

PEDIATRICS

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Learning Objectives

1. Describe the most common pathogens associated with neonatal and pediatric sepsis and meningitis.
 2. Describe current therapeutic options for the management of neonatal and pediatric sepsis and meningitis.
 3. Identify the drugs available for preventing and treating respiratory syncytial virus.
 4. Describe the most common causative organisms of otitis media and potential treatment options.
 5. Identify the recommended pediatric immunization schedule and barriers to routine immunization.
 6. Discuss the differences in anticonvulsant pharmacokinetics and adverse effects between children and adults.
 7. Describe the current drug therapy for treating patients with attention-deficit/hyperactivity disorder.
- D. This patient should receive prophylaxis only if she has additional risk factors such as day care attendance or school-aged siblings.
3. Which is the most accurate statement about prophylaxis of bacterial meningitis?
 - A. Close contacts of patients with pneumococcal meningitis should receive prophylaxis.
 - B. Close contacts of patients with *Haemophilus influenzae* meningitis require prophylaxis only if their immunizations are not up-to-date.
 - C. Rifampin is a first-line agent for prophylaxis against meningococcal meningitis.
 - D. Prophylaxis against bacterial meningitis is no longer recommended regardless of the causative organism.

Self-Assessment Questions

Answers and explanations to these questions can be found at the end of this chapter.

1. A 15-year-old boy with a history of exercise-induced asthma presents with fever, tachypnea, headache, and myalgia. Which is most likely to be isolated from this patient?
 - A. Respiratory syncytial virus (RSV).
 - B. *Streptococcus pneumoniae*.
 - C. Group B *Streptococcus*.
 - D. *Pseudomonas aeruginosa*.
2. Which is the best assessment of the risk of severe RSV infection and subsequent need for prophylaxis in a 3-month-old girl born at 30 weeks' gestation?
 - A. This patient should receive prophylaxis if she is 6 months or younger at the beginning of RSV season.
 - B. This patient is at risk only if she has chronic lung disease (i.e., necessitating more than 21% oxygen for at least the first 28 days of life).
 - C. All neonates born during RSV season should receive prophylaxis.
4. A 6-month-old baby who was born at 24 weeks' gestation is brought to the clinic in October for a routine checkup and immunizations. Which is the best recommendation to make for this patient's immunization schedule?
 - A. Only two of the five immunizations due should be given at the same time; schedule another appointment for the next week to administer the rest.
 - B. Oral polio vaccine should be used to reduce the number of injections required to complete the schedule.
 - C. Vaccines should be based on his corrected gestational age rather than on his chronologic age because he was born prematurely.
 - D. Influenza vaccine should be administered with all other scheduled vaccinations.
5. A physician asks for your recommendation for treating a 5-year-old child with his first case of acute otitis media (AOM). Which statement is the best advice?
 - A. A blood culture should be obtained to identify the causative organism.
 - B. Antibiotics may not be warranted at this time.
 - C. Initiate azithromycin to treat atypical organisms (e.g., mycoplasma).
 - D. Administer intramuscular ceftriaxone.

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6. A 16-year-old girl with asthma, a history of ventricular septal defect, and attention-deficit/hyperactivity disorder (ADHD) was initially treated with methylphenidate immediate release, but her ADHD symptoms persisted at home and at school. Her therapy was then changed to methylphenidate OROS (Concerta). The dose was maximized during the next several weeks; however, her symptoms were still not well controlled throughout the day. She and her family report adherence to the treatment regimen. Which is the best recommendation to make for treating her ADHD?
- A. Switch to clonidine.
 - B. Switch to extended-release mixed amphetamine salts (i.e., Adderall XR).
 - C. Switch to methylphenidate transdermal system (i.e., Daytrana).
 - D. Switch to atomoxetine.
7. A 7-year-old child with absence seizures is having breakthrough episodes on ethosuximide. Which is the most appropriate alternative therapy?
- A. Valproic acid.
 - B. Phenytoin.
 - C. Phenobarbital.
 - D. Gabapentin.
8. In a retrospective study of the risk of loss of appetite in adolescents taking a specific stimulant agent for ADHD management, 7 of 200 patients exposed to the stimulant showed appetite loss, compared with 1 of 198 control subjects (unexposed). Which choice best reflects the correct odds ratio of developing loss of appetite for the case subjects compared with the control subjects?
- A. 3.
 - B. 6.
 - C. 7.
 - D. 8.
9. An investigator wants to establish a causal relationship between the use of ceftriaxone in premature neonates and the incidence of kernicterus. Which study design is best to use?
- A. Case series.
 - B. Randomized controlled.
 - C. Retrospective cohort.
 - D. Crossover.
10. An 8-month-old, former 36-week gestational-age infant with hypoplastic left heart disease is admitted during RSV season for stage II (of III) repair of his heart defect. Which statement is most accurate about the use of palivizumab for RSV prophylaxis in this patient?
- A. He is not at significant risk of severe RSV infection; therefore, palivizumab is not indicated.
 - B. Palivizumab is indicated to reduce nosocomial transmission of RSV in high-risk patients.
 - C. Palivizumab is not indicated because he has undergone surgical repair of his heart defect.
 - D. A dose of palivizumab should be administered postoperatively and continued throughout the RSV season.

I. SEPSIS AND MENINGITIS

A. Clinical Presentation

1. Signs and symptoms
 - a. Neonates: Temperature instability, feeding intolerance, lethargy, grunting, flaring, retractions, apnea, bulging fontanelle, and seizures
 - b. Children: Fever, loss of appetite, emesis, myalgias, arthralgias, cutaneous manifestations (e.g., petechiae, purpura, rash), nuchal rigidity, back pain, Kernig sign, Brudzinski sign, headache, photophobia, altered mental status, and seizures
2. Early versus late neonatal sepsis
 - a. Onset
 - i. Early: Within 72 hours of birth
 - ii. Late: After the first 3 days of life
 - b. Risk factors
 - i. Early: Very low birth weight, prolonged rupture of amniotic membranes, prolonged labor, maternal endometritis, or chorioamnionitis
 - ii. Late:
 - (a) Unrelated to obstetric risk factors
 - (b) Usually related to iatrogenic factors (e.g., endotracheal tubes, central venous catheters)
 - c. Incidence
 - i. Early
 - (a) 0.7–3.7 of 1000 live births (8 of 1000 very-low-birth-weight infants)
 - (b) Meningitis occurs in less than 10% of cases.
 - ii. Late
 - (a) 0.5–1.8 of 1000 live births
 - (b) Meningitis occurs in 60% of cases.
3. Cerebrospinal fluid findings

Table 1. Cerebrospinal Fluid Findings

Laboratory Value	Normal Child	Normal Newborn	Bacterial Meningitis	Viral Meningitis
WBC (cells/mL)	0–6	0–30	>1000	100–500
Neutrophils (%)	0	2–3	>50	<40
Glucose (mg/dL)	40–80	32–121	<30	>30
Protein (mg/dL)	20–30	19–149	>100	50–100
RBC (cells/mL)	0–2	0–2	0–10	0–2

RBC = red blood cell count; WBC = white blood cell count.

Adapted with permission from the American Academy of Pediatrics. Wubbel L, McCracken GH. Management of bacterial meningitis: 1998. *Pediatr Rev* 1998;19:78-84.

Patient Case

1. A baby born at 36 weeks' gestation develops respiratory distress, hypotension, and mottling at 5 hours of life. The baby is transported to the neonatal intensive care unit, where he has a witnessed seizure, and cultures are drawn. Maternal vaginal cultures are positive for group B *Streptococcus*, and three doses of penicillin were given to the mother before delivery. Which is the best empiric antibiotic regimen?
 - A. Vancomycin.
 - B. Ampicillin plus gentamicin.
 - C. Ampicillin plus ceftriaxone.
 - D. Ceftazidime plus gentamicin.

B. Common Pathogens

Table 2. Common Pathogens

Age	Organism
0–1 month	Group B <i>Streptococcus</i> <i>Escherichia coli</i> <i>Listeria monocytogenes</i> Viral (e.g., herpes simplex virus) Coagulase-negative staphylococcus (nosocomial) Gram-negative bacteria (e.g., <i>Pseudomonas</i> spp., <i>Enterobacter</i> spp.; nosocomial)
1–3 months	Neonatal pathogens (see above) <i>Haemophilus influenzae</i> type B <i>Neisseria meningitidis</i> <i>Streptococcus pneumoniae</i>
3 months–12 years	<i>H. influenzae</i> type B ^a <i>N. meningitidis</i> <i>S. pneumoniae</i>
>12 years	<i>N. meningitidis</i> <i>S. pneumoniae</i>

^a*H. influenzae* is no longer a common pathogen in areas where the vaccine is routinely used.

C. Potential Antibiotic Regimens

Table 3. Potential Antibiotic Regimens

Age	Regimen
0–1 month	Ampicillin + gentamicin OR ampicillin + cefotaxime
1–3 months	Ampicillin + cefotaxime/ceftriaxone
3 months–12 years	Ceftriaxone ± vancomycin ^a
>12 years	Ceftriaxone ± vancomycin ^a

^aAddition of vancomycin should be based on the regional incidence of resistant *Streptococcus pneumoniae*.

Patient Cases

2. Culture results for the patient in question 1 reveal gram-negative rods in the cerebrospinal fluid. Which recommendation regarding antibiotic prophylaxis is best?
 - A. The patient's 5-month-old stepsister is at high risk because she is not fully immunized; the patient should therefore receive rifampin.
 - B. The patient should receive rifampin to eliminate nasal carriage of the pathogen.
 - C. Antibiotic prophylaxis is not indicated in this case.
 - D. All close contacts should receive rifampin for prophylaxis.

3. A 6-year-old boy presents to the emergency department with a temperature of 104°F, altered mental status, and petechiae. There is no history of trauma. A toxicology screen is negative. A complete blood cell count reveals 32×10^3 cells/mm³ white blood cells/mL with 20% bands. Culture results are pending. The patient has no known drug allergies. Which antibiotic regimen provides the best empiric coverage?
 - A. Ampicillin plus gentamicin.
 - B. Cefuroxime.
 - C. Ceftriaxone plus vancomycin.
 - D. Rifampin.

D. Sequelae of Meningitis

1. Hearing loss
2. Mental retardation and learning deficits
3. Visual impairment
4. Seizures
5. Hydrocephalus

E. Chemoprophylaxis of Bacterial Meningitis

1. Purpose: Prevent the spread of *H. influenzae* and *Neisseria meningitidis*
2. High-risk groups
 - a. Household contacts
 - b. Nursery or day care center contacts
 - c. Direct contact with index patient's secretions
3. Regimen

Table 4. Regimens for Chemoprophylaxis^a

Drug	<i>Neisseria meningitidis</i>	<i>Haemophilus influenzae</i>
Rifampin	<1 month old: 5 mg/kg/dose PO every 12 hours × 2 days ≥1 month old: 10 mg/kg/dose PO every 12 hours × 2 days Adults: 600 mg PO every 12 hours × 2 days	20 mg/kg/dose (maximum 600 mg) PO daily × 4 days
Ceftriaxone	<15 years old: 125 mg IM × 1 dose ≥15 years old: 250 mg IM × 1 dose	Not indicated

^aCiprofloxacin and azithromycin are possible alternatives but not routinely recommended.
IM = intramuscularly; PO = orally.

