

1132 Part XV ◆ Allergic Disorders

Table 149-1 Symptoms and Signs of Anaphylaxis in Infants

ANAPHYLAXIS SYMPTOMS THAT INFANTS CANNOT DESCRIBE	ANAPHYLAXIS SIGNS THAT MAY BE DIFFICULT TO INTERPRET/UNHELPFUL IN INFANTS, AND WHY	ANAPHYLAXIS SIGNS IN INFANTS
GENERAL Feeling of warmth, weakness, anxiety, apprehension, impending doom	Nonspecific behavioral changes such as persistent crying, fussing, irritability, fright, suddenly becoming quiet	
SKIN/MUCUS MEMBRANES Itching of lips, tongue, palate, uvula, ears, throat, nose, eyes, etc.; mouth-tingling or metallic taste	Flushing (may also occur with fever, hyperthermia, or crying spells)	Rapid onset of hives (potentially difficult to discern in infants with acute atopic dermatitis; scratching and excoriations will be absent in young infants); angioedema (face, tongue, oropharynx)
RESPIRATORY Nasal congestion, throat tightness; chest tightness; shortness of breath	Hoarseness, dysphonia (common after a crying spell); drooling or increased secretions (common in infants)	Rapid onset of coughing, choking, stridor, wheezing, dyspnea, apnea, cyanosis
GASTROINTESTINAL Dysphagia, nausea, abdominal pain/cramping	Spitting up/regurgitation (common after feeds), loose stools (normal in infants, especially if breastfed); colicky abdominal pain	Sudden, profuse vomiting
CARDIOVASCULAR Feeling faint, presyncope, dizziness, confusion, blurred vision, difficulty in hearing	Hypotension (need appropriate-size blood pressure cuff; low systolic blood pressure for children is defined as <70 mm Hg from 1 mo to 1 yr, and less than $(70 \text{ mm Hg} + [2 \times \text{age in yr}])$ from 1-10 yr; tachycardia, defined as >140 beats/min from 3 mo to 2 yr, inclusive; loss of bowel and bladder control (ubiquitous in infants))	Weak pulse, arrhythmia, diaphoresis/sweating, collapse/unconsciousness
CENTRAL NERVOUS SYSTEM Headache	Drowsiness, somnolence (common in infants after feeds)	Rapid onset of unresponsiveness, lethargy, or hypotonia; seizures

Adapted from Simons FER. Anaphylaxis in infants: can recognition and management be improved? *J Allergy Clin Immunol* 120:537–540, 2007.

Table 149-2 Anaphylaxis Triggers in the Community*

ALLERGEN TRIGGERS (IgE-DEPENDENT IMMUNOLOGIC MECHANISM)*
Foods (e.g., peanut, tree nuts, shellfish, fish, milk, egg, wheat, soy, sesame, meat [galactose- α -1,3-galactose])
Food additives (e.g., spices, colorants, vegetable gums, and contaminants)
Stinging insects: Hymenoptera species (e.g., bees, yellow jackets, wasps, hornets, and fire ants)
Medications (e.g., β -lactam antibiotics, ibuprofen)
Biologic agents (e.g., monoclonal antibodies [infliximab, omalizumab] and allergens [challenge tests, specific immunotherapy])
Natural rubber latex
Vaccines
Inhalants (rare) (e.g., horse or hamster dander, grass pollen)
Previously unrecognized allergens (foods, venoms, biting insect saliva, medications, biologic agents)
OTHER IMMUNE MECHANISMS (IGE INDEPENDENT)
IgG mediated (infliximab, high-molecular-weight dextrans)
Immune aggregates (IVIG)
Drugs (aspirin, NSAID, opiates, contrast material, ethylene oxide/dialysis tubing)
Complement activation
Physical factors (e.g., exercise [†] , cold, heat, sunlight/ultraviolet radiation)
Ethanol
Idiopathic*

*In the pediatric population, some anaphylaxis triggers, such as hormones (progesterone), seminal fluid, and occupational allergens, are uncommon, as is idiopathic anaphylaxis.

[†]Exercise with or without a cotrigger, such as a food or medication, cold air, or cold water.

IVIG, intravenous immunoglobulin; NSAID, nonsteroidal antiinflammatory drug.

Adapted from Leung DYM, Sampson HA, Geha RS, et al: Pediatric allergy principles and practice, New York, 2010, Elsevier, p. 652.

Table 149-3 Patient Risk Factors for Anaphylaxis**AGE-RELATED FACTORS**

Infants: anaphylaxis can be hard to recognize, especially if the first episode; patients cannot describe symptoms
 Adolescents and young adults: increased risk taking behaviors such as failure to avoid known triggers and to carry an epinephrine autoinjector consistently
 Pregnancy: risk of iatrogenic anaphylaxis—for example, from β lactam antibiotics to prevent neonatal group B streptococcal infection, agents used perioperatively during caesarean sections, and natural rubber latex
 Older people: increased risk of death because of concomitant disease and drugs

CONCOMITANT DISEASES

Asthma and other chronic respiratory diseases
 Cardiovascular diseases
 Mastocytosis
 Allergic rhinitis and eczema*
 Depression, cognitive dysfunction, substance misuse

DRUGS

β -Adrenergic blockers[†]
 Angiotensin-converting enzyme (ACE) inhibitors[†]
 Sedatives, antidepressants, narcotics, recreational drugs, and alcohol may decrease the patient's ability to recognize triggers and symptoms

COFACTORS THAT AMPLIFY ANAPHYLAXIS

Exercise: anaphylaxis associated with exercise may be food dependent or food independent; nonsteroidal antiinflammatory drugs and other listed cofactors may also be relevant
 Acute infection such as an upper respiratory tract infection
 Fever
 Emotional stress
 Disruption of routine—for example, travel and jet lag
 Premenstrual status in women and girls

*Atopic diseases are a risk factor for anaphylaxis triggered by food, latex, and exercise, but not for anaphylaxis triggered by most drugs or by insect stings

[†]Patients taking β -adrenergic blockers or ACE inhibitors seem to be at increased risk for severe anaphylaxis. In addition, those taking β -adrenergic blockers may not respond optimally to epinephrine treatment and may need glucagon, a polypeptide with non-catecholamine-dependent inotropic and chronotropic cardiac effects, atropine for persistent bradycardia, or ipratropium for persistent bronchospasm.

Table 149-4 Diagnosis of Anaphylaxis

Anaphylaxis is highly likely when any 1 of the following 3 criteria is fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin and/or mucosal tissue (e.g., generalized hives, pruritus or flushing, swollen lips/tongue/uvula)
AND AT LEAST 1 OF THE FOLLOWING:
 - a. Respiratory compromise (e.g., dyspnea, wheeze/bronchospasm, stridor, reduced peak PEF, hypoxemia)
 - b. Reduced BP or associated symptoms of end-organ dysfunction (e.g., hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a *likely* allergen for that patient (minutes to several hours):
 - a. Involvement of the skin/mucosal tissue (e.g., generalized hives, itch/flush, swollen lips/tongue/uvula)
 - b. Respiratory compromise (e.g., dyspnea, wheeze/bronchospasm, stridor, reduced PEF, hypoxemia)
 - c. Reduced BP or associated symptoms (e.g., hypotonia [collapse], syncope, incontinence)
 - d. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)
3. Reduced BP following exposure to *known* allergen for that patient (minutes to several hours):
 - a. Infants and children: low systolic BP (age-specific) or >30% drop in systolic BP
 - b. Adults: systolic BP <90 mm Hg or >30% drop from patient's baseline

Table 160-2 Classification of Raynaud Phenomenon

Isolated Raynaud phenomenon

Occupational Raynaud phenomenon:

Cold injury
 Vibrating tools
 Polyvinyl chloride exposure

Secondary Raynaud phenomenon:

Systemic sclerosis
 Mixed connective tissue disease
 Sjögren syndrome
 Systemic lupus erythematosus
 Polymyositis/dermatomyositis
 Rheumatoid arthritis
 Arteritis
 Antiphospholipid antibody syndrome
 Primary biliary cirrhosis
 Carpal tunnel syndrome
 Cryoglobulinemia
 Leukemia
 Vasospastic disorders (migraine, Prinzmetal angina)

Infection:

Hepatitis B and C (cryoglobulinemia)
 Cytomegalovirus (?)

Obstructive vascular disease:

Thromboangiitis obliterans
 Thoracic outlet syndrome (cervical rib)

Metabolic syndrome:

Hypothyroid
 Carcinoid syndrome

Drug-induced:

Antimigraine medications
 β -Blocker
 Bleomycin
 Interferons
 Ergotamine derivatives

1134 Part XV ◆ Allergic Disorders

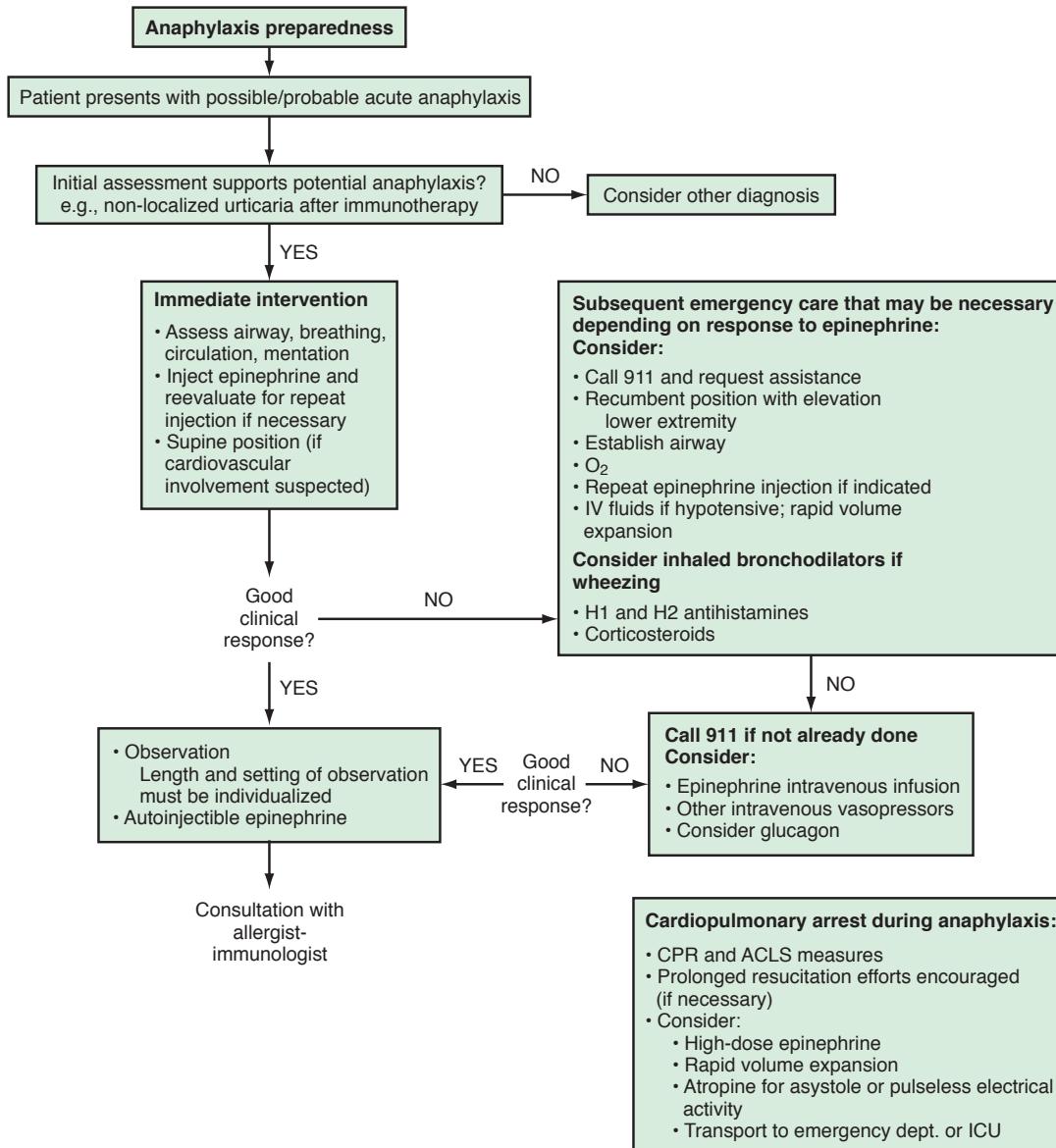


Figure 149-1 Algorithm for the treatment of anaphylactic event in the outpatient setting. IV, Intravenous. (From Lieberman P, Nicklas RA, Oppenheimer J, et al: The diagnosis and management of anaphylaxis practice parameter: 2010 update, *J Allergy Clin Immunol* 126:477-480 e471-442, 2010 [Fig. E2].)

Table 149-5 Management of a Patient with Anaphylaxis

TREATMENT	MECHANISM(S) OF EFFECT	DOSAGE(S)	COMMENTS; ADVERSE REACTIONS
PATIENT EMERGENCY MANAGEMENT (DEPENDENT ON SEVERITY OF SYMPTOMS)			
Epinephrine (adrenaline)	α_1 , β_1 , β_2 adrenergic effects	0.01 mg/kg up to 0.5 mg IM in lateral thigh Weight 8-25 kg: Adrenaclick, Auvi-Q, EpiPen Jr (0.15 mg) IM Weight >25 kg: Adrenaclick, Auvi-Q, EpiPen (0.3 mg) IM	Tachycardia, hypertension, nervousness, headache, nausea, irritability, and tremor
Cetirizine (liquid)	Antihistamine (competitive of H ₁ receptor)	Cetirizine liquid-5 mg/5 mL 0.25 mg/kg up to 10 mg PO	Hypotension, tachycardia, and somnolence
Alt: diphenhydramine	Antihistamine (competitive of H ₁ receptor)	1.25 mg/kg up to 50 mg PO or IM	Hypotension, tachycardia, somnolence, and paradoxical excitement
Transport to an Emergency Facility			
EMERGENCY PERSONNEL MANAGEMENT (DEPENDENT ON SEVERITY OF SYMPTOMS)			
Epinephrine (adrenaline)	α_1 , β_1 , β_2 adrenergic effects	0.01 mg/kg up to 0.5 mg IM in lateral thigh Epinephrine autoinjector: 0.15 mg for 8-25kg, 0.3 mg for >25 kg 0.01 mL/kg/dose of 1:1,000 solution up to 0.5 mL IM May repeat every 10-15 min For severe hypotension: 0.01 mL/kg/dose of 1:10,000 slow IV push	Tachycardia, hypertension, nervousness, headache, nausea, irritability, and tremor
Supplemental oxygen and airway management			
Volume expanders			
Crystalloids (normal saline or Ringer lactate)		30 mL/kg in 1st hr	Rate titrated against blood pressure response If tolerated, place patient supine with legs raised
Colloids (hydroxyethyl starch)		10 mL/kg rapidly followed by slow infusion	Rate titrated against blood pressure response If tolerated, place patient supine with legs raised
Antihistamines			
Cetirizine (liquid)	Antihistamine (competitive of H ₁ receptor)	Cetirizine liquid-5 mg/5 mL 0.25 mg/kg up to 10 mg PO	Hypotension, tachycardia, and somnolence
Alt: diphenhydramine	Antihistamine (competitive of H ₁ receptor)	1.25 mg/kg up to 50 mg PO, IM, or IV	Hypotension, tachycardia, somnolence, and paradoxical excitement
Ranitidine	Antihistamine (competitive of H ₂ receptor)	1 mg/kg up to 50 mg IV Should be administered slowly	Headache, mental confusion
Alt: cimetidine	Antihistamine (competitive of H ₂ receptor)	4 mg/kg up to 200 mg IV Should be administered slowly	Headache, mental confusion
Corticosteroids			
Methylprednisolone	Antiinflammatory	Solu-Medrol (IV) 1-2 mg/kg up to 125 mg IV Depo-Medrol (IM) 1 mg/kg up to 80 mg IM	Hypertension, edema, nervousness, and agitation
Prednisone	Antiinflammatory	1 mg/kg up to 75 mg PO	Hypertension, edema, nervousness, and agitation
Nebulized albuterol	β -Agonist	(0.83 mg/mL [3 mL]) via mask with O ₂	Palpitations, nervousness, central nervous system stimulation, tachycardia; use to supplement epinephrine when bronchospasm appears unresponsive; may repeat
POSTEMERGENCY MANAGEMENT			
Antihistamine		Cetirizine (5-10 mg qd) or loratadine (5-10 mg qd) for 3 days	
Corticosteroids		Optional: Oral prednisone (1 mg/kg up to 75 mg) daily for 3 days	
Preventive treatment			
Prescription for epinephrine autoinjector and antihistamine			
Provide written plan outlining patient emergency management (may download form from http://www.foodallergy.org)			
Follow-up evaluation to determine/confirm etiology			
Immunotherapy for insect sting allergy			
Patient education			
Instruction on avoidance of causative agent			
Information on recognizing early signs of anaphylaxis			
Stress early treatment of allergic symptoms to avoid systemic anaphylaxis			
Encourage wearing medical identification jewelry			

IM, intramuscularly; IV, intravenously; PO, by mouth.

1138 Part XV ◆ Allergic Disorders

Table 151-1 Adverse Food Reactions

FOOD INTOLERANCE (NON-IMMUNE SYSTEM-MEDIATED, NONTOXIC, NONINFECTIOUS)	
Host factors	
Enzyme deficiencies—lactase (primary or secondary), sucrase/isomaltase, hereditary fructose intolerance, galactosemia	
Gastrointestinal disorders—inflammatory bowel disease, irritable bowel syndrome, pseudoobstruction, colic	
Idiosyncratic reactions—caffeine in soft drinks ("hyperactivity")	
Psychologic—food phobias, obsessive-compulsive disorder	
Migraines (rare)	
Food factors (toxic or infectious or pharmacologic)	
Infectious organisms— <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Clostridium perfringens</i> , <i>Shigella</i> , botulism, <i>Salmonella</i> , <i>Yersinia</i> , <i>Campylobacter</i>	
Toxins—histamine (scombroid poisoning), saxitoxin (shellfish)	
Pharmacologic agents—caffeine, theobromine (chocolate, tea), tryptamine (tomatoes), tyramine (cheese), benzoic acid in citrus fruits (perioral flare)	
Contaminants—heavy metals, pesticides, antibiotics	
FOOD ALLERGY	
IgE-mediated	
Cutaneous—urticaria, angioedema, morbilliform rashes, flushing, contact urticaria	
Gastrointestinal—oral allergy syndrome, gastrointestinal anaphylaxis	
Respiratory—acute rhinoconjunctivitis, bronchospasm	
Generalized—anaphylactic shock, exercise induced anaphylaxis	
Mixed IgE and non-IgE-mediated	
Cutaneous—atopic dermatitis, contact dermatitis	
Gastrointestinal—allergic eosinophilic esophagitis and gastroenteritis	
Respiratory—asthma	
Non-IgE-mediated	
Cutaneous—contact dermatitis, dermatitis herpetiformis (celiac disease)	
Gastrointestinal—food protein-induced enterocolitis, proctocolitis, and enteropathy syndromes, celiac disease, food protein induced enteropathy	
Respiratory—food-induced pulmonary hemosiderosis (Heiner syndrome)	
Unclassified	

IgE, immunoglobulin E.

Table 151-2 Differential Diagnosis of Adverse Food Reactions

GASTROINTESTINAL DISORDERS (WITH VOMITING AND/OR DIARRHEA)	
Structural abnormalities (pyloric stenosis, Hirschsprung disease, reflux)	
Enzyme deficiencies (primary or secondary):	
Disaccharidase deficiency—lactase, fructase, sucrase-isomaltase	
Galactosemia	
Malignancy with obstruction	
Other: pancreatic insufficiency (cystic fibrosis), peptic disease	
CONTAMINANTS AND ADDITIVES	
Flavorings and preservatives—rarely cause symptoms:	
Sodium metabisulfite, monosodium glutamate, nitrates	
Dyes and colorings—very rarely cause symptoms (urticaria, eczema): Tartrazine	
Toxins:	
Bacterial, fungal (aflatoxin), fish-related (scombroid, ciguatera)	
Infectious organisms:	
Bacteria (<i>Salmonella</i> , <i>Escherichia coli</i> , <i>Shigella</i>)	
Virus (rotavirus, enterovirus)	
Parasites (<i>Giardia</i> , <i>Akis simplex</i> [in fish])	
Accidental contaminants:	
Heavy metals, pesticides	
Pharmacologic agents:	
Caffeine, glycosidal alkaloid solanine (potato spuds), histamine (fish), serotonin (banana, tomato), tryptamine (tomato), tyramine (cheese)	
PSYCHOLOGIC REACTIONS	
Food phobias	

Table 151-3 Natural History of Food Allergy and Cross-Reactivity Between Common Food Allergies

FOOD	USUAL AGE AT ONSET OF ALLERGY	CROSS REACTIVITY	USUAL AGE AT RESOLUTION
Hen's egg white	0-1 yr	Other avian eggs	7 yr (75% of cases resolve)*
Cow's milk	0-1 yr	Goat's milk, sheep's milk, buffalo milk	5 yr (76% of cases resolve)*
Peanuts	1-2 yr	Other legumes, peas, lentils; coreactivity with tree nuts	Persistent (20% of cases resolve)
Tree nuts	1-2 yr; in adults, onset occurs after cross reactivity to birch pollen	Other tree nuts; coreactivity with peanuts	Persistent (9% of cases resolve)
Fish	Late childhood and adulthood	Other fish (low cross-reactivity with tuna and swordfish)	Persistent†
Shellfish	Adulthood (in 60% of patients with this allergy)	Other shellfish	Persistent
Wheat*	6-24 mo	Other grains containing gluten (rye, barley)	5 yr (80% of cases resolve)
Soybeans*	6-24 mo	Other legumes	2 yr (67% of cases resolve)
Kiwi	Any age	Banana, avocado, latex	Unknown
Apples, carrots, and peaches§	Late childhood and adulthood	Birch pollen, other fruits, nuts	Unknown

*Recent studies suggest that resolution may occur at a later age, especially in children with multiple food allergies and lifetime peak food-specific IgE >50 kU/L.

†Fish allergy that is acquired in childhood can resolve.

§Allergy to fresh apples, carrots, and peaches (oral allergy syndrome) is commonly caused by heat-labile proteins. Fresh fruit causes oral pruritus, but cooked fruit is tolerated. There is generally no risk of anaphylaxis, although in rare cases, allergies to cross-reactive lipid transfer protein can cause anaphylaxis after ingestion of fruits (e.g., peach) and vegetables.

Modified from Lack G: Food allergy, N Engl J Med 359:1252-1260, 2008, Table 1.

Table 151-4 Prevention of Food Allergy	
Exclusive breast feeding for 4-6 mo	
Introduce solid (complementary) foods after 4-6 mo of exclusive breast feeding	
Introduce low-risk complementary foods 1 at a time	
Introduce potentially highly allergenic foods (fish, eggs, peanut products, milk, wheat) soon after the lower-risk foods (no need to avoid or delay)	
Don't avoid allergenic foods during pregnancy or nursing	
Soy-based formulas do not prevent allergic disease	

Table 154-1 Multidisciplinary Treatment of Rheumatic Diseases in Childhood	
Accurate diagnosis and education of family	Pediatric rheumatologist Pediatrician Nurse: <ul style="list-style-type: none">• Disease-related education• Medication administration (injection teaching)• Safety monitoring Social worker: <ul style="list-style-type: none">• Facilitation of school services• Resource identification (community, government, financial, advocacy groups, vocational rehabilitation)
Physical medicine and rehabilitation	Physical therapy: <ul style="list-style-type: none">• Addressing deficits in joint or muscle mobility, limb length discrepancies, gait abnormalities, weakness Occupational therapy: <ul style="list-style-type: none">• Splinting to reduce joint contractures/deformities and lessen stress on joints; adaptive devices for activities of daily living
Consultant team	Ophthalmology: <ul style="list-style-type: none">• Eye screening for uveitis (see Table 155-4)• Screening for medication-related ocular toxicity (hydroxychloroquine, glucocorticoids) Nephrology Orthopedics Dermatology Gastroenterology
Physical and psychosocial growth and development	Nutrition: <ul style="list-style-type: none">• Addressing undernourishment from systemic illness, obesity/overnourishment from glucocorticoids School integration: <ul style="list-style-type: none">• Individualized Educational Plan (IEP) or 504 plan Peer group relationships Individual and/or family counseling
Coordination of care	Involvement of patient and family as active team members Communication among healthcare providers Involvement of school (school nurse) and community (social worker) resources

Table 151-5 Symptoms of Food-Induced Allergic Reactions		
TARGET ORGAN	IMMEDIATE SYMPTOMS	DELAYED SYMPTOMS
Cutaneous	Erythema Pruritus Urticaria Morbilloform eruption Angioedema	Erythema Flushing Pruritus Morbilloform eruption Angioedema Eczematous rash
Ocular	Pruritus Conjunctival erythema Tearing Periorbital edema	Pruritus Conjunctival erythema Tearing Periorbital edema
Upper respiratory	Nasal congestion Pruritus Rhinorrhea Sneezing Laryngeal edema Hoarseness Dry staccato cough	
Lower respiratory	Cough Chest tightness Dyspnea Wheezing Intercostal retractions Accessory muscle use	Cough, dyspnea, and wheezing
GI (oral)	Angioedema of the lips, tongue, or palate Oral pruritus Tongue swelling	
GI (lower)	Nausea Colicky abdominal pain Reflux Vomiting Diarrhea	Nausea Abdominal pain Reflux Vomiting Diarrhea Hematochezia Irritability and food refusal with weight loss (young children)
Cardiovascular	Tachycardia (occasionally bradycardia in anaphylaxis) Hypotension Dizziness Fainting Loss of consciousness	
Miscellaneous	Uterine contractions Sense of "impending doom"	

Note: This table is presented as Table IV in the Guidelines.

GI, gastrointestinal.

From Boyce JA, Assaad A, Burks AW, et al: Guideline for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel, J Allergy Clin Immunol 126(6):S1-S58, 2010 (Table IV, p. S19).

Table 151-8 ACIP and AAP Red Book Recommendations for Administering Vaccines to Patients with Egg Allergy		
VACCINE	ACIP	AAP RED BOOK
MMR/MMRV	May be used	May be used
Influenza	Receive with some precautions*	Receive with some precautions*
Rabies	Use caution	No specific recommendation
Yellow fever	Contraindicated, but desensitization protocols may be followed to administer vaccine if necessary (citing PI)	Contraindicated, but desensitization protocols may be followed to administer vaccine if necessary (citing PI)

AAP, American Academy of Pediatrics; ACIP, Advisory Committee on Immunization Practices.

From Boyce JA, Assaad A, Burks AW, et al: Guideline for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel, J Allergy Clin Immunol 126(6):S1-S58, 2010 (Table V, p S31).

*In 2012, recommendations changed to suggest those with mild egg allergy receive the inactivated influenza vaccine in the primary care setting with a 30 minute observation and preparedness to treat anaphylaxis. Those with severe egg allergy are referred to an allergist.

1140 Part XV ◆ Allergic Disorders

Table 151-6 | Food Protein-Induced Gastrointestinal Syndromes

	FPIES	PROCTOCOLITIS	ENTEROPATHY	EOSINOPHILIC GASTROENTEROPATHIES*
Age at onset	1 day–1 year	1 day–6 months	Dependent of age of exposure to antigen, cow's milk and soy up to 2 yr	Infant to adolescent
Food proteins implicated				
Most common	Cow's milk, soy	Cow's milk, soy	Cow's milk, soy	Cow's milk, soy, egg white, wheat, peanut
Less common	Rice, chicken, turkey, fish, pea	Egg, corn, chocolate	Wheat, egg	Meats, corn, rice, fruits, vegetables, fish
Multiple food hypersensitivities	>50% both cow's milk and soy	40% both cow's milk and soy	Rare	Common
Feeding at the time of onset	Formula	>50% exclusive breast feeding	Formula	Formula
Atopic background				
Family history of atopy	40-70%	25%	Unknown	~50% (often history of eosinophilic esophagitis)
Personal history of atopy	30%	22%	22%	~50%
Symptoms				
Emesis	Prominent	No	Intermittent	Intermittent
Diarrhea	Severe	No	Moderate	Moderate
Bloody stools	Severe	Moderate	Rare	Moderate
Edema	Acute, severe	No	Moderate	Moderate
Shock	15%	No	No	No
Failure to thrive	Moderate	No	Moderate	Moderate
Laboratory findings				
Anemia	Moderate	Mild	Moderate	Mild-moderate
Hypoalbuminemia	Acute	Rare	Moderate	Mild-severe
Methemoglobinemia	May be present	No	No	No
Allergy evaluation				
Food prick skin test	Negative [†]	Negative	Negative	Positive in ~50%
Serum food allergen IgE	Negative [†]	Negative	Negative	Positive in ~50%
Total IgE	Normal	Negative	Normal	Normal to elevated
Peripheral blood eosinophilia	No	Occasional	No	Present in <50%
Biopsy findings				
Colitis	Prominent	Focal	No	May be present
Lymph nodular hyperplasia	No	Common	No	Yes
Eosinophils	Prominent	Prominent	Few	Prominent; also neutrophilic infiltrates, papillary elongation and basal zone hyperplasia
Food challenge	Vomiting in 2-4 hr; diarrhea in 5-8 hr	Rectal bleeding in 6-72 hr	Vomiting, diarrhea, or both in 40-72 hr	Vomiting and diarrhea in hours to days
Treatment	Protein elimination, 80% respond to casein hydrolysate and symptoms clear in 3-10 days; rechallenge in 1.5-2 yr	Protein elimination, symptoms clear in 3 days with casein hydrolysate, resume/continue breastfeeding on maternal antigen-restricted diet	Protein elimination, symptoms clear in 1-3 wk, rechallenge and biopsy in 1-2 yr	Protein elimination, good response to casein hydrolysate, excellent response to elemental diet, symptoms clear within 2-3 wk, excellent acute response to steroids; rechallenge and biopsy in 1-2 yr
Natural history	Cow's milk: 60% resolved by 2 yr Soy: 25% resolved by 2 yr	Resolved by 9-12 months	Most cases resolve in 2-3 yr	Typically a prolonged, relapsing course
Reintroduction of the food	Inpatient food challenge	At home, gradually advancing from 1 oz to full feedings over 2 weeks	Home, gradually advancing	Home, gradually advancing

*Eosinophilic gastroenteropathies encompass esophagitis, gastritis, gastroenterocolitis.

[†]If positive, may be a risk factor for persistent disease.

FPIES, food protein-induced enterocolitis syndrome.

From Nowak-Wegrzyn A, Muraro A: Food protein-induced enterocolitis syndrome. Curr Opin Allergy Immunol 9:371-377, 2009 (Table 1, p. 372).

1142 Part XV ◆ Allergic Disorders

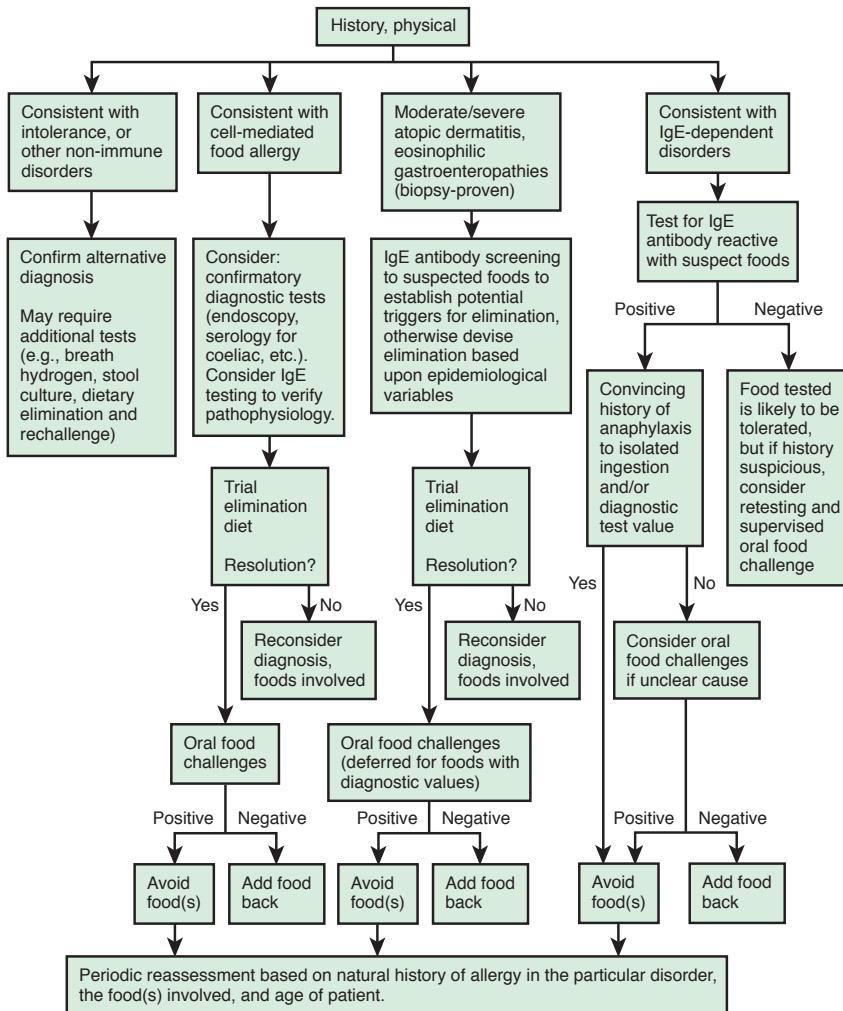


Figure 151-1 General scheme for diagnosis of food allergy. (From Sicherer SH: Food allergy, Lancet 360:701–710, 2002.)

Table 151-7 Clinical Implications of Cross-Reactive Proteins in IgE-Mediated Allergy

FOOD FAMILY	RISK OF ALLERGY TO ≥1 MEMBER (%; APPROXIMATE)	FEATURE(S)
Legumes	5	Main causes of reactions are peanut, soybean, lentil, lupine, and garbanzo (chickpea)
Tree nuts (e.g., almond, cashew, hazelnut, walnut, brazil)	35	Reactions are often severe
Fish	50	Reactions can be severe
Shellfish	75	Reactions can be severe
Grains	20	
Mammalian milks	90	Cow's milk is highly cross reactive with goat's or sheep's milk (92%) but not with mare's milk (4%)
Rosaceae (pitted fruits)	55	Risk of reactions to more than three related foods is very low (<10%), symptoms are usually mild (oral allergy syndrome)
Latex-food	35	For individuals allergic to latex, banana, kiwi, fig, chestnut, and avocado are the main causes of reactions
Food-latex	11	Individuals allergic to banana, kiwi, fig, chestnut, and avocado may be at an increased risk of reactions to latex

Modified from Sicherer SH: Food allergy, Lancet 360:701–710, 2002.

Rheumatic Diseases of Childhood

Table 153-1 Symptoms Suggestive of Rheumatic Disease

SYMPTOM	RHEUMATIC DISEASE(S)	POSSIBLE NONRHEUMATIC DISEASES CAUSING SIMILAR SYMPTOMS
Fevers	Systemic JIA, SLE, vasculitis, acute rheumatic fever, sarcoidosis, MCTD	Malignancies, infections and post-infectious syndromes, inflammatory bowel disease, periodic fever (autoinflammatory) syndromes, Kawasaki disease, HSP
Arthralgias	JIA, SLE, rheumatic fever, JDM, vasculitis, scleroderma, sarcoidosis	Hypothyroidism, trauma, endocarditis, other infections, pain syndromes, growing pains, malignancies, overuse syndromes
Weakness	JDM, myositis secondary to SLE, MCTD, and deep localized scleroderma	Muscular dystrophies, metabolic and other myopathies, hypothyroidism
Chest pain	Juvenile rheumatoid arthritis, SLE (with associated pericarditis or costochondritis)	Costochondritis (isolated), rib fracture, viral pericarditis, panic attack, hyperventilation
Back pain	Enthesitis related arthritis, juvenile ankylosing spondylitis	Vertebral compression fracture, diskitis, intraspinal tumor, spondylolisthesis, bone marrow-occupying malignancy, pain syndromes, osteomyelitis, muscle spasm, injury
Fatigue	SLE, JDM, MCTD, vasculitis, JIA	Pain syndromes, chronic infections, chronic fatigue syndrome, depression

HSP, Henoch-Schönlein purpura; JDM, juvenile dermatomyositis; JIA, juvenile idiopathic arthritis; MCTD, mixed connective tissue disease; SLE, systemic lupus erythematosus.

Table 153-2 Signs Suggestive of Rheumatic Disease

SIGN	RHEUMATIC DISEASES	COMMENTS	NONRHEUMATIC CAUSES
Malar rash	SLE, JDM	SLE classically spares nasolabial folds	Sunburn, parvovirus B19 (fifth disease), Kawasaki disease
Oral ulcers	SLE, Behçet disease	Behçet disease also associated with genital ulcers	HSV infection, PFAPA syndrome
Purpuric rash	Vasculitis, e.g., ANCA-associated vasculitis, HSP	HSP typically starts as small lesions on lower extremities and buttocks that coalesce	Meningococcemia, thrombocytopenia, clotting disorders
Gottron papules	JDM	Look for associated heliotrope rash, periungual telangiectasias	Psoriasis, eczema
Arthritis	Juvenile idiopathic arthritis, SLE, vasculitis, HSP, MCTD, scleroderma, acute rheumatic fever, reactive arthritis	Chronic joint swelling (>6 wk) required for diagnosis of chronic arthritis of childhood; MCTD associated with diffuse puffiness of hands	Postviral arthritis, reactive arthritis, trauma, infection, Lyme disease, Kawasaki disease, malignancy, overuse syndromes

ANCA, antineutrophil cytoplasmic antibody; HSP, Henoch-Schönlein purpura; HSV, herpes simplex virus; JDM, juvenile dermatomyositis; MCTD, mixed connective tissue disease; PFAPA, periodic fever, aphthous stomatitis, pharyngitis and adenitis; SLE, systemic lupus erythematosus.

Table 153-3 Autoantibody Specificity and Disease Associations

ANTIBODY	DISEASE	PREVALENCE (%)	SPECIFICITY
Antinuclear antibody (ANA)	SLE, juvenile rheumatoid arthritis, dermatomyositis, scleroderma, psoriatic arthritis, MCTD	—	Associated with increased risk of uveitis in JIA and psoriatic arthritis Up to 30% of children testing positive for ANAs have no underlying rheumatic disease
Double-stranded DNA (dsDNA)	SLE	60-70	High specificity for SLE; associated with lupus nephritis
Smith (Sm)	SLE	20-30	Highly specific for SLE; associated with lupus nephritis
Smooth muscle (Sm)	Autoimmune hepatitis	—	—
Pm-Scl (polymyositis-scleroderma)	Sclerodermatomyositis	—	—
SSA (Ro)	SLE, Sjögren syndrome	25-30	Associated with neonatal lupus syndrome, subacute cutaneous lupus, thrombocytopenia
SSB (La)	SLE, Sjögren syndrome	25-30	Usually coexists with anti-SSA antibody
Ribonuclease protein (RNP)	MCTD, SLE	30-40	Suggestive of MCTD unless meets criteria for SLE
Histone	Drug-induced lupus, SLE	—	—
Centromere	Limited cutaneous systemic sclerosis	70	Nonspecific for systemic sclerosis
Topoisomerase I (Scl-70)	Systemic sclerosis	—	Rare in childhood
Antineutrophil cytoplasmic antibodies (ANCA)	Vasculitis	—	—
Cytoplasmic (cANCA)/ PR3-ANCA		—	cANCA associated with granulomatosis with polyangiitis (Wegener), cystic fibrosis
Perinuclear (pANCA)/ MPO-ANCA		—	pANCA associated with microscopic polyangiitis, polyarteritis nodosa, SLE, inflammatory bowel disease, cystic fibrosis, primary sclerosing cholangitis, Henoch-Schönlein purpura, Kawasaki disease, Churg-Strauss syndrome
Anticitrullinated protein (ACPA) also called anti-cyclic citrullinated protein (anti-CCP)	RF positive JIA	50-90	Specific for JIA (RF+), may be positive before RF

MCTD, mixed connective tissue disease; MPO-ANCA, antimyeloperoxidase; PR3-ANCA, antiproteinase 3; RF, rheumatoid factor; SLE, systemic lupus erythematosus.
Modified from Aggerwal A: Clinical application of tests used in rheumatology, Indian J Pediatr 69:889-892, 2002.

Table 153-4 Evaluation Based on Suspected Diagnosis

SUSPECTED RHEUMATIC DISEASE(S)	INITIAL EVALUATION	FURTHER EVALUATION	SUBSPECIALTY EVALUATION
SLE, MCTD	CBC, ESR, ANA, ALT, AST, CPK, creatinine, albumin, total protein, urinalysis, BP, thyroid profile	If ANA test result is positive: anti-SSA (Ro), anti-SSB (La), anti-Smith, and anti-RNP Abs; anti-dsDNA Ab, C3, C4, Coombs, spot urine protein/creatinine ratio, CXR	Antiphospholipid Abs, lupus anticoagulant, anti-β ₂ -glycoprotein, echocardiogram; consider renal biopsy, PFTs, bronchoscopy with lavage, HRCT of chest; consider lung biopsy
JDM	CBC, CPK, ALT, AST, LDH, aldolase, ANA; check gag reflex	Consider MRI of muscle	Consider electromyography and possible muscle biopsy, PFTs, swallowing study, serum neopterin
JIA	CBC, ESR, creatinine, ALT, AST, consider anti-streptolysin O/anti-DNAase B for streptococcus-induced arthritis, Epstein-Barr virus titers, Lyme titer, parvovirus B19 titer, plain radiograph of joints	Consider Ab titers to unusual infectious agents, purified protein derivative, RF, ANA, HLA-B27, anti-CCP	MRI
Granulomatosis with polyangiitis (Wegener granulomatosis)	CBC, ANCA, AST, ALT, albumin, creatinine, ESR, urinalysis, CXR, BP	Spot urine protein/creatinine ratio, anti-myeloperoxidase and anti-proteinase-3 Abs, PFTs	Bronchoscopy with lavage, HRCT chest; consider lung and kidney biopsies
Sarcoidosis	CBC, electrolytes, AST, ALT, albumin, creatinine, calcium, phosphorous, ACE, BP	CXR, PFTs	Consider testing for Blau syndrome in infants (see Chapter 159); HRCT of chest; consider renal and lung biopsy
Localized scleroderma	Skin biopsy, CBC, ESR		Serum immunoglobulin G, ANA, RF, single-stranded DNA Ab, antihistone Ab, CPK
Systemic scleroderma	ANA, CBC, ESR, BP, AST, ALT, CPK, creatinine, CXR	Anti-Scl70, PFTs	HRCT of chest, echocardiogram, upper gastrointestinal radiography series

Ab, antibody; ACE, angiotensin-converting enzyme (normally elevated in childhood; interpret with caution); ALT, alanine aminotransferase; ANA, antinuclear antibody; anti-dsDNA Ab, anti-double stranded DNA antibody; AST, aspartate aminotransferase; BP, blood pressure; CBCD, complete blood count with differential; CCP, cyclic citrullinated protein; CPK, creatine phosphokinase; CXR, chest radiograph; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; HRCT, high-resolution CT; LDH, lactate dehydrogenase; PFTs, pulmonary function tests; RF, rheumatoid factor.

Table 155-5 Frequency of Ophthalmologic Examination in Patients with Juvenile Idiopathic Arthritis

TYPE	ANTINUCLEAR ANTIBODY TEST RESULT	AGE AT ONSET (Yr)	DURATION OF DISEASE (Yr)	RISK CATEGORY	EYE EXAMINATION FREQUENCY (Mo)
Oligoarthritis or polyarthritis	+	≤6	≤4	High	3
	+	≤6	>4	Moderate	6
	+	≤6	>7	Low	12
	+	>6	≤4	Moderate	6
	+	>6	>4	Low	12
	-	≤6	≤4	Moderate	6
	-	≤6	>4	Low	12
Systemic disease	NA	NA	NA	Low	12

From Cassidy J, Kivlin J, Lindsley C, et al: Section on Rheumatology; Section on Ophthalmology: Ophthalmologic examinations in children with juvenile rheumatoid arthritis, Pediatrics 117:1843–1845, 2006.

Table 154-2 Therapeutics for Childhood Rheumatic Diseases*

CLASSIFICATION	THERAPEUTIC [†]	DOSE	INDICATION [†]	ADVERSE REACTIONS	MONITORING
Nonsteroidal antinflammatory drugs (NSAIDs) [‡]	Etodolac ^a	PO once-daily dose: 20-30 kg: 400 mg 31-45 kg: 600 mg 46-60 kg: 800 mg >60 kg: 1,000 mg	JIA Spondyloarthropathy Pain Seritis Cutaneous vasculitis Uveitis	GI intolerance (abdominal pain, nausea), gastritis, hepatitis, tinnitus, anemia, pseudoporphyria, aseptic meningitis, headache, renal disease	CBC, LFTs, BUN/creatinine, urinalysis at baseline, then every 6-12 mo
	Ibuprofen ^a	40 mg/kg/day PO divided 3 times daily Max 2400 mg per day			
	Naproxen ^a	15 mg/kg/day PO in 2 divided doses Maximum 1,000 mg per day			
	Celecoxib ^a	10-25 kg: 50 mg PO twice daily >25 kg: 100 mg PO twice daily			
	Meloxicam ^a	0.125 mg/kg, maximum 7.5 mg, PO once daily			
Disease modifying antirheumatic drugs (DMARDs)	Methotrexate ^a	10-20 mg/m ² /wk (0.35-0.65 mg/kg/wk) PO 20-30 mg/m ² /wk (0.65-1 mg/kg/wk) SC; higher doses better absorbed by SC injection	JIA Uveitis	GI intolerance (nausea, vomiting), hepatitis, myelosuppression, mucositis, teratogenesis, lymphoma, interstitial pneumonitis	CBC, LFTs at baseline, monthly × 3, then every 8-12 wk
	Leflunomide	PO once daily: 10 to <20 kg: 10 mg 20-40 kg: 15 mg >40 kg: 20 mg	JIA	hepatitis, hepatic necrosis, cytopenias, mucositis, teratogenesis, peripheral neuropathy	CBC, LFTs, at baseline, monthly × 6, then every 8-12 wk
	Hydroxychloroquine	5-6 mg/kg PO once daily; do not exceed 6.5 mg/kg/daily Maximum dose 400 mg daily	SLE JDMS Antiphospholipid antibody syndrome	Retinal toxicity, GI intolerance, rash, skin discoloration, anemia, cytopenias, myopathy, CNS stimulation, death (overdose)	Ophthalmologic screening every 6-12 mo
	Sulfasalazine ^a	30-50 mg/kg/day divided in twice-daily doses Adult maximum 3 g/day	Spondyloarthropathy, JIA	GI intolerance, rash, hypersensitivity reactions, Stevens-Johnson syndrome, cytopenias, hepatitis, headache	CBC, LFTs, BUN/creatinine, urinalysis at baseline, every other wk × 3 mo, monthly × 3, then every 3 mo
Tumor necrosis factor α (TNF- α) antagonists	Adalimumab ^a	SC once every other wk: 15 to <30 kg: 20 mg ≥30 kg: 40 mg	JIA, spondyloarthropathy, psoriatic arthritis, uveitis	Injection site reaction, infection, rash, cytopenias, lupus-like syndrome, potential increased malignancy risk	TB test; anti-dsDNA, CBC
	Etanercept ^a	0.8 mg/kg SC once weekly (maximum 50 mg/dose) or 0.4 mg/kg SC twice weekly (maximum 25 mg/dose)	JIA	Injection site reactions, infections, rash, demyelinating disorders, cytopenias, potential increased malignancy risk	TB test; CBC
	Infliximab	5-10 mg/kg IV q4-8wk	JIA Spondyloarthropathy Uveitis Sarcoidosis	Infusion reactions, hepatitis, potential increased malignancy risk	TB test; anti-dsDNA, LFTs

*Consult a clinical pharmacology reference for current dosing and monitoring guidelines, and complete list of known adverse effects.

Continued

1156 Part XVI ◆ Rheumatic Diseases of Childhood

Table 154-2 Therapeutics for Childhood Rheumatic Diseases—cont'd

CLASSIFICATION	THERAPEUTIC [†]	DOSE	INDICATION [†]	ADVERSE REACTIONS	MONITORING
Modulate T-cell activation	Abatacept ^a	IV every 2 wk × 3 doses, then monthly for ≥6 yr of age: <75 kg: 10 mg/kg 75-100 kg: 750 mg >100 kg: 1,000 mg	JIA	Infection, headache, potential increased malignancy risk	
Anti-CD20 (B cell) antibody	Rituximab	575 mg/m ² , maximum 1,000 mg, IV on days 1 and 15	SLE	Infusion reactions, lymphopenia, reactivation hepatitis B, rash, serum sickness, arthritis, PML	CBC, BMP; consider monitoring quantitative IgG
Anti-BLyS antibody	Belimumab ^e	10 mg/kg IV every 2 wk × 3 doses, then every 4 wk	SLE	Infusion reactions, infection, depression	
Interleukin 1 antagonist	Anakinra	1-2 mg/kg/daily Adult maximum 100 mg	Systemic JIA CAPS	Injection site reactions, infection	CBC
	Canakinumab ^b	Given SC every 8 wk (CAPS) every 4 wk (Systemic JIA): 15-40 kg: 2 mg/kg (up to 3 mg/kg if needed) >40 kg: 150 mg	CAPS Systemic JIA	Injection site reaction, infection, diarrhea, nausea, vertigo, headache	
Interleukin-6 antagonist	Tocilizumab ^a	≥2 yr and ≥30 kg, 8 mg/kg/dose every 2 wk; ≥2 yr and ≤30 kg, 12 mg/kg/dose every 2 wk	Systemic JIA	Infusion reactions, elevated LFTs, elevated lipids, thrombocytopenia, infections	CBC, LFTs, platelet count, serum lipid profile
Intravenous immunoglobulin	IVIG ^c	1,000-2,000 mg/kg IV infusion For JDMS, give monthly	Kawasaki disease JDMS SLE	Infusion reaction, aseptic meningitis, renal failure	Serum creatinine, BUN, IgG level
Cytotoxic	Cyclophosphamide	0.5-1 g/m ² IV (maximum 1.5 g) monthly for 6-mo induction, then every 2-3 mo Oral regimen: 1-2 mg/kg/daily; maximum 150 mg/daily	SLE Vasculitis JDMS Pulmonary hemorrhage	Nausea, vomiting, myelosuppression, mucositis, hyponatremia, alopecia, hemorrhagic cystitis, gonadal failure, teratogenesis, secondary malignancy	CBC
Immunosuppressive	Mycophenolate mofetil	Oral suspension: maximum 1,200 mg/m ² /day PO (up to 2 g/day) divided twice daily Capsules: maximum 1,500 mg/day PO for BSA 1.25-1.5 m ² , 2 g/day PO for BSA >1.5 m ² divided twice daily	SLE Uveitis	GI intolerance (diarrhea, nausea, vomiting), renal impairment, neutropenia, teratogenesis, secondary malignancy, PML	CBC, BMP

Table 154-2 Therapeutics for Childhood Rheumatic Diseases—cont'd

CLASSIFICATION	THERAPEUTIC [†]	DOSE	INDICATION [†]	ADVERSE REACTIONS	MONITORING
Glucocorticoids	Prednisone ^{a,d,f}	0.5-2 mg/kg/day PO given in 1-4 divided doses; maximum varies by individual (80 mg/daily) Adverse effects are dose dependent; lowest effective dose should be used	SLE JDMS Vasculitis JIA Uveitis Sarcoidosis	Cushing syndrome, osteoporosis, increased appetite, weight gain, striae, hypertension, adrenal suppression, hyperglycemia, infection, avascular necrosis	Blood glucose, potassium Blood pressure
	Methylprednisolone ^{a,d,g}	0.5-1.7 mg/kg/day or 5-25 mg/m ² /day IM/IV in divided doses q6-12h For severe manifestations: 30 mg/kg/dose (maximum 1 g) daily for 1-5 days	SLE JDMS Vasculitis Sarcoidosis Localized scleroderma		
	Intraarticular	Dose varies by joint and formulation	JIA	Subcutaneous atrophy, skin hypopigmentation, calcification, infection	
	Prednisolone ophthalmic suspension	1-2 drops into eye up to every hr while awake Needs monitoring by ophthalmologist	Uveitis	Ocular hypertension, glaucoma, nerve damage, cataract, infection	Ophthalmologic exam

Blys, B-lymphocyte stimulator; BMP, basic metabolic panel; BSA, body surface area; BUN, blood urea nitrogen; CAPS, cryopyrin-associated periodic syndrome; CBC, complete blood count; CNS, central nervous system; dsDNA, double-stranded DNA; GI, gastrointestinal; Ig, immunoglobulin; IM, intramuscular(ly); IV, intravenous(ly); IVIG, intravenous immunoglobulin; JDMS, juvenile dermatomyositis; JIA, juvenile idiopathic arthritis; LFTs, liver function tests; PML, progressive multifocal leukoencephalopathy; PO, by mouth; SC, subcutaneous(ly); SLE, systemic lupus erythematosus; TB, tuberculosis.

