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NR 602 Midterm Review

Chalazion

Chalazion is a chronic sterile inflammation of the eyelid resulting from a lipogranuloma of the meibomian glands that line the posterior margins of the eyelids (see Fig. 29-7). It is deeper in the eyelid tissue than a hordeolum and may result from an internal hordeolum or retained lipid granular secretions.

Clinical Findings

Initially, mild erythema and slight swelling of the involved eyelid are seen. After a few days the inflammation resolves, and a slow growing, round, nonpigmented, painless (key finding) mass remains. It may persist for a long time and is a commonly acquired lid lesion seen in children (see Fig. 29-7).

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Management

- Acute lesions are treated with hot compresses.
- Refer to an ophthalmologist for surgical incision or topical intralesional corticosteroid injections if the condition is unresolved or if the lesion causes cosmetic concerns.. A chalazion can distort vision by causing astigmatism as a result of pressure on the orbit.

Complications

Recurrence is common. Fragile, vascular granulation tissue called *pyogenic granuloma* that enlarges and bleeds rapidly can occur if a chalazion breaks through the conjunctival surface.

Types of Conjunctivitis

Type	Incidence/Etiology	Clinical Findings	Diagnosis	Management*
Ophthalmia neonatorum	Neonates: *Chlamydia trachomatis, Staphylococcus aureus, Neisseria gonorrhoeae,* HSV (silver nitrate reaction occurs in 10% of neonates)	Erythema, chemosis, purulent exudate with *N*	Culture (ELISA, PCR), Gram stain, R/O *N. gonorrhoeae,* chlamydia	Saline irrigation to eyes until exudate gone; follow with erythromycin ointment For *N. gonorrhoeae:*ceftriaxone or IM or IV

Type	Incidence/Etiology	Clinical Findings	Diagnosis	Management*
		. *gonorrhoeae*; clear to mucoid exudate with chlamydia		For chlamydia: erythromycin or possibly azithromycin PO For HSV: antivirals IV or PO
Bacterial conjunctivitis	In neonates 5 to 14 days old, preschoolers, and sexually active teens: *Haemophilus influenzae*(nontypeable), *Streptococcus pneumoniae, S. aureus, N. gonorrhoeae*	Erythema, chemosis, itching, burning, mucopurulent exudate, matter in eyelashes; ↑ in winter	Cultures (required in neonate); Gram stain (optional); chocolate agar (for *N. gonorrhoeae*) R/O pharyngitis, *N. gonorrhoeae*, AOM, URI, seborrhea	Neonates: Erythromycin 0.5% ophthalmic ointment ≥1 year old: Fourth-generation fluoroquinolone For concurrent AOM: Treat accordingly for AOM Warm soaks to eyes three times a day until clear No sharing towels, pillows No school until treatment begins
Chronic bacterial conjunctivitis	School-age children and teens: Bacteria, viruses, *C. trachomatis*	Same as above; foreign body sensati	Cultures, Gram stain; R/O dacryostenosis, blepharitis, corneal ulcers,	Depends on prior treatment, laboratory results, and differential diagnoses Review

Type	Incidence/Etiology	Clinical Findings	Diagnosis	Management*
(unresponsive conjunctivitis previously treated as bacterial in etiology)		on	trachoma	compliance and prior drug choices of conjunctivitis treatment Consult with ophthalmologist
Inclusion conjunctivitis	Neonates 5 to 14 days old and sexually active teens: *C. trachomatis*	Erythema, chemosis, clear or mucoid exudate, palpebral follicles	Cultures (ELISA, PCR), R/O sexual activity	Neonates: Erythromycin or azithromycin PO Adolescents: Doxycycline, azithromycin, EES, erythromycin base, levofloxacin PO
Viral conjunctivitis	Adenovirus 3, 4, 7; HSV, herpes zoster, varicella	Erythema, chemosis, tearing (bilateral); HSV	Cultures, R/O corneal infiltration	Refer to ophthalmologist if HSV or photophobia present Cool compresses three or four times a day

Type	Incidence/Etiology	Clinical Findings	Diagnosis	Management*
		and herpes zoster: unilateral with photophobia, fever; zoster: nose lesion; spring and fall		
Allergic and vernal conjunctivitis	Atopy sufferers, seasonal	Stringy, mucoid exudate, swollen eyelids and conjunctivae, itching (key finding), tearing, palpebral follicles, headac	Eosinophils in conjunctival scrapings	Naphazoline/ pheniramine, naphazoline/antazoline ophthalmic solution (see text) Mast cell stabilizer (see text) Refer to allergist if needed

Type	Incidence/Etiology	Clinical Findings	Diagnosis	Management*
		he, rhinitis		

*See text for dosages.

Blepharitis

Blepharitis is an acute or chronic inflammation of the eyelash follicles or meibomian sebaceous glands of the eyelids (or both). It is usually bilateral. There may be a history of contact lens wear or physical contact with another symptomatic person. It is commonly caused by contaminated makeup or contact lens solution. Poor hygiene, tear deficiency, rosacea, and seborrheic dermatitis of the scalp and face are also possible etiologic factors. The ulcerative form of blepharitis is usually caused by *S. aureus*. Nonulcerative blepharitis is occasionally seen in children with psoriasis, seborrhea, eczema, allergies, lice infestation, or in children with trisomy 21.

Clinical Findings

- Swelling and erythema of the eyelid margins and palpebral conjunctiva

- Flaky, scaly debris over eyelid margins on awakening; presence of lice
- Gritty, burning feeling in eyes
- Mild bulbar conjunctival injection
- Ulcerative form: Hard scales at the base of the lashes (if the crust is removed, ulceration is seen at the hair follicles, the lashes fall out, and an associated conjunctivitis is present)

Differential Diagnosis

Pediculosis of the eyelashes.

Management

Explain to the patient that this may be chronic or relapsing. Instructions for the patient include:

- Scrub the eyelashes and eyelids with a cotton-tipped applicator containing a weak (50%) solution of no-tears shampoo to maintain proper hygiene and debride the scales.
- Use warm compresses for 5 to 10 minutes at a time two to four times a day and wipe away lid debris.
- At times antistaphylococcal antibiotic (e.g., erythromycin 0.5% ophthalmic ointment) is used until symptoms subside and for at least 1 week thereafter. Ointment is preferable to eye drops because of increased duration of contact with the ocular tissue. Azithromycin 1% ophthalmic solution for 4 weeks may also be used (Shtein, 2014).
- Treat associated seborrhea, psoriasis, eczema, or allergies as indicated.
- Remove contact lenses and wear eyeglasses for the duration of the treatment period. Sterilize or clean lenses before reinserting.
- Purchase new eye makeup; minimize use of mascara and eyeliner.
- Use artificial tears for patients with inadequate tear pools.

Chronic staphylococcal blepharitis and meibomian keratoconjunctivitis respond to oral erythromycin. Doxycycline, tetracycline, or minocycline can be used chronically in children older than 8 years old.

Hand-Foot-Mouth Syndrome

Enteroviruses

Nonpolio Enteroviruses

Of the more than 100 serotypes of nonpolio RNA enteroviruses, 10 to 15 serotypes account for most diseases. They are grouped into four genomic classifications: human 495enteroviruses (HEVs) A, B, C, and D. Coxsackieviruses and echoviruses are subgroups of HEVs. Hand-foot-mouth, herpangina, pleurodynia, acute hemorrhagic conjunctivitis, myocarditis, pericarditis, pancreatitis, orchitis, and dermatomyositis-like syndrome are manifestations of infection. These enteroviruses are the most common cause of aseptic meningitis and have also been associated with paralysis, neonatal sepsis, encephalitis, and other respiratory and GI symptoms. The specific serotype may not be unique to any given disease (Abzug, 2011).

As evidenced by the name, enteroviruses concentrate on the GI tract as their primary invasion, replication, and transmission site; they spread by fecal-oral contamination, especially in diapered infants. They are also transmitted via the respiratory route and vertically either prenatally, during parturition, or possibly by way of breastfeeding by an infected mother who lacks antibodies to that particular serotype. Transplacental infection can lead to serious disseminated disease in the neonate that involves multiorgan systems (liver, heart, meninges, and adrenal cortex).

Enteroviruses have worldwide distribution, occurring in temperate climates during the summer and fall and in tropical climates year round. In known cases, infants younger than 12 months old have the highest prevalence rate (>25%), and HEVs account for 55% to 65% of hospitalizations for suspected infant sepsis. Illness occurs more frequently in males; those living in crowded, unsanitary conditions; and in those of lower socioeconomic status (Abzug, 2011). Infection can range from asymptomatic to undifferentiated febrile illness to severe illness. Young children are more likely to be symptomatic. The incubation period is 3 to 6 days (less for hemorrhagic conjunctivitis). After infection, the virus is shed from the respiratory tract for up to 3 weeks and from the GI tract for up to 7 to 11 weeks; it is viable on environmental surfaces for long periods.

Nonpolio enteroviral infection is not a reportable disease, nor is it routinely tested for in the clinical setting, so the overall incidence rate is not known. The CDC administers the National Respiratory and Enteric Virus Surveillance System (NREVSS) and the National Enterovirus 496Surveillance System (NESS) to monitor detection patterns of respiratory and enteric adenoviruses. The 2014 outbreak of an illness in children referred to as *acute flaccid myelitis* bears some similarity to infections caused by viruses, including enterovirus; epidemiologic studies are ongoing (CDC, 2015f).

Clinical Findings

History.

General symptoms include:

- A mild upper respiratory infection (URI) is common and may include complaints of sore throat, fever, vomiting, diarrhea, anorexia, coryza, abdominal pain, rash, and headache.
- Nonspecific febrile illness of at least 3 days: In young children, there is an undifferentiated abrupt-onset febrile illness (101° to 104° F [38.5° to 40°

C]) associated with myalgias, malaise, irritability; fever may wax and wane over several days.

- Onset of viral symptoms within 1 to 2 weeks after delivery for neonates infected transplacentally.

Physical Examination.

General findings include mild conjunctivitis, pharyngeal infection, and/or cervical adenopathy. Other findings include:

- Skin: Rash may be macular, macular-papular, urticarial, vesicular, or petechial. May imitate the rash of meningitis, measles, or rubella.
- Herpangina: There is a sudden onset of high fever (up to 106° F [41° C]) lasting 1 to 4 days. Loss of appetite, sore throat, and dysphagia are common, with vomiting and abdominal pain in 25% of cases. Small vesicles (from one to more than 15 lesions of 1 to 2 mm each) appear and enlarge to ulcers (3 to 4 mm) on the anterior pillars of the fauces, tonsils, uvula, and pharynx and the edge of the soft palate. The vesicles commonly have red areolas up to 10 mm in diameter. This self-limiting infection usually lasts 3 to 7 days.
- Acute lymphonodular pharyngitis: This manifests as an acute sore throat lasting approximately 1 week.
- Hand-foot-mouth disease: This is a clinical entity evidenced by fever, vesicular eruptions in the oropharynx that may ulcerate, and a maculopapular rash involving the hands and feet. The rash evolves to vesicles, especially on the dorsa of the hands and the soles of the feet, and lasts 1 to 2 weeks (Fig. 24-1).

Pharyngitis

Pharyngitis, Tonsillitis, and Tonsillopharyngitis

Pharyngitis is an inflammation of the mucosa lining the structures of the throat, including the tonsils, pharynx, uvula, soft palate, and nasopharynx. It can be due to infectious agents or noninfectious causes, such as smoke or other air irritants. The illness is generally acute and involves an inflammatory response, including erythema, exudate, or ulceration.

The etiology could include a number of viruses and bacteria. If there are nasal symptoms, it is called *nasopharyngitis,* but if there are no nasal symptoms, the disease is called *pharyngitis* or *tonsillopharyngitis.* Most cases of pharyngitis are caused by viruses (Gereige and Cunill-De Sautu,

2011). Adenovirus is the most common cause of nasopharyngitis (Cherry, 2009c). Other viruses include Epstein-Barr virus (EBV), herpes simplex virus (HSV), cytomegalovirus (CMV), enterovirus, influenza virus, parainfluenza, and human immunodeficiency virus (HIV). The viral organisms generally present with upper nasal symptoms. The common bacterial etiology is GABHS in children between 5 and 11 years old, whereas 40% of reported cases of gonococcal infections occur in females 15 to 19 years old. Other organisms include *Corynebacterium diphtheriae, Arcanobacterium haemolyticum, Neisseria gonorrhoeae,* group C and group G streptococci, *Chlamydia trachomatis, Francisella tularensis*, and *Mycoplasma pneumonia* (Gereige and Cunill-De Sautu, 2011).

Acute Viral Pharyngitis, Tonsillitis, or Tonsillopharyngitis

Adenoviruses are more likely to cause pharyngitis as a prominent symptom. Other viruses (e.g., rhinovirus) are associated with pharyngitis as a minor symptom and rhinorrhea or cough as predominant features. The enterovirus (coxsackievirus, echovirus), herpesvirus, and EBV are also common. Viral infections occur year-round, but adenovirus presenting as pharyngoconjunctival fever occurs in outbreaks during the summer due to contaminated swimming pools (Gereige and Cunill-De Sautu, 2011). It is helpful to know what agents are currently infecting children in the community. However, when a patient only has a sore throat, it is difficult to differentiate viral from bacterial causes. Hoarseness, cough, coryza, conjunctivitis, and diarrhea are classic features of a viral infection (Gereige and Cunill-De Sautu, 2011).

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Clinical Findings

History

The following may be reported:

- Pain
- Myalgia and arthralgia
- Fever
- Sore throat and dysphagia
- Rhinitis, cough, hoarseness, stomatitis, stridor and conjunctivitis, nonspecific rash, or diarrhea points to a viral cause (Gereige and Cunill-De Sautu, 2011)

- Acute onset of sore throat with headache, nausea, vomiting, and abdominal pain in the winter and early spring points to GABHS (Gereige and Cunill-De Sautu, 2011)

Physical Examination

Common findings include:

- Erythema of the tonsils and the pharynx
- Reactive cervical lymphadenopathy

Virus-specific physical findings include the following:

- EBV can produce exudate on the tonsils, soft palate petechiae, and diffuse adenopathy.
- Adenovirus can cause a follicular pattern on the pharynx (Cherry, 2009c).
- Enterovirus can produce vesicles or ulcers on the tonsillar pillars and posterior fauces; coryza, vomiting, or diarrhea may be present.
- Herpesvirus produces ulcers anteriorly and marked adenopathy.
- Parainfluenza and RSVs cause more lower respiratory tract disease (e.g., croup, pneumonia, and bronchiolitis) with their typical respiratory signs of stridor, rales, or wheezing.
- Influenza usually is associated with a cough, fever, and multiple systemic complaints.

Diagnostic Studies

A RADT and/or culture should be performed in children older than 3 years old with pharyngitis, because it is difficult to distinguish viral and streptococcal infections by history and physical examination. The incidence of GABHS is rare in children younger than 3 years; however, if there is a child in the household with a positive test for GABHS, children younger than 3 years can be tested (Shulman et al, 2012). In children and adolescents, negative RADT should be backed up by a throat culture, but positive tests do not need a backup due to high specificity of RADT testing (Gereige and Cunill-De Sautu, 2011; Shulman et al, 2012). This careful screening avoids the use of unnecessary antibiotics. Most viral causes of pharyngitis are benign, and other diagnostic studies are not usually used.

Management

For viral infection, only supportive care is needed, including fever and sore throat pain relief with acetaminophen or ibuprofen. Adequate fluid intake should be encouraged.

Acute Bacterial Pharyngitis and Tonsillitis

The most common bacterial cause of pharyngitis and tonsillitis in children and adolescents is GABHS, which accounts for about 15% to 30% of infections in children with acute sore throat and fever. Group C and group G streptococci can cause pharyngitis, but antibiotic treatment does not prevent its only nonsuppurative complication, glomerulonephritis (Shulman et al, 2012). *A. haemolyticum* is more common in adolescents but is difficult to culture, because the organism grows slowly (Martin, 2010). *N. gonorrhoeae* is a cause of adolescent pharyngitis if the patient engages in oral sex. *M. pneumoniae* and *Chlamydophila pneumoniae* are associated with cough along with pharyngitis. *C. diphtheriae* is an extremely rare cause of pharyngitis in the United States. See the GABHS discussion in Chapter 24.