II. RESPIRATORY SYNCYTIAL VIRUS INFECTION

A. Clinical Presentation

1. Seasonal occurrence: Typically November through April, depending on geographic location
2. Signs and symptoms
 - a. Neonates and infants: Lower respiratory tract symptoms (e.g., bronchiolitis and pneumonia), wheezing, lethargy, irritability, poor feeding, and apnea
 - b. Older children: Upper respiratory tract symptoms

B. Risk Factors for Severe Disease

1. Premature birth
2. Chronic lung disease or bronchopulmonary dysplasia
3. Cyanotic or complicated congenital heart disease
4. Immunodeficiency
5. Airway abnormalities or neuromuscular conditions compromising the handling of respiratory secretions
6. Other
 - a. Lower socioeconomic status
 - b. Passive smoking
 - c. Day care attendance
 - d. Siblings younger than 5 years

Patient Case

4. You are screening babies during the current respiratory syncytial virus (RSV) season for risk factors associated with the development of severe RSV infection. Which is the best recommendation about the use of palivizumab for RSV prophylaxis?
 - A. Palivizumab should be prescribed for an 18-month-old, former 26-week premature infant with a history of chronic lung disease who has not received oxygen or medications during the past 8 months.
 - B. Palivizumab should be prescribed for a 5-month-old, former 28-week premature infant with a history of chronic lung disease who was discharged from the hospital without oxygen or medications.
 - C. Palivizumab should be prescribed for a 41-day-old baby, born at 31 weeks' gestation, without a history of chronic lung disease who will attend day care.
 - D. Palivizumab should be prescribed for a 10-month-old baby, born at 37 weeks' gestation, with a surgically repaired congenital heart defect.

C. Prophylaxis

1. Nonpharmacologic: Avoid crowds during RSV season and conscientiously use good handwashing practice.
2. Palivizumab (Synagis)
 - a. Dosing: 15 mg/kg/dose intramuscularly, given monthly during RSV season
 - b. Effects on outcomes
 - i. A 55% reduction in hospitalizations for RSV
 - ii. Safe in patients with cyanotic congenital heart disease. There is a 58% decrease in palivizumab serum concentration after cardiopulmonary bypass; therefore, a postoperative dose of palivizumab is recommended as soon as the patient is medically stable.

- iii. No reduction in overall mortality
- iv. Does not interfere with the response to vaccines
- v. Not recommended for the prevention of nosocomial transmission of RSV
- c. American Academy of Pediatrics (AAP) recommendations for use were updated in 2014 (Table 5) and contain several significant changes from their 2009 policy statement.
 - i. Routine prophylaxis is no longer recommended for neonates born at 29 weeks' gestation or later; previously all neonates born at less than 32 weeks' gestation were recommended to receive routine prophylaxis.
 - ii. Risk factors for RSV infection such as day care attendance or siblings younger than 5 years of age are no longer considered when determining the need for prophylaxis.
 - iii. Prophylaxis is not recommended in the second year of life based on a history of prematurity alone; previously neonates born at less than 28 weeks' gestation could be considered for prophylaxis during their second RSV season.
 - iv. Prophylaxis should be discontinued if an RSV hospitalization occurs; previously palivizumab was continued to complete 5 monthly doses regardless of hospitalization.

Table 5. AAP Guidelines for Palivizumab Use

Gestational Age (weeks)	Age at Start of RSV Season (months)	Other Required Criteria	Maximal Doses
<29 + 0 days	<12		5
<32 + 0 days	<12	Chronic lung disease requiring more than 21% oxygen for at least the first 28 days of life	5
<32 + 0 days	<24	Consider prophylaxis for a second RSV season if chronic lung disease requiring medical therapy within the 6 months preceding the start of RSV season	5
Any	<12	Hemodynamically significant acyanotic ^a congenital heart disease receiving medication for congestive heart failure AND will require cardiac surgery	5
Any	<12	Moderate to severe pulmonary hypertension	5
Any	<12	Congenital abnormalities of airway or neuromuscular disease	5
Any	<24	Profound immunocompromise	5

^aInfants with **cyanotic** heart defects may be considered for prophylaxis after consultation with a pediatric cardiologist.

AAP = American Academy of Pediatrics.

Patient Case

5. An 18-month-old baby with a history of premature birth and chronic lung disease is admitted to the pediatric intensive care unit with fever, respiratory distress requiring intubation, and a 3-day history of cold-like symptoms. A nasal swab is positive for RSV. Which is the best intervention?
- A. Palivizumab.
 - B. Corticosteroids.
 - C. Cefuroxime.
 - D. Intravenous fluids and supportive care.

D. Treatment

1. Supportive care
 - a. Hydration
 - b. Supplemental oxygen
 - c. Mechanical ventilation as needed
2. Ribavirin
 - a. Active against RSV replication
 - b. Not shown to reduce mortality in immunocompetent patients
 - c. Not shown to reduce ventilator days, stay in the intensive care unit or hospital, or hospital cost
 - d. The AAP states that ribavirin “may be considered” in a select group of high-risk patients (e.g., those with complicated congenital heart disease, chronic lung disease or bronchopulmonary dysplasia, immunocompromise).
3. β_2 -Agonists, racemic epinephrine
 - a. Not shown to improve outcome measures
 - b. Some practitioners may give a trial of these therapies, but this is not considered the standard of care.
4. Corticosteroids
 - a. Not shown to improve outcome measures
 - b. Use is not recommended.
5. Hypertonic saline
 - a. Should not be administered in the emergency department
 - b. May be considered for hospitalized patients; however, the evidence supporting use is weak.
6. Antibiotics: Not indicated unless secondary bacterial infection develops

III. OTITIS MEDIA**A. Clinical Presentation**

1. Definitions
 - a. Acute otitis media (AOM): Presence of middle ear effusion and evidence of middle ear inflammation
 - i. Middle ear effusion may be indicated by bulging tympanic membrane, decreased or no mobility of the tympanic membrane, purulent fluid in the middle ear.
 - ii. Inflammation of the middle ear may be indicated by erythema of the tympanic membrane or otalgia.
 - b. Otitis media with effusion (OME): Fluid in the middle ear without evidence of local or systemic illness

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- c. Recurrent AOM: Three or more episodes of acute otitis within 6 months or four episodes within 1 year
 2. Risk factors
 - a. Day care attendance
 - b. Family history of AOM
 - c. Positioning during feeding (e.g., supine position during bottle-feeding allows reflux into eustachian tubes)
 - d. Lower socioeconomic status
 - e. Smokers in the household
 - f. Craniofacial abnormalities or cleft palate
- B. Common Pathogens
1. Viral
 2. *S. pneumoniae*
 3. Nontypeable *H. influenzae*
 4. *Moraxella catarrhalis*
- C. Treatment
1. General principles
 - a. Clinical resolution will occur in a significant number of cases without antibiotic therapy.
 - b. Immediate antibiotic therapy is warranted for AOM with bulging tympanic membrane, perforation, or otorrhea.
 - c. Delayed antibiotic prescribing (i.e., treatment only if otalgia persists for more than 48–72 hours or temperature greater than 39°C in past 48 hours) is an acceptable strategy in children older than 2 years with AOM without severe systemic symptoms.
 - i. Analgesics are more beneficial than antibiotics for relieving otalgia within the first 24 hours and are recommended regardless of antibiotic use.
 - ii. Antibiotics also may be deferred in otherwise healthy children between 6 months and 2 years of age if their symptoms are mild and otitis media is unilateral (as opposed to bilateral).
 - iii. Caregiver must be reliable to recognize worsening of condition and gain immediate access to medical care, if needed.
 - iv. Not recommended for infants younger than 6 months
 - d. Persistence of middle ear fluid is likely after treatment for AOM and does not warrant repeated treatment.
 - e. Antibiotics are not generally warranted for OME because of the high rate of spontaneous resolution.
 - i. Antibiotics are recommended only if bilateral effusions persist for more than 3 months.
 - ii. Corticosteroids, antihistamines, and decongestants are not recommended.
 2. Suggested treatment algorithm

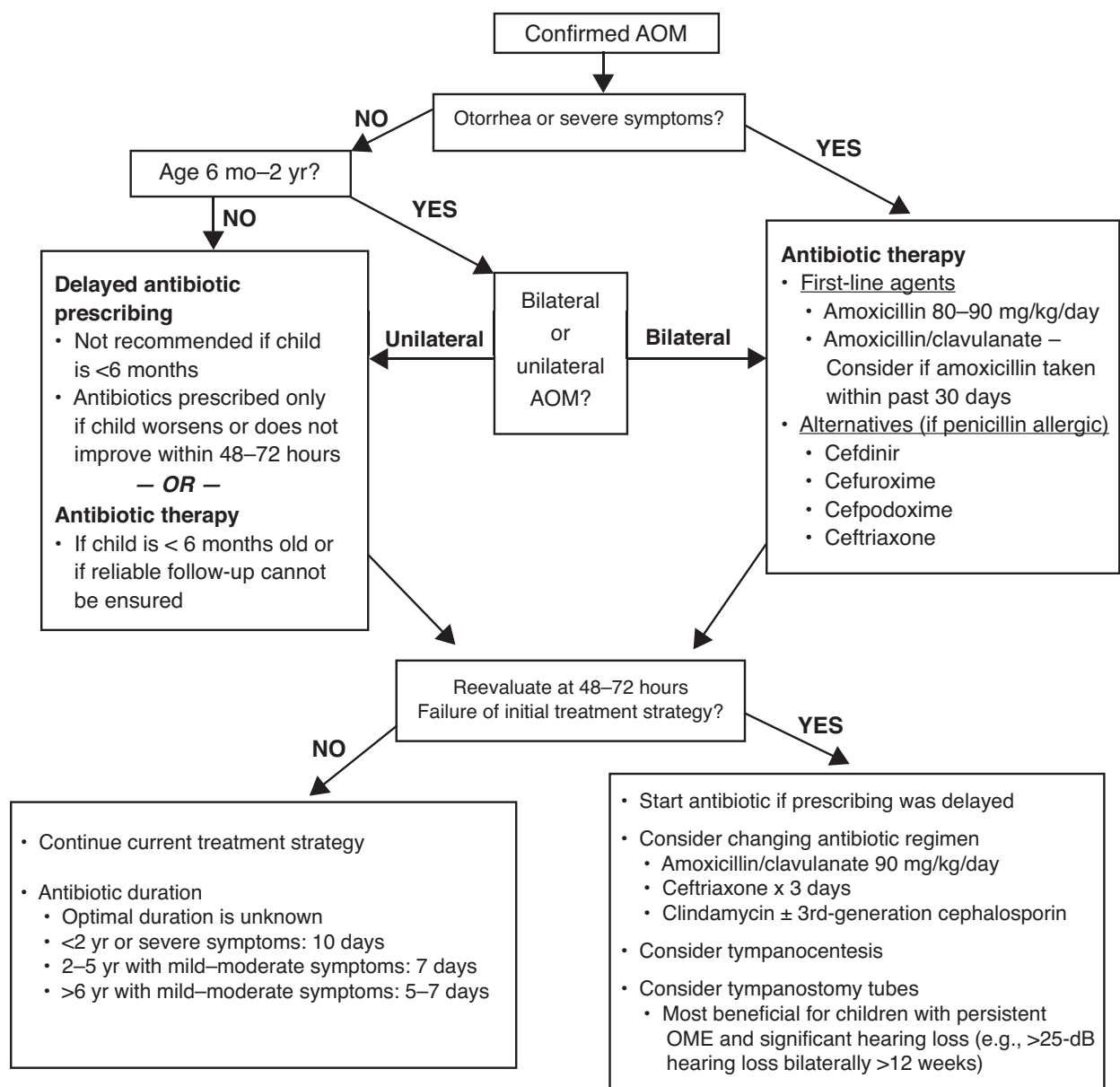


Figure 1. AOM Suggested Treatment Algorithm

D. Prevention Strategies

1. Antibiotic prophylaxis

- Reduces occurrence by about one episode per year
- The risk of promoting bacterial resistance may outweigh the slight benefit.
- AAP recommends against routine use for children with recurrent AOM.

