual practices (eg, digital-vaginal contact, penetrative sex item, etc) and behaviors (eg, sharing of sex items).

Transgender women:
- The prevalence of HIV infection is high in this population (27.7% for all transgender women, 56.3% for black transgender women). However, data about other STIs are limited. STI screening recommendations depend on anatomic considerations and sexual practices.

Transgender men:
- Little information exists regarding the prevalence of STIs among transgender men, though HIV infection is less common than in transgender women. STI screening recommendations depend on anatomic considerations and sexual practices.

In addition to screening practices, the CDC and other organizations have published recommendations for pre- and postexposure strategies to control STIs. These include:
- Postexposure prophylaxis following sexual assault (CDC recommendations)**:**
  - Empiric treatment for *C trachomatis*, *N gonorrhoeae*, and trichomoniasis infection
  - Emergency contraception for women
  - Hepatitis B immunization without hepatitis B immunoglobulin (if the hepatitis status of the assailant is unknown and the survivor has not previously been immunized)
  - Human papillomavirus immunization (if the survivor has not previously been immunized)
  - HIV postexposure prophylaxis depending on risk (see: CDC Sexually Transmitted Diseases Treatment Guidelines, https://www.cdc.gov/std/tg2015/default.htm and below)
- Preexposure prophylaxis to prevent HIV infection:
  - Daily antiretroviral therapy to reduce transmission for individuals at high risk for infection.
- Nonoccupational postexposure prophylaxis to prevent HIV infection:
  - Typically, a 2- or 3-drug regimen to prevent HIV infection after injection drug use, sexual, or other nonoccupational exposure.
  - Nonoccupational postexposure prophylaxis should be initiated as soon as possible after exposure (ideally within 72 hours) and continued for 28 days.
  - Consultation regarding nonoccupational postexposure prophylaxis is available from the National HIV/AIDS Clinician's Consultation PEPline at 1-888-448-4911.

PREP Pearls
- Sexually active adolescent girls should be screened annually for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using a urine or vaginal swab specimen for nucleic acid amplification testing (NAAT).
- Routine screening for *C trachomatis* and *N gonorrhoeae* in sexually active adolescent boys is not recommended. However, screening may be offered to those at high risk for infection.
- Cervical cancer screening by cervical cytology (ie, the Papanicolaou test) is recommended beginning at age 21 years with repeat testing every 3 years until age 29 years.

MOCA-Peds Objective
- Provide guidance regarding methods of contraception

ABP Content Specifications(s)
- Understand the indications for a Papanicolaou test in female adolescents
- Plan an appropriate screening evaluation for sexually transmitted infections in various adolescent populations
- Plan appropriate prophylaxis following possible exposure to sexually transmitted infection

Suggested Readings
- Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep.* 2015;64(No. RR-3):1-137.
- Centers for Disease Control and Prevention. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV – United States, 2016. http://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf .
- Practice bulletin number 157 summary: cervical cancer screening and prevention. *Obstet Gynecol.* 2016;127:185–187. doi: http://dx.doi.org/10.1097/AOG.0000000000001256.
- Summaries for patients: screening for HIV—US Preventive Services Task Force Recommendation Statement. *Ann Intern Med.* 2013;159:51–60. doi: http://dx.doi.org/10.7326/0003-4819-159-1-201307020-00647.
- US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States 2014. A Clinical Practice Guideline. http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf.

Question 247

You are called to the nursery to evaluate a 36-hour-old full-term neonate who has not passed meconium. The mother is a 34-year-old gravida 3, para 1 woman with mild intermittent asthma and gestational diabetes that was treated with glyburide. The neonate was born vaginally with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. The neonate has been both breast and bottle feeding well, but had nonbilious vomiting twice in the past 12 hours. On physical examination, you note mild abdominal distension, without tenderness on palpation. You obtain a contrast enema (Item Q247).

Item Q247: Contrast enema radiograph for the neonate described in the vignette.
Courtesy of T. Levin

Of the following, the MOST likely diagnosis in this neonate is

 A. cystic fibrosis
 B. Hirschsprung disease
 C. malrotation
 D. meconium peritonitis
 E. small left colon syndrome

Correct Answer: E

For the neonate in the vignette, the most likely diagnosis is small left colon syndrome. In the United States, approximately 3% to 5% of term neonates are born to mothers with diabetes. There are a number of neonatal findings associated with gestational and pregestational diabetes. The most common of these is hypoglycemia, which occurs in response to maternal hyperglycemia. Other associated complications include macrosomia, prematurity, asymmetric septal hypertrophy causing cardiac outflow obstruction, respiratory distress syndrome, caudal regression syndrome, and small left colon syndrome.

Nearly 50% of cases of small left colon syndrome occur in neonates born to mothers with diabetes. Clinically, these neonates present with functional small bowel obstruction, abdominal distension, and delayed passage of meconium. They may develop vomiting, and in rare instances, bowel perforation. Though the pathogenesis is unknown, abnormal glucagon metabolism has been implicated. A contrast enema is both diagnostic and therapeutic in these cases. The radiographs will demonstrate a transition zone between the splenic flexure and small left colon. Infants may spontaneously pass a meconium plug with resolution of symptoms (**Item C247**). Typically, no further intervention is required. Stooling patterns should be monitored closely after passage of a meconium plug. If abnormal stooling patterns persist, a rectal biopsy for Hirschsprung disease would be indicated.

Item C247: Passed meconium plug
Courtesy of M. LaTuga

Neonates with cystic fibrosis may have delayed passage of stool because of higher protein levels in their meconium. This abnormal meconium, sometimes described as viscous, may cause a meconium ileus or meconium plug. With both meconium ileus and meconium plugs, neonates have abdominal distension with or without vomiting. In meconium ileus, inspissated meconium may be visualized on abdominal radiography as uneven filling of bowel loops. With meconium plugs, abdominal radiography typically shows a nonspecific gas pattern. For both entities, contrast enema shows a colon of normal caliber, in contrast to the small left colon noted in this

neonate's study. The contrast enema may be therapeutic, resulting in passage of an inspissated plug of meconium.

Neonates with Hirschsprung disease will also present with delayed passage of meconium and abdominal distension. However, a contrast enema will demonstrate a transition zone between the normal and aganglionic zone in the rectum. A rectal examination typically results in passage of a large stool. The diagnosis must be confirmed with suction rectal biopsy, which shows aganglionosis.

Neonates with malrotation may also present with abdominal distension, similar to the neonate in the vignette. They may have bilious emesis and tenderness on palpation of the abdomen. Malrotation is diagnosed on upper gastrointestinal series, with the third segment of the duodenum inappropriately located on the patient's right side. Malrotation with volvulus is a surgical emergency. Therefore, bilious emesis in a neonate must be evaluated immediately with a contrast study.

With meconium peritonitis, on abdominal radiography, opaque densities can be seen extraluminally in the abdominal cavity. Often, in these cases, there is an underlying intestinal atresia or stenosis which leads to a bowel perforation before birth. Neonates with meconium peritonitis may be asymptomatic or present with small bowel obstruction.

PREP Pearls
- The most common neonatal complication associated with gestational and pregestational diabetes is hypoglycemia, which occurs in response to exposure to maternal hyperglycemia.
- Other than hypoglycemia, associated complications of gestational diabetes include macrosomia, prematurity, asymmetric septal hypertrophy causing cardiac outflow obstruction, respiratory distress syndrome, caudal regression syndrome, and small left colon syndrome.
- Bilious emesis in a neonate must be evaluated immediately with a contrast study to ensure that an intestinal malrotation is not present.

ABP Content Specifications(s)
- Recognize the clinical and laboratory features in an infant of a diabetic mother, and manage appropriately

Suggested Readings
- Maheshwari A, Carlo WA. Digestive system disorders. In: Kliegman RM, Stanton BF, St. Geme J, Schor N, eds. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Saunders Elsevier; 2016:867-880.
- Smith B, Clatworthy HW. Meconium peritonitis: prognostic significance. *Pediatrics*. 1961;27: 967 http://pediatrics.aappublications.org/content/27/6/967.

Question 248

You are seeing a 15-year-old girl for preparticipation evaluation before the start of her high school basketball season. She underwent electrocardiography (ECG) 2 weeks earlier, at a community event that offered free cardiac screening for high school athletes. Her family brings the results of this study. You review her medical and family history, and perform a full review of systems and physical examination.

Of the following, the finding that MOST warrants cardiology evaluation in this girl is

A. blood pressure measurement of 135/90 mm Hg
B. first-degree atrioventricular block noted on ECG
C. heart rate of 45 beats/min
D. history of a grandfather who died of cardiac disease at age 55 years
E. history of an episode of syncope during basketball practice

Correct Answer: E

The adolescent in the vignette has a history of syncope during basketball practice. Syncope with exertional activities is an extremely concerning symptom. She should undergo additional evaluation to look for underlying heart disease before further participation in sports.

Syncope is common in adolescent athletes. In a study by Colivicchi et al, 6% of athletes presenting for preparticipation evaluation (PPE) reported at least 1 episode of syncope in the previous 5 years. However, in most cases, fainting was unrelated to exertion, and the athlete's history was consistent with neurocardiogenic syncope. In this study, heart disease was discovered in one-third of the athletes who experienced syncope during exercise.

Sudden cardiac death is uncommon in high school athletes, with an incidence of about 1 in 100,000. In the sports medicine community, there is considerable debate about whether electrocardiography (ECG) should be added to the PPE to screen for heart disease. Proponents of ECG screening argue that sudden cardiac death may be preventable in many cases and that ECG is an inexpensive, readily available tool. Detractors point out that many conditions are missed by ECG screening and that ECG has a high false-positive rate. If ECG were routinely implemented, many athletes would need to undergo additional testing or be disqualified from sports. In addition, many communities lack physicians with experience in interpreting ECG findings in high school athletes. Bradycardia (unless heart rate is <30 beats/min) and first-degree bundle branch block are examples of findings considered to be normal variants in young athletes that might otherwise be of concern.

The American Heart Association (AHA) does not recommend routine ECG screening for athletes, but has developed a list of 14 history and physical examination elements that should be included during the PPE. Most of these items are incorporated into the standardized history and physical examination form included in the preparticipation evaluation monograph published by the American Academy of Pediatrics. As part of the history, athletes should be asked about any history of cardiac symptoms, such as chest pain and syncope, and any history of previous evaluation for heart disease. Physicians should inquire whether there is a family history of death or disability from heart disease before age 50 years and of heart conditions known to be genetic (eg, hypertrophic cardiomyopathy, long QT syndrome). Important physical examination elements include evaluation for features associated with Marfan syndrome, cardiac auscultation, and assessment of blood pressure and femoral pulses. The AHA recommends that providers use their discretion, but should consider referral for additional evaluation if 1 or more of the history and physical examination elements are positive.

The adolescent in the vignette has a family history of heart disease, but the affected relative had a myocardial infarction at age 55 years. She also had a single high blood pressure measurement. A diagnosis of hypertension requires elevated blood pressure on 3 or more occasions. Stage 1 hypertension (>95th percentile, but ≤99th percentile + 5 mm Hg) in an adolescent may merit additional evaluation, but would not preclude participation in basketball.

PREP Pearls
- Syncope occurring with exertional activities is an extremely concerning symptom that merits additional evaluation for underlying heart disease.
- The American Heart Association (AHA) has developed a list of 14 history and physical examination elements that should be included during the preparticipation physical examination.
- Bradycardia (unless heart rate is <30 beats/min) and first-degree bundle branch block are examples of findings considered to be normal variants in young athletes that might otherwise be of concern.

ABP Content Specifications(s)
- Recognize the cardiac risks associated with sports participation and when cardiac evaluation is required

Suggested Readings
- Bernhardt DT, ed. *Preparticipation Physical Examination*. 4th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2010.
- Colivicchi F, Ammirati F, Biffi A, Verdile L, Pelliccia A, Santini M. Exercise-related syncope in young competitive athletes without evidence of structural heart disease: clinical presentation and long-term outcome. *Eur Heart J.* 2002;23(14):1125-1130.
- Drezner JA, Ackerman MJ, Anderson J, et al. Electrocardiographic interpretation in athletes: the 'Seattle criteria'. *Br J Sports Med.* 2013;47(3):122-124. doi: http://dx.doi.org/10.1136/bjsports-2012-092067.

Question 249

A previously healthy 5-year-old boy is brought to your office for his annual health supervision visit. He has intermittently reported leg pain during soccer practice or when playing outside with his friends. He has had intermittent mild headaches responsive to acetaminophen. His history is otherwise unremarkable. He has a heart rate of 80 beats/min, respiratory rate of 15 breaths/min, blood pressure of 120/80 mm Hg in the right upper extremity, and peripheral oxygen saturation of 98% on room air. His physical examination findings are remarkable for diminished femoral pulses.

Of the following, the BEST next step to determine the diagnosis in this patient is

A. brain magnetic resonance imaging
B. complete blood cell count
C. lower extremity blood pressure
D. lower extremity Doppler ultrasonography
E. renal ultrasonography

Correct Answer: C

The patient in this vignette has intermittent leg pain and headaches with hypertension noted by blood pressure measurement in the right arm and diminished femoral pulses. These findings are suggestive of coarctation of the aorta. A lower extremity systolic blood pressure measurement is the next best step to reveal the suspected diagnosis. A blood pressure in the lower extremities lower than the blood pressure in the right arm would be consistent with coarctation of the aorta. The diagnosis would be confirmed with echocardiography, computed tomography, or magnetic resonance imaging.

Coarctation of the aorta can present in different ways depending on the severity of the narrowing. In the neonatal period, in the setting of a critical coarctation that is ductal dependent for systemic blood flow, a patient may present in shock. At any age, coarctation of the aorta can present as a murmur, diminished femoral pulses, or hypertension in the right upper extremity. Renovascular disease can also cause hypertension. Other secondary reasons for hypertension are noted by age and system in **Item C249**.

Item C249. Differential Diagnosis of Hypertension Among Children, by Age.

Age Range	Primary or Secondary	Most Common Secondary Causes
Birth to 1 y	Secondary (99%)	Cardiac • Coarctation of aorta • Patent ductus arteriosus Renal • Renovascular defect • Renal parenchymal disease Pulmonary • Bronchopulmonary dysplasia Neurologic • Intraventricular hemorrhage • Pain Neoplasia • Wilms tumor • Neuroblastoma Endocrine • Congenital adrenal hyperplasia • Hyperaldosteronism • Hyperthyroidism
Age 1-12 y	Secondary (70%-85%) Primary (15%-30%)	Renal • Renal parenchymal disease • Renovascular defect Cardiac • Coarctation of aorta Urologic • Reflux nephropathy Endocrine • Congenital adrenal hyperplasia • Hyperaldosteronism • Hyperthyroidism Neoplasia • Wilms tumor • Neuroblastoma Miscellaneous
Age 12-18 y	Primary (85%-95%) Secondary (5%-15%)	Same causes as for 1-12 y

Reprinted with permission from Brady, T. Hypertension. *Pediatr Rev.* 2012;33(12):545.

Brain magnetic resonance imaging, a complete blood cell count, lower extremity Doppler ultrasonography, and renal ultrasonography would not be necessary or appropriate at this time. The headaches are caused by the hypertension and therefore brain magnetic resonance imaging would not be needed. There is no lower extremity swelling or tenderness to palpation and therefore lower extremity Doppler ultrasonography is not indicated. Renal ultrasonography could eventually be a part of the evaluation for hypertension, but the history and examination findings in this vignette are suggestive of coarctation. There is no indication for a complete blood cell count.

PREP Pearls
- Coarctation of the aorta can present in a neonate with shock or at any age with murmur, right upper extremity hypertension, diminished femoral pulses, or leg claudication.
- A decreased systolic blood pressure in the leg relative to the right upper extremity is concerning for coarctation of the aorta.
- Renovascular disease is another vascular cause of hypertension.

ABP Content Specifications(s)
- Recognize the cardiovascular causes of hypertension

Suggested Readings
- Brady T. Hypertension. *Pediatr Rev.* 2012;33(12):541–552. doi: http://dx.doi.org/10.1542/pir.33-12-541.
- Feld LG, Corey H. Hypertension in childhood. *Pediatr Rev.* 2007;28(8):283–297. doi: http://dx.doi.org/10.1542/pir.28-8-283.

Question 250

You are examining a 2,500 g male neonate born at 35 weeks of gestation to a 32-year-old woman. She is from El Salvador and immigrated to the United States 6 weeks ago. During the first trimester of the pregnancy, she developed a febrile illness that was characterized by rash and red eyes, and she did not seek medical evaluation for this illness. The neonate is normocephalic and the head circumference measures 33.5 cm (50th percentile). The remainder of the physical examination findings are normal. The mother expresses concern that her illness during the first trimester could have been caused by Zika virus.

Of the following, the BEST next step in the evaluation of this neonate is

A. head ultrasonography
B. lumbar puncture
C. ophthalmologic examination
D. Zika virus testing in mother
E. Zika virus testing in neonate

Correct Answer: A

The best next step in the evaluation of the neonate in this vignette is head ultrasonography. The mother of the infant lived in a country with endemic transmission of Zika virus, and during the first trimester she developed an illness that could be consistent with Zika virus infection. Because the infant in this vignette did not have abnormalities identified via physical examination, head ultrasonography would help determine if abnormalities are present.

Women can acquire Zika virus through the bite of an infected mosquito or via sexual contact. The fetus becomes infected via the transplacental route. Abnormalities associated with congenital Zika syndrome include microcephaly, intracranial calcifications (typically subcortical), other brain malformations, and eye anomalies, including abnormalities of the retinal and optic nerves. Fetal brain disruption sequence, characterized by severe microcephaly, overlapping of cranial sutures, prominent occipital bone, and redundant scalp skin has been described in infants with congenital Zika syndrome. Neurologic examination can reveal problems with tone, spasticity, and hyperreflexia. Clubfoot and arthrogryposis have also been associated with congenital Zika syndrome.

Lumbar puncture is not specifically warranted in the evaluation of congenital Zika virus infection. However, if a lumbar puncture is being performed for other reasons, such as evaluation of other congenital infections, cerebrospinal fluid can be evaluated for Zika virus by polymerase chain reaction and testing for anti–Zika virus IgM.

Ophthalmologic examination is recommended for infants with abnormalities suggestive of congenital Zika virus infection or infants with laboratory-confirmed infection. Ophthalmologic evaluation should take place within the first month after birth.

Zika virus testing in the mother should be performed if there is concern for Zika virus infection during the pregnancy based on an associated epidemiologic link. However, it is recommended that molecular testing be performed within 2 weeks of exposure and that serology be performed within 2 to 12 weeks of exposure. The mother in this vignette was not tested in this time frame; thus, while testing could be pursued, negative results would not exclude infection.

Zika virus testing in the neonate is recommended if maternal testing is positive or if the infant has abnormalities consistent with Zika virus infection on physical examination or neuroimaging and there is a maternal epidemiologic link that suggests the possibility of Zika virus infection.

PREP Pearls
- Abnormalities associated with congenital Zika syndrome include microcephaly, intracranial calcifications (typically subcortical), other brain malformations, and eye anomalies, including abnormalities of the retinal and optic nerves.
- Zika virus testing in the mother should be performed if there is concern for Zika virus infection during the pregnancy based on an associated epidemiologic link.
- Zika virus testing in the neonate is recommended if maternal testing is positive or if the infant has abnormalities consistent with Zika virus infection on physical examination or neuroimaging and there is a maternal epidemiologic link that suggests the possibility of Zika virus infection.
- All infants born to mothers with risk factors for Zika virus infection that did not have testing before delivery should have postnatal head ultrasonography, irrespective of physical examination findings.

ABP Content Specifications(s)
- Identify the measures to prevent tick- and mosquito-borne infections

Suggested Readings
- Moore C, Staples J, Dobyns W, et al. Characterizing the pattern anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA Pediatr.* 2017;171(3):288–295. doi: http://dx.doi.org/10.1001/jamapediatrics.2016.3982.
- Russell K, Oliver S, Lewis L, et al. Update: interim guidance for the evaluation and management of infants with possible congenital Zika virus infection—United States, August 2016. MMWR Morb Mortal Wkly Rep. 2016;65(33):870–878. doi: http://dx.doi.org/10.15585/mmwr.mm6533e2.

Question 251

A 3-month-old infant is brought to the emergency department because of a 4-day history of diarrhea and vomiting. His mother informs you that he has had no wet diapers in the last 12 hours. The infant is sleepy but lets out a high-pitched cry as you examine him. He has a temperature of 38°C, heart rate of 170 beats/min, respiratory rate of 50 breaths/min, and a blood pressure of 60/35 mm Hg. He has dry mucous membranes, depressed anterior fontanelle, decreased skin turgor, and deep respirations. His capillary refill time is 5 seconds, and his extremities appear cool and mottled. His serum chemistry results are consistent with hypernatremic dehydration (sodium, 166 mEq/L [166 mmol/L]).

Of the following, the MOST accurate statement in this infant with dehydration is

  A. his degree of dehydration may be overestimated
  B. his intravascular volume is not preserved
  C. neurologic sequelae are common
  D. only the maintenance and fluid deficit need to be replaced
  E. serum sodium should be corrected at a rate greater than 1 mEq/L/h

Correct Answer: C

The clinical symptoms and signs of the patient in this vignette are indicative of dehydration. A patient with dehydration may present with low (hyponatremic), normal (isonatremic), or elevated (hypernatremic) serum sodium concentration. The serum sodium concentration in dehydrated patients is influenced by the balance of the compensatory responses of thirst and antidiuretic hormone secretion. Additionally, inappropriately prepared formula may worsen hyponatremia or hypernatremia.

Hypernatremic dehydration with gastrointestinal losses is more frequently associated with decreased water intake and can be seen in patients with altered sensorium or developmental delay and in infants who receive inadequate fluid intake from their caregivers. In patients with recurrent episodes of hypernatremic dehydration, disorders associated with increased free water loss, such as diabetes mellitus (osmotic diuresis) and diabetes insipidus (antidiuretic hormone disorders), should be suspected. Diabetes insipidus occurs secondary to decreased secretion of antidiuretic hormone (central diabetes insipidus) or secondary to renal resistance to antidiuretic hormone (nephrogenic diabetes insipidus). The clinical presentation of diabetes insipidus includes polyuria, polydipsia, and increased thirst.

Clinical features of hypernatremic dehydration are less marked than clinical features in hyponatremic dehydration, which is caused by fluid shifts from the the intracellular compartment to the intravascular compartment to maintain serum osmolality. This leads to underestimation of the degree of dehydration associated with hypernatremia. It is suggested that 3% to 5% should be added to the degree of dehydration as estimated by clinical features (**Item C251**) in patients with hypernatremic dehydration.

Item C251. Clinical Features of Dehydration.*

Clinical Signs	Mild (3%-5%)	Moderate (6%-9%)	Moderate (≥10%)
Systemic signs	Increased thirst	Irritable	Lethargic
Urine output	Decreased	Decreased (<1 mL/kg/hr)	Decreased (oliguria/anuria)
Mucous membranes	Tacky	Dry	Parched
Skin turgor†	Normal	Reduced	Tenting
Capillary refill†	Normal	Mildly delayed	Markedly delayed
Skin temperature	Normal	Cool	Cool, mottled
Anterior fontanelle	Normal	Sunken	Markedly sunken
Heart rate	Normal	Increased	Markedly increased or ominously low
Blood pressure	Normal	Normal to low	Low
Respirations†	Normal	Deep rate, may be increased	Deep rate, may be increased, decreased or absent

* These findings for isonatremic dehydration overestimate the degree if dehydration with hyponatremia and underestimate the degree of dehydration with hypernatremia.
† Best predictors of dehydration

Reprinted with permission from Powers KS. Dehydration: isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev.* 2015;36(7):277.