Clinical Findings

History

The following characterize GABHS infection:

- Most commonly found in 5- to 13-year-old children; infrequent in children younger than 3 years old
- Abrupt onset without nasal symptoms
- Constitutional symptoms, such as arthralgia, myalgia, headache
- Moderate to high fever, malaise, prominent sore throat, dysphagia
- Nausea, abdominal discomfort, vomiting, headache
- Presentation in late winter or early spring
- Lack of a cough or nasal symptoms, along with an exudative, erythematous pharyngitis with a follicular pattern and typical historical findings point to GABHS

Physical Examination

The following may be seen in GABHS:

- Petechiae on soft palate and pharynx, swollen beefy-red uvula, red enlarged tonsillopharyngeal tissue
- Tonsillopharyngeal exudate that is yellow, blood-tinged (frequently)
- Tender and enlarged anterior cervical lymph nodes
- Bad breath

- Stigmata of scarlet fever may be seen—scarlatiniform rash, strawberry tongue, circumoral pallor
- Other bacterial infections may present with similar clinical findings:
  - *A. haemolyticum* causes an exudative pharyngitis with marked erythema and a pruritic, fine, scarlatiniform rash (Martin, 2010)
  - Adolescents and young adults with pharyngitis caused by *A. haemolyticum* may present with a scarlatiniform rash similar to scarlet fever
- Variable presentation; may have mild pharyngeal erythema without tonsillar exudate or cervical adenopathy

Diagnostic Studies

It is important to use RADT for patients with clinical features consistent with GABHS to increase the yield of 805positive tests and avoid false-positive tests on patients who are carriers of streptococcus and do not need treatment. A RADT has a high specificity but variable sensitivity; therefore, a positive test indicates that a symptomatic person has strep infection and should be treated. However, a negative test does not mean that streptococcal infection is not present (Shulman et al, 2012). It is important not to do a strep test unless the patient has signs and symptoms, because a positive rapid strep test or a positive throat culture can identify a carrier state.

Anti-streptococcal antibody titers, such as anti-streptolysin O (ASO) and anti-deoxyribonuclease B tests (anti-DNase B), are not useful in the diagnosis of acute pharyngitis, because the titers remain elevated for months after an acute infection. Anti-streptolysin O (ASO) is the most common test used to document past GABHS infection. ASO and anti-DNase B testing involves documenting antibody titers in response to streptolysin O or deoxyribonuclease B, respectively (Shulman et al, 2012). These two tests are often done together. The ASO titer rises 1 week postinfection and peaks 3 to 6 weeks after infection. Measurement of anti-streptococcal antibody titers is useful in the diagnosis of the nonsuppurative complications of GABHS, such as rheumatic fever or acute glomerulonephritis. The anti-DNase B test rises 1 to 2 weeks after infection, peaks 6 to 8 weeks following infection, and remains elevated for months even in the face of a mild infection with GABHS. As a result, these tests should not be used to diagnosis acute GABHS infection in a patient.

Rare bacterial causes of pharyngitis that need treatment with antibiotics include *C. diphtheriae* and *N. gonorrhoeae*. Adolescents who have oral to genital sex with individuals who have *N. gonorrhoeae* of the genital region

can develop pharyngitis from *N. gonorrhoeae*. *A. haemolyticum* is found in adolescents and young adults with a sore throat, and they may have a scarlatiniform rash similar to scarlet fever. These specimens need to be sent out for a culture with specific instructions to evaluate for these organisms.

If infectious mononucleosis is suspected in a child, a complete blood count (CBC) can identify a lymphocytosis with atypical lymphocytes. This is a nonspecific test, because reactive (atypical) lymphocytes can occur in EBV, acquired CMV, viral hepatitis, rubella, roseola, and mumps (Jensen, 2011). Heterophile antibody testing can be helpful in school-age children and adolescents after the first week of infection but may yield a false negative in preschool and younger children (Gereige and Cunill-De Sautu, 2011). EBV-specific antibody testing is used to confirm acute or past infection. The presence of EBV immunoglobulin M (IgM), EBV IgG, and the late response (3 to 4 months) of antibodies to Epstein-Barr nuclear antigens (anti-EBNA) helps to confirm the diagnosis of EBV. The presence of IgM antibody to the viral capsid antigen is the specific serologic test for EBV infection and generally confirms the diagnosis of acute infection; however, its presence is time sensitive (Jensen, 2011).

Management

Antibiotics should only be used in a symptomatic child with GABHS when the RADT or throat culture is positive due to increasing antibiotic resistance associated with overuse (Shulman et al, 2012). The goal of antibiotic therapy is to shorten the course and severity of illness, prevent the spread of illness to others, and prevent the development of suppurative and nonsuppurative complications. The use of beta-lactam antibiotics during an acute CMV or EBV infection causes a diffuse, morbilliform skin eruption (Schleiss, 2012) and should not be prescribed. It is important to treat these children within 9 days to prevent the nonsuppurative complication of rheumatic fever (Shulman et al, 2012). The management plan includes the following:

- Antimicrobial therapy is based on positive tests results in a symptomatic patient (Shulman et al, 2012):
  - Penicillins (drugs of choice due to cost, efficacy, and infrequent adverse reactions):
    - Penicillin V potassium: Children (27 kg): 250 mg twice daily or three times daily; children (greater than 27 kg), adolescents, and adults: 500 mg twice daily or three times daily for 10 days; can do 250 mg four times a day with teens (Taketomo et al, 2014)

- Amoxicillin suspension is more palatable (efficacy seems equal to penicillin): 50 mg/kg once daily (maximum dose = 1000 mg); alternate: 25 mg/kg (maximum dose = 500 mg) twice daily for 10 days
- Benzathine penicillin G intramuscular (IM): 600,000 units as a single dose if less than 27 kg; 1.2 million units as a single dose for larger children and adults

- If allergic to penicillin:
  - Pen Cephalexin: 20 mg/kg/dose twice daily (maximum dose = 500 mg/dose) for 10 days but should be avoided in patients with moderate hypersensitivity reaction to penicillin.
  - Cefadroxil: 30 mg/kg/day divided twice daily (maximum daily dose = 2 gms/day) for 10 days but should be avoided with moderate hypersensitivity reaction to penicillin.
  - Clindamycin: 7 mg/kg/dose three times daily (maximum dose = 300 mg/dose) for 10 days.
  - Azithromycin: 12 mg/kg once a day to a maximum of 500 mg. It should be noted that macrolide resistance is variable in the United States (Shulman et al, 2012).
  - Clarithromycin: 7.5 mg/kg/dose to a maximum of 250 mg twice per day for 10 days.

- Supportive care: Antipyretics, fluids, and rest.
- Use of corticosteroids is not indicated (Shulman et al, 2012).
- Repeat culture is not generally needed except in situations where it is necessary to ensure eradication of the organism.
- Continued symptoms of streptococcal pharyngitis and a positive culture for streptococcus may represent an actual 806treatment failure or a new infection with a different serologic type of streptococcus.
- Noncompliance with pharmacologic therapy can explain treatment failure, and in these instances, an injection of benzathine penicillin is recommended.
- Fomites, such as bathroom cups, toothbrushes, or orthodontic devices, may harbor GABHS and should be cleaned or discarded.
- Children can return to school when they are afebrile and have been taking antibiotics for at least 24 hours.
- Streptococcal treatment guidelines may include tonsillectomy as an intervention for recurrent GABHS; note that tonsillectomy should only be considered for the rare child who fails to improve over time despite good

compliance (Shulman et al, 2012). This recommendation is different from the guidelines issued for tonsillectomy discussed earlier (Belderbos et al, 2011).

- Treatment of chronic symptomatic carriage of GABHS:
  - Clindamycin: 20 to 30 mg/kg/day in three doses (maximum dose = 300 mg/dose) for 10 days
  - Amoxicillin-clavulanic acid: 40 mg/kg/day in three doses (maximum daily dose = 2000 mg/day) for 10 days
  - Penicillin V: 50 mg/kg/day in four doses for 10 days (maximum dose = 2000 mg/day) with the use of rifampin: 20 mg/kg/day in one dose (maximum dose = 600 mg/day) during the last 4 days of treatment
  - Benzathine penicillin G: 600,000 units for less than 27 kg and 1,200,000 units for 27 kg or greater; rifampin: 20 mg/kg/day in two doses (maximum dose = 600 mg/day)
  - If clinical relapse occurs, a second course of antibiotic is indicated, as discussed earlier. If recurrent infection is a problem, culturing of the family for the chronic carrier state is advised.

Complications

Major nonsuppurative late complications caused by GABHS are rheumatic fever, poststreptococcal reactive arthritis, and acute glomerulonephritis. Suppurative complications include cervical adenitis, rhinosinusitis, otitis media, pneumonia, mastoiditis, and retropharyngeal or peritonsillar abscess. Retropharyngeal abscess is more common in children younger than 6 years old, whereas peritonsillar abscess is more common from the ages of 20 to 40 years old (Gereige and Cunill-De Saut, 2011). Recurrent GABHS tonsillopharyngitis can also be a problem. Sydenham chorea is linked to GABHS infection. Pediatric autoimmune neuropsychiatric disorder syndrome (PANDAS) is characterized by various movement disorders, including tics, hyperactivity, paroxysmal and stereotypic motor movement, and psychiatric symptoms (e.g., obsessions and compulsions) and is associated with prior GABHS infection. There are five clinical criteria to diagnosis PANDAS. The child must have an (1) obsessive-compulsive disorder and/or other tic disorders; (2) onset of the disease must be prepubertal (3 years old to pubertal onset); (3) abrupt onset with a symptom course that is relapsing and remitting; (4) clear association with GABHS infection; and (5) neurologic abnormalities, such as motor hyperactivity or adventitious movements associated with exacerbations (Esposito et al, 2014). Due to the difficulties in establishing the temporal relationship between

GABHS infection and the onset of neuropsychiatric symptoms and the lack of improvement with antibiotic therapy, it has been suggested that the diagnosis be changed to pediatric acute neuropsychiatric symptoms (PA6NS). This would require a complete history and examination confirming the sudden acute onset of neuropsychiatric symptoms with therapies based on treatment of the symptoms (Swedo et al, 2012).

Congenital Heart Defects

CHD is caused by an alteration in development of or failure of the embryonic heart to progress beyond an early developmental stage. This alteration occurs in the 2nd to 8th weeks of gestation due to genetic, environmental, or multifactorial influences. Most cases of CHD have no identifiable cause. With the publication of the human genome and advances in molecular techniques, more genetic factors have been identified as playing a possible role in CHD. This is increasingly important as more children with CHD survive to their own childbearing years.
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Two percent to 4% of CHD is caused by teratogens, maternal conditions, or environmental influences. Drugs or teratogens linked to CHD include lithium, retinoic acid, antiepileptics, ibuprofen and naproxen, angiotensin-converting enzyme (ACE) inhibitors, tricyclic antidepressants, sulfonamides, sulfasalazine, tobacco, alcohol, cocaine, and marijuana. Environmental exposures to organic solvents, pesticides, and air pollution have also been implicated in CHD. Exposure to these agents during the vulnerable period (2 to 8 weeks of gestation) is best avoided, although often women do not know they are pregnant this early in gestation. Maternal illnesses (such as, diabetes mellitus, connective tissue disorders, phenylketonuria, rubella, and febrile illnesses—especially influenza) have also been implicated with CHD (van der Bom et al, 2011) (see Box 31-1).

Many genes have etiologic roles in the development of human CHD. Most infants born with CHD do not have other birth defects, but CHD does occur in association with other anomalies or syndromes in 25% to 40% of cases. Children with an abnormal chromosomal number (aneuploidy) account for a significant percentage of these children (Richards and Garg, 2010). Table 31-7 lists the most common known genetic syndromes, aneuploidies, single 770gene defects, and microdeletions associated with heart disease. (See Additional Resources on the Evolve site for information on genetic tests and specific genetic defects or syndromes.)

Congenital Malformation Syndromes Associated with Selected Congenital Heart Disease

Disorders	Resultant Heart Defect(s)/Occurrence
Syndromes with Aneuploidy (Abnormal Chromosome Number) or Microdeletion (≈10% of Congenital Heart Disease)	
Trisomy 21 (Down syndrome)	AV septal defect, VSD, ASD, PDA, TOF (50%)
Trisomy 18 (Edwards syndrome)	VSD, ASD, PDA, COA, bicuspid aortic or pulmonary valve (99%)
Trisomy 13 (Patau syndrome)	VSD, PDA, dextrocardia (90%)
Monosomy X (Turner syndrome)	Bicuspid aortic valve, COA (35%), pulmonic stenosis
Klinefelter variant (XXXXY)	PDA, ASD (15%)
22q11.2 deletion (DiGeorge syndrome)	Interrupted aortic arch, truncus arteriosus, TOF, perimembranous VSD, aortic arch anomalies

Disorders	**Resultant Heart Defect(s)/Occurrence**
7q11.23 deletion (Williams syndrome)	Pulmonic stenosis, supravalvular aortic stenosis
Syndromes with Congenital Heart Disease from Single Gene Defects	
Marfan syndrome (FBN1, TGFBR1, TGFBR2)	Mitral valve prolapse, aortic root dilation
Noonan syndrome (PTPN11)	Valvular pulmonic stenosis, HCM
Costello syndrome (HRAS)	Pulmonary stenosis, HCM, conduction abnormalities
Alagille syndrome (JAG1, NOTCH2)	Pulmonic stenosis, TOF, ASD, peripheral pulmonic stenosis
Heterotaxy syndrome (ZIC3, CFC1)	DILV, DORV, d-TGA, AVSD
CHARGE (CHD7, SEMA3E)	Truncus arteriosus, interrupted aortic arch

Disorders	**Resultant Heart Defect(s)/Occurrence**
Jacobsen (11q23 deletion)	HLHS, COA
Holt-Oram syndrome (TBX5)	ASD, VSD
Cri du chat syndrome (5p)	VSD, PDA, ASD (25%)
Neurofibromatosis	Pulmonic stenosis, COA
Leopard syndrome (PTPN11, RAF 1)	Pulmonic stenosis, conduction abnormalities
Nonhereditary Syndromes (Fetal Exposure)	
Fetal alcohol syndrome	VSD, PDA, ASD, TOF (25% to 30%)
Fetal hydantoin syndrome	Pulmonic stenosis, aortic stenosis, COA, PDA, VSD, ASD (<5%)
Fetal trimethadione syndrome	TGA, VSD, TOF (15% to 30%)

Disorders	Resultant Heart Defect(s)/Occurrence
Infant of diabetic mother	TGA, VSD, COA (3% to 5%); cardiomyopathy (10% to 20%)

Specific Congenital Heart Diseases

Congestive Heart Failure

CHF refers to a progressive clinical and pathophysiologic syndrome found in many children with heart problems. The symptoms vary with age of the child and the root cardiac problem (Box 31-4). Besides functional changes, CHF is marked by changes in neurohormonal and molecular changes within the heart.

Box 31-4

Signs and Symptoms of Congestive Heart Failure

Infants

Tachypnea
Tachycardia
Rales or wheezing
Cardiomegaly and hepatomegaly
Periorbital edema
Poor feeding/tires easily when feeding
Poor weight gain
Diaphoresis

Children and Teens

Tachypnea
Tachycardia
Rales or wheezing
Cardiomegaly and hepatomegaly
Orthopnea
Shortness of breath or dyspnea with exertion
Peripheral edema
Poor growth and development

CHF in children can be caused by congenital malformations leading to volume overload (such as, a large VSD) or pressure overload (such as, aortic stenosis) or more complex heart disease. CHF can also occur in children with structurally normal hearts due to

cardiomyopathy or secondary to arrhythmias, ischemia, toxins, or infections (Table 31-8). CHF is estimated to affect 12,000 to 35,000 children each year (Simpson and Canter, 2012).

TABLE 31-8

Conditions Associated with Congestive Heart Failure in Children

Age	Condition
Premature infant	Patent ductus arteriosus (PDA)
Birth to 1 week old	Hypoplastic left heart syndrome (HLHS)
	Coarctation of the aorta (COA)
	Critical aortic stenosis
	Interrupted aortic arch
	Arteriovenous malformations
	Tachycardia
	Cardiomyopathy
1 week to 3 months old	Ventricular septal defect (VSD)
	Truncus arteriosus
	Atrioventricular (AV) canal (endocardial cushion defect)
	Total anomalous pulmonary venous return
	Coarctation

	Tachycardia
	PDA
	Aortic stenosis
	Tricuspid atresia
Older than 1 year	Bacterial endocarditis
	Rheumatic fever
	Myocarditis

The largest group of infants and children with CHF are those with excessive left to right shunting through unrepaired congenital defects. CHF is somewhat of a misnomer in these cases, because the myocardium generally responds quite well to the challenge of excessive blood volume for a long time, and cardiac output remains adequate. However, the compensatory response to this excessive workload for the lungs and some heart chambers includes electrolyte and fluid imbalances and neurohormonal changes. Children with heart failure from systolic or diastolic cardiac dysfunction caused by infections, obstruction, or arrhythmias also need treatment to ameliorate fluid and electrolyte imbalances, increase contractility, and decrease cardiac afterload.
Depending on the underlying pathophysiology, elevated neurohormonal and inflammatory mediators (aldosterone, norepinephrine, natriuretic peptides, tumor necrosis factor, and renin) circulate in children with CHF. Large-scale studies in adult populations show the value of blocking some of the chronic neurohormonal changes in CHF with agents, such as aldosterone inhibitors, angiotensin inhibitors, and sympathetic inhibitors (beta-blockers). Various studies show that the use of neurohormonal agents is more complex in children than adults. Whether a given neurohormonal agent benefits or harms depends on the underlying cause of CHF (CHD, infection, or other) as well as the degree of heart failure (Simpson and Canter, 2012).
The traditional heart failure therapies (i.e., diuretics, inotropes,

and afterload reducers) are still used in many cases, although further elucidation of the neurohormonal responses in children with the different conditions listed in Table 31-7 may change this. Pulmonary vasodilators (such as, sildenafil) have been shown to be helpful in single ventricle heart failure. Monitoring B natriuretic peptides (amino acid polypeptides secreted by the *ventricles* in

response to stretching) in the management of CHF may be helpful in bi-ventricular heart failure but is not recommended in single ventricle disease (Simpson and Canter, 2012). Future approaches to heart failure that are being studied include agents to decrease or block myocardial fibrosis, myocardial cell regeneration, and use of stem cell and microRNA to facilitate remodeling of the heart (Burns et al, 2014).