2. Immunization – Pneumococcal and influenza vaccines should be administered according to the AAP and Advisory Committee on Immunization Practices (ACIP) recommendations.

Patient Cases

6. A 5-month-old infant who was born at term and is otherwise healthy was treated for her first case of otitis media with amoxicillin 45 mg/kg/day for 7 days. On follow-up examination, her pediatrician noticed fullness in the middle ear and a cloudy tympanic membrane with decreased mobility. She is now afebrile and eating well. Which is the best recommendation for her treatment?
 - A. No antibiotics at this time.
 - B. High-dose (90 mg/kg/day) amoxicillin for 7 days.
 - C. Decongestant and antihistamine daily until resolution.
 - D. Azithromycin.

7. A 4-year-old boy receives a diagnosis of his fourth case of otitis media within 12 months. He has not shown evidence of hearing loss or delay in language skills. Which is the best intervention at this point?
 - A. Giving long-term antibiotic prophylaxis.
 - B. Inserting tympanostomy tubes.
 - C. Administering high-dose amoxicillin and ensuring that he is up to date on his pneumococcal and influenza vaccines.
 - D. No antibiotic therapy warranted.

IV. IMMUNIZATIONS**A. Recommended Schedule**

1. Few major changes have been made to the routine childhood schedule since 2009.
 - a. Replacement of 7-valent conjugated pneumococcal vaccine with 13-valent conjugated pneumococcal vaccine (PCV13, Prevnar 13) for all children younger than 6 years
 - b. Human papillomavirus vaccine (HPV4, Gardasil) received a U.S. Food and Drug Administration (FDA) label-approved indication in males 9–26 years old for prevention of genital warts. Now recommended for routine vaccination of adolescent males
 - c. For children and adolescents who have a delayed start to immunizations, a catch-up schedule exists.
 - d. Refer to the National Immunization Program Web site (www.cdc.gov/vaccines).

Patient Case

8. A 1-year-old boy with a history of Kawasaki disease treated 4 months ago with intravenous immunoglobulin (IVIG) is being seen by his pediatrician for a well-child checkup. He is due for the measles, mumps, and rubella (MMR) and varicella vaccines. He has no known drug allergies, but he has many food allergies, including peanuts, eggs, and shellfish. His mother has several concerns about administering these vaccines. Which concern is the best reason to defer administering vaccines in this patient?
 - A. Association between MMR vaccine administration and the development of autism.
 - B. Allergic reaction after MMR administration in a patient with an egg allergy.
 - C. Many concurrent vaccines can overload the patient's immune system.
 - D. Decreased vaccine efficacy because of previous IVIG administration.

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2. Combination vaccines
 - a. Main advantage: Reduction in the number of injections required to complete recommended schedule
 - b. The FDA mandates that the safety and efficacy of combination products not be less than those of the individual components.
 - c. Products
 - i. The DTaP-Hib (*H. influenzae* type B) combination
 - (a) The Hib antibody response is markedly lower after the combination product is administered than when the Hib vaccine is administered separately for primary immunization.
 - (b) Product (TriHIBit) withdrawn from U.S. market
 - ii. The DTaP-IPV (inactivated poliovirus) combination
 - (a) Studies indicate that this combination has no consistent effect on antibody responses.
 - (b) Indicated only for the fifth dose of DTaP and fourth dose of IPV in the routine series
 - (c) Kinrix
 - iii. The DTaP-HepB (hepatitis B) combination: Product is available outside the United States and provides good safety and antibody concentrations.
 - iv. The DTaP-HepB-Hib combination: The Hib antibody levels are lower than after separate administration.
 - v. The DTaP-HepB-IPV combination
 - (a) At least as immunogenic as individual components when administered at 2, 4, and 6 months
 - (b) Not indicated for infants younger than 6 weeks or children older than 7 years
 - (c) Pediarix
 - vi. The HepB-Hib combination
 - (a) Not indicated for infants younger than 6 weeks because of possible decreased immune response
 - (b) Comvax
 - vii. The Hib-DTaP-IPV combination
 - (a) Approved for use in children 6 weeks through 4 years of age
 - (b) Pentacel
 - viii. The HepA-HepB combination
 - (a) Approved for use in adults 18 years and older
 - (b) Twinrix
 - ix. The MMR vaccine and varicella combination
 - (a) Research from the Centers for Disease Control and Prevention and manufacturer indicated a higher incidence of febrile seizures in children 12–23 months of age who received the combination product compared with those who received the separate MMR and varicella vaccines.
 - (b) Since June 2009, ACIP has expressed a preference for separate MMR and varicella vaccines as the first dose given to children 12–47 months of age. The combination product may be used for the second dose at any age and for the first dose in children 48 months or older.
 - (c) ProQuad
 - x. Adding HepB to combination products may result in an extra dose being provided (e.g., monovalent HepB given at birth and then combination products at 2, 4, and 6 months); however, ACIP states that this is a safe practice.
 3. Interchangeability of products
 - a. ACIP recommends that the same product be used throughout the primary series; however, if the previous product's identity is not known or is no longer available, any product may be used.
 - b. For DTaP: The current standard of care is to use the same product for at least the first three doses of the five-dose series; however, if the product used previously is not known or is unavailable, any product may be used.
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- c. For Tdap: BOOSTRIX or ADACEL may be used for the booster dose, regardless of the manufacturer of the DTaP product administered during the primary immunization series.
 - d. For HepB: It is acceptable to use ENGERIX-B and RECOMBIVAX HB interchangeably.
 - e. For polio: Oral polio vaccine and inactivated poliovirus vaccine provide equivalent protection against paralytic poliomyelitis; however, because the only cases of polio in the United States since 1979 have been vaccine associated (i.e., from the live virus in oral polio vaccine), oral polio vaccine is no longer recommended.
 - f. For Hib: These products may be used interchangeably; however, if the regimen is completed using PedvaxHIB exclusively, only three doses are required; regimens using HibTITER or ActHIB require four doses.
 - g. For HPV: The products differ in the HPV types against which they provide protection. HPV4 (Gardasil) protects against types 6, 11, 16, and 18. HPV2 (Cervarix) protects against types 16 and 18. HPV types 6 and 11 are associated with genital warts; types 16 and 18 are associated with gynecologic, anal, and penile cancers.
- B. Barriers to Routine Immunization
- 1. Contraindications
 - a. Anaphylactic reaction to vaccine or any of its components
 - i. Inactivated poliovirus vaccine, MMR, and varicella contain neomycin.
 - ii. Influenza vaccine: Live attenuated influenza vaccine (LAIV) should be avoided in patients with severe egg allergy; inactivated influenza vaccine may be administered with close monitoring.
 - iii. Severe egg allergy is not considered a contraindication to MMR, which is grown in chick embryo tissue.
 - b. Acute moderate to severe febrile illness
 - c. Immunodeficiency: Oral polio vaccine, MMR, varicella
 - d. Pregnancy: MMR, varicella
 - e. Recent administration of immune globulin: MMR, varicella
 - i. Delay administration of vaccine product.
 - ii. Interval between immune globulin dose and administration of vaccine depends on indication for and dose of immune globulin.
 - f. Encephalopathy within 7 days after administration of a previous dose of DTaP
 - g. History of intussusception: rotavirus vaccine
 - 2. Misconceptions about contraindications (i.e., these are NOT contraindications)
 - a. Mild acute illness
 - b. Current antimicrobial therapy
 - c. Reaction to DTaP involving only soreness, redness, or swelling at the site
 - d. Pregnancy of the mother of the vaccine recipient
 - e. Breastfeeding
 - f. Allergies to antibiotics other than neomycin or streptomycin
 - g. Family history of an adverse effect after vaccine administration
 - 3. Other factors associated with underimmunization
 - a. Low socioeconomic status
 - b. Late start of vaccination series
 - c. Missed opportunities
 - i. Provider unaware that vaccination is due
 - ii. Failure to provide simultaneous vaccines
 - iii. Inappropriate contraindications (see previous discussion)

- d. Concern about potential adverse reactions
 - i. Autism: The association with MMR vaccine has not been proved.
 - ii. Guillain-Barré syndrome: The association with meningococcal conjugate vaccine has not been proved.
 - (a) 15 reported cases in adolescents after receiving meningococcal vaccine
 - (b) ACIP continues to recommend the routine use of meningococcal vaccine.
 - iii. Intussusception: An association with rotavirus vaccine led to the market withdrawal of RotaShield; two currently available products:
 - (a) Live, oral human-bovine reassortant rotavirus vaccine (RotaTeq, licensed in 2006)
 - (b) Live, attenuated human rotavirus vaccine (Rotarix, licensed in 2008)
 - (c) Neither product has been associated with intussusception.

Patient Case

9. The following patients are seeing their pediatrician today and are due for immunizations according to the routine schedule. For which patient would it be best to recommend deferring immunizations until later?
 - A. A 12-month-old boy who recently completed a cycle of chemotherapy for acute lymphocytic leukemia.
 - B. A 6-month-old girl receiving amoxicillin for otitis media.
 - C. A 12-month-old HIV-positive boy whose most recent CD4 count was greater than 1000.
 - D. A 12-year-old girl completing a prednisone “burst” (1 mg/kg/day for 5 days) for asthma exacerbation.

C. Considerations in Special Populations

1. Preterm infants
 - a. Immunize according to chronologic age.
 - b. Do not lower vaccine doses.
 - c. If birth weight is less than 2 kg, delay HepB vaccine because of reduced immune response until the patient is 30 days old or at hospital discharge if it occurs before 30 days of age (unless the mother is positive for HepB surface antigen).
2. Children who are immunocompromised
 - a. Should not receive live vaccines
 - b. Inactivated vaccines and immune globulins are appropriate.
 - c. Household contacts should not receive oral polio vaccine; however, MMR, influenza, varicella, and rotavirus vaccines are recommended.
3. Patients receiving corticosteroids
 - a. Live vaccines may be administered to patients receiving the following:
 - i. Topical corticosteroids
 - ii. Physiologic maintenance doses
 - iii. Low or moderate doses (less than 2 mg/kg/day of prednisone equivalent)
 - b. Live vaccines may be given immediately after discontinuation of high doses (2 mg/kg/day or more of prednisone equivalent) of systemic steroids given for less than 14 days.
 - c. Live vaccines should be delayed at least 1 month after discontinuing high doses (2 mg/kg/day or more of prednisone equivalent) of systemic steroids given for more than 14 days.
4. Patients with HIV infection
 - a. MMR should be administered unless patient is severely immunocompromised.
 - b. Varicella should be considered for asymptomatic or mildly symptomatic patients.
 - c. Inactivated vaccines should be administered routinely.