[†]Therapeutics used in practice may not have a FDA-approved indication. Individual therapeutics annotated with FDA-approved indication as follows: a, JIA; b, CAPS; c, Kawasaki disease; d, sarcoidosis; e, SLE; f, uveitis; g, dermatomyositis.

[‡]Many more products available in this class.

Table 155-1 Criteria for the Classification of Juvenile Rheumatoid Arthritis

Age at onset: <16 yr
Arthritis (swelling or effusion, or the presence of 2 or more of the following signs: limitation of range of motion, tenderness or pain on motion, increased heat) in ≥1 joint
Duration of disease: ≥6 wk
Onset type defined by type of articular involvement in the 1st 6 mo after onset:
Polyarthritis: ≥5 inflamed joints
Oligoarthritis: ≤4 inflamed joints
Systemic-onset disease: arthritis with rash and a characteristic quotidian fever
Exclusion of other forms of juvenile arthritis

Modified from Cassidy JT, Levison JE, Bass JC, et al: A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis, *Arthritis Rheum* 29:174-181, 1986.

Table 154-3 Summary of Biologic Therapies Studied in Juvenile Idiopathic Arthritis and Their Method of Action

DRUG	METHOD OF ACTION
Etanercept	Soluble TNF p75 receptor fusion protein that binds to and inactivates TNF-α
Infliximab	Chimeric human/mouse monoclonal antibody that binds to soluble TNF-α and its membrane-bound precursor, neutralizing its action
Adalimumab	A humanized IgG ₁ monoclonal antibody that binds to TNF-α
Abatacept	Soluble, fully human fusion protein of the extracellular domain of CTLA-4, linked to a modified Fc portion of the human IgG ₁ . It acts as a costimulatory signal inhibitor by binding competitively to CD80 or CD86, where it selectively inhibits T-cell activation
Tocilizumab	A humanized anti-human IL-6 receptor monoclonal antibody
Anakinra	An IL-1 receptor antagonist (IL-1RA)

CTLA, cytotoxic T lymphocyte-associated antigen; Ig, immunoglobulin; IL, interleukin; TNF, tumor necrosis factor.

From Beresford MW, Baidam EM: New advances in the management of juvenile idiopathic arthritis—2: the era of biologics, *Arch Dis Child Educ Pract Ed* 94:151-156, 2009.

Table 155-2 International League of Associations for Rheumatology Classification of Juvenile Idiopathic Arthritis (JIA)

CATEGORY	DEFINITION	EXCLUSIONS
Systemic	Arthritis in ≥ 1 joint with, or preceded by, fever of at least 2 wk in duration that is documented to be daily ("quotidian" [*]) for at least 3 days and accompanied by ≥ 1 of the following: 1. Evanescent (nonfixed) erythematous rash 2. Generalized lymph node enlargement 3. Hepatomegaly or splenomegaly or both 4. Serositis [†]	a. Psoriasis or a history of psoriasis in the patient or a 1st-degree relative b. Arthritis in an HLA-B27-positive boy beginning after the 6th birthday c. Ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with inflammatory bowel disease, Reiter syndrome, or acute anterior uveitis, or a history of one of these disorders in a 1st-degree relative d. Presence of immunoglobulin M RF on at least 2 occasions at least 3 mo apart
Oligoarthritis	Arthritis affecting 1-4 joints during the 1st 6 mo of disease. Two subcategories are recognized: 1. Persistent oligoarthritis—affecting ≤ 4 joints throughout the disease course 2. Extended oligoarthritis—affecting >4 joints after the 1st 6 mo of disease	a, b, c, d (above) plus e. Presence of systemic JIA in the patient
Polyarthritis (RF-negative)	Arthritis affecting ≥ 5 joints during the 1st 6 mo of disease; a test for RF is negative	a, b, c, d, e
Polyarthritis (RF-positive)	Arthritis affecting ≥ 5 joints during the 1st 6 mo of disease; ≥ 2 tests for RF at least 3 mo apart during the 1st 6 mo of disease are positive	a, b, c, e
Psoriatic arthritis	Arthritis and psoriasis, or arthritis and at least 2 of the following: 1. Dactylitis [‡] 2. Nail pitting [§] and onycholysis 3. Psoriasis in a 1st-degree relative	b, c, d, e
Enthesitis-related arthritis	Arthritis and enthesitis, or arthritis or enthesitis with at least 2 of the following: 1. Presence of or a history of sacroiliac joint tenderness or inflammatory lumbosacral pain or both [¶] 2. Presence of HLA-B27 antigen 3. Onset of arthritis in a male >6 yr old 4. Acute (symptomatic) anterior uveitis 5. History of ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with inflammatory bowel disease, Reiter syndrome, or acute anterior uveitis in a 1st-degree relative	a, d, e
Undifferentiated arthritis	Arthritis that fulfills criteria in no category or in ≥ 2 of the above categories.	

RF, rheumatoid factor.

^{*}Quotidian fever is defined as a fever that rises to 39°C (102.2°F) once a day and returns to 37°C (98.6°F) between fever peaks.[†]Serositis refers to pericarditis, pleuritis, or peritonitis, or some combination of the 3.[‡]Dactylitis is swelling of ≥ 1 digits, usually in an asymmetric distribution, that extends beyond the joint margin.[§]A minimum of 2 pits on any 1 or more nails at any time.^{||}Enthesitis is defined as tenderness at the insertion of a tendon, ligament, joint capsule, or fascia to bone.[¶]Inflammatory lumbosacral pain refers to lumbosacral pain at rest with morning stiffness that improves on movement.

From Firestein GS, Budd RC, Harris ED Jr, et al, editors: Kelley's textbook of rheumatology, ed 8, Philadelphia, 2009, Saunders.

Table 155-3 Characteristics of the American College of Rheumatology (ACR) and International League of Associations for Rheumatology (ILAR) Classifications of Childhood Chronic Arthritis

PARAMETER	ACR (1977)	ILAR (1997)
Term	Juvenile rheumatoid arthritis (JRA)	Juvenile idiopathic arthritis (JIA)
Minimum duration	≥ 6 wk	≥ 6 wk
Age at onset	<16 yr	<16 yr
≤ 4 joints in 1st 6 mo after presentation	<ul style="list-style-type: none"> • Pauciarticular 	<ul style="list-style-type: none"> • Oligoarthritis: <ul style="list-style-type: none"> a. Persistent: <4 joints for course of disease b. Extended: >4 joints after 6 mo • Polyarthritis rheumatoid factor-negative • Polyarthritis rheumatoid factor-positive
>4 joints in 1st 6 mo after presentation	<ul style="list-style-type: none"> • Polyarticular 	
Fever, rash, arthritis	<ul style="list-style-type: none"> • Systemic-onset 	<ul style="list-style-type: none"> • Systemic
Other categories included	Exclusion of other forms	<ul style="list-style-type: none"> • Psoriatic arthritis • Enthesitis-related arthritis • Undifferentiated: <ul style="list-style-type: none"> a. Fits no other category b. Fits more than 1 category
Inclusion of psoriatic arthritis, inflammatory bowel disease, ankylosing spondylitis	No (see Chapter 156)	Yes

Table 155-4 Overview of the Main Features of the Subtypes of Juvenile Idiopathic Arthritis

INTERNATIONAL LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY SUBTYPE	PEAK AGE OF ONSET (Yr)	FEMALE:MALE RATIO	PERCENTAGE OF ALL JIA CASES	ARTHRITIS PATTERN	EXTRAARTICULAR FEATURES	LABORATORY INVESTIGATIONS	NOTES ON THERAPY
Systemic arthritis	1-5	1:1	5-15	Polyarticular; often affecting knees, wrists, and ankles; also fingers, neck, and hips	Daily fever; evanescent rash; pericarditis; pleuritis	Anemia; WBC ↑↑; ESR ↑↑; CRP ↑↑; ferritin ↑↑; platelets ↑↑ (normal or ↓ in MAS)	Less responsive to standard treatment with MTX and anti-TNF agents; consider IL-1 or IL-6 inhibitors in resistant cases or as first-line therapy
Oligoarthritis	2-4	3:1	40-50 (but ethnic variation)	Knees ++; ankles, fingers +	Uveitis in ≈30% of cases	NSAIDs and intraarticular steroids; MTX occasionally required	
Polyarthritis: RF-negative	2-4 and 10-14	3:1 and 10:1	20-35	Symmetric or asymmetric; small and large joints; cervical spine; temporomandibular joint	Uveitis in ≈10%	ANA positive in ≈60%; other test results usually normal; may have mildly ↑ ESR/CRP	
RF-positive	9-12	9:1	<10	Aggressive symmetric polyarthritis	Rheumatoid nodules in 10%; low-grade fever	Standard therapy with MTX and NSAIDs; then, if nonresponsive, anti-TNF agents or other biologics, including abatacept, indicated as first-line therapy	Long-term remission unlikely; early aggressive therapy is warranted
Psoriatic arthritis	2-4 and 9-11	2:1	5-10	Asymmetric arthritis of small or medium-sized joints	Uveitis in 10%; psoriasis in 50%	ANA positive in 50%; ESR ↑↑; CRP ↑↑/normal; mild anemia	NSAIDs and intraarticular steroids; MTX, anti-TNF agents
Enthesitis-related arthritis	9-12	1:7	5-10	Predominantly lower limb joints affected; sometimes axial skeleton (but less than in adult, ankylosing spondylitis)	Acute anterior uveitis; association with reactive arthritis and inflammatory bowel disease	80% of patients positive for HLA-B27	NSAIDs and intra-articular steroids; consider sulfasalazine as alternative to MTX; anti-TNF agents

ANA, antinuclear antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; JIA, juvenile idiopathic arthritis; MAS, macrophage activation syndrome; MTX, methotrexate; NSAID, nonsteroidal antiinflammatory drug; RF, rheumatoid factor; TNF, tumor necrosis factor; WBC, white blood cell count.

From Firestein GS, Budd RC, Harris ED Jr, et al, editors: Kelley's textbook of rheumatology, ed 8, Philadelphia, 2009, Saunders.

Table 155-7 Conditions Causing Arthritis or Extremity Pain

RHEUMATIC AND INFLAMMATORY DISEASES	BONE AND CARTILAGE DISORDERS
Juvenile idiopathic arthritis	Trauma
Systemic lupus erythematosus	Patellofemoral syndrome
Juvenile dermatomyositis	Hypermobility syndrome
Polyarteritis nodosa	Osteochondritis dissecans
Scleroderma	Avascular necrosis (including Legg-Calvé-Perthes disease)
Sjögren syndrome	Hypertrophic osteoarthropathy
Behçet disease	Slipped capital femoral epiphysis
Overlap syndromes	Osteolysis
Antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis	Benign bone tumors (including osteoid osteoma)
Sarcoidosis	Histiocytosis
Kawasaki syndrome	Rickets
Henoch-Schönlein purpura	
Chronic recurrent multifocal osteomyelitis	
SERONEGATIVE SPONDYLOARTHROPATHIES	NEUROPATHIC DISORDERS
Juvenile ankylosing spondylitis	Peripheral neuropathies
Inflammatory bowel disease	Carpal tunnel syndrome
Psoriatic arthritis	Charcot joints
Reactive arthritis associated with urethritis, iridocyclitis, and mucocutaneous lesions	
INFECTIOUS ILLNESSES	NEOPLASTIC DISORDERS
Bacterial arthritis (septic arthritis, <i>Staphylococcus aureus</i> , <i>Kingella kingae</i> , pneumococcus, gonococcus, <i>Haemophilus influenzae</i>)	Leukemia
Lyme disease	Neuroblastoma
Viral illness (parvovirus, rubella, mumps, Epstein-Barr virus, hepatitis B, Chikungunya virus)	Lymphoma
Fungal arthritis	Bone tumors (osteosarcoma, Ewing sarcoma)
Mycobacterial infection	Histiocytic syndromes
Spirochetal infection	Synovial tumors
Endocarditis	
REACTIVE ARTHRITIS	HEMATOLOGIC DISORDERS
Acute rheumatic fever	Hemophilia
Reactive arthritis (postinfectious caused by <i>Shigella</i> , <i>Salmonella</i> , <i>Yersinia</i> , <i>Chlamydia</i> , or meningococcus)	Hemoglobinopathies (including sickle cell disease)
Serum sickness	
Toxic synovitis of the hip	MISCELLANEOUS DISORDERS
Postimmunization	Autoinflammatory diseases
IMMUNODEFICIENCIES	Recurrent multifocal osteomyelitis
Hypogammaglobulinemia	Pigmented villonodular synovitis
Immunoglobulin A deficiency	Plant-thorn synovitis (foreign-body arthritis)
Human immunodeficiency virus	Myositis ossificans
CONGENITAL AND METABOLIC DISORDERS	Eosinophilic fasciitis
Gout	Tendinitis (overuse injury)
Pseudogout	Raynaud phenomenon
Mucopolysaccharidoses	
Thyroid disease (hypothyroidism, hyperthyroidism)	PAIN SYNDROMES
Hyperparathyroidism	Fibromyalgia
Vitamin C deficiency (scurvy)	Growing pains
Hereditary connective tissue disease (Marfan syndrome, Ehlers-Danlos syndrome)	Depression (with somatization)
Fabry disease	Reflex sympathetic dystrophy
Farber disease	Regional myofascial pain syndromes
Amyloidosis (familial Mediterranean fever)	

Table 155-6 Main Clinical, Laboratory, and Pathologic Features of Macrophage Activation Syndrome

LABORATORY CRITERIA	
1.	Cytophenias
2.	Abnormal liver function tests
3.	Coagulopathy (hypofibrinogenemia)
4.	Decreased erythrocyte sedimentation rate
5.	Hypertriglyceridemia
6.	Hyponatremia
7.	Hypoalbuminemia
8.	Hyperferritinemia
9.	Elevated sCD25 and sCD163
CLINICAL CRITERIA	
1.	Nonremitting fever
2.	Hepatomegaly
3.	Splenomegaly
4.	Lymphadenopathy
5.	Hemorrhages
6.	Central nervous system dysfunction (headache, seizures, lethargy, coma, disorientation)
HISTOPATHOLOGIC CRITERIA	
1.	Macrophage hemophagocytosis in the bone marrow aspirate
2.	Increased CD163 staining of the bone marrow

Table 156-2 Etiologic Microorganisms of Reactive Arthritis

PROBABLE	POSSIBLE
<i>Chlamydia trachomatis</i>	<i>Neisseria gonorrhoeae</i>
<i>Shigella flexneri</i>	<i>Mycoplasma fermentans</i>
<i>Salmonella enteritidis</i>	<i>Mycoplasma genitalium</i>
<i>Salmonella typhimurium</i>	<i>Ureaplasma urealyticum</i>
<i>Yersinia enterocolitica</i>	<i>Escherichia coli</i>
<i>Yersinia pseudotuberculosis</i>	<i>Cryptosporidium</i>
<i>Campylobacter jejuni</i>	<i>Entamoeba histolytica</i>
	<i>Giardia lamblia</i>
	<i>Brucella abortus</i>
	<i>Clostridium difficile</i>
	<i>Streptococcus pyogenes</i>
	<i>Chlamydia pneumoniae</i>
	<i>Chlamydia psittaci</i>

From Kim PS, Klausmeier TL, Orr DP: Reactive arthritis: a review. J Adolesc Health 44:309–315, 2009, Table 2, p. 311.

Table 155-8 Pharmacologic Treatment of Juvenile Idiopathic Arthritis (JIA)

TYPICAL MEDICATIONS	TYPICAL DOSES	JIA SUBTYPE	SIDE EFFECT(S)
NONSTEROIDAL ANTIINFLAMMATORY DRUGS			
Naproxen	15 mg/kg/day PO divided bid (maximum dose 500 mg bid)	Polyarthritis Systemic Oligoarthritis	Gastritis, renal and hepatic toxicity, pseudoporphyria
Ibuprofen	40 mg/kg/day PO divided tid (maximum dose 800 mg tid)	Same as above	Same as above
Meloxicam	0.125 mg/kg PO once daily (maximum dose 15 mg daily)	Same as above	Same as above
DISEASE-MODIFYING ANTIRHEUMATIC DRUGS			
Methotrexate	0.5-1 mg/kg PO or SC weekly (maximum dose 25 mg/wk)	Polyarthritis Systemic Persistent or extended oligoarthritis	Nausea, vomiting, oral ulcerations, hepatic toxicity, blood count dyscrasias, immunosuppression, teratogenicity
Sulfasalazine	Initial 12.5 mg/kg PO daily; increase by 10 mg/kg/day Maintenance: 40-50 mg/kg divided bid (maximum dose 2 g/day)	Polyarthritis	GI upset, allergic reaction, pancytopenia, renal and hepatic toxicity, Stevens- Johnson syndrome
Leflunomide*	10-20 mg PO daily	Polyarthritis	GI upset, hepatic toxicity, allergic rash, alopecia (reversible), teratogenicity (needs washout with cholestyramine)
BIOLOGIC AGENTS			
<i>Anti-Tumor Necrosis Factor-α</i>			
Etanercept	0.8 mg/kg SC weekly or 0.4 mg/kg SC twice weekly (maximum dose 50 mg/wk)	Polyarthritis Systemic Persistent or extended oligoarthritis	Immunosuppressant, concern for malignancy, demyelinating disease, lupus-like reaction, injection site reaction
Infliximab*	3-10 mg/kg IV q4-8wk	Same as above	Same as above, infusion reaction
Adalimumab	<30 kg: 20 mg SC every other week >30 kg: 40 mg SC every other week	Same as above	Same as above
<i>Anticytotoxic T-Lymphocyte-Associated Antigen-4 Immunoglobulin</i>			
Abatacept	<75 kg: 10 mg/kg/dose IV q4wk 75-100 kg: 750 mg/dose IV q4wk >100 kg: 1,000 mg/dose IV q4wk	Polyarthritis	Immunosuppressant, concern for malignancy, infusion reaction
<i>Anti-CD20</i>			
Rituximab*	750 mg/m ² IV 2 wk × 2 (maximum dose 1,000 mg)	Polyarthritis	Immunosuppressant, infusion reaction, progressive multifocal encephalopathy
<i>Interleukin-1 Inhibitors</i>			
Anakinra*	1-2 mg/kg SC daily (maximum dose 100 mg/day)	Systemic	Immunosuppressant, GI upset, injection site reaction
Canakinumab	15-40 kg: 2 mg/kg/dose SC q8wk >40 kg: 150 mg SC q8wk	Systemic	Immunosuppressant, headache, GI upset, injection site reaction
Rilonacept*	2.2 mg/kg/dose SC weekly (maximum dose 160 mg)	Systemic	Immunosuppressant, allergic reaction, dyslipidemia, injection site reaction
<i>Interleukin-6 Receptor Antagonist</i>			
Tocilizumab	<30 kg: 12 mg/kg/dose q2wk >30 kg: 8 mg/kg/dose q2wk (maximum dose 800 mg)	Systemic Polyarthritis	Immunosuppressant, hepatic toxicity, dyslipidemia, cytopenias, GI upset, infusion reaction

bid, Twice daily; GI, gastrointestinal; IV, intravenous; PO, oral; SC, subcutaneous; tid, 3 times daily.

*Not indicated by the U.S. Food and Drug Administration for use in JIA.

Table 156-1 Overlapping Characteristics of the Spondyloarthritides

CHARACTERISTIC	JUVENILE ANKYLOSING SPONDYLITIS	JUVENILE PSORIATIC ARTHRITIS	INFLAMMATORY BOWEL DISEASE	REACTIVE ARTHRITIS
Enthesitis	+++	+	+	++
Axial arthritis	+++	++	++	+
Peripheral arthritis	+++	+++	+++	+++
HLA-B27 positive	+++	+	+++	+++
Antinuclear antibody positive	-	++	-	-
Rheumatoid factor positive	-	-	-	-
Systemic disease:				
Eyes	+	+	+	+
Skin	-	+++	+	+
Mucous membranes	-	-	+	+
Gastrointestinal tract	-	-	+++	+++

Frequency of characteristics: -, absent; +, <25%; ++, 25-50%; +++, 50-75%; ++++, 75% or more.

From Cassidy JT, Petty RE: Textbook of pediatric rheumatology, ed 6, Philadelphia, 2011, Elsevier/Saunders.

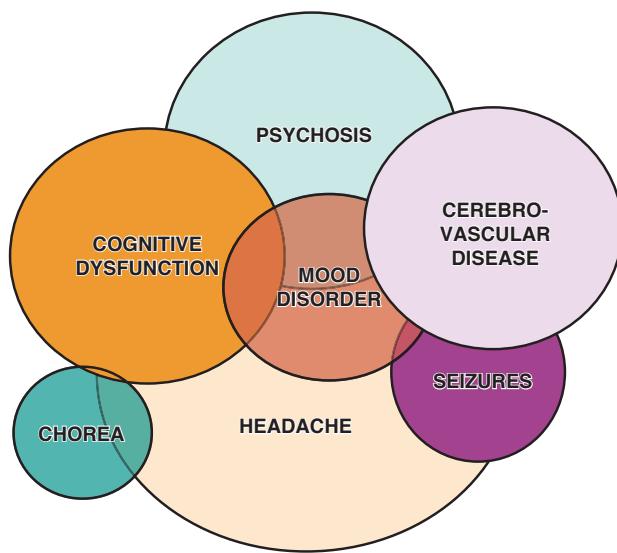


Figure 158-2 Overlapping neuropsychiatric symptoms in pediatric SLE. Patients with pediatric SLE most commonly have more than 1 neuropsychiatric symptom—in particular for seizures. (From Silverman E, Eddy A: Systemic lupus erythematosus. In Cassidy JT, Petty RE, Laxer RM, et al, editors, Textbook of pediatric rheumatology, ed 6, Philadelphia, 2011, Saunders/Elsevier, Fig. 21-17, p. 329.)

Table 158-2

American College of Rheumatology 1997 Revised Classification Criteria for Systemic Lupus Erythematosus*

- Malar rash
- Discoid rash
- Photosensitivity
- Oral or nasal ulcers
- Arthritis
 - Nonerosive, ≥2 joints
- Serositis
 - Pleuritis, pericarditis or peritonitis
 - Renal manifestations†
 - Consistent renal biopsy
 - Persistent proteinuria or renal casts
 - Seizure or psychosis
 - Hematologic manifestations†
 - Hemolytic anemia
 - Leukopenia (<4,000 leukocytes/mm³)
 - Lymphopenia (<1,500 leukocytes/mm³)
 - Thrombocytopenia (<100,000 thrombocytes/mm³)
 - Immunologic abnormalities†
 - Positive anti-double-stranded or anti-Smith antibody
 - False-positive rapid plasma regain test result, positive lupus anticoagulant test result, or elevated anticardiolipin immunoglobulin (Ig) G or IgM antibody
 - Positive antinuclear antibody test result

*The presence of 4 of 11 criteria establishes the diagnosis of SLE. These criteria were developed for classification in clinical trials and not for clinical diagnosis.

†Each of these criteria counts as a single criterion whether 1 or more definitions are satisfied.

Adapted from Hochberg MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus, Arthritis Rheum 40:1725, 1997.

Table 158-3 Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for Systemic Lupus Erythematosus*

CLINICAL CRITERIA

- Acute cutaneous lupus
 - Malar rash, bullous lupus, toxic epidermal necrolysis variant of SLE, maculopapular lupus rash, photosensitive lupus rash, or subacute cutaneous lupus
- Chronic cutaneous lupus
 - Classic discoid rash, lupus panniculitis, mucosal lupus, lupus erythematosus tumidus, chilblains lupus, discoid lupus/lichen planus overlap
- Oral or nasal ulcers
- Nonscarring alopecia
- Synovitis (≥2 joints)
- Serositis
 - Pleurisy or pericardial pain ≥1 day, pleural effusion or rub, pericardial effusion or rub, ECG evidence of pericarditis
- Renal
 - Presence of red blood cell casts or urine protein/creatinine ratio representing >500 mg protein/24 hours
- Neurologic
 - Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy, or acute confusional state
- Hemolytic anemia
- Leukopenia (<4,000/mm³) or lymphopenia (<1,000/mm³)
- Thrombocytopenia (<100,000/mm³)

IMMUNOLOGIC CRITERIA

- Positive antinuclear antibody
- Positive double-stranded DNA antibody
- Positive anti-Smith antibody
- Antiphospholipid antibody positivity
 - Positive lupus anticoagulant, false-positive test for rapid plasma regain, medium to high titer anticardiolipin antibody level (IgA, IgG, IgM), or positive anti-B₂-glycoprotein I antibody (IgA, IgG, IgM)
- Low complement
 - Low C3, C4, or CH50 level
- Positive direct Coombs test (in the absence of hemolytic anemia)

*The presence of 4 criteria (including at least 1 clinical and 1 immunologic criterion) establishes the diagnosis of SLE. Biopsy-proven lupus nephritis with positive ANA or anti-double-stranded DNA also satisfies the diagnosis of SLE. These criteria were developed for classification in clinical trials and not for clinical diagnosis.

Adapted from Petri M: Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus, Arthritis Rheum 64(8):2677–2686, 2012.

Table 158-4 Medications Associated with Drug-Induced Lupus**DEFINITE ASSOCIATION**

Minocycline, procainamide, hydralazine, isoniazid, penicillamine, diltiazem, interferon- α , methyldopa, chlorpromazine, etanercept, infliximab, adalimumab

PROBABLE ASSOCIATION

Phenytoin, ethosuximide, carbamazepine, sulfasalazine, amiodarone, quinidine, rifampin, nitrofurantoin, beta blockers, lithium, captopril, interferon- γ , hydrochlorothiazide, glyburide, docetaxel, penicillin, tetracycline, statins, gold, valproate, griseofulvin, gemfibrozil, propylthiouracil

Table 158-6 Morbidity in Childhood Lupus

Renal	Hypertension, dialysis, transplantation
Central nervous system	Organic brain syndrome, seizures, psychosis, neurocognitive dysfunction
Cardiovascular	Atherosclerosis, myocardial infarction, cardiomyopathy, valvular disease
Immune	Recurrent infection, functional asplenia, malignancy
Musculoskeletal	Osteopenia, compression fractures, avascular necrosis
Ocular	Cataracts, glaucoma, retinal detachment, blindness
Endocrine	Diabetes, obesity, growth failure, infertility, fetal wastage

Table 159-2 Clinical Features of Juvenile Dermatomyositis During the Course of the Disease

FEATURE	%
Muscle weakness	90-100
Dysphagia or dysphonia	13-40
Muscle atrophy	10
Muscle pain and tenderness	30-83
Skin lesions	85-100
Heliotrope rash of eyelids	66-83
Gottron papules	57-91
Erythematous rash of malar/facial area	42-100
Periungual capillary changes	80
Photosensitive rash	5-42
Ulcerations	22-30
Calcinosis	12-30
Lipodystrophy	11-14
Raynaud phenomenon	2-15
Arthritis and arthralgia	22-58
Joint contractures	26-27
Fever	16-46
Gastrointestinal signs and symptoms	8-22
Restrictive pulmonary disease	4-32
Interstitial lung disease	1-7
Cardiac involvement	0-3

Table 158-5 Autoantibodies Commonly Associated with Systemic Lupus Erythematosus (SLE)

ANTIBODY	CLINICAL ASSOCIATION
Anti-double-stranded DNA	Correlates with disease activity, especially nephritis, in some with SLE
Anti-Smith antibody	Specific for the diagnosis of SLE
Antiribonucleoprotein antibody	Increased risk for Raynaud phenomenon and pulmonary hypertension High titer may suggest diagnosis of mixed connective tissue disorder
Anti-Ro antibody (anti-SSA antibody)	Associated with sicca syndrome May suggest diagnosis of Sjögren syndrome
Anti-La antibody (anti-SSB antibody)	Increased risk of neonatal lupus in offspring (congenital heart block) May be associated with cutaneous and pulmonary manifestations of SLE May be associated with isolated discoid lupus
Antiphospholipid antibodies (including anticardiolipin antibodies)	Increased risk for venous and arterial thrombotic events
Antihistone antibodies	Present in a majority of patients with drug-induced lupus May be present in SLE

Table 158-1 Potential Clinical Manifestations of Systemic Lupus Erythematosus

TARGET ORGAN	POTENTIAL CLINICAL MANIFESTATIONS
Constitutional	Fatigue, anorexia, weight loss, fever, lymphadenopathy
Musculoskeletal	Arthritis, myositis, tendonitis, arthralgias, myalgias, avascular necrosis, osteoporosis
Skin	Malar rash, discoid (annular) rash, photosensitive rash, cutaneous vasculitis (petechiae, palpable purpura, digit ulcers, gangrene, urticaria), livedo reticularis, periungual capillary abnormalities, Raynaud phenomenon, alopecia, oral and nasal ulcers, panniculitis, chilblains, alopecia
Renal	Hypertension, proteinuria, hematuria, edema, nephrotic syndrome, renal failure
Cardiovascular	Pericarditis, myocarditis, conduction system abnormalities, Libman-Sacks endocarditis
Neurologic	Seizures, psychosis, cerebritis, stroke, transverse myelitis, depression, cognitive impairment, headaches, migraines, pseudotumor, peripheral neuropathy (mononeuritis multiplex), chorea, optic neuritis, cranial nerve palsies, acute confusional states, dural sinus thrombosis
Pulmonary	Pleuritis, interstitial lung disease, pulmonary hemorrhage, pulmonary hypertension, pulmonary embolism
Hematologic	Immune-mediated cytopenias (hemolytic anemia, thrombocytopenia or leukopenia), anemia of chronic inflammation, hypercoagulability, thrombocytopenic thrombotic microangiopathy
Gastroenterology	Hepatosplenomegaly, pancreatitis, vasculitis affecting bowel, protein-losing enteropathy, peritonitis
Ocular	Retinal vasculitis, scleritis, episcleritis, papilledema, dry eyes, optic neuritis

Table 159-3 Phenotypic Characteristics of the Clinical Subgroups of Juvenile Myositis*

CHARACTERISTIC	JDM	JPM	JCTM
<i>Demographics</i>			
Median age at diagnosis (yr)	Youngest (7.4 yr)	Oldest (12.1 yr)	Intermediate (10.2 yr)
Race	Predominantly white (71.2%)	Black (39.4%)	Black or other (49.0%)
Severity at onset	Mild or moderate severity	Severe or very severe onset	Mild or moderate severity
Median delay to diagnosis (mo)	4 mo	3.5 mo	Longer delay (7 mo)
<i>Clinical features</i>			
	Gottron papules Heliotrope rash Periungual capillary abnormalities Malar rash <i>Photosensitivity</i> <i>Linear extensor erythema[†]</i> Cuticular overgrowth Mucous membrane involvement "V-sign" and "shawl-sign" rashes Skin ulcerations Dyspnea on exertion	Weight loss Falling episodes Raynaud phenomenon Abnormal PFT Dyspnea on exertion Cardiac abnormalities on EKG or ECHO	Gottron papules Heliotrope rash Malar rash Raynaud phenomenon Interstitial lung disease Arthralgia <i>Linear extensor erythema[†]</i> <i>Mucous membrane involvement</i> Arthritis Photosensitivity Sclerodactyly Periungual capillary abnormalities[†] Cuticular overgrowth Abdominal pain, GI bleeding Dyspnea on exertion Weight loss
Autoantibodies	Intermediate ANA titer (median, 1:320) <i>Anti-p155/140[†]</i> Anti-MJ Anti-Mi-2	Intermediate ANA titer (median, 1:320) Anti-SRP Anti-aminoacyl-tRNA synthetase (anti-Jo-1)	Highest ANA titer (median, 1:1280) Anti-U1-RNP Anti-PM-Scl Anti-Ro Anti-SM Anti-La All other U-RNP autoantibodies
Laboratory features	Lowest CK level (median, 829 U/L)	Highest CK level (median, 5027 U/L) Highest levels of aldolase and ALT	Intermediate CK level (median 1208 U/L)
Outcome	Low mortality (2.4%) Calcinosis (34.0%)	Medium mortality (6.3%) Frequently hospitalized (71.9%) Wheelchair use	Highest mortality (14.6%)

ALT, alanine aminotransferase; ANA, antinuclear antibody; CK, creatine kinase; ECHO, echocardiogram; EKG, electrocardiogram; GI, gastrointestinal; JCTM, juvenile myositis overlapping with another autoimmune or connective tissue disease; JDM, juvenile dermatomyositis; JPM, juvenile polymyositis; PFT, pulmonary function test; tRNA, transfer RNA.

*Bold indicates significant in logistic regression; *italics* indicates top variables entered in pruned-down random forest models. Other variables included in this table were significant in univariable analysis to $p \leq 0.01$.

[†]Removed from logistic regression analyses because variable was either 100% or 0% in 1 of the compared subgroups. Gottron papules and heliotrope rash, which were part of the definition of cases of dermatomyositis, were not entered into multivariable analyses.

Modified from Shah M, Mamyrina G, Targoff IN, et al: The clinical phenotypes of the juvenile idiopathic inflammatory myopathies. Medicine (Baltimore) 92:25–41, 2013, Table 9, p. 36.

Table 160-3 Provisional Criteria for the Classification of Juvenile Systemic Sclerosis (SSc)

MAJOR CRITERION (REQUIRED)*
Proximal skin sclerosis/induration of the skin proximal to metacarpophalangeal or metatarsophalangeal joints
MINOR CRITERIA (AT LEAST 2 REQUIRED)
Cutaneous: sclerodactyly
Peripheral vascular: Raynaud phenomenon, nailfold capillary abnormalities (telangiectasias), digital tip ulcers
Gastrointestinal: dysphagia, gastroesophageal reflux
Cardiac: Arrhythmias, heart failure
Renal: Renal crisis, new-onset arterial hypertension
Respiratory: pulmonary fibrosis (high-resolution computed tomography/radiography), decreased diffusing capacity for carbon monoxide, pulmonary arterial hypertension
Neurologic: neuropathy, carpal tunnel syndrome
Musculoskeletal: tendon friction rubs, arthritis, myositis
Serologic: antinuclear antibodies—SSc-selective autoantibodies (anticentromere, antitopoisomerase I [Scl-70], antifibrillarin, anti-PM/Scl, antifibrillin or anti-RNA polymerase I or III)

*Diagnosis requires at least 1 major and at least 2 minor criteria.

Table 159-1 Diagnostic Criteria for Juvenile Dermatomyositis

Classic rash	Heliotrope rash of the eyelids Gottron papules
Plus 3 of the following:	
Weakness	Symmetric Proximal
Muscle enzyme elevation (≥ 1)	Creatine kinase Aspartate aminotransferase Lactate dehydrogenase Aldolase
Electromyographic changes	Short, small polyphasic motor unit potentials Fibrillations Positive sharp waves Insertional irritability
Muscle biopsy	Bizarre, high-frequency repetitive discharges Necrosis Inflammation

Table 160-1 Classification of Pediatric Scleroderma (Morphea)**LOCALIZED SCLERODERMA*****Plaque Morphea***

Confined to dermis, occasionally superficial panniculus
Well-circumscribed circular area of induration, often a central waxy, ivory-colored area surrounded by a violaceous halo; unilateral

Generalized Morphea

Involves dermis primarily, occasionally panniculus
Defined as confluence of individual morphea plaques or lesions in 3 or more anatomic sites; more likely to be bilateral

Bullous Morphea

Bullous lesions that can occur with any of the subtypes of morphea

Linear Scleroderma

Linear lesions can extend through the dermis, subcutaneous tissue, and muscle to underlying bone; more likely unilateral

Limbs/trunk:

One or more linear streaks of the extremities or trunk
Flexion contracture occurs when lesion extends over a joint; limb length discrepancies

En coup de sabre:

Involves the scalp and/or face; lesions can extend into the central nervous system, resulting in neurologic sequelae, most commonly seizures and headaches

Parry Romberg syndrome:

Hemifacial atrophy without a clearly definable en coup de sabre lesion; can also have neurologic involvement

Deep Morphea

Involves deeper layers, including panniculus, fascia, and muscle; more likely to be bilateral

Subcutaneous morphea:

Primarily involves the panniculus or subcutaneous tissue
Plaques are hyperpigmented and symmetric

Eosinophilic fascitis:

Fascitis with marked blood eosinophilia
Fascia is the primary site of involvement; typically involves extremities
Classic description is "peau d'orange" or orange peel texture, but early disease manifests as edema (see Fig. 160-2)

Morphea profunda:

Deep lesion extending to fascia and sometimes muscle, but may be limited to a single plaque, often on trunk

Disabling pansclerotic morphea of childhood:

Generalized full-thickness involvement of skin on the trunk, face and extremities, sparing finger tips and toes

SYSTEMIC SCLEROSIS***Diffuse***

Most common type in childhood

Symmetric thickening and hardening of the skin (sclerosis) with fibrous and degenerative changes of viscera

Limited

Rare in childhood

Previously known as CREST (calcinosis cutis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasia) syndrome

Table 160-1 Classification of Pediatric Scleroderma (Morphea)**LOCALIZED SCLERODERMA*****Plaque Morphea***

Confined to dermis, occasionally superficial panniculus
Well-circumscribed circular area of induration, often a central waxy, ivory-colored area surrounded by a violaceous halo; unilateral

Generalized Morphea

Involves dermis primarily, occasionally panniculus
Defined as confluence of individual morphea plaques or lesions in 3 or more anatomic sites; more likely to be bilateral

Bullous Morphea

Bullous lesions that can occur with any of the subtypes of morphea

Linear Scleroderma

Linear lesions can extend through the dermis, subcutaneous tissue, and muscle to underlying bone; more likely unilateral

Limbs/trunk:

One or more linear streaks of the extremities or trunk
Flexion contracture occurs when lesion extends over a joint; limb length discrepancies

En coup de sabre:

Involves the scalp and/or face; lesions can extend into the central nervous system, resulting in neurologic sequelae, most commonly seizures and headaches

Parry Romberg syndrome:

Hemifacial atrophy without a clearly definable en coup de sabre lesion; can also have neurologic involvement

Deep Morphea

Involves deeper layers, including panniculus, fascia, and muscle; more likely to be bilateral

Subcutaneous morphea:

Primarily involves the panniculus or subcutaneous tissue
Plaques are hyperpigmented and symmetric

Eosinophilic fascitis:

Fascitis with marked blood eosinophilia
Fascia is the primary site of involvement; typically involves extremities
Classic description is "peau d'orange" or orange peel texture, but early disease manifests as edema (see Fig. 160-2)

Morphea profunda:

Deep lesion extending to fascia and sometimes muscle, but may be limited to a single plaque, often on trunk

Disabling pansclerotic morphea of childhood:

Generalized full-thickness involvement of skin on the trunk, face and extremities, sparing finger tips and toes

SYSTEMIC SCLEROSIS***Diffuse***

Most common type in childhood

Symmetric thickening and hardening of the skin (sclerosis) with fibrous and degenerative changes of viscera

Limited

Rare in childhood

Previously known as CREST (calcinosis cutis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasia) syndrome

Table 161-1 Criteria of the International Study Group for the Diagnosis of Behcet disease

CRITERION	DESCRIPTION
Recurrent oral ulceration	Minor aphthous, major aphthous, or herpetiform ulceration recurring at least 3 times in one 12 mo period, observed by physician or patient
Plus 2 of the following:	
Recurrent genital ulcers	Aphthous ulceration or scarring observed by physician or patient
Eye lesions	Anterior uveitis, posterior uveitis, cells in vitreous on slit-lamp examination, or retinal vasculitis observed by an ophthalmologist
Skin lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis or papulopustular lesions, or acneiform nodules observed by physician in postadolescent patient not on corticosteroid treatment
Pathergy	Skin reaction to a needle prick observed by physician at 24-48 hr

Table 162-1 Proposed Criteria for Pediatric Sjögren Syndrome

- I. CLINICAL SYMPTOMS
 1. Oral: recurrent parotitis or enlargement of parotid gland, dry mouth (xerostomia)
 2. Ocular: dry eyes (xerophthalmia) recurrent conjunctivitis without obvious allergic or infectious etiology, keratoconjunctivitis sicca
 3. Other mucosal: recurrent vaginitis
 4. Systemic: fever, non-inflammatory arthralgias, hypokalemic paralysis, abdominal pain
- II. IMMUNOLOGIC ABNORMALITIES: presence of at least 1 of the following antibodies: anti-SSA, anti-SSB, high titer antinuclear antibody, rheumatoid factor
- III. OTHER ABNORMALITIES OR INVESTIGATIONS
 1. Biochemical: elevated serum amylase
 2. Hematologic: leukopenia, high sedimentation rate
 3. Immunologic: polyclonal hyperimmunoglobulinemia
 4. Renal: renal tubular acidosis
 5. Histologic proof of lymphocytic infiltration of salivary glands or other organs (i.e., liver)
 6. Objective documentation of ocular dryness (Bengal red staining or Schirmer test)
 7. Positive findings of parotid gland scintigraphy
- IV. Exclusion of all other autoimmune diseases

Diagnosis requires ≥4 criteria.

Table 163-1 Differential Diagnosis of Familial Autoinflammatory Syndromes

	Cryopyrin-Associated Periodic Syndrome (CAPS)					
	TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME (TRAPS)	FAMILIAL COLD AUTOINFLAMMATORY SYNDROME (FCAS)	MUCKLE-WELLS SYNDROME (MWS)	NEUROLOGIC CUTANEOUS AND ARTICULAR SYNDROME (CINCA)	DEFICIENCY OF IL-1 RECEPTOR ANTAGONIST (DIRA)	CHRONIC INFANTILE NEUROLOGIC DISEASE
Mode of Inheritance	Autosomal recessive	Autosomal recessive	Autosomal dominant	Autosomal dominant	Autosomal dominant	Autosomal recessive
Age at Onset (yr)	<20	<1	<20	<1	<20	Birth, <4 wk
Duration of attack (days)*	<2	4–6	>4	<2	1–2	Continuous
Cutaneous Involvement	Erysipelas-like erythema	Maculopapular rash	Morbilliform rash	Migratory rash, overlying area of myalgia	Cold-induced urticaria-like lesions	Urticaria-like lesions
Musculoskeletal Involvement	Monoarthritis common	Arthralgia, occasional oligoarthritis	Arthralgia common	Severe myalgia common; occasional frank monoarthritis	Athralgia common; occasional mild myalgia	Generalized pustulosis
Abdominal Involvement	Sterile peritonitis common	Splenomegaly, severe pain common	Splenomegaly, pain may occur	Severe pain common	None	May occur
Eye Involvement	Uncommon	Uncommon	Uncommon	Conjunctivitis and periocular edema common	Conjunctivitis	Papilledema with possible loss of vision, uveitis
Distinguishing Clinical Symptoms	Erysipelas-like erythema	Prominent cervical lymphadenopathy	Dysmorphic features, neurologic symptoms	Migratory nature of myalgia and rash, periocular edema	Cold-induced urticaria-like lesions	Conjunctivitis; sometimes optic nerve elevation
Gene Involved	MEFV	MVK	TNFRSF1A	CIAS1 = NLRP3	CIAS1 = NLRP3	IL-1RN
Protein Involved	Pyrin (marenostrin)	Mevalonate kinase	Mevalonate kinase	Type 1 tumor necrosis factor receptor	Cryopyrin	Cryopyrin

Note: For details on Blau syndrome, DIRA, and pyogenic sterile arthritis, pyoderma gangrenosum, and acne (PAPA) syndrome, see text.

*Duration may vary; this is a typical duration.

Modified from Hall KM, Shoham N, Chae JJ, et al: The expanding spectrum of systemic autoinflammatory disorders and their rheumatic manifestations, *Curr Opin Rheumatol* 15:61–69, 2003.

Table 163-1 Differential Diagnosis of Familial Autoinflammatory Syndromes

	Cryopyrin-Associated Periodic Syndrome (CAPS)					
	TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME (TRAPS)	FAMILIAL COLD AUTOINFLAMMATORY SYNDROME (FCAS)	MUCKLE-WELLS SYNDROME (MWS)	CUTANEOUS AND ARTICULAR SYNDROME (CINCA)	NEUROLOGIC DEFICIENCY OF IL-1 RECEPTOR ANTAGONIST (DIRA)	CHRONIC INFANTILE NEUROLOGIC AND ARTICULAR SYNDROME (CINCA)
Mode of Inheritance	Autosomal recessive	Autosomal recessive	Autosomal dominant	Autosomal dominant	Autosomal dominant	Autosomal recessive
Age at Onset (yr)	<20	<1	<20	<1	<20	Birth, <4 wk
Duration of attack (days)*	<2	4–6	>4	<2	1–2	Continuous
Cutaneous Involvement	Erysipelas-like erythema	Maculopapular rash	Morbilliform rash	Migratory rash, overlying area of myalgia	Cold-induced urticaria-like lesions	Urticaria-like lesions
Musculoskeletal Involvement	Monoarthritis common	Arthralgia, occasional oligoarthritis	Arthralgia common	Severe myalgia common; occasional frank monoarthritis	Athralgia common; occasional mild myalgia	Generalized pustulosis
Abdominal Involvement	Sterile peritonitis common	Splenomegaly, severe pain common	Splenomegaly, pain may occur	Severe pain common	None	May occur
Eye Involvement	Uncommon	Uncommon	Uncommon	Conjunctivitis and periorbital edema common	Conjunctivitis	Conjunctivitis; sometimes optic nerve elevation
Distinguishing Clinical Symptoms	Erysipelas-like erythema	Prominent cervical lymphadenopathy	Dysmorphic features, neurologic symptoms	Migratory nature of myalgia and rash, periorbital edema	Cold-induced urticaria-like lesions	Papilledema with possible loss of vision, uveitis
Gene Involved	MEFV	MVK	TNFRSF1A	CIAS1 = NLRP3	CIAS1 = NLRP3	IL-1RN
Protein Involved	Pyrin (marenostrin)	Mevalonate kinase	Mevalonate kinase	Type 1 tumor necrosis factor receptor	Cryopyrin	Cryopyrin

Note: For details on Blau syndrome, DIRA, and pyogenic sterile arthritis, pyoderma gangrenosum, and acne (PAPA) syndrome, see text.

*Duration may vary; this is a typical duration.

Modified from Hall KM, Shoham N, Chae JJ, et al: The expanding spectrum of systemic autoinflammatory disorders and their rheumatic manifestations, *Curr Opin Rheumatol* 15:61–69, 2003.

Chapter 163 ◆ Hereditary Periodic Fever Syndromes and Other Systemic Autoinflammatory Diseases 1195

Table 163-2 Clinical Grouping of Autoinflammatory Diseases by Fever and Skin Manifestations

1. Nonspecific maculopapular rashes with recurrent episodic fever and abdominal pain (the classic "periodic fever syndromes")
 - Recurrent fever attacks of short duration (typically <7 days)**
 - FMF: familial Mediterranean fever
 - HIDS: mevalonate kinase deficiency/hyperimmunoglobulinemia D with periodic fever syndrome
 - Recurrent fever attacks of longer duration (typically >7 days)**
 - TRAPS: TNF receptor-associated periodic fever syndrome
2. Neutrophilic urticaria (the cryopyrinopathies)
 - Recurrent fever attacks of short duration (typically <24 hr)**
 - CAPS/FCAS: familial cold autoinflammatory syndrome
 - CAPS/MWS: Muckle-Wells syndrome
 - Continuous low-grade fever**
 - CAPS/NOMID: neonatal onset multisystem inflammatory disease (NOMID)/chronic infantile neurologic cutaneous and articular syndrome (CINCA)
3. Granulomatous skin lesions and minimal or low-grade fever attacks
 - Blau syndrome/early-onset sarcoidosis (pediatric granulomatous arthritis)
4. Pustular skin rashes and episodic fever
 - With inflammatory bone disease**
 - DIRA: deficiency of interleukin-1 receptor antagonist
 - Majeed syndrome
 - With pyogenic arthritis**
 - PAPA: pyogenic arthritis, pyoderma gangrenosum, and acne syndrome
 - With inflammatory bowel disease**
 - Early-onset inflammatory bowel disease
 - Without other organ involvement**
 - DITRA: deficiency of interleukin-36-receptor antagonist
 - CAMPS: CARD14-mediated psoriasis
5. Atypical neutrophilic dermatosis with histiocytic-like infiltrate
 - PRAAS: proteasome associated autoinflammatory syndromes
6. Syndromes with autoinflammation and immunodeficiency
 - PLAID: PLC γ 2-associated antibody deficiency and immune dysregulation
 - APLAID: autoinflammation and PLC γ 2-associated antibody deficiency and immune dysregulation
 - HOIL-1 deficiency

From Almeida de Jesus A, Goldbach-Mansky R: Monogenic autoinflammatory diseases: concept and clinical manifestations. Clin Immunol 147:155-174, 2013, Table 1.