Left-to-Right Shunting Congenital Heart Disease (Acyanotic)

Pulmonary overflow lesions have communication between the two sides of the heart through which extra blood shunts from the high-pressure, oxygenated left side of the heart to the low-pressure, deoxygenated right side of the heart. The result is an increase in pulmonary blood flow. These lesions are acyanotic in nature. Fig. 31-6 lists the various left-to-right versus right-to-left shunting disorders.

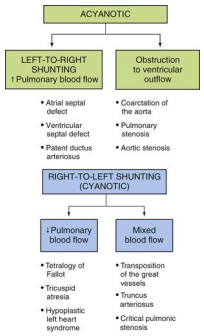

FIGURE 31-6 Classification of congenital heart disease (CHD).

Atrial Septal Defect

An atrial septal defect (ASD) is a defect or hole in the atrial septum. Of the four types of ASD, the most common involves the midseptum in the area of the foramen ovale and is called an *ostium secundum-type defect* (Fig. 31-7). Defects of the sinus venosus type are high in the atrial septum, near the entry of the SVC, or low near the IVC, and are frequently associated with anomalous pulmonary venous return. A primum ASD is in the lower portion of the septum and is most often seen in children with Down

syndrome. The rarest form of ASD is an unroofed coronary sinus. The incidence is 5% to 10% of all CHDs with a female to male ratio of 2 : 1 (Park, 2014). Usually ASDs occur spontaneously; however, there are a few identified genetic mutations that cause familial ASDs (Park, 2014).

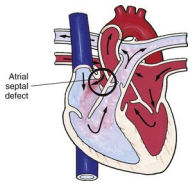

FIGURE 31-7 Atrial septal defect (ASD). (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

The child is often completely asymptomatic and may fatigue easily or have exertional dyspnea, be somewhat thin, and have a history of frequent upper respiratory tract infections or pneumonia. Symptoms may become more common in late adolescence or early adulthood.

Physical Examination.

- Typically a murmur may not be noticed until the child is 2 to 3 years old.
- Possible mild left anterior chest bulge or palpable lift at the left sternal border.
- S_1 is normal or split, with accentuation of the tricuspid valve closure sound.
- S_2 is often split widely and is relatively fixed.
- A grade I to III/VI, widely radiating, medium-pitched, not harsh systolic crescendo-decrescendo murmur is heard best at the pulmonic area. This murmur is not due to flow across the atrial septum, but it is due to increased flow across the pulmonary valve.

Diagnostic Studies.

- Chest radiography may reveal cardiac enlargement, especially of the right atrium and right ventricle. The main pulmonary artery may be dilated and pulmonary vascular markings increased.
- The ECG shows right axis deviation with right atrial enlargement. Lead V_1 usually shows a right bundle branch block with an rSR′ pattern. P wave may be tall

showing right atrial enlargement. The PR interval may be prolonged. However, the ECG can be normal in small left-to-right defects. The ECG should be assessed for AV prolongation.

- The echocardiogram identifies the specific location of the defect in the atrial septum and will show right-sided chamber enlargement.

- Cardiac catheterization is rarely necessary unless the diagnosis is in doubt, the site of pulmonary venous return is questionable, or when a device closure is planned (Park, 2014).

Management

- Small defects found in infancy may close spontaneously.
- Larger defects require intervention, usually after the child is 1 year old and before school entry or when the defect is identified in an older child. Most ASDs can now be closed in the cardiac catheterization lab with a closure device. If the defect is large or unfavorable to device closure, cardiac surgery is indicated. Surgical mortality rate is less than 0.5% (Park, 2014).
- SBE prophylaxis (see Table 31-6) precautions are necessary only in the first 6 months after cardiac surgery or device closure (81 mg of aspirin daily for 6 months may be prescribed after device closure).
- Long-term outcome is excellent after ASD repair. However, there is a small incidence of atrial arrhythmias in teenagers and adults (Sachdeva, 2013).
- Left untreated, with time ASDs can result in right ventricular enlargement, fibrosis, and failure; although rare in children, paradoxical emboli can occur (a thrombus transverses the intracardiac defect and enters the systemic circulation).
- Some with uncorrected ASDs develop severe irreversible pulmonary hypertension that is disabling and life-shortening.
- Exercise restriction is unnecessary (Park, 2014).

Ventricular Septal Defect

A VSD is a hole or defect in one of the areas of the ventricular septum and accounts for between 20% and 30% of all CHDs (Rubio and Lewin, 2013). There are four types of VSDs: perimembranous, supracristal (occurs in the outflow part of the right ventricle above crista supraventricularis), inlet, and muscular. The most common type is the perimembranous VSD (Fig. 31-8). VSDs are associated with many congenital defects, but 95% demonstrate no chromosomal anomaly (see Table 31-7). Approximately 30% to 50% of these defects are small; the vast majority of these close by 4 years old (Park, 2014).

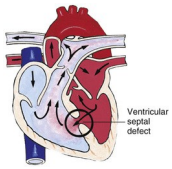

FIGURE 31-8 Ventricular septal defect (VSD). (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

- A murmur is often not heard immediately after birth. When pulmonary vascular resistance falls (normally at 2 to 8 weeks old), more blood is shunted across the VSD from left ventricle to right ventricle and hence to the pulmonary circulation. This causes a classic loud murmur. Early signs and symptoms of CHF may also begin at this time.
- Parents may note signs and symptoms of CHF (see Box 31-4).
- Small defects may be completely asymptomatic at birth, appearing by 6 months old.

Physical Examination.

- Small VSD
- Harsh, high-pitched, grade II to IV/VI holosystolic murmur at left lower sternal border (LLSB)
- All other findings within normal limits
- Large VSD
- Low-pitched, grade II to V/VI holosystolic murmur at LLSB
- VSD murmur that becomes higher pitched over time indicates that the defect is becoming smaller
- Diastolic rumble at the apex
- Thrill along the left sternal border
- Signs of progressing CHF after the first weeks of life
- S_3 or S_4 gallop if CHF is present

Diagnostic Studies.

- Chest radiography findings vary depending on the shunt's size. Children with small shunts have a normal heart size and pulmonary vascular markings that are just beyond the upper limits of normal. Those with large shunts have cardiac enlargement involving both left and right ventricles and left atrium, as well as pulmonary vascular markings that are significantly increased (see Fig. 31-4).
- The ECG is normal with small defects and may show left ventricular hypertrophy (LVH) or biventricular hypertrophy (BVH) with large shunts.
- Echocardiography provides visualization of defects and pinpoints the exact anatomic location. In “pinhole” VSDs, a murmur may be present; however, a defect may not be visualized on the echocardiogram.

- Cardiac catheterization is rarely necessary except when there is a question of elevated pulmonary vascular resistance or when the VSD can be closed in the catheterization laboratory (Park, 2014).

Management

- Infants with small defects and no symptoms of CHF are monitored every 6 months throughout the first year of life and then biannually to assess for closure of the VSD. Some defects may never close and cause no difficulty. SBE prophylaxis is not recommended.
- Larger defects with signs of CHF are managed as follows:
- Lanoxin, diuretics, ACE inhibitors, and beta-blocker dosages are prescribed, as needed, by the pediatric cardiologist.
- Nutritional intake and weight gain must be monitored in infants and children. It is also important to teach families to fortify an infant's calories to 24, 27, or 30 kcal/oz, as needed. Arrange for enteric nutritional support via nasogastric tube for young infants struggling to meet their caloric needs..
- Families must be taught the signs and symptoms of developing or progressing CHF.
- Surgery or device closure is performed if no improvement is seen over weeks or months; the long-term outcome is excellent after repair (Park, 2014).
- SBE prophylaxis precautions are necessary for 6 months after surgery (see Box 31-3 and Table 31-6).

Atrioventricular Septal Defect (Atrioventricular Canal Defect or Endocardial Cushion Defect)

The endocardial cushion is a central cardiac structure that includes the septal portions of the mitral and tricuspid valves and the lower portion of the atrial septum and upper portion of the ventricular septum. Variable portions of the endocardial cushion are absent. Complete AV septal defect implies the absence of this cushion, leading to a primum ASD, a single AV valve (composed of leaflets of the intended mitral and tricuspid valves), and an inlet VSD. There may also be partial, transitional, and intermediate defects with less profound abnormalities and usually less severe symptoms (Fig. 31-9). These complete or partial AV canal defects account for 4% to 5% of all CHDs; trisomy 21 (Down) syndrome children with CHD have a 45% incidence of AV canal defects (Cetta et al, 2013).

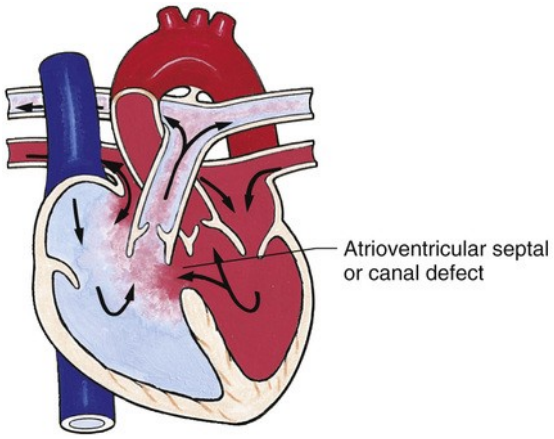

FIGURE 31-9 Complete atrioventricular (AV) septal defect (also known as AV canal defect or complete endocardial cushion defect). (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

Children with only a primum ASD (partial AV canal) may not manifest symptoms. In infants with complete AV canal defects, parents may note signs and symptoms of CHF (see Box 31-4); recurrent pneumonia is common.

Physical Examination.

- Partial AV canal (primum ASD) findings are the same as those with secundum ASD. There may also be a soft blowing murmur of mitral regurgitation in the apex and/or infrascapular area.
- Complete AV canal defect findings:
- Low-pitched, grade II to V/VI holosystolic murmur at LLSB. A murmur may not be evident at birth but increases in loudness at 2 to 8 weeks after pulmonary vascular resistance falls.
- Diastolic rumble at the apex; thrill along the left sternal border.
- Signs of progressing CHF after the first weeks of life; S_3 or S_4 gallop if CHF is present.
- Some infants, particularly those with trisomy 21, maintain neonatal high pulmonary vascular resistance and do not show signs of CHF. Instead they may manifest signs of pulmonary hypertension with loud single S_2, precordial heave, minimal murmur, and desaturation with agitation or effort (Park, 2014).

Diagnostic Studies.

- Chest radiography findings vary depending on the size of the shunt. Children with small shunts have a normal heart size and pulmonary vascular markings just beyond the upper limits of normal. Those with large shunts (complete AV canal defect) have cardiac enlargement involving both the left and right ventricles and left atrium, as well as increased pulmonary vascular markings

(see Fig. 31-4).
- The ECG usually shows superior axis between −40 and −160 degrees. Right ventricular hypertrophy is usually present, and left- or bi-ventricular hypertrophy in large shunts may be present. In 50% of children, the PR interval is prolonged.
- Echocardiography (two-dimensional, Doppler, or transesophageal) provides visualization of the size of ASD and VSD defects, size and other characteristics of the AV valve(s), and relative sizes of the ventricles.
- Cardiac catheterization may be performed if there is a question of elevated pulmonary vascular resistance or discrepancy in ventricular size.

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Management

- Children with a partial AV canal defect that consists of a primum ASD and possibly a cleft mitral valve are monitored every 3 to 6 months throughout the first year of life and then biannually until the defect is closed surgically during toddler or preschool years. They usually do not have signs of CHF but may gain weight slowly. They rarely manifest difficulty with pulmonary hypertension after surgery.
- Infants with a complete AV canal defect usually need surgical correction before they reach 6 months of life. Infants who desaturate or develop CHF should see a cardiologist to determine surgical timing. Medical management before surgery may include:
- Digoxin, diuretics, ACE inhibitors, and beta-blockers.
- Monitoring nutritional intake and weight and fortifying breast milk or infant formulas; enteric nutritional support via nasogastric tube may be needed.
- Educating families on the signs and symptoms of developing or progressing CHF.

Surgical repair consists of closure of the defect and reconstruction of the common AV valve into separate tricuspid and mitral valves. Residual mitral and/or tricuspid insufficiency is common after surgery. Surgical mortality is between 3% and 10% for those with complete AV defects and 3% for those with partial defects (Park, 2014); SBE prophylaxis precautions are necessary for only 6 months.

Patent Ductus Arteriosus

Normal functional closure of the ductus arteriosus occurs in the first 12 to 72 hours after birth. Permanent sealing occurs in 2 to 3 weeks. The ductus arteriosus may remain patent in some infants and leave a connection between the aorta and the pulmonary

artery. As pulmonary vascular resistance falls, aortic blood is shunted into the pulmonary artery and recirculates through the lungs (Fig. 31-10). The incidence is 5% to 10% of all CHDs with a female to male ratio of 3 : 1 (Park, 2014). The frequency of a PDA increases with decreasing gestational age of premature infants; it is as high as 45% to 80% in very young infants less than 1750 g (Park, 2014). This condition occurs with many congenital malformation syndromes (see Table 31-7).

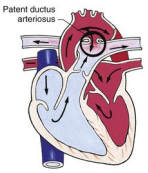

FIGURE 31-10 Patent ductus arteriosus (PDA). (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

The infant or child may be asymptomatic if the PDA is small. Increasing signs of CHF may appear in the first weeks of life in larger PDAs. PDA usually is evident by 3 months old.

Physical Examination.

- In the immediate postnatal period, the murmur is soft, systolic, and heard along the left sternal border, under the left clavicle, and in the back.
- After the first weeks of life, a typical grade II to V/VI, harsh, rumbling, continuous “machinery murmur” is heard in the left infraclavicular fossa and pulmonic area with a thrill at the base.
- Physical findings of CHF may be present with a large shunt.

Diagnostic Studies.

- Chest radiographic findings: With a small to moderate shunt, the heart is not enlarged; with larger shunts, both the left atrium and left ventricle can show enlargement. Pulmonary vascular markings may be increased.
- ECG: Large shunts show LVH; QRS axis is normal or rightward.
- Echocardiogram: Demonstrates the patent ductus and usually enlargement of the left atrium.

Management

- Indomethacin or ibuprofen may be given to preterm infants to effect closure when there is significant left-to-right shunt. It is contraindicated and ineffective in term or older infants (Park, 2014).
- An asymptomatic infant with a small left-to-right shunt from a PDA is followed for spontaneous closure or device closure in the catheterization laboratory, preferably before 1 year old. Infants with large shunts or pulmonary hypertension should have their

PDA surgically closed within the first few months of life to prevent the development of progressive pulmonary vascular obstruction. Surgical ligation of the ductus is a low-risk procedure because cardiopulmonary bypass is not necessary (Park, 2014).

- Interventional cardiologists now close many PDAs in children older than 8 months old by inserting coils or closure plugs into the shunt in the cardiac catheterization laboratory.
- Families should be reassured that their child will live an active, normal life.
- SBE prophylaxis precautions are recommended for the 6-month period after the surgical or device closure.

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Right-to-Left Shunting Congenital Heart Disease (Cyanotic)

Cyanotic CHD represents 10% to 18% of all congenital heart lesions (Park, 2014). Cardiac cyanosis is due to obstruction of pulmonary blood flow or mixing of oxygenated and unoxygenated blood. Visible cyanosis occurs when oxygen saturation in blood reaches around 85%. Cyanosis is more readily apparent with polycythemia and less readily apparent with anemia or the presence of fetal hemoglobin. Polycythemia is a compensatory mechanism to increase the oxygen-carrying capacity in cyanotic patients; however, it increases the risk for cerebral thromboses (Park, 2014).The most common heart conditions causing cyanosis in the immediate newborn period are listed in Fig. 31-6.

Transposition of the Great Arteries

Dextro-transposition of the great arteries (d-TGA) results from incomplete septation and migration of the truncus arteriosus during fetal development. In d-TGA, the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle. The aorta receives the deoxygenated systemic venous blood and returns it to the systemic arteries. The pulmonary artery receives oxygenated pulmonary venous blood and returns it to the pulmonary circulation (Fig. 31-11). There may be a number of comorbid heart malformations with d-TGA—most commonly VSD, PDA, and coronary artery defects. The incidence is 5% to7% of all CHDs with a male to female ratio of 3 : 1 (Park, 2014).