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16-18 yrs
Hepatitis B (HepB)	1 st dose	←.....2 nd dose.....→			←.....3 rd dose.....→											
Rotavirus ² (RV) RV1 (2-dose series); RV5 (3-dose series)		1 st dose	2 nd dose	See footnote 2												
Diphtheria, tetanus, & acellular pertussis ³ (DTaP; <7 yrs)		1 st dose	2 nd dose	3 rd dose			←.....4 th dose.....→					5 th dose				
Tetanus, diphtheria, & acellular pertussis ⁴ (Tdap; ≥7 yrs)													(Tdap)			
<i>Haemophilus influenzae</i> type b ⁵ (Hib)		1 st dose	2 nd dose	See footnote 5			←.....3 rd or 4 th dose.....→ See footnote 5									
Pneumococcal conjugate ⁶ (PCV13)		1 st dose	2 nd dose	3 rd dose			←.....4 th dose.....→									
Pneumococcal polysaccharide ⁶ (PPSV23)																
Inactivated poliovirus ⁷ (IPV; <18 yrs)		1 st dose	2 nd dose	3 rd dose			←.....4 th dose.....→									
Influenza ⁸ (IV; LAIV) 2 doses for some: See footnote 8							←.....3 rd dose.....→									
Measles, mumps, rubella ⁹ (MMR)						Annual vaccination (IV only) 1 or 2 doses						Annual vaccination (LAIV or IV) 1 or 2 doses		Annual vaccination (LAIV or IV) 1 dose only		
Varicella ¹⁰ (VAR)					See footnote 9		←.....1 st dose.....→					2 nd dose				
Hepatitis A ¹¹ (HepA)							←.....1 st dose.....→					2 nd dose				
Human papillomavirus ¹² (HPV2; females only; HPV4; males and females)							←.....2-dose series. See footnote 11.....→									
Meningococcal ¹³ (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)						See footnote 13										Booster

Range of recommended ages for catch-up immunization
 Range of recommended ages for certain high-risk groups
 Range of recommended ages during which catch-up is encouraged and for certain high-risk groups
 Not routinely recommended

This schedule includes recommendations in effect as of January 1, 2015. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at <http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Reporting System (VAERS) online (<http://www.vaers.hhs.gov>) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (<http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm>) or by telephone (800-CDC-INFO [800-232-4636]).

This schedule is approved by the Advisory Committee on Immunization Practices (<http://www.cdc.gov/vaccines/acip>), the American Academy of Pediatrics (<http://www.aap.org>), the American College of Obstetricians and Gynecologists (<http://www.acog.org>), and the American College of Family Physicians (<http://www.aafp.org>).

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Figure 2. Recommended immunization schedule for persons aged 0-18 years – 2015
 For those who fall behind or start late, see the catch-up schedule at <http://www.cdc.gov/vaccines/schedules/hcp/imz/catchup.html>

Footnotes — Recommended immunization schedule for persons aged 0 through 18 years—United States, 2015

For further guidance on the use of the vaccines mentioned below, see: <http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

For vaccine recommendations for persons 19 years of age and older, see the Adult Immunization Schedule.

Additional information

- For contraindications and precautions to use of a vaccine and for additional information regarding that vaccine, vaccination providers should consult the relevant ACIP statement available online at <http://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.
- For purposes of calculating intervals between doses, 4 weeks = 28 days. Intervals of 4 months or greater are determined by calendar months.
- Vaccine doses administered 4 days or less before the minimum interval are considered valid. Doses of any vaccine administered ≥ 5 days earlier than the minimum interval or minimum age should not be counted as valid doses and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval. For further details, see MMWR, General Recommendations on Immunization and Reports / Vol. 60 / No. 2; Table 1. Recommended and minimum ages and intervals between vaccine doses available online at <http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf>.
- Information on travel vaccine requirements and recommendations is available at <http://wwwnc.cdc.gov/travel/destinations/list>.
- For vaccination of persons with primary and secondary immunodeficiencies, see Table 13, "Vaccination of persons with primary and secondary immunodeficiencies," in General Recommendations on Immunization (ACIP), available at <http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf>; and American Academy of Pediatrics. "Immunization in Special Clinical Circumstances," in Pickering LK, Baker CJ, Kimberlin DW, Long SS eds. Red Book: 2012 report of the Committee on Infectious Diseases. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics.

1. Hepatitis B (HepB) vaccine. (Minimum age: birth)**Routine vaccination:****At birth:**

- Administer monovalent HepB vaccine to all newborns before hospital discharge.
- For infants born to hepatitis B surface antigen (HBsAg)-positive mothers, administer HepB vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. These infants should be tested for HBsAg and antibody to HBsAg (anti-HBs) 1 to 2 months after completion of the HepB series at age 9 through 18 months (preferably at the next well-child visit).
- If mother's HBsAg status is unknown, within 12 hours of birth administer HepB vaccine regardless of birth weight. For infants weighing less than 2,000 grams, administer HBIG in addition to HepB vaccine within 12 hours of birth. Determine mother's HBsAg status as soon as possible and, if mother is HBsAg-positive, also administer HBIG for infants weighing 2,000 grams or more as soon as possible, but no later than age 7 days.

Doses following the birth dose:

- The second dose should be administered at age 1 or 2 months. Monovalent HepB vaccine should be used for doses administered before age 6 weeks.
- Infants who did not receive a birth dose should receive 3 doses of a HepB-containing vaccine on a schedule of 0, 1 to 2 months, and 6 months starting as soon as feasible. See Figure 2.
- Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks), administer the third dose at least 8 weeks after the second dose AND at least 16 weeks after the first dose. The final (third or fourth) dose in the HepB vaccine series should be administered no earlier than age 24 weeks.
- Administration of a total of 4 doses of HepB vaccine is permitted when a combination vaccine containing HepB is administered after the birth dose.

Catch-up vaccination:

- Unvaccinated persons should complete a 3-dose series.
- A 2-dose series (doses separated by at least 4 months) of adult formulation Recombivax HB is licensed for use in children aged 11 through 15 years.
- For other catch-up guidance, see Figure 2.

2. Rotavirus (RV) vaccines.**(Minimum age: 6 weeks for both RV1 [Rotarix] and RV5 [RotaTeq])****Routine vaccination:**

Administer a series of RV vaccine to all infants as follows:

1. If Rotarix is used, administer a 2-dose series at 2 and 4 months of age.
2. If RotaTeq is used, administer a 3-dose series at ages 2, 4, and 6 months.
3. If any dose in the series was RotaTeq or vaccine product is unknown for any dose in the series, a total of 3 doses of RV vaccine should be administered.

Catch-up vaccination:

- The maximum age for the first dose in the series is 14 weeks, 6 days; vaccination should not be initiated for infants aged 15 weeks, 0 days or older.
- The maximum age for the final dose in the series is 8 months, 0 days.
- For other catch-up guidance, see Figure 2.

3. Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine. (Minimum age: 6 weeks. Exception: DTaP-IPV [Kinrix]: 4 years)**Routine vaccination:**

- Administer a 5-dose series of DTaP vaccine at ages 2, 4, 6, 15 through 18 months, and 4 through 6 years. The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose. However, the fourth dose of DTaP need not be repeated if it was administered at least 4 months after the third dose of DTaP.

Catch-up vaccination:

- The fifth dose of DTaP vaccine is not necessary if the fourth dose was administered at age 4 years or older.
- For other catch-up guidance, see Figure 2.

4. Tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccine. (Minimum age: 10 years for both Boostrix and Adacel)**Routine vaccination:**

- Administer 1 dose of Tdap vaccine to all adolescents aged 11 through 12 years.
- Tdap may be administered regardless of the interval since the last tetanus and diphtheria toxoid-containing vaccine.
- Administer 1 dose of Tdap vaccine to pregnant adolescents during each pregnancy (preferred during 27 through 36 weeks' gestation) regardless of time since prior Td or Tdap vaccination.

Catch-up vaccination:

- Persons aged 7 years and older who are not fully immunized with DTaP vaccine should receive Tdap vaccine as 1 dose (preferably the first) in the catch-up series; if additional doses are needed, use Td vaccine. For children 7 through 10 years who receive a dose of Tdap as part of the catch-up series, an adolescent Tdap vaccine dose at age 11 through 12 years should NOT be administered. Td should be administered instead 10 years after the Tdap dose.
- Persons aged 11 through 18 years who have not received Tdap vaccine should receive a dose followed by tetanus and diphtheria toxoid (Td) booster doses every 10 years thereafter.
- Inadvertent doses of DTaP vaccine:
 - If administered inadvertently to a child aged 7 through 10 years may count as part of the catch-up series. This dose may count as the adolescent Tdap dose, or the child can later receive a Tdap booster dose at age 11 through 12 years.
 - If administered inadvertently to an adolescent aged 11 through 18 years, the dose should be counted as the adolescent Tdap booster.
- For other catch-up guidance, see Figure 2.

5. Haemophilus influenzae type b (Hib) conjugate vaccine. (Minimum age: 6 weeks for PRP-T [ACTHIB, DTaP-IPV/Hib (Pentacel) and Hib-MenCY (MenHibrix)], PRP-OMP [PedvaxHIB or COMVAX], 12 months for PRP-T [Hiberix])**Routine vaccination:**

- Administer a 2- or 3-dose Hib vaccine primary series and a booster dose (dose 3 or 4 depending on vaccine used in primary series) at age 12 through 15 months to complete a full Hib vaccine series.
- The primary series with ActHIB, MenHibrix, or Pentacel consists of 3 doses and should be administered at 2, 4, and 6 months of age. The primary series with PedvaxHib or COMVAX consists of 2 doses and should be administered at 2 and 4 months of age; a dose at age 6 months is not indicated.
- One booster dose (dose 3 or 4 depending on vaccine used in primary series) of any Hib vaccine should be administered at age 12 through 15 months. An exception is Hiberix vaccine. Hiberix should only be used for the booster (final) dose in children aged 12 months through 4 years who have received at least 1 prior dose of Hib-containing vaccine.
- For recommendations on the use of MenHibrix in patients at increased risk for meningococcal disease, please refer to the meningococcal vaccine footnotes and also to MMWR February 28, 2014 / 63(RR01):1-13, available at <http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf>.

Catch-up vaccination:

- If dose 1 was administered at ages 12 through 14 months, administer a second (final) dose at least 8 weeks after dose 1, regardless of Hib vaccine used in the primary series.
- If both doses were PRP-OMP (PedvaxHIB or COMVAX), and were administered before the first birthday, the third (and final) dose should be administered at age 12 through 59 months and at least 8 weeks after the second dose.
- If the first dose was administered at age 7 through 11 months, administer the second dose at least 4 weeks later and a third (and final) dose at age 12 through 15 months or 8 weeks after second dose, whichever is later.

- If first dose is administered before the first birthday and second dose administered at younger than 15 months, a third (and final) dose should be given 8 weeks later.
- For unvaccinated children aged 15 months or older, administer only 1 dose.
- For other catch-up guidance, see Figure 2. For catch-up guidance related to MenHibrix, please see the meningococcal vaccine footnotes and also MMWR February 28, 2014 / 63(RR01);1-13, available at <http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf>.