Neurologic sequelae occur in up to 50% of infants with hypernatremic dehydration, with severe neurologic sequelae reported in 5% to 10%. Infants with hypernatremic dehydration have increased sleepiness and can be hyperirritable with a high-pitched cry. Hypertonicity causes brain shrinkage due to neural cell dehydration, increasing the risk for the rupture of bridging

veins and leading to subdural, subarachnoid, or intraparenchymal brain hemorrhage. Additionally, patients with hypernatremic dehydration are at increased risk for venous thrombosis.

Fluid management in patients with hypernatremia includes replacement of free water deficit along with any ongoing losses and maintenance fluids. Free water deficit is calculated by using the formula:

$0.6 \times$ weight (kg) $\times$ ([serum sodium /140] -1)

Free water deficit is replaced over a period of 48 to 72 hours to avoid rapid decrease in serum osmolality. A safe rate at which the serum sodium concentration should be lowered is 10 to 12 mEq/L/d (0.4-0.5 mEq/L/h). It is important to account for ongoing losses (eg, urine output, gastrointestinal fluid losses, chest tube drainage) in fluid management because ongoing losses would lead to persistent or worsening hypernatremia despite fluid resuscitation. A rapid decrease in serum osmolality and sodium is associated with an increased risk for cerebral edema due to 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. Serum sodium greater than 160 mEq/L and correction of hypernatremia at a rate greater than 0.5 mEq/L/h for 48 hours is associated with higher morbidity and mortality.

Isonatremic dehydration is the most common presentation in patients with dehydration. It is associated with proportional losses of solute and water. Isonatremic dehydration has the best prognosis as compared to hyponatremic and hypernatremic dehydration. Oral rehydration solution is recommended as the preferred therapy for mild or moderate isonatremic dehydration. Intravenous hydration is the preferred therapy for severe isonatremic dehydration and failure of oral rehydration therapy.

Hyponatremia in patients with dehydration occurs because of replacement of gastrointestinal losses with free water or low-sodium content fluids (ginger ale, juice, water). Hyponatremia associated with low serum osmolality leads to fluid shifts from the extracellular to intracellular compartment to maintain serum osmolality. Patients with hyponatremic dehydration therefore present with severe dehydration and require immediate intravenous rehydration.

PREP Pearls
- Hypernatremic dehydration with gastrointestinal losses is more frequently associated with decreased water intake that occurs in patients with altered sensorium (ie, developmental delay) or infants who receive inadequate fluid intake from their caregivers.
- Clinical features of dehydration are less marked in patients with hypernatremia, leading to underestimation of the degree of dehydration.
- Neurologic sequelae are frequently seen in infants with hypernatremic dehydration.
- A safe rate at which the serum sodium concentration should be lowered in patients with hypernatremic dehydration is 10 to 12 mEq/L/d (0.4-0.5 mEq/L/h) over 48 to 72 hours.

ABP Content Specifications(s)
- Recognize the clinical and laboratory abnormalities associated with hypernatremic dehydration, and manage appropriately
- Recognize the laboratory abnormalities associated with isotonic dehydration, and manage appropriately
- Recognize the clinical and laboratory abnormalities associated with hyponatremic dehydration, and manage appropriately

Suggested Readings
- Jain A. Body fluid composition. *Pediatr Rev*. 2015;36(4):141–152. http://dx.doi.org/10.1542/pir.36-4-141.
- Moritz ML, Ayus JC. Misconceptions in the treatment of dehydration in children. *Pediatr Rev*. 2016;37(7):e29–e31. http://dx.doi.org/10.1542/pir.2016-003.
- Powers KS. Dehydration: isonatremic, hyponatremic, and hypernatremic recognition and management. *Pediatr Rev*. 2015;36(7):274–285. http://dx.doi.org/10.1542/pir.36-7-274.

Question 252

A 3-year-old girl presents to your clinic for evaluation of bilateral intoeing. Her parents are unsure how long this has been present. The girl's preschool teacher recently pointed out her unusual gait while walking and running. The girl is healthy, has met gross motor milestones on time, and does not complain of any leg pain. She seems to trip more often than other children her age. There is no family history of intoeing or lower extremity abnormalities. On physical examination, the girl has moderate, symmetric intoeing with walking. She has mild, symmetric genu valgum. Her thigh-foot angle is neutral bilaterally. In the prone position, her hip internal rotation is 75 degrees bilaterally and hip external rotation is 25 degrees bilaterally. Lower extremity tone and reflexes are normal.

Of the following, the BEST next step in management for this girl is

 A. orthopedic consultation for bracing
 B. orthopedic consultation for surgical correction
 C. reassurance that this is a normal variant
 D. physical therapy for gait training
 E. shoe inserts with arch support

Correct Answer: C

The child in the vignette has intoeing caused by increased femoral anteversion (antetorsion). Increased or "excessive" femoral anteversion is a common, normal variant.

The femoral head and neck are typically in a position of slight anterior rotation (anteversion). The degree of anteversion is highest at birth and gradually decreases until the preadolescent years. Individuals with excessive femoral anteversion have increased internal rotation of the hip and decreased external rotation. Children with structurally normal hip joints should have a total rotation (internal plus external) of at least 90 degrees. Those with femoral anteversion have significantly more internal rotation than external rotation.

At birth, infants typically have contractures of the lateral hip muscles because of in utero positioning. These contractures keep the hips in an externally rotated position that can mask increased femoral anteversion. The hip muscles gradually loosen by 6 to 12 months after children begin walking; thus, the parents of children with increased femoral anteversion typically notice bilateral, symmetric intoeing around the age of 2 to 3 years. Often there is a history of increased tripping and falling. Parents may report that their child can sit in a "W" position (**Item C252**).

Item C252: Child sitting in a W-position
Courtesy of R. Carl

On physical examination, affected children have symmetric hip internal rotation of 65 degrees or more and normal total rotation. Hip and pelvis radiographs should be obtained for children with asymmetric or limited hip motion. Femoral anteversion gradually decreases with growth, but some children have increased internal rotation into adulthood. Increased anteversion has been associated with knee pain, however, studies have not demonstrated subsequent development of arthritis. Sitting in a "W" position has not been associated with future hip or knee problems, and many orthopaedists feel that children should be allowed to sit in the position they find most comfortable.

Internal tibial torsion is another normal variant that leads to intoeing. Internal tibial torsion occurs as a result of in utero position, and typically results in unilateral or asymmetric intoeing. Most parents notice the intoeing when their children begin to walk, between the ages of 12 and 18 months. This condition almost always resolves by age 8 to 10 years of age without intervention.

Braces do not alter the natural history for rotational causes of intoeing. Physical therapy will not change the bone rotation, but may be helpful for gait training in an older child with tripping that limits activities. Osteotomy (bone-cutting) surgery is very rarely indicated; it is reserved for treatment of children and teens who are near skeletal maturity with persistent intoeing that leads to chronic pain or functional disturbances (eg, frequent tripping, difficulty with sports). Shoe inserts do not help correct rotational deformities.

PREP Pearls
- Increased or excessive femoral anteversion is a common, normal variant that results in symmetric intoeing.
- Children with increased femoral anteversion have at least 65 degrees of internal hip rotation and normal total hip rotation.
- Hip and pelvis radiographs should be obtained for children with asymmetric or limited hip motion.
- Braces have not been shown to alter the natural history of rotational causes of intoeing.

ABP Content Specifications(s)
- Understand the natural history of femoral anteversion
- Plan the appropriate clinical and diagnostic evaluation of femoral anteversion

Suggested Readings
- Sarwark JF, LaBella CR, eds. *Pediatric Orthopaedics and Sports Injuries: A Quick Reference Guide*. 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:51,57,217 .
- Schoeneker P, Rich M, Gordon JE. The lower extremity. In: Weinstein SL, Flynn HM, eds. *Lovell and Winter's Pediatric Orthopaedics*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:chap 27:1261-1340.

Question 253

A 12-year-old boy who has been your patient since birth is brought for a sick visit because of headaches that started 6 weeks ago. The headaches have been increasing in frequency and intensity; they now occur almost daily and are worse in the late afternoon. They are nonfocal and described as pounding. The boy does not experience associated photophobia, visual changes, or nausea. An examination by a pediatric optometrist last week showed that he has 20/20 vision in both eyes without correction, and a dilated fundoscopic examination revealed no optic disc edema or other ocular abnormality. He has been taking ibuprofen 10 mg/kg as needed with partial relief. He has not been taking any other medications.

He has not traveled outside of the United States or had any major life changes over the last 12 months. He attends the seventh grade where he has performed well academically, and he reports having lots of friends. He has a normal, generally healthy diet as described by his parents.

His medical history is remarkable for standard-risk acute B lymphoblastic leukemia that was diagnosed at 6 years of age. He completed all chemotherapy treatments at 9 years of age. Since that time, he has been leukemia-free and has had normal growth and development. His immunizations are up to date.

Laboratory data are shown:

Laboratory Test	Result
White blood cell count	6,100/µL (6.1 x 10^9/L)
Hemoglobin	12.9 g/dL (129 g/L)
Platelet count	186 x 10^3/µL (186 x 10^9/L)
Neutrophils	56%
Lymphocytes	41%
Monocytes	3%

No blasts are reported.

Of the following, the BEST next step is to

A. contact his oncologist to arrange for a lumbar puncture
B. obtain a more detailed social history
C. prescribe sumatriptan 3 mg/kg subcutaneously once
D. reassure his parents that headaches are common as boys begin puberty
E. refer him to an ophthalmologist for a more complete eye examination

Correct Answer: A

Headaches in childhood are very common, with 58% of children reporting having had headache in the past year. Headaches can be classified by their presentation, frequency, and intensity into acute, episodic recurrent, new daily persistent, chronic progressive, or chronic nonprogressive. **Item C253** shows the causes of childhood headache divided into these categories.

Item C253. Causes of Pediatric Headache.

Acute headache
- Migraine
- Viral respiratory infection
- Streptococcal pharyngitis
- Meningitis/encephalitis
- Intracranial hemorrhage
- Tumor
- Toxic exposures: alcohol, toxins, illicit drugs, medications
- Trauma
- Stroke
- Malignant hypertension
- Vasculitis

Episodic recurrent headaches
- Tension-type headache
- Migraine with or without aura
- Fasting/eating disorders
- Recurrent toxic exposures: alcohol, toxins, illicit drugs, medications
- Recurrent sinus disease
- Seizure-associated headache
- Mitochondrial disease
- Trigeminal autonomic cephalalgias

Chronic progressive headaches
- Elevated intracranial pressure
- Tumor
- Vascular malformations
- Infection
- Sinus venous thrombosis
- Idiopathic intracranial hypertension
- Endocrine disease: thyroid or parathyroid disease
- Chiari malformation
- Vasculitis

Chronic nonprogressive headaches
- Chronic tension-type headaches
- Chronic or transformed migraine
- New daily persistent headache
- Chronic sinus disease
- Dental disease
- Sleep apnea
- Idiopathic intracranial hypertension
- Thyroid disease
- Chiari malformation
- Fasting/eating disorders
- Chronic posttraumatic headache
- Chronic trigeminal autonomic cephalalgias

Adapted and reprinted with permission from Blume HK. Pediatric headache: a review. Pediatr Rev. 2012;

The boy in this vignette has had headaches that have increased in frequency and intensity over the last few weeks, falling into the category of acute headache. While over 90% of children treated for standard-risk childhood acute lymphoblastic leukemia will be cured of their disease, approximately 10% will have progressive disease or relapse. Based on his history of having completed chemotherapy for acute lymphoblastic leukemia 3 years ago, there should be immediate concern for a central nervous system (CNS) recurrence of the leukemia. The CNS is a

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sanctuary site for acute lymphoblastic leukemia. The blood-brain barrier does not protect the brain from leukemic cells, which are abnormal lymphoblasts that are still recognized by the immune system as self. However, the blood-brain barrier does protect the CNS from many systemic chemotherapeutics. Thus, leukemic cells in the CNS are shielded from exposure to systemic chemotherapy. When multiple-agent chemotherapy was first introduced for leukemia, many children achieved a complete bone marrow remission but relapsed quickly in the CNS. As a consequence, CNS prophylaxis with intrathecal chemotherapy (chemotherapy administered directly into the spinal fluid) was instituted for all children with acute leukemia. Despite this prophylaxis, there are still some treatment failures, and children who had been in a complete remission can relapse. Relapse can occur in the bone marrow, the CNS, the testes (the blood-testicular barrier behaves in a similar way to the blood-brain barrier), or any combination of these sites. When leukemia relapses only in the CNS, it is termed an isolated CNS relapse. Most headaches reported by survivors of childhood leukemia are not caused by a relapse; however, given this child's temporal proximity to treatment, a relapse must be ruled out by lumbar puncture to test for leukemic blasts in the spinal fluid and potentially by magnetic resonance imaging of the brain.

Given the highly varied presentation and broad differential, obtaining a complete history is critical to finding the underlying cause of headaches in children. A reasonably detailed social history was obtained for the child in this vignette, and a more detailed social history would not further narrow the differential. While the child's presentation could be consistent with migraine, a recurrence of leukemia needs to be ruled out before prescribing treatment with sumatriptan. Headaches occur more commonly in boys than girls, but they are not part of normal pubertal development. The boy in this vignette recently had a dilated eye examination, and a repeat evaluation will not narrow the differential diagnosis.

PREP Pearls
- Headaches are common in children, and the differential diagnosis can be narrowed by obtaining a detailed history of the frequency, chronicity, and intensity of the headaches.
- The central nervous system is a sanctuary site for acute leukemia because of the inability of some systemic chemotherapies to cross the blood-brain barrier. Thus, children with a history of leukemia can experience isolated central nervous system relapse.
- If a central nervous system relapse of leukemia is suspected, a lumbar puncture with examination of the cerebral spinal fluid for leukemic blasts should be performed.

ABP Content Specifications(s)
- Identify disorders associated with an increased risk of leukemia
- Understand the outcome associated with treated acute lymphoblastic leukemia
- Recognize clinical findings associated with leukemia, including sites of relapse
- Understand that management of leukemia is dependent on its type

Suggested Readings

- Blume HK. Pediatric headache: a review. *Pediatr Rev*. 2012;33(12):562–576. http://dx.doi.org/10.1542/pir.33-12-562.
- Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. *N Engl J Med*. 2015;373(16):1541–1552. http://dx.doi.org/10.1056/NEJMra1400972.
- Hutter JJ. Childhood leukemia. *Pediatr Rev*. 2010;31(6):234–241. http://dx.doi.org/10.1542/pir.31-6-234.

Question 254

You are caring for a 2-year-old girl with severe anoxic brain injury resulting from a prolonged cardiac arrest after drowning in her family's swimming pool 4 days ago. Her vital signs are as follows: temperature, 37.0°C; heart rate, 120 beats/min, respiratory rate, 16 breaths/min, and blood pressure, 100/60 mm Hg. Her oxygen saturation is 100% on 30% oxygen, with the ventilator rate set at 16. She has not received any sedatives, her toxicology screening result was negative, and her electrolyte levels are normal. On physical examination, the girl does not exhibit any spontaneous movement or any movement with painful stimuli. She does not breathe over the ventilator. Her pupils are 7 mm and fixed, and her cough and gag reflexes are absent. Her eyes do not move relative to her head when it is moved from side to side, nor do they move on cold caloric stimulation of the ears.

Of the following, the MOST appropriate next step in the girl's care is to

  A. consult neurology
  B. declare death by neurologic criteria
  C. obtain a cerebral blood flow scan
  D. perform computed tomography of the head
  E. perform apnea testing

Correct Answer: E

The girl in the vignette suffered a prolonged cardiac arrest resulting in severe anoxic brain injury. Because she does not have any signs of brain activity, a brain death evaluation should be conducted. The neurologic examination component of the brain death examination has already been performed, and revealed no evidence of brain function. Therefore, the most appropriate next step is to perform apnea testing.

In 1981, the United States President's Commission released the Uniform Determination of Death Act, which defined death as either the irreversible cessation of all circulatory and respiratory functions, or the irreversible cessation of all functions of the entire brain, including the brainstem. In effect, this formally established 2 paths for the declaration of death. Declaring death when breathing and circulation have stopped, and resuscitation is either ineffective or not undertaken, fits well with societal and cultural norms of death, in which the deceased appears cold and lifeless. The declaration of brain death can be challenging for clinicians because the deceased has a beating heart, functioning lungs, and often normal vital signs. It can be even more difficult for families to understand, because their loved one may be warm and pink with the appearance of a peacefully sleeping child.
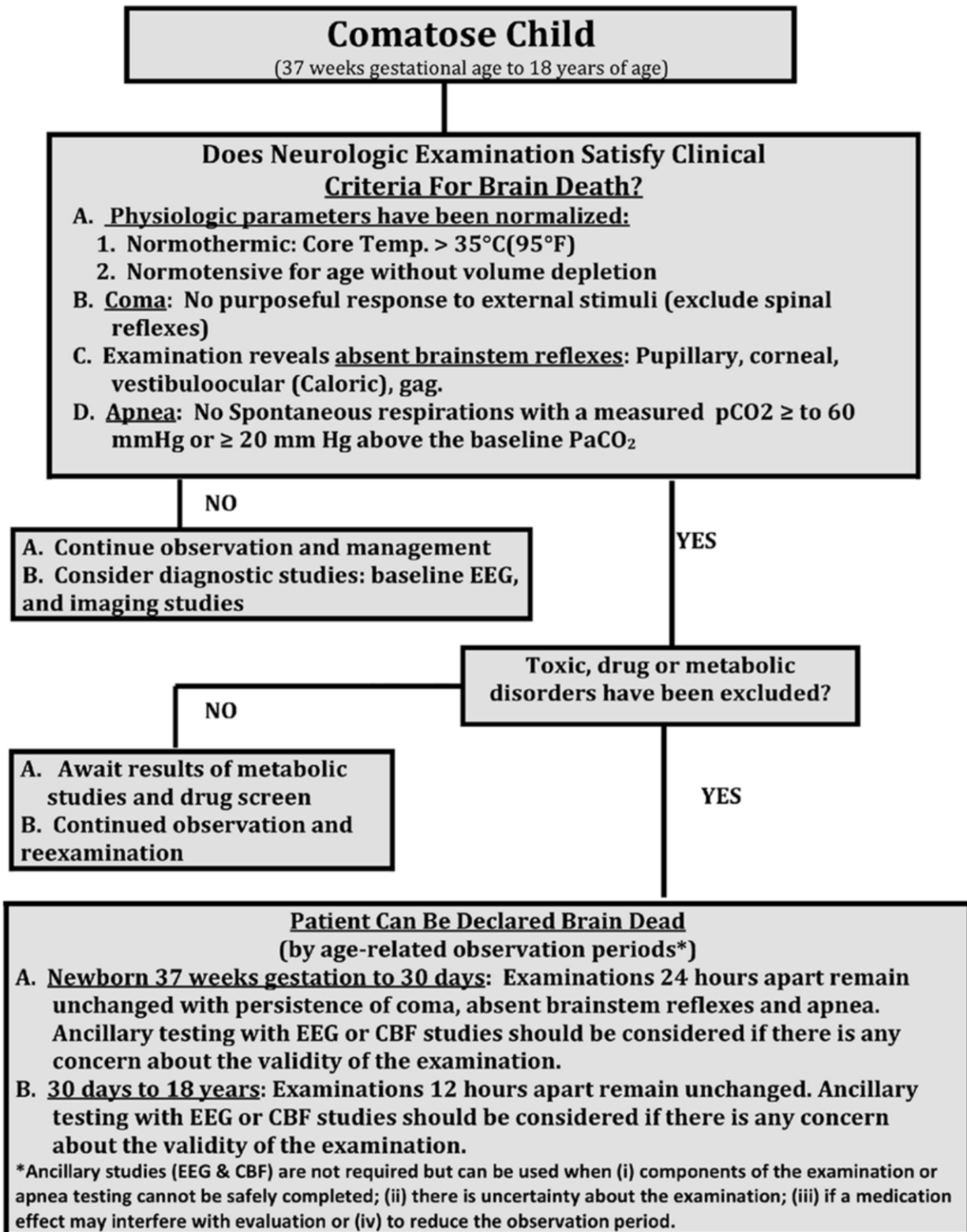
The diagnosis of brain death requires formal testing, which should be undertaken as soon as this condition is considered a possibility. A delay in the diagnosis of death can have several negative consequences, including inappropriate resource utilization, negative impact on the grieving process for families, difficulties in organ recovery, and confusion regarding the diagnosis. Testing should be initiated if there is a known irreversible cause of coma in a child with no evidence of neurologic function. If there is any a priori evidence of neurologic function, such as breathing over the ventilator, cranial nerve function, or response to stimuli outside of spinal reflexes, brain death testing should not be initiated. Other prerequisites for initiating testing include ruling out reversible causes of coma and correction of hypotension, hypothermia, or metabolic disturbances. Some electrolyte abnormalities and therapeutic levels of sedatives may be present, but whether they are severe enough to cause coma in any individual case must be determined by the medical team.

Brain death testing consists of a clinical neurologic examination and the performance of an apnea test. Guidelines for determining brain death in children were first published by the American Academy of Pediatrics in 1987 and updated in 2011 (**Item C254A** and **Item C254B**). Brainstem reflexes must be absent, including pupillary, bulbar response (facial movement with temporomandibular joint pressure), cough, gag, suck, corneal, and oculovestibular. There must be flaccid tone and the absence of spontaneous or induced movement other than spinal reflexes. Apnea testing is consistent with brain death if there is a complete lack of respiratory effort despite a partial pressure of arterial carbon dioxide greater than 60 mm Hg and greater than 20 mm Hg above baseline. If testing reveals any evidence of neurologic function, the test should be stopped and determined to be inconsistent with brain death.

Item C254A. Brain Death Examination in Infants and Children.

Brain Death Examination for Infants and Children
Two physicians must perform independent examinations separated by specified intervals.

Age of Patient	Timing of first exam	Inter-exam. interval
Term newborn 37 weeks gestational age and up to 30 days old	☐ First exam may be performed 24 hours after birth OR following cardiopulmonary resuscitation or other severe brain injury	☐ At least 24 hours ☐ Interval shortened because ancillary study (section 4) is consistent with brain death
31 days to 18 years old	☐ First exam may be performed 24 hours following cardiopulmonary resuscitation or other severe brain injury	☐ At least 12 hours OR ☐ Interval shortened because ancillary study (section 4) is consistent with brain death

Section 1. PREREQUISITES for brain death examination and apnea test

A. IRREVERSIBLE AND IDENTIFIABLE Cause of Coma (Please check)

☐ Traumatic brain injury   ☐ Anoxic brain injury   ☐ Known metabolic disorder   ☐ Other (Specify)
_____

B. Correction of contributing factors that can interfere with the neurologic examination	Examination One		Examination Two	
a. Core Body Temp is over 95° F (35° C)	☐ Yes	☐ No	☐ Yes	☐ No
b. Systolic blood pressure or MAP in acceptable range (Systolic BP not less than 2 standard deviations below age appropriate norm) based on age	☐ Yes	☐ No	☐ Yes	☐ No
c. Sedative/analgesic drug effect excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No
d. Metabolic intoxication excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No
e. Neuromuscular blockade excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No

☐If ALL prerequisites are marked YES, then proceed to section 2, OR

☐ _____ confounding variable was present. Ancillary study was therefore performed to document brain death. (Section 4).