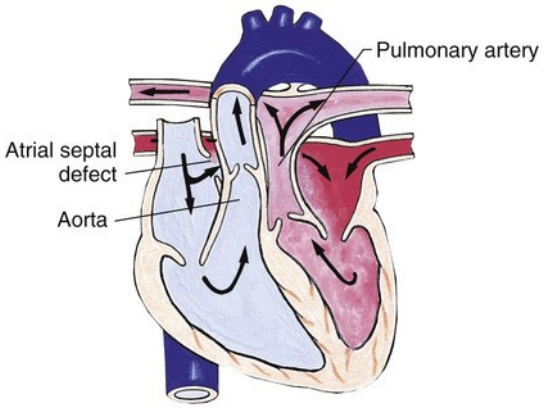

FIGURE 31-11 Complete transposition of the great vessels. (Modified from Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

- Cyanosis is immediately evident by 1 hour of birth (52%) or within the first day after birth (92%). Because d-TGA allows mixing of oxygenated and unoxygenated blood, occasionally less cyanotic infants may present as late as 3 months old.
- CHF symptoms may be present.
- Affected infants are often large for gestational age with retardation of growth and development after the neonatal period.

Physical Examination.

Infants may have no murmur at birth or may have a murmur characteristic of associated lesions, such as VSD, ASD, or PDA. The S_2 is loud and single because of the anatomic placement of the great arteries.

Diagnostic Studies.

- Chest radiography and ECG findings may be normal in the early newborn period, or the heart may appear egg shaped.
- ECG findings show right axis deviation and right ventricular hypertrophy.
- Echocardiography shows the pulmonary artery arising from the left ventricle and the aorta arising from the right.

Management

- Immediate referral to a pediatric cardiac center is necessary. Correction of electrolyte and acid-base imbalance may be necessary.
- Intravenous prostaglandin E_1 (PGE_1) is given to delay closure or reopen the ductus arteriosus.
- A balloon atrial septostomy may be performed in the catheterization laboratory to promote mixing of oxygenated and unoxygenated blood in the atria.
- The arterial switch (Jatene procedure) is usually performed in the first few days of life. If this is not possible, a number of other

operations may be performed, such as the Nakaidoh, Damus-Kaye-Stansel or réparation à l'étage ventriculaire (REV) procedures.
• Children are monitored closely throughout life with annual echocardiogram follow-up.
• SBE prophylaxis precautions are indicated for life.

Prognosis

Without treatment, there is a 50% mortality rate in the first month of life and 90% by the first year. Operative mortality is from 5% to 17%; there are excellent long-term results after surgery (Tabbutt et al, 2012). However, close monitoring for long-term patency and growth of the coronary arteries is warranted. Neopulmonic stenosis and neoaortic regurgitation may occur after the arterial switch. Refer any patient with a history of arterial or atrial switch to a pediatric cardiologist, especially with a history of palpitations, syncope, and/or shortness of breath with exertion.

Tetralogy of Fallot

Tetralogy of Fallot (TOF; also referred to as TET) is a combination of four anatomic cardiac defects resulting in right ventricular outflow tract obstruction: (1) pulmonary valve stenosis, (2) right ventricular hypertrophy, (3) VSD, and (4) an aorta that overrides the ventricular septum (Fig. 31-12). It is the most common cyanotic cardiac lesion

(5% to 10% of all CHDs), occurs slightly more in males, and has a spectrum of severity (Park, 2014). The most severe forms involve non-patent pulmonary valve and artery atresia. This is referred to as *TOF pulmonary atresia,* and these infants are quite cyanotic as newborns. In the mildest form, “pink TETs,” the infant may not display signs of cyanosis because the valvular stenosis is mild, and their symptoms may be similar to a large VSD. However, in most cases of TOF, right-to-left shunting across the VSD and cyanosis increase over the first months of life. This is a result of increasing obstruction in the right ventricular outflow tract. Children with chromosome 22q11.2 deletion syndrome or Down syndrome have a higher risk of this defect.

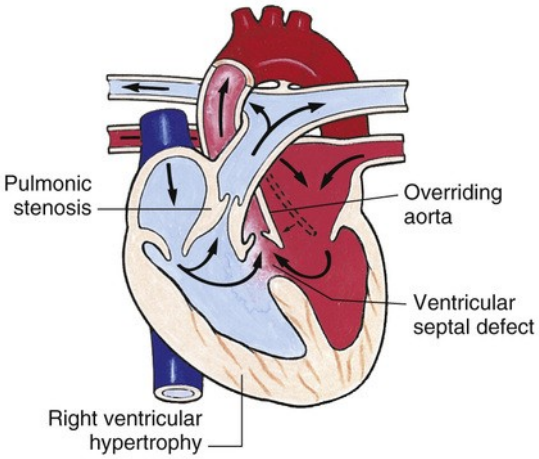

FIGURE 31-12 Tetralogy of Fallot (TOF). (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

The severity of symptoms with TOF depends on the degree of right ventricular outflow obstruction. Symptoms include:

- Cyanosis in cases with mild right ventricular outflow obstruction, cyanosis may be so slight that it is not initially evident, or it may be present at birth (with severe obstruction). Cyanosis is usually present by 6 months old.
- Dyspnea and cyanosis (including hypercyanotic episodes, or "TET spells") increase by 2 to 4 months old, especially with crying, feeding, and/or defecation. The infant may have a history of poor weight gain.

Physical Examination.

The following findings may be evident:

- Cyanosis of the mucous membranes and dyspnea
- A grade III to V/VI, harsh systolic ejection murmur at the left mid- to upper sternal border (VSD murmur and symptoms of a large VSD). There may be a palpable thrill and a holosystolic murmur at the LLSB.
- Sternal lift secondary to right ventricular hypertrophy.

Diagnostics

Chest radiography may show a boot-shaped heart with decreased pulmonary vascular markings.

- ECG shows right ventricular hypertrophy and right axis deviation and may show a conduction delay in V_1.
- An echocardiogram shows the extent of the pulmonary obstruction and demonstrates the anatomy of the overriding aorta and VSD.

- Pulse oximetry values decrease over time, with resultant increase in hemoglobin and hematocrit values.
- Cardiac catheterization may be performed, in the most severe forms, to delineate pulmonary artery anatomy.

Management

- In neonates with severe pulmonary obstruction, the ductus arteriosus is maintained or reopened with PGE_1 until more definitive repair or palliation is possible.
- For hypercyanotic episodes, the child should be cradled in a knee-chest position, soothed, and given oxygen and perhaps morphine sulfate subcutaneously until the spell subsides. The knee-chest maneuver increases systemic resistance, decreases right-to-left shunting, and increases pulmonary blood flow, hopefully alleviating symptoms. Immediate intervention is required for infants who are "spelling," especially if the previously mentioned maneuvers do not end the spell. Most children are surgically repaired before hypercyanotic spells begin.
- Complete repair with open-heart surgery is usually performed in infancy.
- Lifelong cardiology follow-up for pulmonic regurgitation or late arrhythmias is required. Recent studies indicate that progressive right ventricular dilation leads to increasing QRS duration on ECG. QRS duration of 180 ms significantly increases the risk of ventricular tachycardia and sudden death. A cardiology consult is indicated before clearing for sports participation (Park, 2014).
- SBE prophylaxis is indicated before surgery and usually for 6 months after repair.

Tricuspid Atresia, Hypoplastic Left Heart Syndrome, and Other Single Ventricle Defects

Tricuspid atresia, pulmonary atresia/intact ventricular septum, and hypoplastic left heart syndrome (HLHS) are the most common types of single ventricle defects. In most cases, there is functionally only one ventricle of either right or left morphology that must do the work of pumping blood to both the systemic and pulmonary circulations. Oxygenated and deoxygenated blood mix in this ventricle, and the child is cyanotic. Most of these children require palliative cardiac procedures to survive.

Tricuspid atresia results in a small right ventricle without access from the right atrium. Blood returning from the systemic circulation must pass over an ASD to the left atrium and then left ventricle before being pumped to either the lungs or the body (Fig. 31-13). TGA also occurs in 50% of these patients. Less than 3% of all children with CHD have tricuspid atresia; its etiology is unknown (Epstein, 2013).

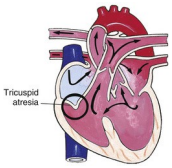

FIGURE 31-13 Tricuspid atresia. (Modified from Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

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HLHS occurs in less than 4% of congenital heart defects (Tweddell et al, 2013). Intrauterine stenosis of either the mitral or aortic valves or both, results in a small left ventricle and hypoplasia of the ascending aorta and arch (Fig. 31-14). The cause is unknown although it is linked to some genetic syndromes, such as Jacobsen syndrome and Turner syndrome in 10% of cases. Central nervous system abnormalities have also been associated with HLHS in 10% to 29% of cases (Park, 2014).

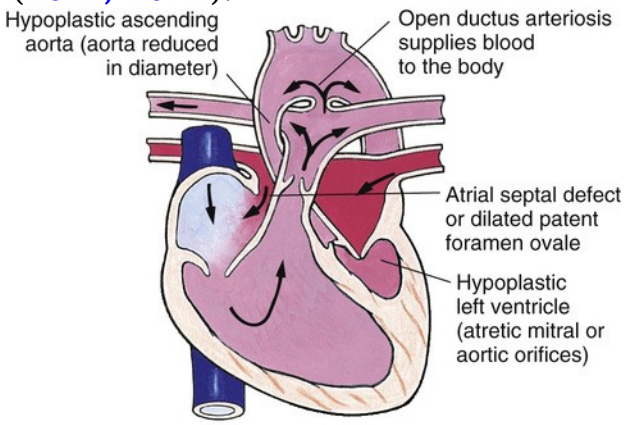

FIGURE 31-14 Hypoplastic left heart syndrome (HLHS). (Modified from Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

Cyanosis occurs soon after birth with increased respiratory rate, fatigue with the effort of crying, or feeding with subsequent poor weight gain. This often progresses to cardiorespiratory shock as the ductus arteriosus closes.

Physical Examination.

- A grade I to III/VI early systolic murmur may be present; usually a single S_2 is heard.
- Cyanosis is generally evident as soon as the ductus arteriosus closes.
- Hepatomegaly (may or may not be present)

Diagnostic Studies.

- Heart size on chest radiography is generally normal initially. Cardiomegaly and decreased pulmonary blood flow occur over time.
- ECG findings depend on the type of single ventricle disease but

are always abnormal for age. Right ventricular forces are diminished in tricuspid atresia.
- Two-dimensional echocardiography is diagnostic and shows the specifics of the anatomy.

Management

- Intravenous PGE_1 may be indicated in newborns. Most children are initially palliated with aortopulmonary shunts or other procedures depending on their anatomy. At 4 to 6 months old, palliation is continued with a bidirectional anastomosis of the SVC to the pulmonary artery. The third stage of palliation (Fontan procedure) occurs at 2 to 4 years old; the IVC is connected to the pulmonary artery. Some children are considered for cardiac transplantation early in life if their anatomy is not amenable to the Fontan pathway, or heart function and pulmonary vascular resistance do not allow completion of palliative staging (Park, 2014).
- Families require support throughout the child's life. Frequent surgeries and hospitalizations can interfere with normal social development. Early recognition and intervention for developmental delays are important.
- SBE prophylaxis is recommended while the child remains cyanotic (see Box 31-3 and Table 31-6).

Complications

Complications include development of collateral arterial and venous vessels, protein-losing enteropathy, arrhythmias, thromboembolic events including strokes, and many others. A decrease in exercise tolerance throughout life can be expected, in addition to left or right ventricular dysfunction. There may be fewer complications with surgical palliation at earlier ages. For those with severe long-term complications, heart transplantation can be an option.

Obstructive Cardiac Lesions

Aortic Stenosis and Insufficiency

Aortic stenosis or narrowing may occur at the aortic valvular, subvalvular, or supravalvular level. Valvular stenosis is the most common form (Fig. 31-15). The stenotic aortic valve is usually bicuspid rather than tricuspid. Stenosis causes increased pressure load on the left ventricle leading to LVH and, ultimately, ventricular failure. The imbalance between increased myocardial oxygen demand of hypertrophied myocardium and coronary blood supply may lead to ischemia and fatal ventricular arrhythmias. The bicuspid aortic valve generally becomes more stenotic and often

regurgitant (insufficient) over time. Some infants are born with critical aortic stenosis and require urgent intervention, usually a balloon valvuloplasty early in life. Children with only a congenital bicuspid aortic valve and no stenosis or

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regurgitation are at risk of developing symptoms by adolescence. Aortic stenosis occurs in 3% to 8% of all CHDs with a male to female ratio of approximately 4 : 1 (Schneider and Moore, 2013).Thirty percent of females with Turner syndrome have obstruction at some level of the left heart outflow tract (Richards and Garg, 2010).

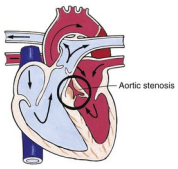

FIGURE 31-15 Aortic stenosis. (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

- Growth and development may be normal.
- Activity intolerance, fatigue, chest pain (angina pectoris), or syncope can develop or increase with age.
- CHF, low cardiac output, and shock may be evident in newborns with severe aortic stenosis.
- Sudden death, presumably due to arrhythmias, can occur with increasing severity of stenosis and exertion.

Physical Examination.

- BP may reveal a narrow pulse pressure. The apical impulse may be pronounced with moderate to severe stenosis.
- A grade III to IV/VI, loud, harsh systolic crescendo-decrescendo murmur is best heard at the upper right sternal border with radiation to the neck, LLSB, and apex.
- With a valvular lesion, a faint, early systolic click at the LLSB may be heard.
- With aortic insufficiency, an early diastolic blowing murmur is heard at the LLSB to apex.
- In the most severe lesions, S_2 is single or closely split; S_3 or S_4 heart sounds may also be heard.
- A thrill may be present at the suprasternal notch.

Diagnostic Studies.

- Chest radiographs are usually normal or may show LVH. Adults frequently develop radiographic evidence of calcification on the aortic valve over time.
- ECG can be normal or reveal LVH and inverted T-waves.

- A 24-hour Holter monitor or 30-day event monitor demonstrates ventricular arrhythmia.
- Echocardiogram is the diagnostic examination of choice.

Management

- The type and timing of treatment depends on the severity of the obstruction.
- Balloon valvuloplasty of the stenotic valve is the initial palliative treatment in the newborn. However, the aortic valve generally needs further intervention.
- In older children, surgical division of fused valve commissures may relieve stenosis but often valve replacement is necessary for severe aortic stenosis and/or insufficiency. Unfortunately, none of the current replacement options are ideal or enduring for children. Mechanical valves are prothrombotic and require anticoagulation with warfarin. Heterograph and homograft valves have limited durability in the aortic position, and the Ross procedure requires placement of the homograft in the pulmonic position, leading to future replacements of that valve as it becomes stenosed.
- Children with subaortic stenosis require surgical resection when the gradient is greater than 35 mm Hg.
- Patients with supravalvar aortic stenosis require resection of the narrowed area with patch material.
- Children with mild aortic stenosis can participate in all sports but should have annual cardiac examinations. Those with moderate aortic stenosis should choose low-intensity sports (such as, golf, bowling, table tennis, or softball) as guided by their cardiologist. Children with severe aortic stenosis or moderate aortic stenosis with symptoms should avoid competitive or intensive sports because of the risk of sudden death from ventricular arrhythmias (Park, 2014) (see Chapter 13, Table 13-6).
- Any aortic root dilation (commonly seen with bicuspid or stenotic aortic valves) may require intervention to prevent aortic dissection.
- SBE prophylaxis is necessary for 6 months after surgery.
- Anticoagulation is necessary with mechanical valve replacement (Park, 2014).

Pulmonic Stenosis

Normally the pulmonary valve opens to allow the flow of blood from the right ventricle into the pulmonary artery. In pulmonic stenosis, there is narrowing at the subpulmonic, valvular, or supravalvular area. Right-sided pressure is increased as the ventricle pumps

against the obstruction. Right ventricular hypertrophy occurs as a result of this increased load. Pulmonary stenosis can also occur in the main and/or branch pulmonary arterial system. Mild pulmonic stenosis is usually identified on routine examination. Many also develop poststenotic dilation of the pulmonary artery. Isolated pulmonic stenosis occurs in 8% to 12% of all CHDs (Park, 2014). (See Table 31-7 for associated congenital malformation syndromes.)

Clinical Findings

History.

• The child is usually asymptomatic, with a murmur noted on routine physical examination in the newborn to school-age child.

• Exertional dyspnea and fatigue are noticeable as stenosis progresses.
• Cyanosis from right-to-left shunting over the foramen ovale may be evident with critical pulmonic stenosis in the newborn.
• Growth and development are usually normal except in cases of Turner or Noonan syndrome in which short stature is common (Park, 2014).

Physical Examination.