Vaccination of persons with high-risk conditions:

- Children aged 12 through 59 months who are at increased risk for Hib disease, including chemotherapy recipients and those with anatomic or functional asplenia (including sickle cell disease), human immunodeficiency virus (HIV) infection, immunoglobulin deficiency, or early component complement deficiency, who have received either no doses or only 1 dose of Hib vaccine before 12 months of age, should receive 2 additional doses of Hib vaccine 8 weeks apart; children who received 2 or more doses of Hib vaccine before 12 months of age should receive 1 additional dose.
- For patients younger than 5 years of age undergoing chemotherapy or radiation treatment who received a Hib vaccine dose(s) within 14 days of starting therapy or during therapy, repeat the dose(s) at least 3 months following therapy completion.
- Recipients of hematopoietic stem cell transplant (HSCT) should be revaccinated with a 3-dose regimen of Hib vaccine starting 6 to 12 months after successful transplant, regardless of vaccination history; doses should be administered at least 4 weeks apart.
- A single dose of any Hib-containing vaccine should be administered to unimmunized* children and adolescents 15 months of age and older undergoing an elective splenectomy; if possible, vaccine should be administered at least 14 days before procedure.
- Hib vaccine is not routinely recommended for patients 5 years or older. However, 1 dose of Hib vaccine should be administered to unimmunized* persons aged 5 years or older who have anatomic or functional asplenia (including sickle cell disease) and unvaccinated persons 5 through 18 years of age with human immunodeficiency virus (HIV) infection.

* Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months of age are considered unimmunized.

6. Pneumococcal vaccines. (Minimum age: 6 weeks for PCV13, 2 years for PPSV23)

Routine vaccination with PCV13:

- Administer a 4-dose series of PCV13 vaccine at ages 2, 4, and 6 months and at age 12 through 15 months.
- For children aged 14 through 59 months who have received an age-appropriate series of 7-valent PCV (PCV7), administer a single supplemental dose of 13-valent PCV (PCV13).

Catch-up vaccination with PCV13:

- Administer 1 dose of PCV13 to all healthy children aged 24 through 59 months who are not completely vaccinated for their age.
- For other catch-up guidance, see Figure 2.

Vaccination of persons with high-risk conditions with PCV13 and PPSV23:

- All recommended PCV13 doses should be administered prior to PPSV23 vaccination if possible.
- For children 2 through 5 years of age with any of the following conditions: chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure); chronic lung disease (including asthma if treated with high-dose oral corticosteroid therapy); diabetes mellitus; cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease; solid organ transplantation; or congenital immunodeficiency:
 1. Administer 1 dose of PCV13 if any incomplete schedule of 3 doses of PCV (PCV7 and/or PCV13) were received previously.
 2. Administer 2 doses of PCV13 at least 8 weeks apart if unvaccinated or any incomplete schedule of fewer than 3 doses of PCV (PCV7 and/or PCV13) were received previously.
 3. Administer 1 supplemental dose of PCV13 if 4 doses of PCV7 or other age-appropriate complete PCV7 series was received previously.
 4. The minimum interval between doses of PCV (PCV7 or PCV13) is 8 weeks.
 5. For children with no history of PPSV23 vaccination, administer PPSV23 at least 8 weeks after the most recent dose of PCV13.
- For children aged 6 through 18 years who have cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease; generalized malignancy; solid organ transplantation; or multiple myeloma:

1. If neither PCV13 nor PPSV23 has been received previously, administer 1 dose of PCV13 now and 1 dose of PPSV23 at least 8 weeks later.
2. If PCV13 has been received previously but PPSV23 has not, administer 1 dose of PPSV23 at least 8 weeks after the most recent dose of PCV13.
3. If PPSV23 has been received but PCV13 has not, administer 1 dose of PCV13 at least 8 weeks after the most recent dose of PPSV23.

- For children aged 6 through 18 years with chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure), chronic lung disease (including asthma if treated with high-dose oral corticosteroid therapy), diabetes mellitus, alcoholism, or chronic liver disease, who have not received PPSV23, administer 1 dose of PPSV23. If PCV13 has been received previously, then PPSV23 should be administered at least 8 weeks after any prior PCV13 dose.

- A single revaccination with PPSV23 should be administered 5 years after the first dose to children with sickle cell disease or other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin's disease; generalized malignancy; solid organ transplantation; or multiple myeloma.

7. Inactivated poliovirus vaccine (IPV). (Minimum age: 6 weeks)

Routine vaccination:

- Administer a 4-dose series of IPV at ages 2, 4, 6 through 18 months, and 4 through 6 years. The final dose in the series should be administered on or after the fourth birthday and at least 6 months after the previous dose.

Catch-up vaccination:

- In the first 6 months of life, minimum age and minimum intervals are only recommended if the person is at risk of imminent exposure to circulating poliovirus (i.e., travel to a polio-endemic region or during an outbreak).
- If 4 or more doses are administered before age 4 years, an additional dose should be administered at age 4 through 6 years and at least 6 months after the previous dose.
- A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.
- If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered.
- Regardless of the child's current age, IPV is not routinely recommended for U.S. residents aged 18 years or older.
- For other catch-up guidance, see Figure 2.

8. Influenza vaccines. (Minimum age: 6 months

for inactivated influenza vaccine [IIV], 2 years for live, attenuated influenza vaccine [LAIV])

Routine vaccination:

- Administer influenza vaccine annually to all children beginning at age 6 months. For most healthy, nonpregnant persons aged 2 through 49 years, either LAIV or IIV may be used. However, LAIV should NOT be administered to some persons, including 1) persons who have experienced severe allergic reactions to LAIV, any of its components, or to a previous dose of any other influenza vaccine; 2) children 2 through 17 years receiving aspirin or aspirin-containing products; 3) persons who are allergic to eggs; 4) pregnant women; 5) immunosuppressed persons; 6) children 2 through 4 years of age with asthma or who had wheezing in the past 12 months; or 7) persons who have taken influenza antiviral medications in the previous 48 hours. For all other contraindications and precautions to use of LAIV, see MMWR August 15, 2014 / 63(32);691-697 [40 pages] available at <http://www.cdc.gov/mmwr/pdf/wk/mm6332.pdf>.

For children aged 6 months through 8 years:

- For the 2014-15 season, administer 2 doses (separated by at least 4 weeks) to children who are receiving influenza vaccine for the first time. Some children in this age group who have been vaccinated previously will also need 2 doses. For additional guidance, follow dosing guidelines in the 2014-15 ACIP influenza vaccine recommendations, MMWR August 15, 2014 / 63(32);691-697 [40 pages] available at <http://www.cdc.gov/mmwr/pdf/wk/mm6332.pdf>.
- For the 2015-16 season, follow dosing guidelines in the 2015 ACIP influenza vaccine recommendations.

For persons aged 9 years and older:

- Administer 1 dose.

9. Measles, mumps, and rubella (MMR) vaccine.

(Minimum age: 12 months for routine vaccination)

Routine vaccination:

- Administer a 2-dose series of MMR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 4 weeks have elapsed since the first dose.
- Administer 1 dose of MMR vaccine to infants aged 6 through 11 months before departure from the United States for international travel. These children should be revaccinated with 2 doses of MMR vaccine, the first at age 12 through 15 months (12 months if the child remains in an area where disease risk is high), and the second dose at least 4 weeks later.

- Administer 2 doses of MMR vaccine to children aged 12 months and older before departure from the United States for international travel. The first dose should be administered on or after age 12 months and the second dose at least 4 weeks later.

Catch-up vaccination:

- Ensure that all school-aged children and adolescents have had 2 doses of MMR vaccine; the minimum interval between the 2 doses is 4 weeks.

10. Varicella (VAR) vaccine. (Minimum age: 12 months)**Routine vaccination:**

- Administer a 2-dose series of VAR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 3 months have elapsed since the first dose. If the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid.

Catch-up vaccination:

- Ensure that all persons aged 7 through 18 years without evidence of immunity (see MMWR 2007 / 56 [No. RR-4], available at <http://www.cdc.gov/mmwr/pdf/rr/rr5604.pdf>) have 2 doses of varicella vaccine. For children aged 7 through 12 years, the recommended minimum interval between doses is 3 months (if the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid); for persons aged 13 years and older, the minimum interval between doses is 4 weeks.

11. Hepatitis A (HepA) vaccine.**(Minimum age: 12 months)****Routine vaccination:**

- Initiate the 2-dose HepA vaccine series at 12 through 23 months; separate the 2 doses by 6 to 18 months.
- Children who have received 1 dose of HepA vaccine before age 24 months should receive a second dose 6 to 18 months after the first dose.
- For any person aged 2 years and older who has not already received the HepA vaccine series, 2 doses of HepA vaccine separated by 6 to 18 months may be administered if immunity against hepatitis A virus infection is desired.

Catch-up vaccination:

- The minimum interval between the two doses is 6 months.

Special populations:

- Administer 2 doses of HepA vaccine at least 6 months apart to previously unvaccinated persons who live in areas where vaccination programs target older children, or who are at increased risk for infection. This includes persons traveling to or working in countries that have high or intermediate endemicity of infection; men having sex with men; users of injection and non-injection illicit drugs; persons who work with HAV-infected primates or with HAV in a research laboratory; persons with clotting-factor disorders; persons with chronic liver disease; and persons who anticipate close personal contact (e.g., household or regular babysitting) with an international adoptee during the first 60 days after arrival in the United States from a country with high or intermediate endemicity. The first dose should be administered as soon as the adoption is planned, ideally 2 or more weeks before the arrival of the adoptee.

12. Human papillomavirus (HPV) vaccines.**(Minimum age: 9 years for HPV2 [Cervarix] and HPV4 [Gardasil])****Routine vaccination:**

- Administer a 3-dose series of HPV vaccine on a schedule of 0, 1-2, and 6 months to all adolescents aged 11 through 12 years. Either HPV4 or HPV2 may be used for females, and only HPV4 may be used for males.
- The vaccine series may be started at age 9 years.
- Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks); administer the third dose 24 weeks after the first dose and 16 weeks after the second dose (minimum interval of 12 weeks).

Catch-up vaccination:

- Administer the vaccine series to females (either HPV2 or HPV4) and males (HPV4) at age 13 through 18 years if not previously vaccinated.
- Use recommended routine dosing intervals (see Routine vaccination above) for vaccine series catch-up.

13. Meningococcal conjugate vaccines.**(Minimum age: 6 weeks for Hib-MenCY [MenHibrix], 9 months for MenACWY-D [Menactra], 2 months for MenACWY-CRM [Menveo])****Routine vaccination:**

- Administer a single dose of Menactra or Menveo vaccine at age 11 through 12 years, with a booster dose at age 16 years.

- Adolescents aged 11 through 18 years with human immunodeficiency virus (HIV) infection should receive a 2-dose primary series of Menactra or Menveo with at least 8 weeks between doses.

- For children aged 2 months through 18 years with high-risk conditions, see below.

Catch-up vaccination:

- Administer Menactra or Menveo vaccine at age 13 through 18 years if not previously vaccinated.
- If the first dose is administered at age 13 through 15 years, a booster dose should be administered at age 16 through 18 years with a minimum interval of at least 8 weeks between doses.
- If the first dose is administered at age 16 years or older, a booster dose is not needed.
- For other catch-up guidance, see Figure 2.