Table 163-3 Autoinflammatory Bone Disorders

	CRMO	Majeed Syndrome	DIRA	Cherubism	cmo and lupo Mice
Ethnicity	Worldwide, but mostly European	Arabic	European, Puerto Rican, Arabic	Worldwide	Occurs in various backgrounds
Fever	Uncommon	Common	Uncommon	No	Not assessed
Sites of osseous involvement	Metaphyses of long bones > vertebrae, clavicle, sternum, pelvis, others	Similar to CRMO	Anterior rib ends, metaphyses of long bones, vertebrae, others	Mandible > maxilla Rarely ribs	Vertebrae hind > forefoot
Extraosseous manifestations	PPP, psoriasis, IBD, others	Dyserythropoietic anemia, Sweet syndrome, HSM, growth failure	Generalized pustulosis, nail changes, lung disease, vasculitis	Cervical lymphadenopathy	Dermatitis, extramedullary hematopoiesis, splenomegaly
Family history of inflammatory disorders	Psoriasis, PPP, arthritis, IBD, others	Psoriasis in some obligate carriers	No known associations	No known associations	Heterozygotes normal
Inheritance	Not clear	Autosomal recessive	Autosomal recessive	Autosomal dominant; incomplete penetrance	Autosomal recessive
Gene defect	Unknown	<i>LPIN2</i>	<i>IL1RN</i>	<i>SH3BP2</i> >> <i>PTPN11</i>	<i>PstPIP2</i>
Protein name	?	Lipin2	IL-1Ra	SH3BP2	PSTPIP2 (a.k.a. MAYP)
Protein function	?	Fat metabolism: (PAP enzyme activity), ↑ message to oxidative stress, ? role in mitosis	Antagonist of IL-1 receptor	↑ Myeloid cell response to M-CSF and RANKL, ↑ TNF- α expression in macrophages	Macrophage proliferation, macrophage recruitment to sites of inflammation, cytoskeletal function
Cytokine abnormalities	↑ serum TNF- α	Not tested	↑ IL-1 α , IL-1 β , MIP-1 α , TNF- α , IL-8, IL-6 ex vivo monocyte assay; skin reveals ↑ IL-17 staining	↑ serum TNF- α in mouse model	cmo: ↑ serum IL-6, MIP-1 α , TNF- α , CSF-1, IP-10 Lupo: ↑ serum MIP-1 α , IL-4, RANTES, TGF- β

CRMO, chronic recurrent multifocal osteomyelitis; CSF, colony-stimulating factor; DIRA, deficiency of interleukin-1 receptor antagonist; HSM, hepatosplenomegaly; IBD, inflammatory bowel disease; IL, interleukin; IL-1Ra, interleukin-1 receptor antagonist; IP-10, interferon-inducible protein-10; M-CSF, macrophage-colony-stimulating factor; MIP-1 α , macrophage inflammatory protein-1 α ; PAP, phosphatidylethanolamine N-acetylgalactosaminidase; PPP, palmar-plantar pustulosis; PSTPIP2, proline-serine-threonine phosphatase interacting protein; RANKL, receptor activator of nuclear factor- κ B ligand; RANTES, regulated upon activation, normal T-cell expressed and secreted; SH3BP2, SH3 binding protein 2; TGF, transforming growth factor; TNF- α , tumor necrosis factor α .

From Ferguson PJ, Laxer RM: Autoinflammatory bone disorders. In Cassidy JT, Petty RE, Laxer RM, et al, editors: Textbook of pediatric rheumatology, ed 6, Philadelphia, 2010, Saunders, Table 44-2.

Chapter 163 ◆ Hereditary Periodic Fever Syndromes and Other Systemic Autoinflammatory Diseases 1197

Table 163-4 Clues That May Assist in the Diagnosis of Autoinflammatory Syndromes	
AGE OF ONSET	
At birth	NOMID, DIRA, FCAS
Infancy and 1st yr of life	HIDS, FCAS, NLRP12
Toddler	PFAPA
Late childhood	PAPA
Most common of autoinflammatory syndromes to have onset in adulthood	TRAPS, DITRA
Variable (mostly in childhood)	All others
ETHNICITY AND GEOGRAPHY	
Armenians, Turks, Italian, Sephardic Jews	FMF
Arabs	FMF, DITRA (Arab Tunisian)
Dutch, French, German, Western Europe	HIDS, MWS, NLRP12
United States	FCAS
Can occur in blacks (West Africa origin)	TRAPS
Eastern Canada, Puerto Rico	DIRA
Worldwide	All others
TRIGGERS	
Vaccines	HIDS
Cold exposure	FCAS, NLRP12
Stress, menses	FMF, TRAPS, MWS, PAPA, DITRA
Minor trauma	PAPA, MWS, TRAPS, HIDS
Exercise	FMF, TRAPS
Pregnancy	DITRA
Infections	All, especially DITRA
ATTACK DURATION	
<24 h	FCAS, FMF
1–3 d	FMF, MWS, DITRA (fever)
3–7 d	HIDS, PFAPA
>7 d	TRAPS, PAPA
Almost always "in attack"	NOMID, DIRA
INTERVAL BETWEEN ATTACKS	
3–6 wk	PFAPA, HIDS
>6 wk	TRAPS
Mostly unpredictable	All others
Truly periodic	PFAPA, cyclic neutropenia
USEFUL LABORATORY TESTS	
Acute-phase reactants must be normal between attacks	PFAPA
Urine mevalonic acid in attack	HIDS
IgD > 100 mg/dL	HIDS
Proteinuria (amyloidosis)	FMF, TRAPS, MWS, NOMID
RESPONSE TO THERAPY	
Corticosteroid dramatic	PFAPA
Corticosteroid partial	TRAPS, FCAS, MWS, NOMID, PAPA*
Colchicine	FMF, PFAPA (30% effective)
Cimetidine	PFAPA (30% effective)
Etanercept	TRAPS, FMF arthritis
Anti-IL-1 dramatic	DIRA (anakinra), FCAS, MWS, NOMID, PFAPA
Anti-IL-1 mostly	TRAPS, FMF
Anti-IL-1 partial	HIDS, PAPA

DIRA, deficiency of the IL-1 receptor antagonist; DITRA, deficiency of the IL-36 receptor antagonist (generalized pustular psoriasis); FCAS, familial cold autoinflammatory syndrome; FMF, familial Mediterranean fever; HIDS, hyperimmunoglobulinemia D syndrome; IL, interleukin; MWS, Muckle-Wells syndrome; NLRP, nucleotide oligomerization domain-like receptor family, pyrin domain; NOMID, neonatal-onset multisystem inflammatory disorder; PAPA, pyogenic sterile arthritis, pyoderma gangrenosum, acne syndrome; PFAPA, periodic fever, aphthous stomatitis, pharyngitis, adenitis; TRAPS, tumor necrosis factor receptor-associated periodic syndrome.

*For intraarticular steroids.

From Hashkes PJ, Toker O: Autoinflammatory syndromes. *Pediatr Clin North Am* 59:447–470, 2012, Table 2.

Table 163-5 Differential Diagnosis of Periodic Fever	
1	Hereditary (see <i>Table 163-1</i>)
2	Nonhereditary
a	Infectious <ul style="list-style-type: none"> i Hidden infectious focus (e.g., aortoenteric fistula, Caroli disease) ii Recurrent reinfection (e.g., chronic meningococcemia, host defense defect) iii Specific infection (e.g., Whipple disease, malaria)
b	Noninfectious inflammatory disorder, e.g.: <ul style="list-style-type: none"> i Adult-onset Still disease ii Juvenile chronic rheumatoid arthritis iii Periodic fever, aphthous stomatitis, pharyngitis, and adenitis iv Schnitzler syndrome v Behçet syndrome vi Crohn disease vii Sarcoidosis viii Extrinsic alveolitis ix Humidifier lung, polymer fume fever
c	Neoplastic <ul style="list-style-type: none"> i Lymphoma (e.g., Hodgkin disease, angioimmunoblastic lymphoma) ii Solid tumor (e.g., pheochromocytoma, myxoma, colon carcinoma)
d	Vascular (e.g., recurrent pulmonary embolism)
e	Hypothalamic
f	Psychogenic periodic fever
g	Factitious or fraudulent

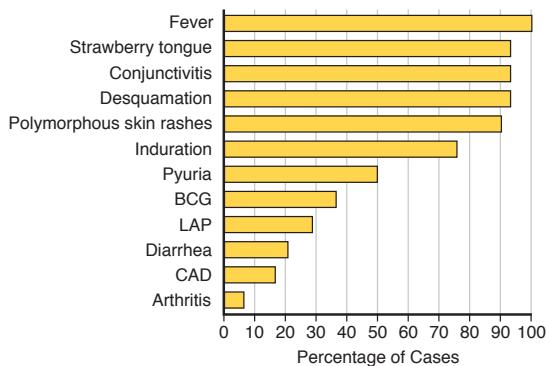


Figure 166-1 Clinical symptoms and signs of Kawasaki disease. A summary of the clinical features from 110 cases of Kawasaki disease seen in Kaohsiung, Taiwan. LAP, lymphadenopathy in head and neck area; BCG, reactivation of bacille Calmette-Guérin inoculation site; CAD, coronary artery dilation, defined by an internal diameter >3 mm. (From Wang CL, Wu YT, Liu CA, et al: Kawasaki disease: infection, immunity and genetics, *Pediatr Infect Dis J* 24:998–1004, 2005.)

Table 166-2 Differential Diagnosis of Kawasaki Disease

VIRAL INFECTIONS

- Adenovirus
- Enterovirus
- Measles
- Epstein-Barr virus
- Cytomegalovirus

BACTERIAL INFECTIONS

- Scarlet fever
- Rocky Mountain spotted fever
- Leptospirosis
- Bacterial cervical lymphadenitis
- Meningococcemia

RHEUMATOLOGIC DISEASE

- Systemic-onset juvenile idiopathic arthritis
- Behçet disease

OTHER

- Toxic shock syndromes
- Staphylococcal scalded skin syndrome
- Drug hypersensitivity reactions
- Stevens-Johnson syndrome

Table 167-5 Classification Criteria for Henoch-Schönlein Purpura*

AMERICAN COLLEGE OF RHEUMATOLOGY

CLASSIFICATION CRITERIA†

Two of the following criteria must be present:

- Palpable purpura
- Age at onset ≤20 yr
- Bowel angina (postprandial abdominal pain, bloody diarrhea)
- Biopsy demonstrating intramural granulocytes in small arterioles and/or venules

EUROPEAN LEAGUE AGAINST RHEUMATISM/PEDIATRIC RHEUMATOLOGY EUROPEAN SOCIETY CRITERIA‡

Palpable purpura (in absence of coagulopathy or thrombocytopenia) and 1 or more of the following criteria must be present:

- Abdominal pain (acute, diffuse, colicky pain)
- Arthritis or arthralgia
- Biopsy of affected tissue demonstrating predominant immunoglobulin A deposition
- Renal involvement (proteinuria >3 grams/24 hr), hematuria or red cell casts

*Classification criteria are developed for use in research and not validated for clinical diagnosis.

†Developed for use in adult and pediatric populations. Adapted from Mills JA, Michel BA, Bloch DA, et al: The American College of Rheumatology 1990 criteria for classification of Henoch-Schönlein purpura, *Arthritis Rheum* 33:1114–1121, 1990.

Table 166-1 Clinical and Laboratory Features of Kawasaki Disease

EPIDEMIOLOGIC CASE DEFINITION (CLASSIC CLINICAL CRITERIA)*

Fever persisting at least 5 days†

Presence of at least 4 principal features:

Changes in extremities:

Acute: Erythema of palms, soles; edema of hands, feet

Subacute: Periungual peeling of fingers, toes in weeks 2 and 3

Polymorphous exanthem

Bilateral bulbar conjunctival injection without exudate

Changes in lips and oral cavity: erythema, lip cracking, strawberry tongue, diffuse injection of oral and pharyngeal mucosa

Cervical lymphadenopathy (>1.5 cm diameter), usually unilateral

Exclusion of other diseases with similar findings‡

OTHER CLINICAL AND LABORATORY FINDINGS

Cardiovascular findings:

Congestive heart failure, myocarditis, pericarditis, valvular regurgitation

Coronary artery abnormalities

Aneurysms of medium-size noncoronary arteries

Raynaud phenomenon

Peripheral gangrene

Musculoskeletal system:

Arthritis, arthralgias

Gastrointestinal tract:

Diarrhea, vomiting, abdominal pain

Hepatic dysfunction

Hydrops of gallbladder

Central nervous system:

Extreme irritability

Aseptic meningitis

Sensorineural hearing loss

Genitourinary system:

Urethritis/meatitis

Other findings:

Erythema, induration at bacille Calmette-Guérin inoculation site

Anterior uveitis (mild)

Desquamating rash in groin

LABORATORY FINDINGS IN ACUTE KAWASAKI DISEASE

Leukocytosis with neutrophilia and immature forms

Elevated erythrocyte sedimentation rate

Elevated C-reactive protein

Anemia

Abnormal plasma lipids

Hypoalbuminemia

Hyponatremia

Thrombocytosis after week 1§

Sterile pyuria

Elevated serum transaminases

Elevated serum gamma glutamyl transpeptidase

Pleocytosis of cerebrospinal fluid

Leukocytosis in synovial fluid

*Patients with fever at least 5 days and <4 principal criteria can be diagnosed with Kawasaki disease when coronary artery abnormalities are detected by 2-dimensional echocardiography or angiography.

†In the presence of ≥4 principal criteria, Kawasaki disease diagnosis can be made on day 4 of illness. Experienced clinicians who have treated many patients with Kawasaki disease may establish diagnosis before day 4.

‡See differential diagnosis (Table 166-2).

§Some infants present with thrombocytopenia and disseminated intravascular coagulation.

Table 166-3 Treatment of Kawasaki Disease**ACUTE STAGE**

- Intravenous immunoglobulin 2 g/kg over 10-12 hr and
- Aspirin 80-100 mg/kg/day divided every 6 hr orally until patient isafebrile for at least 48 hr

CONVALESCENT STAGE

- Aspirin 3-5 mg/kg once daily orally until 6-8 wk after illness onset if normal coronary findings throughout course

LONG-TERM THERAPY FOR PATIENTS WITH CORONARY ABNORMALITIES

- Aspirin 3-5 mg/kg once daily orally
- Clopidogrel 1 mg/kg/day (maximum: 75 mg/day)
- Most experts add warfarin or low-molecular-weight heparin for those patients at particularly high risk of thrombosis

ACUTE CORONARY THROMBOSIS

- Prompt fibrinolytic therapy with tissue plasminogen activator or other thrombolytic agent under supervision of a pediatric cardiologist

Table 167-1 Common Disease Associations with Antibodies to Neutrophil Cytoplasmic Antigens

ANTIGEN	ANCA PATTERN	DISEASE ASSOCIATION	FREQUENCY (%)
PR3	cANCA	Wegener granulomatosis Churg-Strauss	30 to 90 25 to 50
MPO	pANCA	Microscopic polyarteritis Ulcerative colitis Sclerosing cholangitis Crohn disease	25 to 75 40 to 80 65 to 85 10 to 40
BPI	ANCA	Cystic fibrosis	80 to 90
Actin	pANCA	Autoimmune hepatitis type 1	70 to 75

ANCA, Antibodies directed at neutrophil cytoplasmic antigen; BPI, Bactericidal permeability increasing protein. cANCA, cytoplasmic ANCA; pANCA, perinuclear ANCA.

From Cabral D, Benseler S: Granulomatous vasculitis, microscopic polyangiitis and primary angiitis of the central nervous system. In Cassidy JT, Petty RE, Laxer RM, Lindsley CB, editors, Textbook of pediatric rheumatology, ed 6, Philadelphia, 2011, Elsevier/Saunders, Table 34-3, p. 526.

Table 167-6 Proposed Classification Criteria for Pediatric-Onset Takayasu Arteritis

Angiographic abnormalities (conventional, CT, or magnetic resonance angiography) of the aorta or its main branches and at least one of the following criteria:

- Decreased peripheral artery pulse(s) and/or claudication of extremities
- Blood pressure difference between arms or legs of >10 mm Hg
- Bruits over the aorta and/or its major branches
- Hypertension (defined by childhood normative data)
- Elevated acute phase reactant (erythrocyte sedimentation rate or C-reactive protein)

Table 167-2 Classification of Childhood Vasculitis

- I. Predominantly Large Vessel Vasculitis
 - Takayasu arteritis
- II. Predominantly Medium Vessel Vasculitis
 - Childhood polyarteritis nodosa
 - Cutaneous polyarteritis nodosa
 - Kawasaki disease
- III. Predominantly Small Vessel Vasculitis
 - A. Granulomatous:
 - Granulomatosis with polyangiitis (Wegener granulomatosis)*
 - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)*
 - B. Nongranulomatous:
 - Microscopic polyangiitis*
 - Henoch-Schönlein purpura
 - Isolated cutaneous leukocytoclastic vasculitis
 - Hypocomplementemic urticarial vasculitis
- IV. Other Vasculitides
 - Behçet disease
 - Vasculitis secondary to infection (including hepatitis B-associated polyarteritis nodosa), malignancies, and drugs, including hypersensitivity vasculitis
 - Vasculitis associated with connective tissue disease
 - Isolated vasculitis of the central nervous system
 - Cogan syndrome
 - Unclassified

*Associated with antineutrophil cytoplasmic antibody.

Adapted from Ozen S, Pistorio A, Iusan SM, et al: EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis 69:798-806, 2010.

Table 167-3 Features That Suggest a Vasculitic Syndrome**CLINICAL FEATURES**

- Fever, weight loss, fatigue of unknown origin
Skin lesions (palpable purpura, vasculitic urticaria, livedo reticularis, nodules, ulcers)
Neurologic lesions (headache, mononeuritis multiplex, focal central nervous system lesions)
Arthralgia or arthritis, myalgia, or myositis
Serositis
Hypertension
Pulmonary infiltrates or hemorrhage

LABORATORY FEATURES

- Increased erythrocytes sedimentation rate or C-reactive protein level
Leukocytosis, anemia
Eosinophilia
Antineutrophil cytoplasmic antibodies
Elevated factor VIII-related antigen (von Willebrand factor)
Cryoglobulins
Circulating immune complexes
Hematuria, proteinuria, elevated serum creatinine

From Cassidy JT, Petty RE: Textbook of pediatric rheumatology, ed 5, Philadelphia, 2005, Elsevier/Saunders.

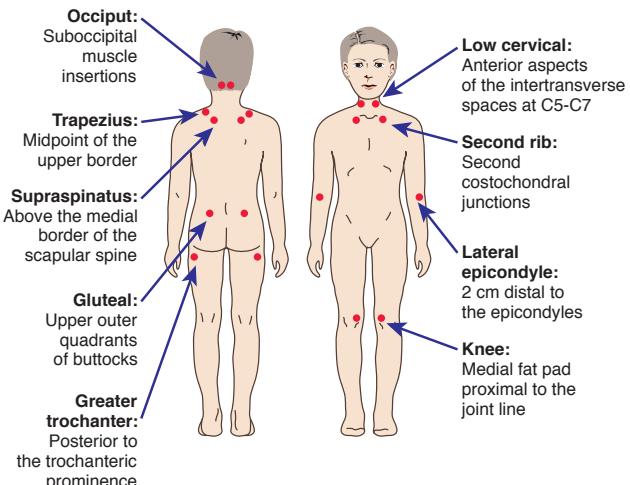


Figure 168-1 Fibromyalgia tender points.

1216 Part XVI ◆ Rheumatic Diseases of Childhood

Table 167-4 Clinical and Pathologic Characteristics of Some Vasculitides in Childhood

SYNDROME	FREQUENCY	VESSELS AFFECTED	CHARACTERISTIC PATHOLOGY
POLYARTERITIS			
Polyarteritis nodosa	Rare	Medium-size and small muscular arteries and sometimes arterioles	Focal segmental (often near bifurcations); fibrinoid necrosis; gastrointestinal, renal microaneurysms; lesions at various stages of evolution
Kawasaki disease	Common	Coronary and other muscular arteries	Thrombosis, fibrosis, aneurysms, especially of coronary vessels
LEUKOCYTOCLASTIC VASCULITIS			
Henoch-Schönlein purpura	Common	Arterioles and venules, often small arteries and veins	Leukocytoclasia; mixed cells, eosinophils, immunoglobulin A deposits in affected vessels
Hypersensitivity angitis	Rare	Arterioles and venules	Leukocytoclastic or lymphocytic, varying eosinophils, occasionally granulomatous; widespread lesions at same stage of evolution
GRANULOMATOUS VASCULITIS			
Granulomatosis with polyangiitis	Rare	Small arteries and veins, occasionally larger vessels	Upper and lower respiratory tract, necrotizing granulomata glomerulonephritis
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)	Rare	Small arteries and veins, often arterioles and venules	Necrotizing extravascular granulomata; lung involvement; eosinophilia
GIANT CELL ARTERITIS			
Takayasu arteries	Uncommon	Large arteries	Granulomatous inflammation, giant cells; aneurysms, dissection
Temporal arteritis	Rare	Medium-size and large arteries	Granulomatous inflammation, giant cell arteritis

Table 167-8 EULAR/PReS Classification Criteria for Pediatric-Onset Granulomatosis with Polyangiitis*

Histopathology showing granulomatous inflammation
Upper airway involvement
Laryngeal, tracheal or bronchial involvement
ANCA positivity
Renal involvement
Proteinuria, hematuria, red blood cell casts, necrotizing pauci-immune glomerulonephritis

*Diagnosis requires 3 of 6 criteria.

Table 167-7 Proposed Classification Criteria for Pediatric-Onset Polyarteritis Nodosa*

Histopathology	Necrotizing vasculitis in medium or small arteries
Angiographic abnormalities	Angiography showing aneurysm, stenosis, or occlusion of a medium or small size artery not from a noninflammatory cause
Cutaneous findings	Livedo reticularis, tender subcutaneous nodules, superficial skin ulcers, deep skin ulcers, digital necrosis, nail bed infarctions or splinter hemorrhages
Muscle involvement	Myalgia or muscle tenderness
Hypertension	Systolic or diastolic blood pressure >95th percentile for height
Peripheral neuropathy	Sensory peripheral neuropathy, motor mononeuropathy multiplex
Renal involvement	Proteinuria (>300 mg/24 hr equivalent), hematuria or red blood cell casts, impaired renal function (glomerular filtration rate <50% normal)

*The presence of all 5 criteria provides 89.6% sensitivity and 99.6% specificity for the diagnosis of childhood onset polyarteritis nodosa.

Table 167-9 Differential Diagnostic Features of Small Vessel Vasculitis

FEATURE	HENOCH-SCHÖNLEIN PURPURA	GRANULOMATOSIS WITH POLYANGIITIS	CHURG-STRAUSS SYNDROME	MICROSCOPIC POLYANGIITIS
Signs and symptoms of small vessel vasculitis*	+	+	+	+
Immunoglobulin A-dominant immune deposits	+	-	-	-
Circulating antineutrophil cytoplasmic antibodies	-	+(PR3)	+(MPO > PR3)	+(MPO)
Necrotizing vasculitis	-	+	+	+
Granulomatous inflammation	-	+	+	-
Asthma and eosinophilia	-	-	+	-

MPO, myeloperoxidase-reactive antibodies; PR3, proteinase 3-reactive antibodies; +, presence; -, absent.

*Signs and symptoms of small vessel vasculitis include purpura, other rash, arthralgias, arthritis, and constitutional symptoms.

1226 Part XVI ◆ Rheumatic Diseases of Childhood

Table 168-2 Common Musculoskeletal Pain Syndromes in Children by Anatomic Region

ANATOMICAL REGION	PAIN SYNDROMES	
Shoulder	Impingement syndrome	
Elbow	Little League elbow Avulsion fractures Osteochondritis dissecans	Tennis elbow Panner disease
Arm	Localized hypermobility syndrome Complex regional pain syndrome	
Pelvis and hip	Avulsion injuries Legg-Calvé-Perthes syndrome	Slipped capital femoral epiphysis Congenital hip dysplasia
Knee	Osteochondritis dissecans Osgood-Schlatter disease Sinding-Larsen syndrome	Patellofemoral syndrome Malalignment syndromes
Leg	Growing pains Complex regional pain syndrome Localized hypermobility syndrome	Shin splints Stress fractures Compartment syndromes
Foot	Plantar fasciitis Tarsal coalition Stress fractures	Achilles tendonitis Juvenile bunion
Spine	Musculoskeletal strain Spondylolisthesis Spondylolysis	Scoliosis Scheuermann disease (kyphosis) Low back pain
Generalized	Hypermobility syndrome Juvenile fibromyalgia Generalized pain syndrome	

Table 168-1 Potential Indicators of Benign Versus Serious Causes of Musculoskeletal Pain

CLINICAL FINDING	BENIGN CAUSE OF MUSCULOSKELETAL PAIN	SERIOUS CAUSE OF MUSCULOSKELETAL PAIN
Effects of rest versus activity on pain	Relieved by rest and worsened by activity	Relieved by activity and present at rest
Time of day pain occurs	End of the day and nights	Morning*
Objective joint swelling	No	Yes
Joint characteristics	Hypermobile/normal	Stiffness, limited range of motion
Bony tenderness	No	Yes
Muscle strength	Normal	Muscle weakness
Growth	Normal growth pattern or weight gain	Poor growth and/or weight loss
Constitutional symptoms (e.g., fever, malaise)	Fatigue without other constitutional symptoms	Yes
Lab findings	Normal CBC, ESR, CRP	Abnormal CBC, raised ESR and CRP
Radiographic findings	Normal	Effusion, osteopenia, radiolucent metaphyseal lines, joint space loss, bony destruction

CBC, complete blood count; CRP, C-reactive protein level; ESR, erythrocyte sedimentation rate.

*Cancer pain is often severe and worst at night.

Adapted from Malleson PN, Beauchamp RD: *Diagnosing musculoskeletal pain in children*. CMAJ 165:183–188, 2001.**Table 168-3** Definition of “Growing Pains”

	INCLUSIONS	EXCLUSIONS
Nature of pain	Intermittent; some pain-free days and nights, deep aching, cramping	Persistent; increasing intensity, pain during the day
Unilateral or bilateral	Bilateral	Unilateral
Location of pain	Anterior thigh, calf, posterior knee—in muscles	Articular, back, or groin pain
Onset of pain	Late afternoon or evening	Pain still present next morning
Physical findings	Normal	Swelling, erythema, tenderness; local trauma or infection; reduced joint range of motion; limping, fever, weight loss, mass
Laboratory findings	Normal	Objective evidence of abnormalities; increased erythrocyte sedimentation rate, C-reactive protein, abnormal complete blood count, radiography, bone scan or MRI

Infectious Diseases

1246 Part XVII ◆ Infectious Diseases

Table 172-3 Currently* Available Vaccines in the United States by Type			
PRODUCT	TYPE	PRODUCT	TYPE
Anthrax vaccine adsorbed	Cell-free filtrate of components including protective antigen	Japanese encephalitis vaccine	Inactivated whole virus that is purified
Bacille Calmette-Guérin (BCG) vaccine	Live-attenuated mycobacterial strain used to prevent tuberculosis in very limited circumstances	Measles, mumps, rubella (MMR) vaccine	Live-attenuated viruses
Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine	Toxoids of diphtheria and tetanus and purified and detoxified components from <i>Bordetella pertussis</i>	Measles, mumps, rubella, varicella (MMRV) vaccine	Live-attenuated viruses
DTaP-hepatitis B-inactivated polio vaccine (DTaP-HepB-IPV)	DTaP with hepatitis B surface antigen (HBsAg) produced through recombinant techniques in yeast with inactivated whole polioviruses	Meningococcal conjugate vaccine against serogroups A, C, W135, and Y (MCV4)	Polysaccharide from each serogroup conjugated to diphtheria toxoid or CRM 197
DTaP with IPV and Hib (DTaP-IPV/Hib)	DTaP with inactivated whole polioviruses and Hib polysaccharide conjugated to tetanus toxoid	Meningococcal conjugate vaccine against serogroups C and Y and Hib conjugate vaccine	Polysaccharide from each serogroup conjugated to diphtheria toxoid and Hib polysaccharide conjugated to tetanus toxoid
DTaP and inactivated polio vaccine (DTaP-IPV)	DTaP with inactivated whole polioviruses	Meningococcal polysaccharide vaccine against serogroups A, C, W135, and Y (MPSV4)	Polysaccharides from each of the serogroups
Hib conjugate vaccine (Hib)	Polysaccharide conjugated to either tetanus toxoid or meningococcal group B outer membrane protein	Pneumococcal conjugate vaccine (13 valent) (PCV13)	Pneumococcal polysaccharides conjugated to a nontoxic form of diphtheria toxin CRM197 Contains 13 serotypes that accounted for >80% of invasive disease in young children prior to vaccine licensure
Hepatitis A vaccine (HAV)	Inactivated whole virus	Pneumococcal polysaccharide vaccine (23 valent) (PPSV23)	Pneumococcal polysaccharides of 23 serotypes responsible for 85-90% of bacteremic disease in the United States
Hepatitis A-hepatitis B vaccine (HAV-HBV)	Combined hepatitis A and B vaccine	Poliomyelitis (inactivated, enhanced potency) (IPV)	Inactivated whole virus
Hepatitis B vaccine (HBV)	HBsAg produced through recombinant techniques in yeast	Rabies vaccines (human diploid and purified chick embryo cell)	Inactivated whole virus
Hepatitis B-Hib vaccine (Hib-HBV)	Combined hepatitis B-Hib vaccine; the Hib component is polysaccharide conjugated to meningococcal group B outer membrane protein	Rotavirus vaccines (RV5 and RV1)	Bovine rotavirus pentavalent vaccine (RV5) live reassortment attenuated virus, and human live-attenuated virus (RV1)
Human papillomavirus vaccine (bivalent) (HPV2), (quadrivalent) (HPV4), and 9-valent (HPV9)	The L1 capsid proteins of HPV types 6, 11, 16, and 18 to prevent cervical cancer and genital warts (HPV4) and types 16 and 18 to prevent cervical cancer (HPV2); HPV9 also contains types 31, 33, 45, 52, and 58.	Smallpox vaccine	Vaccinia virus, an attenuated poxvirus that provides cross-protection against smallpox
Influenzavirus vaccine inactivated (IIV)	Available either as trivalent (A/H ₃ N ₂ , A/H ₁ N ₁ , and B) split and purified inactivated vaccines containing the hemagglutinin (H) and neuraminidase (N) of each type or as quadrivalent preparations (which include representative strains from 2 B-lymphocyte clades in addition to the 2 influenza A strains in trivalent inactivated influenza vaccine)	Tetanus and diphtheria toxoids, adsorbed (Td, adult use)	Tetanus toxoid plus a reduced quantity of diphtheria toxoid compared to diphtheria toxoid used for children <7 yr of age
Influenzavirus vaccine live, intranasal (LAIV)	Live-attenuated, temperature-sensitive, cold-adapted trivalent vaccine containing the H and N genes from the wild strains reassorted to have the 6 other genes from the cold-adapted parent, only available as quadrivalent preparation	Tetanus and diphtheria toxoids adsorbed plus acellular pertussis (Tdap) vaccine	Tetanus toxoid plus a reduced quantity of diphtheria toxoid plus acellular pertussis vaccine to be used in adolescents and adults and in children 7 through 9 yr of age who have not been appropriately immunized with DTaP
		Typhoid vaccine (polysaccharide)	Vi capsular polysaccharide of <i>Salmonella typhi</i>
		Typhoid vaccine (oral)	Live-attenuated Ty21a strain of <i>S. typhi</i>
		Varicella vaccine	Live-attenuated Oka strain
		Yellow fever vaccine	Live-attenuated 17D strain

*As of January 2015.

Data from Centers for Disease Control and Prevention: U.S. vaccine names. <http://www.cdc.gov/vaccines/about/terms/USvaccines.html>

1244 Part XVII ◆ Infectious Diseases

PRODUCT	MAJOR INDICATIONS
Immunoglobulin for intramuscular injection	Replacement therapy in primary immunodeficiency disorders Hepatitis A prophylaxis Measles prophylaxis
Intravenous immunoglobulin (IVIG)	Replacement therapy in primary immune-deficiency disorders Kawasaki disease Pediatric HIV infection Hypogammaglobulinemia in chronic B-lymphocyte lymphocytic leukemia Immune-mediated thrombocytopenia Hematopoietic cell transplantation in adults to prevent graft-versus-host disease and infection May be useful in a variety of other conditions
Hepatitis B immunoglobulin (IM)	Postexposure prophylaxis Prevention of perinatal infection in infants born to hepatitis B surface antigen-positive mothers
Rabies immunoglobulin (IM)	Postexposure prophylaxis
Tetanus immunoglobulin (IM)	Wound prophylaxis Treatment of tetanus
Varicella-zoster immunoglobulin (IM) or IVIG	Postexposure prophylaxis of susceptible people at high risk for complications from varicella
Cytomegalovirus IVIG	Prophylaxis of disease in seronegative transplant recipients
Subcutaneous immunoglobulin	Treatment of patients with primary immunodeficiencies
Vaccinia immunoglobulin (IV)	Prevent or modify serious adverse events following smallpox vaccination caused by vaccinia replication
Botulism IVIG human	Treatment of infant botulism
Diphtheria antitoxin, equine	Treatment of diphtheria
Heptavalent botulinum antitoxin against all 7 (A-G) botulinum toxin types	Treatment of food and wound botulism
Palivizumab (monoclonal antibody) (IM)	Prophylaxis for infants against respiratory syncytial virus (see Chapter 260)

**Figure 172-2 Recommended immunization schedule for persons aged 0 through 18 years—United States, 2015.
(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 172-3].)**

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 172-2. To determine minimum intervals between doses, see the catch-up schedule (Figure 172-3). School entry and adolescent vaccine age groups are shaded.

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 ¹ (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 ⁷ (PPSV23)																
Inactivated poliovirus ⁸ (IPV: <18 yrs)			1 st dose	2 nd dose		3 rd dose					4 th dose					
Influenza ⁹ (IIV; LAIV) 2 doses for some; See footnote 8							Annual vaccination (IIV only) 1 or 2 doses			Annual vaccination (LAIV or IIV) 1 or 2 doses			Annual vaccination (LAIV or IIV) 1 dose only			
Measles, mumps, rubella ⁹ (MMR)					See footnote 9		1 st dose			2 nd dose						
Varicella ¹⁰ (VAR)							1 st dose			2 nd dose						
Hepatitis A ¹¹ (HepA)							2-dose series, See footnote 11									
Human papillomavirus ¹² (HPV2: females only; HPV4: males and females)													(3-dose series)			
Meningococcal ¹³ (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)					See footnote 13							1 st dose			Booster	

Range of recommended ages for all children 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 Event Reporting System (VAERS) online (<http://www.vaers.hrsa.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 Academy of Family Physicians (<http://www.aafp.org>), and the American College of Obstetricians and Gynecologists (<http://www.acog.org>).

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

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 172-3.

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:

- If Rotarix is used, administer a 2-dose series at 2 and 4 months of age.
- If RotaTeq is used, administer a 3-dose series at ages 2, 4, and 6 months.
- 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 172-3.

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.

Figure 172-2 Recommended immunization schedule for persons aged 0 through 18 yr—United States, 2015. (From Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>)

Continued

3. Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine (cont'd)**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 172-2.

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 172-3.

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/r6301.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 172-3. 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/r6301.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 complement component 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(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 172-3.

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 172-3.**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>.

Figure 172-2, cont'd

**Figure 172-2 Recommended immunization schedule for persons aged 0 through 18 years—United States, 2015.
(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 172-3].)**

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 172-2. To determine minimum intervals between doses, see the catch-up schedule (Figure 172-3). School entry and adolescent vaccine age groups are shaded.

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 ¹ (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 ⁷ (PPSV23)																	
Inactivated poliovirus ⁸ (IPV; <18 yrs)			1 st dose	2 nd dose		3 rd dose					4 th dose						
Influenza ⁹ (IIV; LAIV) 2 doses for some; See footnote 8							Annual vaccination (IIV only) 1 or 2 doses			Annual vaccination (LAIV or IIV) 1 or 2 doses			Annual vaccination (LAIV or IIV) 1 dose only				
Measles, mumps, rubella ⁹ (MMR)					See footnote 9		1 st dose			2 nd dose							
Varicella ¹⁰ (VAR)							1 st dose			2 nd dose							
Hepatitis A ¹¹ (HepA)							2-dose series, See footnote 11										
Human papillomavirus ¹² (HPV2; females only; HPV4; males and females)													(3-dose series)				
Meningococcal ¹³ (MenB; MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)					See footnote 13							1 st dose			Booster		
	Range of recommended ages for all children	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 Event Reporting System (VAERS) online (<http://www.vaers.hrsa.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 Academy of Family Physicians (<http://www.aafp.org>), and the American College of Obstetricians and Gynecologists (<http://www.acog.org>).

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

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 172-3.

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:

- If Rotarix is used, administer a 2-dose series at 2 and 4 months of age.
- If RotaTeq is used, administer a 3-dose series at ages 2, 4, and 6 months.
- 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 172-3.

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.

Figure 172-2 Recommended immunization schedule for persons aged 0 through 18 yr—United States, 2015. (From Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>)

Continued

3. Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine (cont'd)**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 172-2.

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 172-3.

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/r6301.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 172-3. 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/r6301.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 complement component 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 172-3.

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 172-3.**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>.

Figure 172-2, cont'd

- 8. Influenza vaccines (cont'd)**
- 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:**
- Institute 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 172-3.
- 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):
 - Menveo
 - Children who initiate vaccination at 8 weeks through 6 months:* Administer doses at 2, 4, 6, and 12 months of age.
 - 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.
 - Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart.
 - MenHibrix
 - Children 6 weeks through 18 months:* Administer doses at 2, 4, 6, and 12 through 15 months of age.
 - 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.*
 - Menactra
 - 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:
 - Menveo
 - Children who initiate vaccination at 8 weeks through 6 months:* Administer doses at 2, 4, 6, and 12 months of age.
 - 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.
 - Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart.
 - MenHibrix
 - Children 6 weeks through 18 months:* Administer doses at 2, 4, 6, and 12 through 15 months of age.
 - 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.*
 - Menactra
 - Children 9 through 23 months:* Administer 2 primary doses at least 12 weeks apart.
 - 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 a complete 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/mmwrhtml/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>.

Figure 172-2, cont'd

1254 Part XVII ◆ Infectious Diseases

FIGURE 172-3. Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind—United States, 2015.

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Figure 1 and the footnotes that follow.

Children age 4 months through 6 years					
Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Hepatitis B ¹	Birth	4 weeks	8 weeks and at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks.		
Rotavirus ²	6 weeks	4 weeks	4 weeks ³		
Diphtheria, tetanus, and acellular pertussis ⁴	6 weeks	4 weeks	4 weeks	6 months	6 months ³
<i>Haemophilus influenzae type b⁵</i>	6 weeks	4 weeks if first dose was administered before the 1 st birthday. 8 weeks (as final dose) if first dose was administered at age 12 through 14 months. No further doses needed if first dose was administered at age 15 months or older.	4 weeks ³ if current age is younger than 12 months and first dose was administered at younger than age 7 months, and at least 1 previous dose was PRP-T (ActHib, Pentacell) or unknown. 8 weeks and age 12 through 59 months (as final dose) ³ • if current age is younger than 12 months and first dose was administered at age 7 through 11 months; OR • if current age is 12 through 59 months and first dose was administered before the 1 st birthday, and second dose administered at younger than 15 months; OR • if both doses were PRP-OMP (PedvaxHib; Comvax) and were administered before the 1 st birthday. No further doses needed if previous dose was administered at age 15 months or older.	8 weeks (as final dose) This dose only necessary for children age 12 through 59 months who received 3 doses before the 1 st birthday.	
Pneumococcal ⁶	6 weeks	4 weeks if first dose administered before the 1 st birthday. 8 weeks (as final dose for healthy children) if first dose was administered at the 1 st birthday or after. No further doses needed for healthy children if first dose administered at age 24 months or older.	4 weeks if current age is younger than 12 months and previous dose given at <7 months old. 8 weeks (as final dose for healthy children) if previous dose given between 7–11 months (wait until at least 12 months old); OR if current age is 12 months or older and at least 1 dose was given before age 12 months. No further doses needed for healthy children if previous dose administered at age 24 months or older.	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus ⁷	6 weeks	4 weeks ⁸	4 weeks ⁹	6 months ⁷ (minimum age 4 years for final dose).	
Meningococcal ¹²	6 weeks	8 weeks ¹²	See footnote 13	See footnote 13	
Measles, mumps, rubella ⁸	12 months	4 weeks			
Varicella ¹⁰	12 months	3 months			
Hepatitis A ¹¹	12 months	6 months			
Children and adolescents age 7 through 18 years					
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis ⁹	7 years ⁴	4 weeks	4 weeks if first dose of DTaP/DT was administered before the 1 st birthday. 6 months (as final dose) if first dose of DTaP/DT was administered at or after the 1 st birthday.	6 months ⁷ if first dose of DTaP/DT was administered before the 1 st birthday.	
Human papillomavirus ¹²	9 years		Routine dosing intervals are recommended. ¹²		
Hepatitis A ¹¹	Not applicable (N/A)	6 months			
Hepatitis B ¹	N/A	4 weeks	8 weeks and at least 16 weeks after first dose.		
Inactivated poliovirus ⁷	N/A	4 weeks	4 weeks ⁹	6 months ⁷	
Meningococcal ¹²	N/A	8 weeks ¹²			
Measles, mumps, rubella ⁸	N/A	4 weeks			
Varicella ¹⁰	N/A	3 months if younger than age 13 years. 4 weeks if age 13 years or older.			

NOTE: The above recommendations must be read along with the footnotes of this schedule in Fig. 172-2.

Figure 172-3 Catch-up immunization schedule for persons aged 4 mo through 18 yr who start late or who are more than 1 mo old—United States, 2015. (From Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/vaccines/schedules/downloads/child/catchup-schedule-pr.pdf>)

Table 172-6 Combination Vaccines Licensed and Available in the United States

VACCINE PRODUCT (MANUFACTURER)*	TRADE NAME (YEAR LICENSED)	COMPONENTS	Recommended Ages	
			PRIMARY SERIES	BOOSTER DOSE
Hib-HepB ¹⁺ (Merck & Co, Inc.)	Comvax (1996)	PRP-OMP + HepB vaccine	2, 4 mo of age	12 through 15 mo of age
MenCY/Hib (GlaxoSmithKline)	MenHibRix (2013)	MenCY + PRP-T	2, 4, 6 mo of age	12 through 15 mo of age
DTaP-IPV/Hib (Sanofi Pasteur)	Pentacel (2008)	DTaP-IPV + PRP-T	2, 4, 6 mo of age	15 through 18 mo of age
DTaP-HepB-IPV (GlaxoSmithKline)	Pediarix (2002)	DTaP + HepB + IPV	2, 4, 6 mo of age	
DTaP-IPV (GlaxoSmithKline)	Kinrix (2008)	DTaP + IPV		4 through 6 yr of age: • booster for 5th dose of DTaP • booster for 4th dose of IPV
HepA-HepB (GlaxoSmithKline)	Twinrix (2001)	HepA + HepB	>18 yr of age; 0, 1, and 6 mo schedule	
MMRV (Merck & Co, Inc.)	ProQuad (2005)	MMR + varicella	12 through 15 mo of age	4 through 6 yr of age

*Dash (-) indicates that products are supplied in their final form by the manufacturer and do not require mixing or reconstitution by user; slash (/) indicates that products are mixed or reconstituted by user.

¹If a PRP-OMP vaccine is not administered as both doses in the primary series or if there is uncertainty about which products were administered previously, a 3rd dose of Hib conjugate vaccine is needed to complete the primary series.

²Preferred for American Indian/Alaska Native children.

³DTaP, diphtheria and tetanus toxoids and acellular pertussis vaccine; HepA, hepatitis A vaccine; HepB, hepatitis B vaccine; IPV/Hib, trivalent inactivated polio vaccine and *Haemophilus influenzae* type b vaccine; MMRV, measles-mumps-rubella and varicella vaccine.

1256 Part XVII ◆ Infectious Diseases

Table 172-8 Recommended Immunizations for Travelers to Developing Countries*

IMMUNIZATIONS	Length of Travel		
	BRIEF, <2 WK	INTERMEDIATE, 2 WK-3 MO	LONG-TERM RESIDENTIAL, >3 MO
Review and complete age-appropriate childhood and adolescent schedule (see text for details)	+	+	+
• DTaP, poliovirus, pneumococcal, and <i>Haemophilus influenzae</i> type b vaccines may be given at 4-wk intervals if necessary to complete the recommended schedule before departure			
• Measles: 2 additional doses given if <12 mo of age at 1st dose			
• Rotavirus			
• Varicella			
• HPV			
• Hepatitis B [†]			
• Tdap			
• MCV4			
Yellow fever [‡]	+	+	+
Hepatitis A [§]	+	+	+
Typhoid fever	±	+	+
Meningococcal disease [¶]	±	±	±
Rabies**	±	+	+
Japanese encephalitis ^{††}	±	±	+

*See disease-specific chapters in the Red Book for details. For further sources of information, see text.

[†]If there is insufficient time to complete 6 mo primary series, accelerated series can be given.[‡]For regions with endemic infection, see Health Information for International Travel (<http://www.cdc.gov/travel>).[§]Indicated for travelers to areas with intermediate or high endemic rates of hepatitis A virus infection.^{||}Indicated for travelers who will consume food and liquids in areas of poor sanitation.[¶]Recommended for regions of Africa with endemic infection and during local epidemics, and required for travel to Saudi Arabia for the Hajj.^{**}Indicated for people with high risk for animal exposure (especially to dogs) and for travelers to countries with endemic infection.^{††}For regions with endemic infection (see Health Information for International Travel). For high-risk activities in areas experiencing outbreaks, vaccine is recommended, even for brief travel.

+, Recommended; ±, consider; DTaP, diphtheria and tetanus toxoids and acellular pertussis.

Modified Pickering LK, Baker CJ, Kimberlin DW, Long SL, editors: Red Book 2012: report of the Committee on Infectious Diseases, Elk Grove Village, IL, 2012,

Table 172-7 Vaccines Recommended for Children and Adolescents with Underlying Conditions or at High Risk

VACCINES	CONDITIONS
PCV13 (and PPSV23 in certain conditions)	<ul style="list-style-type: none"> Immunocompetent children with: <ul style="list-style-type: none"> 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 leaks Cochlear implant Anatomic or functional asplenia (including sickle cell disease and other hemoglobinopathies, congenital or acquired asplenia or splenic dysfunction) Immunocompromising conditions: HIV infection; chronic renal failure and nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease or solid organ transplantation; congenital immunodeficiency
MCV4	<ul style="list-style-type: none"> Anatomic or functional asplenia (including sickle cell disease) Persistent complement component deficiency Residents of or travelers to countries in African meningitis belt or pilgrims on the Haj During outbreaks caused by a vaccine serogroup
Hib	<ul style="list-style-type: none"> Anatomic or functional asplenia (including sickle cell disease) Immunocompromising conditions: HIV disease; immunosuppressive therapy for malignant neoplasms; immunoglobulin deficiency including immunoglobulin G₂ subclass deficiency or early complement deficiency; recipients of a hematopoietic stem cell transplant (HSCT)

Table 172-9 Vaccination of Persons with Primary and Secondary Immune Deficiencies

PRIMARY				
CATEGORY	SPECIFIC IMMUNODEFICIENCY	CONTRAINDICATED VACCINES*	RISK-SPECIFIC RECOMMENDED VACCINES*	EFFECTIVENESS AND COMMENTS
B lymphocyte (humoral)	Severe antibody deficiencies (e.g., X-linked agammaglobulinemia and common variable immunodeficiency)	OPV [†] Smallpox LAIV BCG Ty21a (live typhoid) YF	Pneumococcal Consider measles and varicella vaccination	The effectiveness of any vaccine will be uncertain if it depends only on the humoral response (e.g., PPSV, MPSV) IVIG interferes with the immune response to measles vaccine and possibly varicella vaccine
	Less-severe antibody deficiencies (e.g., selective IgA deficiency and IgG subclass deficiency)	OPV [†] BCG YF Other live vaccines appear to be safe	Pneumococcal	All vaccines probably effective Immune response may be attenuated
T lymphocyte (cell-mediated and humoral)	Complete defects (e.g., SCID, complete DiGeorge syndrome)	All live vaccines ^{‡§}	Pneumococcal	Vaccines may be ineffective
	Partial defects (e.g., most patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia)	All live vaccines ^{‡§}	Pneumococcal Meningococcal Hib (if not administered in infancy)	Effectiveness of any vaccine depends on degree of immune suppression
Complement	Persistent complement, properdin, or factor B deficiency	None	Pneumococcal	All routine vaccines probably effective
Phagocytic function	Chronic granulomatous disease, leukocyte adhesion defect, and myeloperoxidase deficiency	Live bacterial vaccines [‡]	Meningococcal Pneumococcal [¶]	All inactivated vaccines safe and probably effective Live viral vaccines probably safe and effective
SECONDARY				
SPECIFIC IMMUNODEFICIENCY	CONTRAINDICATED VACCINES*	RISK-SPECIFIC RECOMMENDED VACCINES*		EFFECTIVENESS AND COMMENTS
HIV/AIDS	OPV [†] Smallpox BCG LAIV Withhold MMR and varicella in severely immunocompromised persons	Pneumococcal Consider Hib (if not administered in infancy) and meningococcal vaccination		MMR, varicella, rotavirus, and all inactivated vaccines, including inactivated influenza, may be effective [*]
Malignant neoplasm, transplantation, immunosuppressive or radiation therapy	Live viral and bacterial, depending on immune status ^{‡§}	Pneumococcal		Effectiveness of any vaccine depends on degree of immune suppression
Asplenia	None	Pneumococcal Meningococcal Hib (if not administered in infancy)		All routine vaccines probably effective
Chronic renal disease	LAIV	Pneumococcal Hepatitis B ^{**}		All routine vaccines probably effective

*Other vaccines that are universally or routinely recommended should be given if not contraindicated.

[†]OPV is no longer recommended for routine use in the United States.

[‡]Live bacterial vaccines: BCG and oral Ty21a *Salmonella typhi* vaccine.

[§]Live viral vaccines: MMR, MMRV, OPV, LAIV, YF, zoster, rotavirus, and varicella (smallpox). Smallpox vaccine is not recommended for children or the general public.

^{||}Regarding T-lymphocyte immunodeficiency as a contraindication for rotavirus vaccine, data exist only for SCID.

[¶]Pneumococcal vaccine is not indicated for children with chronic granulomatous disease beyond age-based universal recommendations for PCV. Children with chronic granulomatous disease are not at increased risk for pneumococcal disease.

^{*}HIV-infected children should receive immunoglobulin after exposure to measles and may receive varicella, measles, and YF vaccine if CD4+ lymphocyte count is greater than 15%. (For YF vaccine, CD4+ T-lymphocyte count between 15% and 24% is a precaution.)

^{**}Indicated based on the risk from dialysis-based bloodborne transmission.

BCG, bacille Calmette-Guérin vaccine; Hib, *Haemophilus influenzae* type b vaccine; HIV/AIDS, human immunodeficiency virus/acquired immunodeficiency syndrome; IVIG, intravenous immunoglobulin; LAIV, live-attenuated influenza vaccine; MMR, measles, mumps, rubella vaccine; MPSV/quadrivalent meningococcal polysaccharide vaccine; OPV, oral poliovirus vaccine (live); PPSV, pneumococcal polysaccharide vaccine; SCID, severe combined immunodeficiency disease; YF, yellow fever.