• A grade II to IV/VI, harsh, mid- to late systolic ejection murmur is heard at the upper left sternal border over the pulmonic region with transmission along the left sternal border, neck and back, and into both lung fields.
• An intermittent systolic ejection click may be evident in the pulmonic area that decreases with inspiration and increases with expiration.
• Cyanosis and symptoms of right-sided CHF can occur in severe pulmonic stenosis in the newborn.

Diagnostic Studies.

• Chest radiographs may be within normal limits in infants or show prominent main pulmonary artery segments. Right-sided cardiac enlargement and decreased peripheral pulmonary vascular markings may be evident if heart failure develops.
• ECG may be normal with mild stenosis; with moderate to severe pulmonic stenosis, right axis deviation and right ventricular hypertrophy occur.
• Echocardiograms confirm the diagnosis, identifying the gradient and monitoring progression of the stenosis.
• Cardiac catheterization may be used to delineate location of the main and branch pulmonary artery stenosis.

Management

• Balloon valvuloplasty in neonates and older children with stenosis

greater than 50 mm Hg are performed. If unsuccessful, surgical valvuloplasty or replacement may be indicated. Stents and balloons are also used for branch stenosis.
- With mild stenosis, families must be encouraged to treat their children normally and not limit their activity. Moderate stenosis can progress to severe narrowing during periods of rapid growth, such as during infancy or adolescence (Park, 2014).
- SBE prophylaxis is not considered necessary except in the 6-month postoperative period or if prosthetic material is used (see Box 31-3).

Coarctation of the Aorta

Coarctation of the aorta (COA) is a narrowing of a small or long segment of the aorta (Fig. 31-16). Coarctation may occur as a single defect caused by a disturbance in the development of the aorta or may be secondary to constriction of the ductus arteriosus. The severity of the coarctation, its location, and the degree of obstruction determine the clinical presentation. Systolic and diastolic hypertension exists in vessels proximal to the narrowing, whereas hypotension is present in vessels below the narrowing. COA accounts for 6% to 8% of all congenital heart defects and occurs slightly more in males (Beckman, 2013). The incidence in females with Turner syndrome is close to 30%; it is also commonly associated with a bicuspid aortic valve in greater than 50% of cases (Park, 2014).

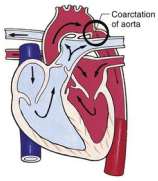

FIGURE 31-16 Coarctation of the aorta (COA). (From Hockenberry M, Wilson D: *Nursing care of infants and children,* ed 10, St. Louis, 2015, Mosby/Elsevier.)

Clinical Findings

History.

In newborns, COA is not always apparent until the ductus closes and decreases blood flow to the lower body. Severe coarctation in infants is apparent in the first 6 weeks; symptoms include tachypnea, poor feeding, and possibly cool lower extremities. In children 3 to 5 years old, coarctation may go unnoticed until hypertension or a murmur is detected. Retrospectively, children with coarctation may have had complaints of leg pain with exercise or headaches.

Physical Examination.

- Upper extremity hypertension with lower extremity hypotension

are present, although milder cases may cause only a minimal discrepancy between upper and lower extremity BPs. In severe cases, poor lower extremity perfusion may be noticed with lower body mottling or pallor.
• Delayed timing and absent or weak arterial and other distal arterial pulses may occur.
• Bounding brachial, radial, and carotid pulses may occur.
• Signs of CHF may be evident.
• A systolic ejection murmur may be detected in the left infraclavicular region with transmission to the back.
• A ventricular heave at the apex may be palpated.
• A gallop rhythm may occur in infants with CHF.

Diagnostic Studies.

• Chest radiography may reveal a normal or slightly enlarged heart and normal to increased pulmonary vascular markings; rib notching may be seen.
• ECG findings depend on the severity of the lesion and the age of the child. In infants, right ventricular

hypertrophy may be seen; in older children, LVH develops secondary to hypertension.
• Echocardiography is helpful in confirming the diagnosis and locating the constricted aortic segment. It may also show associated cardiac abnormalities. In newborns with a PDA diagnosis by echocardiogram can be challenging.
• MRI can define the location, severity, and anatomy of the aortic arch.

Management

• In critical neonatal coarctation, PGE_1 is used to maintain or reopen the ductus.
• If possible, surgical resection of the constricted area and anastomosis of the upper and lower portions of the aorta is performed. Restenosis is more likely to occur if repair was before 1 year old (Park, 2014). Cardiologists may dilate or stent the coarcted area in recoarctation or mild coarctation. Other procedures, including bypass grafting, may be necessary with unusually long coarcted segments. Surgical mortality is rare. Some centers choose balloon valvuloplasty or stent procedures for initial coarctation management (Park, 2014).
• In older children with long-standing hypertension, antihypertensive medication may be required for several months after repair. Long-term prognosis is excellent unless there are associated intracardiac defects. BP should be monitored postoperatively for recoarctation..

- Children with previous coarctation repairs may participate in any competitive sport if residual BP gradient between arm and legs is less than 20 mm Hg and peak systolic BP is normal at rest and with exercise. However, during the first year after surgery, high-intensity static exercises, such as weight lifting and wrestling, should be avoided (Park, 2014).
- Lifelong follow-up is necessary due to risk of recoarctation, residual hypertension, and often associated bicuspid aortic valve.
- SBE prophylaxis is no longer considered necessary except in the 6-month postoperative period or if prosthetic material is used (see Box 31-3).

Kawasaki Disease

KD (also known as *mucocutaneous lymph node syndrome* or *infantile polyarteritis*) is the second most common

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childhood vasculitis with a varying incidence from country to country, with Japan having the highest incidence of 239.6 per 100,000. The incidence is increasing in Japan, the United Kingdom, and India (Saundankar et al, 2014). The disease is characterized by an acute generalized systemic medium vessel vasculitis occurring throughout the body. Although its cause is unknown, it is believed that an infectious agent activates the immune system in a genetically susceptible host. Genetics may explain the higher incidence in Asia as well as a higher incidence in children of parents or siblings with a history of the disease. Recent data suggest T-cell activation plays a role in disease severity and susceptibility (Scuccimarri, 2012).

KD exhibits geographic and seasonal outbreaks, in the late winter and early spring. Person-to-person spread is low. Referral of these children to a pediatrician is necessary. It is self-limited and the most common cause of acquired heart disease in children in Japan and the United States (Saundankar et al, 2014). The EULAR/PReS classification for KD includes a persistent fever for at least 5 days plus four of the following (Ozen et al, 2010):

- Bilateral conjunctival injection
- Changes of the lips and oral cavity
- Cervical lymphadenopathy
- Polymorphous exanthema
- Changes in the peripheral extremities (swelling of the hands or feet) or perineal area

Clinical Findings

Despite accepted KD guidelines, children can have atypical or

incomplete KD with coronary anomalies shown by echocardiogram. Children younger than 6 to 12 months old may have more atypical findings. In atypical KD, the child may fulfill the criteria but has an additional feature that is not usually seen in KD. In incomplete KD, the fever may last for 5 days or more, but the child will only meet two or three of the other criteria. Incomplete KD is more common in children younger than 1 year old and older than 9 years old. Thus, incomplete KD without nodal involvement is possible. Coronary artery involvement is found more frequently in children with incomplete KD, so based on the frequency of the disease, an index of suspicion should be maintained in infancy and older school-age children (Scuccimarri, 2012). If KD is untreated, the normal course of fever is 10 to 14 days.

Other clinical features associated with KD include irritability, aseptic meningitis, mild acute iridocyclitis or anterior uveitis, otitis media due to inflammation rather than infection of the drum, urethritis, hydrops of the gallbladder, and facial nerve palsy. In children who have received BCG, there may be erythema and induration at the site of injection. Two rare complications are MAS and peripheral gangrene (Scuccimarri, 2012).

Stage 1: Acute Phase

The acute phase (days 0 to 14) begins with an abrupt onset of high fever (greater than 102.2° F [39° C]) that is unresponsive to antipyretics or antibiotics. Significant irritability, bilateral nonpurulent conjunctival injection, erythema of the oropharynx, dryness and fissuring of the lips, “strawberry tongue,” cervical lymphadenopathy, a polymorphous rash, erythema of the urethral meatus, tachycardia, and edema of the extremities are typically noted. During the acute phase, there may be pericardial, myocardial, endocardial, and coronary artery inflammation. The child typically is tachycardic and has a hyperdynamic precordium with a gallop rhythm and a flow murmur. Rarely, children have low cardiac output syndrome from poor myocardial function.

Stage 2: Subacute Phase

The subacute phase (2 to 4 weeks after illness onset) begins with resolution of the fever and lasts until all other clinical signs have disappeared. Irritability may be prolonged throughout this phase. Desquamation of the fingers (at the junction of nail tip and digit) occurs first, followed by desquamation of the toes. Transient jaundice, abnormal liver function tests, arthralgia or arthritis, transient diarrhea, orchitis, facial palsy, and sensorineural hearing loss may occur. Coronary artery aneurysms appear during this period—more so in untreated children. Common sites for aneurysms, in order of frequency, are the proximal left anterior

descending coronary, proximal right coronary, left main coronary, left circumflex, and distal right coronary artery.

Stage 3: Convalescent Phase

During the convalescent phase, all clinical signs of KD have resolved, but laboratory values may not have returned to normal. This phase is complete when all blood values are normal (6 to 8 weeks from onset). However, nail changes including Beau lines (deep transverse grooves across the nails) may be seen (Scuccimari, 2012).

Although some researchers note a chronic phase lasting from 40 days to years after illness onset, this phase is not present in all patients. Although coronary complications, if present, can persist into adulthood, a recent study of 564 patients with KD revealed a low incidence of side effects in children who were followed to 21 years of age (Holve et al, 2014).

Diagnostic Studies

KD is a diagnosis of exclusion. Results of lab investigations are not diagnostic but rather help rule in other diagnoses. Although the acute phase reactants (ESR and CRP) are usually increased, they may be normal early in the course of the illness. A CBC may show an increased WBC with a predominance of neutrophils with toxic granulation. Anemia may follow with prolonged inflammation. A marked thrombocytosis with values greater than 1 million follow in the second week of illness in the subacute phase. The comprehensive metabolic profile may show an increase in serum transaminases and hypoalbuminemia. Sterile pyuria may occur. Leukopenia and thrombocytopenia in

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KD may occur in association with the life-threatening MAS.

- Stage 1 is typified by an elevated ESR and platelet count (as high as 700,000/mm^3), elevated CRP, leukocytosis with left shift, slight decreases in red blood cells and hemoglobin, hypoalbuminemia, increased α_2-globulin, and sterile pyuria. The platelet count may be initially normal with gradual increase after the seventh day of fever.
- Blood, urine, cerebrospinal fluid, and group A beta-hemolytic streptococci (GABHS) pharyngeal cultures may be indicated given the symptomatology (to rule out other sources of fever).
- Echocardiograms at acute illness, 2 weeks and 6 to 8 weeks after onset of fever, are performed to evaluate for coronary, myocardial, and pericardial inflammation. Angiography, MRI, and cardiac stress testing may be considered.

Differential Diagnosis

The differential diagnosis includes viral infections (e.g., measles,

adenovirus, EBV, enterovirus, influenza, or roseola) and bacterial infections (e.g., cervical adenitis, scarlet fever, staphylococcal scalded skin syndrome, toxic shock syndrome, leptospirosis, or Rickettsia illness, such as Rocky Mountain spotted fever). Immune-mediated diseases may need to be considered and include Steven-Johnson syndrome, serum sickness, RF, SJIA or other JIA, or connective tissue diseases, such as SLE. Other differential diagnoses include mercury poisoning, or tumor necrosis factor receptor–associated periodic syndromes, such as hyper IgM syndrome (Scuccimarri, 2012).

Management

- Early diagnosis is essential to prevent aneurysms in the coronary and extraparenchymal muscular arteries. Treatment goals include: (1) evoking a rapid anti-inflammatory response, (2) preventing coronary thrombosis by inhibiting platelet aggregation, and (3) minimizing long-term coronary risk factors by exercise, a heart healthy diet, and smoking prevention. The child should be referred for initial treatment that includes the following medications and agents (Scuccimarri, 2012):
- Intravenous immunoglobulin (IVIG) therapy (a single dose of 2 g/kg over 12 hours, ideally in the first 10 days of the illness) to reduce the incidence of coronary artery abnormalities. The use of immunoglobulin after the tenth day must be individualized. If a child is found to have an abnormal echocardiogram, fever, tachycardia, or other signs of inflammation beyond the tenth day, then immunoglobulin is still indicated. Retreatment with immunoglobulin may be useful for persistent or recurrent fevers.
- High-dose aspirin is given for its anti-inflammatory properties (80 to 100 mg/kg/day in four divided doses—every 6 hours initially) until afebrile for at least 48 to 72 hours, then lowering the aspirin dose to 3 to 5 mg/kg/day until 6 to 8 weeks and then can discontinue if the echocardiogram is normal. If significant coronary artery abnormalities develop and do not resolve, aspirin or other antiplatelet therapy is used indefinitely.
- For patients with IVIG-resistant disease as indicated by a persistent fever 48 hours after treatment with IVIG and aspirin, a second treatment of IVIG at 2 mg/kg over 12 hours is initiated. If this is not successful, then methylprednisone IV at 30 mg/kg over 3 hours once a day for 1 to 3 days may be initiated. Infliximab 5 mg/kg may also be used. If the patient is still febrile, then the opposite anti-inflammatory can be used. (Methylprednisone in the infliximab groups, or infliximab in

the methylprednisone group.) Other options include cyclosporine A, methotrexate or cyclophosphamide (Saneeymehri et al, 2015).

- An echocardiogram should be obtained as soon as the diagnosis is established as a baseline study, with subsequent studies at 2 weeks and 6 to 8 weeks after onset of illness. If a child is found to have abnormalities, more frequent evaluations may be indicated.
- All children on chronic aspirin therapy should receive inactivated influenza vaccination. If varicella or influenza develops, aspirin treatment should be stopped for 6 weeks and another antiplatelet drug substituted to minimize the risk of Reye syndrome.
- Live virus vaccines should be delayed until 11 months after administration of IVIG (AAP Red Book, 2015).
- Children without coronary or cardiac changes should be followed by a cardiologist during the first year after the onset of KD.. If there are no cardiac changes during that first year, then the PCP may follow the patient with no activity restrictions imposed at that point.
- Patients with any range of transient coronary artery dilation (including giant aneurysms) should be followed by a cardiologist for years; physical activity limitations may be imposed..
- Follow and counsel all KD patients about a heart-healthy diet.

Complications and Prognosis

The acute disease is self-limited; however, during the initial stage (acute phase), inflammation of the arterioles, venules, and capillaries of the heart occurs and can later progress to coronary artery aneurysm in 15% to 25% of untreated children (less than 5% when treated appropriately). The process of aneurysm formation and subsequent thrombosis or scarring of the coronary artery may occur as late as 6 months after the initial illness. Other possible complications include recurrence of KD (less than 2%); CHF or massive myocardial infarction; myocarditis or pericarditis, or both (30%); pericardial effusion; and mitral valve insufficiency. Mortality (1.25%) from KD occurs from cardiac sequelae 15 to 45 days after onset of fever. Children with coronary dilation or aneurysms (especially those greater than 4 mm) may have long-term coronary endothelial changes that place the child at risk for early ischemic disease;

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they may also develop dyslipidemias (Wood and Tulloh, 2009). Studies from Japan raise concern about risk of early atherosclerosis (due to arterial damage, ongoing inflammatory process, and alteration in lipid profile and other atherosclerosis

risk factors) even in children without coronary changes during acute febrile illness (Fukazawa and Ogawa, 2009).
The risk of coronary aneurysm is reduced in patients older than 1 year old if IVIG is given within 10 days of the illness. Aneurysm regression occurs in half of all patients who develop them, commonly by 1 year after the illness (80% resolve within 5 years), but vessels do not dilate normally in response to increased oxygen demand by the myocardium. Prompt treatment of chest pain, dyspnea, extreme lethargy, or syncope is always warranted. Surgical revascularization and transcatheter revascularization are used for some coronary sequelae of KD (Wood and Tulloh, 2009).

Acute Rheumatic Fever

ARF is a nonsuppurative complication following a Lancefield GAS pharyngeal infection that results in an autoimmune inflammatory process involving the joints (polyarthritis), heart (rheumatic heart disease), CNS (Sydenham chorea), and subcutaneous tissue (subcutaneous nodules and erythema marginatum). Recurrent ARF with its multisystem responses can follow with subsequent GAS pharyngeal infections. Long-term effects on tissues are generally minimal except for the damage done to cardiac valves that leaves fibrosis and scarring and results in rheumatic heart disease. ARF is diagnosed based on a set of criteria called the *revised Jones criteria* (1992). These criteria are used for the initial attack of ARF. Further modifications of the Jones criteria are used for recurrent ARF.