Section 2. Physical Examination (Please check) NOTE: SPINAL CORD REFLEXES ARE ACCEPTABLE	Examination One Date/ time: _____		Examination Two Date/ Time: _____	
a. Flaccid tone, patient unresponsive to deep painful stimuli	☐ Yes	☐ No	☐ Yes	☐ No
b. Pupils are midposition or fully dilated and light reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
c. Corneal, cough, gag reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
Sucking and rooting reflexes are absent (in neonates and infants)	☐ Yes	☐ No	☐ Yes	☐ No
d. Oculovestibular reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
e. Spontaneous respiratory effort while on mechanical ventilation is absent	☐ Yes	☐ No	☐ Yes	☐ No

☐The _____ (specify) element of the exam could not be performed because_____.
Ancillary study (EEG or radionuclide CBF) was therefore performed to document brain death. (Section 4).

Section 3. APNEA Test	Examination One Date/ Time_____	Examination Two Date/ Time_____
No spontaneous respiratory efforts were observed despite final $PaCO_2 \geq 60$ mm Hg and a ≥ 20 mm Hg increase above baseline. (Examination One) No spontaneous respiratory efforts were observed despite final $PaCO_2 \geq 60$ mm Hg and a ≥ 20 mm Hg increase above baseline. (Examination Two)	Pretest $PaCO_2$: _____ Apnea duration: _____min Posttest $PaCO_2$: _____	Pretest $PaCO_2$: _____ Apnea duration: _____min Posttest $PaCO_2$: _____

Apnea test is contraindicated or could not be performed to completion because_____.
Ancillary study (EEG or radionuclide CBF) was therefore performed to document brain death. (Section 4).

Section 4. ANCILLARY testing is required when (1) any components of the examination or apnea testing cannot be completed; (2) if there is uncertainty about the results of the neurologic examination; or (3) if a medication effect may be present. **Ancillary testing can be performed to reduce the inter-examination period however a second neurologic examination is required. Components of the neurologic examination that can be performed safely should be completed in close proximity to the ancillary test**	Date/Time: _____	
☐ Electroencephalogram (EEG) report documents electrocerebral silence OR	☐ Yes	☐ No
☐ Cerebral Blood Flow(CBF) study report documents no cerebral perfusion	☐ Yes	☐ No

Section 5. Signatures

Examiner One

I certify that my examination is consistent with cessation of function of the brain and brainstem. Confirmatory exam to follow.

_____   _____
(Printed Name)   (Signature)

_____   _____   _____
(Specialty)   (Pager #/License #)   (Date mm/dd/yyyy)   (Time)

Examiner Two

☐I certify that my examination☐ and/or ancillary test report ☐confirms unchanged and irreversible cessation of function of the brain and brainstem. The patient is declared brain dead at this time.
Date/Time of death: _____

_____   _____
(Printed Name)   (Signature)

_____   _____   _____
(Specialty)   (Pager #/License #)   (Date mm/dd/yyyy)   (Time)

Item C254B. Algorithim to Diagnose Brain Death in Infants and Children.

Comatose Child
(37 weeks gestational age to 18 years of age)

Does Neurologic Examination Satisfy Clinical Criteria For Brain Death?

A. Physiologic parameters have been normalized:
   1. Normothermic: Core Temp. > 35°C(95°F)
   2. Normotensive for age without volume depletion
B. Coma: No purposeful response to external stimuli (exclude spinal reflexes)
C. Examination reveals absent brainstem reflexes: Pupillary, corneal, vestibuloocular (Caloric), gag.
D. Apnea: No Spontaneous respirations with a measured pCO2 ≥ to 60 mmHg or ≥ 20 mm Hg above the baseline $PaCO_2$

NO

A. Continue observation and management
B. Consider diagnostic studies: baseline EEG, and imaging studies

YES

Toxic, drug or metabolic disorders have been excluded?

NO

A. Await results of metabolic studies and drug screen
B. Continued observation and reexamination

YES

Patient Can Be Declared Brain Dead
(by age-related observation periods*)

A. Newborn 37 weeks gestation to 30 days: Examinations 24 hours apart remain unchanged with persistence of coma, absent brainstem reflexes and apnea. Ancillary testing with EEG or CBF studies should be considered if there is any concern about the validity of the examination.
B. 30 days to 18 years: Examinations 12 hours apart remain unchanged. Ancillary testing with EEG or CBF studies should be considered if there is any concern about the validity of the examination.

*Ancillary studies (EEG & CBF) are not required but can be used when (i) components of the examination or apnea testing cannot be safely completed; (ii) there is uncertainty about the examination; (iii) if a medication effect may interfere with evaluation or (iv) to reduce the observation period.

Reprinted with permission from Nakagawa TA, Ashwal S, Mathur M, Mysore M; Society of Critical Care Medicine, Section on Critical Care and Section on Neurology of American Academy of Pediatrics; Child Neurology Society. Guidelines for the determination of brain death in infants and children: an update of the 1987 task force recommendations. *Pediatrics.* 2011;128:e720-740.

A newborn from 37 weeks' gestation to 30 days of age can be declared brain dead if results of 2 examinations conducted 24 hours apart are both consistent with brain death. A child between 30 days and 18 years of age can be declared brain dead after results of 2 examinations conducted 12 hours apart meet the criteria. Once brain death is determined, time of death should be declared. If there is any concern about the validity of the clinical examination, an ancillary test, such as electroencephalography or cerebral blood flow study, should be performed. For example, if a child becomes unstable during the apnea testing, the test should be aborted and an ancillary test should be performed. However, ancillary testing should not be obtained if the neurologic examination and apnea test can be reliably performed and are consistent with brain death.

The child in this vignette cannot be declared brain dead at this point, because the first examination is not yet complete, and 2 examinations conducted 12 hours apart are necessary. Any physician can perform brain death testing, thus neurology consultation is not necessary in this case. A cerebral blood flow scan or other ancillary test should be performed when brain death testing is equivocal, or otherwise cannot be conducted, but that is not the case for the child in this vignette. Lastly, computed tomography is not helpful in a diagnosis of brain death.

Organ procurement organizations (OPOs) should be notified early in the treatment course of a comatose child, perhaps even before brain death is suspected. However, it is inappropriate for them to interact with the family until death is suspected. A reasonable time for representatives of an OPO to approach the family is between the first and second brain death examinations. It is recommended that the discussion of organ donation be initiated by the OPO as opposed to the medical team, to improve consent rates as well as mitigate concerns of conflict of interest.

PREP Pearls
- Death is medically, legally, and ethically established by either irreversible cessation of all circulatory and respiratory functions, or irreversible cessation of all functions of the entire brain, including the brainstem.
- The diagnosis of brain death requires 2 clinical examinations, 12 or 24 hours apart depending on the child's age, each including a clinical neurologic examination and apnea testing.
- Ancillary testing, such as electroencephalography or cerebral blood flow scanning, should be undertaken to help determine brain death, only if the clinical examination is equivocal or cannot be reliably performed.

ABP Content Specifications(s)
- Understand the criteria for brain death and the role of neurodiagnostic studies in making that determination

Suggested Readings
- Booth CM, Boone RH, Tomlinson G, Detsky AS. Is this patient dead, vegetative, or severely neurologically impaired? assessing outcome for comatose survivors of cardiac arrest. *JAMA*. 2004;291(7):870–879. http://dx.doi.org/10.1001/jama.291.7.870.
- Mathur M, Petersen L, Stadtler M, et al. Variability in pediatric brain death determination and documentation in southern California. *Pediatrics*. 2008;121(5):988–993. http://dx.doi.org/10.1542/peds.2007-1871.
- Nakagawa TA, Ashwal S, Mathur M, Mysore M; Society of Critical Care Medicine, Section on Critical Care and Section on Neurology of American Academy of Pediatrics; Child Neurology Society. Guidelines for the determination of brain death in infants and children: an update of the 1987 task force recommendations. *Pediatrics*. 2011;128:e720–740. http://dx.doi.org/10.1542/peds.2011-1511.

Question 255

You are seeing a 4-year-old boy in your clinic for frequent eye blinking. His medical history is unremarkable, with no chronic medical problems. His father reports that, for the past 1 to 2 months, the boy's right eye will twitch or blink rhythmically for 3 to 5 minutes. At the same time, his right cheek will also twitch. During these episodes, the boy is awake and can respond to simple questions, but seems "spacey." These episodes occur once or twice a week. His parents have not noticed any triggers for these events.The boy's physical examination findings are within normal parameters.

Of the following, the BEST next step in this boy's diagnosis and management is to

A. obtain an anti-DNA-ase B test, antistreptolysin antibodies, and inflammatory markers
B. obtain serum electrolytes and liver function tests
C. order electroencephalography
D. provide reassurance
E. start clonidine

Correct Answer: C

The boy in the vignette is having focal seizures involving his face, which is associated with an alteration of his mental status. Focal seizures are also called complex partial seizures. The best next step in his diagnosis and management is to order an electroencephalogram to confirm the diagnosis. He will likely also need magnetic resonance imaging of the brain to look for a focal lesion that may be causing the seizures.

Focal seizures can have various clinical presentations, depending on the location in the brain where the seizure starts. These include hemifacial twitching (usually involving the eye, cheek, and sometimes mouth), focal limb jerking, or automatisms such as purposeless, repetitive hand movements; activities such as nose wiping, fumbling with clothes or arranging small items; or uttering repetitive stereotyped phrases such as "I'm OK! I'm OK! I'm OK." During the seizure, the child may be able to respond to simple requests, but is not able to have a normal conversation. Focal seizures typically last 2 to 30 minutes or longer. Sometimes there is an aura before the seizure, such as a feeling of fear, a noxious smell, or a sense of deja vu. In most cases, an individual's focal seizures are the same every time they have them. This can help differentiate focal seizures from other phenomena, such as parasomnias or nonepileptic seizures, which can have different clinical presentations and different durations from event to event.

Obtaining an anti-DNA-ase B test, antistreptolysin antibodies, and inflammatory markers would be helpful if the boy in the vignette had chorea. Chorea typically presents with random, jerky movements without alteration in consciousness, which is different from this boy's presentation. Serum electrolytes and liver function tests are rarely abnormal even in the setting of new seizures in children. Because this boy has been having seizures for 1 to 2 months, these tests are not likely to help in diagnosis. Reassurance would be appropriate if there were no concern for focal seizure, but this boy presented with typical symptoms of focal seizures. Clonidine is frequently used off-label to treat tics. Like chorea, tics do not present with altered mental status, so starting clonidine in this case is not likely to be helpful.

PREP Pearls
- Focal seizures (also called complex partial seizures) can have various clinical presentations, such as hemifacial twitching (usually involving the eye, cheek, and sometimes mouth), focal limb jerking, automatisms such as purposeless, repetitive hand movements; activities such as nose wiping, fumbling with clothes, or arranging small items; or uttering repetitive stereotyped phrases.
- Mental status is usually altered during a focal seizure.
- An individual's clinical presentation of a focal seizure usually stays the same (ie, type and duration) for each event.

ABP Content Specifications(s)
- Recognize the clinical findings associated with complex partial seizures, and manage appropriately

Suggested Readings
- International League Against Epilepsy. www.epilepsydiagnosis.org .
- Sidhu R, Velayudam K, Barnes G. Pediatric seizures. *Pediatr Rev*. 2013;34(8):333-342. http://dx.doi.org/10.1542/pir.34-8-333.

Question 256

A 3-year-old girl is brought to your office for evaluation of short stature, progressive learning difficulties, and unusual facial features. She is also showing signs of developmental regression. Her mother notes that she has loud snoring, hearing problems, and frequent ear, nose, and throat infections. Her facial features appear coarse with midfacial hypoplasia, flat nasal bridge, thickened lips and tongue, and a dark synophrys (Item Q256). Her eye examination reveals corneal clouding. The remainder of the physical examination shows a loud systolic murmur, umbilical hernia, gibbus deformity of the lower spine, joint stiffness, and hepatosplenomegaly.

Item Q256: Girl described in the vignette.
Courtesy of L. Parsley

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

A. biotinidase deficiency
B. galactosemia
C. Hunter syndrome
D. Hurler syndrome
E. phenylketonuria

Correct Answer: D

The patient in this vignette has Hurler syndrome, mucopolysaccharidosis type I (MPS I), which is a progressive multisystem neurodegenerative disorder. In severe MPS I, infants will appear normal at birth but over time will develop coarsening of the facial features, most evident after 1 year of age. Other manifestations include severe cognitive decline, macrocephaly with or without communicating hydrocephalus, gibbus deformity of the lower spine, progressive skeletal dysplasia (dysostosis multiplex), short stature, hearing loss, frequent upper respiratory infections, umbilical/inguinal hernias, hepatosplenomegaly, and corneal clouding. Cardiac involvement includes cardiac valvular thickening, cardiomyopathy, arrhythmias, coronary artery disease, and ultimately cardiovascular collapse with most patients dying before 10 years of age.

Fortunately, there are medical treatments that can prevent or delay some of the primary manifestations of MPS I. If performed early, hematopoietic stem cell transplant can improve growth, reduce facial coarsening, reduce hepatosplenomegaly, improve hearing, and amend the natural history of the progressive cardiac and respiratory involvement, increasing survival. Hematopoietic stem cell transplant has less impact on skeletal manifestations and corneal clouding. Enzyme replacement therapy with laronidase is also available for treating the non–central nervous system manifestations of MPS I. Enzyme replacement therapy does not prevent the cognitive decline in MPS I because of its inability to cross the blood-brain barrier. It will reduce hepatic size, improve linear growth and joint mobility, and ameliorate the respiratory complications of MPS I. A multispecialty team approach is mandatory and should include a neurologist, ophthalmologist, orthopedic surgeon, cardiologist, audiologist, otolaryngologist, rehabilitation specialist, and a primary care physician.

Urine glycosaminoglycans and a skeletal survey are effective screening tests for MPS, but they are not specific to MPS I. Definitive diagnosis is established through identification of biallelic pathogenic mutations in *IDUA* or demonstration of deficient α-L-iduronidase lysosomal enzyme activity.

Mucopolysaccharidosis type I is an autosomal recessive condition caused by biallelic inheritance of pathogenic gene mutations in *IDUA*. Each child of a couple who both have heterozygous *IDUA* mutations will have a 25% chance of being affected, a 25% chance of being unaffected and not a carrier, and a 50% chance of being a carrier.

Hunter syndrome, also known as MPS II, is an X-linked recessive condition predominantly affecting male individuals that manifests very similarly to the neurodegenerative and multisystem features of MPS I, except for the corneal clouding, which is not a typical feature of MPS II. Because the patient in this vignette is a girl, a diagnosis of Hunter syndrome would be less likely.

Biotinidase deficiency presents with extensive neurologic abnormalities including seizures, ataxia, low muscle tone, developmental delay, vision problems, and hearing loss. Children will often have cutaneous abnormalities including alopecia, skin rash, and recurrent candidiasis. Children with biotinidase deficiency identified on newborn screening can immediately be treated

with daily lifelong biotin therapy, avoiding the neurologic consequences of this disorder and optimizing their chances of a normal outcome through early intervention and detection.

Galactosemia presents with life-threatening manifestations in early infancy including feeding problems, failure to thrive, bleeding, hepatic failure, and *Escherichia coli* sepsis. These symptoms will quickly resolve with a lactose-restricted diet in the first 2 weeks after birth. This disorder is included in all newborn screening protocols given that early detection and treatment dramatically improves outcomes. However, even with early treatment, children can still experience speech delay, learning disabilities, and premature ovarian insufficiency.

Phenylketonuria presents with progressive severe and irreversible intellectual disability if a phenylalanine-restricted diet is not implemented in early infancy. Because of a deficiency of phenylalanine hydroxylase, children are unable to break down phenylalanine into tyrosine, resulting in excess phenylalanine levels and low tyrosine levels. These biochemical abnormalities cause rapid neurocognitive decline, epilepsy, autistic features, musty body odor, eczema, and light skin and hair pigmentation. This disorder is included in newborn screening panels given that early detection and treatment dramatically improves outcomes.

Biotinidase deficiency, galactosemia, and phenylketonuria do not present with skeletal dysplasia and coarse facial features.

PREP Pearls
- Hurler syndrome, mucopolysaccharidosis type I, is a progressive multisystem neurodegenerative disorder where infants appear normal at birth but develop coarsening of the facial features, most evident after 1 year of age. Other manifestations include a severe cognitive decline, macrocephaly with or without communicating hydrocephalus, gibbus deformity of the lower spine, progressive skeletal dysplasia (dysostosis multiplex), short stature, hearing loss, frequent upper respiratory infections, umbilical/inguinal hernias, hepatosplenomegaly, and corneal clouding.

ABP Content Specifications(s)
- Recognize the clinical features associated with the mucopolysaccharidoses, including Hurler syndrome
- Recognize the laboratory features associated with mucopolysaccharidosis

Suggested Readings
- Clarke LA. Mucopolysaccharidosis type I. *GeneReviews*. 2016.
- Jameson E, Jones S, Remmington T. Enzyme replacement therapy with laronidase (Aldurazyme(®)) for treating mucopolysaccharidosis type I. *Cochrane Database Syst Rev*. 2016;4:CD009354. http://dx.doi.org/10.1002/14651858.CD009354.pub4.
- Wraith JE, Jones S. Mucopolysaccharidosis type I. *Pediatr Endocrinol Rev*. 2014;12(suppl 1):102–106.

Question 257

A 13-year-old adolescent boy is brought to your office by his parents for behavioral concerns. His parents report that for the past month, their son has been withdrawn and uninterested in participating in any family activities. He quit the baseball team and his grades have dropped. He spends most of his time in his room. He is irritable when his parents talk to him and hard to wake in the morning for school. The boy has been healthy and is not taking any medications or supplements. When you interview him apart from his parents, his responses are brief and unrevealing. The review of systems is otherwise negative, and the boy's physical examination findings are within normal limits. You recommend evaluation and treatment by a psychologist to address the adolescent's symptoms.

Of the following, the MOST evidence-based treatment for the adolescent's condition is

  A. cognitive behavioral therapy
  B. dialectical behavior therapy
  C. family therapy
  D. interpersonal therapy
  E. psychodynamic therapy

Correct Answer: A

The adolescent boy in the vignette is exhibiting signs and symptoms of depression. Among the response choices, the most evidence-based treatment for this condition is cognitive behavioral therapy (CBT).

There is substantial evidence regarding the effectiveness of CBT in treating depression. Unlike interpersonal therapy which focuses on relationships, and psychodynamic therapy which focuses on past experiences, CBT focuses on present thoughts, feelings, and behaviors. The therapist works with the patient on reframing negative thoughts into healthier thoughts, thereby resulting in more positive feelings and behaviors. Dialectical behavioral therapy is based on CBT, but works toward the acceptance of distressing thoughts, emotions, and behaviors. Family therapy, which focuses on improving communication and conflict resolution among family members, can be used as an adjunct to other treatments for depression, but is not effective when used by itself. Of the therapies offered as responses, CBT is the best-established treatment for depression.

Depression is characterized by at least 2 weeks of depressed or irritable mood and/or decreased pleasure or interest in activities (ie, anhedonia). These symptoms are accompanied by appetite or weight changes, sleep changes (eg, insomnia, hypersomnia), activity changes (eg, psychomotor agitation or retardation), lack of energy, feelings of guilt or worthlessness, poor concentration, and/or suicidality. Children may not express sadness or a depressed mood, but instead present with irritability, declining academic achievement, social withdrawal, poor self-esteem, difficulty concentrating, or disruptive behaviors. Younger children may present with somatic symptoms (eg, headache, stomach ache), whereas adolescents may demonstrate psychomotor retardation, hopelessness, or risk-taking behaviors (eg, substance use). Although typical adolescents may demonstrate mood swings, irritability, impulsivity, and changes in their sleep patterns, adolescents with depression respond to the stress and events in their lives with emotions that are more intense and longer-lasting. In addition, they have other depressive symptoms (eg, anhedonia, difficulty concentrating) and have impairment in function (eg, decline in school grades and behavior, poor relationships with peers and family).

Evidence-based tools, such as the Patient Health Questionnaire and the Beck Depression Inventory, can be used to screen children for depression. Information should be gathered from parents, but adolescents and children with concerning signs or symptoms should also be interviewed alone. Suicidal ideation and risk factors for suicide (eg, previous attempt, access to firearms, substance use, family history of suicide) should be assessed, and emergent evaluation by psychiatry is indicated if there is immediate concern of self harm. Coexisting conditions should be identified, because most children and adolescents with depressive disorders have coexisting conditions that increase their complexity of management. Anxiety disorders, substance abuse disorders, and disruptive behavior disorders are the most common comorbid conditions.

There are multiple contributors to depression. Genetic factors are important; children of depressed adults are more likely to have depression. Molecular genetic studies indicate that differences in the serotonin transporter gene may confer vulnerability to depression. Functional

imaging studies demonstrate differences in such areas as the medial prefrontal cortex and amygdala. Mood may be influenced by environmental stress through production of epigenetic effects or by hypothalamic-pituitary-adrenal axis dysregulation. Children with psychosocial stressors such as abuse, trauma, parental divorce, family conflict, and low socioeconomic status are at increased risk for depression. Risk factors also include chronic medical problems and other mental health conditions (eg, anxiety, conduct disorder). Close family relationships, special skills, or other strengths may be protective.

Management begins with psychoeducation about depression and the options for treatment. Evidence-based treatments include psychotherapy and medication. The recommended treatment for mild to moderate depression is psychotherapy. Moderate to severe depression is best treated with a combination of psychotherapy and medication. Treatment with combined CBT and medication is more effective than either treatment alone for adolescent depression.

Selective serotonin reuptake inhibitors are the recommended first-line medications for treating depression in children. Fluoxetine is approved by the US Food and Drug Administration for treating childhood and adolescent depression; escitalopram is also approved for treating adolescent depression. The depressed child's family should be referred to mental health resources and supports, and a safety plan should be developed defining what the adolescent should do if symptoms worsen (eg, contacting an adult or physician, calling 911). Frequent monitoring of treatment goals and outcomes is essential. Referral to a mental health specialist is recommended for patients with complex conditions, those who do not respond to treatment, or those who are acutely suicidal or psychotic.

Pediatricians are vital to the identification, management, and treatment of children and adolescents with depression. Resources such as the Guidelines for Adolescent Depression in Primary Care and Bright Futures in Practice: Mental Health are available to support the pediatric health care provider in the care of these patients.