1258 Part XVII ◆ Infectious Diseases

Table 174-1 Infectious Diseases in the Childcare Setting	
DISEASE	INCREASED INCIDENCE WITH CHILDCARE
RESPIRATORY TRACT INFECTIONS	
Otitis media	Yes
Sinusitis	Probably
Pharyngitis	Probably
Pneumonia	Yes
GASTROINTESTINAL TRACT INFECTIONS	
Diarrhea (rotavirus, calicivirus, astrovirus, enteric adenovirus, <i>Giardia lamblia</i> , <i>Cryptosporidium</i> , <i>Shigella</i> , <i>Escherichia coli</i> O157:H7, and <i>Clostridium difficile</i>)	Yes
Hepatitis A	Yes
SKIN DISEASES	
Impetigo	Probably
Scabies	Probably
Pediculosis	Probably
Tinea (ringworm)	Probably
INVASIVE BACTERIA INFECTIONS	
<i>Haemophilus influenzae</i> type b	No*
<i>Neisseria meningitidis</i>	Probably
<i>Streptococcus pneumoniae</i>	Yes
ASEPTIC MENINGITIS	
Enteroviruses	Probably
HERPESVIRUS INFECTIONS	
Cytomegalovirus	Yes
Varicella-zoster virus	Yes
Herpes simplex virus	Probably
BLOOD-BORNE INFECTIONS	
Hepatitis B	Few case reports
HIV	No cases reported
Hepatitis C	No cases reported
VACCINE-PREVENTABLE DISEASES	
Measles, mumps, rubella, diphtheria, pertussis, tetanus	Not established
Polio	No
<i>H. influenzae</i> type b	No*
Varicella	Yes
Rotavirus	Yes

*Not in the postvaccine era; yes in the prevaccine era

Table 172-10 Standards for Child and Adolescent Immunization Practices	
AVAILABILITY OF VACCINES	
Vaccination services are readily available. Vaccinations are coordinated with other healthcare services and provided in a medical home when possible. Barriers to vaccination are identified and minimized. Patient costs are minimized.	
ASSESSMENT OF VACCINATION STATUS	
Healthcare professionals review the vaccination and health status of patients at every encounter to determine which vaccines are indicated. Healthcare professionals assess for and follow only medically accepted contraindications.	
EFFECTIVE COMMUNICATION ABOUT VACCINE BENEFITS AND RISKS	
Parents or guardians and patients are educated about the benefits and risks of vaccination in a culturally appropriate manner and in easy-to-understand language.	
PROPER STORAGE AND ADMINISTRATION OF VACCINES AND DOCUMENTATION OF VACCINATIONS	
Healthcare professionals follow appropriate procedures for vaccine storage and handling. Up-to-date, written vaccination protocols are accessible at all locations where vaccines are administered. Persons who administer vaccines and staff who manage or support vaccine administration are knowledgeable and receive ongoing education. Healthcare professionals simultaneously administer as many indicated vaccine doses as possible. Vaccination records for patients are accurate, complete, and easily accessible. Healthcare professionals report adverse events following vaccination promptly and accurately to the Vaccine Adverse Event Reporting System (VAERS) and are aware of a separate program, the National Vaccine Injury Compensation Program (VICP). All personnel who have contact with patients are appropriately vaccinated.	
IMPLEMENTATION OF STRATEGIES TO IMPROVE VACCINATION COVERAGE	
Systems are used to remind parents or guardians, patients, and healthcare professionals when vaccinations are due and to recall those who are overdue. Office- or clinic-based patient record reviews and vaccination coverage assessments are performed annually. Healthcare professionals practice community-based approaches.	

Table 173-3 Common Surgical Procedures for Which Perioperative Prophylactic Antibiotics Are Recommended			
SURGICAL PROCEDURE	LIKELY PATHOGENS	RECOMMENDED DRUGS	NON-β-LACTAM ALTERNATIVE
CLEAN WOUNDS			
Cardiac surgery (e.g., open heart surgery)	Skin flora, enteric Gram-negative bacilli	Cefazolin or cefuroxime	Clindamycin or vancomycin
Vascular surgery			
Neurosurgery			
Orthopedic surgery (e.g., joint replacement)			
CLEAN CONTAMINATED WOUNDS			
Head and neck surgery involving the oral cavity or pharynx	Skin flora, oral anaerobes, oral streptococci	Cefazolin + metronidazole, ampicillin-sulbactam	Clindamycin
Gastrointestinal and genitourinary surgery	Enteric Gram-negative bacilli, anaerobes, Gram-positive cocci	Cefazolin + metronidazole, cefotetan or piperacillin-tazobactam If colon is involved, consider bacterial reduction with PO neomycin and erythromycin	Clindamycin
CONTAMINATED WOUNDS			
Traumatic wounds (e.g., compound fracture)	Skin flora	Cefazolin	Clindamycin, vancomycin
DIRTY WOUNDS			
Appendectomy, penetrating abdominal wounds, colorectal surgery	Enteric Gram-negative bacilli, anaerobes, Gram-positive cocci	Cefazolin + metronidazole, cefoxitin, cefotetan or ampicillin-sulbactam	Clindamycin + aminoglycoside

Table 174-2 Disease- or Condition-Specific Recommendations for Exclusion of Children in Out-of-Home Childcare—cont'd

CONDITION	MANAGEMENT OF CASE	MANAGEMENT OF CONTACTS
Measles	Exclusion until 4 days after beginning of rash and when the child is able to participate	Immunize exposed children without evidence of immunity within 72 hr of exposure Children who do not receive vaccine within 72 hr or who remain unimmunized after exposure should be excluded until at least 2 wk after onset of rash in the last case of measles
Mumps	Exclusion until 5 days after onset of parotid gland swelling	In outbreak setting, people without documentation of immunity should be immunized or excluded Immediate readmission may occur following immunization Unimmunized people should be excluded for ≥26 days following onset of parotitis in last case
Pediculosis capitis (head lice)	Treatment at end of program day and readmission on completion of 1st treatment	Household and close contacts should be examined and treated if infested No exclusion is necessary
Pertussis	Exclusion until 5 days of appropriate antimicrobial therapy course have been completed	Immunization and chemoprophylaxis should be administered as recommended for household contacts Symptomatic children and staff should be excluded until completion of 5 days of antimicrobial therapy course Untreated adults should be excluded until 21 days after onset of cough
Rubella	Exclusion until 6 days after onset of rash for postnatal infection	Pregnant contacts should be evaluated
Salmonella serotype Typhi infection	Exclusion until diarrhea resolves 3 Negative stool culture results required before readmission	Stool cultures should be performed for attendees and staff; infected people should be excluded on the basis of age
Non-serotype Typhi <i>Salmonella</i> infection	Exclusion until diarrhea resolves. Negative stool culture results not required for non-serotype Typhi <i>Salmonella</i> species	Symptomatic contacts should be excluded until symptoms resolve Stool cultures are not required for asymptomatic contacts Antimicrobial therapy is not recommended for asymptomatic infection or uncomplicated diarrhea or for contacts
Scabies	Exclusion until after treatment given	Close contacts with prolonged skin-to-skin contact should have prophylactic therapy Bedding and clothing in contact with skin of infected people should be laundered
Shiga toxin-producing <i>Escherichia coli</i> , including <i>E. coli</i> O157:H7, or <i>Shigella</i> infection	Exclusion until diarrhea resolves and results of 2 stool cultures are negative for these organisms, depending on state regulations	Meticulous hand hygiene; stool cultures should be performed for contacts Center(s) with cases should be closed to new admissions during <i>E. coli</i> O157:H7 outbreak
<i>Staphylococcus aureus</i> skin infections	Exclusion only if skin lesions are draining and cannot be covered with a watertight dressing	Meticulous hand hygiene Cultures of contacts are not recommended
Streptococcal pharyngitis	Exclusion until 24 hr after treatment has been initiated and the child is able to participate in activities	Symptomatic contacts of documented cases of group A streptococcal infection should be tested and treated if test results are positive
Tuberculosis	For active disease, exclusion until determined to be noninfectious by physician or health department authority May return to activities after therapy is instituted, symptoms have diminished, and adherence to therapy is documented No exclusion for latent tuberculosis infection	Local health department personnel should be informed for contact investigation
Varicella	Exclusion until all lesions have dried and crusted, usually 6 days after onset of rash in immunocompetent people; may be longer in immunocompromised people	Varicella vaccine should be administered by 3-5 days after exposure, and varicella-zoster Ig should be administered up to 96 hr after exposure when indicated

HAV, hepatitis A virus; Ig, immunoglobulin.

Table 174-2 Disease- or Condition-Specific Recommendations for Exclusion of Children in Out-of-Home Childcare

CONDITION	MANAGEMENT OF CASE	MANAGEMENT OF CONTACTS
HAV infection	Serologic testing to confirm HAV infection in suspected cases Exclusion until 1 wk after onset of jaundice	If ≥1 case is confirmed in child or staff attendees or ≥2 cases in households of staff or attendees, HAV vaccine or Ig should be administered within 14 days of exposure to unimmunized staff and attendees In centers without diapered children, HAV vaccine or Ig should be given to unimmunized classroom contacts of index case Asymptomatic Ig recipients may return after receipt of Ig
Impetigo	Exclusion until 24 hr after treatment has been initiated Lesions on exposed skin covered with watertight dressing	No intervention needed unless additional lesions develop

Table 174-3 General Recommendations for Exclusion of Children in Out-of-Home Childcare

SYMPTOM(S)	MANAGEMENT
Illness preventing participation in activities, as determined by childcare staff	Exclusion until illness resolves and able to participate in activities
Illness that requires care greater than staff can provide without compromising health and safety of others	Exclusion or placement in care environment where appropriate care can be provided without compromising care of others
Severe illness suggested by fever with behavior changes, lethargy, irritability, persistent crying, difficulty breathing, progressive rash	Medical evaluation and exclusion until symptoms have resolved
Rash with fever or behavioral change	Medical evaluation and exclusion until illness is determined not to be communicable
Persistent abdominal pain (≥ 2 hr) or intermittent abdominal pain associated with fever, dehydration, or other systemic signs and symptoms	Medical evaluation and exclusion until symptoms have resolved
Vomiting ≥ 2 times in preceding 24 hr	Exclusion until symptoms have resolved, unless vomiting is determined to be caused by a noncommunicable condition and child is able to remain hydrated and participate in activities
Diarrhea or stools containing blood or mucus	Medical evaluation and exclusion until symptoms have resolved
Oral lesions	Exclusion until child or staff member is considered to be noninfectious (lesions crusted and dry)

Table 175-1 Travel Vaccinations for Children

VACCINE	PRIMARY SERIES	AGE AT VACCINATION	BOOSTER/COMMENTS
HEPATITIS A			
Havrix, Vaqta	0.5 mL IM $\times 2$ doses ≥ 6 mo apart	>1 yr	No booster; see text about off-label administration (age 6-11 mo)
Immunoglobulin (Ig)	Travel <2 mo: 0.02 mL/kg IM once Travel >2 mo: 0.06 mL/kg IM once	Birth	See text about restrictions with live virus vaccinations (i.e., MMR) following Ig administration
INFLUENZA			
Inactivated	6-35 mo: 0.25 mL IM, 1 or 2 doses 3-8 yr: 0.5 mL IM, 1 or 2 doses >9 yr: 0.5 mL IM once	>6 mo	New vaccine yearly In children 6 mo-9 yr, 2 doses should be given ≥ 1 mo apart if no prior vaccination
Live-attenuated	0.25 mL in each nostril, 1 or 2 doses	>2 yr	New vaccine yearly
JAPANESE B ENCEPHALITIS			
Ixiaro (inactivated)	2 mo-2 yr: 0.25 mL IM on days 0 and 28 >3 yr: 0.5 mL IM on days 0 and 28	2 mo to <3 yr >3 yr	Booster 1-2 yr after primary series Booster 1-2 yr after primary series
MEASLES			
MMR	Recommended schedule: 12-15 mo and 4-6 yr If >12 mo and traveling internationally, 2nd MMR dose can be administered 4 wk later	>6-11 mo: 1 dose recommended if traveling to measles-endemic area	See text. MMR at 6-11 mo does not count toward primary series; MMR should be administered simultaneously with other recommended/required live-virus travel vaccines (yellow fever)
MENINGOCOCCAL DISEASE			
Conjugate A/C/Y/W-135	0.5 mL IM 9-23 mo: 2 doses, 3 mo apart 0.5 mL IM once	9-23 mo >2-6 yr >7 yr	Booster 3 yr after primary series Booster after 3 yr (age 2-6 yr) Booster after 5 yr (age >7 yr) Children with functional/anatomic asplenia receive 2 dose primary series, 2 mo apart; conjugate vaccine recommended over polysaccharide A/C/Y/W-135
Polysaccharide A/C/Y/W-135	0.5 mL SC once	>2 yr	<4 yr of age: every 2 yr >4 yr of age: every 3-5 yr
RABIES			
	Preexposure: 1.0 mL IM $\times 3$ doses, days 0, 7, and 21 or 28 days	Any age	See text for follow-up vaccination if bitten
TYPHOID			
Intramuscular Vi	0.5 mL IM once	≥ 2 yr	Every 2-3 yr
Oral Ty21	4 doses: 1 capsule PO every other day	≥ 6 yr	Every 5 yr; see text for administration
YELLOW FEVER			
	0.5 mL SC once	>9 mo	Every 10 yr (see text)

A/C/Y/W-135, serogroup A, C, Y, and W¹³⁵ meningococcal vaccine.

1278 Part XVII ◆ Infectious Diseases

RISK GROUP	DIAGNOSTIC CONSIDERATIONS
IMMUNOCOMPETENT PATIENTS	
Neonates (<28 days)	Sepsis and meningitis caused by group B <i>Streptococcus</i> , <i>Escherichia coli</i> , <i>Listeria monocytogenes</i> ; neonatal herpes simplex virus infection, enteroviruses, parechovirus
Infants 1-3 mo	Serious bacterial disease in 5-15%, including bacteremia in 5%; urinary tract infection most common serious bacterial infection; <i>E. coli</i> most common pathogen; enterovirus, parechovirus, influenza
Infants and children 3-36 mo	Occult bacteremia in <0.5% of children immunized with both <i>Haemophilus influenzae</i> type b and pneumococcal conjugate vaccines; urinary tract infections
Hyperpyrexia (>40°C [104°F])	Meningitis, bacteremia, pneumonia, heatstroke, hemorrhagic shock-encephalopathy syndrome
Fever with petechiae	Bacteremia and meningitis caused by <i>Neisseria meningitidis</i> , <i>H. influenzae</i> type b, and <i>Streptococcus pneumoniae</i> Rickettsial disease Viral exanthem
IMMUNOCOMPROMISED PATIENTS	
Sickle cell disease	Sepsis, pneumonia, and meningitis caused by <i>S. pneumoniae</i> , osteomyelitis caused by <i>Salmonella</i> and <i>Staphylococcus aureus</i>
Asplenia	Bacteremia and meningitis caused by <i>N. meningitidis</i> , <i>H. influenzae</i> type b, <i>S. pneumoniae</i> , and <i>Capsacystophaga</i> sp.
Complement or properdin deficiency	Sepsis caused by <i>N. meningitidis</i>
Agammaglobulinemia	Bacteremia, sinopulmonary infections
AIDS	<i>S. pneumoniae</i> , <i>H. influenzae</i> type b, and <i>Salmonella</i> infections
Congenital heart disease	Infective endocarditis; brain abscess with right-to-left shunting
Central venous line	<i>S. aureus</i> , coagulase-negative staphylococci, <i>Candida</i>
Malignancy	Bacteremia with gram-negative enteric bacteria, <i>S. aureus</i> , and coagulase-negative staphylococci; fungemia with <i>Candida</i> and <i>Aspergillus</i>

INFECTIOUS CAUSES
Relapsing fever (<i>Borrelia recurrentis</i>)
Trench fever (<i>Bartonella quintana</i>)
Q fever (<i>Coxiella burnetii</i>)
Typhoid fever (<i>Salmonella typhi</i>)
Syphilis (<i>Treponema pallidum</i>)
Tuberculosis
Histoplasmosis
Coccidioidomycosis
Blastomycosis
Melioidosis (<i>Pseudomonas pseudomallei</i>)
Lymphocytic choriomeningitis (LCM) infection
Dengue fever
Yellow fever
Chronic meningococcemia
Colorado tick fever
Leptospirosis
Brucellosis
Oroya fever (<i>Bartonella bacilliformis</i>)
Acute rheumatic fever
Rat bite fever (<i>Spirillum minus</i>)
Visceral leishmaniasis
Lyme disease (<i>Borrelia burgdorferi</i>)
Malaria
Babesiosis
Noninfluenza respiratory viral infection
Epstein-Barr virus infection
NONINFECTIOUS CAUSES
Behcet disease
Crohn disease
Weber-Christian disease (panniculitis)
Leukoclastic angiitis syndromes
Sweet syndrome
Systemic lupus erythematosus and other autoimmune disorders
PERIODIC FEVER SYNDROMES (see Chapter 163)
Familial Mediterranean fever
Cyclic neutropenia
Periodic fever, aphthous stomatitis, pharyngitis, adenopathy (PFAPA)
Hyperimmunoglobulin D syndrome
Hibernal fever (tumor necrosis factor superfamily immunoglobulin A-associated syndrome [TRAPS])
Muckle-Wells syndrome
Others

Table 176-2 Evaluation of Acute Fever
Thorough history: onset, other symptoms, exposures (daycare, school, family, pets, playmates), travel, medications, other underlying disorders, immunizations
Physical examination: complete, with focus on localizing symptoms
Laboratory studies on a case-by-case basis:
<ul style="list-style-type: none"> • Rapid antigen testing • Nasopharyngeal: respiratory viruses by polymerase chain reaction • Throat: group A <i>Streptococcus</i> • Stool: rotavirus • Blood: complete blood count, blood culture, C-reactive protein, sedimentation rate, procalcitonin • Urine: urinalysis, culture • Stool: Hemoccult, culture • Cerebrospinal fluid: cell count, glucose, protein, Gram stain, culture • Chest radiograph or other imaging studies on a case-by-case basis

Table 177-3 Management of Fever Without Localizing Signs

GROUP	MANAGEMENT
Any toxic-appearing child 0-36 mo and temperature $\geq 38^{\circ}\text{C}$ (100.4°F)	Hospitalize, broad cultures plus other tests,* parenteral antibiotics
Child <1 mo and temperature $\geq 38^{\circ}\text{C}$ (100.4°F)	Hospitalize, broad cultures plus other tests,* parenteral antibiotics
Child 1-3 mo and temperature $\geq 38^{\circ}\text{C}$ (100.4°F)	Two-step process 1. Determine risk based on history, physical examination, and laboratory studies. Low risk: <ul style="list-style-type: none">• Uncomplicated medical history• Normal physical examination• Normal laboratory studies• Urine: negative leukocyte esterase, nitrite and <10 WBC/HPF• Peripheral blood: 5,000-15,000 WBC/mm3; <1,500 bands or band: total neutrophil ratio <0.2• Stool studies if diarrhea (no RBC and <5 WBC/HPF)• CSF cell count (<8 WBC/μL) and negative Gram stain• Chest radiograph without infiltrate 2. If child fulfills all low-risk criteria, administer no antibiotics, ensure follow-up in 24 hr and access to emergency care if child deteriorates. Daily follow-up should occur until blood, urine, and CSF cultures are final. If any cultures are positive, child returns for further evaluation and treatment. If child does not fulfill all low-risk criteria, hospitalize and administer parenteral antibiotics until all cultures are final and definitive diagnosis determined and treated
Child 3-36 mo and temperature $38\text{-}39^{\circ}\text{C}$ ($100.4\text{-}102.2^{\circ}\text{F}$)	Reassurance that diagnosis is likely self-limiting viral infection, but advise return with persistence of fever, temperatures $>39^{\circ}\text{C}$ (102.2°F), and new signs and symptoms
Child 3-36 mo and temperature $>39^{\circ}\text{C}$ (102.2°F)	Two-step process: 1. Determine immunization status 2. If received conjugate pneumococcal and <i>Haemophilus influenzae</i> type b vaccines, obtain urine studies (urine WBC, leukocyte esterase, nitrite, and culture) for all girls, all boys <6 mo old, all uncircumcised boys <2 yr, all children with recurrent urinary tract infections If did not receive conjugate pneumococcal and <i>H. influenzae</i> type b vaccines, manage according to the 1993 Guidelines (see Baraff et al. <i>Ann Emerg Med</i> 22:1198-1210, 1993.)

*Other tests may include chest radiograph, stool studies, herpes simplex polymerase chain reaction.

CSF, cerebrospinal fluid; HPF, high-powered field; RBC, red blood cell; WBC, white blood cell.

Table 177-4 Summary of Definitions and Major Features of the 4 Subtypes of Fever of Unknown Origin

FEATURE	CLASSIC FUO	HEALTHCARE-ASSOCIATED FUO	IMMUNE-DEFICIENT FUO	HIV-RELATED FUO
Definition	$>38^{\circ}\text{C}$ (100.4°F), >3 wk, >2 visits or 1 wk in hospital	$\geq 38^{\circ}\text{C}$ (100.4°F), >1 wk, not present or incubating on admission	$\geq 38^{\circ}\text{C}$ (100.4°F), >1 wk, negative cultures after 48 hr	$\geq 38^{\circ}\text{C}$ (100.4°F), >3 wk for outpatients, >1 wk for inpatients, HIV infection confirmed
Patient location	Community, clinic, or hospital	Acute care hospital	Hospital or clinic	Community, clinic, or hospital
Leading causes	Cancer, infections, inflammatory conditions, undiagnosed, habitual hyperthermia	Healthcare-associated infections, postoperative complications, drug fever	Majority caused by infections, but cause documented in only 40-60%	HIV (primary infection), typical and atypical mycobacteria, CMV, lymphomas, toxoplasmosis, cryptococcosis, immune reconstitution inflammatory syndrome (IRIS)
History emphasis	Travel, contacts, animal and insect exposure, medications, immunizations, family history, cardiac valve disorder	Operations and procedures, devices, anatomic considerations, drug treatment	Stage of chemotherapy, drugs administered, underlying immunosuppressive disorder	Drugs, exposures, risk factors, travel, contacts, stage of HIV infection
Examination emphasis	Fundi, oropharynx, temporal artery, abdomen, lymph nodes, spleen, joints, skin, nails, genitalia, rectum or prostate, lower-limb deep veins	Wounds, drains, devices, sinuses, urine	Skin folds, IV sites, lungs, perianal area	Mouth, sinuses, skin, lymph nodes, eyes, lungs, perianal area
Investigation emphasis	Imaging, biopsies, sedimentation rate, skin tests	Imaging, bacterial cultures	CXR, bacterial cultures	Blood and lymphocyte count; serologic tests; CXR; stool examination; biopsies of lung, bone marrow, and liver for cultures and cytologic tests; brain imaging
Management	Observation, outpatient temperature chart, investigations, avoidance of empirical drug treatments	Depends on situation	Antimicrobial treatment protocols	Antiviral and antimicrobial protocols, vaccines, revision of treatment regimens, good nutrition
Time course of disease	Months	Weeks	Days	Weeks to months
Tempo of investigation	Weeks	Days	Hours	Days to weeks

CMV, cytomegalovirus; CXR, chest radiograph; FUO, fever of unknown origin.

Adapted from Mandell GL, Bennett JE, Dolin R, editors: Mandell, Douglas, and Bennett's principles and practice of infectious diseases, ed 7, Philadelphia, 2010, Churchill Livingstone/Elsevier, p. 780, Table 51-1.

Table 177-5 Diagnostic Considerations of Fever of Unknown Origin in Children

ABSCESSES	RHEUMATOLOGIC DISEASES
Abdominal	Behçet disease
Brain	Juvenile dermatomyositis
Dental	Juvenile idiopathic arthritis
Hepatic	Rheumatic fever
Pelvic	Systemic lupus erythematosus
Perinephric	
Rectal	
Subphrenic	
Psoas	
BACTERIAL DISEASES	HYPERSensitivity DISEASES
Actinomycosis	Drug fever
<i>Bartonella henselae</i> (cat-scratch disease)	Hypersensitivity pneumonitis
Brucellosis	Serum sickness
<i>Campylobacter</i>	Weber-Christian disease
<i>Francisella tularensis</i> (tularemia)	
<i>Listeria monocytogenes</i> (listeriosis)	
Meningococcemia (chronic)	
<i>Mycoplasma pneumoniae</i>	
Rat bite fever (<i>Streptobacillus moniliformis</i> ; streptobacillary form of rat bite fever)	
<i>Salmonella</i>	
Tuberculosis	
Whipple disease	
Yersiniosis	
LOCALIZED INFECTIONS	NEOPLASMS
Cholangitis	Atrial myxoma
Infective endocarditis	Cholesterol granuloma
Mastoiditis	Hodgkin disease
Osteomyelitis	Inflammatory pseudotumor
Pneumonia	Leukemia
Pyelonephritis	Lymphoma
Sinusitis	Pheochromocytoma
SPIROCHETES	Neuroblastoma
<i>Borrelia burgdorferi</i> (Lyme disease)	Wilms tumor
Relapsing fever (<i>Borrelia recurrentis</i>)	
Leptospirosis	
Rat bite fever (<i>Spirillum minus</i> ; spirillary form of rat bite fever)	
Syphilis	
FUNGAL DISEASES	GRANULOMATOUS DISEASES
Blastomycosis (extrapulmonary)	Crohn disease
Coccidioidomycosis (disseminated)	Granulomatous hepatitis
Histoplasmosis (disseminated)	Sarcoidosis
<i>Chlamydia</i>	Angitis
Lymphogranuloma venereum	
Psittacosis	
RICKETTSIA	FAMILIAL AND HEREDITARY DISEASES
<i>Ehrlichia canis</i>	Anhidrotic ectodermal dysplasia
Q fever	Autonomic neuropathies
Rocky Mountain spotted fever	Fabry disease
Tick-borne typhus	Familial dysautonomia
VIRUSES	Familial Hibernian fever
Cytomegalovirus	Familial Mediterranean fever and the many other autoinflammatory diseases (see Chapter 163)
Hepatitis viruses	Hypertriglyceridemia
HIV	Ichthyosis
Epstein-Barr virus	Sickle cell crisis
PARASITIC DISEASES	Spinal cord/brain injury
Amebiasis	
Babesiosis	
Giardiasis	
Malaria	
Toxoplasmosis	
Trichinosis	
Trypanosomiasis	
Visceral larva migrans (<i>Toxocara</i>)	
	MISCELLANEOUS
	Addison disease
	Castleman disease
	Chronic active hepatitis
	Cyclic neutropenia
	Diabetes insipidus (nonnephrogenic and nephrogenic)
	Factitious fever
	Hemophagocytic syndromes
	Hypothalamic-central fever
	Infantile cortical hyperostosis
	Inflammatory bowel disease
	Kawasaki disease
	Kikuchi-Fujimoto disease
	Metal fume fever
	Pancreatitis
	Periodic fever syndromes
	Poisoning
	Pulmonary embolism
	Thrombophlebitis
	Thyrotoxicosis, thyroiditis

Table 177-6 Examples of Subtle Physical Findings Having Special Significance in Patients with Fever of Unknown Origin

BODY SITE	PHYSICAL FINDING	DIAGNOSIS
Head	Sinus tenderness	Sinusitis
Temporal artery	Nodules, reduced pulsations	Temporal arteritis
Oropharynx	Ulceration	Disseminated histoplasmosis, SLE, IBD, Behcet syndrome, periodic fever syndromes
	Tender tooth	Periapical abscess
Fundi or conjunctivae	Choroid tubercle Petechiae, Roth spot	Disseminated granulomatosis* Endocarditis
Thyroid	Enlargement, tenderness	Thyroiditis
Heart	Murmur	Infective or marantic endocarditis
Abdomen	Enlarged iliac crest lymph nodes, splenomegaly	Lymphoma, endocarditis, disseminated granulomatosis*
Rectum	Perirectal fluctuance, tenderness Prostatic tenderness, fluctuance	Abscess Abscess
Genitalia	Testicular nodule Epididymal nodule	Periarteritis nodosa, cancer Disseminated granulomatosis
Lower extremities	Deep venous tenderness	Thrombosis or thrombophlebitis
Skin and nails	Petechiae, splinter hemorrhages, subcutaneous nodules, clubbing	Vasculitis, endocarditis

*Includes tuberculosis, histoplasmosis, coccidioidomycosis, sarcoidosis, granulomatosis with polyangiitis, and syphilis.

From Mandell GL, Bennett JE, Dolin R, editors: Mandell, Douglas, and Bennett's principles and practice of infectious diseases, ed 7, Philadelphia, 2010, Churchill Livingstone/Elsevier, p. 785, Table 51-8.

Table 177-2 Low-Risk Criteria in a Child 1-3 Months Old with Fever

BOSTON CRITERIA	
Infants are at low risk if they appear well, have a normal physical examination, and have a caretaker reachable by telephone and if laboratory tests are as follows:	
• CBC: <20,000 WBC/ μ L	
• Urine: negative leukocyte esterase	
• CSF: leukocyte count less than 10×10^6 /L	
PHILADELPHIA PROTOCOL	
Infants are at low risk if they appear well and have a normal physical examination and if laboratory tests are as follows:	
• CBC: <15,000 WBC/ μ L; band: total neutrophil ratio <0.2	
• Urine: <10 WBC/HPF; no bacteria on Gram stain	
• CSF: <8 WBC/ μ L; no bacteria on Gram stain	
• Chest radiograph: no infiltrate	
• Stool: no RBC; few to no WBC	
PITTSBURGH GUIDELINES	
Infants are at low risk if they appear well and have a normal physical examination and if laboratory tests are as follows:	
• CBC: 5,000-15,000 WBC/ μ L; peripheral absolute band count <1,500/ μ L	
• Urine (enhanced urinalysis): 9 WBC/ μ L and no bacteria on Gram stain	
• CSF: 5 WBC/ μ L and negative Gram stain; if bloody tap, then WBC:RBC $\leq 1:500$	
• Chest radiograph: no infiltrate	
• Stool: 5 WBC/HPF with diarrhea	
ROCHESTER CRITERIA	
Infants are at low risk if they appear well and have a normal physical examination and if laboratory findings are as follows:	
• CBC: 5,000-15,000 WBC/ μ L; absolute band count $\leq 1,500/\mu$ L	
• Urine: <10 WBC/HPF at 40x	
• Stool: <5 WBC/HPF if diarrhea	

CBC, complete blood count; CSF, cerebrospinal fluid; HPF, high-powered field; RBC, red blood cell; WBC, white blood cell.

Table 178-3 Possible Causes of Fever in Neutropenic Patients Not Responding to Broad-Spectrum Antibiotics

CAUSES	APPROXIMATE FREQUENCY IN HIGH-RISK PATIENTS (%)
Fungal infections susceptible to empirical therapy	40
Fungal infections resistant to empirical antifungal therapy	5
Bacterial infections (with cryptic foci, biofilms, and resistant organisms)	10
Toxoplasma gondii, mycobacteria, or fastidious pathogens (<i>Legionella</i> , <i>Mycoplasma</i> , <i>Chlamydophila pneumoniae</i> , <i>Bartonella</i>)	5
Viral infections (herpesviruses, cytomegalovirus, Epstein-Barr virus, human herpesvirus 6, varicella-zoster virus, herpes simplex virus, parainfluenza virus, respiratory syncytial virus, influenza viruses)	5
Graft-versus-host disease after hematopoietic stem cell transplantation	10
Undefined (e.g., drug fever, toxic effects of chemotherapy, antitumor responses, undefined pathogens)	25

Table 178-2 Most Common Causes of Infections in Immunocompromised Children**BACTERIA, AEROBIC***

Acinetobacter
Bacillus
Burkholderia cepacia
Citrobacter
Corynebacterium
Enterobacter spp.
Enterococcus faecalis
Enterococcus faecium
Escherichia coli
Klebsiella spp.
Listeria monocytogenes
Mycobacterium spp.
Neisseria meningitidis
Nocardia
Pseudomonas aeruginosa
Staphylococcus aureus
Staphylococcus, coagulase-negative
Streptococcus pneumoniae
Streptococcus, viridans group

BACTERIA, ANAEROBIC*

Bacillus
Clostridium
Fusobacterium
Peptococcus
Peptostreptococcus
Propionibacterium
Veillonella

FUNGI*

Aspergillus
Candida albicans
Other Candida spp.
Cryptococcus neoformans
Fusarium spp.
Pneumocystis jiroveci
Zygomycoses (Mucor, Rhizopus, Rhizomucor)

VIRUSES*

Adenoviruses
Cytomegalovirus
Epstein-Barr virus
Herpes simplex virus
Human herpesvirus 6
Polyomavirus (BK)
Respiratory and enteric community-acquired viruses
Varicella-zoster virus

PROTOZOA*

Cryptosporidium parvum
Giardia lamblia
Toxoplasma gondii

*Listed alphabetically.

Table 178-1 Major Causes of Increased Risk for Infection in Immunocompromised Hosts**PRIMARY IMMUNODEFICIENCIES**

Antibody deficiency (B-cell defects; see Chapter 124)

- X-linked agammaglobulinemia
- Common variable immunodeficiency
- Selective immunoglobulin IgA deficiency
- IgG subclass deficiencies
- Hyper-IgM syndrome
- Transient hypogammaglobulinemia of infancy

Cell-mediated deficiency (T-cell defects)

- Thymic dysplasia (DiGeorge syndrome)
- Defective T-cell receptor
- Defective cytokine production
- T-cell activation defects
- CD8 lymphocytopenia
- Chronic mucocutaneous candidiasis

Combined B- and T-cell defects (see Chapter 126)

- Severe combined immunodeficiency
- Combined immunodeficiency
- Omenn syndrome
- Thrombocytopenia and eczema (Wiskott-Aldrich syndrome)
- Ataxia-telangiectasia
- Hyper-IgE syndrome

Phagocyte defects (see Chapter 130)

- Leukocyte adhesion deficiency
- Chédiak-Higashi syndrome
- Myeloperoxidase deficiency
- Chronic granulomatous disease

Leukopenia (see Chapter 131)

- Congenital neutropenia (Kostmann syndrome)
- Shwachman-Diamond syndrome

Disorders of the complement system (see Chapter 133)

SECONDARY IMMUNODEFICIENCIES

HIV (see Chapter 276)
Malignancies (and cancer chemotherapy)
Transplantation (see Chapters 135, 339, 368, 443, 444, and 536)

- Bone marrow and hematopoietic stem cell
- Solid organ

Burns
Sickle cell disease
Cystic fibrosis (see Chapter 403)
Diabetes mellitus
Immunosuppressive drugs
Asplenias including heterotaxy syndrome
Implanted foreign body
Malnutrition

Table 178-4 Host Defense Defects and Common Pathogens by Time After Bone Marrow Transplantation/Hematopoietic Stem Cell Transplantation			
TIME PERIOD	HOST DEFENSE DEFECTS	CAUSES	COMMON PATHOGENS
Pretransplant	Neutropenia Abnormal anatomic barriers	Underlying disease Prior chemotherapy	Aerobic Gram-negative bacilli
Preegraftment	Neutropenia Abnormal anatomic barriers	Chemotherapy Radiation Indwelling catheters	Aerobic Gram-positive cocci Aerobic Gram-negative bacilli <i>Candida</i> <i>Aspergillus</i> Herpes simplex virus (in previously infected patients) Community-acquired viral pathogens
Postengraftment	Abnormal cell-mediated immunity Abnormal anatomic barriers	Chemotherapy Immunosuppressive medications Radiation Indwelling catheters Unrelated cord blood donor	Gram-positive cocci Aerobic Gram-negative bacilli Cytomegalovirus Adenoviruses Community-acquired viral pathogens <i>Pneumocystis jiroveci</i>
Late posttransplant	Delayed recovery of immune function (cell-mediated, humoral, and abnormal anatomic barriers)	Time required to develop donor-related immune function Graft-versus-host disease	Varicella-zoster virus <i>Streptococcus pneumoniae</i>

Table 178-6 Timing of Infectious Complications Following Solid-Organ Transplantation

EARLY PERIOD (0-30 DAYS)

Bacterial Infections

Gram-negative enteric bacilli

- Small bowel, liver, neonatal heart

Pseudomonas, Burkholderia, Stenotrophomonas, Alcaligenes

- Cystic fibrosis lung

Gram-positive organisms

- All transplant types

Fungal Infections

All transplant types

Viral Infections

Herpes simplex virus

- All transplant types

Nosocomial respiratory viruses

- All transplant types

MIDDLE PERIOD (1-6 MO)

Viral Infections

Cytomegalovirus

- All transplant types

• Seronegative recipient of seropositive donor

Epstein-Barr virus

- All transplant types (small bowel highest risk group)

- Seronegative recipient

Varicella-zoster virus

- All transplant types

- Opportunistic infections

Pneumocystis jiroveci

- All transplant types

Toxoplasma gondii

- Seronegative recipient of cardiac transplant from a seropositive donor

Bacterial Infections

Pseudomonas, Burkholderia, Stenotrophomonas, Alcaligenes

- Cystic fibrosis lung

Gram-negative enteric bacilli

- Small bowel

LATE PERIOD (>6 MO)

Viral Infections

Epstein-Barr virus

- All transplant types, but less risk than middle period

Varicella-zoster virus

- All transplant types

Community-acquired viral infections

- All transplant types

Bacterial Infections

Pseudomonas, Burkholderia, Stenotrophomonas, Alcaligenes

- Cystic fibrosis lung

- Lung transplants with chronic rejection

Gram-negative bacillary bacteremia

- Small bowel

Fungal Infections

Aspergillus

- Lung transplants with chronic rejection

Table 178-5 Risk Factors for Infections Following Solid-Organ Transplantation in Children

PRETRANSPLANTATION FACTORS

Age of patient

Underlying disease, malnutrition

Specific organ transplanted

Previous exposures to infectious agents

Previous immunizations

Presence of infection in the donor

INTRAOPERATIVE FACTORS

Duration of transplant surgery

Exposure to blood products

Technical problems

Organisms transmitted with donor organ

POSTTRANSPLANTATION FACTORS

Immunosuppression

Induction immunosuppression

Maintenance immunosuppression

Augmented treatment for rejection

Indwelling catheters

Nosocomial exposures

Community exposures

Table 180-3 | Antibacterial Medications (Antibiotics)*

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Amikacin sulfate Amikin Injection: 50 mg/mL, 250 mg/mL	Aminoglycoside antibiotic active against Gram-negative bacilli, especially <i>Escherichia coli</i> , <i>Klebsiella</i> , <i>Proteus</i> , <i>Enterobacter</i> , <i>Serratia</i> , and <i>Pseudomonas</i> Neonates: Postnatal age ≤7 days: weight 1,200-2,000 g: 7.5 mg/kg q 12-18 hr IV or IM; weight >2,000 g: 10 mg/kg q 12 hr IV or IM; postnatal age >7 days: weight 1,200-2,000 g IV or IM: 7.5 mg/kg q 8-12 hr IV or IM; weight >2,000 g: 10 mg/kg q 8 hr IV or IM Children: 15-25 mg/kg/24 hr divided q 8-12 hr IV or IM Adults: 15 mg/kg/24 hr divided q 8-12 hr IV or IM	Cautions: Anaerobes, <i>Streptococcus</i> (including <i>S. pneumoniae</i>) are resistant. May cause ototoxicity and nephrotoxicity. Monitor renal function. Drug eliminated renally. Administered IV over 30-60 min Drug interactions: May potentiate other ototoxic and nephrotoxic drugs Target serum concentrations: Peak 25-40 mg/L; trough <10 mg/L
Amoxicillin Amoxil, Polymox Capsule: 250, 500 mg Tablet: chewable: 125, 250 mg Suspension: 125 mg/5 mL, 250 mg/5 mL Drops: 50 mg/mL	Penicillinase-susceptible β-lactam: Gram-positive pathogens except <i>Staphylococcus</i> ; <i>Salmonella</i> , <i>Shigella</i> , <i>Neisseria</i> , <i>E. coli</i> , and <i>Proteus mirabilis</i> Children: 20-50 mg/kg/24 hr divided q 8-12 hr PO. Higher dose of 80-90 mg/kg 24 hr PO for otitis media Adults: 250-500 mg q 8-12 hr PO Uncomplicated gonorrhea: 3 g with 1 g probenecid PO	Cautions: Rash, diarrhea, abdominal cramping. Drug eliminated renally Drug interaction: Probenecid
Amoxicillin-clavulanate Augmentin Tablet: 250, 500, 875 mg Tablet, chewable: 125, 200, 250, 400 mg Suspension: 125 mg/5 mL, 200 mg/5 mL, 250 mg/5 mL, 400 mg/5 mL	β-Lactam (amoxicillin) combined with β-lactamase inhibitor (clavulanate) enhances amoxicillin activity against penicillinase-producing bacteria. <i>S. aureus</i> (not methicillin-resistant organism), <i>Streptococcus</i> , <i>Haemophilus influenzae</i> , <i>Moraxella catarrhalis</i> , <i>E. coli</i> , <i>Klebsiella</i> , <i>Bacteroides fragilis</i> Neonates: 30 mg/kg/24 hr divided q 12 hr PO Children: 20-45 mg/kg 24 hr divided q 8-12 hr PO. Higher dose 80-90 mg/kg/24 hr PO for otitis media	Cautions: Drug dosed on amoxicillin component. May cause diarrhea, rash. Drug eliminated renally Drug interaction: Probenecid Comment: Higher dose may be active against penicillin-tolerant/resistant <i>S. pneumoniae</i>
Ampicillin Polycillin, Omnipen Capsule: 250, 500 mg Suspension: 125 mg/5 mL, 250 mg/5 mL, 500 mg/5 mL Injection	β-Lactam with same spectrum of antibacterial activity as amoxicillin Neonates: Postnatal age ≤7 days weight ≤2,000 g: 50 mg/kg/24 hr IV or IM q 12 hr (meningitis: 100 mg/kg/24 hr divided q 12 hr IV or IM); weight >2,000 g: 75 mg/kg/24 hr divided q 8 hr IV or IM (meningitis: 150 mg/kg/24 hr divided q 8 hr IV or IM). Postnatal age >7 days weight <1,200 g: 50 mg/kg/24 hr IV or IM q 12 hr (meningitis: 100 mg/kg/24 hr divided q 12 hr IV or IM); weight 1,200-2,000 g: 75 mg/kg/24 hr divided q 8 hr IV or IM (meningitis: 150 mg/kg/24 hr divided q 8 hr IV or IM); weight >2,000 g: 100 mg/kg/24 hr divided q 6 hr IV or IM (meningitis: 200 mg/kg/24 hr divided q 6 hr IV or IM) Children: 100-200 mg/kg/24 hr divided q 6 hr IV or IM (meningitis: 200-400 mg/kg/24 hr divided q 4-6 hr IV or IM) Adults: 250-500 mg q 4-8 hr IV or IM	Cautions: Less bioavailable than amoxicillin, causing greater diarrhea Drug interaction: Probenecid
Ampicillin-sulbactam Unasyn Injection	β-Lactam (ampicillin) and β-lactamase inhibitor (sulbactam) enhances ampicillin activity against penicillinase-producing bacteria: <i>S. aureus</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>E. coli</i> , <i>Klebsiella</i> , <i>B. fragilis</i> Children: 100-200 mg/kg/24 hr divided q 4-8 hr IV or IM Adults: 1-2 g q 6-8 hr IV or IM (max daily dose: 8 g)	Cautions: Drug dosed on ampicillin component. May cause diarrhea, rash. Drug eliminated renally Note: Higher dose may be active against penicillin-tolerant/resistant <i>S. pneumoniae</i> Drug interaction: Probenecid

*In the Drug column, the generic drug name is in bold. In the Indications column, bold indicates major organisms targeted and mechanisms of action. Continued

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Azithromycin Zithromax Tablet: 250 mg Suspension: 100 mg/5 mL, 200 mg/5 mL	Azalide antibiotic with activity against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>Mycoplasma</i> , <i>Legionella</i> , <i>Chlamydia trachomatis</i> Children: 10 mg/kg PO on day 1 (max dose: 500 mg) followed by 5 mg/kg PO q 24 hr for 4 days Group A streptococcus pharyngitis: 12 mg/kg/24 hr PO (max dose: 500 mg) for 5 days. Adults: 500 mg PO day 1 followed by 250 mg for 4 days Uncomplicated <i>C. trachomatis</i> infection: single 1 g dose PO	Note: Very long half-life permitting once-daily dosing. No metabolic-based drug interactions (unlike erythromycin and clarithromycin), limited gastrointestinal distress. Shorter-course regimens (e.g., 1-3 days) under investigation. 3 day, therapy (10 mg/kg/24 hr × 3 days) and single-dose therapy (30 mg/kg): use with increasing frequency (not for streptococcus pharyngitis)
Aztreonam Azactam Injection	β-Lactam (monobactam) antibiotic with activity against Gram-negative aerobic bacteria, <i>Enterobacteriaceae</i> , and <i>Pseudomonas aeruginosa</i> Neonates: Postnatal age ≤7 days weight ≤2,000 g: 60 mg/kg/24 hr divided q 12 hr IV or IM; weight >2,000 g: 90 mg/kg/24 hr divided q 8 hr IV or IM; postnatal age >7 days weight <1,200 g: 60 mg/kg/24 hr divided q 12 hr IV or IM; weight 1,200-2,000 g: 90 mg/kg/24 hr divided q 8 hr IV or IM; weight >2,000 g: 120 mg/kg/24 hr divided q 6-8 hr IV or IM Children: 90-120 mg/kg/24 hr divided q 6-8 hr IV or IM. For cystic fibrosis up to 200 mg/kg/24 hr IV Adults: 1-2 g IV or IM q 8-12 hr (max dose: 8 g/24 hr)	Cautions: Rash, thrombophlebitis, eosinophilia. Renally eliminated Drug interaction: Probenecid
Carbenicillin Geopen Injection Geocillin oral tablet	Extended-spectrum penicillin (remains susceptible to penicillinase destruction) active against <i>Enterobacter</i> , indole-positive <i>Proteus</i> , and <i>Pseudomonas</i> Neonates: Postnatal age ≤7 days weight ≤2,000 g: 225 mg/kg/24 hr divided q 8 hr IV or IM; weight >2,000 g: 300 mg/kg/24 hr divided q 6 hr IV or IM; >7 days: 300-400 mg/kg/24 hr divided q 6 hr IV or IM Children: 400-600 mg/kg/24 hr divided q 4-6 hr IV or IM	Cautions: Painful given intramuscularly; rash; each gram contains 5.3 mEq sodium. Interferes with platelet aggregation at high doses, increases in liver transaminase levels. Renally eliminated. Oral tablet for treatment of urinary tract infection only Drug interaction: Probenecid
Cefaclor Ceclor Capsule: 250, 500 mg Suspension: 125 mg/5 mL, 187 mg/5 mL, 250 mg/5 mL, 375 mg/5 mL	Second-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> including <i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 20-40 mg/kg/24 hr divided q 8-12 hr PO (max dose: 2 g) Adults: 250-500 mg q 6-8 hr PO	Cautions: β-Lactam safety profile (rash, eosinophilia) with high incidence of serum sickness reaction. Renally eliminated Drug interaction: Probenecid
Cefadroxil Duricef, Ultracef Capsule: 500 mg Tablet: 1,000 mg Suspension: 125 mg/5 mL, 250 mg/5 mL, 500 mg/5 mL	First-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 30 mg/kg/24 hr divided q 12 hr PO (max dose: 2 g) Adults: 250-500 mg q 8-12 hr PO	Cautions: β-lactam safety profile (rash, eosinophilia). Renally eliminated. Long half-life permits q 12-24 hr dosing Drug interaction: Probenecid
Cefazolin Ancef, Kefzol Injection	First-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> Neonates: Postnatal age ≤7 days 40 mg/kg/24 hr divided q 12 hr IV or IM; >7 days 40-60 mg/kg/24 hr divided q 8 hr IV or IM Children: 50-100 mg/kg/24 hr divided q 8 hr IV or IM Adults: 0.5-2 g q 8 hr IV or IM (max dose: 12 g/24 hr)	Caution: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Does not adequately penetrate CNS Drug interaction: Probenecid
Cefdinir Omnicef Capsule: 300 mg Oral suspension: 125 mg/5 mL	Extended-spectrum, semisynthetic cephalosporin Children 6 mo-12 yr: 14 mg/kg/24 hr in 1 or 2 doses PO (max dose: 600 mg/24 hr) Adults: 600 mg q 24 hr PO	Cautions: Reduce dosage in renal insufficiency (creatinine clearance <60 mL/min). Avoid taking concurrently with iron-containing products and antacids because absorption is markedly decreased; take at least 2 hr apart Drug interaction: Probenecid
Cefepime Maxipime Injection	Expanded-spectrum, fourth-generation cephalosporin active against many Gram-positive and Gram-negative pathogens, including <i>P. aeruginosa</i> many multidrug-resistant pathogens Children: 100-150 mg/kg/24 hr q 8-12 hr IV or IM Adults: 2-4 g/24 hr q 12 hr IV or IM	Adverse events: Diarrhea, nausea, vaginal candidiasis Cautions: β-lactam safety profile (rash, eosinophilia). Renally eliminated Drug interaction: Probenecid

*In the Drug column, the generic drug name is in bold. In the Indications column, bold indicates major organisms targeted and mechanisms of action.

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Cefixime Suprax Tablet: 200, 400 mg Suspension: 100 mg/5 mL	Third-generation cephalosporin active against <i>streptococci</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>Neisseria gonorrhoeae</i> , <i>Serratia marcescens</i> , and <i>Proteus vulgaris</i> . No antistaphylococcal or antipseudomonal activity Children: 8 mg/kg/24 hr divided q 12-24 hr PO Adults: 400 mg/24 hr divided q 12-24 hr PO	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Does not adequately penetrate CNS Drug interaction: Probenecid
Cefoperazone sodium Cefobid Injection	Third-generation cephalosporin active against many Gram-positive and Gram-negative pathogens Neonates: 100 mg/kg/24 hr divided q 12 hr IV or IM Children: 100-150 mg/kg/24 hr divided q 8-12 hr IV or IM Adults: 2-4 g/24 hr divided q 8-12 hr IV or IM (max dose: 12 g/24 hr)	Cautions: Highly protein-bound cephalosporin with limited potency reflected by weak antipseudomonal activity. Variable Gram-positive activity. Primarily hepatically eliminated in bile Drug interaction: Disulfiram-like reaction with alcohol
Cefotaxime sodium Claforan Injection	Third-generation cephalosporin active against Gram-positive and Gram-negative pathogens. No antipseudomonal activity Neonates: ≤7 days: 100 mg/kg/24 hr divided q 12 hr IV or IM; >7 days: weight <1,200 g 100 mg/kg/24 hr divided q 12 hr IV or IM; weight >1,200 g: 150 mg/kg/24 hr divided q 8 hr IV or IM Children: 150 mg/kg/24 hr divided q 6-8 hr IV or IM (meningitis: 200 mg/kg/24 hr divided q 6-8 hr IV) Adults: 1-2 g q 8-12 hr IV or IM (max dose: 12 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Each gram of drug contains 2.2 mEq sodium. Active metabolite Drug interaction: Probenecid
Cefotetan disodium Cefotan Injection	Second-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>E. coli</i> , <i>Klebsiella</i> , <i>Proteus</i> , and <i>Bacteroides</i> . Inactive against <i>Enterobacter</i> Children: 40-80 mg/kg/24 hr divided IV or IM q 12 hr Adults: 2-4 g/24 hr divided q 12 hr IV or IM (max dose: 6 g/24 hr)	Cautions: Highly protein-bound cephalosporin, poor CNS penetration; β-lactam safety profile (rash, eosinophilia), disulfiram-like reaction with alcohol. Renally eliminated (~20% in bile)
Cefoxitin sodium Mefoxin Injection	Second-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>E. coli</i> , <i>Klebsiella</i> , <i>Proteus</i> , and <i>Bacteroides</i> . Inactive against <i>Enterobacter</i> Neonates: 70-100 mg/kg/24 hr divided q 8-12 hr IV or IM Children: 80-160 mg/kg/24 hr divided q 6-8 hr IV or IM Adults: 1-2 g q 6-8 hr IV or IM (max dose: 12 g/24 hr)	Cautions: Poor CNS penetration; β-lactam safety profile (rash, eosinophilia). Renally eliminated. Painful given intramuscularly Drug interaction: Probenecid
Cefpodoxime proxetil Vantin Tablet: 100 mg, 200 mg Suspension: 50 mg/5 mL, 100 mg/5 mL	Third-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>N. gonorrhoeae</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> . No antipseudomonal activity Children: 10 mg/kg/24 hr divided q 12 hr PO Adults: 200-800 mg/24 hr divided q 12 hr PO (max dose: 800 mg/24 hr) Uncomplicated gonorrhea: 200 mg PO as single-dose therapy	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Does not adequately penetrate CNS. Increased bioavailability when taken with food Drug interaction: Probenecid; antacids and H-2 receptor antagonists may decrease absorption
Ceftaroline fosamil Teflaro Injection	Fifth-generation cephalosporin active against <i>S. aureus</i> (including MRSA when used for skin and soft-tissue infection), <i>Streptococcus pyogenes</i> , <i>Streptococcus agalactiae</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>H. influenzae</i> , and <i>Klebsiella oxytoca</i> *Children: 24 mg/kg/24 hr divided q 8 hr IV (<6 mo of age); 36 mg/kg/24 hr divided q 8 hr IV (weight ≤33 kg); 400 mg q 8 hr IV (weight >33 kg) Adults: 600 mg q 12 hr IV *Suggested dose; safety and effectiveness in pediatric patients have not yet been established	Caution: β-Lactam safety profile (rash, eosinophilia) Drug interaction: Probenecid
Cefprozil Cefzil Tablet: 250, 500 mg Suspension: 125 mg/5 mL, 250 mg/5 mL	Second-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>E. coli</i> , <i>M. catarrhalis</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 30 mg/kg/24 hr divided q 8-12 hr PO Adults: 500-1,000 mg/24 hr divided q 12 hr PO (max dose: 1.5 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Good bioavailability; food does not affect bioavailability Drug interaction: Probenecid

*In the Drug column, the generic drug name is in bold. In the Indications column, bold indicates major organisms targeted and mechanisms of action.