Vaccination of persons with high-risk conditions and other persons at increased risk of disease:

- Children with anatomic or functional asplenia (including sickle cell disease):
 1. Menveo
 - o Children who initiate vaccination at 8 weeks through 6 months: Administer doses at 2, 4, 6, and 12 months of age.
 - o Unvaccinated children 7 through 23 months: Administer 2 doses, with the second dose at least 12 weeks after the first dose AND after the first birthday.
 - o Children 24 months and older who have not received a complete series: Administer 2 primary doses at least 8 weeks apart.
 2. MenHibrix
 - o Children 6 weeks through 18 months: Administer doses at 2, 4, 6, and 12 through 15 months of age.
 - o If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.
 3. Menactra
 - o Children 24 months and older who have not received a complete series: Administer 2 primary doses at least 8 weeks apart. If Menactra is administered to a child with asplenia (including sickle cell disease), do not administer Menactra until 2 years of age and at least 4 weeks after the completion of all PCV13 doses.
- Children with persistent complement component deficiency:
 1. Menveo
 - o Children who initiate vaccination at 8 weeks through 6 months: Administer doses at 2, 4, 6, and 12 months of age.
 - o Unvaccinated children 7 through 23 months: Administer 2 doses, with the second dose at least 12 weeks after the first dose AND after the first birthday.
 - o Children 24 months and older who have not received a complete series: Administer 2 primary doses at least 8 weeks apart.
 2. MenHibrix
 - o Children 6 weeks through 18 months: Administer doses at 2, 4, 6, and 12 through 15 months of age.
 - o If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.
 3. Menactra
 - o Children 9 through 23 months: Administer 2 primary doses at least 12 weeks apart.
 - o Children 24 months and older who have not received a complete series: Administer 2 primary doses at least 8 weeks apart.
- For children who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic, including countries in the African meningitis belt or the Hajj, administer an age-appropriate formulation and series of Menactra or Menveo for protection against serogroups A and W meningococcal disease. Prior receipt of MenHibrix is not sufficient for children traveling to the meningitis belt or the Hajj because it does not contain serogroups A or W.
- For children at risk during a community outbreak attributable to a vaccine serogroup, administer or complete an age- and formulation-appropriate series of MenHibrix, Menactra, or Menveo.
- For booster doses among persons with high-risk conditions, refer to MMWR 2013 / 62(RR02);1-22, available at <http://www.cdc.gov/mmwr/preview/mmwr.html/rr6202a1.htm>.

For other catch-up recommendations for these persons, and complete information on use of meningococcal vaccines, including guidance related to vaccination of persons at increased risk of infection, see MMWR March 22, 2013 / 62(RR02);1-22, available at <http://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf>.

V. PEDIATRIC SEIZURE DISORDERS

A. Treatment Options Based on Seizure Type

Table 6. Treatment Options Based on Seizure Type

Seizure Type	Drugs of Choice	Alternatives
Focal (formerly “partial”)	VPA, CBZ, PHT	PB, gabapentin, lamotrigine, tiagabine, topiramate, oxcarbazepine, zonisamide, levetiracetam, lacosamide
Generalized		
Tonic-clonic	VPA, CBZ, PHT	Lamotrigine, topiramate, zonisamide, levetiracetam
Myoclonic	VPA	Topiramate, zonisamide, levetiracetam
Absence	Ethosuximide, VPA	Lamotrigine, zonisamide, levetiracetam
Lennox-Gastaut	VPA, topiramate, lamotrigine	Rufinamide, clobazam, felbamate, zonisamide
Infantile spasms	ACTH	Vigabatrin, lamotrigine, tiagabine, topiramate, VPA, zonisamide

ACTH = adrenocorticotropic hormone; CBZ = carbamazepine; PB = phenobarbital; PHT = phenytoin; VPA = valproic acid.

B. Comparison of Available Antiepileptic Drugs

Table 7. Comparison of Available Antiepileptic Drugs

Drug	Adverse Effects	Pharmacokinetic Considerations	Other Comments
Carbamazepine	Rash Hyponatremia ↓ Bone density Teratogenic	Autoinduction ↓ Effectiveness of OCs	Significant drug interactions
Clobazam	Somnolence	Dose adjustment required in hepatic impairment Dose adjustment required in CYP2C19 poor metabolizers	
Felbamate	Anorexia, nausea, weight loss Insomnia, somnolence Aplastic anemia Hepatic failure	Clearance ~50:50 renal/hepatic	Significant drug interactions Aplastic anemia: Adults > children Requires signed informed consent
Gabapentin	Somnolence Weight gain	↑ Clearance in children <6 years Dose adjustment required in renal insufficiency Nonlinear pharmacokinetics	Minimal drug interactions Minimal cognitive effects May worsen Lennox-Gastaut
Lacosamide	Prolonged PR interval Dizziness Headache Diplopia	Dose adjustment required in severe renal insufficiency	Use with caution if severe cardiac disease or conduction problems No clinically significant drug interactions
Lamotrigine	Rash Stevens-Johnson syndrome	Autoinduction	Rash: Children > adults Minimal cognitive effects

Table 7. Comparison of Available Antiepileptic Drugs (*continued*)

Drug	Adverse Effects	Pharmacokinetic Considerations	Other Comments
Levetiracetam	Headache Somnolence	Linear pharmacokinetics Renal excretion Clearance 40% ↑ in children No effect on CYP system	Minimal drug interactions
Oxcarbazepine	Hyponatremia (>CBZ) Rash (<CBZ)	Linear pharmacokinetics Clearance 40% ↑ in children <6 years Induces CYP3A4 Inhibits CYP2C19	Hyponatremia more common in adults than in children Minimal cognitive effects
Phenobarbital	Cognitive dysfunction Sedation Rash ↓ Bone density	Linear pharmacokinetics ↓ Effectiveness of OCs	Significant drug interactions
Phenytoin	Rash Gingival hyperplasia Hirsutism ↓ Bone density Teratogenic	Nonlinear pharmacokinetics ↓ Effectiveness of OCs	Significant drug interactions
Rufinamide	Somnolence Rash QT interval shortening	↑ Level with concurrent VPA	Somnolence: Minimized with slow dose titration Rash: All reported cases are in children
Tiagabine	Dizziness Nonconvulsive status epilepticus (case reports)	Clearance 50% ↑ in children	Minimal cognitive effects
Topiramate	Cognitive dysfunction Weight loss Glaucoma Oligohidrosis	↑ Clearance in children Dose adjustment required in renal insufficiency	Weight loss more common in obese patients Children at higher risk of oligohidrosis than adults
Valproic acid	Weight gain Menstrual irregularities Polycystic ovarian syndrome Hyperandrogenism Hepatotoxicity Teratogenic Thrombocytopenia	CYP induction > in children	Significant drug interactions Most cases of hepatotoxicity in children <2 years
Vigabatrin	Vision loss Weight gain		Available only through restricted distribution program
Zonisamide	Weight loss Rash Oligohidrosis Somnolence Agitation Hallucinations	Linear pharmacokinetics Primarily renal excretion No effect on CYP system	Better tolerated by children than by adults

CBZ = carbamazepine; CYP = cytochrome P450; OC = oral contraceptive; PHT = phenytoin; VPA = valproic acid.

Patient Case

10. A 14-year-old moderately obese girl comes to the clinic with an erythematous pruritic rash. She was initiated on oxcarbazepine about 3 weeks ago for the management of partial seizures. Her medical history is significant only for seizures. She recently became sexually active with a male and admits inconsistent contraceptive use. Which intervention is best for her?
- Change to carbamazepine.
 - Change to levetiracetam.
 - Change to valproic acid.
 - No change in therapy is necessary.

VI. ATTENTION-DEFICIT/HYPERACTIVITY DISORDER**A. Clinical Presentation**

- Diagnostic and Statistical Manual for Mental Disorders (DSM-V)* criteria
 - Either (i) or (ii):
 - Six or more of the following symptoms of inattention have been present for at least 6 months to a point that is disruptive and inappropriate:

Inattention

 - Often does not give close attention to detail/makes careless mistakes
 - Often has trouble keeping attention on tasks/activities
 - Often does not seem to listen
 - Often does not follow instructions
 - Often has trouble organizing activities
 - Often avoids or dislikes things that require long periods of mental effort
 - Often loses things needed for tasks or activities
 - Often is easily distracted
 - Often is forgetful
 - Six or more of the following symptoms of hyperactivity-impulsivity have been present for at least 6 months to a point that is disruptive and inappropriate:

Hyperactivity

 - Often fidgets or squirms
 - Often is unable to remain seated when it is expected
 - Often runs or climbs when and where it is not appropriate
 - Often has difficulty with quiet play or activities
 - Often is “on the go”
 - Often talks excessively

Impulsivity

 - Often blurts out answers
 - Often has difficulty waiting one’s turn
 - Often interrupts
 - Some symptoms were present before 7 years of age.
 - Some impairment from the symptoms is present in two or more settings.
 - Clear evidence of significant impairment exists in social, school, or work functioning.
 - No other mental disorder better describes the symptoms.
- Comorbid disease states: 44%–87% of children with ADHD have at least one other disorder:
 - Oppositional defiant disorder

- i. Most common comorbid disorder in adolescents
- ii. Presence of ADHD increases the odds of oppositional defiant disorder almost 11-fold.
- b. Anxiety disorder: May exist in about 25% of children with ADHD
- c. Tics
 - i. 21%–90% of children with Tourette syndrome may also have ADHD.
 - ii. May not be exacerbated by stimulant agents, as once thought

Patient Case

11. A 9-year-old boy has a new diagnosis of ADHD. At school, he is disruptive, talks when the teacher is talking, and runs around the classroom. His parents report extreme difficulty in getting him to do his homework after school. Which is best for his initial drug therapy?
- A. Methylphenidate (OROS) (Concerta) given once daily.
 - B. Methylphenidate immediate release (Ritalin) given twice daily, with doses administered 4 hours apart.
 - C. Guanfacine given at bedtime.
 - D. D-Methylphenidate (Focalin) given twice daily, with doses administered 4 hours apart.

- B. Classification: Based on *DSM-V* Criteria (see previous section)
 - 1. ADHD, Combined Type: Criteria (i) and (ii) both are met.
 - 2. ADHD, Predominantly Inattentive Type: Criterion (i) is met, but (ii) is not met.
 - 3. ADHD, Predominantly Hyperactive-Impulsive Type: Criterion (ii) is met, but (i) is not met.
- C. Treatment Options: Combination of pharmacotherapy and behavioral therapy is more beneficial than either intervention alone.
 - 1. Factors affecting choice of pharmacologic agent
 - a. Desired length of coverage time for symptoms
 - i. Consider time of day when symptoms occur.
 - ii. Consider time of day when child's activities occur (e.g., when is homework done, at what time are teenagers driving, when is child's bedtime).
 - b. Child's ability to swallow pills or capsules
 - c. Concomitant disease states (e.g., tic disorders)
 - d. Adverse effect profile
 - e. Concerns about abuse or diversion potential
 - i. Children with ADHD are more likely to have a concurrent substance use disorder than those without ADHD.
 - ii. Treatment with stimulant medication may reduce the risk of developing a substance use disorder.
 - iii. Children treated with stimulants at a younger age are less likely to misuse or abuse substances than those in whom treatment is delayed.
 - f. Expense
 - 2. Available pharmacologic agents
 - a. Stimulant medications: Some children with ADHD respond better to one stimulant type than another; therefore, both methylphenidate- and amphetamine-containing products should be tried before stimulant treatment is deemed a failure.
 - i. Methylphenidate-containing products
 - (a) Ramp effect: behavioral effects are proportional to the rate of methylphenidate absorption into the central nervous system.