Clinical Findings and History

The diagnosis of an initial attack of ARF is based on the following revised Jones criteria:

- Evidence of documented (culture, rapid streptococcal antigen test, or ASO titer) GAS pharyngeal infection
- Findings of two major manifestations or one major and two minor manifestations of ARF (Berard, 2012; Burke and Chang, 2014)

Major Manifestations

Children with fewer manifestations can also have ARF. Arthritis of large joints occurs in 65% of cases, carditis in 50%, chorea in 15% to 30%, cutaneous nodules in 5%, and subcutaneous nodules in less than 7%. There is some controversy regarding the use of the Jones criteria in developing countries where the ability for diagnostic testing may be limited; therefore,

the World Health Organization (WHO) criteria (Box 25-2) may be used (Ferrieri, 2002; Seckel and Hoke, 2011).

- Carditis is common (pancarditis, valves, pericardium, myocardium) and can cause chronic, life-threatening disease (i.e., congestive heart failure [CHF]) with estimates of 30% to 80% of patients with ARF experiencing carditis; it is more common in younger children than adolescents. The symptoms of carditis may be vague and insidious with decreased appetite, fatigue, and pains. A high-pitched holosystolic murmur is heard at the apex with radiation to the infrascapular area, as well as tachycardia and often a gallop rhythm. Mitral and possibly aortic regurgitation occur in 95% of cases, usually within 2 weeks of RF illness. The mitral valve becomes leaky due to annular dilation and elongation of the chordate that attach leaflets to the left ventricle. With moderate to severe mitral regurgitation CHF develops; recurrent episodes of RF lead to worsening valve disease.
- Polyarthritis (migratory and painful) involving large joints and rarely small or unusual joints (e.g., vertebrae); it is the most common manifestation of ARF.
- Sydenham chorea is uncommon.

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- Erythema marginatum manifested as pink macules on the trunk and extremities; nonpruritic; this sign is uncommon.
- Subcutaneous nodules associated with repeated episodes and severe carditis; this sign is uncommon.

Box 25-2

2002-2003 World Health Organization Criteria for the Diagnosis of Rheumatic Fever and Rheumatic Heart Disease—Based on the Revised Jones Criteria

Diagnostic Categories

- Primary episode of RF*
- Recurrent attack of RF in a patient *without* established rheumatic heart disease†
- Recurrent attack of RF in a patient *with* established rheumatic heart disease
- Rheumatic chorea: Insidious onset rheumatic carditis†
- Chronic valve lesions of rheumatic heart disease (patients presenting for the first time with pure mitral stenosis or mixed mitral valve disease)‡

Criteria

- Two major or one major and two minor manifestations *plus* evidence of a preceding GAS infection
- Two minor manifestations *plus* evidence of a preceding GAS infection[§]
- Other major manifestations or evidence of GAS infection not required
- Do not require any other criteria to be diagnosed as having rheumatic heart disease and/or aortic valve disease

Major Manifestations

- Carditis
- Polyarthritis
- Chorea
- Erythema marginatum
- Subcutaneous nodules

Minor Manifestations

- Clinical fever, polyarthralgia
- Laboratory elevated acute phase reactants (ESR or leukocyte count)

Supporting Evidence of a Preceding Group A Streptococcal Infection within the Past 45 Days

- ECG: Prolonged PR interval
- Elevated or rising ASO or other streptococcal antibody *or*
- A positive throat culture *or*
- Rapid antigen test for GAS *or*
- Recent scarlet fever

ASO, Anti-streptolysin O; *ECG,* electrocardiogram; *ESR,* erythrocyte sedimentation rate; *GAS,* group A streptococcus; *RF,* rheumatic fever.

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[*]Patients may present with polyarthritis (or with only polyarthralgia or monoarthritis) and with several (three or more) other minor manifestations, together with evidence of recent GAS infection. Some of these cases may later turn out to be RF. It is prudent to consider them as cases of "probable RF" (once other diagnoses are excluded) and advise regular secondary prophylaxis. Such patients require close follow-up and regular examination of the heart. This cautious approach is particularly suitable for patients in vulnerable age groups in high-incidence settings.

[†]Infective endocarditis should be excluded.

‡Congenital heart disease should be excluded.
§Some patients with recurrent attacks may not fulfill these criteria.

From World Health Organization (WHO): *Rheumatic fever and rheumatic heart disease: report of a WHO expert consultation*, 2001. Available at www.who.int/cardiovascular_diseases/resources/en/cvd_trs923.pdf. Accessed January 11, 2015, Table 4.1, p 23.

Minor Manifestations

- Fever (101° F to 102° F [38.2° C to 38.9° C]), arthralgia, history of ARF

Diagnostic Studies

- Elevated acute-phase reactants (ESR, white blood cells [WBCs], CRP)
- Leukocytosis
- Prolonged PR interval on ECG

Children may be diagnosed with ARF without evidence of a preceding streptococcal infection in the following two situations: (1) a child with Sydenham chorea or (2) with acquired heart disease (commonly mitral valve regurgitation without a congenitally abnormal or prolapsed valve) that can only be linked to ARF. Approximately 80% of children with ARF have an elevated ASO titer. A combination of both DNase-B testing and ASO rising may confirm the recent infection.

Differential Diagnosis

ARF is a clinical diagnosis associated with rising antibody titers. Arthritis and arthralgia can accompany a variety of diseases including JIA; connective tissue diseases; viral infections, such as parvovirus; inflammatory bowel disease; bacterial infections, such as gonorrhea; hemophilia; infective endocarditis; and Lyme disease (Berard, 2012). A complete history and physical examination with appropriate diagnostic testing are critical to establish the diagnosis.

Management

The treatment of ARF includes the following:

- Antibiotic therapy to eradicate GAS infection: Primary prevention requires that a GAS infection be treated within 10 days of onset. Benzathine penicillin G is the drug of choice unless there is an allergic history; erythromycin is then the drug of choice. Azithromycin and cephalosporins are also sometimes used (Gerber, 2011). A patient with a history of ARF

who has an upper respiratory infection should be treated for GAS whether or not GAS is recovered as asymptomatic infection can trigger a recurrence.

- Anti-inflammatory therapy: Aspirin can be used for arthritis after the diagnosis is established; it is usually 561given only for 2 weeks and then tapered. It is also used to treat mild to moderate carditis. Aspirin and steroids provide symptomatic relief but do not prevent the incidence of chronic heart disease. Steroids have been beneficial in the management of severe carditis, reducing its morbidity and mortality. The association of Reye syndrome with aspirin use is always a concern and must be addressed with parents. Yearly influenza immunization is critical for children on aspirin therapy.
- Chest radiographs, ECG, and echocardiography are indicated; carditis usually develops within the first 3 weeks of symptoms.
- Referral for CHF treatment if needed: medical management and or valve replacement.
- Bed rest is generally indicated only for children with CHF. Children with Sydenham chorea may need to be protected from injury until their choreiform movements are controlled. Steroids in the absence of other symptoms are not useful in the treatment of chorea.
- Children with severe chorea may benefit from the use of antiepileptic agents, such as sodium valproate or carbamazepine.

Prevention of Acute Rheumatic Fever

- Treat GAS pharyngeal infections with appropriate antibiotics. Antibacterial prophylaxis for those with a prior history of ARF is required because of the greatly increased risk of recurrent ARF with subsequent inadequately treated GAS infections. Intramuscular penicillin G (1.2 million units) is more effective than daily penicillin V (Gerber, 2011) and must be given every 4 weeks (every 28 days) not monthly. It can be given every 3 weeks in high-risk children.
- Antibacterial secondary prophylaxis with penicillin is given every 4 weeks for 5 years after the last ARF episode in children without carditis or until 21 years old (whichever is longer). For those with carditis and persistent myocardial or valvular disease, treatment is 10 or more years and may be lifelong (Gerber, 2011). In the majority of patients, valvular disease will resolve if they are compliant in taking antibiotic prophylaxis after the first episode of rheumatic heart disease.

Complications

Chronic CHF can occur after an initial episode of ARF or follow recurrent episodes of ARF. Residual valvular damage is responsible for CHF. The risk of significant cardiac disease increases dramatically with each subsequent episode of ARF; thus prevention of subsequent GAS infections is critical. Engagement in the follow-up is essential to prevent the need for cardiac valvular repair.

Common Neonatal Conditions

Skin Conditions

Table 39-3 lists newborn skin disorders.

TABLE 39-3

Comparison of Newborn Skin Disorders

Rash	Significant Maternal or Infant History	Rash Description	Diagnc
Milia	None	Firm, pearly, white papules over cheeks, nose, and forehead	None
Sebaceous hyperplasia	None	Prominent, yellow-white papules over cheeks, nose, and forehead	None
Erythema toxicum	None Presents at 24 to 48 hours	Yellow-white papules with an erythematous base over cheeks, nose, and forehead	Wright demons large nu eosinop Culture sterile
Transient neonatal pustular melanosis	None More common in darker skinned persons	Vesicopustules that rupture easily and leave a halo of white scales around a central macule of hyperpigmentation on trunk, limbs, palms, and soles	None
Sucking blisters	Results from vigorous sucking	Scattered superficial bullae on the upper arms and lips of infants at birth	None

	in utero on the affected part		
Cutis marmorata	Accentuated physiologic response to cold	Lacy, reticulated, red or blue vascular pattern	None
Harlequin color change	None	Half of the baby's coloring is red and the other pale	None
Nevus sebaceous	None	Yellow, hairless smooth plaque on head or neck	None
Herpes simplex virus (HSV)	Mother may have active lesions or a history of disease	Grouped vesicles on erythematous base	DFA or detecti antigen

DFA, Direct fluorescent antibody; *ELISA*, enzyme-linked immunosorbent assay.

Milia

Milia are multiple, firm, pearly, opalescent white papules scattered over the forehead, nose, and cheeks. Their intraoral counterparts are called *Epstein pearls.* Histologically, milia represent superficial epidermal inclusion cysts filled with keratinous material associated with the developing pilosebaceous follicle. No treatment is necessary because milia exfoliate spontaneously in most infants over the first few weeks of life (Fig. 39-6).

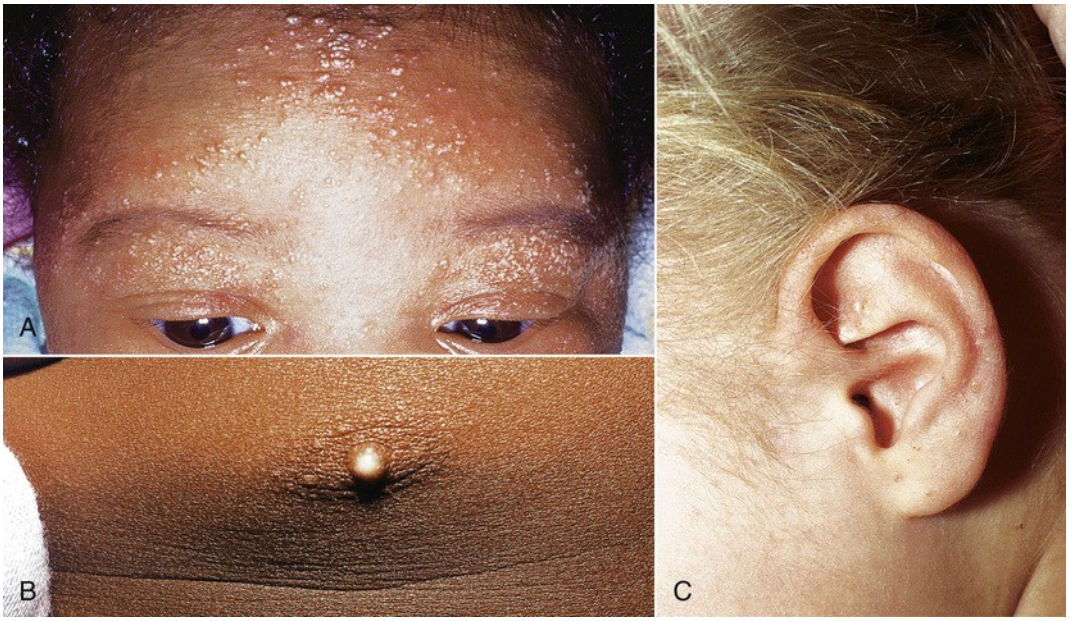

FIGURE 39-6 Milia. (From Cohen BA: *Pediatric dermatology,* ed 4, Philadelphia, 2013, Elsevier, Fig. 2-18A.)

Sebaceous Hyperplasia

Sebaceous hyperplasia is characterized by prominent yellow-white papules at the opening of each pilosebaceous follicle, predominantly over the nose, forehead, upper lip, and cheeks. The overgrowth of sebaceous glands in response to the same androgenic stimulation that occurs in adolescence

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causes sebaceous hyperplasia. No treatment is required. These tiny papules diminish in size and disappear entirely within the first few weeks of life (Fig. 39-7).

Impetigo

Impetigo is a common contagious bacterial infection of the superficial layers of the skin. It has two forms: nonbullous, with honey-colored crusts on the lesions, and bullous (Fig. 37-4). Impetigo is usually caused by group A *streptococcus (Streptococcus pyogenes), Staphylococcus aureus,* or MRSA. Often streptococcus and staphylococcus can be

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cultured from an impetigo lesion. Nonbullous impetigo accounts for more than 70% of cases, with *S. aureus* as the most common pathogen. Nonbullous impetigo usually follows some type of skin trauma (e.g., bites, abrasions, or varicella) or another skin disease, such as atopic dermatitis. Bullous impetigo occurs sporadically, develops on intact skin, and is more common in infants and young

children. Certain epidermal types of *S. aureus* produce a toxin that causes bullous skin lesions.

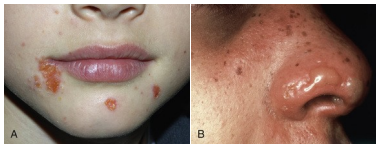

FIGURE 37-4 A, Nonbullous impetigo. **B,** Bullous impetigo. (From Bologia J, Schaffer JV, Duncan KO, et al: *Dermatology essentials*, Philadelphia, 2014, Saunders/Elsevier.)

Bacterial colonization of the skin occurs several days to months before lesions appear; the organism usually spreads from autoinoculation via hands, towels, clothing, nasal discharge, or droplets. Impetigo occurs more frequently with poor hygiene; during the summer months; in warm, humid climates; and in lower socioeconomic groups. Streptococci that cause pharyngitis rarely cause impetigo and vice versa. Secondary bacterial infections of underlying skin problems (dermatitis, varicella, psoriasis) are most commonly caused by staphylococci (Cohen, 2013).

Clinical Findings

History

- Pruritus, spread of the lesion to surrounding skin, and earlier skin disruption at the site
- Weakness, fever, and diarrhea may accompany bullous impetigo

Physical Examination

The following can be found:

- Nonbullous, classic, or common impetigo—begins as 1- to 2-mm erythematous papules or pustules that progress to vesicles or bullae, which rupture, leaving moist, honey-colored, crusty lesions on mildly erythematous, eroded skin; less than 2 cm in size; little pain but rapid spread
- Bullous impetigo—large, flaccid, thin-wall, superficial, annular, or oval pustular blisters or bullae that rupture, leaving thin varnish-like coating or scale

- Lesions are most common on face, hands, neck, extremities, or perineum; satellite lesions may be found near the primary site, although they can be anywhere on the body
- Regional lymphadenopathy

Diagnostic Studies

Gram stain and culture are ordered if identification of the organism is needed in recalcitrant or severe cases.

Differential Diagnosis

Herpes simplex, varicella, nummular eczema, contact dermatitis, tinea, kerion, and scabies are included in the differential diagnosis.

Management

Management involves the following:

- Topical antibiotics may be used if the impetigo is superficial, nonbullous, or localized to a limited area. Topical treatment alone provides clinical improvement but may prolong the carrier state (Weston and Morelli, 2013). In localized regions, topical antibiotics (such as, bacitracin, polymyxin B, and neomycin) may be used, but, given the increasing resistance to traditional topical antibiotics, mupirocin and retapamulin are considered better choices for topical treatment (Cohen, 2013; Weinberg and Tyring, 2010; Weston and Morelli, 2013). Oral antibiotics are recommended for multiple lesions or nonbullous impetigo with infection in multiple family members, child care groups, or athletes. Treat for *S. aureus* and *S. pyogenes* because coexistence is common (Cohen, 2013).
- Cephalexin: 40 mg/kg/day for 7 to 10 days
- Amoxicillin/clavulanate: 50 to 90 mg/kg/day for 7 to 10 days
- Dicloxacillin: 15 to 50 mg/kg/day for 7 to 10 days
- Cloxacillin: 50 to 100 mg/kg/day for 7 to 10 days
- Clindamycin: 10 to 25 mg/kg/day for 7 to 10 days
- For widespread infection with constitutional symptoms and deeper skin involvement, use an oral antibiotic active against beta-lactamase–producing strains of *S. aureus,* such as amoxicillin/clavulanate, dicloxacillin, cloxacillin, or cephalexin.
- If an infant has bullous impetigo, use parenteral beta-lactamase–resistant antistaphylococcal penicillin, such as methicillin, oxacillin, or nafcillin.
- If there is no response in 7 days, swab beneath the crust, and do Gram stain, culture, and sensitivities. Community-acquired MRSA should be considered. This organism is more susceptible to clindamycin and trimethoprim-sulfamethoxazole (TMP-SMX) (see Chapter 24 for treatment of MRSA).
- Educate regarding cleanliness, hand washing, and spread of disease.
- Exclude from day care or school until treated for 24 hours.
- Schedule a follow-up appointment in 48 to 72 hours if not improved.