Continued

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Ceftazidime Fortaz, Ceptaz, Tazicef, Tazidime Injection	Third-generation cephalosporin active against Gram-positive and Gram-negative pathogens, including <i>P. aeruginosa</i> Neonates: Postnatal age ≤7 days: 100 mg/kg/24 hr divided q 12 hr IV or IM; >7 days weight ≤1,200 g: 100 mg/kg/24 hr divided q 12 hr IV or IM; weight >1,200 g: 150 mg/kg/24 hr divided q 8 hr IV or IM Children: 150 mg/kg/24 hr divided q 8 hr IV or IM (meningitis: 150 mg/kg/24 hr IV divided q 8 hr) Adults: 1-2 g q 8-12 hr IV or IM (max dose: 8-12 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Increasing pathogen resistance developing with long-term, widespread use Drug interaction: Probenecid
Ceftizoxime Cefizox Injection	Third-generation cephalosporin active against Gram-positive and Gram-negative pathogens. No antipseudomonal activity Children: 150 mg/kg/24 hr divided q 6-8 hr IV or IM Adults: 1-2 g q 6-8 hr IV or IM (max dose: 12 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated Drug interaction: Probenecid
Ceftriaxone sodium Rocephin Injection	Third-generation cephalosporin active against Gram-positive and Gram-negative pathogens. No antipseudomonal activity Neonates: 50-75 mg/kg q 24 hr IV or IM Children: 50-75 mg/kg q 24 hr IV or IM (meningitis: 75 mg/kg dose 1 then 80-100 mg/kg/24 hr divided q 12-24 hr IV or IM) Adults: 1-2 g q 24 hr IV or IM (max dose: 4 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Eliminated via kidney (33-65%) and bile; can cause sludging. Long half-life and dose-dependent protein binding favors q 24 hr rather than q 12 hr dosing. Can add 1% lidocaine for IM injection Drug interaction: Probenecid. In neonates, coadministration with calcium-containing products can result in severe precipitation and attendant embolic complications
Cefuroxime (cefuroxime axetil for oral administration) Ceftin, Kefurox, Zinacef Injection Suspension: 125 mg/5 mL Tablet: 125, 250, 500 mg	Second-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>E. coli</i> , <i>M. catarrhalis</i> , <i>Klebsiella</i> , and <i>Proteus</i> Neonates: 40-100 mg/kg/24 hr divided q 12 hr IV or IM Children: 200-240 mg/kg/24 hr divided q 8 hr IV or IM; PO administration: 20-30 mg/kg/24 hr divided q 8 hr PO Adults: 750-1,500 mg q 8 hr IV or IM (max dose: 6 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated. Food increases PO bioavailability Drug interaction: Probenecid
Cephalexin Keflex, Keftab Capsule: 250, 500 mg Tablet: 500 mg, 1 g Suspension: 125 mg/5 mL, 250 mg/5 mL, 100 mg/mL drops	First-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 25-100 mg/kg/24 hr divided q 6-8 hr PO Adults: 250-500 mg q 6 hr PO (max dose: 4 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated Drug interaction: Probenecid
Cephradine Velosef Capsule: 250, 500 mg Suspension: 125 mg/5 mL, 250 mg/5 mL	First-generation cephalosporin active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 50-100 mg/kg/24 hr divided q 6-12 hr PO Adults: 250-500 mg q 6-12 hr PO (max dose: 4 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated Drug interaction: Probenecid
Chloramphenicol Chloromycetin Injection Capsule: 250 mg Ophthalmic, otic solutions Ointment	Broad-spectrum protein synthesis inhibitor active against many Gram-positive and Gram-negative bacteria, <i>Salmonella</i> , vancomycin-resistant <i>Enterococcus faecium</i> , <i>Bacteroides</i> , other anaerobes, <i>Mycoplasma</i> , <i>Chlamydia</i> , and <i>Rickettsia</i> ; usually inactive against <i>Pseudomonas</i> Neonates: Initial loading dose 20 mg/kg followed 12 hr later by: postnatal age ≤7 days: 25 mg/kg/24 hr q 24 hr IV; >7 days: weight ≤2,000 g: 25 mg/kg/24 hr q 24 hr IV; weight >2,000 g: 50 mg/kg/24 hr divided q 12 hr IV Children: 50-75 mg/kg/24 hr divided q 6-8 hr IV or PO (meningitis: 75-100 mg/kg/24 hr IV divided q 6 hr) Adults: 50 mg/kg/24 hr divided q 6 hr IV or PO (max dose: 4 g/24 hr)	Cautions: Gray-baby syndrome (from too-high dose in neonate), bone marrow suppression aplastic anemia (monitor hematocrit, free serum iron) Drug interactions: Phenytoin, phenobarbital, rifampin may decrease levels Target serum concentrations: Peak 20-30 mg/L; trough 5-10 mg/L

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Ciprofloxacin Cipro Tablet: 100, 250, 500, 750 mg Injection Ophthalmic solution and ointment Otic suspension Oral suspension: 250 and 500 mg/5 mL	Quinolone antibiotic active against <i>P. aeruginosa</i> , <i>Serratia</i> , <i>Enterobacter</i> , <i>Shigella</i> , <i>Salmonella</i> , <i>Campylobacter</i> , <i>N. gonorrhoeae</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , some <i>S. aureus</i> , and some <i>Streptococcus</i> Neonates: 10 mg/kg q 12 hr PO or IV Children: 15-30 mg/kg/24 hr divided q 12 hr PO or IV; cystic fibrosis: 20-40 mg/kg/24 hr divided q 8-12 hr PO or IV Adults: 250-750 mg q 12 hr; 200-400 mg IV q 12 hr PO (max dose: 1.5 g/24 hr)	Cautions: Concerns of joint destruction in juvenile animals not seen in humans; tendonitis, superinfection, dizziness, confusion, crystalluria, some photosensitivity Drug interactions: Theophylline; magnesium-, aluminum-, or calcium-containing antacids; sucralfate; probenecid; warfarin; cyclosporine
Clarithromycin Biaxin Tablet: 250, 500 mg Suspension: 125 mg/5 mL, 250 mg/5 mL	Macrolide antibiotic with activity against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>Legionella</i> , <i>Mycoplasma</i> , and <i>C. trachomatis</i> Children: 15 mg/kg/24 hr divided q 12 hr PO Adults: 250-500 mg q 12 hr PO (max dose: 1 g/24 hr)	Cautions: Adverse events less than erythromycin; gastrointestinal upset, dyspepsia, nausea, cramping Drug interactions: Same as erythromycin: astemizole, carbamazepine, terfenadine, cyclosporine, theophylline, digoxin, tacrolimus
Clindamycin Cleocin Capsule: 75, 150, 300 mg Suspension: 75 mg/5 mL Injection Topical solution, lotion, and gel Vaginal cream	Protein synthesis inhibitor active against most Gram-positive aerobic and anaerobic cocci except <i>Enterococcus</i> Neonates: Postnatal age ≤ 7 days weight <2,000 g: 10 mg/kg/24 hr divided q 12 hr IV or IM; weight >2,000 g: 15 mg/kg/24 hr divided q 8 hr IV or IM; >7 days weight <1,200 g: 10 mg/kg/24 hr IV or IM divided q 12 hr; weight 1,200-2,000 g: 15 mg/kg/24 hr divided q 8 hr IV or IM; weight >2,000 g: 20 mg/kg/24 hr divided q 8 hr IV or IM Children: 10-40 mg/kg/24 hr divided q 6-8 hr IV, IM, or PO Adults: 150-600 mg q 6-8 hr IV, IM, or PO (max dose: 5 g/24 hr IV or IM or 2 g/24 hr PO)	Cautions: Diarrhea, nausea, <i>Clostridium difficile</i> -associated colitis, rash Administer slow IV over 30-60 min Topically active as an acne treatment
Cloxacillin sodium Tegopen Capsule: 250, 500 mg Suspension: 125 mg/5 mL	Penicillinase-resistant penicillin active against <i>S. aureus</i> and other Gram-positive cocci except <i>Enterococcus</i> and coagulase-negative staphylococci Children: 50-100 mg/kg/24 hr divided q 6 hr PO Adults: 250-500 mg q 6 hr PO (max dose: 4 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Primarily hepatically eliminated; requires dose reduction in renal disease. Food decreases bioavailability Drug interaction: Probenecid
Colistin (Colistimethate sodium; polymyxin E) Injection Inhalation	Treatment of multidrug resistant Gram-negative organisms (<i>Enterobacteriaceae</i> including extended-spectrum beta-lactamase and carbapenemase-producing strains) Children: 2.5-5 mg/kg/day divided in 2-4 divided doses IV Adults: 300 mg/day in 2-4 divided doses IV	Cautions: Nephrotoxicity (~3% in young children; higher rates in adolescents and adults); adjust dose for renal insufficiency; neurotoxicity (headaches, paresthesia, ataxia) Drug interactions: Should not be administered concomitantly with polymyxins or aminoglycosides
Co-trimoxazole (trimethoprim-sulfamethoxazole; TMP-SMZ) Bactrim, Cotrim, Septra, Sulfatrim Tablet: SMZ 400 mg and TMP 80 mg Tablet DS: SMZ 800 mg and TMP 160 mg Suspension: SMZ 200 mg and TMP 40 mg/5 mL Injection	Antibiotic combination with sequential antagonism of bacterial folate synthesis with broad antibacterial activity: <i>Shigella</i> , <i>Legionella</i> , <i>Nocardia</i> , <i>Chlamydia</i> , <i>Pneumocystis jiroveci</i> . Dosage based on TMP component Children: 6-20 mg TMP/kg/24 hr or IV divided q 12 hr PO <i>Pneumocystis carinii</i> pneumonia: 15-20 mg TMP/kg/24 hr divided q 12 hr PO or IV <i>P. carinii</i> prophylaxis: 5 mg TMP/kg/24 hr or 3 times/wk PO Adults: 160 mg TMP q 12 hr PO	Cautions: Drug dosed on TMP (trimethoprim) component. Sulfonamide skin reactions: rash, erythema multiforme, Stevens-Johnson syndrome, nausea, leukopenia. Renal and hepatic elimination; reduce dose in renal failure Drug interactions: Protein displacement with warfarin, possibly phenytoin, cyclosporine

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Continued

1306 Part XVII ◆ Infectious Diseases

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Daptomycin Cubicin	Disrupts bacterial cell membrane function, causing depolarization leading to inhibition of protein, DNA and RNA synthesis, which results in bacterial cell death. Active against enterococci (including glycopeptide-resistant strains), staphylococci (including MRSA), streptococci, and corynebacteria. Approved for skin and soft-tissue infections. Acceptable for bacteremia and right-sided endocarditis with susceptible strains Adults: In skin and soft-tissue infections, 4 mg/kg daptomycin is given intravenously once daily. For <i>S. aureus</i> bacteremia or right-sided endocarditis, the approved dose is 6 mg/kg given intravenously once daily Children: Unknown. Doses of 5-9 mg/kg/day in once-daily dosing have been reported in pediatric clinical trials	Cautions: Should not be used for pneumonia as drug inactivated by surfactants. Associated with rash, renal failure, anemia, headache. Is reported to cause myopathy, rhabdomyolysis, and eosinophilic pneumonia Drug interactions: Should not be administered with statins
Demeclocycline Declomycin Tablet: 150, 300 mg Capsule: 150 mg	Tetracycline active against most Gram-positive cocci except <i>Enterococcus</i> , many Gram-negative bacilli, anaerobes, <i>Borrelia burgdorferi</i> (Lyme disease), <i>Mycoplasma</i> , and <i>Chlamydia</i> Children: 8-12 mg/kg/24 hr divided q 6-12 hr PO Adults: 150 mg PO q 6-8 hr Syndrome of inappropriate antidiuretic hormone secretion: 900-1,200 mg/24 hr or 13-15 mg/kg/24 hr divided q 6-8 hr PO with dose reduction based on response to 600-900 mg/24 hr	Cautions: Teeth staining, possibly permanent (if administered <8 yr of age) with prolonged use; photosensitivity, diabetes insipidus, nausea, vomiting, diarrhea, superinfections Drug interactions: Aluminum-, calcium-, magnesium-, zinc- and iron-containing food, milk, dairy products may decrease absorption
Dicloxacillin Dynapen, Pathocil Capsule: 125, 250, 500 mg Suspension: 62.5 mg/5 mL	Penicillinase-resistant penicillin active against <i>S. aureus</i> and other Gram-positive cocci except <i>Enterococcus</i> and coagulase-negative staphylococci Children: 12.5-100 mg/kg/24 hr divided q 6 hr PO Adults: 125-500 mg q 6 hr PO	Cautions: β -Lactam safety profile (rash, eosinophilia). Primarily renally (65%) and bile (30%) elimination. Food may decrease bioavailability Drug interaction: Probenecid
Doripenem Doribax Injection	Carbapenem antibiotic with broad-spectrum activity against Gram-positive cocci and Gram-negative bacilli, including <i>P. aeruginosa</i> and anaerobes Children: dose unknown. Adults: 500 mg q 8 hr IV	Cautions: β -Lactam safety profile; does not undergo hepatic metabolism. Renal elimination (70-75%); dose adjustment for renal failure Drug interactions: Valproic acid, probenecid
Doxycycline Vibramycin, Doxy Injection Capsule: 50, 100 mg Tablet: 50, 100 mg Suspension: 25 mg/5 mL Syrup: 50 mg/5 mL	Tetracycline antibiotic active against most Gram-positive cocci except <i>Enterococcus</i> , many Gram-negative bacilli, anaerobes, <i>B. burgdorferi</i> (Lyme disease), <i>Mycoplasma</i> , and <i>Chlamydia</i> Children: 2-5 mg/kg/24 hr divided q 12-24 hr PO or IV (max dose: 200 mg/24 hr) Adults: 100-200 mg/24 hr divided q 12-24 hr PO or IV	Cautions: Teeth staining, possibly permanent (<8 yr of age) with prolonged use; photosensitivity, nausea, vomiting, diarrhea, superinfections Drug interactions: Aluminum-, calcium-, magnesium-, zinc-, iron-, kaolin-, and pectin-containing products, food, milk, dairy products may decrease absorption. Carbamazepine, rifampin, barbiturates may decrease half-life
Erythromycin E-Mycin, Ery-Tab, Eryc, Ilosone Estolate 125, 500 mg Tablet EES: 200 mg Tablet base: 250, 333, 500 mg Suspension: estolate 125 mg/5 mL, 250 mg/5 mL, EES 200 mg/5 mL, 400 mg/5 mL Estolate drops: 100 mg/mL. EES drops: 100 mg/2.5 mL. Available in combination with sulfisoxazole (Pedazole), dosed on erythromycin content	Bacteriostatic macrolide antibiotic most active against Gram-positive organisms, <i>Corynebacterium diphtheriae</i> , and <i>Mycoplasma pneumoniae</i> Neonates: Postnatal age ≤7 days: 20 mg/kg/24 hr divided q 12 hr PO; >7 days weight <1,200 g: 20 mg/kg/24 hr divided q 12 hr PO; weight >1,200 g: 30 mg/kg/24 hr divided q 8 hr PO (give as 5 mg/kg/dose q 6 hr to improve feeding intolerance) Children: Usual max dose 2 g/24 hr Base: 30-50 mg/kg/24 hr divided q 6-8 hr PO Estolate: 30-50 mg/kg/24 hr divided q 8-12 hr PO Stearate: 20-40 mg/kg/24 hr divided q 6 hr PO Lactobionate: 20-40 mg/kg/24 hr divided q 6-8 hr IV Glucetate: 20-50 mg/kg/24 hr divided q 6 hr IV; usual max dose 4 g/24 hr IV Adults: Base: 333 mg PO q 8 hr; estolate/stearate/base: 250-500 mg q 6 hr PO	Cautions: Motilin agonist leading to marked abdominal cramping, nausea, vomiting, diarrhea. Associated with hypertrophic pyloric stenosis in young infants. Many different salts with questionable tempering of gastrointestinal adverse events. Rare cardiac toxicity with IV use. Dose of salts differ. Topical formulation for treatment of acne Drug interactions: Antagonizes hepatic CYP 3A4 activity: astemizole, carbamazepine, terfenadine, cyclosporine, theophylline, digoxin, tacrolimus, carbamazepine

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Gentamicin Garamycin Injection Ophthalmic solution, ointment, topical cream	Aminoglycoside antibiotic active against Gram-negative bacilli, especially <i>E. coli</i> , <i>Klebsiella</i> , <i>Proteus</i> , <i>Enterobacter</i> , <i>Serratia</i> , and <i>Pseudomonas</i> Neonates: Postnatal age ≤7 days weight 1,200-2,000 g: 2.5 mg/kg q 12-18 hr IV or IM; weight <2,000 g: 2.5 mg/kg q 12 hr IV or IM; postnatal age >7 days weight 1,200-2,000 g: 2.5 mg/kg q 8-12 hr IV or IM; weight >2,000 g: 2.5 mg/kg q 8 hr IV or IM Children: 2.5 mg/kg/24 hr divided q 8-12 hr IV or IM. Alternatively may administer 5-7.5 mg/kg/24 hr IV once daily Intrathecal: Preservative-free preparation for intraventricular or intrathecal use: neonate: 1 mg/24 hr; children: 1-2 mg/24 hr intrathecal; adults: 4-8 mg/24 hr Adults: 3-6 mg/kg/24 hr divided q 8 hr IV or IM	Cautions: Anaerobes, <i>S. pneumoniae</i> , and other <i>Streptococcus</i> are resistant. May cause ototoxicity and nephrotoxicity. Monitor renal function. Drug eliminated renally. Administered IV over 30-60 min Drug interactions: May potentiate other ototoxic and nephrotoxic drugs Target serum concentrations: Peak 6-12 mg/L; trough >2 mg/L with intermittent daily dose regimens only
Imipenem-cilastatin Primaxin Injection	Carbapenem antibiotic with broad-spectrum activity against Gram-positive cocci and Gram-negative bacilli, including <i>P. aeruginosa</i> and anaerobes. No activity against <i>Stenotrophomonas maltophilia</i> Neonates: Postnatal age ≤7 days weight <1,200 g: 20 mg/kg q 18-24 hr IV or IM; weight >1,200 g: 40 mg/kg divided q 12 hr IV or IM; postnatal age >7 days weight 1,200-2,000 g: 40 mg/kg q 12 hr IV or IM; weight >2,000 g: 60 mg/kg q 8 hr IV or IM Children: 60-100 mg/kg/24 hr divided q 6-8 hr IV or IM Adults: 2-4 g/24 hr divided q 6-8 hr IV or IM (max dose: 4 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia), nausea, seizures. Cilastatin possesses no antibacterial activity; reduces renal imipenem metabolism. Primarily renally eliminated Drug interaction: Possibly ganciclovir
Linezolid Zyvox Tablet: 400, 600 mg Oral suspension: 100 mg/5 mL Injection: 100 mg/5 mL	Oxazolidinone antibiotic active against Gram-positive cocci (especially drug-resistant organisms), including <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>E. faecium</i> , and <i>Enterococcus faecalis</i> . Interferes with protein synthesis by binding to 50S ribosome subunit Children: 10 mg/kg q 12 hr IV or PO Adults: Pneumonia: 600 mg q 12 hr IV or PO; skin infections: 400 mg q 12 hr IV or PO	Adverse events: Myelosuppression, pseudomembranous colitis, nausea, diarrhea, headache Drug interaction: Probenecid
Loracarbef Lorabid Capsule: 200 mg Suspension: 100 mg/5 mL, 200 mg/5 mL	Carbacephem very closely related to cefaclor (second-generation cephalosporin) active against <i>S. aureus</i> , <i>Streptococcus</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>E. coli</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 30 mg/kg/24 hr divided q 12 hr PO (max dose: 2 g) Adults: 200-400 mg q 12 hr PO (max dose: 800 mg/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia). Renally eliminated Drug interaction: Probenecid
Meropenem Merrem Injection	Carbapenem antibiotic with broad-spectrum activity against Gram-positive cocci and Gram-negative bacilli, including <i>P. aeruginosa</i> and anaerobes. No activity against <i>S. maltophilia</i> Children: 60 mg/kg/24 hr divided q 8 hr IV meningitis: 120 mg/kg/24 hr (max dose: 6 g/24 hr) q 8 hr IV Adults: 1.5-3 g q 8 hr IV	Cautions: β-Lactam safety profile; appears to possess less CNS excitation than imipenem. 80% renal elimination Drug interaction: Probenecid
Metronidazole Flagyl, Metro I.V., Topical gel, vaginal gel Injection Tablet: 250, 500 mg	Highly effective in the treatment of infections caused by anaerobes. Oral therapy of <i>C. difficile</i> colitis Neonates: weight <1,200 g: 7.5 mg/kg 48 hr PO or IV; postnatal age ≤7 days weight 1,200-2,000 g: 7.5 mg/kg/24 hr q 24 hr PO or IV; weight 2,000 g: 15 mg/kg/24 hr divided q 12 hr PO or IV; postnatal age <7 days weight 1,200-2,000 g: 15 mg/kg/24 hr divided q 12 hr PO or IV; weight >2,000 g: 30 mg/kg/24 hr divided q 12 hr PO or IV Children: 30 mg/kg/24 hr divided q 6-8 hr PO or IV Adults: 30 mg/kg/24 hr divided q 6 hr PO or IV (max dose: 4 g/24 hr)	Cautions: Dizziness, seizures, metallic taste, nausea, disulfiram-like reaction with alcohol. Administer IV slow over 30-60 min. Adjust dose with hepatic impairment Drug interactions: Carbamazepine, rifampin, phenobarbital may enhance metabolism; may increase levels of warfarin, phenytoin, lithium

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Continued

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Mezlocillin sodium Mezlin Infection	Extended-spectrum penicillin active against <i>E. coli</i> , <i>Enterobacter</i> , <i>Serratia</i> , and <i>Bacteroides</i> ; limited antipseudomonal activity Neonates: Postnatal age ≤7 days: 150 mg/kg/24 hr divided q 12 hr IV; >7 days: 225 mg/kg divided q 8 hr IV Children: 200-300 mg/kg/24 hr divided q 4-6 hr IV; cystic fibrosis 300-450 mg/kg/24 hr IV Adults: 2-4 g/dose q 4-6 hr IV (max dose: 12 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 1.8 mEq sodium. Interferes with platelet aggregation with high doses; increases noted in liver function test results. Renally eliminated. Inactivated by β-lactamase enzyme Drug interaction: Probenecid
Mupirocin Bactroban Ointment	Topical antibiotic active against <i>Staphylococcus</i> and <i>Streptococcus</i> Topical application: Nasal (eliminate nasal carriage) and to the skin 2-4 times per day	Caution: Minimal systemic absorption as drug metabolized within the skin.
Nafcillin sodium Nafcil, Unipen Injection Capsule: 250 mg Tablet: 500 mg	Penicillinase-resistant penicillin active against <i>S. aureus</i> and other Gram-positive cocci, except <i>Enterococcus</i> and coagulase-negative staphylococci Neonates: Postnatal age ≤7 days weight 1,200-2,000 g: 50 mg/kg/24 hr divided q 12 hr IV or IM; weight >2,000 g: 75 mg/kg/24 hr divided q 8 hr IV or IM; postnatal age >7 days weight 1,200-2,000 g: 75 mg/kg/q 8 hr; weight >2,000 g: 100 mg/kg divided q 6-8 hr IV (meningitis: 200 mg/kg/24 hr divided q 6 hr IV) Children: 100-200 mg/kg/24 hr divided q 4-6 hr IV Adults: 4-12 g/24 hr divided q 4-6 hr IV (max dose: 12 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia), phlebitis; painful given intramuscularly; oral absorption highly variable and erratic (not recommended) Adverse effect: Neutropenia
Nalidixic acid NegGram Tablet: 250, 500, 1,000 mg Suspension: 250 mg/5 mL	First-generation quinolone effective for short-term treatment of lower urinary tract infections caused by <i>E. coli</i> , <i>Enterobacter</i> , <i>Klebsiella</i> , and <i>Proteus</i> Children: 50-55 mg/kg/24 hr divided q 6 hr PO; suppressive therapy 25-33 mg/kg/24 hr divided q 6-8 hr PO Adults: 1 g q 6 hr PO; suppressive therapy: 500 mg q 6 hr PO	Cautions: Vertigo, dizziness, rash. Not for use in systemic infections Drug interactions: Liquid antacids
Neomycin sulfate Mycifradin Tablet: 500 mg Topical cream, ointment Solution: 125 mg/5 mL	Aminoglycoside antibiotic used for topical application or orally before surgery to decrease gastrointestinal flora (nonabsorbable) and hyperammonemia Infants: 50 mg/kg/24 hr divided q 6 hr PO Children: 50-100 mg/kg/24 hr divided q 6-8 hr PO Adults: 500-2,000 mg/dose q 6-8 hr PO	Cautions: In patients with renal dysfunction because small amount absorbed may accumulate Adverse events: Primarily related to topical application, abdominal cramps, diarrhea, rash Aminoglycoside ototoxicity and nephrotoxicity if absorbed
Nitrofurantoin Furadantin, Furan, Macrodantin Capsule: 50, 100 mg Extended-release capsule: 100 mg Macrocrystal: 50, 100 mg Suspension: 25 mg/5 mL	Effective in the treatment of lower urinary tract infections caused by Gram-positive and Gram-negative pathogens Children: 5-7 mg/kg/24 hr divided q 6 hr PO (max dose: 400 mg/24 hr); suppressive therapy 1-2.5 mg/kg/24 hr divided q 12-24 hr PO (max dose: 100 mg/24 hr) Adults: 50-100 mg/24 hr divided q 6 hr PO	Cautions: Vertigo, dizziness, rash, jaundice, interstitial pneumonitis. Do not use with moderate to severe renal dysfunction Drug interactions: Liquid antacids
Ofloxacin Ocuflax 0.3% ophthalmic solution: 1, 5, 10 mL Floxin 0.3% otic solution: 5, 10 mL	Quinolone antibiotic for treatment of conjunctivitis or corneal ulcers (ophthalmic solution) and otitis externa or chronic suppurative otitis media (otic solution) caused by susceptible Gram-positive, Gram-negative, anaerobic bacteria, or <i>C. trachomatis</i> Child >1-12 yr: Conjunctivitis: 1-2 drops in affected eye(s) q 2-4 hr for 2 days, then 1-2 drops qid for 5 days Corneal ulcers: 1-2 drops q 30 min while awake and at 4 hr intervals at night for 2 days, then 1-2 drops hourly for 5 days while awake, then 1-2 drops q 6 hr for 2 days Otitis externa (otic solution): 5 drops into affected ear bid for 10 days Chronic suppurative otitis media: treat for 14 days Child >12 yr and adults: Ophthalmic solution doses same as for younger children. Otitis externa (otic solution): Use 10 drops bid for 10 or 14 days as for younger children	Adverse events: Burning, stinging, eye redness (ophthalmic solution), dizziness with otic solution if not warmed

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Oxacillin sodium Prostaphlin Injection Capsule: 250, 500 mg Suspension: 250 mg/5 mL	Penicillinase-resistant penicillin active against <i>S. aureus</i> and other Gram-positive cocci, except <i>Enterococcus</i> and coagulase-negative <i>staphylococci</i> Neonates: Postnatal age ≤7 days weight 1,200-2,000 g: 50 mg/kg/24 hr divided q 12 hr IV; weight >2,000 g: 75 mg/kg/24 hr IV divided q 8 hr IV; postnatal age >7 days weight <1,200 g: 50 mg/kg/24 hr IV divided q 12 hr IV; weight 1,200-2,000 g: 75 mg/kg/24 hr divided q 8 hr IV; weight >2,000 g: 100 mg/kg/24 hr IV divided q 6 hr IV Infants: 100-200 mg/kg/24 hr divided q 4-6 hr IV Children: PO 50-100 mg/kg/24 hr divided q 4-6 hr IV Adults: 2-12 g/24 hr divided q 4-6 hr IV (max dose: 12 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia) Moderate oral bioavailability (35-65%) Primarily renally eliminated Drug interaction: Probenecid Adverse effect: Neutropenia
Penicillin G Injection Tablets	Penicillin active against most Gram-positive cocci; <i>S. pneumoniae</i> (resistance is increasing), group A <i>Streptococcus</i> , and some Gram-negative bacteria (e.g., <i>N. gonorrhoeae</i> , <i>N. meningitidis</i>) Neonates: Postnatal age ≤7 days weight 1,200-2,000 g: 50,000 units/kg/24 hr divided q 12 hr IV or IM (meningitis: 100,000 units/kg/24 hr divided q 12 hr IV or IM); weight >2,000 g: 75,000 units/kg/24 hr divided q 8 hr IV or IM (meningitis: 150,000 units/kg/24 hr divided q 8 hr IV or IM); postnatal age >7 days weight ≤1,200 g: 50,000 units/kg/24 hr divided q 12 hr IV (meningitis: 100,000 units/kg/24 hr divided q 12 hr IV); weight 1,200-2,000 g: 75,000 units/kg/24 hr q 8 hr IV (meningitis: 225,000 units/kg/24 hr divided q 8 hr IV); weight >2,000 g: 100,000 units/kg/24 hr divided q 6 hr IV (meningitis: 200,000 units/kg/24 hr divided q 6 hr IV) Children: 100,000-250,000 units/kg/24 hr divided q 4-6 hr IV or IM (max dose: 400,000 units/kg/24 hr) Adults: 2-24 million units/24 hr divided q 4-6 hr IV or IM	Cautions: β-Lactam safety profile (rash, eosinophilia), allergy, seizures with excessive doses particularly in patients with marked renal disease. Substantial pathogen resistance. Primarily renally eliminated Drug interaction: Probenecid
Penicillin G, benzathine Bicillin Injection	Long-acting repository form of penicillin effective in the treatment of infections responsive to persistent, low penicillin concentrations (1-4 wk), e.g., group A <i>Streptococcus</i> pharyngitis, rheumatic fever prophylaxis Neonates weight >1,200 g: 50,000 units/kg IM once Children: 300,000-1.2 million units/kg q 3-4 wk IM (max dose: 1.2-2.4 million units/dose) Adults: 1.2 million units IM q 3-4 wk	Cautions: β-Lactam safety profile (rash, eosinophilia), allergy. Administer by IM injection only. Substantial pathogen resistance. Primarily renally eliminated Drug interaction: Probenecid
Penicillin G, procaine Crysticillin Injection	Repository form of penicillin providing low penicillin concentrations for 12 hr Neonates weight >1,200 g: 50,000 units/kg/24 hr IM Children: 25,000-50,000 units/kg/24 hr IM for 10 days (max dose: 4.8 million units/dose) Gonorrhea: 100,000 units/kg (max dose: 4.8 million units/24 hr) IM once with probenecid 25 mg/kg (max dose: 1 g) Adults: 0.6-4.8 million units q 12-24 hr IM	Cautions: β-Lactam safety profile (rash, eosinophilia) allergy. Administer by IM injection only. Substantial pathogen resistance. Primarily renally eliminated Drug interaction: Probenecid
Penicillin V Pen VK, V-Cillin K Tablet: 125, 250, 500 mg Suspension: 125 mg/5 mL, 250 mg/5 mL	Preferred oral dosing form of penicillin, active against most Gram-positive cocci; <i>S. pneumoniae</i> (resistance is increasing), other streptococci, and some Gram-negative bacteria (e.g., <i>N. gonorrhoeae</i> , <i>N. meningitidis</i>) Children: 25-50 mg/kg/24 hr divided q 4-8 hr PO Adults: 125-500 mg q 6-8 hr PO (max dose: 3 g/24 hr)	Cautions: β-Lactam safety profile (rash, eosinophilia), allergy, seizures with excessive doses particularly in patients with renal disease. Substantial pathogen resistance. Primarily renally eliminated. Inactivated by penicillinase Drug interaction: Probenecid
Piperacillin Pipracil Injection	Extended-spectrum penicillin active against <i>E. coli</i> , <i>Enterobacter</i> , <i>Serratia</i> , <i>P. aeruginosa</i> , and <i>Bacteroides</i> Neonates: Postnatal age ≤7 days 150 mg/kg/24 hr divided q 8-12 hr IV; >7 days; 200 mg/kg divided q 6-8 hr IV Children: 200-300 mg/kg/24 hr divided q 4-6 hr IV; cystic fibrosis: 350-500 mg/kg/24 hr IV Adults: 2-4 g/dose q 4-6 hr (max dose: 24 g/24 hr IV)	Cautions: β-Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 1.9 mEq sodium. Interferes with platelet aggregation/serum sickness-like reaction with high doses; increases in liver function tests. Renally eliminated. Inactivated by penicillinase Drug interaction: Probenecid

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Continued

1310 Part XVII ◆ Infectious Diseases

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Piperacillin-tazobactam Zosyn Injection	Extended-spectrum penicillin (piperacillin) combined with a β -lactamase inhibitor (tazobactam) active against <i>S. aureus</i> , <i>H. influenzae</i> , <i>E. coli</i> , <i>Enterobacter</i> , <i>Serratia</i> , <i>Acinetobacter</i> , <i>P. aeruginosa</i> , and <i>Bacteroides</i> Children: 300-400 mg/kg/24 hr divided q 6-8 hr IV or IM Adults: 3.375 g q 6-8 hr IV or IM	Cautions: β -Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 1.9 mEq sodium Interferes with platelet aggregation, serum sickness-like reaction with high doses, increases in liver function test results. Renally eliminated <i>Drug interaction:</i> Probenecid
Quinupristin/dalfopristin Synercid IV injection: powder for reconstitution, 10 mL contains 150 mg quinupristin, 350 mg dalfopristin	Streptogramin antibiotic (quinupristin) active against vancomycin-resistant <i>E. faecium</i> (VRE) and methicillin-resistant <i>S. aureus</i> (MRSA). Not active against <i>E. faecalis</i> Children and adults: VRE: 7.5 mg/kg q 8 hr IV for VRE; skin infections: 7.5 mg/kg q 12 hr IV	Adverse events: Pain, edema, or phlebitis at injection site, nausea, diarrhea <i>Drug interactions:</i> Synercid is a potent inhibitor of CYP 3A4
Sulfadiazine Tablet: 500 mg	Sulfonamide antibiotic primarily indicated for the treatment of lower urinary tract infections caused by <i>E. coli</i> , <i>P. mirabilis</i> , and <i>Klebsiella</i> Toxoplasmosis: Neonates: 100 mg/kg/24 hr divided q 12 hr PO with pyrimethamine 1 mg/kg/24 hr PO (with folic acid) Children: 120-200 mg/kg/24 hr divided q 6 hr PO with pyrimethamine 2 mg/kg/24 hr divided q 12 hr PO \geq 3 days then 1 mg/kg/24 hr (max dose: 25 mg/24 hr) with folic acid Rheumatic fever prophylaxis: weight \leq 30 kg: 500 mg/24 hr q 24 hr PO; weight $>$ 30 kg: 1 g/24 hr q 24 hr PO	Cautions: Rash, Stevens-Johnson syndrome, nausea, leukopenia, crystalluria. Renal and hepatic elimination; avoid use with renal disease. Half-life ~10 hr <i>Drug interactions:</i> Protein displacement with warfarin, phenytoin, methotrexate
Sulfamethoxazole Gantanol Tablet: 500 mg Suspension: 500 mg/5 mL	Sulfonamide antibiotic used for the treatment of otitis media, chronic bronchitis, and lower urinary tract infections due to susceptible bacteria Children: 50-60 mg/kg/24 hr divided q 12 hr PO Adults: 1 g/dose q 12 hr PO (max dose: 3 g/24 hr)	Cautions: Rash, Stevens-Johnson syndrome, nausea, leukopenia, crystalluria. Renal and hepatic elimination; avoid use with renal disease. Half-life 12 hr. Initial dose often a loading dose (doubled) <i>Drug interactions:</i> Protein displacement with warfarin, phenytoin, methotrexate
Sulfisoxazole Gantrisin Tablet: 500 mg Suspension: 500 mg/5 mL Ophthalmic solution, ointment	Sulfonamide antibiotic used for the treatment of otitis media, chronic bronchitis, and lower urinary tract infections caused by susceptible bacteria Children: 120-150 mg/kg/24 hr divided q 4-6 hr PO (max dose: 6 g/24 hr) Adults: 4-8 g/24 hr divided q 4-6 hr PO	Cautions: Rash, Stevens-Johnson syndrome, nausea, leukopenia, crystalluria. Renal and hepatic elimination; avoid use with renal disease. Half-life ~7-12 hr. Initial dose often a loading dose (doubled) <i>Drug interactions:</i> Protein displacement with warfarin, phenytoin, methotrexate
Ticarcillin Ticar Injection	Extended-spectrum penicillin active against <i>E. coli</i> , <i>Enterobacter</i> , <i>Serratia</i> , <i>P. aeruginosa</i> , and <i>Bacteroides</i> Neonates: Postnatal age \leq 7 days weight $<$ 2,000 g: 150 mg/kg/24 hr divided q 8-12 hr IV; $>$ 7 days weight $<$ 2,000 g: 225 mg/kg/24 hr divided q 8 hr IV; $>$ 7 days weight $<$ 1,200 g: 150 mg/kg/24 hr divided q 12 hr IV; weight 1,200-2,000 g: 225 mg/kg/24 hr divided q 8 hr IV; weight $>$ 2,000 g: 300 mg/kg/24 hr divided q 6-8 hr IV Children: 200-400 mg/kg/24 hr divided q 4-6 hr IV; cystic fibrosis: 400-600 mg/kg/24 hr IV Adults: 2-4 g/dose q 4-6 hr IV (max dose: 24 g/24 hr)	Cautions: β -Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 5-6 mEq sodium. Interferes with platelet aggregation; increases in liver function tests. Renally eliminated. Inactivated by penicillinase <i>Drug interaction:</i> Probenecid
Ticarcillin-clavulanate Timimentin Injection	Extended-spectrum penicillin (ticarcillin) combined with a β -lactamase inhibitor (clavulanate) active against <i>S. aureus</i> , <i>H. influenzae</i> , <i>Enterobacter</i> , <i>E. coli</i> , <i>Serratia</i> , <i>P. aeruginosa</i> , <i>Acinetobacter</i> , and <i>Bacteroides</i> Children: 280-400 mg/kg/24 hr q 4-8 hr IV or IM Adults: 3.1 g q 4-8 hr IV or IM (max dose: 18-24 g/24 hr)	Cautions: β -Lactam safety profile (rash, eosinophilia); painful given intramuscularly; each gram contains 5-6 mEq sodium. Interferes with platelet aggregation; increases in liver function tests. Renally eliminated <i>Drug interaction:</i> Probenecid

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

Table 180-3 Antibacterial Medications (Antibiotics)—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	INDICATIONS (MECHANISM OF ACTION) AND DOSING	COMMENTS
Tigecycline Tygacil Injection	Tetracycline-class antibiotic (glycylcycline) active against Enterobacteriaceae, including extended spectrum β -lactamase producers; streptococci (including VRE); staphylococci (including MRSA); and anaerobes Children: unknown Adults: 100 mg loading dose followed by 50 mg q 12 hr IV	Cautions: Pregnancy; children <8 yr of age; photosensitivity; hypersensitivity to tetracyclines; hepatic impairment (~60% hepatic clearance) Drug interaction: Warfarin; mycophenolate mofetil
Tobramycin Nebcin, Tobrex Injection Ophthalmic solution, ointment	Aminoglycoside antibiotic active against Gram-negative bacilli, especially <i>E. coli</i> , <i>Klebsiella</i> , <i>Enterobacter</i> , <i>Serratia</i> , <i>Proteus</i> , and <i>Pseudomonas</i> Neonates: Postnatal age \leq 7 days, weight 1,200-2,000 g: 2.5 mg/kg q 12-18 hr IV or IM; weight >2,000 g: 2.5 mg/kg q 12 hr IV or IM; postnatal age >7 days, weight 1,200-2,000 g: 2.5 mg/kg q 8-12 hr IV or IM; weight >2,000 g: 2.5 mg/kg q 8 hr IV or IM Children: 2.5 mg/kg/24 hr divided q 8-12 hr IV or IM. Alternatively may administer 5-7.5 mg/kg/24 hr IV. Preservative-free preparation for intraventricular or intrathecal use: neonate: 1 mg/24 hr; children: 1-2 mg/24 hr; adults: 4-8 mg/24 hr Adults: 3-6 mg/kg/24 hr divided q 8 hr IV or IM	Cautions: <i>S. pneumoniae</i> , other <i>Streptococcus</i> , and anaerobes are resistant. May cause ototoxicity and nephrotoxicity. Monitor renal function. Drug eliminated renally. Administered IV over 30-60 min Drug interactions: May potentiate other ototoxic and nephrotoxic drugs Target serum concentrations: Peak 6-12 mg/L; trough <2 mg/L
Trimethoprim Proloprim, Trimpepx Tablet: 100, 200 mg	Folic acid antagonist effective in the prophylaxis and treatment of <i>E. coli</i> , <i>Klebsiella</i> , <i>P. mirabilis</i> , and <i>Enterobacter</i> urinary tract infections; <i>P. carinii</i> pneumonia Children: For urinary tract infection: 4-6 mg/kg/24 hr divided q 12 hr PO Children >12 yr and adults: 100-200 mg q 12 hr PO. <i>P. carinii</i> pneumonia (with dapsone): 15-20 mg/kg/24 hr divided q 6 hr for 21 days PO	Cautions: Megaloblastic anemia, bone marrow suppression, nausea, epigastric distress, rash Drug interactions: Possible interactions with phenytoin, cyclosporine, rifampin, warfarin
Vancomycin Vancocin, Lyphocin Injection Capsule: 125 mg, 250 mg Suspension	Glycopeptide antibiotic active against most Gram-positive pathogens including staphylococci (including MRSA and coagulase-negative staphylococci), <i>S. pneumoniae</i> including penicillin-resistant strains, <i>Enterococcus</i> (resistance is increasing), and <i>C. difficile</i> -associated colitis Neonates: Postnatal age \leq 7 days, weight <1,200 g: 15 mg/kg/24 hr divided q 24 hr IV; weight 1,200-2,000 g: 15 mg/kg/24 hr divided q 12-18 hr IV; weight >2,000 g: 30 mg/kg/24 hr divided q 12 hr IV; postnatal age >7 days, weight <1,200 g: 15 mg/kg/24 hr divided q 24 hr IV; weight 1,200-2,000 g: 15 mg/kg/24 hr divided q 8-12 hr IV; weight >2,000 g: 45 mg/kg/24 hr divided q 8 hr IV Children: 45-60 mg/kg/24 hr divided q 8-12 hr IV; <i>C. difficile</i> -associated colitis: 40-50 mg/kg/24 hr divided q 6-8 hr PO. 40-50 mg/kg/24 hr divided q 6-8 hr PO	Cautions: Ototoxicity and nephrotoxicity particularly when co-administered with other ototoxic and nephrotoxic drugs Infuse IV over 45-60 min. Flushing (red man syndrome) associated with rapid IV infusions, fever, chills, phlebitis (central line is preferred). Renally eliminated Target serum concentrations: Peak (1 hr after 1 hr infusion) 30-40 mg/L; trough 5-10 mg/L

*In the Drug column, the generic drug name is in bold. In the Indications column, **bold** indicates major organisms targeted and mechanisms of action.

1312 Part XVII ◆ Infectious Diseases

Table 180-4 Adverse Reactions to Penicillins*		
TYPE OF REACTION	FREQUENCY (%)	OCCURS MOST FREQUENTLY WITH*
ALLERGIC		
Immunoglobulin E antibody	0.004-0.4	Penicillin G
• Anaphylaxis		
• Early urticaria (<72 hr)		
Cytotoxic antibody	Rare	Penicillin G
• Hemolytic anemia		
Antigen-antibody complex disease	Rare	Penicillin G
• Serum sickness		
Delayed hypersensitivity	4-8	Ampicillin
• Contact dermatitis		
IDIOPATHIC	4-8	Ampicillin
Skin rash		
Fever		
Late-onset urticaria		
GASTROINTESTINAL	2-5	
Diarrhea	2-5	Ampicillin
Enterocolitis	<1	Ampicillin
HEMATOLOGIC		
Hemolytic anemia	Rare	Penicillin G
Neutropenia	1-4	Penicillin G, nafcillin, oxacillin, piperacillin
Platelet dysfunction	3	Ticarcillin
HEPATIC		
Elevated serum aspartate transaminase level	1-4	Flucloxacillin, nafcillin, oxacillin
ELECTROLYTE DISTURBANCE		
Sodium overload	Variable	Ticarcillin
Hypokalemia	Variable	Ticarcillin
Hyperkalemia—acute	Rare	Penicillin G
NEUROLOGIC		
Seizures	Rare	Penicillin G
Bizarre sensations		Procaine penicillin
RENAL		
Interstitial nephritis	<1%	Any penicillin

*All the reactions can occur with any of the penicillins.

Table 180-6 Potential Adverse Effects of Cephalosporins		
TYPE	SPECIFIC	FREQUENCY
Hypersensitivity	Rash Urticaria Serum sickness Anaphylaxis	1-3% <1% <1% 0.01%
Gastrointestinal	Diarrhea Nausea, vomiting Transient transaminase elevation Biliary sludge	1-19% 1-6% 1-7% 20-46%*
Hematologic	Eosinophilia Neutropenia Thrombocytopenia Hypoprothrombinemia Impaired platelet aggregation Hemolytic anemia	1-10% <1% <1-3% <1% <1% <1%
Renal	Interstitial nephritis	<1%
Central nervous system	Seizures Encephalopathy	<1% <1%
False-positive laboratory	Coombs positive Glucosuria Serum creatinine	3% Rare Rare
Other	Drug fever Disulfiram-like reaction* Superinfection Phlebitis Calcium-antibiotic precipitation (ceftriaxone)	Rare Rare Rare Rare Unknown; is associated with embolic events

*Cephalosporins with thiomethyl tetrazole ring (MTT) side chain.

Table 180-5 Classification of Parenteral and Oral Cephalosporins						
CEPHALOSPORINS	FIRST GENERATION	SECOND GENERATION	CEPHAMYCINS	THIRD GENERATION	FOURTH GENERATION	FIFTH GENERATION
Parenteral	Cefazolin (Ancef, Kefzol) Cephalothin (Keflin, Seffin) Cephapirin (Cefadyl) Cephradine (Velosef)	Cefamandole (Mandol) Cefonicid (Monocid) Cefuroxime (Kefurox, Zinacef)	Cefmetazole (Zefazone) Cefotetan (Cefotan) Cefoxitin (Mefoxin)	Cefoperazone (Cefobid) Cefotaxime (Claforan) Ceftazidime (Fortaz) Ceftizoxime (Cefizox) Ceftriaxone (Rocephin)	Cefepime (Maxipime) Cefpirome (Cefrom) Ceftolozane (combined with tazobactam; CXA-101)	Ceftaroline (Teflaro) Ceftobiprole (Zeftera)
Oral	Cefadroxil (Duricef, Ultracet) Cephalexin (Keflex, Biocef, Keftab) Cephradine (Velosef)	Cefaclor (Ceclor) Cefprozil (Cefzil) Cefuroxime-axetil (Ceftin) Loracarbef (Lorabid)		Cefdinir (Omnicef) Cefditoren (Spectracef) Cefixime (Suprax) Cefpodoxime (Vantin) Ceftibuten (Cedax)		

Adapted from Mandell GL, Bennett JE, Dolin R, editors: Principles and practice of infectious diseases, ed 7. Philadelphia, 2010, Elsevier, Table 22-1.

Table 181-1 Parenteral Antimicrobial Agent(s) for Treatment of Bacteremia and Other Serious *Staphylococcus aureus* Infections

SUSCEPTIBILITY	ANTIMICROBIAL AGENTS	COMMENTS
I. INITIAL EMPIRIC THERAPY (ORGANISM OF UNKNOWN SUSCEPTIBILITY)		
Drugs of choice:	Vancomycin (15 mg/kg Q6-H + nafcillin or oxacillin)	For life-threatening infections (i.e., septicemia, endocarditis, CNS infection); linezolid could be substituted if the patient has received several recent courses of vancomycin
	Vancomycin (15 mg/kg Q8H)	For non-life-threatening infection without signs of severe sepsis (e.g., skin infection, cellulitis, osteomyelitis, pyarthritis) when rates of MRSA colonization and infection in the community are substantial
	Clindamycin	For non-life-threatening infection without signs of severe sepsis when rates of MRSA colonization and infection in the community are substantial and prevalence of clindamycin resistance is low
II. METHICILLIN-SUSCEPTIBLE, PENICILLIN-RESISTANT <i>S. AUREUS</i>		
Drugs of choice:	Nafcillin or oxacillin [†]	Only for patients with a serious penicillin allergy and clindamycin-susceptible strain
Alternatives (depending on susceptibility results):	Cefazolin Clindamycin Vancomycin Ampicillin + sulbactam	Only for penicillin- and cephalosporin-allergic patients
III. MRSA (OXACILLIN MIC, 4 µG/ML OR GREATER)		
<i>A. Healthcare-Associated (Multidrug-Resistant)</i>		
Drugs of choice:	Vancomycin + gentamicin [†]	
Alternatives: susceptibility testing results available before alternative drugs are used	Trimethoprim-sulfamethoxazole Linezolid [‡] Quinupristin-dalfopristin [†] Fluoroquinolones	Not recommended for people younger than 18 yr of age or as monotherapy
<i>B. Community (Not Multidrug-Resistant)</i>		
Drugs of choice:	Vancomycin + gentamicin [†] Clindamycin (if strain susceptible) Trimethoprim-sulfamethoxazole	For life-threatening infections For pneumonia, septic arthritis, osteomyelitis, skin or soft tissue infections For skin or soft tissue infections
Alternatives:	Vancomycin	
IV. VANCOMYCIN INTERMEDIATELY SUSCEPTIBLE OR <i>S. AUREUS</i>[‡] (MIC, 4 TO 16 µG/ML)[‡]		
Drugs of choice:	Optimal therapy is not known Linezolid [‡] Daptomycin [§] Quinupristin-dalfopristin [†] Tigecycline [†]	Dependent on in vitro susceptibility test results
Alternatives:	Vancomycin + linezolid ± gentamicin Vancomycin + trimethoprim-sulfamethoxazole [†]	

[†]One of the adjunctive agents, gentamicin or rifampin, should be added to the therapeutic regimen for life-threatening infections such as endocarditis or CNS infection or infections with a vancomycin-intermediate *S. aureus* strain. Consultation with an infectious diseases specialist should be considered to determine which agent to use and duration of use.