PREP Pearls
- There is substantial evidence of the effectiveness of cognitive behavioral therapy (CBT) in treating depression.
- In CBT, the therapist works with the patient on reframing present negative thoughts into healthier thoughts, thereby resulting in more positive feelings and behaviors.
- Depressed children may not express sadness or a depressed mood, but may present with irritability, declining academic achievement, social withdrawal, poor self-esteem, difficulty concentrating, or disruptive behaviors.
- Most children and adolescents with depressive disorders have coexisting conditions such as anxiety, substance abuse, or disruptive behavior disorders.
- Moderate to severe depression is best treated with a combination of psychotherapy and medication. Treatment with CBT combined with medication is more effective than either treatment alone for adolescent depression.

ABP Content Specifications(s)
- Distinguish the findings associated with normal mood swings in an adolescent from those of a depressive disorder
- Recognize co-morbidities commonly associated with depressive disorders in children and adolescents
- Recognize the various environmental and biological contributors to the development of depressive disorders in children and adolescents
- Recognize the clinical findings associated with depressive disorders in children and adolescents, and manage appropriately

Suggested Readings

- Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein RE; GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II, treatment and ongoing management. *Pediatrics*. 2007;120(5):e1313–e1326. http://dx.doi.org/10.1542/peds.2006-1395.
- Maslow GR, Dunlap K, Chung RJ. Depression and suicide in children and adolescents. *Pediatr Rev*. 2015;36(7):299–310. http://dx.doi.org/10.1542/pir.36-7-299.
- Tang MH, Pinsky EG. Mood and affect disorders. *Pediatr Rev*. 2015;36(2):52–61. http://dx.doi.org/10.1542/pir.36-2-52.
- Zuckerbrot RA, Cheung AH, Jensen PS, Stein RE, Laramie D; GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): I, identification, assessment, and initial management. *Pediatrics*. 2007;120(5):e1299–e1312. http://dx.doi.org/10.1542/peds.2007-1144.

Question 258

A 4-year-old girl is brought to your office for evaluation of recurrent crops of pruritic red bumps noted over the past 6 months. Individual lesions resolve in 7 to 10 days, leaving areas of hyperpigmentation. The girl has no other symptoms and takes no medications. She appears well and is afebrile. There are multiple hyperpigmented macules and papules that are concentrated on the extremities (Item Q258).

Item Q258: Hyperpigmented macules and papules as described in the vignette.
Reprinted with permission from Hernandez RG, Cohen BA. *Pediatrics*. 2006;118(1):e189-e195

Of the following, the MOST likely diagnosis is

 A. atopic dermatitis
 B. Gianotti-Crosti disease
 C. papular urticaria
 D. scabies
 E. urticaria

Correct Answer: C

The girl in this vignette has a recurring eruption composed of erythematous papules that last 7 to 10 days. Over time, the lesions become hyperpigmented. These findings are most consistent with a diagnosis of papular urticaria. Atopic dermatitis has a chronic course marked by intermittent flares and, in persons of color, the rash may be papular (**Item C258A**). However, the presence of large individual papules, as exhibited by the girl in this vignette, would be atypical of atopic dermatitis. In atopic dermatitis, the involvement of the antecubital and popliteal fossae, not the extensor surfaces of the extremities, is expected. Gianotti-Crosti disease (papular acrodermatitis of childhood) is a unique viral exanthem composed of erythematous, edematous, monomorphous papules symmetrically distributed on the face, buttocks, and extensor surfaces of the extremities. Papules may coalesce to form large plaques (**Item C258B**). The trunk is usually spared. The eruption may last 8 to 12 weeks but is not recurrent. Scabies is characterized by erythematous papules concentrated in flexural areas (interdigital webs, wrist flexures, axillae). The eruption of scabies would not be expected to recur unless the child had become reinfested. Urticaria appears as wheals, often in a variety of shapes. Although the condition may become chronic, individual lesions last less than 24 hours (usually < 2 to 3 hours).

Item C258A: Papular atopic dermatitis in the antecubital fossa.
Courtesy of D. Krowchuk

Item C258B: Monomorphic papules coalesced on the cheeks of a child with Gianotti-Crosti disease.
Reprinted with permission from Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology. A Quick Reference Guide*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016.Pg 122

Papular urticaria is a reaction to bites from insects, especially fleas, mosquitoes, mites, and bedbugs. Although the pathophysiology is incompletely understood, it is postulated that the biting insect deposits an antigen that is disseminated hematogenously. A type 1 hypersensitivity reaction ensues, leading to the formation of lesions at locations distant from the bite. However, evidence exists supporting a component of delayed-type hypersensitivity (type IV). Papular urticaria occurs most often in children 2 to 10 years of age and is especially prevalent during spring and summer months. The eruption is characterized by grouped erythematous papules or vesicles on exposed surfaces of the extremities. The lesions are intensely pruritic. Some papules exhibit a central punctum (the site of a bite), but other papules do not have a central punctum and are caused by a hypersensitivity reaction. Lesions may become eroded and crusted from scratching or hyperpigmented as the result of the inflammatory process. The treatment of papular urticaria is symptomatic. Because lesions are pruritic, a mid- to high-potency topical corticosteroid may be applied to individual lesions twice daily. If needed, an oral antihistamine can be administered. A central component of management is prevention of insect bites. Families with pets should initiate flea-control measures. For outdoor play, children may wear protective clothing and apply insect repellent to exposed skin surfaces. The prognosis for papular urticaria is excellent. Children ultimately "outgrow" the condition before adolescence.

PREP Pearls
- Papular urticaria is a reaction to bites from insects, especially fleas, mosquitoes, mites, and bedbugs.
- Papular urticaria occurs most often in children 2 to 10 years of age and is especially prevalent during spring and summer months.
- The papular urticaria eruption is characterized by grouped erythematous papules or vesicles located on exposed surfaces of the extremities. Some papules exhibit a central punctum (the site of a bite), but other papules do not have a central punctum and are produced by a hypersensitivity reaction.

ABP Content Specifications(s)
- Recognize the clinical manifestations of papular urticaria
- Know the cause of papular urticaria

Suggested Readings
- Hernandez RG, Cohen BA. Insect bite-induced hypersensitivity and the SCRATCH principles: a new approach to papular urticaria. *Pediatrics*. 2006;118(1):e189–e196. http://dx.doi.org/10.1542/peds.2005-2550.
- Section on Dermatology, American Academy of Pediatrics. Insect bites and papular urticaria. In: Mancini AJ, Krowchuk DP, eds. *Pediatric Dermatology: A Quick Reference Guide*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2016:295–303.

Question 259

A 13-year-old previously healthy boy presents to your office for evaluation of scrotal pain. Five hours ago, the boy awoke from sleep with a sharp pain in his right scrotum. He states that last evening, he played basketball with some friends at a local park and then rode his bicycle home. He does not recall any injury to his scrotum, and he denies any previous episodes of similar pain. He denies any recent fevers, dysuria, difficulty urinating, or flank pain, but complains of "feeling sick to my stomach" since his pain began.

In your office, the boy appears uncomfortable but nontoxic. He is afebrile, and his vital signs are within normal limits for his age. His abdomen is soft with no focal tenderness and normoactive bowel sounds. His right hemiscrotum is moderately swollen and tender to palpation, with erythema of the overlying skin. His left hemiscrotum is nontender without swelling or erythema of the overlying skin. You are able to elicit a cremasteric reflex on the left, but not on the right. A urine test strip analysis is negative.

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

 A. acute orchitis
 B. incarcerated inguinal hernia
 C. testicular torsion
 D. torsion of a testicular appendage
 E. traumatic hematocele

Correct Answer: C

The adolescent boy in the vignette presents with acute onset of severe unilateral scrotal pain and nausea. He has no preceding history of trauma, fever, or other genitourinary symptoms. His physical examination is significant for unilateral swelling, tenderness, and erythema over the right side of his scrotum, with absence of a right cremasteric reflex. These features are consistent with a diagnosis of right testicular torsion.

Testicular torsion occurs due to twisting of the spermatic cord, which impairs testicular blood flow and can lead to permanent ischemic injury to the affected testicle. Therefore, testicular torsion is a true surgical emergency. Classic symptoms of testicular torsion include sudden onset of severe, unrelenting scrotal pain, often with associated nausea and/or vomiting. Physical examination findings include enlargement/swelling of the hemiscrotum, tenderness of the testicle, loss of the cremasteric reflex, and transverse lie of the testis (sometimes with superior displacement) on the affected side. It is important to note that the absence of swelling or erythema over the affected testicle and/or the presence of a cremasteric reflex does *not* rule out the diagnosis of testicular torsion, especially if the onset of pain is recent.

Early recognition of testicular torsion is the key to ensuring the best clinical outcome. Any boy with acute scrotal pain, regardless of age, must be presumed to have testicular torsion until proven otherwise. Furthermore, it is essential that a testicular examination be completed in any male with abdominal pain, because testicular torsion can manifest solely with abdominal pain in some patients. Younger children may not be able to recognize and/or verbalize the presence of scrotal symptoms, while older children may be reluctant to report scrotal symptoms to caregivers and/or medical providers.

All children with suspected testicular torsion should be emergently referred for urologic consultation. Scrotal ultrasonography is the recommended diagnostic study for these patients; however, even if the diagnosis is not confirmed by imaging, urologic consultation is still recommended when testicular torsion is highly suspected. The sole management for testicular torsion is operative reduction and fixation. Although manual detorsion maneuvers may be attempted as a temporizing measure, this treatment alone is not adequate. Significant ischemic damage to the testicle is believed to occur within 4 to 8 hours of torsion, referred to as the "golden window" in some texts. However, patients presenting with testicular torsion who have had symptoms for greater than 8 hours must still be emergently referred for surgical management, because the viability of the testis can be difficult to predict.

Children and adolescents with orchitis may also present with unilateral (or bilateral) scrotal pain, but symptom onset is typically more gradual. Patients with orchitis often have associated fever, and generally do not present with nausea or vomiting.

Children with incarcerated inguinal hernias typically present with pain in the inguinal region with "bulging" of a nonreducible, tender, erythematous/discolored mass through the external inguinal ring. Like testicular torsion, an incarcerated inguinal hernia is a surgical emergency.

This diagnosis is unlikely for the boy in the vignette; he has swelling and tenderness of his right scrotum rather than his inguinal region, and he has no history of inguinal hernia.

Children with torsion of a testicular appendage often report symptoms similar to those of testicular torsion, but the degree of pain reported is generally less severe, and nausea and vomiting are typically not present. The scrotal swelling is less pronounced than that seen with testicular torsion, and these patients typically have a focal tender nodule located at the superior aspect of the affected testis (rather than over the inferior aspect of the testis). The "blue dot" sign is an area of bluish coloration that can be seen through the scrotal skin at the superior pole of the testis. While it is a classic physical examination finding, it is certainly not seen in all children presenting with this diagnosis. Scrotal ultrasonography is indicated in children with findings suggestive of torsion of the testicular appendage, because it is essential to distinguish this condition from testicular torsion.

Patients with a traumatic hematocele may develop scrotal swelling, tenderness, and erythema and/or bruising. However, a history of significant blunt trauma to the perineal region is also universally present in these patients. The boy in the vignette has no reported history of trauma.

PREP Pearls
- Classic symptoms of testicular torsion include sudden onset of severe, unrelenting scrotal pain, often with associated nausea and/or vomiting.
- Physical examination findings of testicular torsion include enlargement/swelling of the hemiscrotum, tenderness of the testicle, loss of the cremasteric reflex, and transverse lie of the testis on the affected side.
- Any boy with acute scrotal pain, regardless of age, must be presumed to have testicular torsion until proven otherwise.
- It is essential that a testicular examination be conducted in *any* boy with abdominal pain, because testicular torsion can manifest solely with abdominal pain.
- Testicular torsion is a true surgical emergency. All boys with suspected testicular torsion should be emergently referred for urologic consultation and scrotal ultrasonography.

ABP Content Specifications(s)
- Recognize the clinical findings associated with testicular torsion, and manage appropriately
- Plan the appropriate diagnostic evaluation of testicular torsion

Suggested Readings

- Gatti JM, Murphy JP. Acute testicular disorders. Pediatr Rev. 2008;29:35. http://dx.doi.org/10.1542/pir.29-7-235.
- Kolon TF, Canning DA. Urologic evaluation of the child. In: Wein AJ, Kavoussi, KR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology*. 11th ed. Philadelphia, PA: Elsevier Inc; 2016;chap 125.
- Weiss DA, Jacobstein CR. Genitourinary emergencies. In: Shaw KN, Bachur RG, eds. *Fleisher and Ludwig's Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Wolters Kluwer; 2016;chap 127:1353–1361.

Question 260

A 10-month-old female infant who was recently adopted from China is brought to the adoption medicine clinic for a follow-up evaluation. Two weeks ago, she had a comprehensive medical evaluation and assessment of her immunizations. She returns today to receive results of testing performed during the last visit. Since she was last seen, she has had several loose stools but has otherwise been well. She has a temperature of 37.2°C, heart rate of 100 beats/min, respiratory rate of 26 breaths/min, and blood pressure of 94/62 mm Hg. She is well nourished and active. The remainder of the physical examination findings are normal. Laboratory data show:

•Hepatitis A virus antibody, positive total (i.e. IgG and IgM)
•Hepatitis A virus IgM, positive

She has been attending a child care center for the last week and is in a classroom composed of 9- to 11-month-old infants.

Of the following, the BEST next step in the management of the children in her classroom is administration of

  A. hepatitis A virus immune globulin
  B. hepatitis A virus immune globulin and vaccine
  C. hepatitis A virus vaccine
  D. interferon
  E. interferon and hepatitis A virus vaccine

Correct Answer: A

The adopted infant in this vignette has had a recent infection with hepatitis A virus (HAV). The best next step in the management of the children in the infant's classroom is to administer hepatitis A virus (HAV) immune globulin. For individuals that have had HAV exposure within the last 2 weeks and are not eligible for HAV vaccine, passive immunization with HAV immune globulin is recommended.

The HAV vaccine is licensed for individuals 12 months to 40 years of age. The vaccine is used for postexposure prophylaxis in unvaccinated individuals 12 months to 40 years of age. Because the children in the classroom range in age from 9 to 11 months, they are not eligible for HAV vaccine as postexposure prophylaxis and should receive HAV immune globulin. Immune globulin can also be used for preexposure prophylaxis for individuals who cannot receive vaccine. Interferon is not used for HAV prophylaxis.

Transmission of HAV is typically person-to-person through the fecal-oral route. Foodborne outbreaks have occurred. Risk factors for infection in the United States include close contact with a child who attends a child care center, close contact with an international adoptee, contact with an infected individual, and international travel. Individuals with illicit drug use and men who have sex with men are additional groups at risk.

The HAV vaccine is administered in a 2-dose series as a part of routine vaccinations to children 12 to 23 months of age. The minimum interval between doses is 6 months. Vaccination is also recommended for individuals at risk of infection or at risk of severe disease including individuals travelling to countries that have high or intermediate endemicity of HAV, individuals who have close contact with an international adoptee in the 60 days after their arrival, men who have sex with men, individuals with illicit drug use, patients with clotting factor disorders, and patients with chronic liver disease. Routine immunization for health care workers or staff of child care centers is not recommended.

The clinical presentation of HAV infection differs between children and adults. The majority of infected young children are asymptomatic. However, if symptomatic, features can include fever, malaise, and nausea. In contrast, the majority of infected older children and adults are symptomatic, and a large portion will develop jaundice.

Serology (IgM and IgG) and molecular assays are available for HAV infection testing. Serology results are positive for IgM in acute/recent infection but can also be positive after vaccination. Typically, IgM against HAV becomes undetectable 6 months after infection.

PREP Pearls
- For individuals who were exposed to hepatitis A virus within the last 2 weeks and are not eligible for hepatitis A virus vaccine, passive immunization with hepatitis A virus immune globulin is recommended.
- The hepatitis A virus vaccine is licensed for individuals 12 months to 40 years of age. The vaccine is used for postexposure prophylaxis for unvaccinated individuals 12 months to 40 years of age.
- Risk factors for hepatitis A virus infection in the United States include close contact with a child who attends a child care center, close contact with an international adoptee, contact with an infected individual, and international travel. Individuals with illicit drug use and men who have sex with men are additional groups at risk.

ABP Content Specifications(s)
- Understand the epidemiology of the hepatitis A virus
- Know the indications and schedule for hepatitis A vaccine
- Plan the appropriate diagnostic evaluation of hepatitis A virus infection
- Recognize the clinical features associated with hepatitis A virus infection in children of various ages

Suggested Readings
- 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.
- Christenson J, Manaloor J. Hepatitis A, B, and C. Pediatr Rev. 2016;37(10):426–438. http://dx.doi.org/10.1542/pir.2015-0075.

Question 261

You are asked to review a case in which platelets were ordered for the wrong neonate, but were not administered. A physician requested a platelet transfusion for Infant A. The nurse placed a verbal order in the computer for a platelet transfusion under Infant B. When the platelets arrived from the blood bank, the bedside nurse for Infant B recognized the error and returned the platelets to the blood bank.

In your review, you note that on the day of the event, the neonatal intensive care unit population was higher than average. The neonates had similar last names. You label the event as an intercepted adverse event.

Of the following, the patient safety measure used to PREVENT this error from reaching the neonate is

A. alternate patient-naming strategies
B. a standardized handoff tool
C. closed loop communication
D. computer patient order entry
E. Swiss cheese model of care

Correct Answer: E

In 1999, the Institute of Medicine published a report highlighting the prevalence of medical errors and their associated complications in the US health care system. By their estimate, 44,000 patients die annually due to preventable medical errors. In response to this report, health care providers and systems have changed how they identify, investigate, and work to eliminate medical errors. Most medical errors occur as a result of systems of practice. However, individual factors must also be considered in the evaluation of medical errors.

Medical errors can be classified as preventable and nonpreventable. Preventable errors may occur due to individual factors, system factors, or a combination thereof. Nonpreventable errors can be considered the baseline complication rate associated with a medical condition. By systematically examining and altering systems of practice, health care organizations have reduced medical errors significantly over the past 15 years.

The Swiss cheese model of care as developed by James Reason illustrates how a medical error was prevented as described in the vignette. In this model, the health care system is viewed as a series of slices of Swiss cheese, each with strengths (areas of intact cheese) and weaknesses (holes). As such, each part of the health care system contributes differently to the risk of error. When a system is designed to prevent errors, the "holes" will not line up. Each layer of care has a unique role in identifying and averting medical errors. In this vignette, the receiving nurse placed the order under the wrong neonate. The bedside nurse recognized that Infant B did not need a platelet transfusion, providing a different line of defense (blocking the hole) and preventing the error from reaching the patient.

Though the neonates involved had similar surnames, there was no alternate naming strategy in place to assist providers in avoiding a mistaken order entry between the 2 patients. Alternate naming strategies and visual cues on patient charts can be used to help avoid medical errors.

With closed loop communication, the recipient repeats the information provided to confirm the original message and clarify any issues of confusion between the 2 parties. In this situation, there is no evidence that the nurse placing the verbal order used closed loop communication.

Computerized provider order entry has been shown to decrease errors in medication prescribing. However, computer order entry systems are not without risk, particularly when providers can bypass safety features. Therefore, vigilance regarding the accuracy of orders must still be maintained. In this vignette, bypassing the computer provider order entry process with acceptance of a verbal order likely contributed to the medical error.

Hand-offs between providers, during which critical information may be transferred, are vulnerable times for medical errors. Based on current medical literature, standardizing the process of hand-offs and the use of a standardized handoff tool, reduce the risk of medical error. In this vignette, care hand-off between providers was not noted.

PREP Pearls
- Preventable medical errors are often the result of a combination of personal and systems factors.
- Health care providers can reduce medical error by using standardized tools when handing off patients.
- In closed loop communication, the recipient summarizes key information and requests clarification of any outstanding issues.

ABP Content Specifications(s)
- Use effective methods of communication to reduce errors in the health-care setting
- Recognize the relative role of systems and individuals in producing medical error and harm

Suggested Readings
- Leonard MS. Patient safety and quality improvement: medical errors and adverse events. *Pediatr Rev*. 2010;31:151. http://dx.doi.org/10.1542/pir.31-4-151.
- Pereira-Argenziano L, Levy FH. Patient safety and quality improvement: terminology. *Pediatr Rev*. 2015;36:403. http://dx.doi.org/10.1542/pir.36-9-403.

Question 262

An 8-year-old girl is brought to the emergency department with a 2-day history of worsening nausea, abdominal pain, and vomiting. Her mother also reports significant fatigue and weight loss. She denies fever, headache, respiratory symptoms, or diarrhea. The girl's medical history is significant for severe persistent asthma, treated with fluticasone 220 μg 2 puffs inhaled twice daily and albuterol 4 puffs inhaled every 4 hours as needed. She recently completed a 2-week course of oral prednisolone for an asthma exacerbation. Her temperature is 37°C, blood pressure is 90/46 mm Hg, heart rate is 110 beats/min, respiratory rate is 16 breaths/min, and oxygen saturation is 98% on room air. She is tired-appearing. Her physical examination is significant for diffuse abdominal tenderness without rebound.

Laboratory evaluation reveals the following:
- White blood cell count, 8,000/μL (8×10^9/L)
- Hemoglobin 12 g/dL (12 g/L)
- Hematocrit, 38%
- Platelets, 253×10^3/μL (253×10^9/L)
- Sodium, 130 mEq/L (130 mmol/L)
- Potassium, 3.9 mEq/L (3.9 mmol/L)
- Chloride, 98 mEq/L (98 mmol/L)
- Bicarbonate, 18 mEq/L (18 mmol/L)
- Blood urea nitrogen, 25 mg/dL (8.9 mmol/L)
- Creatinine, 0.9 mg/dL (80 μmol/L)
- Glucose, 52 mg/dL (2.9 mmol/L)
- Urinalysis: Specific gravity 1.025, pH 5, small ketones, no white blood cells, no red blood cells, no glucose

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

A. adrenal insufficiency
B. gastroenteritis
C. hypothyroidism
D. inappropriate secretion of antidiuretic hormone
E. urinary tract infection

Correct Answer: A

The girl in the vignette has secondary adrenal insufficiency due to hypothalamic-pituitary-adrenal (HPA) suppression by exogenous steroids. Chronic use of high-dose inhaled corticosteroids can cause HPA suppression. Furthermore, this girl was recently treated with 2 weeks of oral prednisolone. She has become symptomatic after steroid withdrawal, as the axis takes time to recover. The girl's fatigue, weight loss, nausea, vomiting, abdominal pain, hypotension, and tachycardia are characteristic of adrenal insufficiency.

Salt craving and generalized skin hyperpigmentation can occur in primary adrenal insufficiency (pathology of the adrenal gland itself), because of mineralocorticoid deficiency and high adrenocorticotropic hormone (ACTH) levels, respectively. In contrast, with ACTH insufficiency, as is the case for the girl in the vignette, adrenal mineralocorticoid production remains sufficient because it is under control of the renin-angiotensin-aldosterone system.

The girl's hyponatremia, hypoglycemia, metabolic acidosis, and laboratory indicators of dehydration are also consistent with adrenal insufficiency. Hyperkalemia occurs in primary adrenal insufficiency because of mineralocorticoid deficiency. An ACTH level in this girl with secondary adrenal insufficiency would be low but would be high in the context of primary adrenal insufficiency. A cortisol level would be low in both cases.

Hypothyroidism and inappropriate secretion of antidiuretic hormone are potential causes of hyponatremia, but volume status would not be depleted in these conditions, as seen in the girl in the vignette. Gastroenteritis and urinary tract infection can present with nausea, vomiting, abdominal pain, and signs of dehydration, but the girl's history of steroid use makes adrenal insufficiency a more likely cause. The findings on complete blood count and urinalysis also make a urinary tract infection less likely.