Complications

- Cellulitis may occur with nonbullous impetigo and present in the form of ecthyma (infection involving entire epidermis) or erysipelas (spreading cellulitis with induration).
- Lymphangitis, suppurative lymphadenitis, guttate psoriasis, erythema multiforme, scarlet fever, or glomerulonephritis may occur following infection with some strains of *Streptococcus.* Acute rheumatic fever is a rare complication of streptococcal skin

infections.

- Staphylococcal scalded skin syndrome (SSSS) is a blistering disease that results from circulating epidermolytic toxin–producing *S. aureus*.. SSSS is most common in neonates (Ritter disease), infants, and children younger than 5 years old. It manifests abruptly with fever, malaise, and tender erythroderma, especially in the neck folds and axillae, rapidly becoming crusty around the eyes, nose, and mouth. Nikolsky sign (peeling of skin with a light rub to reveal a moist red surface) is a key finding. Treatment may include hospitalization and parenteral antibiotics, especially for young children (Berk and Bayliss, 2010). Antibiotics of choice are intravenous (IV) or oral dicloxacillin, a penicillinase-resistant penicillin, first- or second-generation cephalosporins, or clindamycin. Quicker healing without scarring results if steroids are avoided, there is minimal handling of the skin, and ointments and topical mupirocin are used at the infection site (Berk and Bayliss, 2010; Patel and Patel, 2010). Severe cases may need treatment similar to extensive burn care.

Patient and Family Education

- Thorough cleansing of any breaks in the skin helps prevent impetigo.
- Postinflammatory pigment changes can last weeks to months.
- The patient should not return to school or day care until 24 hours of antibiotic treatment is completed.

Herpetic whitlow on hand or fingers: Deep-appearing vesicles (Fig. 37-16)

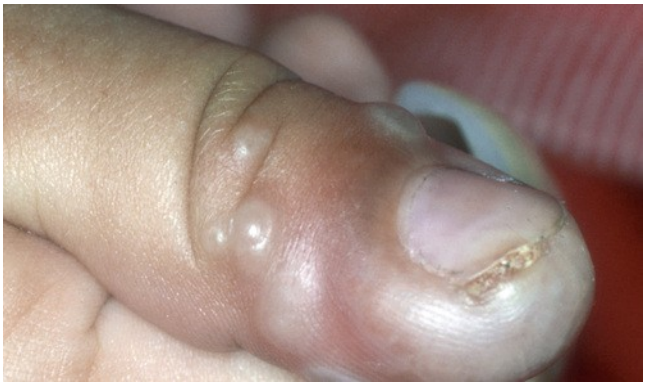

FIGURE 37-16 Herpetic whitlow. (From Cohen B: *Pediatric dermatology*, ed 4, Philadelphia, 2013, Saunders/Elsevier.)

Herpetic whitlow, occurring on a finger or thumb, is a swollen, painful lesion with an erythematous base and ulceration resembling a paronychia. It occurs on fingers of thumb-sucking children with gingivostomatitis or adolescents with genital HSV infection.

Molluscum Contagiosum

A benign common childhood viral skin infection with little health risk, molluscum contagiosum often disappears on its own in a few weeks to months and is not easily treated (Fig. 37-18). This poxvirus replicates in host epithelial cells. It attacks skin and mucous membranes and is spread by direct contact, by fomites, or by autoinoculation (typically scratching). It is commonly found in children and adolescents. The incubation period is about 2 to 7 weeks but may be as long as 6 months (Weston and Morelli, 2013). Infectivity is low but the child is contagious as long as lesions are present.

FIGURE 37-18 Molluscum contagiosum. (From Weston WL, Lane AT, Morelli JG: *Color textbook of pediatric dermatology*, ed 4, St. Louis, 2007, Mosby/Elsevier, p 144.)

Clinical Findings

History

- Itching at the site
- Possible exposure to molluscum contagiosum

Physical Examination

- Very small, firm, pink to flesh-colored discrete papules 1 to 6 mm in size (occasionally up to 15 mm)
- Papules progressing to become umbilicated (may not be evident) with a cheesy core; keratinous contents may extrude from the umbilication
- Surrounding dermatitis is common
- Face, axillae, antecubital area, trunk, popliteal fossae, crural area, and extremities are the most commonly involved areas; palms, soles, and scalp are spared
- Single papule to numerous papules; most often numerous clustered papules and linear configurations
- Sexually active or abused children can have genitally grouped lesions
- Children with eczema or immunosuppression can have severe cases; those with human immunodeficiency virus (HIV) infection or AIDS can have

hundreds of lesions

Differential Diagnosis

Warts, closed comedones, small epidermal cysts, blisters, folliculitis, and condyloma acuminatum are included in the differential diagnosis.

Management

- Untreated lesions usually disappear within 6 months to 2 years but may take up to 4 years to completely go away. There is no consensus on the management of molluscum contagiosum and no evidence-based literature to show that any treatment is superior to placebo. Therapy may be necessary to alleviate discomfort, reduce itching, minimize autoinoculation, limit transmission, and for cosmetic reasons. Genital lesions may need to be treated to prevent spread to sexual partners.
- Mechanical removal of the central core is to prevent spread and autoinoculation. Using eutectic mixture of local anesthetics (EMLA) cream (lidocaine/prilocaine) 30 to 45 minutes before the procedure reduces discomfort. Curettage is done with a sharp blade to remove the papule. Piercing the papule and expressing the plug is an option but is painful.
- There are reports that irritants (such as, surgical tape, adhesive tape, or duct tape) applied each night can result in lesion resolution.
- Topical medications may prove beneficial. Recheck the patient in 1 to 2 weeks to determine need for retreatment.
- Liquid nitrogen applied for 2 to 3 seconds (easiest but also painful).
- Trichloroacetic acid 25% to 50% applied by dropper to the center of the lesion, followed by alcohol (use with caution). Surround the lesion first with petroleum jelly.
- Cantharidin 0.7% in collodion applied by dropper to the center of the lesion, followed by alcohol. Salicylic or lactic acid or KOH or podophyllin can also be used.
- Podofilox 0.5% topical solution or gel, or imiquimod 5% applied daily with a toothpick or cotton-tipped swab.
- Tretinoin or tazarotene cream or gel applied to lesion each night.
- Silver nitrate, iodine 7% to 9%, or phenol 1% applied for 2 to 3 seconds.

- Cimetidine 30 to 40 mg/kg/day in two divided doses orally for 6 weeks if topical treatment fails.
- Sexual abuse of children with genitally grouped lesions should be suspected and evaluated.
- Evaluate for HIV infection if hundreds of lesions are found.
- Wait and see approach—spontaneous clearing occurs over years.

Complications

Molluscum dermatitis, a scaly, erythematous, hypersensitive reaction, can occur and will respond to moisturizer; avoid hydrocortisone because it causes molluscum to flare. Impetiginized lesions, inflammation of the eyes or conjunctiva, and scarring can occur.

Patient and Family Education

Patients are contagious, but there is no need to exclude them from day care or school. Children with impaired immunity, atopic dermatitis, or traumatized skin are at greater risk for broader spread. Severe inflammation is possible several hours after application of cantharidin. Scarring is unusual.

Port wine stains (Nevus flammeus), Salmon Patches, Café au lait Spots, & Hemangioma

Vascular and Pigmented Nevi

Nevi are a common finding in children. The two most common types are vascular nevi (vascular malformations and hemangiomas) and pigmented nevi (e.g., mongolian spots, café au lait spots, acquired melanocytic nevi, atypical nevi, and lentigines).

Vascular nevi are caused by a structural abnormality (malformations) or by an overgrowth of blood vessels (hemangiomas) and are flat, raised, or cavernous. Flat lesions or vascular malformations include salmon patches (also called *macular stains*), an innocent malformation that is a light red macule appearing on the nape of the neck, upper eyelids, and glabella. Approximately 60% to 70% of newborns have a salmon patch on the back of the neck. Port-wine stains occur in 0.2% to 0.3% of newborns (Cohen, 2013). At 1 year old, 10% to 12% of Caucasian infants have a hemangioma —females three times more likely than males. There is also an increased incidence of hemangioma in premature neonates. Vascular malformations are always present at birth and do not resolve spontaneously. Precursor lesions of hemangiomas are present at birth 50% of the time. They undergo rapid growth (proliferative stage), stability (plateau phase), and regression (involution phase); 90% are completely resolved in children 9 to 10 years old (Paller and Mancini, 2011).

Pigmented nevi are caused by an overgrowth of pigment cells. Pigmented nevi most commonly seen are mongolian spots (found in up to 90% of African Americans, 62% to 86% of Asians, 70% of Hispanics, and less than 10% of Caucasians), café au lait spots (found in up to 33% of normal children and in 50% of patients with McCune-Albright syndrome), and acquired melanocytic nevi, the most common tumor of childhood. Atypical nevi, also called *dysplastic nevi,* are potential precursors for malignant

melanoma. Dysplastic nevi are uncommon under 18 years old but have a higher incidence in melanoma-prone families (Paller and Mancini, 2011).

Clinical Findings

History

- Presence from birth, or age first noted
- Progression of lesion
- Familial tendencies for similar nevi, especially for history of melanoma

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Physical Examination

Findings include the following (Box 37-8):

- Vascular malformations or flat vascular nevi are present at birth and grow commensurate with the child's growth.
- Hemangiomas are classified as superficial, deep (cavernous), or mixed. They may or may not be present at birth, but they usually emerge by 2 to 3 weeks of life. They may manifest initially as a pale macule, a telangiectatic lesion, or a bright red nodular papule. After appearing, hemangiomas go through a proliferative phase during which they grow rapidly and form nodular compressible masses, ranging in size from a few millimeters to several centimeters. Occasionally they may cover an entire limb, resulting in asymmetric limb growth. Rapidly growing lesions may ulcerate. The final phase of involution occurs slowly (10% per year) but spontaneously (30% by 3 years old, 50% by 5 years old, 70% by 7 years old, and 90% by 9 to 10 years old). Average involution begins between 12 and 24 months old, heralded by gray areas in the lesion followed by flattening from the center outward. Most hemangiomas appear as normal skin after involution, but others may have residual changes, such as telangiectasias, atrophy, fibrofatty residue, and scarring (Paller and Mancini, 2011).
- Pigmented nevi may be present at birth or acquired during childhood.
- Atypical nevi are larger than acquired nevi; have irregular, poorly defined borders; and have variable pigmentation.

****Common Vascular and Pigmented Lesions *****

I. Vascular malformations or flat vascular nevi

A. Salmon patch or nevus flammeus: Light pink macule of varying size and configuration. Commonly seen on the glabella, back of neck, forehead, or upper eyelids.

B. Port-wine stain: Purple-red macules that occur unilaterally and tend to be large. Usually occur on face, occiput, or neck, although they may be on extremities.

II. Hemangiomas

A. Superficial (strawberry) hemangiomas are found in the upper dermis of the skin and account for the majority of hemangiomas.

B. Deep cavernous hemangiomas are found in the subcutaneous and hypodermal layers of the skin; although similar to superficial hemangiomas, there is a blue tinge to their appearance. With pressure, there is blanching and a feeling of a soft, compressible tumor. Variable in size, they can occur in places other than skin.

C. Mixed hemangiomas have attributes of both superficial and deep hemangiomas.

III. Pigmented nevi

A. Mongolian spots: Blue or slate-gray, irregular, variably sized macules. Common in the presacral or lumbosacral area of dark-skinned infants; also on the upper back, shoulders, and extremities. The majority of the pigment fades as the child gets older and the skin darkens. Solitary or multiple, often covering a large area.

B. Café au lait spots: Tan to light brown macules found anywhere on the skin; oval or irregular shape; increase in number with age.

C. Acquired melanocytic nevi are benign, light brown to dark brown to black, flat, or slightly raised, occurring anywhere on the body, especially on sun-exposed areas above the waist.

1. Junctional nevi represent the initial stage, with tiny, hairless, light brown to black macules.
2. Compound nevi—a few junctional nevi progress to more elevated, warty, or smooth lesions with hair.
3. Dermal nevi are the adult form, dome shaped with coarse hair.
4. Atypical nevi usually appear at puberty, have irregular borders, variegated pigmentation, are larger than normal nevi (6 to 15 mm); usually found on trunk, feet, scalp, and buttocks.
5. Halo nevi appear in late childhood with an area of depigmentation around a pigmented nevus, usually on trunk (see Fig. 37-34).

D. Acanthosis nigricans is velvety brown rows of hyperpigmentation in irregular folds of skin, usually the neck and axilla; tags may also be present.

E. Lentigines are small brown to black macules 1 to 2 mm in size appearing anywhere on the body in school-age children.
F. Freckles: 1 to 5 mm light brown, pigmented macules in sun-exposed areas.

Verruca vulgaris

Common warts (verruca vulgaris) are usually elevated flesh-colored single papules with scaly, irregular surfaces and occasionally black pinpoints, which are thrombosed blood vessels. They are usually asymptomatic and multiple and are found anywhere on the body, although most commonly on the hands, nails, and feet. They may be dome shaped, filiform, or exophytic (Fig. 37-19). Filiform warts project from the skin on a narrow stalk and are usually seen on the face, lips, nose, eyelids, or neck. Periungual warts are common, occurring around the cuticles of the fingers or toes.

Acute Diarrhea

The term *acute gastroenteritis* was formerly used to describe acute diarrhea, but this term is technically a misnomer because the etiology of diarrhea does not technically involve the stomach (Guandalini and Assiri, 2014). With acute diarrhea, there is a disruption of the normal intestinal net absorptive versus secretory mechanisms of fluids and electrolytes, resulting in excessive loss of fluid into the intestinal lumen. This can lead to dehydration, electrolyte imbalance, and in severe cases, death in those also malnourished. In children younger than 2 years old, this translates to a daily stool volume of more than 10 mL/kg (this definition excludes the normal breastfeeding stooling of five or six stools per day). In children older than 2 years old, diarrheal stooling is described as occurring four or more times in 24 hours. The duration can last up to 14 days.

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Viruses can injure the absorptive surface of mature villous cells, which reduces the amount of fluid absorbed. Some can release a viral enterotoxin (e.g., rotavirus). A loss of water and electrolytes ensues, and there can be volumes of watery diarrhea, even if the child is not being fed. Bacterial and parasitic agents can adhere and/or translocate, causing noninflammatory diarrhea. Bacteria can also damage the anatomy and functional ability of the intestinal mucosa by direct invasion. Some bacteria release endotoxins, whereas others release cytotoxins that result in the excretion of fluid, protein, and cells into the intestinal lumen and an inflammatory response in some cases. Abnormal peristalsis for any reason can result in acute diarrhea. The enteric pathogens are spread through the fecal-oral route and by ingestion of contaminated food or water.

Worldwide, the burden of acute diarrhea is huge, resulting in 3 to 5 billion cases and nearly 2 billion deaths (20% of total child deaths) in children younger than 5 years old

(particularly vulnerable) (Bell, 2010; Guandalini and Assiri, 2014; Norman et al, 2010). Developing countries also see their share of the burden of this disease (approximately 10%), attributable to poor water, sanitation, and hygiene (Norman et al, 2010). Globally, females have higher rates of *Campylobacter* species infections and hemolytic uremic syndrome; otherwise the incidence of cases shows no gender preference. Nontyphoidal *Salmonella*, *Shigella, Campylobacter, E. coli* organisms (bacteria); rotavirus, norovirus, enteric adenovirus (viruses); and *Giardia, Cryptosporidium*, and *Strongyloides* (parasites) cause most disease (Ahmed Bhutta, 2011). *Shigella, E. coli, Giardia lamblia, Cryptosporidium parvum,* and *Entamoeba histolytica* are particularly infectious in small amounts. The term "dysentery" is used to indicate infection with specific species of *Shigella*and *Salmonella* (e.g., *Shigella dysenteriae*).

In the United States, those most vulnerable include Native Americans and Native Alaskans, where remote residential locations or living on reservations compomises sanitation and safe water supplies, and where severe rotavirus diarrhea occurs. About 200,000 hospitalizations in the United States occur annually due to diarrheal illness with 300 deaths (Bell, 2010). The most common viral pathogens are noroviruses and rotavirus, followed by adenoviruses and astroviruses. Food-borne bacterial or parasitic diarrheal diseases are most commonly due to *Salmonella* and *Campylobacter*species, followed by *Shigella, Cryptosporidium, E. coli* O157:H7, *Yersinia, Listeria, Vibrio* (*Vibrio cholerae* and other species), and *Cyclospora* species. *C. difficile* has been associated with pseudomembranous colitis and diarrhea after the use of antibiotics, but it is not the causative agent in most antibiotic-associated diarrhea in children in the United States (Ahmed Bhutta, 2011).