[‡]Linezolid, quinupristin-dalfopristin, and tigecycline are agents with activity in vitro and efficacy in adults with multidrug-resistant, Gram-positive organisms, including *S. aureus*. Because experience with these agents in children is limited, consultation with an infectious diseases specialist should be considered before use.

[§]Daptomycin is active in vitro against multidrug-resistant, Gram-positive organisms, including *S. aureus*, but has not been evaluated in children. Daptomycin is approved by the US FDA only for the treatment of complicated skin and skin structure infections and for *S. aureus* bloodstream infections. Daptomycin is ineffective for treatment of pneumonia and is not indicated for patients 18 yr of age and older.

CNS, central nervous system; MRSA, methicillin-resistant *S. aureus*; MIC, minimum inhibitory concentration.

From Pickering LK, editor: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics.

1326 Part XVII ◆ Infectious Diseases

RISK GROUP	UNDERLYING MEDICAL CONDITION	PCV13 RECOMMENDED	PPSV23 RECOMMENDED	REVACCINATION 5 YR AFTER 1ST DOSE
Immunocompetent persons	Chronic heart disease [§] Chronic lung disease Diabetes mellitus Cerebrospinal fluid leaks Cochlear implants Alcoholism Chronic liver disease Cigarette smoking		✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓	
Persons with functional or anatomic asplenia	Sickle cell disease/other hemoglobinopathies Congenital or acquired asplenia	✓ ✓	✓ ✓	✓ ✓

AGE AT 1ST DOSE (MO)	PRIMARY PCV13 SERIES* PCV13 BOOSTER DOSE [†]
2-6	3 doses 1 dose at age 12-15 mo
7-11	2 doses 1 dose at age 12-15 mo
12-23	2 doses —
24-59 (healthy children)	1 dose —
24-71 (children with certain chronic diseases or immunocompromising conditions)	2 doses —

*Minimum interval between doses is 8 wk except for children vaccinated at age <12 mo for whom minimum interval between doses is 4 wk. Minimum age for administration of 1st dose is 6 wk.

[†]Given at least 8 wk after the previous dose.

From Centers for Disease Control and Prevention (CDC): Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children—Advisory Committee on Immunization Practices (ACIP), 2010, MMWR Morb Mortal Wkly Rep 59:258–261, 2010, Table 2.

INFANT SERIES	BOOSTER DOSE	SUPPLEMENTAL PCV13 DOSE		
2 mo	4 mo	6 mo	≥12 mo*	14-59 mo [†]
PCV7	PCV13	PCV13	PCV13	—
PCV7	PCV7	PCV13	PCV13	—
PCV7	PCV7	PCV7	PCV13	—
PCV7	PCV7	PCV7	PCV7	PCV13

*No additional PCV13 doses are indicated for children age 12-23 mo who have received 2 or 3 doses of PCV before age 12 mo and at least 1 dose of PCV13 at age ≥12 mo.

[†]For children with underlying medical conditions (see Table 182-1), a single supplemental PCV13 dose is recommended through age 71 mo.

From Centers for Disease Control and Prevention (CDC): Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children—Advisory Committee on Immunization Practices (ACIP), 2010, MMWR Morb Mortal Wkly Rep 59:258–261, 2010, Table 3.

CLINICAL CRITERIA	
Hypotension plus 2 or more of the following:	
Renal impairment	
Coagulopathy	
Hepatic involvement	
Adult respiratory distress syndrome	
Generalized erythematous macular rash	
Soft-tissue necrosis	
DEFINITE CASE	
Clinical criteria plus group A streptococcus from a normally sterile site	
PROBABLE CASE	
Clinical criteria plus group A streptococcus from a nonsterile site	

Table 181-2 Diagnostic Criteria of Staphylococcal Toxic Shock Syndrome

MAJOR CRITERIA (ALL REQUIRED)

Acute fever; temperature >38.8°C (101.8°F)
Hypotension (orthostatic, shock; blood pressure below age-appropriate norms)
Rash (erythroderma with convalescent desquamation)

MINOR CRITERIA (ANY 3 OR MORE)

Mucous membrane inflammation (vaginal, oropharyngeal or conjunctival hyperemia, strawberry tongue)
Vomiting, diarrhea
Liver abnormalities (bilirubin or transaminase greater than twice upper limit of normal)
Renal abnormalities (urea nitrogen or creatinine greater than twice upper limit of normal, or greater than 5 white blood cells per high-power field)
Muscle abnormalities (myalgia or creatinine phosphokinase greater than twice upper limit of normal)
Central nervous system abnormalities (alteration in consciousness without focal neurologic signs)
Thrombocytopenia (100,000/mm³ or less)

EXCLUSIONARY CRITERIA

Absence of another explanation
Negative blood cultures (except occasionally for *Staphylococcus aureus*)

Data from Pickering LK, editor: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics.

Table 183-2 Guidelines for the Diagnosis of Initial or Recurrent Attack of Rheumatic Fever (Jones Criteria, Updated 2015)¹⁻⁵

MAJOR MANIFESTATIONS	MINOR MANIFESTATIONS	SUPPORTING EVIDENCE OF ANTECEDENT GROUP A STREPTOCOCCAL INFECTION
Carditis Polyarthritis Erythema marginatum Subcutaneous nodules Chorea	Clinical features: Arthralgia Fever Laboratory features: Elevated acute phase reactants: Erythrocyte sedimentation rate C-reactive protein Prolonged P-R interval	Positive throat culture or rapid streptococcal antigen test Elevated or increasing streptococcal antibody titer

From Guidelines for the diagnosis of rheumatic fever. Jones Criteria, 2015 update. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association (in press).

1. Initial attack: 2 major manifestations, or 1 major and 2 minor manifestations, plus evidence of recent GAS infection. Recurrent attack: 2 major, or 1 major and 2 minor, or 3 minor manifestations (the latter only in the Moderate/High-Risk population), plus evidence of recent GAS infection (see text).

2. Low-Risk population is defined as ARF incidence <2 per 100,000 school-age children per year, or all-age RHD prevalence of <1 per 1000 population. Moderate/High-Risk population is defined as ARF incidence >2 per 100,000 school-age children per year, or all-age RHD prevalence of >1 per 1000 population.

3. Carditis is now defined as clinical and/or subclinical (echocardiographic valvulitis). See Table 183-3.

4. Arthritis (major) refers only to polyarthritis in Low-Risk populations, but also to monoarthritis or polyarthralgia in Moderate/High-Risk populations.

5. Minor criteria for Moderate/High-Risk populations only include monoarthralgia (polyarthralgia for Low-Risk populations), fever of >38° C (>38.5° C in Low-Risk populations), ESR >30 mm/hr (>60 mm/hr in Low-Risk populations).

Table 183-5 Chemoprophylaxis for Recurrences of Acute Rheumatic Fever (Secondary Prophylaxis)

DRUG	DOSE	ROUTE
Penicillin G benzathine	600,000 IU for children weighing ≤60 lb 1.2 million IU for children weighing >60 lb, every 4 wk*	Intramuscular
or		
Penicillin V or	250 mg, twice a day	Oral
Sulfadiazine or sulfisoxazole	0.5 g, once a day for patients weighing ≤60 lb 1.0 g, once a day for patients weighing >60 lb	Oral
FOR PEOPLE WHO ARE ALLERGIC TO PENICILLIN AND SULFONAMIDE DRUGS		
Macrolide or azalide	Variable	Oral

*In high-risk situations, administration every 3 wk is recommended.

Table 183-6 Duration of Prophylaxis for People Who Have Had Acute Rheumatic Fever: Recommendations of the American Heart Association

CATEGORY	DURATION
Rheumatic fever without carditis	5 yr or until 21 yr of age, whichever is longer
Rheumatic fever with carditis but without residual heart disease (no valvular disease*)	10 yr or until 21 yr of age, whichever is longer
Rheumatic fever with carditis and residual heart disease (persistent valvular disease*)	10 yr or until 40 yr of age, whichever is longer; sometimes lifelong prophylaxis

*Clinical or echocardiographic evidence.

Table 183-3 Echocardiographic Findings in Rheumatic Valvulitis

PATHOLOGIC MITRAL REGURGITATION (ALL 4 MET)	PATHOLOGIC AORTIC REGURGITATION (ALL 4 MET)
1. Seen in at least 2 views	1. Seen in at least 2 views
2. Jet length ≥2 cm in at least 1 view	2. Jet length ≥1 cm in at least 1 view
3. Peak velocity >3 meters/second	3. Peak velocity >3 meters/second
4. Pan-systolic jet in at least 1 envelope	4. Pan-diastolic jet in at least 1 envelope

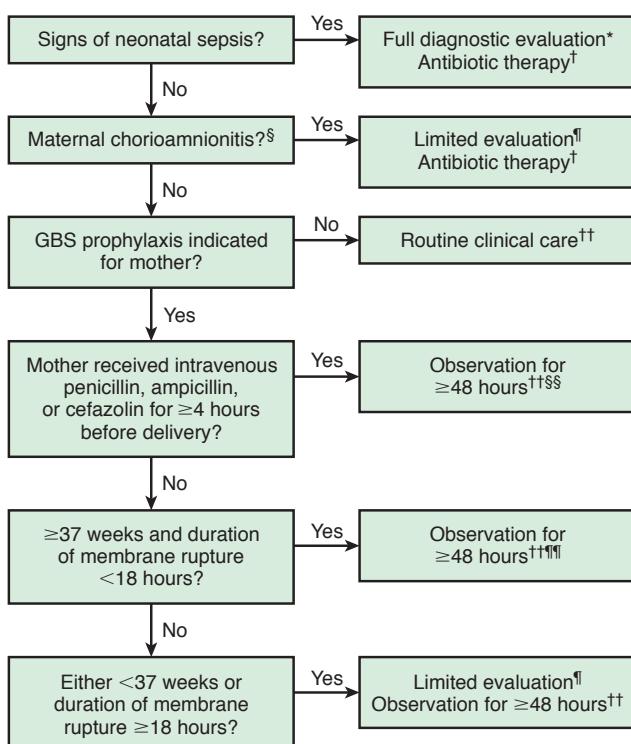
Table 183-4 Differential Diagnosis of Acute Rheumatic Fever

ARTHRITIS	CARDITIS	CHOREA
Juvenile idiopathic arthritis	Viral myocarditis	Huntington chorea
Reactive arthritis (e.g., <i>Shigella</i> , <i>Salmonella</i> , <i>Yersinia</i>)	Viral pericarditis	Wilson disease
Serum sickness	Infective endocarditis	Systemic lupus erythematosus
Sickle cell disease	Kawasaki disease	Cerebral palsy
Malignancy	Congenital heart disease	Tic disorder
Systemic lupus erythematosus	Mitral valve prolapse	Hyperactivity
Lyme disease (<i>Borrelia burgdorferi</i>)	Innocent murmurs	
Pyogenic arthritis		
Poststreptococcal reactive arthritis		

Table 184-1 Characteristics of Early- and Late-Onset Group B Streptococcus Disease

	EARLY-ONSET DISEASE	LATE-ONSET DISEASE
Age at onset	0-6 days	7-90 days
Increased risk after obstetric complications	Yes	No
Common clinical manifestations	Sepsis, pneumonia, meningitis	Bacteremia, meningitis, other focal infections
Common serotypes	Ia, Ib, II, III, V	III predominates
Case fatality rate	4.7%	2.8%

Adapted from Schrag SJ, Zywicki S, Farley MM, et al: Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis, N Engl J Med 342:15-20, 2000.



* Full diagnostic evaluation includes a blood culture, a complete blood count (CBC) including white blood cell differential and platelet counts, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

† Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

‡ Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

¶ Limited evaluation includes blood culture (at birth) and CBC with differential and platelets (at birth and/or at 6–12 hours of life).

†† If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

§§ If ≥37 weeks' gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

¶¶ Some experts recommend a CBC with differential and platelets at age 6–12 hours.

Figure 184-2 Algorithm for secondary prevention of early-onset group B streptococcal disease among newborns.

Table 184-2 Recommended Duration of Therapy for Manifestations of Group B Streptococcus Disease

TREATMENT	DURATION
Bacteremia without a focus	10 days
Meningitis	2-3 wk
Ventriculitis	At least 4 wk
Septic arthritis or osteomyelitis	3-4 wk

Table 188-1 Types of *Listeria monocytogenes* Infections

Listeriosis in pregnancy Neonatal listeriosis: Early onset Late onset Foodborne outbreaks/febrile gastroenteritis Listeriosis in normal children and adults (rare) Focal listeria infections (e.g., meningitis, endocarditis, pneumonia, liver abscess, osteomyelitis, septic arthritis) Listeriosis in immunocompromised persons: Lymphohematogenous malignancies Collagen vascular diseases Diabetes mellitus HIV infection Transplantation Renal failure with peritoneal dialysis Listeriosis in the elderly

Table 188-2 Characteristic Features of Early- and Late-Onset Neonatal Listeriosis

EARLY ONSET (<5 DAYS)	LATE ONSET (≥5 DAYS)
Positive result of maternal <i>Listeria</i> culture	Negative results of maternal <i>Listeria</i> culture
Obstetric complications	Uncomplicated pregnancy
Premature delivery	Term delivery
Low birthweight	Normal birthweight
Neonatal sepsis	Neonatal meningitis
Mean age at onset 1.5 days	Mean age at onset 14.2 days
Mortality rate >30%	Mortality rate <10% Nosocomial outbreaks

Table 188-3 Prevention of Food-Borne Listeriosis

General recommendations to prevent an infection with <i>Listeria</i> :	<p>FDA recommendations for washing and handling food.</p> <ul style="list-style-type: none"> Rinse raw produce, such as fruits and vegetables, thoroughly under running tap water before eating, cutting, or cooking. Even if the produce will be peeled, it should still be washed first. Scrub firm produce, such as melons and cucumbers, with a clean produce brush. Dry the produce with a clean cloth or paper towel. Separate uncooked meats and poultry from vegetables, cooked foods, and ready-to-eat foods. <p>Keep your kitchen and environment cleaner and safer.</p> <ul style="list-style-type: none"> Wash hands, knives, countertops, and cutting boards after handling and preparing uncooked foods. Be aware that <i>Listeria monocytogenes</i> can grow in foods in the refrigerator. Use an appliance thermometer, such as a refrigerator thermometer, to check the temperature inside your refrigerator. The refrigerator should be 4.5°C (40°F) or lower and the freezer –17.8°C (0°F) or lower. Clean up all spills in your refrigerator right away—especially juices from hot dog and lunch meat packages, raw meat, and raw poultry. Clean the inside walls and shelves of your refrigerator with hot water and liquid soap, then rinse. <p>Cook meat and poultry thoroughly.</p> <ul style="list-style-type: none"> Thoroughly cook raw food from animal sources, such as beef, pork, or poultry to a safe internal temperature. For a list of recommended temperatures for meat and poultry, visit the safe minimum cooking temperatures chart at http://www.FoodSafety.gov. <p>Store foods safely.</p> <ul style="list-style-type: none"> Use precooked or ready-to-eat food as soon as you can. Do not store the product in the refrigerator beyond the use-by date; follow USDA refrigerator storage time guidelines: <ul style="list-style-type: none"> Hot dogs—store opened package no longer than 1 wk and unopened package no longer than 2 wk in the refrigerator. Luncheon and deli meat—store factory-sealed, unopened package no longer than 2 wk. Store-opened packages and meat sliced at a local deli no longer than 3-5 days in the refrigerator. Divide leftovers into shallow containers to promote rapid, even cooling. Cover with airtight lids or enclose in plastic wrap or aluminum foil. Use leftovers within 3-4 days. <p>Choose safer foods.</p> <ul style="list-style-type: none"> Do not drink raw (unpasteurized) milk, and do not eat foods that have unpasteurized milk in them.
--	--

Continued

Table 188-3 Prevention of Food-Borne Listeriosis—cont'd

Recommendations for persons at higher risk, such as pregnant women, persons with weakened immune systems, and older adults in addition to the recommendations listed above, include:	<p>Meats</p> <ul style="list-style-type: none"> Do not eat hot dogs, luncheon meats, cold cuts, other deli meats (e.g., bologna), or fermented or dry sausages unless they are heated to an internal temperature of 73.9°C (165°F) or until steaming hot just before serving. Avoid getting fluid from hot dog and lunch meat packages on other foods, utensils, and food preparation surfaces, and wash hands after handling hot dogs, luncheon meats, and deli meats. Pay attention to labels. Do not eat refrigerated pâté or meat spreads from a deli or meat counter or from the refrigerated section of a store. Foods that do not need refrigeration, like canned or shelf-stable pâté and meat spreads, are safe to eat. Refrigerate after opening. <p>Cheeses</p> <ul style="list-style-type: none"> Do not eat soft cheese such as feta, queso blanco, queso fresco, brie, Camembert, blue-veined, or panela (queso panela) unless it is labeled as made with pasteurized milk. Make sure the label says, "MADE WITH PASTEURIZED MILK." <p>Seafood</p> <ul style="list-style-type: none"> Do not eat refrigerated smoked seafood, unless it is contained in a cooked dish, such as a casserole, or unless it is a canned or shelf-stable product. Refrigerated smoked seafood, such as salmon, trout, whitefish, cod, tuna, and mackerel, is most often labeled as "nova-style," "lox," "kippered," "smoked," or "jerky." These fish are typically found in the refrigerator section or sold at seafood and deli counters of grocery stores and delicatessens. Canned and shelf stable tuna, salmon, and other fish products are safe to eat. <p>Follow this general FDA advice for melon safety:</p> <ul style="list-style-type: none"> Consumers and food preparers should wash their hands with warm water and soap for at least 20 sec before and after handling any whole melon, such as cantaloupe, watermelon, or honeydew. Scrub the surface of melons, such as cantaloupes, with a clean produce brush under running water and dry them with a clean cloth or paper towel before cutting. Be sure that your scrub brush is sanitized after each use, to avoid transferring bacteria between melons. Promptly consume cut melon or refrigerate promptly. Keep your cut melon refrigerated at, or less than 4.5°C (40°F) (0-1.1°C [32-34°F] is best), for no more than 7 days. Discard cut melons left at room temperature for more than 4 hr.
--	--

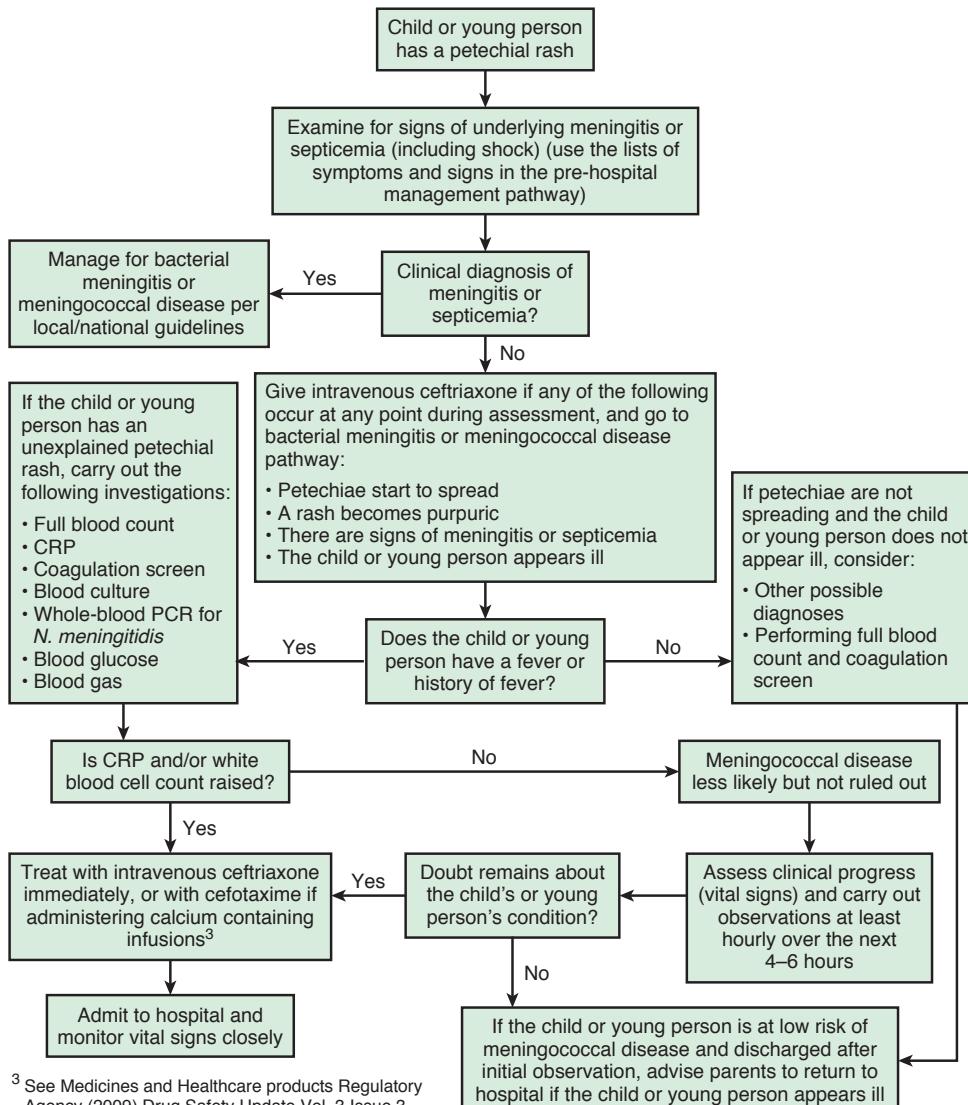
Adapted from the Centers for Disease Control and Prevention: Listeria (Listeriosis): prevention. Available at: <http://www.cdc.gov/listeria/prevention.html>

Table 191-2 Treatment of *Neisseria meningitidis* Invasive Infections

DRUG	ROUTE OF ADMINISTRATION	DOSE	DOSING INTERVAL (hr)	MAXIMUM DAILY DOSE	NOTES
Penicillin G	IM or IV	300,000 units/kg/day	4-6	12-24 million units	Does not clear carriage and "prophylaxis" is required at the end of treatment
Ampicillin	IM or IV	200-400 mg/kg/day	6	6-12 g	Does not clear carriage and "prophylaxis" is required at the end of treatment
Cefotaxime	IM or IV	200-300 mg/kg/day	6-8	8-12 g	Recommended in the neonate
Ceftriaxone	IM or IV	100 mg/kg/day	12-24	2-4 g	Preferred treatment as only once or twice daily and may reduce skin complications
ALTERNATIVE THERAPY IN THE FACE OF LIFE-THREATENING β-LACTAM ALLERGY					
Chloramphenicol ^a	IV	50-100 mg/kg/day	6	2-4 g	
Ciprofloxacin ^b	IV	30-40 mg/kg/day	12	1-1.5 g	
Meropenem ^c	IV	60-120 mg/kg/day	8	1.5-6 g	

^aMonitor blood levels to avoid toxicity.^bLicensed for individuals older than age 18 yr.^cRate of crossreactivity in penicillin-allergic adults is 2-3%.

IM, intramuscular; IV, intravenous.

Management of Petechial Rash

³ See Medicines and Healthcare products Regulatory Agency (2009) Drug Safety Update Vol. 3 Issue 3. Available from www.mhra.gov.uk

Figure 191-3 An approach to management of petechial rash. (From National Collaborating Center for Women's and Children's Health (UK): Bacterial meningitis and meningococcal septicaemia: management of bacterial meningitis and meningococcal septicaemia in children and young people younger than 16 years in primary and secondary care. NICE clinical guidelines, No. 102. London, 2010, RCOG Press.)

Table 198-3 Treatment of *Salmonella* Gastroenteritis

ORGANISM AND INDICATION	DOSE AND DURATION OF TREATMENT
<i>Salmonella</i> infections in infants <3 mo of age or immunocompromised persons (in addition to appropriate treatment for underlying disorder)	Cefotaxime 100-200 mg/kg/day every 6-8 hr for 5-14 days or Ceftriaxone 75 mg/kg/day once daily for 7 days or Ampicillin 100 mg/kg/day every 6-8 hr for 7 days or Cefixime 15 mg/kg/day for 7-10 days

Table 191-3 Antibiotic Prophylaxis to Prevent *Neisseria meningitidis* Infection*

DRUG	DOSE	DURATION
RIFAMPIN [†]		
Infants <1 mo	5 mg/kg PO every 12 hr	2 days (4 doses)
Children ≥1 mo	10 mg/kg PO every 12 hr (maximum: 600 mg)	2 days (4 doses)
Adults	600 mg PO every 12 hr	2 days (4 doses)
CEFTRIAXONE		
Children <15 yr	125 mg IM	1 dose
Children ≥15 yr	250 mg IM	1 dose
CIPROFLOXACIN		
Children ≥1 mo [‡]	20 mg/kg (maximum: 500 mg) PO	1 dose

*Recommended for household and kissing contacts. In the United States, chemoprophylaxis is recommended for:

- Household contact, especially children younger than 2 yr of age
- Childcare or preschool contact at any time during 7 days before onset of illness
- Direct exposure to index patient's secretions through kissing, sharing toothbrushes or eating utensils at any time during 7 days before onset of illness
- Mouth-to-mouth resuscitation, unprotected contact during endotracheal intubation during 7 days before onset of illness
- Frequently slept in same dwelling as index patient during 7 days before onset of illness
- Passengers seated directly next to the index case during airline flights lasting more than 8 hr

[†]Not recommended for pregnant women.

[‡]Not recommended routinely for people younger than 18 yr of age; use only if fluoroquinolone-resistant strains of *N. meningitidis* have not been identified in the community.

IM, intramuscular; PO, by mouth.

Table 198-5 Common Clinical Features of Typhoid Fever in Children*

FEATURE	RATE (%)
High-grade fever	95
Coated tongue	76
Anorexia	70
Vomiting	39
Hepatomegaly	37
Diarrhea	36
Toxicity	29
Abdominal pain	21
Pallor	20
Splenomegaly	17
Constipation	7
Headache	4
Jaundice	2
Obtundation	2
Ileus	1
Intestinal perforation	0.5

Table 191-4 Recommendations for Meningococcal Vaccination

GENERAL POPULATION			
<2 YR	2-10 YR	11-21 YR	22-55 YR
Not recommended	Not recommended	A single dose of MenACWY-D or MenACWY-CRM at age 11-12 yr or at 13-18 yr if not previously vaccinated. Age 19-21 yr: not routinely recommended but may be given as catch-up for those who have not received a dose after their 16th birthday. A booster dose 5 yr later (see text)*	Not recommended
SPECIAL POPULATIONS AT INCREASED RISK OF MENINGOCOCCAL DISEASE†			
RISK FACTOR	2-18 MONTHS	9-23 MONTHS	2-55 YR‡
Persistent complement deficiencies, functional or anatomic asplenia	4 doses of Hib-MenCY-TT at 2, 4, 6, and 12-15 months	2 doses of MenACWY-D 12 wk apart§	2 doses of MenACWY 8-12 wk apart
At risk during a community outbreak with a vaccine serogroup	4 doses of Hib-MenCY-TT at 2, 4, 6, and 12-15 months	2 doses of MenACWY-D 12 wk apart	1 dose of MenACWY
Travel to or resident of countries where meningococcal disease is hyperendemic or epidemic¶	Should receive a quadrivalent meningococcal vaccination licensed for children aged ≥9 mo prior to travel	2 doses of MenACWY-D 12 wk apart**	1 dose of MenACWY
Have HIV, if another indication for vaccination exists	—	2 doses of MenACWY-D 12 wk apart	2 doses of MenACWY 8-12 wk apart
Other risk factors	—	—	1 dose MenACWY

*Otherwise healthy adolescents who received a 1st dose at age 11-12 yr should receive a booster dose of a meningococcal conjugate vaccine at 16 yr of age. For those given a 1st dose at age 13-15 yr, and who have not yet reached their 21st birthday, the booster dose should be given 5 yr after the 1st dose.

†Assuming not previously vaccinated.

‡Persons previously vaccinated at 7 yr of age or older who are at prolonged increased risk should be revaccinated 5 yr after their previous meningococcal vaccine and every 5 yr thereafter. Persons previously vaccinated at ages 2 mo-6 yr who are at prolonged increased risk should be revaccinated 3 yr after their previous meningococcal vaccination and every 5 yr thereafter.

§Because of high risk for invasive pneumococcal disease, children with functional or anatomic asplenia should not be immunized with MenACWY-D before age 2 yr to avoid interference with the immune response to the pneumococcal conjugate vaccine (PCV).

||If MenACWY-D is used, it should be administered at least 4 wk after completion of all PCV doses.

¶For example, visitors to the "meningitis belt" of sub-Saharan Africa. Vaccination also is required by the government of Saudi Arabia for all travelers to Mecca during the annual Hajj.

**If receiving the vaccine prior to travel, 2 doses may be administered as early as 8 wk apart.

Adapted from American Academy of Pediatrics Committee on Infectious Diseases: Updated recommendations on the use of meningococcal vaccines. Pediatrics 134:400-403, 2014.

Table 197-2 Recommended Antimicrobial Treatment and Postexposure Prophylaxis for Pertussis, By Age Group

AGE GROUP	Primary Agents		Alternate Agent*	
	AZITHROMYCIN	ERYTHROMYCIN	CLARITHROMYCIN	TMP-SMZ
<1 mo	Recommended agent 10 mg/kg/day in a single dose for 5 days (only limited safety data available)	Not preferred Erythromycin is substantially associated with infantile hypertrophic pyloric stenosis Use if azithromycin is unavailable; 40-50 mg/kg/day in 4 divided doses for 14 days	Not recommended (safety data unavailable)	Contraindicated for infants <2 mo of age (risk for kernicterus)
1-5 mo	10 mg/kg/day in a single dose for 5 days	40-50 mg/kg/day in 4 divided doses for 14 days	15 mg/kg/day in 2 divided doses for 7 days	Contraindicated at age <2 mo For infants age ≥2 mo: TMP 8 mg/kg/day plus SMZ 40 mg/kg/day in 2 divided doses for 14 days
Infants age ≥6 mo and children	10 mg/kg in a single dose on day 1 (maximum: 500 mg), then 5 mg/kg/day (maximum: 250 mg) on days 2-5	40-50 mg/kg/day (maximum: 2 g/day) in 4 divided doses for 14 days	15 mg/kg/day in 2 divided doses (maximum: 1 g/day) for 7 days	TMP 8 mg/kg/day plus SMZ 40 mg/kg/day in 2 divided doses (maximum TMP: 320 mg/day) for 14 days
Adults	500 mg in a single dose on day 1 then 250 mg/day on days 2-5	2 g/day in 4 divided doses for 14 days	1 g/day in 2 divided doses for 7 days	TMP 320 mg/day, SMZ 1,600 mg/day in 2 divided doses for 14 days

*Trimethoprim-sulfamethoxazole (TMP-SMZ) can be used as an alternative agent to macrolides in patients age ≥2 mo who are allergic to macrolides, who cannot tolerate macrolides, or who are infected with a rare macrolide-resistant strain of *Bordetella pertussis*.

From Centers for Disease Control and Prevention (CDC): Recommended antimicrobial agents for treatment and postexposure prophylaxis of pertussis: 2005 CDC guidelines, MMWR Morb Mortal Wkly Rep 54:1-16, 2005.

Table 198-6 Extraintestinal Infectious Complications of Typhoid Fever Caused By *Salmonella enterica* Serotype Typhi

ORGAN SYSTEM INVOLVED	PREVALENCE (%)	RISK FACTORS	COMPLICATIONS
Central nervous system	3-35	Residence in endemic region, malignancy, endocarditis, congenital heart disease, paranasal sinus infections, pulmonary infections, meningitis, trauma, surgery, and osteomyelitis of the skull	Encephalopathy, cerebral edema, subdural empyema, cerebral abscess, meningitis, ventriculitis, transient parkinsonism, motor neuron disorders, ataxia, seizures, Guillain-Barré syndrome, psychosis
Cardiovascular system	1-5	Cardiac abnormalities—e.g., existing valvular abnormalities, rheumatic heart disease, or congenital heart defects	Endocarditis, myocarditis, pericarditis, arteritis, congestive heart failure
Pulmonary system	1-6	Residence in endemic region, past pulmonary infection, sickle cell anemia, alcohol abuse, diabetes, HIV infection	Pneumonia, empyema, bronchopleural fistula
Bone and joint	<1	Sickle cell anemia, diabetes, systemic lupus erythematosus, lymphoma, liver disease, previous surgery or trauma, extremes of age, and steroid use	Osteomyelitis, septic arthritis
Hepatobiliary system	1-26	Residence in endemic region, pyogenic infections, intravenous drug use, splenic trauma, HIV, hemoglobinopathy	Cholecystitis, hepatitis, hepatic abscesses, splenic abscess, peritonitis, paralytic ileus
Genitourinary system	<1	Urinary tract, pelvic pathology, and systemic abnormalities	Urinary tract infection, renal abscess, pelvic infections, testicular abscess, prostatitis, epididymitis
Soft-tissue infections	At least 17 cases reported in the English language literature	Diabetes	Psoas abscess, gluteal abscess, cutaneous vasculitis
Hematologic	At least 5 cases reported in the English language literature		Hemophagocytosis syndrome

From Huang DB, DuPont HL: Problem pathogens: extra-intestinal complications of *Salmonella enterica* serotype Typhi infection, Lancet Infect Dis 5:341-348, 2005.

Table 198-7 Treatment of Typhoid Fever in Children

SUSCEPTIBILITY	Optimal Therapy			Alternative Effective Drugs		
	ANTIBIOTIC	DAILY DOSE (mg/kg/day)	DAYS	ANTIBIOTIC	DAILY DOSE (mg/kg/day)	DAYS
UNCOMPLICATED TYPHOID FEVER						
Fully sensitive	Chloramphenicol	50-75	14-21	Fluoroquinolone, e.g., ofloxacin or ciprofloxacin	15	5-7*
Multidrug-resistant	Amoxicillin	75-100	14	Azithromycin	8-10	7
	Fluoroquinolone or Cefixime	15	5-7			
Quinolone-resistant [†]	Azithromycin or Ceftriaxone	15-20 8-10	7-14 7	Cefixime Ceftriaxone	15-20 20	7-14 7-14
		75	10-14			
SEVERE TYPHOID FEVER						
Fully sensitive	Fluoroquinolone, e.g., ofloxacin	15	10-14	Chloramphenicol	100	14-21
Multidrug-resistant	Fluoroquinolone	15	10-14	Amoxicillin Ceftriaxone or Cefotaxime	100 60	10-14
Quinolone-resistant	Ceftriaxone	60	10-14	Azithromycin	80	10-14
	Cefotaxime	80	10-14	Fluoroquinolone	10-20 20	7 7-14

*A 3-day course is also effective, particularly for epidemic containment.

[†]The optimum treatment for quinolone-resistant typhoid fever has not been determined. Azithromycin, third-generation cephalosporins, or high-dose fluoroquinolones for 10-14 days is effective.

Modified from World Health Organization: Treatment of typhoid fever. In: World Health Organization: Background document: the diagnosis, prevention and treatment of typhoid fever. Communicable disease surveillance and response: vaccines and biologicals, Geneva, 2003, World Health Organization, pp. 19-23. Available at: http://whqlibdoc.who.int/hq/2003/WHO_V&B_03.07.pdf

Table 200-1Clinical Characteristics, Pathogenesis, and Diagnosis of Diarrheagenic *E. coli*

PATHOGEN	POPULATIONS AT RISK	Characteristics of Diarrhea			Main Virulence Factors		DIAGNOSIS
		WATERY	BLOODY	DURATION	ADHERENCE FACTORS	TOXINS	
ETEC	>1 yr old and travelers	+++	—	Acute	Colonization factor antigens (CFs or CFAs); ECP	Heat-labile enterotoxin (LT) Heat-stable enterotoxin (ST)	Detection of enterotoxins (LT and ST) by enzyme immunoassays or PCR (lt, st)
EIEC	>1 yr old	+	++	Acute	Invasion plasmid antigen (IpABCD)		Detection of invasion plasmid antigen of <i>Shigella</i> (ipaH) by PCR
EPEC	<2 yr old	+++	+	Acute, prolonged or persistent	A/E lesion, intimin/Tir, EspABD, Bfp	EspF, Map, EAST1, SPATEs (EspC)	Detection of intimin gene (eae) ± bundle-forming pili (bfpA) by PCR, and absence of Shiga toxins; HEp-2 cells adherence assay (LA, LLA)
STEC (EHEC/ VTEC)	6 mo-10 yr and the elderly	+	+++	Acute	A/E lesion, intimin/Tir, EspABD	Shiga toxins (Stx1, Stx2, and variants of Stx2)	Detection of Shiga toxins by enzyme immunoassays or PCR (Stx1, Stx2); stool culture on MacConkey-sorbitol media to detect <i>E. coli</i> O157. Simultaneous culture for O157 and nonculture assays to detect Shiga toxins
EAEC	<2 yr old, HIV-infected patients, and travelers	+++	+	Acute, prolonged, or persistent	Aggregative adherence fimbriae (AAF)	SPATEs (Pic, Pet), ShET1, EAST1	Detection of Aggr, AA plasmid, and other virulence genes: aap, aatA, astA, set1A by PCR; HEp-2 cells adherence assay (AA)
DAEC	>1 yr old and travelers	++	—	Acute	Afa/Dr, AIDA-I	SPATEs (Sat)	Detection of Dr adhesins (daaC or daaD) and Dr-associated genes by PCR; HEp-2 cells adherence assay (DA)

—, Not present; +, present; ++, common; +++, very common; A/E lesion, attaching and effacing lesion; AA, aggregative adherence; Bfp, bundle-forming pili; DA, diffuse adherence; DAEC, diffusely adherent *E. coli*; EAEC, enteroaggregative *E. coli*; EAST1, enteroaggregative heat stable toxin; ECP, *E. coli* common pilus; EHEC, enterohemorrhagic *E. coli*; EIEC, enteroinvasive *E. coli*; EPEC, enteropathogenic *E. coli*; EspABD, *E. coli* secreted proteins A, B, and D; ETEC, enterotoxigenic *E. coli*; LA, localized adherence; LLA, localized-like adherence; PCR, polymerase chain reaction; ShET1, *Shigella* enterotoxin 1; SPATEs, serine protease autotransporter of Enterobacteriaceae; STEC, Shiga toxin-producing *E. coli*; Tir, translocated intimin receptor; VTEC, verotoxin-producing *E. coli*.

Table 210-1

Diagnoses Considered in Subsequently Laboratory-Confirmed Cases of Infant Botulism

ADMISSION DIAGNOSIS	SUBSEQUENTLY CONSIDERED DIAGNOSES
Suspected sepsis, meningitis	Guillain-Barré syndrome
Pneumonia	Myasthenia gravis
Dehydration	Disorders of amino acid metabolism
Viral syndrome	Hypothyroidism
Hypotonia of unknown etiology	Drug ingestion Organophosphate poisoning
Constipation	Brainstem encephalitis
Failure to thrive	Heavy metal poisoning (Pb, Mg, As)
Spinal muscular atrophy type 1 (Werdnig-Hoffmann disease)	Poliomyelitis Viral polyneuritis Hirschsprung disease Metabolic encephalopathy Medium chain acetyl-coenzyme A dehydrogenase deficiency

Table 210-2

Diagnoses Considered in Foodborne and Wound Botulism

Acute gastroenteritis
Myasthenia gravis
Guillain-Barré syndrome
Organophosphate poisoning
Meningitis
Encephalitis
Psychiatric illness
Cerebrovascular accident
Poliomyelitis
Hypothyroidism
Aminoglycoside-associated paralysis
Tick paralysis
Hypocalcemia
Hypermagnesemia
Carbon monoxide poisoning
Hyperemesis gravidarum
Laryngeal trauma
Diabetic complications
Inflammatory myopathy
Overexertion

Table 205-1 *Pseudomonas aeruginosa* Infections

INFECTION	COMMON CLINICAL CHARACTERISTICS
Endocarditis	Native right-sided (tricuspid) valve disease with intravenous drug abuse
Pneumonia	Compromised local (lung) or systemic host defense mechanisms; nosocomial (respiratory), bacteremic (malignancy), or abnormal mucociliary clearance (cystic fibrosis) may be pathogenetic; cystic fibrosis is associated with mucoid <i>P. aeruginosa</i> organisms producing capsular slime
Central nervous system infection	Meningitis, brain abscess; contiguous spread (mastoiditis, dermal sinus tracts, sinusitis); bacteremia or direct inoculation (trauma, surgery)
External otitis	Swimmer's ear; humid warm climates, swimming pool contamination
Malignant otitis externa	Invasive, indolent, febrile toxic, destructive necrotizing lesion in young infants, immunosuppressed neutropenic patients, or diabetic patients; associated with 7th nerve palsy and mastoiditis
Chronic mastoiditis	Ear drainage, swelling, erythema; perforated tympanic membrane
Keratitis	Corneal ulceration; contact lens keratitis
Endophthalmitis	Penetrating trauma, surgery, penetrating corneal ulceration; fulminant progression
Osteomyelitis/septic arthritis	Puncture wounds of foot and osteochondritis; intravenous drug abuse; fibrocartilaginous joints, sternum, vertebrae, pelvis; open fracture osteomyelitis; indolent pyelonephritis and vertebral osteomyelitis
Urinary tract infection	Iatrogenic, nosocomial; recurrent urinary tract infections in children, instrumented patients, and those with obstruction or stones
Intestinal tract infection	Immunocompromised, neutropenia, typhlitis, rectal abscess, ulceration, rarely diarrhea; peritonitis in peritoneal dialysis
Ecthyma gangrenosum	Metastatic dissemination; hemorrhage, necrosis, erythema, eschar, discrete lesions with bacterial invasion of blood vessels; also subcutaneous nodules, cellulitis, pustules, deep abscesses
Primary and secondary skin infections	Local infection; burns, trauma, decubitus ulcers, toe web infection, green nail (paronychia); whirlpool dermatitis; diffuse, pruritic, folliculitis, vesiculopustular or maculopapular, erythematous lesions

Table 207-1 Recommended Therapy for the Treatment of Brucellosis

AGE AND CONDITION	ANTIMICROBIAL AGENT	DOSE	ROUTE	DURATION
≥8 yr	Doxycycline + Rifampin Alternative: Doxycycline + Streptomycin or Gentamicin	2-4 mg/kg/day; maximum: 200 mg/day 15-20 mg/kg/day; maximum: 600-900 mg/day 2-4 mg/kg/day; maximum: 200 mg/day 15-30 mg/kg/day; maximum: 1 g/day 3-5 mg/kg/day	PO PO PO IM IM/IV	6 wk 6 wk 6 wk 2-3 wk 1-2 wk
	Trimethoprim-sulfamethoxazole (TMP-SMZ) + Rifampin	TMP (10 mg/kg/day; maximum: 480 mg/day) and SMZ (50 mg/kg/day; maximum: 2.4 g/day) 15-20 mg/kg/day	PO	4-8 wk 6 wk
	Doxycycline + Gentamicin ± Rifampin	2-4 mg/kg/day; maximum: 200 mg/day 3-5 mg/kg/day 15-20 mg/kg/day; maximum: 600-900 mg/day	PO IV PO	4-6 mo 1-2 wk 4-6 mo

Table 211-1 Tetanus Prophylaxis in Routine Wound Management

HISTORY OF ABSORBED TETANUS TOXOID	Clean, Minor Wounds		All Other Wounds*	
	TDAP OR TD†	TIG‡	TDAP OR TD†	TIG‡
Uncertain or <3 doses	Yes	No	Yes	Yes
3 or more doses	No§	No	No	No

*Such as, but not limited to, wounds contaminated with dirt, feces, and saliva; puncture wounds; avulsions; wounds resulting from missiles, crushing, burns, and frostbite.

†For children younger than 7 yr of age, DTaP is preferred to tetanus toxoid alone if <3 doses of DTaP have been previously given. If pertussis vaccine is contraindicated, DT is given. For persons 7 yr of age or older, Td (or Tdap for adolescents 11-18 yr of age) is preferred to tetanus toxoid alone. Tdap is preferred to Td for adolescents 11-18 yr of age who have never received Tdap. Td is preferred to tetanus toxoid for adolescents who received Tdap previously or when Tdap is not available.

‡TIG should be administered for tetanus-prone wounds in HIV-infected patients regardless of the history of tetanus immunizations.

§Yes, if 10 yr or longer since the last tetanus toxoid-containing vaccine dose.

||Yes, if 5 yr or longer since the last tetanus toxoid-containing vaccine dose. (More frequent boosters are not needed and can accentuate adverse events.)

TD, diphtheria and tetanus toxoid vaccine; DTaP, combined diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine; Td, tetanus toxoid and reduced diphtheria toxoid vaccine; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; TIG, tetanus immune globulin.

Table 213-1 Infections Associated with Anaerobic Bacteria

SITE AND INFECTION	MAJOR RISK FACTORS	ANAEROBIC BACTERIA*
CENTRAL NERVOUS SYSTEM		
Cerebral abscess	Cyanotic heart disease Cystic fibrosis Penetrating trauma	Polymicrobial
Epidural and subdural empyemas, meningitis	Direct extension from contiguous sinusitis, otitis media, mastoiditis, or anatomic defect involving the dura	<i>Bacteroides fragilis</i> [†] <i>Fusobacterium</i> <i>Peptostreptococcus</i> <i>Veillonella</i>
UPPER RESPIRATORY TRACT		
Dental abscess	Poor periodontal hygiene	<i>Peptostreptococcus</i>
Ludwig angina (cellulitis of sublingual-submandibular space)	Drugs producing gingival hypertrophy	<i>Fusobacterium</i>
Necrotizing gingivitis (Vincent stomatitis)		<i>Prevotella melaninogenica</i>
Chronic otitis-mastoiditis-sinusitis		
Peritonsillar abscess	Tympanic perforation	
Retropharyngeal abscess	Tympanostomy tubes	
Lemierre syndrome	Streptococcal pharyngitis Penetrating injury Preexisting viral or bacterial pharyngitis	<i>Fusobacterium</i>
LOWER RESPIRATORY TRACT		
Aspiration pneumonia	Periodontal disease	Polymicrobial
Necrotizing pneumonitis	Bronchial obstruction	<i>P. melaninogenica</i>
Lung abscess	Altered gag or consciousness Aspirated foreign body Sequestered lobe Vascular anomaly	<i>Bacteroides intermedius</i> <i>Fusobacterium</i> <i>Peptostreptococcus, Eubacterium</i> <i>B. fragilis, Veillonella</i> <i>Fusobacterium</i>
Septic pulmonary emboli		
INTRAABDOMINAL		
Abscess	Appendicitis	Polymicrobial
Secondary peritonitis	Penetrating trauma (especially of the colon)	<i>Bacteroides</i> spp. <i>Clostridium</i> <i>Peptostreptococcus</i> <i>Eubacterium</i> <i>Fusobacterium</i>
FEMALE GENITAL TRACT		
Bartholin abscess	Vaginosis	<i>B. fragilis</i>
Tuboovarian abscess	Intrauterine device	<i>Bacteroides bivius</i>
Endometritis		<i>Peptostreptococcus</i>
Pelvic thrombophlebitis		<i>Clostridium</i>
Salpingitis		<i>Mobiluncus</i>
Chorioamnionitis		<i>Actinomyces</i>
Septic abortion		<i>Clostridium</i>
SKIN AND SOFT TISSUE		
Cellulitis	Decubitus ulcers	Varies with site and contamination with oral or enteric flora
Perirectal cellulitis	Abdominal wounds	<i>Clostridium perfringens</i> (myonecrosis)
Myonecrosis (gas gangrene)	Pilonidal sinus	<i>Bacteroides</i>
Necrotizing fasciitis and synergistic gangrene	Trauma Human and animal bites Immunosuppressed or neutropenic patients Varicella	<i>Clostridium tertium</i> <i>Clostridium septicum</i> Anaerobic streptococci
BLOOD		
Bacteremia	Intraabdominal infection, abscesses, myonecrosis, necrotizing fasciitis	<i>B. fragilis</i> <i>Clostridium</i> <i>Peptostreptococcus</i> <i>Fusobacterium</i>

*Infections may also be from or may involve aerobic bacteria as the sole agent or as part of a mixed infection; brain abscess may contain microaerophilic streptococci; intraabdominal infections may contain Gram-negative enteric organisms and enterococci; and salpingitis may contain *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.

[†]*Bacteroides fragilis* is usually isolated from infections below the diaphragm except for brain abscesses.

Table 210-3 Complications of Infant Botulism

Acute respiratory distress syndrome
Aspiration
<i>Clostridium difficile</i> enterocolitis
Hypotension
Inappropriate antidiuretic hormone secretion
Long bone fractures
Misplaced or plugged endotracheal tube
Nosocomial anemia
Otitis media
Pneumonia
Pneumothorax
Recurrent atelectasis
Seizures secondary to hyponatremia
Sepsis
Subglottic stenosis
Tracheal granuloma
Tracheitis
Transfusion reaction
Urinary tract infection

Table 214-2 Isoniazid Drug-Drug Interactions

DRUG USED WITH ISONIAZID	EFFECTS
Acetaminophen, alcohol, rifampin	Increased hepatotoxicity of isoniazid or listed drugs
Aluminum salts (antacids)	Decreased absorption of isoniazid
Carbamazepine, phenytoin, theophylline, diazepam, warfarin	Increased level, effect, or toxicity of listed drugs due to decreased metabolism
Itraconazole, ketoconazole, oral hypoglycemic agents	Decreased level or effect of listed drugs due to increased metabolism
Cycloserine, ethionamide	Increased central nervous system adverse effects of cycloserine and ethionamide
Prednisolone	Increased isoniazid metabolism

Table 214-1 Recommended Treatment Regimens for Drug-Susceptible Tuberculosis in Infants, Children, and Adolescents

INFECTION OR DISEASE CATEGORY	REGIMEN	REMARKS
LATENT TUBERCULOSIS INFECTION*		
Isoniazid susceptible	9 mo of isoniazid, once a day	If daily therapy is not possible, DOT twice a week can be used for 9 mo
Isoniazid resistant	6 mo of rifampin, once a day	If daily therapy is not possible, DOT twice a week can be used for 6 mo
Isoniazid-rifampin resistant [†]	Consult a tuberculosis specialist	
PULMONARY AND EXTRAPULMONARY INFECTION		
Except meningitis	2 mo of isoniazid, rifampin, pyrazinamide, and ethambutol daily, followed by 4 mo of isoniazid and rifampin [‡] by DOT [§] for drug-susceptible <i>Mycobacterium tuberculosis</i> 9-12 mo of isoniazid and rifampin for drug-susceptible <i>Mycobacterium bovis</i>	If possible drug resistance is a concern (see text), another drug (ethambutol or an aminoglycoside) is added to the initial 3 drug therapy until drug susceptibilities are determined; DOT is highly desirable If hilar adenopathy only, a 6-mo course of isoniazid and rifampin is sufficient Drugs can be given 2 or 3x/wk under DOT in the initial phase if nonadherence is likely
Meningitis	2 mo of isoniazid, rifampin, pyrazinamide, and an aminoglycoside or ethambutol or ethionamide, once a day, followed by 7-10 mo of isoniazid and rifampin, once a day or twice a week (9-12 mo total) for drug-susceptible <i>M. tuberculosis</i> ≥12 mo of therapy without pyrazinamide for drug-susceptible <i>M. bovis</i>	A 4th drug, such as an aminoglycoside, is given with initial therapy until drug susceptibility is known For patients who might have acquired tuberculosis in geographic areas where resistance to streptomycin is common, kanamycin, amikacin, or capreomycin can be used instead of streptomycin

*Positive TST or IGRA result, no disease.