PREP Pearls
- Long-term use of high-dose inhaled corticosteroids can cause hypothalamic-pituitary-adrenal axis suppression and significant signs and symptoms of adrenal insufficiency.
- Hyponatremia, hypoglycemia, metabolic acidosis, and laboratory indicators of dehydration are consistent with adrenal insufficiency.
- Hyperkalemia occurs in primary adrenal insufficiency because of mineralocorticoid deficiency.

MOCA-Peds Objective
- Recognize the complications of chronic corticosteroid therapy

ABP Content Specifications(s)
- Differentiate the clinical and laboratory findings associated with adrenal insufficiency from those of the inappropriate secretion of antidiuretic hormone
- Recognize the clinical and laboratory manifestations of adrenal insufficiency

Suggested Readings
- Auron M, Raissouni N. Adrenal insufficiency. *Pediatr Rev*. 2015;36(3):92–102; quiz 103, 129. http://dx.doi.org/10.1542/pir.36-3-92.
- Kapadia CR, Nebesio TD, Myers SE, et al; Drugs and Therapeutics Committee of the Pediatric Endocrine Society. Endocrine effects of inhaled corticosteroids in children. *JAMA Pediatr*. 2016;170(2):163-170.

Question 263

You are advising a medical student who is preparing for a rotation in Bangladesh. There is a high incidence of childhood blindness in the village she will be going to, and she asks you about potential causes of this blindness. You review the photograph from her orientation material of a child from this area (Item Q263).

Item Q263: Ocular findings referred to in the vignette.
Reprinted with permission from Ferrari G, Viganó M. *N Engl J Med*. 2013;368(22):e29

Of the following, this child's condition MOST likely results from a(n)

A. genetic disorder
B. infection
C. micronutrient deficiency
D. toxic exposure
E. traumatic incident

Correct Answer: C

The child in this photograph has Bitot spots, which are associated with vitamin A deficiency. Bitot spots are not caused by a genetic condition, infection, toxic exposure, or trauma. Globally, vitamin A deficiency is the most common cause of preventable childhood blindness. Vitamin A is a fat-soluble vitamin found in green leafy vegetables, sweet potatoes, carrots, and liver. It is absorbed in the small intestine, converted to a stable form, and then stored in the liver. Vitamin A is essential for the normal function of epithelial cells in the eyes and the respiratory, gastrointestinal, and genitourinary tracts.

Vitamin A deficiency can present with:
- Ophthalmologic symptoms
    - Decreased visual acuity in low light (night blindness)
    - Foamy accumulations of dead epithelial cells on the conjunctiva (Bitot spots)
    - Corneal ulcerations or infection
- Dry scaly skin
- Failure to thrive
- Impaired immune function, including increased susceptibility to diarrhea and respiratory infections

Ophthalmologic symptoms typically present early in the course of vitamin A deficiency and may be reversible unless corneal ulceration has occurred.

Vitamin A deficiency can be prevented by encouraging breastfeeding for infants and by ensuring a varied diet for older children. Patients with intestinal disease causing malabsorption are also at risk for deficiency. Treatment is with supplemental vitamin A. Hypervitaminosis A can lead to fatigue, hair loss, arthralgia, increased intracranial pressure, and carotenemia (reversible orange coloration of the skin).

PREP Pearls
- Vitamin A is essential for the normal function of the epithelial cells of the eye and the respiratory, gastrointestinal, and genitourinary tracts.
- Vitamin A deficiency is the most common cause of preventable childhood blindness worldwide. It can cause night blindness, Bitot spots, and corneal ulcerations, as well as dry skin, failure to thrive, and increased susceptibility to infection.
- Vitamin A is found in green leafy vegetables, sweet potatoes, carrots, and liver. Deficiency can be prevented by breastfeeding infants and ensuring a varied diet in older children.
- Individuals with intestinal malabsorption are also at risk of vitamin A deficiency. Treatment is with supplemental vitamin A.

ABP Content Specifications(s)
- Recognize the signs, symptoms, and causes of vitamin A deficiency, and manage appropriately

Suggested Readings
- Ferrari G, Viganó M. Images in clinical medicine: Bitot's spot in vitamin A deficiency. *N Engl J Med*. 2013;368(22):e29. http://dx.doi.org/10.1056/NEJMicm1205309.
- Lauer B, Spector N. Vitamins. *Pediatr Rev*. 2012;33(8):339–351. http://dx.doi.org/10.1542/pir.33-8-339.

Question 264

A 12-year-old girl presents to the emergency department complaining of decreased appetite, fatigue, vomiting, and increased thirst and urination of 2 weeks' duration. Her vital signs include a temperature of 37°C, heart rate of 140 beats/min, respiratory rate of 36 breaths/min, and a blood pressure of 100/60 mm Hg. She is awake and alert. Her mucous membranes are dry. She has sunken eyes and skin tenting. The girl's breathing is rapid and deep. Her lungs are clear to auscultation bilaterally with good aeration. The remainder of her examination findings are unremarkable.

Laboratory results are as follows:

Sodium	135 mEq/L (135 mmol/L)
Potassium	7.0 mEq/L (7.0 mmol/L)
Chloride	100 mEq/L (100 mmol/L)
Bicarbonate	5 mEq/L (5 mmol/L)
Serum urea nitrogen	30 mg/dL (10.7 mmol/L)
Creatinine	0.8 mg/dL (70.7 µmol/L)
Glucose	810 mg/dL (45.0 mmol/L)
Capillary blood gas pH	7.05
Partial pressure of carbon dioxide	14 mm Hg (1.8 kPa)
Base deficit	-25

Of the following, the MOST likely explanation for this girl's hyperkalemia is

 A. decreased intracellular potassium shift
 B. decreased renal excretion of potassium
 C. increased intracellular potassium production
 D. increased muscle breakdown
 E. increased total body content of potassium

Correct Answer: A

The girl in the vignette has diabetic ketoacidosis (DKA) with hyperkalemia. The most likely explanation for her hyperkalemia is decreased intracellular potassium shift as a result of the acidosis.

Diabetic ketoacidosis is a condition caused by insulin deficiency, resulting in failure of intracellular glucose transport. The inability to use glucose as a substrate for cellular respiration leads to lipolysis, gluconeogenesis, and glycogenolysis. The resulting use of free fatty acids as a source of energy causes the accumulation of ketone bodies and acidic by-products, including beta-hydroxybutyrate and acetoacetic acid. Hyperglycemia causes osmotic diuresis and dehydration. The continued inability of tissue glucose uptake further increases the release of counterregulatory hormones including growth hormone, epinephrine, and glucagon, leading to a vicious cycle.

Potassium is the body's major intracellular cation. Approximately 98% of total body potassium is contained in the intracellular fluid (ICF), whereas 2% is contained in the extracellular fluid (ECF). The K+ equilibrium between the ICF and the ECF is tightly controlled by the sodium-potassium-adenosine triphosphatase (Na-K-ATPase) pump located on the membranes of all cells. Generally, fluctuations in total body potassium do not cause significant changes in serum potassium levels, because the function of the Na-K-ATPase pump uses the large intracellular stores of potassium to maintain homeostasis.

Serum potassium levels are elevated in DKA because, with insulin deficiency, the usual process of shifting potassium intracellularly is impaired. Furthermore, metabolic acidosis itself causes hyperkalemia, as hydrogen ion shifts intracellularly in exchange for the positively charged potassium ion. However, in DKA, there is significant total body potassium deficit. In the context of osmotic diuresis, the potassium burden to the renal tubules exceeds its capacity for normal reabsorption. Thus, a total body potassium deficit can be present even if the serum potassium level is normal or high. Although it can be life-threatening in other conditions, hyperkalemia is rarely dangerous in DKA, and is best treated with an insulin infusion to treat the underlying condition.

Increased muscle breakdown can cause a rapid increase in serum potassium levels, but that condition is not common in DKA. Intracellular potassium production is not increased in DKA; in fact, because the total body content of potassium is decreased and serum potassium is increased, it follows that intracellular potassium is decreased. In addition, renal excretion of potassium is increased because of osmotic diuresis.

PREP Pearls

- Diabetic ketoacidosis can be associated with hyperkalemia, but total body potassium is decreased because of osmotic diuresis.
- Acidosis causes hyperkalemia because hydrogen ion moves intracellularly in exchange for potassium.
- Ninety-eight percent of total body potassium is intracellular. Homeostasis is maintained by the sodium-potassium-adenosine triphosphatase pump located on the plasma membrane.

ABP Content Specifications(s)

- Understand that serum potassium concentration does not reflect total body content of potassium

Suggested Readings

- Roberts KB. Hyperkalemia. *Pediatr Rev*. 1996;17:106 http://pedsinreview.aappublications.org/content/17/3/106.
- Rodan AR. Potassium: friend or foe. *Pediatr Nephrol*. 2016; (32)7:1109-1121. http://dx.doi.org/10.1007/s00467-016-3411-8 .
- Zacchia M, Abategiovanni ML, Stratigis S. Potassium: from physiology to clinical implications. *Kidney Dis*. 2016;2:72–79.

Question 265

A 12-year-old boy comes to your office for an acute care visit for evaluation of abdominal pain. The boy reports that he has epigastric abdominal pain that began about 4 to 5 weeks ago and is not improving. The pain is described as a burning sensation with a severity of 4 to 7 on a 10-point scale. He reports an association with gastroesophageal reflux and nausea. He has lost 8 lb (3.6 kg) due to decreasing appetite. There has been some improvement with over-the-counter calcium carbonate tablets and ranitidine.

His vital signs are normal for his age. His abdomen is soft and tender to palpation in the epigastric region without guarding or rebound. He has no masses. The remainder of his examination findings are unremarkable.

Of the following, the compound MOST responsible for his symptoms is

A. gastrin
B. gastrin inhibitory peptide
C. pepsin
D. pepsinogen
E. somatostatin

Correct Answer: A

Gastrin is a hormone secreted by G cells in the stomach in response to the presence of amino acids or peptides, gastric distention, or vagal stimulation. Gastrin results in increased H^+ secretion into the stomach. Excess H^+ secretion can result in gastritis and development of gastroesophageal reflux disease because of the imbalance between cytoprotection and toxic effects in the stomach.

Acid-peptic disorder in children can present as recurrent epigastric or periumbilical abdominal pain. Nocturnal pain that awakens the child from sleep and postprandial pain may be reported. Many patients also experience gastroesophageal reflux with acid-peptic disease. Nausea is often reported, and vomiting may be present. Less common presentations include gastrointestinal bleeding and weight loss.

Following a complete history and physical examination, evaluation may include the following laboratory studies: complete blood cell count with differential, erythrocyte sedimentation rate, liver function tests, electrolytes, celiac disease screen, and stool pathogen panel. Urinalysis and urine culture should be obtained if clinically indicated.

An empiric trial of acid blockade with either an H_2-blocker or proton pump inhibitor is indicated in a child with suspected acid-peptic disorder. If there is improvement within 2 to 4 weeks, an 8- to 12-week course should be completed with a slow taper off the medication. If there is no improvement with acid blockade or return of symptoms after the medication is stopped, additional evaluation including upper gastrointestinal endoscopy with biopsies may be indicated. Endoscopy should also be completed for gastrointestinal bleeding, feeding difficulties, and abnormal radiographic imaging studies. Upper gastrointestinal imaging may be obtained to evaluate anatomy and gastric emptying. A pH impedance study can be used to quantify acid and nonacid reflux and correlate symptoms and reflux. Stool studies, endoscopic biopsy, and urea-breath tests can be used to test for *Helicobacter pylori* infection.

The risk factors for peptic disease include *H pylori* infection, other infectious etiologies (viral, bacterial, and parasitic), family history of peptic ulcer disease, medications, stress associated with illness, eosinophilic esophagitis, inflammatory bowel disease, and celiac disease.

Management of acid-peptic disease includes H_2-receptor antagonists, proton pump inhibitors, and cytoprotective agents (sucralfate and polyaluminum hydroxide) when lesions are identified. The first-line therapy is H_2-receptor antagonists with transition to proton pump inhibitors if there is no benefit in 2 to 4 weeks. H_2-receptor antagonists decrease both gastric secretions and gastric acid secretion. Proton pump inhibitors are irreversible inhibitors of the H^+/K^+-ATPase and are potent inhibitors of acid secretion. Cytoprotective agents form a thick protective layer in acidic environments. **Item C265** shows the medical therapy for acid-peptic disease.

Item C265. Medical Therapy for Acid-Peptic Disease.

Medication	Pediatric Dose	Possible Side Effects
H$_2$-receptor antagonists:		
Famotidine	1-1.2 mg/kg/d up to 20 mg twice daily	Famotidine may cause headache, dizziness, constipation, diarrhea, and drowsiness.
Ranitidine	2-4 mg/kg/d up to 150 mg twice daily	Ranitidine may cause headache, gastrointestinal disturbance, malaise, insomnia, sedation, arthralgia, and hepatotoxicity.
Proton pump inhibitors:		
Esomeprazole	0.8-1 mg/kg/d	
Lansoprazole	0.8-1 mg/kg/d	Lansoprazole may cause headache and diarrhea.
Omeprazole	0.8 mg/kg/d with an effective dosage range of 0.3-3.3 mg/kg per 24 hours	Omeprazole may cause headache, diarrhea, nausea, and vomiting.
Cytoprotective:		
Sucralfate	40-80 mg/kg/d divided 4 times/day	Constipation

Adapted and reprinted with permission from Chelimsky G, Czinn S. Peptic ulcer disease in children. *Pediatr Rev*. 2001;22(10):349-355.

Gastrin inhibitory peptide reduces gastric secretion and therefore reduces gastric acid secretion. Pepsinogen is secreted by gastric chief cells and is converted to the active form pepsin following acid cleavage in the stomach. Pepsin, an enzyme that hydrolyzes proteins, is secreted in response to gastric stimulation, but does not cause increased gastric acid secretion. Somatostatin is an inhibitor of acid secretion.

PREP Pearls
- Gastrin is the hormone responsible for gastric acid secretion.
- Acid-peptic disorder can present as recurrent epigastric or periumbilical abdominal pain in children.
- Nocturnal pain that wakens a child from sleep and postprandial pain may be reported with acid-peptic disorder.
- Evaluation of acid-peptic disorder should include a complete history and physical examination as well as laboratory studies, radiographic studies, and endoscopic procedures as indicated.

ABP Content Specifications(s)
- Plan the appropriate evaluation of suspected ulcer disease not caused by Helicobacter pylori
- Identify the risk factors associated with ulcer disease (other than that caused by Helicobacter pylori) in childhood
- Recognize the clinical features associated with acid-peptic disorder in a patient with recurrent abdominal pain
- Plan the appropriate management of ulcer disease not caused by Helicobacter pylori infection

Suggested Readings
- Chelimsky G, Czinn S. Peptic ulcer disease in children. *Pediatr Rev*. 2001;22(10):349–355. http://dx.doi.org/10.1542/pir.22-10-349.
- Vandenplas Y, Hauser B, Devreker T. Infant regurgitation and pediatric gastroesophageal reflux disease. In: Faure C, Di Lorenzo C, Thapar N, eds. *Pediatric Neurogastroenterology*. New York, NY: Springer; 2013:331–346.
- Ward RM, Kearns GL. Proton pump inhibitors in pediatrics: mechanism of action, pharmacokinetics, pharmacogenetics, and pharmacodynamics. *Pediatr Drugs*. 2013;15(2):119–131. http://dx.doi.org/10.1007/s40272-013-0012-x.

Question 266

An 18-year-old girl is brought to your office for concerns of irregular periods. She reports that her last menstrual period was 4 months ago. She denies having ever had sex. On physical examination, she is overweight with moderate facial acne and a Ferriman-Gallwey score of 9. Her urine pregnancy test result is negative. You suspect that she has polycystic ovary syndrome. The medical student who has been shadowing you suggests an alternative diagnosis of nonclassic congenital adrenal hyperplasia.

Of the following, the finding that would MOST likely support this diagnosis is

A. 11-deoxycortisol value less than 50 ng/dL
B. 17-hydroxyprogesterone value greater than 200 ng/dL
C. serum dehydroepiandrosterone-sulfate level greater than 400 μg/dL
D. serum morning cortisol level less than 10 μg/dL
E. serum potassium value greater than 6.0 mEq/L

Correct Answer: B

The finding that would most likely support a diagnosis of nonclassic congenital adrenal hyperplasia (NCCAH) is a 17-hydroxyprogesterone (17-OHP) value greater than 200 ng/dL. There is considerable overlap in the clinical features of polycystic ovary syndrome (PCOS) and NCCAH. However, an elevated 17-OHP level is key to the diagnosis of NCCAH. An Endocrine Society guideline recommends using an early-morning, follicular-phase 17-OHP level as a screen for NCCAH, with a cutoff of 200 to 400 ng/dL depending on the assay. For values close to the cutoff, an adrenocorticotropic hormone (ACTH) stimulation test is indicated. Stimulated 17-OHP values greater than 1,000 ng/dL are consistent with NCCAH.

Nonclassic congenital adrenal hyperplasia affects 1 to 2 in 1,000 in the general population and is caused by mutations in the gene coding for the 21-hydroxylase enzyme in the adrenal steroid pathway. Mutations in the same gene are also responsible for the most common classic form of congenital adrenal hyperplasia. However, there is a spectrum of clinical severity depending on the degree of enzyme impairment. There is less enzyme deficiency in NCCAH than the classic form, resulting in milder clinical features that present later in childhood, adolescence, or adulthood. The enzyme deficiency results in accumulation of the 17-OHP precursor, the key steroid intermediate for making the diagnosis. The 17-OHP and other accumulated adrenal steroid intermediates are converted to androgens, resulting in excess adrenal androgen secretion. In NCCAH, mineralocorticoid secretion is normal and the impairment in cortisol biosynthesis is usually not clinically significant. Thus, a serum potassium value greater than 6.0 mEq/L (6.0 mmol/L), which would be suggestive of mineralocorticoid deficiency, and a serum morning cortisol level less than 10 µg/dL, are not characteristic of NCCAH.

Those with NCCAH most often present with signs and symptoms of androgen excess. NCCAH can also be asymptomatic. Children may present with early development of pubic hair, axillary hair, or body odor. The most common presenting features in adolescent females are hirsutism, menstrual irregularities, and acne, which are also the most common presenting features of PCOS. Adult women can present with fertility problems.

Treatment of NCCAH with glucocorticoid may be indicated for symptoms of androgen excess (eg, to regulate menses, prevent progression of hirsutism and acne, and for fertility) but benefits should be weighed against potential adverse effects (eg, iatrogenic adrenal suppression). Oral contraceptives and antiandrogens (eg, spironolactone) also help treat the irregular menses and hirsutism.

Polycystic ovary syndrome is a heterogeneous disorder that affects up to 10% of reproductive-age females. The etiology is multifactorial but many have associated insulin resistance. Obesity is common in those with PCOS. Diagnostic criteria require both abnormal menses and evidence of hyperandrogenism, which may be clinical or biochemical, and must be otherwise unexplained. Thus NCCAH, hypothyroidism, hyperprolactinemia, androgen-secreting tumors, and Cushing syndrome should be excluded before diagnosing PCOS.

Clinical evidence of hyperandrogenism includes hirsutism and acne. The Ferriman-Gallwey scoring system (**Item 266**) is commonly used as an objective measure of hirsutism. Terminal hair growth over 9 areas of the body are scored from 0 to 4. A total score of 8 or greater is abnormal. The increased androgen production in PCOS may be of both ovarian and adrenal origin. Elevated total and/or free testosterone levels are characteristic of PCOS and originate from the ovaries. Dehydroepiandrosterone sulfate (DHEA-S) originates from the adrenal glands and levels are elevated in about half of those with PCOS. Thus, an elevated serum dehydroepiandrosterone-sulfate (DHEA-S) level greater than 400 µg/dL would not distinguish NCCAH from PCOS.
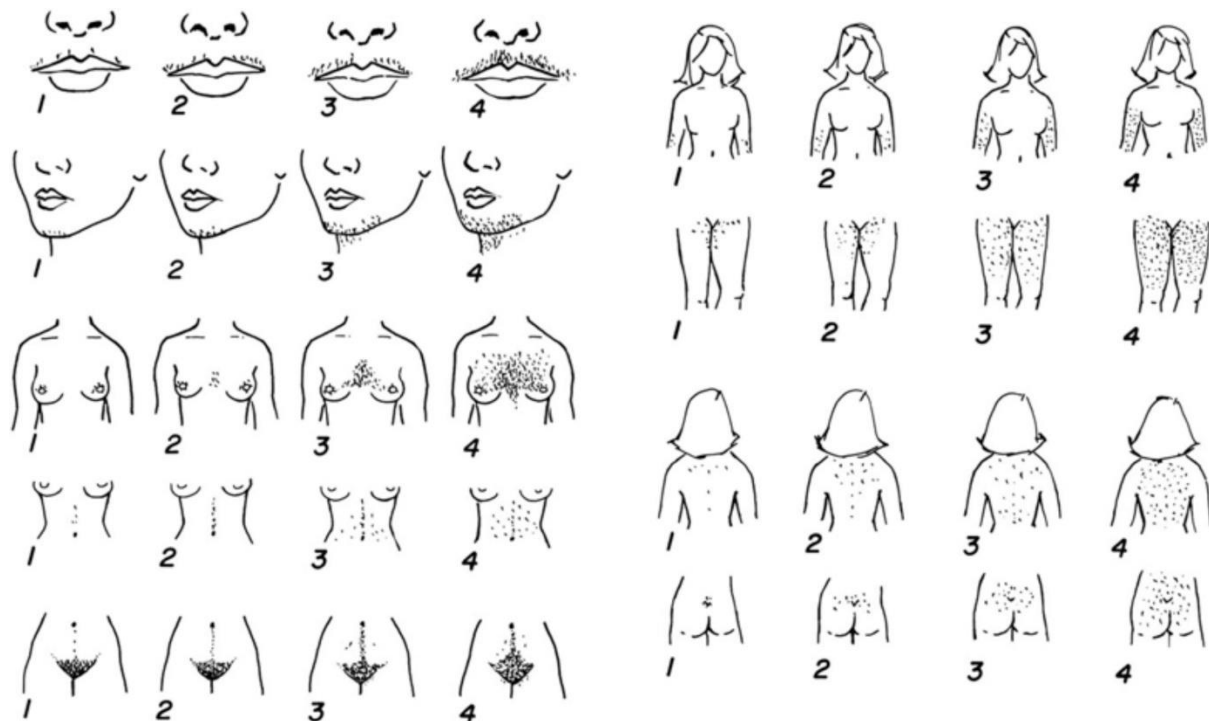
Item C266: Ferriman-Gallwey hirsutism scoring system. Each of the 9 body areas most sensitive to androgen is assigned a score from 0 (no hair) to 4 (frankly virile), and these separate scores are summed to provide a hormonal hirsutism score. Generalized hirsutism (score = 8) is abnormal in the general US and UK populations, whereas locally excessive hair growth (score, 8) is a common normal variant. The normal score is lower in Asian populations and higher in Mediterranean populations.