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- (b) See Table 8 for a comparison of available products.
 - (c) Adverse effects and precautions
 - (1) Headache, stomachache, loss of appetite, and insomnia
 - (2) Use with caution in patients with glaucoma, tics, psychosis, and concomitant monoamine oxidase inhibitor use.
 - (3) Insomnia, anorexia, and tics occur more often with transdermal patch, also mild skin reactions.
 - ii. Amphetamine-containing products
 - (a) See Table 8 for a comparison of available products.
 - (b) Adverse effects and precautions
 - (1) Loss of appetite, insomnia, abdominal pain, and nervousness
 - (2) May exacerbate preexisting hypertension and tic disorders
 - (3) Labeling change warns of potential association with sudden cardiac death (SCD); therefore, not recommended for patients with known structural heart defects.
 - iii. Potential association with SCD
 - (a) No established evidence of causative relationship between stimulants and SCD
 - (b) The frequency of SCD is no higher in children taking stimulants than in the general pediatric population.
 - (c) The AAP recommends targeted cardiac history and careful physical examination before initiating stimulant therapy.
 - (1) Routine electrocardiography is not recommended unless history and physical examination suggest cardiac disease.
 - (2) For otherwise healthy children, stimulant therapy should not be withheld because of the inability to obtain an electrocardiogram or assessment by a pediatric cardiologist.
 - b. Nonstimulant medications
 - i. Norepinephrine reuptake inhibitors (see Table 9)
 - (a) Adverse effects: Dyspepsia, decreased appetite, weight loss, and fatigue
 - (b) Labeling change warns of potential for severe liver injury, although routine monitoring of hepatic function is not required.
 - (c) Black box warning about increased risk of suicidal ideation in children and adolescents
 - (d) Does not exacerbate tics
 - ii. α -Adrenergic receptor agonists: See Table 9 for a comparison of available products.
 - iii. Antidepressants: Non-FDA label approved for the treatment of ADHD
 - (a) Noradrenergic antidepressant (e.g., bupropion [Wellbutrin])
 - (1) May use immediate- or extended-release product given in two or three doses
 - (2) Contraindicated for children with active seizure disorder
 - (b) Tricyclic antidepressants (e.g., imipramine, nortriptyline)
 - (1) Baseline electrocardiogram is recommended before therapy initiation and after each dose increase.
 - (2) Desipramine should be used with extreme caution because of reports of sudden death.

Table 8. Stimulant Agents for the Treatment of ADHD

Methylphenidate-Containing Products				
Medication	Doses per Day	Onset of Effect	Duration of Effect (hours)	Other Comments
Methylphenidate immediate release (Ritalin)	2 or 3	20–60 minutes	3–5	50:50 racemic mixture of L-threo and D-threo isomers
Dexmethylphenidate (Focalin)	2 or 3	20–60 minutes	3–5	Only D-threo isomer, thought to be pharmacologically active enantiomer D-Threo isomer has not been shown to hinder effectiveness or increase adverse effects Recommended doses are half those of methylphenidate immediate release Offers no proven pharmacoeconomic benefit over methylphenidate immediate-release products
Methylphenidate sustained release (Ritalin SR)	1 or 2	1–3 hours	2–6	
Methylphenidate extended release (Ritalin LA)	1	20–60 minutes	6–8	Contains 50% immediate-release and 50% extended-release beads Capsule may be opened and sprinkled on applesauce Efficacy may wane in after-school or late-afternoon hours, necessitating addition of methylphenidate immediate release for later-day coverage
Methylphenidate modified release (Metadate CD)	1	20–60 minutes	6–8	Capsule contains 30% immediate-release and 70% extended-release beads (slowly released about 4 hours after ingestion) Capsule may be opened and sprinkled on applesauce Efficacy may wane in after-school or late-afternoon hours, necessitating addition of methylphenidate immediate release for later-day coverage
Methylphenidate extended release (Methylin ER)	1	20–60 minutes	8	
Dexmethylphenidate extended release (Focalin XR)	1	20–60 minutes	8–12	Bimodal drug release results in peak serum concentrations at 1½ and 6½ hours after dose administration Shorter duration of action than methylphenidate OROS, so afternoon symptom control is not as good
Methylphenidate OROS (Concerta)	1	20–60 minutes	12	Outer capsule contains ~22% of the drug, allowing immediate release; tablet core contains remainder of drug, which is released over 10 hours, minimizing peak to trough fluctuations Swallow whole; do NOT chew, crush, or divide

Table 8. Stimulant Agents for the Treatment of ADHD (*continued*)

Methylphenidate-Containing Products				
Medication	Doses per Day	Onset of Effect	Duration of Effect (hours)	Other Comments
Methylphenidate transdermal system (Daytrana)	1	60 minutes	11–12	Apply to hip 2 hours before effect is needed Recommended to remove 9 hours after application, may be worn up to 16 hours Duration of effect is ~3 hours after patch removal May be worn while swimming or exercising
Amphetamine-Containing Products				
Medication	Doses per Day	Onset of Effect	Duration of Effect (hours)	Other Comments
Mixed amphetamine salts immediate release (Adderall)	1 or 2	20–60 minutes	6	
Mixed amphetamine salts extended release (Adderall XR)	1	20–60 minutes	10	Contains 50% immediate-release and 50% extended-release beads (released 4 hours after ingestion) May be sprinkled on applesauce
Lisdexamfetamine dimesylate (Vyvanse)	1	60 minutes	10–12	Prodrug with D-amphetamine covalently bound to L-lysine Designed for less abuse potential than amphetamine No clinical evidence of superiority over other amphetamine products

Table 9. Nonstimulant Agents for the Treatment of ADHD

Norepinephrine Reuptake Inhibitor				
Medication	Doses per Day	Onset of Effect (weeks)	Duration of Effect (hours)	Other Comments
Atomoxetine (Strattera)	1 or 2	1–2	10–12	May be considered first-line therapy for children with active substance abuse problem, comorbid anxiety, or tics Metabolized through cytochrome P450 2D6
α-Adrenergic Receptor Agonists				
Clonidine extended release (Kapvay)	1 or 2	1–2	10–12	May be more effective for hyperactivity than for inattention symptoms Lessens severity of tics, especially when used in combination with methylphenidate Primary adverse effect is sedation
Guanfacine extended release (Intuniv)	1	1–2	10–12	Improves comorbid tic disorder Less sedating than clonidine Abrupt discontinuation may cause rebound hypertension

Patient Case

12. The patient in question 11 has been doing well in school since methylphenidate (OROS) (Concerta) was initiated 6 months ago. His late-afternoon symptoms are well controlled; however, he has had insomnia since drug therapy initiation. Which is the best modification to his treatment regimen?
- A. Administer the Concerta dose later in the day.
 - B. Change to methylphenidate modified release (Metadate CD) once a day.
 - C. Change to methylphenidate transdermal patch (Daytrana).
 - D. Change to atomoxetine at bedtime.

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ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. Answer: B

Group B *Streptococcus*, *Escherichia coli*, *Klebsiella* spp., and *Listeria* are the most likely pathogens of neonatal sepsis or meningitis. Ampicillin plus gentamicin administered in meningitic doses would provide reasonable empiric coverage. Although coagulase-negative *Staphylococcus* is the most likely cause of nosocomial neonatal sepsis, this patient's early presentation makes a hospital-acquired pathogen extremely unlikely. Therefore, vancomycin is unnecessary. Ampicillin plus ceftriaxone would provide adequate empiric antimicrobial coverage for the most likely pathogens. However, ceftriaxone use can result in biliary sludging, leading to reduced elimination of bilirubin and a potential risk of kernicterus in neonates. Ceftazidime plus gentamicin lacks coverage for *Listeria* and group B *Streptococcus*, which is still necessary empirically even though the mother received penicillin before delivery. In addition, empiric double-coverage of gram-negative organisms is not necessary for early neonatal sepsis.

2. Answer: C

Given this patient's age and culture results, the most likely infecting organism is *E. coli* or *Klebsiella* spp. (gram-negative rods), for which antimicrobial prophylaxis is not indicated. The most common pathogens causing meningitis in neonates do not warrant antimicrobial prophylaxis. If this patient had been older and infected with *N. meningitidis* or *H. influenzae*, antibiotic prophylaxis with rifampin would have been indicated for all close contacts, regardless of age or immunization status. Rifampin prophylaxis to eliminate nasal carriage is also indicated for people who receive index diagnoses of *N. meningitidis* and treatment with an antibiotic other than ceftriaxone.

3. Answer: C

The most likely causative organisms of sepsis or meningitis in this age group are *S. pneumoniae* and *N. meningitidis*. Therefore, a regimen of ceftriaxone plus vancomycin would provide appropriate empiric coverage. Depending on the regional incidence of resistant *S. pneumoniae*, empiric vancomycin may not be necessary. Ampicillin plus gentamicin would not provide adequate coverage. Cefuroxime does not provide

reliable penetration into the cerebrospinal fluid, so it would not be appropriate empiric coverage because this patient's presentation suggests he has meningitis. Rifampin would be the drug of choice for the prophylaxis of close contacts if this patient receives a diagnosis of meningococcal meningitis; however, it is inadequate for treatment.

4. Answer: B

Palivizumab is the drug of choice for prophylaxis against RSV infection in high-risk patient populations, including those born before 29 weeks' gestation, regardless of risk factors, who are 12 months or younger during RSV season. Patients born between 29 weeks' gestation and 32 weeks' gestation are no longer considered high risk based solely on their gestational age. To be considered as candidates for palivizumab prophylaxis, these infants must have a disease state (e.g., chronic lung disease, hemodynamically significant heart disease, airway anomalies, neuromuscular disease, or profound immunodeficiency) that puts them at risk for severe RSV infection. Other potential risk factors (e.g., siblings younger than 5 years or day care attenders) are no longer considered when determining the appropriateness of palivizumab prophylaxis. Patients with complex heart defects requiring surgical repair are at high risk of developing severe RSV infections; however, after the repair is complete, palivizumab is no longer warranted. Patients with a history of chronic lung disease who are 24 months or younger and who are receiving, or have received in the past 6 months, oxygen or medical management for chronic lung disease are also at risk of severe RSV infection.

5. Answer: D

There is no specific treatment of RSV infection. Intravenous fluids, oxygen, and mechanical ventilation, if needed, are indicated. Palivizumab is the drug of choice for RSV prophylaxis, but it has no role in treatment. Corticosteroids have not been shown to be of benefit and are therefore not indicated. Secondary bacterial infection with *H. influenzae* or *M. catarrhalis* may occur; however, empiric antibiotic therapy is not indicated.