[†]Duration of therapy is longer for human immunodeficiency virus (HIV)-infected people, and additional drugs may be indicated.

[‡]Medications should be administered daily for the 1st 2 wk to 2 mo of treatment and then can be administered 2-3x/wk by DOT.

[§]If initial chest radiograph shows cavitary lesions and sputum after 2 mo of therapy remains positive, duration of therapy is extended to 9 mo.

DOT, directly observed therapy; IGRA, interferon- γ release assay; TST, tuberculin skin test.

From American Academy of Pediatrics: *Tuberculosis*. In Pickering LK, Baker CJ, Kimberlin DW, Long SS, editors: Red book 2012: report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics.

Table 214-3 Treatment of Nontuberculous Mycobacteria Infections in Children

ORGANISM	DISEASE	TREATMENT
SLOWLY GROWING SPECIES		
<i>Mycobacterium avium</i> complex (MAC); <i>Mycobacterium haemophilum</i> ; <i>Mycobacterium lentiflavum</i>	Lymphadenitis	Complete excision of lymph nodes; if excision is incomplete or disease recurs, clarithromycin or azithromycin plus ethambutol or rifampin (or rifabutin)
	Pulmonary infection	Clarithromycin or azithromycin plus ethambutol with rifampin or rifabutin (pulmonary resection in some patients who fail to respond to drug therapy). For severe disease, an initial course of amikacin or streptomycin often is included. Clinical data in adults support that 3x/wk therapy is as effective as daily therapy, with less toxicity. For patients with advanced disease, drugs should be given daily
<i>Mycobacterium kansasii</i>	Disseminated	See text
	Pulmonary infection	Rifampin plus ethambutol with isoniazid
	Osteomyelitis	Surgical debridement and prolonged antimicrobial therapy using rifampin plus ethambutol with isoniazid
<i>Mycobacterium marinum</i>	Cutaneous infection	Trimethoprim-sulfamethoxazole, clarithromycin, or doxycycline for mild disease; ethambutol with clarithromycin or rifampicin for extensive disease; extensive lesions might require surgical debridement.
<i>Mycobacterium ulcerans</i>	Cutaneous and bone infections	Daily intramuscular streptomycin and oral rifampin × 8 wk; excision of tissue
RAPIDLY GROWING SPECIES		
<i>Mycobacterium fortuitum</i> group	Cutaneous infection	Initial therapy for serious disease is amikacin plus cefoxitin or imipenem IV, followed by clarithromycin, doxycycline,* or trimethoprim-sulfamethoxazole or ciprofloxacin, orally, on the basis of in vitro susceptibility testing; might require surgical excision
	Catheter infection	Catheter removal and amikacin plus cefoxitin or imipenem, IV; clarithromycin, trimethoprim-sulfamethoxazole, or ciprofloxacin, orally, on the basis of in vitro susceptibility testing
<i>Mycobacterium abscessus</i>	Otitis media	Clarithromycin plus initial course of amikacin plus cefoxitin or imipenem; might require surgical debridement. Base regimen on in vitro susceptibility testing (50% are amikacin resistant)
	Pulmonary infection (in cystic fibrosis)	Serious disease, clarithromycin, amikacin, and cefoxitin on the basis of susceptibility testing; might require surgical resection
<i>Mycobacterium cheloneae</i>	Catheter infection	Catheter removal and tobramycin (initially) plus clarithromycin
	Disseminated cutaneous infection	Tobramycin and ciprofloxacin or linezolid (initially) plus clarithromycin

*Doxycycline should not be given to children younger than 8 yr of age unless the benefits of therapy are greater than the risks of dental staining. Only 50% of isolates of *Mycobacterium marinum* are susceptible to doxycycline.

From American Thoracic Society/Infectious Disease Society of America Statement: Diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 175:367-416, 2007.

Table 215-1 Groups at High Risk for Acquiring Tuberculosis Infection and Developing Disease in Countries with Low Incidence

RISK FACTORS FOR TUBERCULOSIS INFECTION
Children exposed to high-risk adults
Foreign-born persons from high-prevalence countries
Homeless persons
Persons who inject drugs
Present and former residents or employees of correctional institutions, homeless shelters, and nursing homes
Healthcare workers caring for high-risk patients (if infection control is not adequate)
RISK FACTORS FOR PROGRESSION OF LATENT TUBERCULOSIS INFECTION TO TUBERCULOSIS DISEASE
Infants and children ≤4 yr of age, especially those <2 yr of age
Adolescents and young adults
Persons coinfected with HIV
Persons with skin test conversion in the past 1-2 yr
Persons who are immunocompromised, especially in cases of malignancy and solid organ transplantation, immunosuppressive medical treatments including anti-tumor necrosis factor therapies, diabetes mellitus, chronic renal failure, silicosis, and malnutrition
RISK FACTORS FOR DRUG-RESISTANT TUBERCULOSIS
Personal or contact history of treatment for tuberculosis
Contacts of patients with drug-resistant tuberculosis
Birth or residence in a country with a high rate of drug resistance
Poor response to standard therapy
Positive sputum smears (acid-fast bacilli) or culture ≥2 mo after initiating appropriate therapy

Table 215-3

Definitions of Positive Tuberculin Skin Test Results in Infants, Children, and Adolescents*

INDURATION ≥5 MM

Children in close contact with known or suspected contagious people with tuberculosis disease

Children suspected to have tuberculosis disease:

- Findings on chest radiograph consistent with active or previously tuberculosis disease
- Clinical evidence of tuberculosis disease[†]

Children receiving immunosuppressive therapy[‡] or with immunosuppressive conditions, including HIV infection

INDURATION ≥10 MM

Children at increased risk of disseminated tuberculosis disease:

- Children younger than 4 yr of age
- Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition (see Table 215-2)

Children with increased exposure to tuberculosis disease:

- Children born in high-prevalence regions of the world
- Children often exposed to adults who are HIV infected, homeless, users of illicit drugs, residents of nursing homes, incarcerated or institutionalized, or migrant farm workers
- Children who travel to high-prevalence regions of the world

INDURATION ≥15 MM

Children ≥4 yr of age without any risk factors

*These definitions apply regardless of previous bacille Calmette-Guérin (BCG) immunization; erythema at TST site does not indicate a positive test result. Tests should be read at 48–72 hr after placement.

[†]Evidence by physical examination or laboratory assessment that would include tuberculosis in the working differential diagnosis (e.g., meningitis).

[‡]Including immunosuppressive doses of corticosteroids or tumor necrosis factor- α antagonists.

HIV, human immunodeficiency virus; TST, tuberculin skin test.

Table 215-4

Recommendations for Use of the Tuberculin Skin Test and an Interferon- γ Release Assay in Children

TST preferred, IGRA acceptable

- Children <5 yr of age*
- IGRA preferred, TST acceptable
- Children >5 yr of age who have received the BCG vaccine
- Children >5 yr of age who are unlikely to return for TST reading
- TST and IGRA should be considered when:
 - The initial and repeat IGRA are indeterminate
 - The initial test (TST or IGRA) is negative and:
 - Clinical suspicion for tuberculosis disease is moderate to high[†]
 - Risk of progression and poor outcome is high[†]
 - The initial TST is positive and:
 - >5 yr of age and history of BCG vaccination
 - Additional evidence needed to increase compliance
 - Nontuberculous mycobacterial disease is suspected

*Positive result of either test is considered significant in these groups.

[†]IGRAs should not be used in children younger than 2 yr of age unless tuberculosis disease is suspected. In children 2–4 yr of age, there are limited data about the usefulness of IGRAs in determining tuberculosis infection, but IGRA testing can be performed if tuberculosis disease is suspected.

IGRA indicates interferon- γ release assay; TST, tuberculin skin test.

Table 215-2

Tuberculin Skin Test Recommendations for Infants, Children, and Adolescents*

CHILDREN FOR WHOM IMMEDIATE TST OR IGRA IS INDICATED[†]:

- Contacts of people with confirmed or suspected contagious tuberculosis (contact investigation)
- Children with radiographic or clinical findings suggesting tuberculosis disease
- Children immigrating from countries with endemic infection (e.g., Asia, Middle East, Africa, Latin America, countries from the former Soviet Union), including international adoptees
- Children with travel histories to countries with endemic infection and substantial contact with indigenous people from such countries[‡]
- Children who should have annual TST or IGRA:
 - Children infected with HIV

CHILDREN AT INCREASED RISK FOR PROGRESSION OF LTBI TO TUBERCULOSIS DISEASE

Children with other medical conditions, including diabetes mellitus, chronic renal failure, malnutrition, and congenital or acquired immunodeficiencies deserve special consideration. Without recent exposure, these children are not at increased risk of acquiring tuberculosis infection. Underlying immunodeficiencies associated with these conditions theoretically would enhance the possibility for progression to severe disease. Initial histories of potential exposure to tuberculosis should be included for all of these patients. If these histories or local epidemiologic factors suggest a possibility of exposure, immediate and periodic TST should be considered. An initial TST or IGRA should be performed before initiation of immunosuppressive therapy, including prolonged steroid administration, use of tumor necrosis factor- α antagonists, or immunosuppressive therapy in any child requiring these treatments.

*Bacille Calmette-Guérin immunization is not a contraindication to a TST.

[†]Beginning as early as 3 mo of age.

[‡]If the child is well and has no history of exposure, the TST or IGRA should be delayed up to 10 wk after return.

HIV, human immunodeficiency virus; IGRA indicates interferon- γ release assay; LTBI, latent tuberculosis infection; TST, tuberculin skin test.

From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, p. 740.

Table 215-6 Less-Commonly Used Drugs for Treating Drug-Resistant Tuberculosis in Infants, Children, and Adolescents*				
DRUGS	DOSAGE, FORMS	DAILY DOSAGE, mg/kg	MAXIMUM DOSE	ADVERSE REACTIONS
Amikacin [†]	Vials: 500 mg, 1 g	15-30 (IV or IM administration)	1 g	Auditory and vestibular toxic effects, nephrotoxic effects
Capreomycin [†]	Vials: 1 g	15-30 (IM administration)	1 g	Auditory and vestibular toxicity and nephrotoxic effects
Cycloserine	Capsules: 250 mg	10-20, given in 2 divided doses	1 g	Psychosis, personality changes, seizures, rash
Ethionamide	Tablets: 250 mg	15-20, given in 2-3 divided doses	1 g	Gastrointestinal tract disturbances, hepatotoxic effects, hypersensitivity reactions, hypothyroidism
Kanamycin	Vials: 75 mg/2 mL 500 mg/2 mL 1 g/3 mL	15-30 (IM or IV administration)	1 g	Auditory and vestibular toxic effects, nephrotoxic effects
Levofloxacin [†]	Tablets: 250 mg 500 mg 750 mg Vials: 25 mg/mL	Adults: 750-1000 mg (once daily) Children: 15 mg/kg daily	1 g	Theoretic effect on growing cartilage, gastrointestinal tract disturbances, rash, headache, restlessness, confusion
Ofloxacin	Tablets: 200 mg 300 mg 400 mg Vials: 20 mg/mL 40 mg/mL	Adults and adolescents: 800 mg Children 15-20 mg/kg daily	800 mg	Arthropathy, arthritis
Moxifloxacin	Tablets: 400 mg IV solution: 400 mg/250 mL in 0.8% saline	Adults and adolescents: 400 mg Children: 7.5-10 mg/kg daily	400 mg	Arthropathy, arthritis
Paraaminosalicylic acid (PAS)	Packets: 3 g	200-300 (2-4 times a day)	10 g	Gastrointestinal tract disturbances, hypersensitivity, hepatotoxic effects
Streptomycin [†]	Vials: 1 g 4 g	20-40 (IM administration)	1 g	Auditory and vestibular toxic effects, nephrotoxic effects, rash

*These drugs should be used in consultation with a specialist in tuberculosis.

[†]Dose adjustment in renal insufficiency.

[‡]Levofloxacin currently is not approved for use in children younger than 18 yr of age; its use in younger children necessitates assessment of the potential risks and benefits.

From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, p. 748.

Table 215-5 Commonly Used Drugs for the Treatment of Tuberculosis in Infants, Children, and Adolescents					
DRUG	DOSAGE FORMS	DAILY DOSAGE, mg/kg	TWICE A WEEK DOSAGE, mg/kg PER DOSE	MAXIMUM DOSE	ADVERSE REACTIONS
Ethambutol	Tablets: 100 mg 400 mg	20	50	2.5 g	Optic neuritis (usually reversible), decreased red-green color discrimination, gastrointestinal tract disturbances, hypersensitivity
Isoniazid*	Scored tablets: 100 mg 300 mg Syrup: 10 mg/mL	10-15 [†]	20-30	Daily, 300 mg Twice a week, 900 mg	Mild hepatic enzyme elevation, hepatitis, [‡] peripheral neuritis, hypersensitivity
Pyrazinamide*	Scored tablets: 500 mg	30-40	50	2 g	Hepatotoxic effects, hyperuricemia, arthralgias, gastrointestinal tract upset
Rifampin*	Capsules: 150 mg 300 mg Syrup formulated from capsules	10-20	10-20	600 mg	Orange discoloration of secretions or urine, staining of contact lenses, vomiting, hepatitis, influenza-like reaction, thrombocytopenia, pruritus; oral contraceptives may be ineffective

*Rifamate is a capsule containing 150 mg of isoniazid and 300 mg of rifampin. Two capsules provide the usual adult (i.e., person weighing >50 kg) daily doses of each drug. Rifater, in the United States, is a capsule containing 50 mg of isoniazid, 120 mg of rifampin, and 300 mg of pyrazinamide. Isoniazid and rifampin also are available for parenteral administration.

[†]When isoniazid in a dosage exceeding 10 mg/kg per day is used in combination with rifampin, the incidence of hepatotoxic effects may be increased.

From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, p. 748.

1464 Part XVII ◆ Infectious Diseases

Table 216-1 NHDP Recommended Multidrug Therapy Regimens for Hansen Disease in the United States				
Type of Leprosy	Antimicrobial Therapy	Adult Dosing (Given Orally)	Pediatric Dosing* (Given Orally)	Duration of Therapy
MULTIBACILLARY LEPROSY (LL, BL, BB)	Dapsone and Rifampin and Clofazimine	100 mg/day 600 mg/day 50 mg/day	1 mg/kg/day 10-20 mg/kg/day 1 mg/kg/day [†]	24 months 24 months 24 months
PAUCIBACILLARY LEPROSY (TT, BT)	Dapsone and Rifampin	100 mg/day 600 mg/day	1-2 mg/kg/day 10-20 mg/kg/day	12 months 12 months

NHDP multidrug therapy is daily and of longer duration than World Health Organization recommended regimen.

*Daily pediatric mg/kg dose should not exceed adult daily maximum.

[†]Clofazimine is only available through NHDP Investigational New Drug (IND) program; minimum formulation is 50 mg and capsules should not be cut. Alternative dosing includes: clofazimine 2 mg/kg every other day or clarithromycin 7.5 mg/kg/day.

BB, borderline; BL, borderline lepromatous; BT, borderline tuberculoid; LL, lepromatous; NHDP, National Hansen's Disease Program; TT, tuberculoid.

Table 216-2 World Health Organization Recommended Multidrug Therapy Regimens for Hansen Disease				
Type of Leprosy	Antimicrobial Therapy			Duration of Therapy
	Monthly (Supervised)		Daily (Self-administered)	
Multibacillary (LL, BL, BB)	Adult Pediatric*	Rifampicin 600 mg and clofazimine 300 mg Rifampicin 450 mg and clofazimine 150 mg	Dapsone 100 mg and clofazimine 50 mg Dapsone 50 mg and clofazimine 50 mg every other day	12-24 months
Paucibacillary (TT, BT)	Adult Pediatric*	Rifampicin 600 mg Rifampicin 450 mg	Dapsone 100 mg Dapsone 50 mg	6-12 months 6 months
Paucibacillary (single lesion) [†]	Rifampicin 600 mg and ofloxacin 400 mg and minocycline 100 mg			One time, single dose

*In children younger than 10 yr of age, dosages of multidrug therapy should be in mg/kg, not to exceed the adult daily maximum: rifampicin 10 mg/kg once monthly, dapsone 2 mg/kg/day, clofazimine 1 mg/kg on alternate days.

[†]Paucibacillary single-lesion, one-time single-dose therapy may be less effective than the 6 mo paucibacillary multidrug therapy regimen.

BB, borderline; BL, borderline lepromatous; BT, borderline tuberculoid; LL, lepromatous; TT, tuberculoid.

Table 217-1 Diseases Caused by Nontuberculous Mycobacterial Species		
Clinical Disease	Common Species	Less-Common Species
Cutaneous infection	<i>Mycobacterium chelonae</i> , <i>Mycobacterium fortuitum</i> , <i>Mycobacterium abscessus</i> , <i>Mycobacterium marinum</i>	<i>Mycobacterium ulcerans</i> *
Lymphadenitis	MAC	<i>Mycobacterium kansasii</i> , <i>Mycobacterium haemophilum</i> , <i>Mycobacterium malmoense</i> [†]
Otologic infection	<i>M. abscessus</i> , MAC	<i>M. fortuitum</i>
Pulmonary infection	MAC, <i>M. kansasii</i> , <i>M. abscessus</i>	<i>Mycobacterium xenopi</i> , <i>Mycobacterium malmoense</i> [†] , <i>Mycobacterium szulgai</i> , <i>M. fortuitum</i> , <i>Mycobacterium simiae</i>
Catheter-associated infection	<i>M. chelonae</i> , <i>M. fortuitum</i>	<i>M. abscessus</i>
Skeletal infection	MAC, <i>M. kansasii</i> , <i>M. fortuitum</i>	<i>M. chelonae</i> , <i>M. marinum</i> , <i>M. abscessus</i> , <i>M. ulcerans</i> *
Disseminated	MAC	<i>M. kansasii</i> , <i>Mycobacterium genavense</i> , <i>M. haemophilum</i> , <i>M. chelonae</i>

*Endemic in West Africa and Australia, minor foci in East Asia and Latin America.

[†]Found primarily in Northern Europe.

MAC, *Mycobacterium avium* complex.

From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, p. 761.

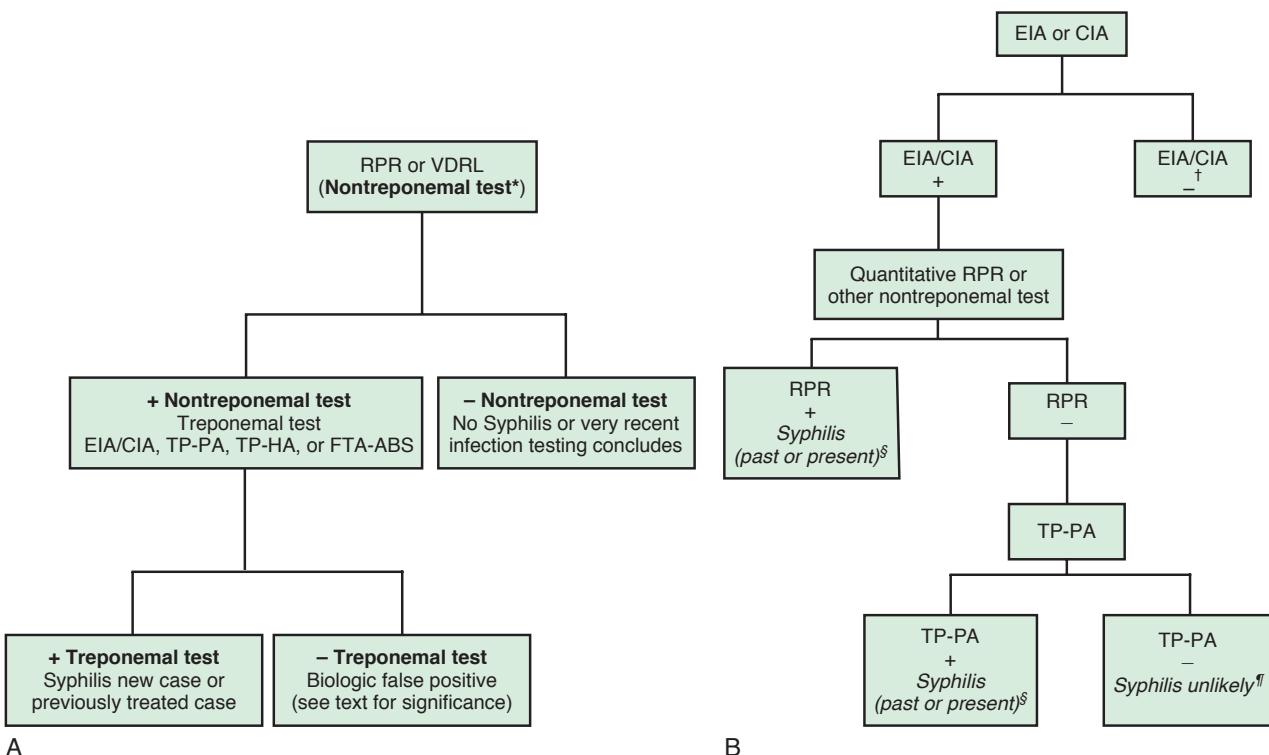


Figure 218-9 A, Traditional laboratory testing algorithm for syphilis. B, CDC-recommended algorithm for reverse sequence syphilis screening (treponemal test screening followed by nontreponemal test confirmation). Despite these recommendations for reverse sequence screening, the CDC continues to recommend the traditional algorithm with reactive nontreponemal tests confirmed by treponemal testing. EIA/CIA, enzyme immunoassay/chemiluminescence immunoassay; FTA-ABS, fluorescent treponemal antibody absorption; RPR, rapid plasma reagins; TP-HA, *Treponema pallidum* hemagglutination; TP-PA, Treponema pallidum particle agglutination; VDRL, Venereal Disease Research Laboratory. *If nontreponemal test is positive qualitatively, a titer is then quantitated. †If incubating or primary syphilis is suspected, treat with benzathine penicillin G 2.4 million units intramuscularly in a single dose. §Evaluate clinically, determine whether treated for syphilis in the past, assess risk for infection, and administer therapy according to CDC's 2010 STD Treatment Guidelines (available at <http://www.cdc.gov/std/treatment/2010>). ¶If at risk for syphilis, repeat RPR in several weeks. (A based on data from Workowski KA, Berman S; Centers for Diseases Control and Prevention [CDC]: Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep 59[RR-12]:1-110, 26-29, 2010; B from Centers for Disease Control and Prevention [CDC]: Discordant results from reverse sequence syphilis screening—five laboratories, United States, 2006-2010. MMWR Morb Mortal Wkly Rep 60(5):133-137, 2011.)

Table 234-1 Dosing of Antifungal Agents in Infants* and Number of Infants Younger Than 1 Yr of Age Studied with Reported Pharmacokinetic Parameters

DRUG	INFANTS STUDIED	SUGGESTED DOSE
Amphotericin B deoxycholate	27	1 mg/kg/day
Amphotericin B lipid complex	28	5 mg/kg/day
Liposomal amphotericin B	17	5 mg/kg/day
Amphotericin B colloidal dispersion	0	5 mg/kg/day
Fluconazole [†]	65	12 mg/kg/day
Micafungin [‡]	120	10 mg/kg/day
Caspofungin [§]	22	50 mg/m ² /day
Anidulafungin [‡]	15	1.5 mg/kg/day

*Voriconazole dosing has not been investigated in the nursery.

[†]A loading dose of 25 mg/kg of fluconazole is necessary to achieve therapeutic serum concentrations in the early days of therapy.

[‡]Micafungin has been studied in infants <120 days of life at this dosage.

[§]Caspofungin and anidulafungin should generally be avoided because dosing sufficient to penetrate brain tissue has not been studied.

Table 234-2 Dosing of Antifungal Agents in Children Older Than 1 Year of Age for Treatment of Invasive Disease

DRUG	SUGGESTED DOSAGE
Amphotericin B deoxycholate	1 mg/kg/day
Amphotericin B lipid complex	5 mg/kg/day
Liposomal amphotericin B	5 mg/kg/day
Amphotericin B colloidal dispersion	5 mg/kg/day
Fluconazole [†]	12 mg/kg/day
Voriconazole	8 mg/kg every 12 hr
Micafungin [*]	2-4 mg/kg/day
Caspofungin	50 mg/m ² /day
Anidulafungin	1.5 mg/kg/day

*Use adult dosages in children older than 8 yr of age.

[†]Loading doses should be used for fluc^onazol^e (25 mg/kg), voriconazole (9 mg/kg q 12 × 24 hr), caspofungin (70 mg/m²), and anidulafungin (3 mg/kg).

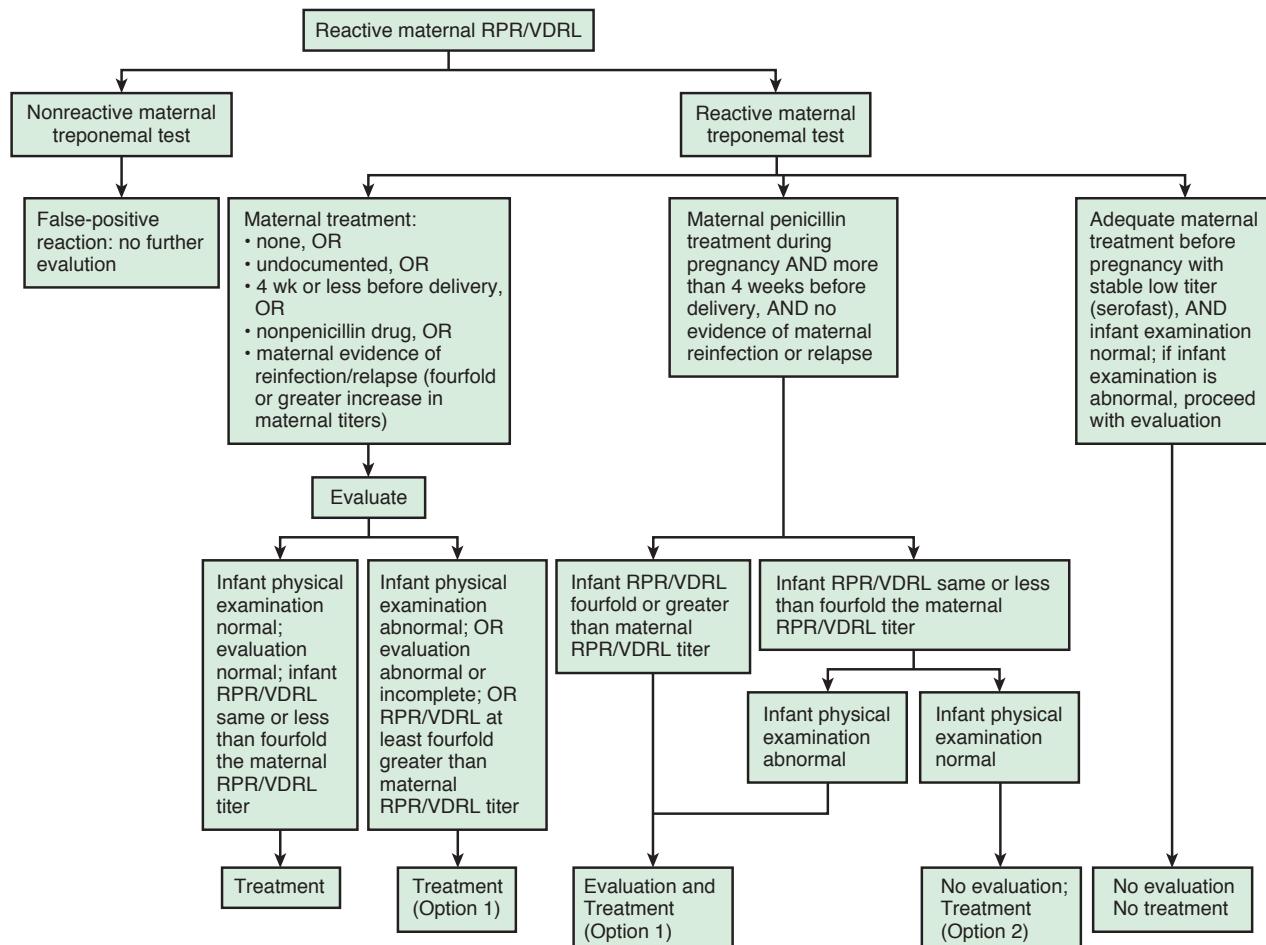


Figure 218-11 Algorithm for evaluating and treating infants born to mothers with reactive serologic tests for syphilis. (From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, Fig. 3-7, p. 695.)

Table 233-1 Suggested Dosing of Antifungal Agents in Children and Neonates

DRUG	FORMULATIONS	SUGGESTED PEDIATRIC DOSAGE	COMMENTS
Amphotericin B deoxycholate	IV	1 mg/kg/day	Generally less toxicity in children than adults; do not start with smaller test doses
Lipid amphotericin B formulations	IV	5 mg/kg/day	Generally all lipid formulations are dosed the same; there is no clear indication of one formulation over another for clinical efficacy
Fluconazole	IV, PO	12 mg/kg/day	Loading dose (25 mg/kg) is suggested based on pharmacokinetic simulations, but insufficiently studied
Itraconazole	IV, PO	2.5 mg/kg/dose bid	Divide dosage twice daily in children; follow trough levels
Voriconazole	IV, PO	8 mg/kg/dose bid IV maintenance; 9 mg/kg/dose bid oral maintenance	Linear pharmacokinetics in children requires higher dosing than in adults; 9 mg/kg/dose bid IV loading, followed by maintenance dosing; follow trough levels
Posaconazole	PO	12-24 mg/kg/day divided tid	Dosage unclear in children at present In adults, max dosage is 800 mg/day, and optimally divide this into 2 or 3 doses; follow trough levels
Micafungin	IV	2-10 mg/kg/day	Highest dosages in neonates (10 mg/kg/day), and lower dosages in children; older than 8 yr of age, use adult dosage
Anidulafungin	IV	1.5 mg/kg/day	Loading dose of 3 mg/kg/day
Caspofungin	IV	50 mg/m ² /day	Load with 70 mg/m ² /day, then 50/mg/m ² /day as maintenance dosage

Table 218-2 Clues That Suggest a Diagnosis of Congenital Syphilis*

EPIDEMIOLOGIC BACKGROUND	CLINICAL FINDINGS
Untreated early syphilis in the mother	Osteochondritis, periostitis
Untreated latent syphilis in the mother	Snuffles, hemorrhagic rhinitis
An untreated mother who has contact with a known syphilitic during pregnancy	Condylomata lata
Mother treated for syphilis during pregnancy with a drug other than penicillin	Bullous lesions, palmar or plantar rash
Mother treated for syphilis during pregnancy without follow-up to demonstrate 4-fold change in titer	Mucous patches
Mother coinfected with HIV	Hepatomegaly, splenomegaly
	Jaundice
	Nonimmune hydrops fetalis
	Generalized lymphadenopathy
	Central nervous system signs; elevated cell count or protein in cerebrospinal fluid
	Hemolytic anemia, diffuse intravascular coagulation, thrombocytopenia
	Pneumonitis
	Nephrotic syndrome
	Placental villitis or vasculitis (unexplained enlarged placenta)
	Intrauterine growth restriction

*Arranged in decreasing order of confidence of diagnosis.

Modified from Remington JS, Klein JO, Wilson CB, et al, editors: Infectious diseases of the fetus and newborn infant, ed 6. Philadelphia, 2006, WB Saunders, p. 556.

Table 218-3 Recommended Management of Neonates (≤ 1 Month of Age) Born to Mothers with Serologic Tests for Syphilis

CLINICAL STATUS	EVALUATION (IN ADDITION TO PHYSICAL EXAMINATION AND QUANTITATIVE NONTREPONEMAL TESTING)	ANTIMICROBIAL THERAPY*
Proven or highly probable disease [†]	CSF analysis for VDRL, cell count, and protein CBC and platelet count Other tests as clinically indicated (e.g., long-bone radiography, liver function tests, ophthalmologic examination)	Aqueous crystalline penicillin G, 100,000-150,000 units/kg/day, administered as 50,000 units/kg/dose IV q12hr during the 1st 7 days of life and 18 hr thereafter for a total of 10 days or Penicillin G procaine, 50,000 units/kg/day IM in a single dose $\times 10$ days
NORMAL PHYSICAL EXAMINATION AND SERUM QUANTITATIVE NONTREPONEMAL TITER ≤ 4 TIMES THE MATERNAL TITER: (a) (i) Mother was not treated or inadequately treated or has no documented treatment; (ii) mother was treated with erythromycin or other nonpenicillin regimen; (iii) mother received treatment ≤ 4 wk before delivery; (iv) maternal evidence of reinfection or relapse (<4-fold decrease in titers) (b) (i) Adequate maternal therapy given >4 wk before delivery; (ii) mother has no evidence of reinfection or relapse (c) Adequate therapy before pregnancy and mother's nontreponemal serologic titer remained low and stable during pregnancy and at delivery	CSF analysis for VDRL, cell count, and protein [§] CBC and platelet count [§] Long-bone radiography [§] None None	Aqueous crystalline penicillin G IV $\times 10$ days [§] or Penicillin G procaine [†] 50,000 units/kg IM in a single dose $\times 10$ days [§] or Penicillin G benzathine [†] 50,000 units/kg IM in a single dose [§] Clinical, serologic follow-up, and penicillin G benzathine 50,000 units/kg IM in a single dose None [¶]

*If more than 1 day of therapy is missed, the entire course should be restarted.

[†]Abnormal physical examination, serum quantitative nontreponemal titer that is 4-fold greater than the mother's titer, or positive result of darkfield or fluorescent antibody test of body fluid(s).[‡]Penicillin G benzathine and penicillin G procaine are approved for IM administration only.[§]A complete evaluation (CSF analysis, bone radiography, CBC) is not necessary if 10 days of parenteral therapy is administered, but it may be useful to support a diagnosis of congenital syphilis. If a single dose of penicillin G benzathine is used, then the infant must be evaluated fully, results of the full evaluation must be normal, and follow-up must be certain. If any part of the infant's evaluation is abnormal or not performed or if the CSF analysis is uninterpretable, the 10-day course of penicillin is required.^{||}Some experts would not treat the infant but would provide close serologic follow-up.[¶]Some experts would treat with penicillin G benzathine, 50,000 units/kg, as a single IM injection, if follow-up is uncertain.

CBC, complete blood cell count; CSF, cerebrospinal fluid; VDRL, Venereal Disease Research Laboratory.

From American Academy of Pediatrics: Red book: 2009 report of the Committee on Infectious Diseases, 28/e. Elk Grove Village, IL, 2009, American Academy of

Table 218-4 Recommended Treatment for Syphilis in Patients Older Than 1 Month of Age

STATUS	CHILDREN	ADULTS
Congenital syphilis	Aqueous crystalline penicillin G 200,000-300,000 units/kg/day IV administered as 50,000 units/kg q4-hr × 10 days*	
Primary, secondary, and early latent syphilis†	Penicillin G benzathine,‡ 50,000 units/kg, IM, up to the adult dose of 2.4 million units in a single dose	Penicillin G benzathine,‡ 2.4 million units IM in a single dose or If allergic to penicillin and not pregnant, doxycycline 100 mg PO bid × 14 days or Tetracycline 500 mg PO qid × 14 days
Late latent syphilis§ or syphilis of unknown duration	Penicillin G benzathine,‡ 50,000 units/kg IM up to the adult dose of 2.4 million units, administered as 3 single doses at 1 wk intervals (total 150,000 units/kg, up to the adult dose of 7.2 million units)	Penicillin G benzathine,‡ 7.2 million units total administered as 3 doses of 2.4 million units IM, each at 1 wk intervals or If allergic to penicillin and not pregnant, doxycycline 100 mg PO bid × 4 wk or Tetracycline 500 mg PO qid × 4 wk
Tertiary syphilis		Penicillin G benzathine,‡ 7.2 million units total, administered as 3 doses of 2.4 million units IM at 1 wk intervals If allergic to penicillin and not pregnant, same as for late latent syphilis
Neurosyphilis	Aqueous crystalline penicillin G 200,000-300,000 units/kg/day q4-hr × 10-14 days in doses not to exceed the adult dose	Aqueous crystalline penicillin G 18-24 million units/day administered as 3-4 million units IV q4hr × 10-14 days¶ or Penicillin G procaine,‡ 2.4 million units IM once daily plus probenecid 500 mg PO qid, both × 10-14 days

*If the patient has no clinical manifestations of disease, the CSF examination is normal, and the CSF VDRL result is negative, some experts would treat with up to 3 weekly doses of penicillin G benzathine 50,000 units/kg IM. Some experts also suggest giving these patients a single dose of penicillin G benzathine 50,000 units/kg IM after the 10-day course of IV aqueous penicillin.

†Early latent syphilis is defined as being acquired within the preceding year.

‡Penicillin G benzathine and penicillin G procaine are approved for IM administration only.

§Late latent syphilis is defined as syphilis beyond 1 year's duration.

||Patients who are allergic to penicillin should be desensitized.

¶Some experts administer penicillin G benzathine 2.4 million units IM, once per week for up to 3 wk after completion of these neurosyphilis treatment regimens. CSF, cerebrospinal fluid; VDRL, Venereal Disease Research Laboratory.

From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, p. 698, Table 3.72.

Table 222-2 Recommended Treatment of Lyme Disease	
DRUG	PEDIATRIC DOSING
Amoxicillin	50 mg/kg/day in 3 divided doses (max: 1,500 mg/day)
Doxycycline	4 mg/kg/day in 2 divided doses (max: 200 mg/day) (see text regarding doxycycline use in children)
Cefuroxime axetil	30 mg/kg/day in 2 divided doses (max: 1,000 mg/day)
Ceftriaxone (IV)*†	50-75 mg/kg/day once daily (max: 2,000 mg/day)
RECOMMENDED THERAPY BASED ON CLINICAL MANIFESTATION	
Erythema migrans	Oral regimen, 14-21 days
Meningitis	Ceftriaxone, 10-28 days
Cranial nerve palsy	Oral regimen, 14-21 days (see text regarding possible need for lumbar puncture)
Cardiac disease	Oral regimen or ceftriaxone, 14-21 days (see text for specifics)
Arthritis‡	Oral regimen, 28 days
Late neurologic disease	Ceftriaxone, 14-28 days

*Cefotaxime and penicillin G are alternative parenteral agents.

†Doses of 100 mg/kg/day should be used for meningitis.

‡Persistent arthritis can be treated with a second oral regimen or ceftriaxone.

From Wormser GP, Dattwyler RJ, Shapiro ED, et al: The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America, Clin Infect Dis 43:1089-1134, 2006.

Table 222-1 Clinical Stages of Lyme Disease		
DISEASE STAGE	TIMING AFTER TICK BITE	TYPICAL CLINICAL MANIFESTATIONS
Early localized	3-30 days	Erythema migrans (single), variable constitutional symptoms (headache, fever, myalgia, arthralgia, fatigue)
Early disseminated	3-12 wk	Erythema migrans (single or multiple), worse constitutional symptoms, cranial neuritis, meningitis, carditis, ocular disease
Late	>2 mo	Arthritis

Table 245-1 Currently Licensed Antiviral Drugs*		
ANTIVIRAL	TRADE NAME	MECHANISM OF ACTION
Acyclovir	Zovirax	Inhibits viral DNA polymerase
Adefovir	Hepsera	Nucleotide reverse transcriptase inhibitor
Amantadine	Symmetrel	Blocks M2 protein ion channel
Cidofovir	Vistide	Inhibits viral DNA polymerase
Famciclovir	Famvir	Inhibits viral DNA polymerase
Fomivirsen	Vitravene	Phosphorothioate oligonucleotide inhibits viral replication via antisense mechanism
Foscarnet	Foscavir	Inhibits viral DNA polymerase and reverse transcriptase at pyrophosphate-binding site
Ganciclovir	Cytovene	Inhibits viral DNA polymerase
Iodoxuridine	Herplex	Inhibits viral DNA polymerase
Interferon- α	Intro-A (interferon- α 2b) Roferon-A (interferon- α 2a) Infergen (interferon alfacon-1)	Produces multiple effector proteins that exert antiviral effects; also directly interacts with immune system components
Interferon- α 2b plus ribavirin	Rebetron	Not established
Lamivudine	Epivir	Inhibits viral DNA polymerase and reverse transcriptase
Oseltamivir	Tamiflu	Neuraminidase inhibitor; interference with deaggregation and release of viral progeny
Pegylated interferon	PEG-Intron (α 2b), Pegasys (α 2a)	Same as interferon
Penciclovir	Denavir	Inhibits viral DNA polymerase
Ribavirin	Virazole, Rebetol, Copegus	Interference with viral messenger RNA
Rimantadine	Flumadine	Blocks M2 protein ion channel
Trifluridine	Viroptic	Inhibits viral DNA polymerase
Valacyclovir	Valtrex	Same as acyclovir
Valganciclovir	Valcyte	Same as ganciclovir
Vidarabine	ara-A	Inhibits viral DNA polymerase (and to lesser extent, cellular DNA polymerase)
Zanamivir	Relenza	Neuraminidase inhibitor; interference with deaggregation and release of viral progeny
FDA-APPROVED COMBINATION THERAPIES		
Interferon- α 2b + ribavirin	Rebetron (Intron-A plus Rebetol)	
Interferon- α 2a + ribavirin	Roferon-A + ribavirin	
Pegylated interferon- α 2b + ribavirin	PEG-Intron + Rebetol	
Pegylated interferon- α 2a + ribavirin	Pegasys + Copegus	

*See Chapter 276 for antiretroviral drugs.

Table 246-2 Recommendations for Measles Immunization	
CATEGORY	RECOMMENDATIONS
Unimmunized, no history of measles (12-15 mo of age)	A 2 dose schedule (with MMR) is recommended The 1st dose is recommended at 12-15 mo of age; the 2nd is recommended at 4-6 yr of age
Children 6-11 mo of age in epidemic situations or prior to international travel	Immunize with MMR vaccine, but this dose is not considered valid, and 2 valid doses administered on or after the 1st birthday are required. The 1st valid dose should be administered at 12-15 mo of age. The 2nd valid dose is recommended at least 28 days later and is given at 4 through 6 yr of age
Students in kindergarten or elementary, middle, and high school who have received 1 dose of measles vaccine at 12 mo of age or older	Administer the 2nd dose
Students in college and other post-high school institutions who have received 1 dose of measles vaccine at \geq 12 mo of age	Administer the 2nd dose
History of immunization before the 1st birthday	Do not consider valid and immunize (2 doses)
History of receipt of inactivated measles vaccine or unknown type of vaccine, 1963-1967	Do not consider valid and immunize (2 doses)
Further attenuated or unknown vaccine given with Ig	Do not consider valid and immunize (2 doses)
Allergy to eggs	Immunize; no reactions likely
Neomycin allergy, nonanaphylactic	Immunize; no reactions likely
Severe hypersensitivity (anaphylaxis) to neomycin or gelatin	Avoid immunization
Tuberculosis	Immunize; if patient has untreated tuberculosis disease, start antituberculosis therapy before immunizing
Measles exposure	Immunize and/or give Ig, depending on circumstances
HIV-infected	Immunize (2 doses) unless severely immunocompromised, and give Ig if exposed to measles
Personal or family history of seizures	Immunize; advise parents of slightly increased risk of seizures
Ig or blood recipient	Immunize at the appropriate interval (see Table 246-3)

Ig, immunoglobulin; MMR, measles-mumps-rubella vaccine.

From American Academy of Pediatrics: Red book: 2012 report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics, p. 494.

Table 245-2 Antiviral Therapies for Non-HIV Clinical Conditions

VIRUS	CLINICAL SYNDROME	ANTIVIRAL AGENT OF CHOICE	ALTERNATIVE ANTIVIRAL AGENTS
Influenza A	Treatment	Oseltamivir (>1 yr old)	Rimantadine Amantadine Amantadine Rimantadine Zanamivir (>7 yr old)
	Prophylaxis	Oseltamivir (>1 yr old)	
Influenza B	Treatment	Oseltamivir	Zanamivir (>7 yr old)
Respiratory syncytial virus	Bronchiolitis or pneumonia in high-risk host	Ribavirin aerosol	
Cytomegalovirus (CMV)	Congenital CMV infection	Ganciclovir (IV)	Valganciclovir (if oral therapy appropriate; long-term oral valganciclovir investigational but may improve developmental and hearing outcomes)
	Retinitis in AIDS patients	Valganciclovir	Ganciclovir Cidofovir Foscarnet Ganciclovir ocular insert Foscarnet Cidofovir Valganciclovir
	Pneumonitis, colitis; esophagitis in immunocompromised patients	Ganciclovir (IV)	
Herpes simplex virus (HSV)	Neonatal herpes Suppressive therapy following neonatal herpes with central nervous system involvement	Acyclovir (IV) Acyclovir (PO)	
	HSV encephalitis	Acyclovir (IV)	Acyclovir (IV)
	HSV gingivostomatitis	Acyclovir (PO)	Valacyclovir Famciclovir
	First episode genital infection	Acyclovir (PO)	Acyclovir (IV) (severe disease) Valacyclovir Famciclovir Valacyclovir Famciclovir Penciclovir (topical)
	Recurrent genital herpes	Acyclovir (PO)	
	Suppression of genital herpes	Acyclovir (PO)	
	Cutaneous HSV (whitlow, herpes gladiatorum) Eczema herpeticum	Acyclovir (PO) Acyclovir (PO)	Acyclovir (IV) (severe disease) Acyclovir (PO) (if outpatient therapy acceptable)
	Mucocutaneous infection in immunocompromised host (mild)	Acyclovir (IV)	
	Mucocutaneous infection in immunocompromised host (moderate to severe)	Acyclovir (IV)	
	Prophylaxis in bone marrow transplant recipients	Acyclovir (IV)	Valacyclovir Famciclovir Cidofovir Vidarabine
Varicella-zoster virus	Acyclovir-resistant HSV Keratitis or keratoconjunctivitis	Foscarnet Trifluridine	
	Chickenpox, healthy child	Supportive care	Acyclovir (PO)
	Chickenpox, immunocompromised child	Acyclovir (IV)	
	Zoster (not ophthalmic branch of trigeminal nerve), healthy child	Supportive care	Acyclovir (PO)
	Zoster (ophthalmic branch of trigeminal nerve), healthy child	Acyclovir (IV)	
	Zoster, immunocompromised child	Acyclovir (IV)	Valacyclovir

Modified from Kimberlin DW: Antiviral therapies in children: Has their time arrived? *Pediatr Clin North Am* 52:837–867, 2005.

Table 246-3 Suggested Intervals Between Immunoglobulin Administration and Measles Immunization*

INDICATION FOR IMMUNOGLOBULIN	ROUTE	Dose		
		UNITS (U) OR MILLILITERS (mL)	mg IgG/kg	INTERVAL (mo) [†]
Tetanus (as tetanus Ig)	IM	250 U	10	3
Hepatitis A prophylaxis (as Ig): Contact prophylaxis International travel	IM	0.02 mL/kg	3.3	3
	IM	0.06 mL/kg	10	3
Hepatitis B prophylaxis (as hepatitis B Ig)	IM	0.06 mL/kg	10	3
Rabies prophylaxis (as rabies Ig)	IM	20 IU/kg	22	4
Varicella prophylaxis (as VarizIG)	IM	125 U/10 kg (maximum 625 U)	20-40	5
Measles prophylaxis (as Ig): Standard Immunocompromised host	IM	0.25 mL/kg	40	5
	IM	0.50 mL/kg	80	6
Respiratory syncytial virus prophylaxis (palivizumab monoclonal antibody) [‡]	IM	—	15 mg/kg (monoclonal)	None
Cytomegalovirus immune globulin	IV	3 mL/kg	150	6
Blood transfusion: Washed RBCs	IV	10 mL/kg	Negligible	0
RBCs, adenine-saline added	IV	10 mL/kg	10	3
Packed RBCs	IV	10 mL/kg	20-60	5
Whole blood	IV	10 mL/kg	80-100	6
Plasma or platelet products	IV	10 mL/kg	160	7

Continued

Table 246-3 Suggested Intervals Between Immunoglobulin Administration and Measles Immunization*—cont'd

INDICATION FOR IMMUNOGLOBULIN	ROUTE	Dose		
		UNITS (U) OR MILLILITERS (mL)	mg IgG/kg	INTERVAL (mo) [†]
Replacement (or therapy) of immune deficiencies (as IVIG)	IV	—	300-400	8
ITP (as IVIG)	IV	—	400	8
ITP	IV	—	1,000	10
ITP or Kawasaki disease	IV	—	1,600-2,000	11

*Immunization in the form of measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV), or monovalent measles vaccine.

[†]These intervals should provide sufficient time for decreases in passive antibodies in all children to allow for an adequate response to measles vaccine. Physicians should not assume that children are fully protected against measles during these intervals. Additional doses of Ig or measles vaccine may be indicated after exposure to measles (see text).[‡]Monoclonal antibodies, such as palivizumab, do not interfere with the immune response to vaccines.

Ig, immunoglobulin; IgG, immunoglobulin G; ITP, immune (formerly termed "idiopathic") thrombocytopenic purpura; IVIG, intravenous Ig; RBCs, red blood cells.

Table 247-2 Clinical Manifestations of Congenital Rubella Syndrome in 376 Children Following Maternal Rubella*

MANIFESTATION	RATE (%)
Deafness	67
Ocular	71
Cataracts	29
Retinopathy	39
Heart disease [†]	48
Patent ductus arteriosus	78
Right pulmonary artery stenosis	70
Left pulmonary artery stenosis	56
Valvular pulmonic stenosis	40
Low birthweight	60
Psychomotor retardation	45
Neonatal purpura	23
Death	35

*Other findings: hepatitis, linear streaking of bone, hazy cornea, congenital glaucoma, delayed growth.

[†]Findings in 87 patients with congenital rubella syndrome and heart disease who underwent cardiac angiography.