Reproduced with permission from Martin KA, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL, et al. Evaluation and treatment of hirsutism in premenopausal women: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrin Metab*. 2008;93:1107

An 11-deoxycortisol value is not useful in the evaluation of NCCAH or PCOS. This adrenal steroid intermediate is important in the diagnosis of congenital adrenal hyperplasia due to 11-hydroxylase deficiency and would be elevated in this condition. Deficiency of 11-hydroxylase is not an important cause of NCCAH.

PREP Pearls
- Common presenting features of both polycystic ovary syndrome (PCOS) and nonclassic congenital adrenal hyperplasia (NCCAH) in adolescent females are hirsutism, menstrual irregularities, and acne. PCOS affects up to 10% of reproductive-age females. NCCAH affects 1 to 2 in 1,000 in the general population.
- An early-morning, follicular-phase 17-hydroxyprogesterone greater than 200 ng/dL is suggestive of NCCAH. An adrenocorticotropic hormone (ACTH) stimulated level higher than 1,000 ng/dL confirms the diagnosis of NCCAH.
- Although elevated total and/or free testosterone levels, secreted by the ovaries, are characteristic of polycystic ovary syndrome, the adrenal glands may also be a source of excess androgen.

MOCA-Peds Objective
- Recognize and plan initial evaluation of a child with suspected congenital adrenal hyperplasia

ABP Content Specifications(s)
- Know that there is an overlap between adrenal and ovarian androgen production in some women with PCOS (VII.B.5.c.10 (2312))
- Know how to differentiate PCOS from late onset congenital adrenal hyperplasia (VII.B.5.c.11 (2313))

Suggested Readings
- Gray SH. Menstrual disorders. *Pediatr Rev*. 2013;34(1):6–17. http://dx.doi.org/10.1542/pir.34-1-6 .
- Rosenfield RL. The diagnosis of polycystic ovary syndrome in adolescents. *Pediatrics*. 2015;136(6):1154–1165. http://dx.doi.org/10.1542/peds.2015-1430 .
- Speiser PW, Azziz R, Baskin LS, et al; Endocrine Society. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2010 Sep;95(9):4133–4160. http://dx.doi.org/10.1210/jc.2009-2631. Erratum in: *J Clin Endocrinol Metab*. 2010 Nov;95(11):5137.
- Witchel SF, Azziz R. Nonclassic congenital adrenal hyperplasia. *Int J Pediatr Endocrinol*. 2010;2010:625105. http://dx.doi.org/10.1155/2010/625105.

Question 267

You receive a phone call from an otolaryngologist regarding a patient of yours who has had chronic ear drainage since tube placement 4 months ago. He has received multiple courses of topical quinolone-corticosteroids and 2 courses of oral amoxicillin without resolution. The otolaryngologist reports that on otomicroscopy, there is a large central tympanic membrane perforation, but no cholesteatoma. He recommends that the child receive parenteral antibiotics to treat the chronic suppurative otitis media. He has sent a sample of the ear discharge to the laboratory for culture and sensitivity testing to guide treatment.

Of the following, the MOST likely pathogen the culture will isolate is

A. methicillin-resistant Staphylococcus aureus
B. Moraxella catarrhalis
C. nontypeable Haemophilus influenzae
D. Streptococcus pneumoniae
E. Proteus mirabilis

Correct Answer: A

Chronic suppurative otitis media (CSOM) is defined by the World Health Organization (WHO) as "chronic inflammation of the middle ear and mastoid cavity which presents with recurrent ear discharge or otorrhea through a tympanic perforation" (**Item C267**). The duration of discharge required to make the diagnosis varies among authors, from 2 weeks (WHO) to as long as 3 months. Although CSOM often follows an episode of acute otitis media (AOM), the bacteriology of the 2 conditions is distinct. In contrast to the usual respiratory pathogens associated with AOM (pneumococcus, *Haemophilus influenzae, Moraxella),* CSOM is caused by biofilm-producing organisms, most often *Pseudomonas aeruginosa* or *Staphylococcus aureus.* Less commonly, CSOM is caused by *Escherichia coli, Streptococcus pyogenes, Proteus mirabilis, Klebsiella* spp or anaerobes (eg, *Bacteroides, Peptostreptococcus, Propionibacterium*). Among the response choices, methicillin-resistant *S aureus* is the most likely causative organism for the boy in the vignette.
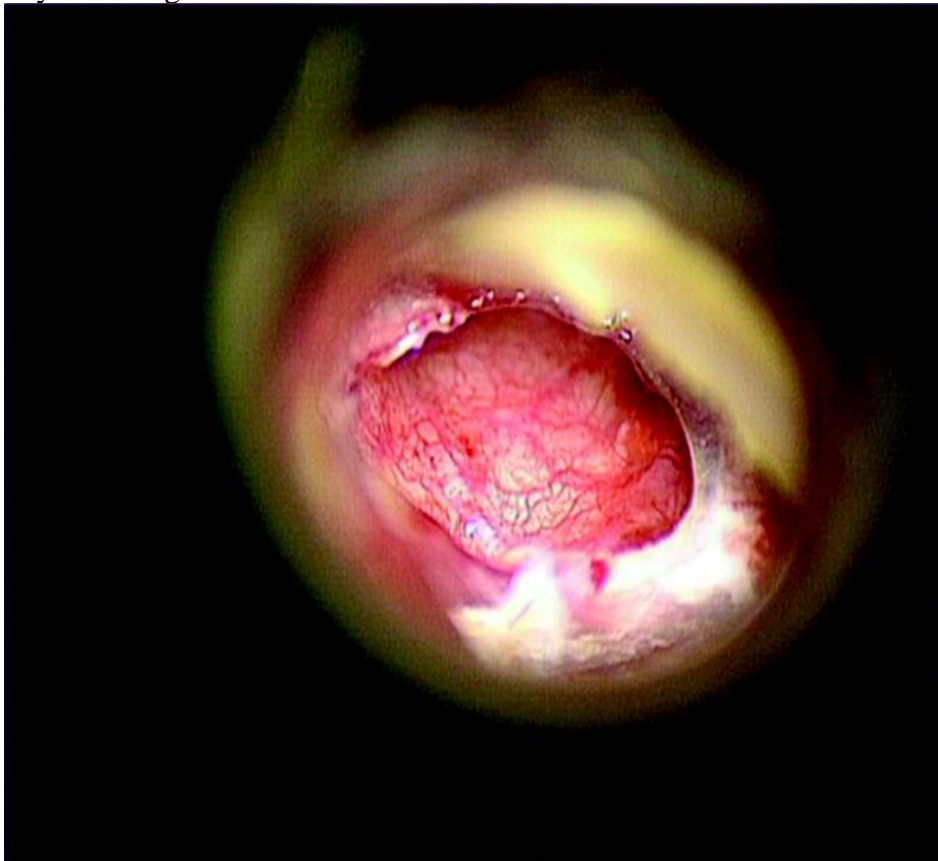
Item C267: Tympanic membrane with central perforation
Reprinted with permission from Yadiel A. Alameda, MD, Caribbean Sinus and Ear Institute, Puerto Rico and Rosa-Olivares, J. et al. Otitis media: to treat, to refer or to do nothing, a review for the practitioner. *Pediatr Rev*. 2015; 36:480-486.

The prevalence and impact of CSOM has declined dramatically since the introduction of antibiotics in the 1930s and 1940s. In the developed world, the prevalence is estimated to be 0.2% to 1.2% of children, and the most important risk factor is having undergone tympanostomy

tube placement. Other risk factors include having more than 3 upper respiratory infections in the past 6 months; older siblings; low parental education level; day care attendance; and more than 3 episodes of AOM in the past year. In contrast, the largest disease burden from CSOM occurs in the developing world, especially where access to medical care or antibiotics is limited, most notable in the Western Pacific region. Various indigenous groups including Inuit, southwestern American Indians (primarily the Navajo), Australian aborigines, and Greenlanders demonstrate particular susceptibility to CSOM.

The most frequent consequence of CSOM is mild to moderate hearing impairment, often in the 30- to 60-dB range. As many as 50% of children with CSOM will suffer such impairment, and it is the most common cause of moderate hearing loss in resource-poor countries. In addition, infection from CSOM can spread both contiguously and hematogenously, resulting in intra- and extracranial complications. Chronic mastoiditis from CSOM can cause a subperiosteal abscess and labyrinthine fistula presenting with facial nerve paralysis, postauricular swelling and tenderness, and otalgia. The most common intracranial complication of CSOM is meningitis; it can also lead to sinus thrombosis and brain abscess.

There are both medical and surgical approaches to the treatment of CSOM, with the goal of eradicating the infection and closing the tympanic perforation. Medical therapies include aural hygiene, antiseptics, topical antibiotics (with or without corticosteroids), and systemic antibiotics (oral or parenteral). The most efficient treatment for children with CSOM is a topical antibiotic administered after aural cleaning (often performed with the help of an otomicroscope). Many experts prefer fluoroquinolone otic drops; they may be more effective in clearing otorrhea and they are not ototoxic. Data are insufficient to determine if topical corticosteroids in combination with topical antibiotics confer any benefit beyond topical antibiotics alone. Aural antiseptics (eg, borax + alum, acetic acid) may be included as part of aural cleaning, but are less effective than topical antibiotics as a sole treatment for CSOM. Systemic antibiotics reduce otorrhea in children with CSOM, but recurrences are frequent. Studies with anti-*Pseudomonas* intravenous antibiotics (eg, ceftazidime) showed good results in producing a dry ear before surgical procedures. Systemic antibiotics are more costly than topical treatment.

Mastoidectomy and/or tympanoplasty are the most frequent surgical procedures used to treat and cure CSOM. During mastoidectomy, the surgeon removes the mastoid air cells, granulations, and inflammatory debris, clearing much of the inflammation of CSOM. Tympanoplasty is frequently necessary to close the tympanic perforation, typically with a soft tissue graft. At times this is performed after the ossicular chain is reconstructed. If a cholesteatoma is involved, it must also be removed surgically.

PREP Pearls
- The bacteria most commonly associated with chronic suppurative otitis media (CSOM) are *Pseudomonas aeruginosa* and *Staphylococcus aureus.*
- The most common complication associated with CSOM is mild to moderate hearing loss.
- The most efficient treatment for CSOM is topical antibiotics; fluoroquinolones are the most frequently recommended.
- Surgical treatment is often required for CSOM, and may include tympanoplasty and mastoidectomy.
- The greatest disease burden of CSOM occurs in resource-poor countries, particularly in the western Pacific, southeast Asia, and certain African nations.

ABP Content Specifications(s)
- Distinguish the pathogens associated with chronic suppurative otitis media from those of acute otitis media
- Plan the appropriate management of chronic suppurative otitis media in patients of various ages

Suggested Readings
- Acuin J, World Health Organization. Chronic suppurative otitis media: burden of illness and management options. World Health Organization. 2004. Accessed at http://apps.who.int/iris/handle/10665/42941.
- Acuin J. Chronic suppurative otitis media. *BMJ Clin Evid*. 2007;2:507.
- 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;36:480–486. http://dx.doi.org/10.1542/pir.36-11-480.

Question 268

A 16-month-old girl is brought to the emergency department by her parents for a rash and a nosebleed. They noticed the rash for the first time this morning on her chest. Since that time, the rash has spread to cover her trunk, legs, arms, and face. Her nosebleed started about 2 hours ago and has waxed and waned over that time despite having pressure applied. Otherwise, she has been well and has not had a fever. Her appetite has been normal, and she has been happy and playful. No other family members are ill.

She was born full term following an uncomplicated pregnancy in the United States and has no travel history. She has had normal growth and development. She has never been hospitalized, has never undergone surgery, and has not been taking any medications. Her immunizations are up-to-date, and she received the MMR (measles, mumps, and rubella) vaccine 2 weeks ago.

She has a temperature of 37°C, heart rate of 98 beats/min, and blood pressure of 96/64 mm Hg. She is sitting on her mother's lap and babbling happily. Both nostrils trickle blood when her mother removes the tissue that has been held to them. She has normal heart, lung, and abdominal examination findings with no hepatosplenomegaly. She has nonblanching, red, macular pin-prick lesions over her face, trunk, arms, and legs that are particularly dense at the site where a tourniquet was placed to collect blood.

Laboratory studies show:

Laboratory Test	Result
White blood cell count	6,100/µL (6.1 x 10^9/L)
Hemoglobin	12.9 g/dL (129 g/L)
Platelet count	3 x 10^3/µL (3 x 10^9/L)
Neutrophils	56%
Lymphocytes	41%
Monocytes	3%
Blood type	O+

Results of a chemistry panel are normal.

Of the following, the MOST appropriate next step is to

A. admit her to the hematology service for the administration of intravenous immune globulin 1 g/kg
B. discharge her after arranging follow-up care with pediatric hematology for the next day
C. immediately transfuse 10 mL/kg of single-donor platelets
D. order immediate computed tomography of the head to rule out an intracranial bleed
E. send peripheral blood for flow cytometry to rule out leukemia

Correct Answer: A

The girl in this vignette has been well until very recently when she developed a petechial rash and mucosal bleeding associated with severe isolated thrombocytopenia (only one blood cell line with a decreased count). This is a classic presentation for acute immune thrombocytopenic purpura (ITP). Acute ITP occurs when the body develops antibody-mediated autoimmunity to platelet antigens. This condition can be primary, meaning that it occurs without association to an underlying disorder, or secondary, meaning that it occurs as a symptom of a larger disorder of autoimmunity. In younger children, acute ITP is most commonly primary, but in older children and adolescents it is often the presenting sign of a broader autoimmune disease. Although primary acute ITP most often does not have an identifiable trigger, it has been associated with the administration of some vaccines, most notably the measles, mumps, and rubella vaccine.

The treatment of ITP is based on immune modulation. The 4 commonly used therapeutic approaches are corticosteroids, intravenous immune globulin, anti-Rh immune globulin, and watchful waiting. The selection of the therapeutic approach is dependent on the platelet count, the severity of bleeding symptoms, the age of the child, and the presence of other associated cytopenias, signs, or symptoms. Although European treatment guidelines only address ITP pharmacologically when there are significant bleeding symptoms, guidelines from the American Society of Hematology suggest treating children if the platelet count is less than 10,000/µL (10 x 10^9/L), even in the absence of bleeding symptoms. This treatment approach is used because of the potential increased risk for spontaneous intracranial bleeding when the platelet count is less than 10,000/µL. For children with platelet counts greater than 10,000/µL and no bleeding, it is reasonable to just monitor the platelet count over time. About 80% of children with acute ITP have complete resolution within 6 months.

Given that the girl in this vignette has a platelet count less than 10,000/µL and has mucosal bleeding, it would be most appropriate to treat her with intravenous immune globulin. Platelet transfusion in the setting of ITP is contraindicated unless there is a major hemorrhage, because the transfused platelets will present antigens that will continue to drive the autoimmune process. The girl in this vignette has had no head trauma and no symptoms of an intracranial hemorrhage; therefore, computed tomography of the head is not needed. In the absence of additional cytopenias or symptoms, it is extremely unlikely for this presentation to be that of acute lymphoblastic leukemia. Studies of the bone marrow of patients with ITP have found few or no cases of leukemia in patients with isolated severe thrombocytopenia and no other symptoms.

PREP Pearls
- Immune thrombocytopenic purpura is an antibody-mediated autoimmunity to platelet antigens.
- In younger children, immune thrombocytopenic purpura tends to be primary, but in older children and adolescents it can be the presenting sign of a broader autoimmune disorder.
- There are several possible therapies for immune thrombocytopenic purpura, including corticosteroids, intravenous immune globulin, anti-Rh immune globulin, and watchful waiting.

- About 80% of children diagnosed with acute immune thrombocytopenic purpura will have resolution of the disorder within 6 months, irrespective of therapy.

ABP Content Specifications(s)
- Understand the natural history of immune thrombocytopenia purpura
- Recognize the clinical and laboratory findings associated with immune thrombocytopenia purpura, and manage appropriately
- Recognize complications associated with immune thrombocytopenia purpura

Suggested Readings
- Blanchette V, Bolton-Maggs P. Childhood immune thrombocytopenic purpura: diagnosis and management. *Pediatr Clin N Am*. 2008;55(2):393–420. http://dx.doi.org/10.1016/j.pcl.2008.01.009.
- Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190–4207. http://dx.doi.org/10.1182/blood-2010-08-302984.
- Schultz CL, Mitra N, Schapira MM, Lambert MP. Influence of the American Society of Hematology guidelines on the management of newly diagnosed childhood immune thrombocytopenia. *JAMA Pediatr*. 2014;168(10):e142214. http://dx.doi.org/10.1001/jamapediatrics.2014.2214.

Question 269

A 10-year-old previously healthy girl is brought to the emergency department with a 1-day history of fever, headache, and vomiting. There are no sick contacts, no pets at home, and no recent travel. She had not received routine childhood vaccinations for philosophical reasons. She is irritable and has a temperature of 40°C, heart rate of 126 beats/min, and respiratory rate of 22 breaths/min. Her blood pressure is normal. There is nuchal rigidity and positive Kernig and Brudzinski signs. The remainder of the physical examination findings are unremarkable. Her blood glucose level is 100 mg/dL (5.6 mmol/L). Gram stain of the cerebrospinal fluid is shown in Item Q269. Data from cerebrospinal fluid analysis are shown:

Laboratory Test	Result
White blood cell count	5,200/µL (5.2 x 10^9/L)
Neutrophils	96%
Glucose	10 mg/dL
Protein	215 mg/dL
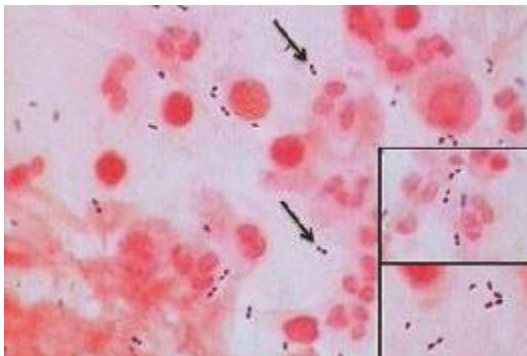
Item Q269: Gram stain of cerebrospinal fluid
Courtesy of the Centers for Disease Control and Prevention.

The girl is admitted to the hospital with a diagnosis of meningitis.

Of the following, the BEST antimicrobial treatment is

 A. ampicillin and ceftriaxone
 B. ampicillin, ceftriaxone, and vancomycin
 C. ceftriaxone and vancomycin
 D. ceftriaxone, nafcillin, and vancomycin
 E. meropenem and vancomycin

Correct Answer: C

The ill-appearing, unvaccinated girl in this vignette exhibits the clinical features and cerebrospinal fluid (CSF) profile (marked pleocytosis with neutrophil predominance, elevated protein level, low CSF glucose to serum glucose ratio (< 0.6), and pairs of gram-positive diplococci) consistent with acute bacterial meningitis caused by *Streptococcus pneumoniae*. *Streptococcus pneumoniae* and *Neisseria meningitidis* are the 2 most common bacterial causes of meningitis in otherwise healthy children older than 1 month in the United States. In unvaccinated infants and children younger than 4 years, *Haemophilus influenzae* type b must also be included in the differential diagnosis.

In neonates, the most common causes of bacterial meningitis are group B *Streptococcus*, *Escherichia coli, a*nd *Listeria monocytogenes*. Children with certain underlying conditions or compromised immune status are at greater risk for developing bacterial meningitis caused by certain microorganisms. Pneumococcal meningitis is associated with CSF fluid leak, otic fistula, cochlear implant, asplenia, nephrotic syndrome, sickle cell disease, and HIV infection. Invasive meningococcal infection is associated with terminal complement deficiency disorders. Meningitis caused by S*taphylococcus aureus, Streptococcus*, and gram-negative enteric bacilli may occur after penetrating head trauma, neurosurgery, or placement of ventriculoperitoneal shunt. Immunocompromised patients, especially patients with T-lymphocyte deficiency or renal transplant patients, are at greater risk for developing meningitis caused by *L monocytogenes*. *Streptococcus pneumoniae* is an encapsulated, lancet-shaped, α-hemolytic, catalase-negative, gram-positive diplococcus that is part of the human nasopharyngeal flora. *Streptococcus pneumoniae* is the most common pathogen of bacterial meningitis in children older than 1 month. Children younger than 2 years, adults 65 years of age or older, immunocompromised individuals as well as African American, some Alaskan native, and Apache populations remain at highest risk for invasive pneumococcal disease, defined as isolation of *S pneumoniae* from a normally sterile body fluid.

The introduction of conjugate *H influenzae* type b vaccine in 1990 has resulted in near complete elimination of invasive *H influenzae* type b disease in the United States. In 2000, following introduction of pneumococcal conjugate vaccine (PCV7), rates of pneumococcal meningitis decreased by 59% among children younger than 2 years. Nonimmunized children and adults were also protected because of herd immunity. From 2001 through 2004, PCV7 prevented an estimated 3,330 hospitalizations and 394 deaths from pneumococcal meningitis in persons of all ages. In a United States population-based surveillance study, the overall rate of pneumococcal meningitis caused by PCV7 serotypes decreased significantly (from 59% in 1998-1999 to 23% in 2004-2005). However, disease rates caused by non-PCV7 serotypes increased significantly (from 28% in 1998-1999 to 65% in 2004-2005), with most increase associated with serotypes 19A and 22F. In 2010, PCV13 replaced PCV7 in the United States childhood immunization schedule to address the problem of pneumococcal serotype replacement disease. Recent data from population-based surveillance indicate a continued decrease in rates of invasive pneumococcal disease in all age groups following implementation of PCV13.

Nasopharyngeal colonization with *S pneumoniae* is a critical first step in the pathogenesis of invasive pneumococcal disease. Viral respiratory tract infections, especially influenza, may facilitate pneumococcal infection and spread. Transmission of pneumococcus occurs via respiratory droplet contact. The spread of *S pneumoniae* to the meninges typically occurs via the hematogenous route. The clinical features of pneumococcal meningitis can vary from an insidious onset of illness after an upper respiratory tract infection to a rapidly fulminant course resulting in death within 24 hours of presentation. Pneumococcal meningitis is associated with substantial morbidity and mortality. Neurologic sequelae (eg, sensorineural hearing loss, paresis, and cognitive impairment) occur in 25% to 56% of survivors and mortality occurs in 5% to 15% of cases.

The isolation of pneumococcus from CSF usually confirms the diagnosis of pneumococcal meningitis. The Clinical and Laboratory Standards Institute has defined breakpoints for in vitro susceptibility and nonsusceptibility of nonmeningeal and meningeal pneumococcal isolates (**Item C269A**). Combination therapy consisting of vancomycin plus cefotaxime or ceftriaxone is recommended for the treatment of proven or suspected pneumococcal meningitis (such as for the girl in this vignette) given the concerns of nonsusceptibility to penicillin, cefotaxime, and ceftriaxone. Cefotaxime or ceftriaxone would also provide empiric appropriate therapy for meningococcal meningitis. The recommended dose of vancomycin therapy for bacterial meningitis is 60 mg/kg/d in 4 divided doses. To maintain the target trough concentration of 15 to 20 µg/ml needed to achieve adequate CSF concentrations, the dose and frequency of vancomycin may be individualized. The recommended doses of cefotaxime and ceftriaxone for bacterial meningitis are 225 to 300 mg/kg/d in 3 divided doses and 100 mg/kg/d in 2 divided doses, respectively. Antibiotic therapy can be adjusted based on the antimicrobial susceptibility test results (**Item C269B**).