6. Answer: A

Persistence of middle ear fluid after an episode of AOM is common. If these findings are not associated with signs and symptoms of infection, a diagnosis of OME is made. The AAP practice guideline for the management of OME recommends watchful waiting. A watch-and-wait approach would not be appropriate for this patient if she were given a diagnosis of AOM rather than OME because she is younger than 6 months. Spontaneous resolution of OME occurs within 3 months in 75%–90% of cases after AOM without residual morbidities. Children at high risk of speech and learning problems (e.g., craniofacial anomalies, Down syndrome, severe visual impairment) may require earlier, more aggressive intervention (e.g., tympanostomy tubes). Decongestants and antihistamines do not promote resolution or improve symptoms. Antibiotics are not effective in treating OME. However, high-dose amoxicillin (80–100 mg/kg/day) is considered first-line therapy for AOM, so if this patient's treatment with the initial course of lower-dose amoxicillin fails (which is not a recommended regimen) or if she develops new signs of infection, then high-dose amoxicillin will be an appropriate treatment choice. Up to 74% of streptococcal strains have been reported to be resistant to azithromycin, which also has poor activity against *H. influenzae*, so this would not be the best antibiotic option if an infection developed.

7. Answer: C

Four cases of otitis media in 12 months is considered recurrent otitis media, for which the watch-and-wait approach is not recommended. Previously, this patient would have been a candidate for antibiotic prophylaxis; however, this practice has fallen out of favor because of the significant risk of antimicrobial resistance compared with the minor reduction in the occurrence of otitis media. Tympanostomy tubes are typically reserved for patients in whom aggressive antibiotic therapy fails and may be effective only in otitis with bulging tympanic membrane. In addition, the greatest benefit of tympanostomy tubes may be in patients with persistent OMEs resulting in significant hearing loss. As long as this patient continues to respond to high-dose amoxicillin, this will be considered a first-line regimen. In addition, the pneumococcal and influenza vaccines should be administered according to the recommended schedule because these organisms are common causes of AOM.

8. Answer: D

Vaccines are often deferred for inappropriate reasons, leading to missed opportunities for immunization. Previous administration of IVIG can decrease the efficacy of live vaccines such as MMR and varicella, but it does not affect the efficacy of inactivated products. The suggested interval between an IVIG dose and the administration of live vaccines depends on the immune globulin product and indication. Concerns about an association between MMR vaccine and the development of autism and immunizations overwhelming the immune system have been disproved by scientific evaluation. The MMR vaccine is grown in chick embryo tissue; however, an egg allergy is not a contraindication to its administration.

9. Answer: A

Immunocompromised patients should not receive live vaccines; therefore, the MMR and varicella vaccines should be deferred in these patients. Mild cold-like symptoms, or administration of antibiotics for mild illnesses such as otitis media, are not a contraindication to vaccination, and deferring immunizations for such reasons is considered a missed opportunity. Patients with HIV, especially those with asymptomatic disease, should be considered candidates for all age-appropriate vaccines, including those containing live virus and the pneumococcal vaccine. Corticosteroid administration is an indication for deferral of live vaccines only if the patient is receiving high doses (more than 2 mg/kg/day of prednisone equivalent) for more than 14 days.

10. Answer: B

Rash associated with antiepileptic drugs is a common adverse effect and generally resolves within a few days after discontinuation. There is no reliable method to determine whether the rash will remain benign or progress to a more severe skin reaction, so discontinuation of the offending drug is warranted. Carbamazepine has a higher incidence of rash than oxcarbazepine, and cross-reactivity has been noted. Valproic acid is a good choice for managing partial seizures and has a low incidence of rash. However, the principal adverse effects of valproic acid include weight gain and menstrual irregularities, both of which would be undesirable in this overweight teenage girl. In addition, valproic acid is a known teratogen (pregnancy category D) that should be avoided if other options are available in females of

reproductive age who are unreliable in their use of contraception. Levetiracetam (pregnancy category C) has a low incidence of rash and minimal drug interactions.

11. Answer: A

Stimulants, especially methylphenidate, are generally considered first-line therapy for treating ADHD. Because this patient shows symptoms at school and at home, the short duration of action (about 6–8 hours) of a twice-daily methylphenidate immediate-release regimen will probably not provide adequate symptom relief. Likewise, D-methylphenidate has a short duration of action. In addition, D-methylphenidate is no more effective and has no fewer adverse effects than methylphenidate immediate release. Therefore, D-methylphenidate is generally not considered cost-beneficial. Extended-release guanfacine was recently FDA label approved for the treatment of ADHD, but it should be reserved for patients with ADHD and tic disorders or those who have not responded to stimulant agents. Methylphenidate (OROS) with its longer duration of action (10–12 hours) would provide the best coverage. Therapy with this drug may be initiated without previous titration using methylphenidate immediate release.

12. Answer: C

Changing to a methylphenidate transdermal patch allows flexibility in the duration of drug effect. Wearing the patch for 9 hours results in about 12 hours of therapeutic effect; however, the patch may be removed sooner, thus reducing the duration of effect and allowing serum concentrations to decrease before bedtime. Response rates to atomoxetine are lower than to methylphenidate (OROS) in children with ADHD. In addition, the onset of therapeutic effect for atomoxetine is delayed (typically 2–4 weeks). Atomoxetine does not have the adverse effect of insomnia. Rather, fatigue and drowsiness are more common, the tolerability of which is improved with the initiation of atomoxetine at low doses with a gradual titration. The dose may also be administered in the evening to improve tolerability. Because this patient responded well to stimulant therapy with methylphenidate and there are disadvantages to atomoxetine (i.e., lower response rates and delayed onset), it would be best to manage the adverse effect of insomnia by altering the stimulant regimen. Administering methylphenidate OROS later in the day

would probably worsen the insomnia. A better recommendation would be to administer methylphenidate OROS earlier in the morning, which would allow more time in the late afternoon and evening for the serum concentration to decrease before bedtime. Changing to a shorter-acting methylphenidate product (e.g., methylphenidate CD or LA) might improve the insomnia, but because of its shorter duration of action, it might compromise late-afternoon symptom control.

ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: B

The pathogens most likely to cause pediatric sepsis or meningitis are *S. pneumoniae*, *N. meningitidis*, and *H. influenzae*. *P. aeruginosa* is more commonly associated with nosocomial sepsis. Adolescents who develop an RSV infection typically present with mild upper respiratory tract symptoms, whereas this patient's presentation suggests meningitis.

2. Answer: B

Before the 2014 publication of the AAP's updated guidelines, infants who were born before 31 weeks' gestation who were 6 months or younger at the beginning of RSV season were considered at high risk of severe infection; therefore, routine palivizumab prophylaxis was recommended based solely on their prematurity. The 2014 guidelines changed the prematurity-based criteria for routine palivizumab prophylaxis to include only infants born before 29 weeks' gestation who are younger than 12 months at the beginning of RSV season. According to the new guidelines, infants born between 29 weeks' and 32 weeks' gestation must have chronic lung disease, hemodynamically significant congenital heart disease, airway anomalies, neuromuscular disease, or profound immunocompromise to be considered candidates for palivizumab prophylaxis. Risk factors such as day care attendance and school-aged siblings are no longer considered when determining whether prophylaxis is warranted. Routine prophylaxis for otherwise healthy, full-term neonates is not recommended because evidence of benefit is lacking.

3. Answer: C

Prophylaxis with rifampin is recommended for close contacts of patients with *N. meningitidis* or *H. influenzae*, regardless of their immunization status. Postexposure prophylaxis against pneumococcal meningitis is not recommended.

4. Answer: D

All scheduled immunizations should be given during the same visit. Delaying some vaccines until a later date is considered a missed opportunity. Oral polio vaccine is no longer recommended as part of the routine schedule because of the risk of vaccine-associated poliomyelitis,

which accounts for most newly diagnosed cases in the United States since 1979. Premature neonates should be vaccinated according to chronologic age, and doses should not be reduced. As of 2008, influenza vaccine is recommended for all children 6 months to 18 years of age during influenza season.

5. Answer: B

Otitis media is most commonly caused by *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, and viruses. Blood culture results do not predict causative organisms of otitis media. If the patient is older than 2 years and does not have severe symptoms (i.e., moderate to severe otalgia or temperature of 39°C or greater), delaying the decision to prescribe antibiotics is an acceptable strategy. If otalgia or fever persists for more than 48–72 hours, then antibiotic therapy is acceptable, but if these symptoms resolve spontaneously within this time, antibiotics are not necessary. If antibiotics are warranted and the patient does not have an allergy, high-dose amoxicillin is the treatment of choice rather than azithromycin. Broad-spectrum antibiotics such as ceftriaxone should be reserved for resistant cases.

6. Answer: D

In general, patients who do not respond to one stimulant agent should be treated with a different stimulant before they are considered not to have responded to this class of drug therapy. However, switching from a methylphenidate-containing stimulant to extended-release mixed amphetamine salts (a different stimulant) should be avoided in this patient because amphetamine-containing products have been associated with SCD in children with structural heart defects. The methylphenidate transdermal system has a duration of action and efficacy similar to those of methylphenidate OROS; therefore, it is unlikely to benefit this patient because her therapy with methylphenidate immediate release and methylphenidate OROS has already failed. If adherence or difficulty swallowing pills were a suspected cause of treatment failure in this patient, a patch might be a reasonable alternative. Clonidine may be added as an adjunctive therapy for patients whose treatment with a single stimulant agent fails; however, it should not be used as the sole agent for treating ADHD. Atomoxetine, a nonstimulant, would be a

reasonable alternative to the stimulant class of agents in this patient because some patients respond better to one class of agent than another.

7. Answer: A

Valproic acid is considered a first-line therapy for treating absence seizures. If the patient is having breakthrough seizures on ethosuximide—also a first-line therapy—and the dose has been maximized, it is reasonable to switch to valproic acid. Phenytoin, phenobarbital, and gabapentin have not been shown effective in treating absence seizures.

8. Answer: C

	Adverse Event (loss of appetite)	
	Yes	No
Exposure (stimulant)		
Yes	7 (<i>a</i>)	193 (<i>b</i>)
No	1 (<i>c</i>)	197 (<i>d</i>)

$$\begin{aligned} \text{Odds ratio} &= (a/c)/(b/d) \\ &= (7/1)/(193/197) \\ &= 7.15 \end{aligned}$$

9. Answer: C

A case series does not reliably establish a causal relationship but rather suggests a potential hypothesis to be further studied. Given the current knowledge about the potential risk of kernicterus related to ceftriaxone use, obtaining investigational review board approval for a randomized controlled or a crossover trial design would be difficult, given ethical considerations, although this study design is the gold standard for establishing a causal relationship. Therefore, a retrospective cohort would be best to investigate a causal relationship in this instance.

10. Answer: D

Patients with congenital heart defects, particularly those with hemodynamically significant lesions, are at high risk of severe RSV infection regardless of their gestational age. These patients are considered to be at high risk if they are younger than 12 months at the beginning of RSV season and have not undergone definitive surgical repair of their heart defect. It is not recommended that palivizumab be initiated as routine prophylaxis in hospitalized patients because it does not reduce

the incidence of nosocomial-acquired RSV infection. However, patients currently receiving a course of palivizumab (one dose per month for 5 months) at the time of hospital admission should have that intervention continued. In addition, cardiopulmonary bypass reduces palivizumab serum concentrations; therefore, patients undergoing congenital heart defect repair during RSV season should receive a postoperative dose of palivizumab as soon as they are medically stable, regardless of when their next scheduled dose is due.