Table 249-1 Differential Diagnosis of Acute Flaccid Paralysis

SITE, CONDITION, FACTOR, OR AGENT	CLINICAL FINDINGS	ONSET OF PARALYSIS	PROGRESSION OF PARALYSIS	SENSORY SIGNS AND SYMPTOMS	REDUCTION OR ABSENCE OF DEEP TENDON REFLEXES	RESIDUAL PARALYSIS	PLEOCYTOSIS
ANTERIOR HORN CELLS OF SPINAL CORD							
Poliomyelitis (wild and vaccine-associated paralytic poliomyelitis)	Paralysis	Incubation period 7-14 days (range: 4-35 days)	24-48 hr to onset of full paralysis; proximal → distal, asymmetric	No	Yes	Yes	Aseptic meningitis (moderate polymorphonuclear leukocytes at 2-3 days)
Nonpolio enteroviruses	Hand-foot-and-mouth disease, aseptic meningitis, acute hemorrhagic conjunctivitis, possibly idiopathic epidemic flaccid paralysis	As in poliomyelitis	As in poliomyelitis	No	Yes	Yes	As in poliomyelitis
West Nile virus	Meningitis/encephalitis	As in poliomyelitis	As in poliomyelitis	No	Yes	Yes	Yes
OTHER NEUROTROPIC VIRUSES							
Rabies virus		Month-year	Acute, symmetric, ascending	Yes	Yes	No	±
Varicella-zoster virus	Exanthematous vesicular eruptions	Incubation period 10-21 days	Acute, symmetric, ascending	Yes	±	±	Yes
Japanese encephalitis virus		Incubation period 5-15 days	Acute, proximal, asymmetric	±	±	±	Yes
GUILLEN-BARRÉ SYNDROME							
Acute inflammatory polyradiculoneuropathy	Preceding infection, bilateral facial weakness	Hours to 10 days	Acute, symmetric, ascending (days to 4 wk)	Yes	Yes	±	No
Acute motor axonal neuropathy	Fulminant, widespread paralysis, bilateral facial weakness, tongue involvement	Hours to 10 days	1-6 days	No	Yes	±	No

ACUTE TRAUMATIC SCIATIC NEURITS	Acute, asymmetric	Hours to 4 days	Complete, affected limb	Yes	Yes	±	No
Intramuscular gluteal injection		Hours to days	Hours to days	Yes	Yes, early	Yes	Yes
Acute transverse myelitis	Preceding Mycoplasma pneumoniae, Schistosoma, other parasitic or viral infection	Acute, symmetric hypotonia of lower limbs		Yes	Yes	±	Yes
Epidural abscess	Headache, back pain, local spinal tenderness, meningismus	Complete		Yes	Yes	±	Yes
Spinal cord compression; trauma		Complete	Hours to days	Yes	Yes	±	±
NEUROPATHIES							
Exotoxin of <i>Corynebacterium diphtheriae</i>	In severe cases, palatal paralysis, blurred vision	Incubation period 1-8 wk (paralysis 8-12 wk after onset of illness)		Yes	Yes	±	±
Toxin of <i>Clostridium botulinum</i>	Abdominal pain, diplopia, loss of accommodation, mydriasis	Incubation period 18-36 hr	Rapid, descending, ± symmetric	No	No	No	No
Tick bite paralysis	Ocular symptoms	Latency period 5-10 days	Acute, symmetric, ascending	No	Yes	No	No
DISEASES OF THE NEUROMUSCULAR JUNCTION							
Myasthenia gravis	Weakness, fatigability, diplopia, ptosis, dysarthria		Multifocal	No	No	No	No
DISORDERS OF MUSCLE							
Polymyositis	Neoplasm, autoimmune disease	Subacute, proximal → distal	Weeks to months	No	Yes	No	No
Viral myositis		Pseudoparalysis	Hours to days	No	No	No	No
METABOLIC DISORDERS							
Hypokalemic periodic paralysis		Proximal limb, respiratory muscles	Sudden postprandial	No	Yes	±	No
INTENSIVE CARE UNIT WEAKNESS							
Critical illness polyneuropathy	Flaccid limbs and respiratory weakness	Acute, following systemic inflammatory response syndrome/sepsis	Hours to days	±	Yes	±	No

Modified from Marx A, Glass JD, Sutter RW: Differential diagnosis of acute flaccid paralysis and its role in poliomyelitis surveillance, Epidemiol Rev 22:298-316, 2000.

Table 258-3 Centers for Disease Control and Prevention Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis

ANTIVIRAL AGENT	USE	CHILDREN	ADULTS*
Oseltamivir (Tamiflu)	Treatment (5 days)	If child is younger than 1 yr old [†] : 3 mg/kg/dose twice daily [†] If child is 1 yr or older, dose varies by child's weight: 15 kg or less, the dose is 30 mg twice a day >15-23 kg, the dose is 45 mg twice a day >23-40 kg, the dose is 60 mg twice a day >40 kg, the dose is 75 mg twice a day	75 mg twice daily
	Chemoprophylaxis (7 days)	If child is younger than 3 mo old, use of oseltamivir for chemoprophylaxis is not recommended unless situation is judged critical because of limited data in this age group If child's age is 3 mo or older and younger than 1 yr old [†] : 3 mg/kg/dose once daily [†] If child is 1 yr or older, dose varies by child's weight: 15 kg or less, the dose is 30 mg once a day >15-23 kg, the dose is 45 mg once a day >23-40 kg, the dose is 60 mg once a day >40 kg, the dose is 75 mg once a day	75 mg once daily
Zanamivir [‡] (Relenza)	Treatment (5 days)	For children age 7 yr and older: 10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) twice daily
	Chemoprophylaxis (7 days)	For children age 5 yr and older: 10 mg (two 5-mg inhalations) once daily	10 mg (two 5-mg inhalations) once daily

Current for 2013-2014 influenza season, United States.

*Intravenous peramivir (Rapivab) was approved on December 19, 2014, for use in the treatment of acute uncomplicated influenza in people 18 years and older.

[†]Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza with twice-daily dosing in persons older than 14 days of age, and for prophylaxis with once-daily dosing in persons 1 yr and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants younger than 14 days old, and for prophylaxis in infants 3 mo to 1 yr of age, is recommended by the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics.

[‡]This is the FDA-approved oral and CDC-recommended oseltamivir treatment dose for infants 14 days and older and less than 1 yr old, and provides oseltamivir exposure in children similar to that achieved by the approved dose of 75 mg orally twice daily for adults, as shown in 2 studies of oseltamivir pharmacokinetics. The American Academy of Pediatrics recommends an oseltamivir treatment dose of 3.5 mg/kg orally twice daily for infants ages 9-11 mo for the 2013-2014 season, on the basis of data that indicated that the higher dose of 3.5 mg/kg was needed to achieve the protocol-defined targeted exposure for this cohort as defined in the Collaborative Antiviral Study Group (CASG) 114 study. It is unknown whether this higher dose will improve efficacy or prevent the development of antiviral resistance. However, there is no evidence that the 3.5 mg/kg dose is harmful or causes more adverse events to infants in this age group.

[§]Inhaled zanamivir is approved for treatment of acute uncomplicated influenza with twice-daily dosing in persons age 7 yr and older, and for prophylaxis with once-daily dosing in persons age 5 yr and older.

Adapted from Centers for Disease Control and Prevention (CDC): Influenza antiviral medications: summary for clinicians. Available at <http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>. For current details, consult annually updated recommendations at <http://www.cdc.gov/flu>.

Table 255-1 Findings in Infants with Symptomatic Congenital Cytomegalovirus Infection Identified Through Newborn Screening Program*

	PERCENTAGE (%) OF INFANTS
CLINICAL FINDINGS	
Prematurity (<37 wk)	24
Jaundice (direct bilirubin >2 mg/dL)	42
Petechiae	54
Hepatosplenomegaly	19
Purpura	3
Microcephaly	35
Small gestational age	28
1 Clinical finding	41
2 Clinical findings	59
LABORATORY FINDINGS	
Elevated alanine aminotransferase (>80 IU/mL)	71
Thrombocytopenia (<100,000/µL)	43
Direct hyperbilirubinemia (>2 mg/dL)	54
Head CT abnormalities	42

*Findings in 70 infants with symptomatic congenital CMV infection identified during the newborn screening program for infants with congenital CMV infection performed at the University of Alabama Hospitals over an approximate 20 yr interval.

Table 250-2 Differential Diagnosis of Enterovirus Infections

CLINICAL MANIFESTATION	BACTERIAL PATHOGENS	VIRAL PATHOGENS
Nonspecific febrile illness	<i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> type b, <i>Neisseria meningitidis</i>	Influenza viruses, human herpesviruses 6 and 7, human parechoviruses
Exanthems/enanthems	Group A streptococcus, <i>Staphylococcus aureus</i> , <i>N. meningitidis</i>	Herpes simplex virus, adenoviruses, varicella-zoster virus, Epstein-Barr virus, measles virus, rubella virus, human herpesviruses 6 and 7, human parechoviruses
Respiratory illness/conjunctivitis	<i>S. pneumoniae</i> , <i>H. influenzae</i> (nontypeable and type b), <i>N. meningitidis</i> , <i>Mycoplasma pneumoniae</i> , <i>Chlamydia pneumoniae</i>	Adenoviruses, influenza viruses, respiratory syncytial virus, parainfluenza viruses, rhinoviruses, human metapneumovirus, coronaviruses
Myocarditis/pericarditis	<i>S. aureus</i> , <i>H. influenzae</i> type b, <i>M. pneumoniae</i>	Adenoviruses, influenza virus, parvovirus, cytomegalovirus
Meningitis/encephalitis	<i>S. pneumoniae</i> , <i>H. influenzae</i> type b, <i>N. meningitidis</i> , <i>Mycobacterium tuberculosis</i> , <i>Borrelia burgdorferi</i> , <i>M. pneumoniae</i> , <i>Bartonella henselae</i> , <i>Listeria monocytogenes</i>	Herpes simplex virus, West Nile virus, influenza viruses, adenoviruses, Epstein-Barr virus, mumps virus, lymphocytic choriomeningitis virus, arboviruses, human parechoviruses
Neonatal infections	Group B streptococcus, Gram-negative enteric bacilli, <i>L. monocytogenes</i> , <i>Enterococcus</i>	Herpes simplex virus, adenoviruses, cytomegalovirus, rubella virus, human parechoviruses

Table 274-1 Rabies Postexposure Prophylaxis Guide

ANIMAL TYPE	EVALUATION AND DISPOSITION OF ANIMAL	POSTEXPOSURE PROPHYLAXIS RECOMMENDATIONS
Dogs, cats, and ferrets	Healthy and available for 10 days of observation Rabid or suspected of being rabid [†] Unknown (escaped)	Prophylaxis only if animal shows signs of rabies* Immediate immunization and RIG Consult public health officials for advice
Bats, skunks, raccoons, foxes, and most other carnivores; woodchucks	Regarded as rabid unless geographic area is known to be free of rabies or until animal proven negative by laboratory tests [†]	Immediate immunization and RIG
Livestock, rodents, and lagomorphs (rabbits, hares, and pikas)	Consider individually	Consult public health officials. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice and other rodents, rabbits, hares, and pikas almost never require antirabies treatment

*During the 10-day observation period, at the first sign of rabies in the biting dog, cat, or ferret, treatment of the exposed person with RIG (human) and vaccine should be initiated. The animal should be euthanized immediately and tested.

[†]The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended. Immunization is discontinued if immunofluorescent test result for the animal is negative.

RIG, rabies immunoglobulin.

From American Academy of Pediatrics: Red book 2012: report of the Committee on Infectious Diseases, ed 29. Elk Grove Village, IL, 2012, American Academy of Pediatrics.

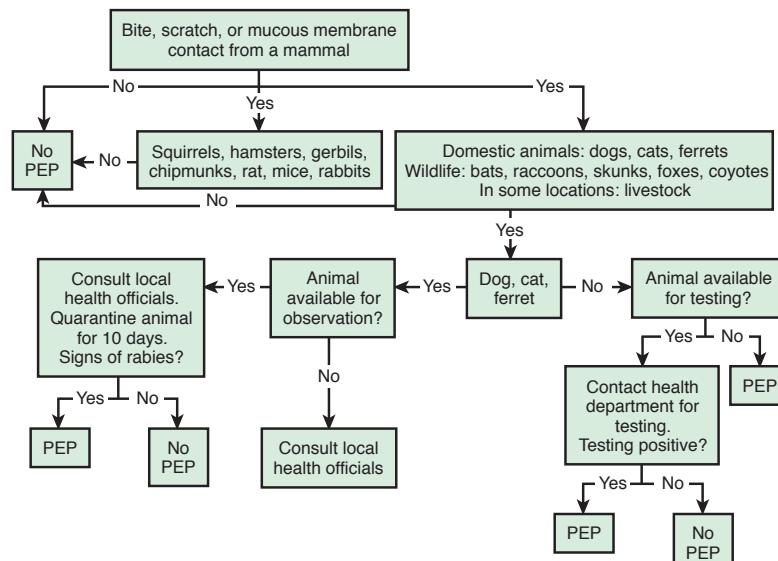


Figure 274-1 Algorithm for evaluating a child for rabies postexposure prophylaxis. This and any other algorithm should be used in concert with local epidemiologic information regarding the incidence of animal rabies in any given location.

Chapter 276 ◆ Acquired Immunodeficiency Syndrome (Human Immunodeficiency Virus) 1651

Table 276-2

Stage 3—Defining Opportunistic Illnesses in HIV Infection

Bacterial infections, multiple or recurrent*
 Candidiasis of bronchi, trachea, or lungs
 Candidiasis of esophagus
 Cervical cancer, invasive†
 Coccidioidomycosis, disseminated or extrapulmonary
 Cryptococcosis, extrapulmonary
 Cryptosporidiosis, chronic intestinal (>1 mo duration)
 Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 mo
 Cytomegalovirus retinitis (with loss of vision)
 Encephalopathy attributed to HIV‡
 Herpes simplex: chronic ulcers (>1 mo duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 mo)
 Histoplasmosis, disseminated or extrapulmonary
 Isosporiasis, chronic intestinal (>1 mo duration)
 Kaposi sarcoma
 Lymphoma, Burkitt (or equivalent term)
 Lymphoma, immunoblastic (or equivalent term)
 Lymphoma, primary, of brain
Mycobacterium avium complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
Mycobacterium tuberculosis of any site, pulmonary,† disseminated, or extrapulmonary
Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
Pneumocystis jiroveci (previously known as *Pneumocystis carinii*) pneumonia
 Pneumonia, recurrent†
 Progressive multifocal leukoencephalopathy
Salmonella septicemia, recurrent
 Toxoplasmosis of brain, onset at age >1 mo
 Wasting syndrome attributed to HIV‡

*Only among children aged <6 yr.

†Only among adults, adolescents, and children aged ≥6 yr.

‡Suggested diagnostic criteria for these illnesses, which might be particularly important for HIV encephalopathy and HIV wasting syndrome, are described in the following references:

Table 276-3

Laboratory Diagnosis of HIV Infection

TEST	COMMENT
HIV DNA PCR	Preferred test to diagnose HIV-1 subtype B infection in infants and children younger than 18 mo of age; highly sensitive and specific by 2 wk of age and available; performed on peripheral blood mononuclear cells. False negatives can occur in non-B subtype HIV-1 infections
HIV culture	Expensive, not easily available, requires up to 4 wk to do test; not recommended
HIV RNA PCR	Preferred test to identify non-B subtype HIV-1 infections. Similar sensitivity and specificity to HIV DNA PCR in infants and children younger than 18 mo of age, but DNA PCR is generally preferred because of greater clinical experience with that assay

Table 276-1

HIV Infection Stage* Based on Age-Specific CD4+ T-Lymphocyte Count or CD4+ T-Lymphocyte Percentage of Total Lymphocytes

Stage	Age on Date of CD4+ T-Lymphocyte Test					
	<1 Yr		1-5 Yr		≥6 Yr	
	CELLS/µL	%	CELLS/µL	%	CELLS/µL	%
1	≥1,500	≥34	≥1,000	≥30	≥500	≥26
2	750-1,499	26-33	500-999	22-29	200-499	14-25
3	<750	<26	<500	<22	<200	<14

*Stage is based primarily on the CD4+ T-lymphocyte count. The CD4+ T-lymphocyte count takes precedence over the CD4+ T-lymphocyte percentage, and the percentage is considered only if the count is missing.

From Centers for Disease Control and Prevention: Revised surveillance case definition for HIV infection—United States, 2014. MMWR 63(No RR-3):1-10, 2014.

Chapter 276 ◆ Acquired Immunodeficiency Syndrome (Human Immunodeficiency Virus) 1655

Table 276-4 Summary of Antiretroviral Therapies Available in 2014

DRUG (TRADE NAMES, FORMULATIONS)	DOSING	SIDE EFFECTS	COMMENTS
NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS		Class adverse effects: Lactic acidosis with hepatic steatosis	
Abacavir (ABC) Ziagen, ABC Tablet: 300 mg Oral solution: 20 mg/mL Trizivir: combination of zidovudine (ZDV), lamivudine, ABC (300, 150, 300 mg) Epzicom: combination of lamivudine, ABC (300, 600 mg)	Children: ≥3 mo to 13 yr: 8 mg/kg bid (maximum dose 300 mg bid) >30 kg: 300 mg bid Children with viral load <40 copies/mm ³ : 16 mg/kg once daily (max 600 mg) Adolescents >16 yr and adults: 600 mg once daily Trizivir (>40 kg): 1 tablet bid Epzicom (>16 yr of age): 1 tablet bid	Common: nausea, vomiting, anorexia, fever, headache, diarrhea, rash Less common: hypersensitivity, lactic acidosis with hepatic steatosis, pancreatitis, elevated triglycerides, myocardial infarction	Can be given with food Genetic screening for HLAB*5701 is recommended prior to initiation of ABC-containing treatment. If test is positive avoid ABC. Do not restart ABC in patients who had hypersensitivity-like symptoms (e.g., flu-like symptoms)
Didanosine Videx, ddI Powder for oral solution (prepared with solution containing antacid): 10 mg/mL	2 wk to <3 mo: 50 mg/m ² bid 3-8 mo: 100 mg/m ² bid >8 mo: 120 mg/m ² (maximum 200 mg per dose) bid Adolescents (>13 yr) and adults <60 kg: 250 mg once daily >60 kg: 400 mg once daily (to increase adherence) If combined with tenofovir <60 kg-200 mg once daily >60 kg-250 mg once daily	Common: diarrhea, abdominal pain, nausea, vomiting Less common: pancreatitis, peripheral neuropathy, electrolyte abnormalities, lactic acidosis with hepatic steatosis, hepatomegaly, retinal depigmentation	Food decreases bioavailability up to 50%. Take 30 min before or 2 hr after meal. Tablets dissolved in water are stable for 1 hr (4 hr in buffered solution) Drug interactions: antacids/gastric acid antagonists may increase bioavailability; possible decreased absorption of fluoroquinolones, ganciclovir, ketoconazole, itraconazole, dapsone, and some protease inhibitors. Combination with d4T enhances toxicity, also common if combined with tenofovir
Videx EC Capsule, delayed release: 125, 200, 250, 400 mg Generic: 200, 250, 400 mg	Children: not established 20-25 kg: 200 mg once daily 25-60 kg: 250 mg once daily ≥60 kg: 400 mg once daily	Same as for ddI	Same as for ddI
Emtricitabine Emtriva, FTC Capsules: 200 mg Oral solution: 10 mg/mL Truvada: combination FTC, tenofovir disoproxil fumarate (TDF) (200, 300 mg) Atripla: Combination FTC, TDF, efavirenz (EFV) (200, 300, 600 mg) Complera: combination of FTC, TDF, rilpivirine (RPV) (200, 300, 25mg) Stribild: combination of FTC, TDF, elvitegravir (EVG), cobicistat (COBI) (200, 300, 150, 150 mg)	Infants: 0-3 mo: 3 mg/kg once daily Children ≥3 mo to 17 yr: 6 mg/kg (maximum 240 mg) once daily >33 kg, adolescent and adult: 200 mg capsule or 240 mg solution once daily Truvada or Atripla or Complera or Stribild adult dose: 1 tablet once daily	Common: headache, insomnia, diarrhea, nausea, skin discoloration Less common: lactic acidosis with hepatic steatosis, neutropenia	Closely monitor patients with hepatitis B coinfection Can be given without regard to food. Oral solution should be refrigerated if temperature above 25°C (77°F)
Lamivudine Epivir, Epivir HBV, 3TC Tablet: 150 (scored), 300 mg (Epivir 100 mg (Epivir HBV) Solution: 5 mg/mL (Epivir HBV), 10 mg/mL (Epivir) Combivir: combination of ZDV, lamivudine (300, 150 mg) Trizivir and Epzicom combination (see abacavir)	Neonates (<30 days): 2 mg/kg bid >1 mo: 4 mg/kg bid (maximum 150 mg bid) ≥30 kg: 150 mg bid or 300 mg once daily Children with VL <40 copies/mL: 8-10 mg/kg qd Combivir, Trizivir (>30 kg): 1 tablet bid Epzicom (>16 yr): 1 tablet qd	Common: headache, nausea Less common: pancreatitis, peripheral neuropathy, lactic acidosis with hepatic steatosis, lipodystrophy	No food restrictions Combination with ZDV may prevent ZDV resistance. Patient should be screened for hepatitis B virus (HBV) and if positive watched for HBV exacerbation when lamivudine is discontinued
Stavudine Zerit, d4T Capsule: 15, 20, 30, 40 mg Solution: 1 mg/mL	Neonates (0-13 days): 0.5 mg/kg bid 14 days to 30 kg: 1 mg/kg bid >30 kg: 30 mg bid	Common: headache, nausea, hyperlipidemia, fat maldistribution Less common: peripheral neuropathy, pancreatitis, lactic acidosis, hepatic steatosis	No food restrictions. Should not be administered with ZDV because of virologic antagonism. Higher incidence of lactic acidosis. Increased toxicity if combined with ddI

Continued

Table 276-4 Summary of Antiretroviral Therapies Available in 2014—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	DOSING	SIDE EFFECTS	COMMENTS
Tenofovir Viread, TDF Tablet: 150, 200, 250, 300 mg Powder: 40 mg per 1 gr powder Truvada: combination of FTC, TDF (200, 300 mg) Atripla: Combination of FTC, TDF, EFV (200, 300, 600 mg) Complera: combination of FTC, TDF, RPV (200, 300, 25 mg) Stribild: combination of FTC, TDF, EVG, COBI (200, 300, 150, 150 mg)	2 to <12 yr: 8 mg/kg qd >12 yr and 35 kg, adolescent >12 yr and 35 kg and adult: 300 mg once daily Truvada, Atripla, Complera, and Stribild (see FTC)	Common: nausea, vomiting, diarrhea Less common: lactic acidosis with hepatic steatosis, hepatomegaly, reduced bone density, renal toxicity	High-fat meal increases absorption; coadministration with ddI may increase ddI toxicity, decrease atazanavir (ATV) levels (therefore boosting ATV with ritonavir is required). ATV and lopinavir (LPV) increase TDF levels and potential toxicity. Screen for HBV before TDF given, as exacerbation of hepatitis may occur when TDF is discontinued
Zidovudine Retrovir, AZT, ZDV Capsule: 100 mg Tablet: 300 mg Syrup: 10 mg/mL Injection: 10 mg/mL Combivir: combination of ZDV, lamivudine (300, 150 mg) Trizivir: Combination of ZDV, lamivudine, ABC (300, 150, 300 mg)	Prophylaxis: 0-6 wk: Premature infants: 1.5 mg/kg IV every 12 hr or 2 mg/kg orally every 12 hr for 2 wk (for gestational age 30 to 35 wk) or 4 wk (for gestational age <30 wk); then increase to 3 mg/kg every 12 hr to complete 6 wk (if needed) For gestational age >35 wk: 3 mg/kg/dose IV every 12 hr or 4 mg/kg orally every 12 hr Treatment: 6 wk to 18 yr: 240 mg/m ² every 12 hr or 4 kg to <9 kg: 12 mg/kg bid 9 kg to <30 kg: 9 mg/kg bid >30 kg, adolescent and adult: 200 mg tid or 300 mg bid Combivir or Trizivir: 1 tablet bid	Common: bone marrow suppression (e.g., macrocytic anemia, leukopenia), headache, nausea, vomiting, anorexia Less common: liver toxicity, lactic acidosis with hepatic steatosis, myopathy, fat redistribution	No food restrictions Drug interactions: should not be given with d4T or doxorubicin Rifampin may increase metabolism Cimetidine, fluconazole, valproic acid may decrease metabolism Ganciclovir, IFN- α , ribavirin increase ZDV toxicity
NONNUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS			
Efavirenz Sustiva, EFV Capsule: 50, 200 mg Tablet: 600 mg Atripla combination of EFV, FTC, TDF (600, 200, 300 mg)	Children <3 yr: consult with expert Children ≥3 yr: 10 to <15 kg: 200 mg qd 15 to <20 kg: 250 mg qd 20 to <25 kg: 300 mg qd 25 to <32.5 kg: 350 mg qd 32.5 to <40 kg: 400 mg qd ≥40 kg: 600 mg qd or 370 mg/m ² body surface area Atripla (see FTC)	Common: skin rashes, CNS abnormalities (e.g., abnormal dreams, impaired concentration, insomnia, depression, hallucination) Less common: increased liver enzymes; potentially teratogenic	Capsules can be opened for mixing in food. Can be given without regard to food except fatty foods (because absorption is increased 50%) Drug interactions: Efavirenz induces/inhibits CYP3A4 enzymes. Increase clearance of drugs metabolized by this pathway (e.g., antihistamines, sedatives and hypnotics, cisapride, ergot derivatives, warfarin, ethinyl estradiol) and several other ARVs (i.e., protease inhibitors). Drugs that induce CYP3A4 (e.g., phenobarbital, rifampin, rifabutin) decrease efavirenz levels. Clarithromycin levels decrease with EFV and azithromycin should be considered
Etravirine (ETR), Intelence, ETR, tablet: 25, 100, 200 mg	Children <6 yr: consult with expert 16 to <20 kg: 100 mg bid 20 to <25 kg: 125 mg bid 25 to <30 kg: 150 mg bid >30 kg, adolescent and adult: 200 mg bid	Common: nausea, rash, diarrhea Less common: hypersensitivity reactions	Given only with food. Tablets can be dispensed in water Inducer of CYP3A4 enzymes and inhibitor of CYP2C9 and CYP2C19, causing multiple interactions that should be checked before initiating ETR. Should not be given in combination with TPV, Fos-APV, ATZ, or other nonnucleoside reverse transcriptase inhibitors

Table 276-4

Summary of Antiretroviral Therapies Available in 2014—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	DOSING	SIDE EFFECTS	COMMENTS
Nevirapine Viramune, NVP Tablet: 200 mg Extended-release (XR) tablet: 100, 400 mg Suspension: 10 mg/mL	Prophylaxis: For infant of woman with no antepartum ARV treatment: 2 mg/kg birth to 48 hr 2 mg/kg 48 hr after 1st dose 2 mg/kg 96 hr after 2nd dose Treatment: <8 yr: 200 mg/m ² once daily for 14 days; then same dose bid (maximum 200 mg per dose) or XR 400 mg qd >8 yr: 120-150 mg/m ² once daily for 14 days; then bid (maximum 200 mg per dose) Adolescent and adult: 200 mg once daily for 14 days; then 200 mg bid or XR 400 mg qd	Common: skin rash, headache, fever, nausea, abnormal liver function tests Less common: hepatotoxicity (rarely life-threatening), hypersensitivity reactions	No food restrictions Drug interactions: induces hepatic CYP450A enzymes (including CYP3A and CYP2B6) activity and decreases protease inhibitor concentrations (e.g., IND, SQV, LPV). Should not be given with ATV. Reduces ketoconazole concentrations (fluconazole should be used as an alternative). Rifampin decreases nevirapine serum levels. Anticonvulsants and psychotropic drugs using same metabolic pathways as NVP should be monitored. Oral contraceptives may also be affected
Rilpivirine Edurant, RPV Tablet: 25 mg Complera combination of RPV, FTC, TDF (25, 200, 300 mg)	Pediatrics: consult with expert Adolescent (>18 yr) and adult: 25 mg	Headache, insomnia, rash, depression, mood changes	Given with food only Should not be used if viral load >100,000 copies/mm ³ or drugs that induce CYP3A or with proton pump inhibitors
PROTEASE INHIBITORS			
Atazanavir Reyataz, ATV Capsules: 100, 150, 200, 300 mg	<6 yr: consult with expert 6-18 yr: 15 to <20 kg: 150 mg + 100 RTV qd 20 to 40 kg: 200 mg + 100 RTV qd >40 kg, adolescent and adult: 300 mg + 100 RTV qd or 400 mg if unboosted with food If given with EFV (600 mg) or TDF (300 mg): 400 mg + 100 RTV qd	Common: elevation of indirect bilirubin; headache, arthralgia, depression, insomnia, nausea, vomiting, diarrhea, paresthesias Less common: prolongation of PR interval on electrocardiogram (ECG); rash, rarely Stevens-Johnson syndrome, diabetes mellitus, nephrolithiasis	Administer with food to increase absorption. Review drug interactions before initiating because ATV inhibits CYP3A4, CYP1A2, CYP2C9, and UGT1A1 enzymes. Use with caution with cardiac conduction disease or liver impairment. Combination with EFV should not be used in treatment-experienced patients because it decreases ATV levels. TDF, antacids, H ₂ -receptor antagonists, and proton-pump inhibitors decrease ATV concentrations. Patients taking buffered ddI should take it at least 2 hr before ATV
Darunavir Prezista, DRV Tablets: 75, 150, 400, 600, 800 mg Suspension: 100 mg/mL	<3 yr: consult with expert 3 to <18 yr: 10 to <15 kg: 20 mg/kg DRV + 3 mg/kg RTV 15 to <30 kg: 375 mg DRV + 50 mg RTV bid 30 to <40 kg: 450 DRV mg + 100 mg RTV bid >40 kg, adolescent and adult: 600 mg DRV + 100 mg RTV bid or Adolescent (>12 yr and 40 kg) and adult: 800 mg DRV + 100 mg RTV qd with food If any DRV resistance is found: 600 mg DRV = 100 mg RTV bid	Common: diarrhea, nausea, vomiting, abdominal pain, fatigue, headache Less common: skin rashes (including Stevens-Johnson syndrome), lipid and liver enzyme elevations, hyperglycemia, fat maldistribution	DRV should not be given without food. Contraindicated for concurrent therapy with cisapride, ergot alkaloids, benzodiazepines, pimozide, or any major CYP3A4 substrates. Use with caution in patients taking strong CYP3A4 inhibitors, or moderate/strong CYP3A4 inducers. Adjust dose with concurrent rifamycin therapy. Contains sulfa moiety: potential for cross-sensitivity with sulfonamide class

Continued

Table 276-4 Summary of Antiretroviral Therapies Available in 2014—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	DOSING	SIDE EFFECTS	COMMENTS
Fosamprenavir Lexiva, FPV Tablets: 700 mg Suspension: 50 mg/mL	6 mo to 18 yr: <11 kg: 45 mg/kg FPV + 7 mg/kg RTV bid 11 to <15 kg: 30 mg/kg + 3 mg/kg RTV bid 15 to <20 kg: 23 mg/kg + 3 mg/kg RTV bid >20 kg: 18 mg/kg (max 700 mg) + 3 mg/kg (max: 100 mg) RTV bid Adolescent >18 yr and adult: FPV 700 mg + RTV 100 mg bid or FPV 1,400 mg + RTV 200 mg qd For protease inhibitor (PI)-experienced, the once daily dose is not recommended	Common: nausea, vomiting, perioral paresthesias, headache, rash, lipid abnormalities Less common: Stevens-Johnson syndrome, fat redistribution, neutropenia, elevated creatine kinase, hyperglycemia, diabetes mellitus, elevated liver enzymes, angioedema, nephrolithiasis	Should be given with food. FPV is an inhibitor of the CYP450 system and an inducer, inhibitor, and substrate of CYP3A4, which can cause multiple drug interactions. Use with caution in sulfa-allergic individuals
Indinavir Crixivan, IDV Capsule: 100, 200, 400 mg	Infants: not approved Children: 500 mg/m ² every 8 hr (max dose: 800 mg per dose) or 400 mg/m ² + RTV 100 mg/m ² bid Adolescent and adult: 800 mg IDV + 100 or 200 mg RTV bid	Common: nausea, abdominal pain, hyperbilirubinemia, headache, dizziness, lipid abnormalities, nephrolithiasis, metallic taste Less common: fat redistribution, hyperglycemia, diabetes mellitus, hepatitis, acute hemolytic anemia	Administer on empty stomach if given without RTV. Reduce dose (600 mg IDV every 8 hr) with mild to moderate liver dysfunction. Adequate hydration (at least 48 oz fluid/day in adults) necessary to minimize risk of nephrolithiasis. IDV is cytochrome P450 3A4 inhibitor and substrate, which can cause multiple drug interactions: rifampin reduces levels; ketoconazole, ritonavir, and other protease inhibitors increase IDV levels. Do not coadminister with EFV, astemizole cisapride, terfenadine
Lopinavir/Ritonavir Kaletra, LPV/r Tablets: 100/25 mg, 200/50 mg Solution: 80/20 mg per/mL (contains 42% alcohol)	14 days to 18 yr: 300 mg/m ² LPV +75 mg/m ² RTV bid Adolescent (>18 yr) and adult: 400 mg LPV +100 mg RTV bid or 800 mg LPV +200 mg RTV qd If taken with NVP, EFV, FPV, or NFV: LPV 600 mg + RTV 150 mg bid	Common: diarrhea, headache, nausea and vomiting, lipid elevation Less common: fat redistribution, hyperglycemia, diabetes mellitus, pancreatitis, hepatitis, PR interval prolongation	No food restrictions. High-fat meal and flavoring of solution to increase palatability are recommended if oral solution is used. Interacts with drugs using CYP3A4, which can cause multiple drug interactions
Nelfinavir Viracept, NFV Tablet: 250, 625 mg	<2 yr: not recommended Children 2-13 yr: 45-55 mg/kg bid Adolescents and adults: 1,250 mg bid	Common: diarrhea, asthenia, abdominal pain, skin rashes, lipid abnormalities Less common: exacerbation of liver disease, fat redistribution, hyperglycemia, diabetes mellitus, elevation of liver enzymes	Administer with a meal to optimize absorption; avoid acidic food or drink (e.g., orange juice). Tablet can be crushed or dissolved in water to administer as a solution Drug interactions: Nelfinavir inhibits CYP3A4 activity, which may cause multiple drug interactions. Rifampin, phenobarbital, and carbamazepine reduce levels. Ketoconazole, ritonavir, indinavir, and other protease inhibitors increase levels. Do not coadminister astemizole, cisapride, terfenadine. RTV boosting has no effect. Because of very high variation in plasma levels, TDM should be used for dose adjustment

Table 276-4 Summary of Antiretroviral Therapies Available in 2014—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	DOSING	SIDE EFFECTS	COMMENTS
Ritonavir Norvir, RTV Capsule: 100 mg Tablet: 100 mg Solution: 80 mg/mL (contains 43% alcohol)	Only use is to enhance other PIs; dose varies (see information for specific PI)	Common: nausea, headache, vomiting, abdominal pain, diarrhea, taste aversion, lipid abnormalities, perioral paresthesias Less common: fat redistribution, hyperglycemia, diabetes mellitus, pancreatitis, hepatitis, PR interval prolongation, allergic reactions	Administration with food enhances bioavailability and reduces gastrointestinal symptoms. RTV solution should not be refrigerated RTV is potent inhibitor of CYP3A4 and CYP2D6 and inducer of CYP3A4 and CYP1A2 that leads to many drug interactions (e.g., protease inhibitors, antiarrhythmics, antidepressants, cisapride). Use cautiously with inhaled steroids
Saquinavir Invirase, SQV Hard gel: 200 mg Film-coated tablets: 500 mg	Infants and children <2 yr: not established SQV must be boosted with RTV >2 yr: 5 to <15 kg: 50 mg/kg + 3 mg/kg RTV bid 15-40 kg: 50 mg/kg + 2.5 mg/kg RTV bid >40: 50 mg/kg + 100 RTV bid Adolescent and adult: SQV 1,000 mg + 100 mg RTV bid	Common: diarrhea, abdominal pain, headache, nausea, skin rashes, lipid abnormalities Less common: exacerbation of chronic liver disease, diabetes mellitus, pancreatitis, elevated liver transaminases, fat maldistribution, increase in both QT and PR in ECG	Administration with a high-fat meal to enhance bioavailability. Use only in combination with ritonavir boosting dose. SQV is metabolized by CYP3A4, which may cause many drug interactions: rifampin, phenobarbital, and carbamazepine decrease serum levels. Saquinavir may decrease metabolism of calcium channel antagonists, azoles (e.g., ketoconazole), macrolides
Tipranavir Aptivus, TPV Capsule: 250 mg Solution 100 mg/mL (contains 116 IU vitamin E/mL)	<2 yr: not established. 2-18 yr: 375 mg/m ² TPV + 150 mg/m ² RTV (maximum 500 mg TPV + 200 mg RTV) bid or 14 mg TPV + 6 mg RTV per kg (maximum-same) bid Adolescent (>18 yr) and adult: 500 mg TPV + 200 mg RTV bid	Common: diarrhea, nausea, vomiting, fatigue, headache, skin rashes, elevated liver enzymes, lipid abnormalities Less common: fat redistribution, hepatitis, hyperglycemia, diabetes mellitus, intracranial hemorrhage	No food restrictions. Better tolerated with meal. TPV must be boosted with RTV. Can inhibit human platelet aggregation: use with caution in patients at risk for increased bleeding (trauma, surgery, etc.) or in patients receiving concurrent medications that may increase the risk of bleeding. TPV is metabolized by CYP3A4, which may cause many drug interactions. Contraindicated in patients with hepatic insufficiency or receiving concurrent therapy with amiodarone, cisapride, ergot alkaloids, benzodiazepines, pimozide. TPV contains sulfonamide moiety and caution should be taken in patients with sulfonamide allergy
FUSION INHIBITORS Enfuvirtide Fuzeon, ENF Injection: lyophilized powder of 108 mg reconstituted in 1.1 mL of sterile water delivers 90 mg/mL	<6 yr: not established Children >6 yr to 16 yr: 2 mg/kg SQ (maximum 90 mg) bid Adolescent and adult: 90 mg SQ bid	Common: Local injection site reactions in 98% (e.g., erythema, induration nodules, cysts, ecchymoses) Less common: increased incidence of bacterial pneumonia, hypersensitivity, fever, nausea, vomiting, chills, elevated liver enzymes, hypotension, immune-mediated reactions (e.g., glomerulonephritis, Guillain-Barré syndrome, respiratory distress)	Must be given subcutaneously. Severity of reactions increased if given intramuscularly. Apply ice after injection and massage the area to reduce local reactions. Injection sites should be rotated

Continued

Table 276-4 Summary of Antiretroviral Therapies Available in 2014—cont'd

DRUG (TRADE NAMES, FORMULATIONS)	DOSING	SIDE EFFECTS	COMMENTS
ENTRY INHIBITORS Maraviroc Selzentry, MVC Tablets: 150, 300 mg	Not approved for children or adolescents <16 yr Adolescents >16 yr and adults: 150 mg bid if given with potent CYP3A inhibitor (e.g., protease inhibitor except TPV) 300 mg bid if given with not potent CYP3A4 inhibitors (e.g., NRTI, TPV, NVP, ENF, RAL) 600 mg bid if given with potent CYP3A4 inducer (e.g., EFV, ETR, rifampin, phenobarbital)	Common: fever, upper respiratory infection-like symptoms, rash, abdominal pain, musculoskeletal symptoms, dizziness Less common: cardiovascular abnormalities, cholestatic jaundice, rhabdomyolysis, myositis, osteonecrosis	No food restrictions. MVC is a CYP3A4 and P-glycoprotein (Pgp) substrate, which may cause many drug interactions Tropism assay to exclude the presence of CXCR4 HIV is required before using MVC. Caution should be used when given to patients with hepatic impairment or cardiac disease or receiving CYP3A4 or Pgp modulating drugs
INTEGRASE INHIBITORS Daltegravir Tivicay, DTG Tablet: 50 mg	Children <12 yr: consult with expert >12 yr and 40 kg, adolescents, and adults: 50 mg qd If taken with EFV, FPV, TPV, or rifampin: 50 mg bid	Insomnia Headache	No food restrictions UGT1A1 and CYP450 (CYP) 3A substrate Should be taken 2 hr before or 6 hr after taking laxatives, sucralfate, iron or calcium supplements, or buffered medications Administer with food EVG is metabolized by CYP3A4 and modestly induces CYP2D6 that can cause multiple drug interactions. Cautiously use with nephrotoxic drugs. Stribild should not be used with ritonavir
Elvitegravir EVG Only as Stribild combination of EVG, FTC, TDF, cobicistat (COBI) (150, 200, 300, 150 mg)	Children and adolescents (<18 yr): not established Adolescent (>18 yr) and adult: 1 tablet qd	Common: nausea, diarrhea Less common: increased serum creatinine, urea, and phosphate, decreased bone density; lactic acidosis, hepatomegaly with stenosis	
Raltegravir Isentress, RAL Film-coated tablet: 400 mg Chewable tablet: 25, 100 mg Solution: 20 mg/ml	Oral solution: 3 to <4 kg: 20 mg bid 4 to <6 kg: 30 mg bid 6 to <8 kg: 40 mg bid 8 to <11 kg: 60 mg bid 11 to <14 kg: 80 mg bid 14 to <20 kg: 100 mg bid Chewable tablet: 10 to <14 kg: 75 mg bid 14 to <20 kg: 100 mg bid 20 to <28 kg: 150 mg bid 28 to <40 kg: 200 mg bid Adolescent (>12 yr) and adult: 400 mg bid	Common: nausea, headache, dizziness, diarrhea, fatigue Less common: abdominal pain, vomiting, itching, creatine phosphokinase elevation, myopathy, rhabdomyolysis, depression, hypersensitivity	No food restrictions Film-coated tablet and chewable tablet are not interchangeable RAL is metabolized by UGT1A1 glucuronidation, and inducers of this system (e.g., rifampin, TPV) will reduce RGV levels, whereas inhibitors (e.g., ATV) will increase it

Antiretroviral drugs often have significant drug-drug interactions, with each other and with other classes of medicines, which should be reviewed before initiating any new medication.

Vaccine	Birth	1 mo	2 mo	4 mo	6 mo	12 mo	15 mo	18 mo	24 mo	4-6 yr	11-12 yr	14-16 yr
Hepatitis B	Hep B	Hep B			Hep B							
Measles, Mumps, Rubella*						MMR†	MMR†					
Influenza					Influenza‡							
Pneumococcal Conjugate and Hemophilus b			PCV Hib	PCV Hib	PCV Hib	PCV Hib					Pneumococcal§	
Diphtheria, Tetanus, Pertussis			DTaP	DTaP	DTaP		DTaP					
Polio (inactivated)			Polio	Polio	Polio							
Varicella					Varicella							
Hepatitis A					Hep A¶							
Rotavirus*		RV¶	RV	RV								

See text.

Contraindicated in children with AIDS or CD4+ <15%. Give 2 doses 1-3 mo apart.

Revaccination is recommended every year. Attenuated vaccine can be used >2 yr of age only if CD4+ >15%.

Revaccination with pneumococcal polysaccharide vaccine (PPV) every 5 yr.

Two doses at least 6 mo apart.

First dose 6 through 14 wk of age and final dose no later than 8 mo 0 days of age. If using Rotarix, only 2 doses (2 and 4 mL) are needed.

Figure 276-4 Routine childhood immunization schedule for HIV-infected children.

Table 276-6 Prophylaxis to Prevent First Episode of Opportunistic Infections Among HIV-Exposed and HIV-Infected Infants and Children, United States*

PATHOGEN	INDICATION	Preventive Regimen	
		FIRST CHOICE	ALTERNATIVE
STRONGLY RECOMMENDED AS STANDARD OF CARE			
<i>Pneumocystis pneumonia</i> [†]	HIV-infected or HIV-indeterminate infants aged 1-12 mo; HIV-infected children aged 1-5 yr with CD4 count of <500 cells/ μ L or CD4 percentage of <15%; HIV-infected children aged 6-12 yr with CD4 count of <200 cells/ μ L or CD4 percentage of <15%	TMP-SMX , 150/750 mg/m ² body surface area per day (max: 320/1600 mg) orally qd or bid 3 times weekly on consecutive days or qd or bid orally 3 times weekly on alternate days	Dapsone : age ≥1 mo: 2 mg/kg (max: 100 mg) orally qd; or 4 mg/kg (max: 200 mg) orally once a week Atovaquone : age 1-3 mo and >24 mo: 30 mg/kg orally qd; age 4-24 mo: 45 mg/kg orally qd Aerosolized pentamidine : age ≥5 yr: 300 mg once a month by Respigrad II (Marquest, Englewood, CO) nebulizer Doxycycline age >8 yr: 2.2 mg/kg qd Doxycycline , 100 mg orally qd for children >8 yr Chloroquine , 5 mg/kg base (equal 7.5 mg/kg chloroquine phosphate) orally up to 300 mg weekly (only for regions where the parasite is sensitive)
Malaria	Living or traveling to area in which malaria is endemic	Same for HIV-infected and HIV-uninfected children. Refer to http://www.cdc.gov/malaria/ for the most recent recommendations. Mefloquine , 5 mg/kg orally 1 time weekly (max: 250 mg) Atovaquone/proguanil (Malarone) qd 11-20 kg: 62.5 mg/25 mg (1 pediatric tablet) 21-30 kg: 2 pediatric tablets 31-40 kg: 3 pediatric tablets >40 kg: 1 adult tablet (250 mg/100 mg)	
<i>Mycobacterium tuberculosis</i> Isoniazid-sensitive	TST reaction ≥5 mm or Prior positive TST result without treatment or Close contact with any person who has contagious TB. TB disease must be excluded before start of treatment	Isoniazid , 10-15 mg/kg body weight (max: 300 mg) qd for 9 mo or 20-30 mg/kg body weight (max: 900 mg) orally 2 times weekly for 9 mo	Rifampin , 10-20 mg/kg body weight (max: 600 mg) orally daily for 4-6 mo
Isoniazid-resistant	Same as previous pathogen; increased probability of exposure to isoniazid-resistant TB	Rifampin , 10-20 mg/kg body weight (max: 600 mg) orally daily for 4-6 mo	Uncertain
Multidrug-resistant (isoniazid and rifampin)	Same as previous pathogen; increased probability of exposure to multidrug-resistant TB	Choice of drugs requires consultation with public health authorities and depends on susceptibility of isolate from source patient	
<i>Mycobacterium avium complex</i> [‡]	For children age ≥6 yr with CD4 count of <50 cells/ μ L; age 2-5 yr with CD4 count of <75 cells/ μ L; age 1-2 yr with CD4 count of <500 cells/ μ L; age <1 yr with CD4 count of <750 cells/ μ L	Clarithromycin , 7.5 mg/kg (max: 500 mg) orally bid or Azithromycin , 20 mg/kg (max: 1,200 mg) orally once a week	Azithromycin , 5 mg/kg body weight (max: 250 mg) orally qd or Children age ≥6 yr or Rifabutin , 300 mg orally qd If VarizIG is not available and <96 hr from exposures, acyclovir 20 mg/kg (max: 800 mg) 4 times a day for 5-7 days or IVIG , 400 mg/kg, administered once
Varicella-zoster virus [§]	Exposure to varicella or shingles with no history of varicella or Zoster or seronegative status for VZV or Lack of evidence for age-appropriate vaccination	Varicella-zoster immunoglobulin (VarizIG), 125 IU per 10 kg (max: 625 IU) IM, administered within 96 hr after exposure	
Vaccine-preventable pathogens	Standard recommendations for HIV-exposed and HIV-infected children	Routine vaccinations (see Fig. 276-3)	

Chapter 276 ◆ Acquired Immunodeficiency Syndrome (Human Immunodeficiency Virus) 1665

Table 276-6 Prophylaxis to Prevent First Episode of Opportunistic Infections Among HIV-Exposed and HIV-Infected Infants and Children, United States—cont'd

PATHOGEN	INDICATION	Preventive Regimen	
		FIRST CHOICE	ALTERNATIVE
USUALLY RECOMMENDED			
Toxoplasma gondii [†]	Seropositive IgG to Toxoplasma and severe immunosuppression: age <6 yr with CD4 <15%; age ≥6 yr with CD4 <100 cells/µL	TMP-SMZ, 150/750 mg/m ² orally bid or Same dosage qd 3 times weekly on consecutive days or bid 3 times weekly on alternate days	Dapsone, age ≥1 mo: 2 mg/kg or 15 mg/m ² (max: 25 mg) orally qd plus Pyrimethamine, 1 mg/kg (max: 25 mg) orally qd plus Leucovorin, 5 mg orally twice a week or Atovaquone, age 1-3 mo and >24 mo, 30 mg/kg orally qd; children age 4-24 mo, 45 mg/kg orally qd with or without pyrimethamine, 1 mg/kg (or 15 mg/m ²) (max: 25 mg) qd plus Leucovorin, 5 mg orally twice a week (3 days apart)
Invasive bacterial infections	Hypogammaglobulinemia (i.e., IgG <400 mg/dL)	IVIG 400 mg/kg body weight every 2-4 wk	
Cytomegalovirus	CMV antibody positivity and severe immunosuppression (CD4 <50 cells/µL)	Valganciclovir, 900 mg orally qd with food for older children who can receive adult dosing	

*Information in these guidelines might not represent FDA approval or FDA-approved labeling for products or indications. Specifically, the terms "safe" and "effective" might not be synonymous with the FDA-defined legal standards for product approval.

[†]Daily trimethoprim-sulfamethoxazole (TMP-SMZ) reduces the frequency of certain bacterial infections. Compared with weekly dapsone, daily dapsone is associated with lower incidence of PCP but higher hematologic toxicity and mortality. Patients receiving therapy for toxoplasmosis with sulfadiazine-pyrimethamine are protected against PCP and do not need TMP-SMZ. TMP-SMZ, dapsone-pyrimethamine, and possibly atovaquone (with or without pyrimethamine) protect against toxoplasmosis; however, data have not been prospectively collected.

[‡]Substantial drug interactions can occur between rifamycins (i.e., rifampin and rifabutin) and protease inhibitors and nonnucleoside reverse transcriptase inhibitors. A specialist should be consulted.

[§]Children routinely being administered intravenous immunoglobulin (IVIG) should receive VariZIG if the last dose of IVIG was administered more than 21 days before exposure.

[¶]As of 2007, VariZIG can be obtained only under a treatment Investigational New Drug protocol (1-800-843-7477, FFF Enterprises, Temecula, CA).

^{**}Protection against toxoplasmosis is provided by the preferred anti-*Pneumocystis* regimens and possibly by atovaquone.

CMV, cytomegalovirus; FDA, U.S. Food and Drug Administration; HIV, human immunodeficiency virus IgG, immunoglobulin G; IM, intramuscularly; IVIG, intravenous immunoglobulin; PCP, *Pneumocystis pneumonia*; TMP-SMZ, trimethoprim-sulfamethoxazole; TB, tuberculosis; TST, tuberculin skin test; VZV, varicella-zoster virus.

From Centers for Disease Control and Prevention (CDC): Guidelines for the prevention and treatment of opportunistic infections among HIV-exposed and HIV-infected children, MMWR Recomm Rep 58(RR-11):127-128, 2009, Table 1.

Table 276-5 Recommendations for PCP Prophylaxis and CD4 Monitoring for HIV-Exposed Infants and HIV-Infected Children, by Age and HIV Infection Status

AGE/HIV INFECTION STATUS	PCP PROPHYLAXIS	CD4 MONITORING
Birth to 4-6 wk, HIV exposed	No prophylaxis	None
HIV infection reasonably excluded*	No prophylaxis	None
<1 yr, HIV-infected or indeterminate	Prophylaxis regardless of CD4 count or percentage	According to local practice for initiation or follow-up of cART
1-5 yr, HIV infected	Prophylaxis if: CD4 <500 cells/µL or <15% [†]	According to local practice for initiation or follow-up of cART
>6 yr, HIV infected	Prophylaxis if: CD4 <200 cells/µL or <15% [‡]	According to local practice for initiation or follow-up of cART

The National Perinatal HIV Hotline (1-888-448-8765) provides consultation on all aspects of perinatal HIV care.

*See text.

[†]More frequent monitoring (e.g., monthly) is recommended for children whose CD4 counts or percentages are approaching the threshold at which prophylaxis is recommended.

[‡]Prophylaxis should be considered on a case-by-case basis for children who might otherwise be at risk for PCP, such as children with rapidly declining CD4 counts or percentages or children with category C conditions. Children who have had PCP should receive PCP prophylaxis until their CD4 count is >20% (for >6 yr of age) or >25% (for 2-5 yr of age) on continuous cART.

cART, combined antiretroviral therapy; PCP, *Pneumocystis carinii* (also called *P. jirovecii*) pneumonia.