Item C269A. In Vitro Susceptibility and Nonsusceptibility of Nonmeningeal and Meningeal Pneumococcal Isolates.

Drug and Isolate Location	Susceptible, µg/mL	Nonsusceptible, µg/mL	
		Intermediate	Resistant
Penicillin (oral)[a]	≤0.06	0.12-1.0	≥2.0
Penicillin (intravenous)[b]			≥8.0
– Nonmeningeal	≤2.0	4.0	≥0.12
– Meningeal	≤0.06	None	≥0.12
Cefotaxime **OR** ceftriaxone			
– Nonmeningeal	≤1.0	2.0	≥4.0
– Meningeal	≤0.5	1.0	≥2.0

[a] Without meningitis.

[b] Treated with intravenous penicillin.

Reprinted with permission from American Academy of Pediatrics. Pneumococcal 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; 2015:626-638.

Item C269B. Antimicrobial Therapy Based on Susceptibility Test Results for Infants and Children with Pneumococcal Meningitis.

Susceptibility Test Results	Antimicrobial Management
Susceptible to penicillin	Discontinue vancomycin **AND** Begin penicillin (and discontinue cephalosporin) **OR** Continue cefotaxime or ceftriaxone alone*
Nonsusceptible to penicillin (intermediate or resistant) **AND** Susceptible to cefotaxime and ceftriaxone	Discontinue vancomycin **AND** Continue cefotaxime or ceftriaxone
Nonsusceptible to penicillin (intermediate or resistant) **AND** Nonsusceptible to cefotaxime and ceftriaxone (intermediate or resistant) **AND** Susceptible to rifampin	Continue vancomycin and high-dose cefotaxime or ceftriaxone **AND** Rifampin may be added in selected circumstances (see text)

Some experts recommend the maximum dosages. Initial therapy of nonallergic children older than 1 month of age should be vancomycin and cefotaxime or ceftriaxone.

*Some physicians may choose this alternative for convenience and cost savings but only in treatment of meningitis.

A combination regimen with ampicillin, nafcillin, or meropenem would not be indicated for empiric therapy of suspected pneumococcal meningitis. Ampicillin is the drug of choice for meningitis caused by *L monocytogenes*, whereas nafcillin is recommended for meningitis caused by methicillin-susceptible *S aureus*. Combination therapy consisting of vancomycin plus rifampin or therapy with meropenem alone should be considered for the treatment of proven or suspected pneumococcal meningitis in patients with serious hypersensitivity reactions to penicillins and cephalosporins.

PREP Pearls
- *Streptococcus pneumoniae* and *Neisseria meningitidis* are the 2 most common bacteria causing pyogenic meningitis in previously healthy children older than 1 month. In unimmunized children younger than 4 years, *Haemophilus influenzae* type b must also be considered.
- The incidence of invasive pneumococcal disease in the United States has decreased significantly following introduction of pneumococcal conjugate vaccines.
- The clinical features of pneumococcal meningitis vary from an insidious onset of illness after an upper respiratory tract infection to a rapidly fulminant course resulting in severe morbidity and death.
- Combination therapy consisting of vancomycin plus cefotaxime or ceftriaxone is recommended for the empiric treatment of acute bacterial meningitis in children older than 1 month.

ABP Content Specifications(s)
- Recognize the clinical features associated with Streptococcus pneumoniae
- Understand the epidemiology of Streptococcus pneumoniae infection
- Plan appropriate management for a patient with Streptococcus pneumoniae infection

Suggested Readings
- American Academy of Pediatrics. Pneumococcal 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; 2015:626–638.
- Maraqa NF. Pneumococcal infections. *Pediatr Rev*. 2015;35(7):299–310. http://dx.doi.org/10.1542/pir.35-7-299.
- Swanson D. Meningitis. *Pediatr Rev*. 2015;36(12):514–526. http://dx.doi.org/10.1542/pir.36-12-514.

Question 270

A 16-year-old adolescent boy presents to your office for a health supervision visit. In response to your questions about alcohol and drug use, he admits to using marijuana on some weekends when hanging out with his closest friend. He states that he does not personally drive under the influence of marijuana, but sometimes rides in a car driven by his friend after they have been using it. The adolescent has been maintaining his grades at school, unlike his friend whose grades have gone down and has been sent to after-school detention several times this past month. He denies using any other illicit substance.

Of the following, the MOST appropriate statement about the boys' level of illicit substance use is that

A. your patient and his friend have problematic use
B. your patient has experimental use and his friend has limited use
C. your patient has experimental use and his friend has problematic use
D. your patient has limited use and his friend has problematic use
E. your patient has problematic use and his friend has substance abuse

Correct Answer: D

Based on the history provided by the boy in the vignette, the most appropriate statement about the level of his illicit substance use is that your patient has limited use and his friend has problematic use.

Understanding the stages of substance use allows the primary care physician to provide appropriate counseling and recommendations for treatment. The spectrum of substance use ranges from abstinence to addiction. Abstinence is the period before alcohol or drug use has begun. Experimentation is the first few times that an adolescent uses substances (eg, alcohol, marijuana, tobacco, prescription medications). Limited use is continued substance use, usually with friends and without adverse effect, as seen with the patient in the vignette. Problematic use, seen in the actions of the boy's friend, is substance use with negative consequences (eg, declining academic performance, detentions, driving under the influence, arrests, fights, injuries). Substance abuse is defined as regular drug use that continues despite interference with functioning. Dependence or addiction is repeated and compulsive substance use leading to tolerance (ie, need for greater amounts of substance to yield desired effects) and withdrawal symptoms between episodes of use.

Anticipatory guidance to prevent substance use can begin at the prenatal or newborn visit with a review of parental and family history of substance use and a discussion of the risks of secondhand tobacco smoke and of substance-impairment in caregivers. At childhood health supervision visits, modeling of alcohol and other substance use by parents, caregivers, and media personalities should be discussed.

All adolescents should be given anticipatory guidance about the adverse consequences of substance use and the risks of driving or riding with a driver under the influence of alcohol or drugs. Adolescents who are abstinent should be praised and given positive reinforcement for their avoidance of substance use. They should be encouraged to continue to abstain. Adolescents in the experimental stage should be educated about the negative impact of substances on the developing brain and body, and should be advised not to use substances. Adolescents with limited use should be guided on reducing the risks of their substance use and exposure; it is particularly important for adolescents to develop a safety plan to avoid risky driving or riding behaviors. Adolescents with problem use of substances should receive a brief office intervention that provides education on risks, recommends cessation of substance use, and negotiates a commitment to at least limit substance use. Adolescents with substance abuse should be referred for outpatient treatment, while those with dependence should be referred for intensive inpatient treatment.

Appreciation of the various factors that influence the likelihood of substance use can help the primary care physician in identifying those patients at highest risk for substance use. Risk factors include early academic failure, family conflict, and abuse. One of the strongest predictors of substance use is having friends who use alcohol or other substances. Protective factors include self-reliance, high self-esteem, and emotional well-being; supportive relationships with

family, school, or community; good parental involvement and modeling; and success in academics or extracurricular activities.

Primary care physicians play an important role in providing anticipatory guidance to prevent substance use in their patients, and in detecting and addressing the spectrum of use that may occur. The American Academy of Pediatrics' Committee on Substance Abuse 2011 policy statement, "Substance Use Screening, Brief Intervention, and Referral to Treatment for Pediatricians," serves as a resource for pediatricians wishing to further their knowledge on how to meet these needs.

PREP Pearls
- One of the strongest predictors of substance use is having friends who use alcohol or other substances.
- All adolescents should be given anticipatory guidance about the adverse consequences of substance use and the risks of driving or riding with a driver under the influence of alcohol or drugs.
- Adolescents with problem use of substances (ie, substance use with negative consequences) should receive a brief office intervention that provides education on risks, recommends cessation of substance use, and negotiates a commitment to at least limit substance use.

ABP Content Specifications(s)
- Provide appropriate anticipatory guidance to patients and families with regard to substance use/abuse
- Recognize the influence of peer groups on substance use/abuse
- Identify factors protective against substance use/abuse
- Recognize the association between early academic failure and substance use/abuse
- Understand the stages of drug/alcohol use

Suggested Readings
- Committee on Substance Abuse, Levy SJ, Kokotailo PK. Substance use screening, brief intervention, and referral to treatment for pediatricians. *Pediatrics*. 2011;128(5):e1330–1340. http://dx.doi.org/10.1542/peds.2011-1754.
- Committee on Substance Abuse. Policy statement: alcohol use by youth and adolescents—a pediatric concern. *Pediatrics*. 2010;125(5):1078–1087. http://dx.doi.org/10.1542/peds.2010-0438.
- Nackers KA, Kokotailo P, Levy SJ. Substance abuse, general principles. *Pediatr Rev*. 2015;36(12):535–544. http://dx.doi.org/10.1542/pir.36-12-535.

Question 271

A 5-year-old, previously healthy boy presents to the emergency department with a 1-month history of progressive fatigue, malaise, and weight loss. He developed a cough and difficulty breathing over the past week, and has needed to be propped up on a pillow to sleep. His temperature is 37.0°C, heart rate is 130 beats/min, respiratory rate is 36 breaths/min, and blood pressure is 90/70 mm Hg. On physical examination, the boy is awake, alert, and in no distress. His breathing is rapid and shallow, but he appears comfortable. There are mild scattered rales bilaterally on lung auscultation. His heart has a regular rhythm without rubs, murmurs, or gallops. His liver is palpable 4 cm below the right costal margin. His extremities are cool, with a capillary refill time of 4 seconds. Echocardiography shows a dilated left atrium and severely decreased left and right ventricular systolic function.

Laboratory results are as follows:

Sodium	128 mEq/L (128 mmol/L)
Potassium	4.5 mEq/L (4.5 mmol/L)
Chloride	98 mEq/L (98 mmol/L)
Bicarbonate	22 mEq/L (22 mmol/L)
Serum urea nitrogen	20 mg/dL (7.1 mmol/L)
Creatinine	0.5 mg/dL (44.2 µmol/L)

Of the following, the MOST likely explanation for this child's hyponatremia is

A. decreased dietary intake of sodium
B. decreased renal excretion of water
C. hypoaldosteronism
D. increased renal excretion of sodium
E. pseudohyponatremia

Correct Answer: B

The boy in the vignette has congestive heart failure, as evidenced by fatigue, weight loss, orthopnea, and suggestive echocardiographic findings. In congestive heart failure, antidiuretic hormone (ADH) release is increased, which decreases the excretion of water in the distal nephron, resulting in hyponatremia.

Sodium is the predominant extracellular cation, as most of the body's stores are in the extracellular compartment. Sodium is also the major determinant of plasma osmolality, which is approximated by the following formula:

Plasma osmolality (mOsm/kg) = 2*Na + BUN / 2.8 + plasma glucose / 18

Plasma osmolality is tightly controlled between 280 and 295 mOsm/kg by osmostatic mechanisms in the posterior pituitary gland through regulation of the thirst mechanism and ADH. Serum sodium level and serum osmolality are lowered both by water intake through the thirst mechanism and by decreased water excretion in response to the action of ADH on the collecting ducts of the nephron. ADH causes insertion of aquaporin channels into the basolateral membrane of the collecting duct cells, resulting in reabsorption of intraluminal water into the bloodstream.

Conditions in which hyponatremia is caused by increased ADH secretion include congestive heart failure, syndrome of inappropriate ADH (SIADH), neurologic conditions such as traumatic brain injury and after neurologic surgery, and pulmonary infections. In many of these conditions sodium stores are normal. These causes of hyponatremia, in which the water content is in excess in relation to sodium, comprise dilutional hyponatremia; this is the most common form of hyponatremia. Water retention and sodium depletion can occur with diarrhea and vomiting in the context of a normal thirst mechanism.

Hypertonic hyponatremia, sometimes referred to as pseudohyponatremia, can occur in the context of elevated osmotically active solutes. The most common presentation is in the setting of hyperglycemia in diabetic ketoacidosis. In response to hyperosmolality, water moves from the intracellular to the extracellular compartment, and dilutes the plasma sodium. Factitious hyponatremia occurs when severe hyperproteinemia and hyperlipidemia cause a laboratory artifact, falsely lowering the serum sodium level. Because these compounds occupy volume in the sample, the sodium distributed in the aqueous compartment of the sample is measured at a lower concentration.

Decreased dietary intake of sodium rarely causes hyponatremia, as the minimum dietary requirement of sodium is easily met, outside of extreme starvation. Hypoaldosteronism can cause hyponatremia, but the aldosterone axis is usually increased in patients with congestive heart failure. Renal excretion of sodium can be increased in cases of cerebral salt wasting, renal tubular dysfunction, or diuretic use, but none of these is present in the boy in the vignette. Pseudohyponatremia can occur in certain hyperosmolar conditions, such as diabetic ketoacidosis, but no such conditions are present in the boy in the vignette.

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PREP Pearls

- Plasma osmolality is tightly controlled between 280 and 295 mOsm/kg by osmostatic mechanisms in the posterior pituitary gland through regulation of the thirst mechanism and antidiuretic hormone (ADH).
- ADH decreases water excretion by the insertion of aquaporin channels into the basolateral membrane of the nephron, causing reabsorption of intraluminal water into the bloodstream.
- Dilutional hyponatremia is the most common cause of hyponatremia, representing conditions of excess water in relation to sodium stores.

MOCA-Peds Objective

- Recognize the features of congestive heart failure

ABP Content Specifications(s)

- Distinguish between dilutional hyponatremia and a total body deficit of sodium
- Plan the laboratory evaluation of hyponatremia while considering the differential diagnoses associated with the disorder

Suggested Readings

- Adrogue HJ, Madias NE. Hyponatremia. *N Engl J Med.* 2000;25;342(21):1581–1589. http://dx.doi.org/10.1056/NEJM200005253422107 .
- Moritz ML, Ayus JC. Maintenance intravenous fluids in acutely ill patients. *N Engl J Med*. 2015;373(14):1350–1360. http://dx.doi.org/10.1056/NEJMra1412877 .
- Reid-Adam J. Hyponatremia. *Pediatr Rev* 2013;34;417–419. http://dx.doi.org/10.1542/pir.34-9-417.

Question 272

A 17-year-old girl presents to your clinic with a complaint of "twitching." For the past 2 weeks, she has noticed her hands and arms suddenly twitch and jerk throughout the day. She says she can stop the twitching for a short time if she concentrates really hard. The twitching interferes with writing and she asks for a doctor's note to be excused from her upcoming advanced placement English test. You ask her about stressors, and she reports that she broke up with her boyfriend a month ago but she is "over it" now. The girl is worried about her college applications and meeting her parents' expectation that she be accepted to the Ivy League institution they both attended. A review of systems reveals fatigue, headaches, chest pain, shortness of breath, abdominal pain, nausea, vomiting, muscle aches, generalized weakness, and a 10-pound weight gain over the past 2 months. Her physical examination findings are normal; there are no unusual movements. However, after the formal examination, you observe irregular, low-amplitude jerks of her fingers and hands that appear involuntary. You obtain an anti-DNA-ase B test, antistreptolysin antibodies, an erythrocyte sedimentation rate, C-reactive protein level, and an electrocardiogram. All of the test results are normal.

Of the following, the test or assessment MOST likely to yield the diagnosis is a(n)

 A. echocardiogram
 B. electroencephalogram
 C. evaluation by a psychologist
 D. ionized calcium level
 E. serum human chorionic gonadotropin level

Correct Answer: E

The girl in the vignette has chorea. Chorea is an involuntary, quick, jerky movement that can involve any part of the body, including the fingers, limbs, trunk, face, or tongue. Like most movement disorders, it can be transiently suppressed. The most commonly seen chorea in children in the United States is Sydenham chorea. Other causes of chorea include basal ganglia brain injury, due to systemic lupus erythematosus or other causes of small vessel vasculitis; medications such as phenytoin; or thyrotoxicosis. Chorea gravidarum occurs during pregnancy and resolves afterwards. For the 17-year-old girl in the vignette, who has new-onset chorea but no signs of Sydenham chorea on laboratory testing, serum human chorionic gonadotropin level is the best response choice to reveal an underlying diagnosis. Magnetic resonance imaging of the brain and testing for hyperthyroidism would also be appropriate.

Echocardiography would be appropriate if the girl's laboratory testing results were consistent with Sydenham chorea. Electroencephalography would be helpful if the jerking were more suggestive of seizures. Focal seizures can present with focal jerking or twitching, but usually these involve just 1 side of the body, and there is often alteration of consciousness. The girl in the vignette may also have anxiety or depression, and she has many acute life stressors, so conversion disorder is an appropriate diagnosis to consider. In conversion disorder, the symptoms often increase during formal examination and dissipate with distraction. Psychological evaluation would be the next best step if conversion disorder were the most likely diagnosis. Hypocalcemia can cause tetany, a muscle spasm usually presenting in the hands, fingers, or toes. Tetany is not suppressible, and the girl in the vignette has no reason to have hypocalcemia, so an ionized calcium level would not be the best next test.

PREP Pearls
- Among children in the United States, the most common cause of chorea is Sydenham chorea.
- When Sydenham chorea has been ruled out as a cause of chorea, further evaluation may include magnetic resonance imaging of the brain, testing for hyperthyroidism, and testing for pregnancy when appropriate.
- Chorea gravidarum is chorea that occurs during pregnancy and resolves afterwards.

ABP Content Specifications(s)
- Understand the etiology of chorea and recognize its clinical manifestations

Suggested Readings
- Leblicq C, Duval M, Carmant L, Vliet GV, Alos N. Rising serum thyroxine levels and chorea in Graves' disease. *Pediatrics.* 2013;131(2):e616–e619. http://dx.doi.org/10.1542/peds.2012-0686.
- Mink JW, Zinner SH. Movement disorders II: chorea, dystonia, myoclonus, and tremor. *Pediatr Rev.* 2010;31(7):287–295. http://dx.doi.org/10.1542/pir.31-7-287 .

Question 273

A 10-year-old girl with autosomal recessive polycystic kidney disease is brought to your office for a health supervision visit. She is afebrile. She has a respiratory rate of 16 breaths/min, heart rate of 70 beats/min, and blood pressure of 130/80 mm Hg. Her height is 110 cm (less than fifth percentile), and her weight is 25 kg (fifth percentile). She started having menstrual periods 6 months ago. Her physical examination is significant for palpable kidneys.

You note that her most recent serum creatinine level is 0.62 mg/dL (54.8 µmol/L). You discuss her underlying kidney disease, glomerular filtration rate, and the associated complications with her parents.

Of the following, you are MOST likely to inform the parents that

A. growth failure needs treatment with recombinant human growth hormone
B. hypertension and deterioration in glomerular filtration rate are unrelated
C. a normal serum creatinine level indicates absence of chronic kidney disease
D. restriction of protein to less than the recommended intake is indicated
E. risk for deteriorating glomerular filtration rate is greatest during puberty

Correct Answer: E

The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical practice guidelines diagnose chronic kidney disease (CKD) in children based on the presence of 1 of the following criteria:

- Glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for greater than 3 months with implications for health, regardless of whether other CKD markers are present
- Glomerular filtration rate greater than 60 mL/min/1.73 m^2 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 by histology or inferred by imaging

The KDIGO guidelines also stage CKD in children (>2 years) for risk stratification into the following groups.

- Stage G1: Normal GFR ($\geq$ 90 mL/min/1.73 m^2)
- Stage G2: GFR between 60 and 89 mL/min/1.73 m^2
- Stage G3a: GFR between 45 and 59 mL/min/1.73 m^2
- Stage G3b: GFR between 30 and 44 mL/min/1.73 m^2
- Stage G4: GFR between 15 and 29 mL/min/1.73 m^2
- Stage G5: GFR less than 15 mL/min/1.73 m^2

Glomerular filtration rate is a measure of kidney function and indicative of the stage of CKD. The Schwartz formula is used to estimate the GFR from the serum creatinine level:

GFR = 0.413 × height (in centimeters) ÷ serum creatinine level (enzymatic method)

The GFR for the patient in this vignette is 73 mL/min/1.73 m^2, which corresponds to CKD stage 2.

In the majority of patients (86%), the diagnosis of CKD is associated with progression of renal disease and impairment of renal function leading to end-stage renal disease, which requires treatment with renal replacement therapy (dialysis or renal transplant). The continued decrease in renal function is caused by repeated acute and chronic insults to the renal parenchyma or by the adaptive hyperfiltration injury (increased glomerular pressure and flow) in the functioning nephrons. As a result of the adaptive hyperfiltration associated with compensatory increased function in the remaining nephrons, GFR is not a good indicator of loss of functioning nephrons in CKD. 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 in size on renal ultrasonography because of compensatory hypertrophy of the functioning nephrons. As the GFR decreases with progressive glomerular injury, the rise in serum creatinine level is also counteracted by increased tubular secretion of endogenous creatinine, leading to no increase or minimal increase in serum creatinine levels. Thus, patients with a decrease in GFR from 120 to 60 mL/min/1.73m^2 may have no change or minimal change in their serum creatinine level. The progression of CKD between stages G1 to G3a is accompanied by minimal initial elevation in serum creatinine but a

major decrease in GFR. Subsequent progression of CKD (stage G3b to G5) is associated with a marked increase in serum creatinine levels but only a small decrease in GFR.

Persistent glomerular hyperfiltration secondary to parenchymal injury leads to glomerular damage, tubulointerstitial inflammation, and fibrosis. These conditions lead to scarring of the renal glomeruli, blood vessels, and tubulointerstitium over a long-term period. Injury is histologically characterized by glomerulosclerosis, vascular sclerosis, and tubulointerstitial fibrosis. In the early stages (G1-G3a), increasing proteinuria or the onset or worsening of hypertension is indicative of progressive CKD despite stable GFR.

The rapid increase in body mass during infancy and puberty leads to increased filtration in the remaining nephrons. Risk for CKD progression is greatest during the growth spurts of infancy and puberty; and children in these growth stages should be monitored closely. According to the the Chronic Kidney Disease in Children study, among 891 children (1-16 years old) with glomerular and nonglomerular renal disease, a urine protein to creatinine ratio greater than 2 mg/mg, hypoalbuminemia, and elevated blood pressure were associated with rapid progression of CKD. In addition to increased risk of progression to end-stage renal disease with low GFR at diagnosis, the rate of decline in renal function is affected by ethnicity, primary renal disease, and genetic or familial risk factors for CKD.

In children with CKD, poor appetite, decreased intestinal absorption of nutrients, and metabolic acidosis leads to malnutrition. Provision of adequate nutrition is important to achieve optimum growth and neurocognitive development. Restriction of protein intake is not recommended in children in view of their needs for growth and neurocognitive development. Also, protein restriction has not been linked with decreased kidney function in children with CKD. Protein intake between 100% and 140% of the dietary reference intake values based on age and sex is recommended for children with CKD and a GFR of 30 to 60 mL/min/1.73m^2. In children with a GFR less than 30 mL/min/1.73m^2, protein intake between 100% and 120% of the dietary reference intake for age and sex is recommended.

Poor growth is a major complication of children with CKD and a marker for disease severity. Inadequate nutrition, fluid and electrolyte abnormalities (including metabolic acidosis), osteodystrophy, and disturbances of the growth hormone/insulin-like growth factor 1 axis contribute to growth impairment in children with CKD. Prior to 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 electrolyte and fluid losses, metabolic acidosis, anemia, and 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.

PREP Pearls

- Serum creatinine level and glomerular filtration rate are not good indicators of loss of functioning nephrons because of the compensatory increased function in the remaining nephrons.
- Increasing proteinuria or the onset or worsening of hypertension is indicative of progressive chronic kidney disease despite a stable glomerular filtration rate.
- A urine protein to creatinine ratio greater than 2 mg/mg, hypoalbuminemia, and elevated blood pressure were associated with rapid chronic kidney disease progression.
- Risk for chronic kidney disease progression is greatest during the growth spurts of infancy and puberty.

ABP Content Specifications(s)

- Recognize laboratory abnormalities associated with chronic kidney disease
- Recognize complications associated with chronic kidney disease

Suggested Readings

- Kidney Disease: Improving Global Outcomes. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney. *Kidney Int Suppl.* 2013;3(1):1–150.
- Massengill SF, Ferris M. Chronic kidney disease in children and adolescents. *Pediatr Rev.* 2014;35(1):16–29. doi:10.1542/pir.35-1-16.
- 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. http://www2.kidney.org/professionals/kdoqi/guidelines_ckd/toc.htm.

Question 274

A 12-year-old previously healthy girl is brought to the emergency department with an abrupt onset of nausea, vomiting, abdominal cramps, and watery diarrhea. One day prior to presentation, she had returned after a 2-week family cruise vacation to Europe. Other family members who traveled with her are also ill. Her temperature is 38°C. She has dry mucous membranes and sunken eyes. Capillary refill time is 3 seconds, and the serum sodium concentration is 130 mEq/L (130 mmol/L).

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

A. astrovirus
B. Bacillus cereus
C. enterovirus
D. norovirus
E. Shigella

Correct Answer: D

The adolescent girl in this vignette has acute gastroenteritis (AGE) after a recent family cruise vacation overseas. A similar illness is affecting other family members. This scenario is consistent with a norovirus infection. Norovirus (genus Norovirus, family Caliciviridae) is the most common etiology of cruise-associated outbreaks of AGE. Other pathogens associated with AGE on cruise ships include enterotoxigenic *Escherichia coli*, *Salmonella enteritidis*, *Shigella* species, *Vibrio* species, *Clostridium perfringens*, *Staphylococcus aureus*, and *Cyclospora*. *Bacillus cereus* is an important toxin-mediated foodborne illness, but it is not transmissible from person to person. Enterovirus and astrovirus can cause diarrheal illness in children, but are not implicated in cruise ship outbreaks of gastroenteritis.

Since the introduction of rotavirus vaccine in the United States, human norovirus (previously known as Norwalk virus) is now the leading cause of both sporadic and epidemic AGE in children younger than 5 years. Each year, norovirus AGE in children in the United States accounts for approximately 1 million health care visits, resulting in substantial disease and economic burden. Norovirus affects both children and adults and is responsible for an estimated 1.7 million office visits, 400,000 emergency department visits, 56,000 to 71,000 hospitalizations, 570 to 800 deaths, and approximately $284 million in health care costs annually in the United States. Globally, norovirus is responsible for 18% of pediatric AGE (17% of hospitalized cases and 24% of community episodes) and is estimated to cause more than 200,000 deaths each year.

With the increased availability of sensitive molecular detection methods such as real-time reverse transcriptase polymerase chain reaction assay, norovirus has been increasingly identified as a principal cause of foodborne illness and foodborne disease outbreaks in the United States (**Item C274**). The outbreaks are commonly associated with food contamination in restaurants during preparation by infected food handlers. The food vehicles implicated in common-source outbreaks include ice, shellfish, and ready-to-eat food products, such as salads, berries, and bakery items. In addition, norovirus has been implicated in health care–acquired infections, travel-associated diarrhea, and outbreaks with high attack rates in diverse settings including long-term care facilities, day care centers, schools, dormitories, military facilities, and cruise ships. The Centers for Disease Control and Prevention reported that norovirus caused 14,911 cases of AGE among cruise passengers and crew members during 2008-2014, representing 0.01% of the estimated number of norovirus cases during the same time period.

Estimated mean percentage and 95% confidence intervals of foodborne disease outbreaks caused by norovirus attributed to each food commodity — Foodborne Disease Outbreak Surveillance System, United States, 1998–2008*
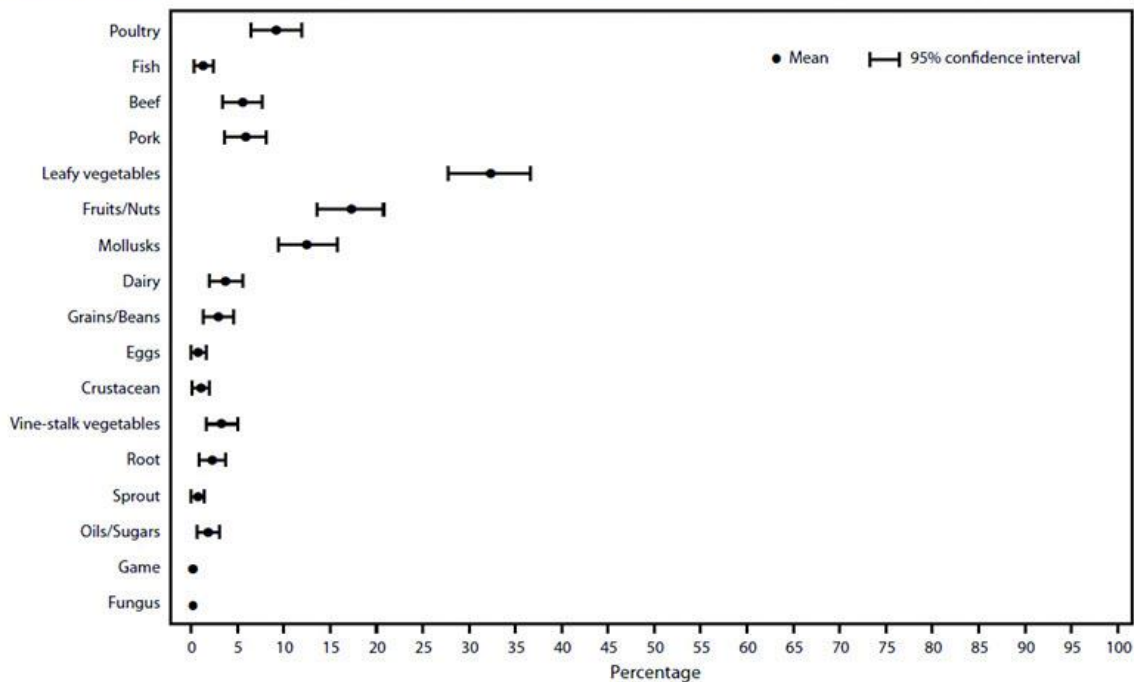
*N = 439.

Item C274: Percentage of Foodborne Outbreaks Caused by Norovirus by Food Type. Reprinted with permission from Frenkel L and Kimberlin DW, et al. *Red Book Online*. Norovirus and Other Human Calicivirus. Elk Grove Village, IL. American Academy of Pediatrics 2015

Norovirus is a nonenveloped, single-stranded RNA virus of the family Caliciviridae. The precise mechanisms of natural immunity to norovirus are not well understood. Immunity from norovirus infection is not permanent, and reinfections can occur throughout life. Infection with 1 norovirus serotype may not necessarily confer cross protection against other serotypes.

Noroviruses are highly contagious and easily transmitted through the fecal-oral or vomitus-oral routes, via consumption of contaminated water or food products or by direct contact with contaminated objects or surfaces. The virus is remarkably stable in the environment and can survive on surfaces for prolonged periods of time. Other factors that promote the transmissibility of norovirus include prolonged viral shedding (up to 3 weeks or more) by infected patients, high virus burden, and a small inoculum dose (< 100 viral particles) needed to cause disease. Norovirus has been detected in stools of healthy subjects, especially in children.

After an incubation period of 12 to 48 hours, norovirus illness often begins with the abrupt onset of vomiting associated with watery diarrhea, abdominal cramps, and nausea. Children may have diarrhea without vomiting. Other systemic symptoms may include fever, malaise, myalgia, loss of appetite, and headache. The usual duration of illness ranges from 1 to 5 days. Gastroenteritis

caused by norovirus can be severe in infants, the elderly, and immunocompromised hosts with a prolonged hospital course and mortality.

The management of norovirus AGE is supportive and aimed at the treatment of dehydration with oral or intravenous rehydration solutions and maintenance of fluid and electrolyte balance. Hospitalized patients with suspected AGE caused by norovirus must be placed on contact precautions until 48 hours after resolution of the illness. Strict adherence to hand hygiene practices remains the mainstay of norovirus infection prevention and control. Use of soap and running water for a minimum of 20 seconds is recommended after contact with a patient with suspected or confirmed norovirus gastroenteritis. Development of an effective norovirus vaccine must remain a priority.

PREP Pearls
- Since the introduction of rotavirus vaccine in the United States, human norovirus is now the leading cause of acute gastroenteritis in children younger than 5 years.
- Norovirus has been associated with foodborne disease outbreaks, health care–acquired infections, travel-associated diarrhea, and outbreaks in long-term care facilities, day care centers, schools, dormitories, and cruise ships.
- Noroviruses are highly contagious and easily transmitted through the fecal-oral or vomitus-oral routes, via consumption of contaminated water or food or by direct contact with contaminated objects or surfaces.
- Norovirus illness often begins with the abrupt onset of vomiting associated with watery diarrhea, abdominal cramps, and nausea.

ABP Content Specifications(s)
- Understand the epidemiology of human calicivirus (norovirus and sapovirus) infection
- Recognize the clinical features associated with calicivirus (norovirus and sapovirus) infection

Suggested Readings
- Centers for Disease Control and Prevention. Vital signs: foodborne norovirus outbreaks— United States, 2009-2012. *MMWR Morb Mortal Wkly Rep.* 2014;63(22):491–495.
- Freeland AL, Vaughan GH Jr, Banerjee SN. Acute gastroenteritis on cruise ships: United States, 2008-2014. *MMWR Morb Mortal Wkly Rep.* 2016;65(1):1–5. http://dx.doi.org/10.15585/mmwr.mm6501a1.
- Payne DC, Vinjé J, Szilagyi PG, et al. Norovirus and medically attended gastroenteritis in U.S. children. N Engl J Med. 2013;368(12):1121–1130. http://dx.doi.org/10.1056/NEJMsa1206589.

Question 275

You are seeing a 3-week-old infant for a health supervision visit. The boy was delivered at 34 weeks' gestation. He was recently discharged from the neonatal intensive care unit, where he was treated for mild respiratory distress syndrome and difficulty with feeding. During the neonate's hospitalization, a chest radiograph incidentally revealed a thoracic hemivertebra and mild right thoracic spinal curvature. Since discharge, he has gained weight appropriately. The infant is vigorous and alert, with normal physical examination findings.

Of the following, the BEST next step in evaluating this child is

  A. echocardiography
  B. magnetic resonance imaging (MRI) of the brain
  C. MRI of the spine
  D. no additional evaluation
  E. renal ultrasonography

Correct Answer: E

The neonate in the vignette has congenital scoliosis. Congenital scoliosis refers to scoliosis that results from the presence of 1 or more congenital vertebral malformations (CVMs). Because renal abnormalities are present in about one-third of children with CVMs, and are not typically detected with a history and physical examination, it is recommended that these children undergo screening with renal ultrasonography.

Hemivertebrae, butterfly vertebrae, and congenital vertebral fusions are examples of CVM. Although the vertebral abnormalities are congenital, arising during embryonic development, scoliosis may be absent at birth and develop later in childhood. Children with CVMs should be referred to an orthopaedic surgeon with experience managing congenital scoliosis.

Congenital vertebral malformations are associated with abnormalities of other organ systems that form during the same period of development. Children with CVMs have an increased risk of spinal cord abnormalities, such as tethered cord and diastematomyelia. If a child exhibits signs of central nervous system dysfunction (eg, lower extremity weakness, cavovarus foot deformity) or midline cutaneous lesions overlying the spine, spinal imaging should be obtained. Spinal ultrasonography would be the best screening test for a newborn, because sedation is not required. Ultrasonography typically provides adequate visualization of the spine in children younger than 4 months of age. In older children, magnetic resonance imaging (MRI) is the best test to look for spinal cord abnormalities.

The incidence of congenital heart disease is increased in children with CVMs. However, an asymptomatic neonate who is growing well and has normal cardiac examination findings is unlikely to have structural heart disease. Therefore, echocardiography is not indicated for the child in the vignette. As noted before, children with CVMs should routinely be evaluated with renal ultrasonography, therefore no additional evaluation would not be the correct response. Screening with brain MRIs is not indicated for children with CVMs.

PREP Pearls
- Congenital scoliosis results from the presence of 1 or more congenital vertebral malformations (CVMs).
- Renal abnormalities are present in about one-third of children with CVMs. Therefore, children with CVMs should be evaluated with renal ultrasonography.
- If a child with CVMs exhibits signs of central nervous system dysfunction or midline cutaneous lesions overlying the spine, spinal imaging should be performed.

ABP Content Specifications(s)
- Recognize conditions commonly associated with congenital scoliosis

Suggested Readings

- Shah SA, Song K. Congenital scoliosis. In: Weinstein SL,Flynn HM, eds. *Lovell & Winter's Pediatric Orthopaedics.* 7th ed. Philadelphia, PA:Lippincott Williams & Wilkins; 2013:chap 18:698–713.

Question 276

A 6-year-old previously healthy boy is brought to your office by his mother for concerns of adult body odor that she first noticed a few months ago. He takes no medication and has had no exogenous exposure to androgen. A review of systems shows unremarkable findings. There is no family history of precocious puberty. On physical examination, his temperature is 37°C, heart rate is 89 beats/min, blood pressure is 98/56 mm Hg, weight is 25 kg (90th percentile), and height is 125 cm (97th percentile). He appears older than his chronologic age, and has comedonal acne on his nose. Examination of his genitalia reveals a normal phallus, pubic hair at sexual maturity rating 2, and testes measuring approximately 6 mL bilaterally. Thinning and reddening of the scrotum are noted. He has a small amount of axillary hair bilaterally. The remainder of the physical examination findings are unremarkable.

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

A. 17-hydroxyprogesterone level
B. brain magnetic resonance imaging
C. dehydroepiandrosterone sulfate level
D. testicular ultrasonography
E. testosterone level

Correct Answer: B

The boy described in the vignette has central precocious puberty. In contrast to girls in whom central precocious puberty is most often idiopathic, in boys it is more often caused by underlying central nervous system (CNS) pathology. Thus, brain magnetic resonance imaging (MRI) is the test most likely to reveal this boy's diagnosis. CNS neoplasms such as hypothalamic hamartomas and optic gliomas can cause central precocious puberty. Optic gliomas can be associated with neurofibromatosis type 1.

Traditionally, precocious puberty is diagnosed when there are signs of puberty before age 8 years in girls and 9 years in boys. Newer evidence suggests that the lower age limit for onset of normal puberty may actually be 7 years for white girls and 6 years for black girls. The boy in the vignette has signs of puberty on his physical examination and tall stature, which may indicate growth acceleration because of sex steroid exposure. Results of a bone age radiograph were not provided in the vignette, but his bone age would likely be advanced.

When evaluating a child with precocious puberty, it is important to distinguish central from peripheral causes. Central precocious puberty results from activation of the hypothalamic-pituitary-gonadal axis. Testes are pubertal in volume (≥4 mL) in central precocious puberty because they are stimulated by luteinizing hormone (LH). Thus, testicular size is an important discriminator between central and peripheral precocious puberty in boys. The boy in the vignette has a testicular volume of 6 mL, which is consistent with central precocious puberty. An LH level of 0.3 IU/L or more (pubertal level) is also consistent with central precocious puberty.

Testes can also be pubertal in volume with tumors secreting human chorionic gonadotropin (hCG; eg, germinomas), because hCG is structurally similar to LH and stimulates LH receptors on the testes. With hCG-secreting tumors, however, testicular volume, although pubertal, is usually smaller than expected for the degree of other pubertal signs.

Peripheral precocious puberty may originate from the adrenal gland, gonad, an hCG-secreting tumor (in boys), exogenous hormone exposure, or severe hypothyroidism. In these conditions, testicular volume is prepubertal (<4 mL), except in cases of hCG-secreting tumors (as described before) and autonomous testosterone production from the testes (activating mutation in the LH receptor). LH is in the prepubertal range (<0.3 IU/L) in peripheral precocious puberty.

A testosterone level would likely be pubertal (≥30 ng/dL depending on laboratory) in this boy because the testes are the primary source of testosterone, but this result would not be helpful in revealing the underlying diagnosis. Testicular ultrasonography would be indicated if a testicular tumor were suspected. In the case of a testicular tumor, a mass may be palpated and the testes are usually asymmetric in size. A 17-hydroxyprogesterone level would be elevated in congenital adrenal hyperplasia; the high androgen levels come from the adrenal gland, so testicular volume would be prepubertal. Similarly, a high dehydroepiandrosterone sulfate level would indicate an adrenal source of androgen and testicular volume would be prepubertal.

PREP Pearls
- 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 because they are stimulated by luteinizing hormone (LH).
- A pubertal LH level of 0.3 IU/L or more is consistent with central precocious puberty.
- Central nervous system pathology is much more common in boys with central precocious puberty than in girls.

MOCA-Peds Objective
- Recognize normal variations in pubertal development

ABP Content Specifications(s)
- Recognize the clinical features associated with precocious puberty, including that caused by tumors

Suggested Readings
- Carel JC, Léger J. Clinical practice: precocious puberty. *N Engl J Med*. 2008;358(22):2366–2377. http://dx.doi.org/10.1056/NEJMcp0800459.
- Long D. Precocious puberty. *Pediatr Rev*. 2015;36(7):319–321. http://dx.doi.org/10.1542/pir.36-7-319.
- Muir A. Precocious puberty. *Pediatr Rev*. 2006;27(10):373–381. http://pedsinreview.aappublications.org/content/27/10/373.

Question 277

An 11-year-old boy is seen for an annual health supervision visit. He received a bone marrow transplant from an unrelated donor for relapsed acute lymphoblastic leukemia at 7 years of age. His transplant conditioning included total body irradiation (1,350 cGy) and cyclophosphamide. He was weaned off of immunosuppressive drugs over a 12-month period, and for the last 3 years he has been healthy and off all medications.

As part of your evaluation, you ask about his school performance. He has been attending the fifth grade, but reports struggling in many classes, especially math and science. Although he and his parents report that he is a serious student and a hard worker, his grades have declined over the last 3 years, and he has become frustrated with his school work. Both of his parents are professionals, and he has 2 older siblings who are excellent students. The boy tells you that he wonders why he does not do as well in school as his siblings.

Of the following, you counsel him and his parents that

A. after undergoing a traumatic medical intervention such as bone marrow transplant, he is most likely focusing on "life" and not giving academics his full effort
B. because he was kept out of school for over a year for the bone marrow transplant, he should repeat the fifth grade
C. bone marrow donors are not screened for intelligence, so his school performance likely reflects his donor's academic potential
D. none of the therapies he received should affect his academic performance, so he should continue to work hard and over time his grades will improve
E. the transplant conditioning, he received puts him at high risk for neurocognitive changes, so you would like to refer him for a formal neurocognitive evaluation

Correct Answer: E

Long-term survivors of childhood cancer and bone marrow transplant are at high risk for chronic diseases and disorders as a consequence of their treatments. These diseases and disorders include cardiovascular disease, pulmonary dysfunction, endocrinopathies, infertility, musculoskeletal disorders, secondary malignant neoplasms, and neurocognitive deficits. Almost every long-term survivor has at least one measurable defect in organ function. The risk for specific late effects is directly related to the chemotherapy, radiation, and surgery exposures the survivor received during treatment. For example, patients who received anthracyclines such as doxorubicin are at higher risk for cardiomyopathy in a dose-dependent manner, and female survivors who received chest radiation have a 35% chance of developing breast cancer by 50 years of age. The Children's Oncology Group has created exposure-based guidelines for the screening of survivors (www.survivorshipguidelines.org). Many pediatric oncology programs have specialized survivorship programs that can assist with formulating personalized screening plans based on exposures.

The central nervous system is a sanctuary site for childhood leukemia; therefore, children treated for leukemia receive central nervous system prophylaxis with intrathecal chemotherapy, which is administered directly into the spinal fluid. Although intrathecal chemotherapy is generally well tolerated, it is often performed during brain development and can cause neurocognitive changes. Radiation therapy to the brain of a child can also impact neurocognition. The child in this vignette underwent a bone marrow transplant for relapsed acute lymphoblastic leukemia. Although the child's chemotherapy and radiation exposures during the initial treatment of the leukemia are not specified, it is very likely that he received multiple intrathecal chemotherapy administrations. In addition, he underwent total body irradiation as part of the conditioning regimen for the bone marrow transplant. Total body irradiation includes radiation to the brain, which can impact cognitive development. The boy in this vignette reports having challenges in school that make his academic experience markedly different than his family's academic achievements. These challenges must be recognized and addressed, because an appropriate education plan in school can prevent further frustration and potential education failure. The boy should have a formal neurocognitive assessment, and any resulting recommendations should be provided to the school. These recommendations can be formally discussed between the school and the family in a 504 meeting (in reference to section 504 of the Americans with Disabilities Act) and then formalized as interventions in an individualized education program.

The boy described in this vignette reports working hard at school, which has been corroborated by his parents. It is important to understand the patient's history so as not to mistake educational challenges for laziness or apathy. The intelligence of the marrow donor should have no bearing on the school performance of the recipient. Although it is likely that the boy in this vignette would benefit from some interventions in school, repeating a grade is not necessarily the best option. He should receive a formal neurocognitive assessment of his academic strengths and weaknesses prior to any recommendations being implemented.

PREP Pearls
- Survivors of childhood cancer and bone marrow transplant are at high risk for late morbidity as a consequence of chemotherapy, radiation, and surgery.
- Childhood cancer survivors who received intrathecal chemotherapy or radiation to the brain are at risk for neurocognitive changes and educational challenges and should therefore undergo formal neurocognitive testing.
- Many pediatric oncology programs have survivorship programs that can assist with formulating individualized, exposure-based screening plans.

ABP Content Specifications(s)
- Recognize psychosocial and family issues associated with transplantation

Suggested Readings
- Landier W, Armenian S, Bhatia S. Late effects of childhood cancer and its treatment. *Pediatr Clin North Am*. 2015;62(1):275–300. http://dx.doi.org/10.1016/j.pcl.2014.09.017.
- Meck MM, Leary M, Sills RH. Late effects in survivors of childhood cancer. *Pediatr Rev*. 2006;27(7):257–262. http://dx.doi.org/10.1542/pir.27-7-257 .
- Hudson MM, Ness KK, Gurney JG, et al. Clinical ascertainment of health outcomes among adults treated for childhood cancer. *JAMA*. 2013;309(22):2371–2381. http://dx.doi.org/10.1001/jama.2013.6296 .
- Children's Oncology Group. Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 4.0. 2014. http://www.survivorshipguidelines.org . Available at: http://www.survivorshipguidelines.org