Tables 33-11 and 33-14 discuss the characteristics of diarrheal diseases caused by bacteria, viruses, and parasites that a primary care provider is more likely to encounter and needs to differentiate. Infections due to *Cryptosporidium, E. coli* O157:H7, *Giardia, Listeria, Salmonella, Shigella,* and *V. cholerae* are required to be reported to the CDC. The enteric pathogens encountered more in day care settings include rotavirus, astrovirus, calicivirus, *Campylobacter, Shigella, Giardia*, and *Cryptosporidium* species (Guandalini and Assisri, 2014).

TABLE 33-11

Diarrheal Illnesses Due to Common Bacterial or Viral Pathogens

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
Campylobacter jejuni	2 to 5 days, but	Diarrhea (foul smelling), cramps,	2 to 10 da	Raw and undercooked	Routine stool culture; *Campylobacter*requires	Rehydration is the mainstay. Azithromycin and

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
	can be longer	fever, nausea and vomiting; diarrhea may be bloody in neonates Occurs in warm weather months	ys	poultry, unpasteurized milk, contaminated water; low inoculum dose produces infection	special media and incubation temperature; positive gross blood, leukocytes; CBC: ↑ WBCs	erythromycin shorten the duration of the illness when given early, and usually eradicates the organism from stool within 2 to 3 days.
Clostridium difficile	Unknown	Variety of symptoms and severity are seen: mild to explosive diarrhea, bloody stools, abdominal pain, fever, nausea, vomiting	During or after several weeks of antibiotic use; can occ	Acquired from the environment or from stool of other colonized or infected people by the	Stool cultures; enzyme immunoassay for toxin A, or A and B; positive gross blood, leukocytes; CBC: ↑ WBCs; ESR normal	Discontinue current antibiotic (any antibiotic, but notably ampicillin, clindamycin, second- and third-generation cephalosporins). Fluids and electrolyt

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
		Mild to moderate illness is characterized by watery diarrhea, low-grade fever, and mild abdominal pain	ur without being associated with such treatment	fecal-oral route		e replacement are usually sufficient. If antibiotic is still needed or illness is severe, treat with oral metronidazole (drug of choice in children) or vancomycin for 7 to 10 days. Supplement with probiotics. Lactobacillus GG, *Saccharomyces boulardii* are recommended (Jones, 2010; Shane,

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
						2010). Complications include pseudomembranous colitis, toxic megacolon, colonic perforation, relapse, intractable proctitis, death in debilitated children.
Enterohemorrhagic *Escherichia coli*(EHEC) including *E. coli* O157: H7 and other Shiga toxin–producing *E. coli*(STEC)	1 to 8 days	Severe diarrhea that is often bloody, abdominal pain and vomiting Usually little or no fever More common in children <4	5 to 10 days	Undercooked beef, especially hamburger, unpasteurized milk and juice, raw fruits,	Stool culture; *E. coli*O157: H7 requires special media to grow. If *E. coli*O157: H7 is suspected, specific testing must be requested. Shiga toxin	Supportive care: Monitor CBC, platelets, and kidney function closely. *E. coli* O157:H7 infection is also associated with HUS, which

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
		years old		vegetables (e.g., sprouts, spinach, lettuce), salami (rarely) Contaminated water; petting zoos	testing may be done using commercial kits; positive isolates should be forwarded to public health laboratories for confirmation and serotyping. Stool grossly positive for blood.	can cause lifelong complications. Studies indicate that antibiotics may promote the development of HUS.
Enterotoxigenic *E. coli*(ETEC) and enteroadherent *E. coli* (frequent cause of traveler's diarrhea)	1 to 3 days	Watery diarrhea, abdominal cramps, some vomiting; often cause of mild traveler's diarrhea	3 to >7 days	Water or food contaminated with human feces	Stool culture. ETEC requires special laboratory techniques for identification. If suspected, must request specific testing.	Supportive care: Antibiotics are rarely needed except in severe cases. Recommended antibiotics include TMP-SMX and quinolon

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
						es. See www.cdc.gov/travel.
Listeria monocytogenes	Variable, ranging from 1 day to more than 3 weeks	Rare, but serious Fever, muscle aches, and nausea or diarrhea Pregnant women may have mild flulike illness, and infection can lead to premature delivery or stillbirth Older adults or immunocompromised patients may have	Variable	Thrives in salty and acidic conditions, such as fresh soft cheeses, ready-to-eat deli meats, hot dogs; also unpasteurized milk, inadequately pasteurized milk;	Blood or cerebrospinal fluid cultures. Asymptomatic fecal carriage occurs; therefore, stool culture usually not helpful. Antibody to listeriolysin O may be helpful to identify outbreak retrospectively.	Initial therapy with IV ampicillin and an aminoglycoside usually gentamicin, recommended for severe infections.

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
		bacteremia or meningitis Infants infected from mother at risk for sepsis or meningitis		multiplies at low temperatures, even in properly refrigerated foods		
Adenovirus, enteric	3 to 10 days	Children >4 years old	Variable	Fecal-oral, throughout year; can remain viable on inanimate objects	Stool specimen for adenovirus antigen via rapid commercial immunoassay techniques or per electron microscopy	Supportive care: Monitor intake and hydration status Preventive care: Good hand washing and diapering precaution
Norovirus	12 to	Abrupt-onset watery	24 to 60 ho	Fecal-oral; conta	No	Supportive care: May

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
	48 hours	diarrhea, nausea, vomiting, abdominal cramps	urs Often associated with closed venues (child care centers, cruise ships)	minated food (ice, shellfish, ready-to-eat foods [e.g., salads, bakery products], or water)	commercial assay available; CDC can support laboratory evaluation or state and local health department laboratories can perform RT-PCR assays.	need to treat dehydration and/or electrolyte imbalance. Preventive care: Hand hygiene, clean surfaces and food preparation areas; no swimming in recreational venues for 2 weeks after symptoms resolve.
Rotavirus	1 to 3 days; prevalent during	Acute-onset fever, vomiting, and watery diarrhea occur 2 to 4 days	3 to 8 days	Fecal-oral; viable on inanimate objects; rarel	Enzyme immunoassay and latex agglutination assays for group A rotavirus antigen;	Supportive care: May need to correct dehydration and electrolyte imbalances. Oral

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
	cooler months in temperate climates	later in children <5 years old, especially those between 3 to 24 months old		y contaminated water or food	virus can be found by electron microscopy and specific nucleic acid amplification methods.	IG has been used in those immunocompromised. Preventive care: Rotavirus vaccine; hygiene and diapering precautions in day care facilities.
Salmonella spp.	1 to 3 days	Diarrhea, fever, abdominal cramps, rebound tenderness, vomiting. *S. typhi* and *S. paratyphi* produce typhoid with insidious onset characterized by	4 to 7 days	Contaminated eggs, poultry, unpasteurized milk or juice, cheese, contaminated raw fruits and veget	Routine stool cultures; positive leukocytes and gross blood. CBC: WBC can be slightly ↑ with left shift, ↓, or normal.	Supportive care: *Only* consider antibiotics (other than for *S. typhi*or *S. paratyphi*) for infants <3 months old, those with chronic GI disease, malignan

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
		fever, headache, constipation, malaise, chills, and myalgia; diarrhea is uncommon, and vomiting is not usually severe		ables (alfalfa sprouts, melons) *S. typhi* epidemics are often related to fecal contamination of water supplies or street-vended foods		t neoplasm, hemoglobinopathies, HIV, other immunosuppressive illnesses or therapies. If indicated, consider ampicillin or amoxicillin, azithromycin, or TMP-SMX; if resistance shown to any of those, use IM ceftriaxone, cefotaxime; or azithromycin or quinolones. A vaccine exists

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
						for *S. typhi* in certain cases.
Shigella spp.	Varies from 1 to 7 days, but typically is 1 to 3 days	Abdominal cramps, fever, and diarrhea; Stools may contain blood and mucus Seen most commonly in those 6 months old to 3 years old	4 to 7 days	Food or water contaminated with human fecal material Usually person-to-person spread, fecal-oral transmission Ready-to-eat foods touched by infected food	Routine stool cultures; gross blood, leukocytes. CBC: normal or slightly ↑ WBCs with left shift	Supportive care: If antibiotics indicated (severe disease, dysentery, immunocompromised), test first for susceptibility. Oral ampicillin (amoxicillin less so) or TMP-SMX recommended in the United States; for organism resistance, use IM ceftriaxone for 2 to 5 days;

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
				workers (e.g., raw vegetables, salads, sandwiches)		PO ciprofloxacin; azithromycin (oral cephalosporins not useful). If child is at risk of malnutrition, supplement with vitamin A (200,000 international units). No swimming in recreational pools/slides for 1 week after symptoms resolve.
*Yersinia enterocolytica*and *Y. pseudotuberculosis*	Typically 4 to 6	Appendicitis-like symptoms (diarrhea and	1 to 3 weeks, usu	Undercooked pork, unpasteuri	Stool, vomitus, or blood culture. *Yersinia*requires special	Supportive care: If septicemia or other invasive

Etiology	Incubation Period	Signs and Symptoms	Duration of Illness	Route of Transmission	Laboratory Testing	Treatment and Complications*
	days with a range of 1 to 14 days	vomiting, fever, and RLQ pain) occur primarily in older children and young adults May have a scarlatiniform rash or erythema nodosum with *Y. pseudotuberculosis* Seen in all ages	ally self-limiting	zed milk, tofu, contaminated water Infection has occurred in infants whose caregivers handled chitterlings	medium to grow. If suspected, must request specific testing. Serology is available in research and reference laboratories.	disease occurs, antibiotic therapy with gentamicin or cefotaxime (doxycycline and ciprofloxacin also effective) after susceptibility testing is done.

*See Table 33-12 for dosages.

CBC, Complete blood count; *CDC,* Centers for Disease Control and Prevention; *ESR,* erythrocyte sedimentation rate; *GI,* gastrointestinal; *HIV,* human immunodeficiency virus; *HUS,* hemolytic uremic syndrome; *IG,* immunoglobulin; *IM,* intramuscular; *IV,* intravenous; *RLQ,* right lower quadrant; *RT-PCR,* reverse transcription-polymerase chain reaction; *TMP-SMX,* trimethoprim-sulfamethoxazole; *WBC,* white blood cell.

Adapted from Department of Health and Human Services, Centers for Disease Control and Prevention (CDC): Diagnosis and management of food borne illnesses: a primer for physicians and other health professionals, *MMWR Morb Mortal Wkly Rep* 53(RR04):7–9,

2004. Additional information from Mezoff EA, Cohen MB: *Clostridium difficile* infection. In Kliegman RM, Behrman RE, Jenson HB, et al: *Nelson textbook of pediatrics,* ed 19, Philadelphia, 2011, Elsevier, p 994; Red book: *2012 report of the committee on infectious diseases,* ed 29, Elk Grove Village, IL, 2012, American Academy of Pediatrics.

Nausea and vomiting are not good indicators of the severity of a condition; however, the absence of or low-grade fever, mild to moderate periumbilical pain, and watery diarrhea are more typically associated with less serious bacterial infection and suggest small intestine involvement (Ahmed Bhutta, 2011). The following are more indicative of potentially serious infection in the upper intestine:

- Food-borne illness suspected
- Bloody diarrhea, weight loss, dehydration, severe abdominal pain, and fever
- Diarrhea lasting several days with more than three stools per day
- Neurologic involvement on physical examination

Clinical Findings

History

- Pattern of diarrhea: Onset, number of stools, volume, frequency
- Appearance of stool: Odor, mucoid, and/or bloody
- Associated symptoms: Abdominal pain, nausea, vomiting, or fever
- Number of wet diapers in the past 24 hours and approximate time of last void
- Dietary consumption: Changes in diet that might correlate with increased stooling; ingestion (and when) of raw or poorly cooked foods (e.g., raw or undercooked eggs, meat, shellfish, fish, poultry), unpasteurized or under-pasteurized milk or juices, home-canned foods, fresh produce (fruits/vegetables), soft cheeses, deli meats
- If given, response to oral rehydration therapy
- Food allergies
- Family members or close friends with similar illness or other GI diseases
- Day care, school attendance, recreational swimming exposure (even if chlorinated): Illness patterns and contacts at these locations; walking in soil without shoes
- Travel history: Foreign or coastal areas; camping or travel where untreated water might have been consumed
- Attendance at picnics or other outings where food was consumed
- Most recent weight and previous growth pattern
- Medications: Antibiotics, laxatives, antacids, opiates (withdrawal), vitamins (toxicity)
- Pica (metals, plants)
- Chemotherapy
- Recent surgeries (abdominal)

Physical Examination

- Complete a physical examination including vital signs and assessment of behavior/mental status changes
- Assess for dehydration (see Table 33-1)

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Diagnostic Studies

Diagnostic studies are ordered if the symptoms (discussed earlier) of more serious infection are present. Some specific diagnostic findings associated with the more common infectious diarrheal illness are found in Table 33-11. Molecular diagnostic tests (e.g., polymerase chain reaction [PCR]) have greatly improved the ability to diagnose diarrheal illness due to bacteria. The following tests may be ordered:

- Stool examination (color, consistency, blood, mucus, pus, odor, volume): In endemic areas, microscopy examination for parasites (e.g., *G. lamblia*and *E. histolytica*).
- Stool: pH (less than 5.5 suggests carbohydrate intolerance typically seen in viral infections), leukocytes (suggest bacterial invasion), reducing substances (viral infections), and occult blood. Normal stool: pH greater than 5.5, carbohydrate negative.
- Stool cultures should be considered early in the course of illness for bloody or prolonged diarrhea; in the presence of leukocytes; if clinical signs of colitis are present; for suspected food-borne illness outbreaks (especially with *E. coli* O157:H7); in the immunocompromised; or after recent travel abroad.
- Electrolytes, if indicated, to evaluate degree of dehydration and for more serious signs and symptoms of infectious disease.
- CBC, as indicated for serious infectious disease.

Differential Diagnosis

Diarrhea from viral etiology and antibiotic use are the most common causes of diarrhea in all age groups. Systemic infection is a common cause in infants and children, and food poisoning is a common cause in children and adolescents. Overfeeding should also be considered in infants. Rare causes of acute diarrhea in infants include primary disaccharidase deficiency, Hirschsprung toxic colitis, adrenogenital syndrome, and neonate opiate withdrawal; toxic ingestion in children; and hyperthyroidism in adolescents.

Management

The foundation of all treatment of acute diarrhea is fourfold:

- Restore and maintain hydration and correct/maintain electrolyte and acid-base balance. Oral rehydration with an oral electrolyte solution should be attempted when dehydration is assessed between 3% and 9%. Administer parenteral hydration if necessary for the following: impaired circulation and possible shock, weight less than 4 to 5 kg or a child younger than 3 months old, intractable diarrhea, lethargy, anatomic anomalies, or failure to gain weight or continued weight loss despite oral fluids (see Table 33-3).

- Maintain nutrition. Resume early refeeding because contents of the bowel stimulate the growth of enterocytes and help facilitate mucosal repair following injury (see Table 33-3).
- Prescribe antibiotics prudently. Antibiotics are recommended for acute diarrhea caused by *G. lamblia, V. cholerae,* and *Shigella* species and can be considered for infections caused by enteropathogenic *E. coli* (if infection prolonged), enteroinvasive *E. coli, Yersinia* for those with sickle cell disease, and *Salmonella* in young infants with fever or positive blood culture findings (Guandalini and Assiri, 2014) (see Tables 33-11 and 33-12). Children with HIV at risk for acute diarrhea may benefit from cotrimoxazole and vitamin A (Humphreys et al, 2010).

TABLE 33-12

Antibiotics More Commonly Used for Diarrheal Infections

Drug	Dosage	Indication
Amoxicillin	25-50 mg divided in three doses, PO, for 7 to 10 days (maximum daily dose 1.5 g)	*Salmonella, Shigella*
Ampicillin	50-100 mg/kg/day divided into four doses for 5 to 10 days (maximum daily dose 4 g)	*Salmonella, Shigella*
Azithromycin	10 mg/kg/day first day, then 5 mg/kg/day days 2 to 5, PO (up to maximum daily dose of 500 mg on day 1; 250 mg on days 2 to 5)	*Clostridium jejuni, Escherichia coli*O157:H7
Cefotaxime	IM: 75-100 mg in three or four doses	*Salmonella*
Ceftriaxone	IM: 50-75 mg in one or two doses, maximum single dose 1000 mg	*Salmonella, Shigella*

Drug	Dosage	Indication
Ciprofloxacin (in pediatric patients, not routinely first-line therapy)	>18 years old: 20-30 mg/kg/day divided into two divided doses, PO (maximum daily dose 1.5 g) for 5 to 10 days for *E. coli*. Same dosage divided in two doses and treated for 7 to 10 days for *Salmonella* and *Shigella;* for 5 to 7 days for *Campylobacter*	*E. coli* O157:H7, *Listeria, Shigella, Salmonella, Campylobacter*
Doxycycline	<8 years old: 2 mg/kg/dose every 12 hours for 3 days >8 years old: 2-4 mg/kg/day in one or two doses, PO for 7 to 10 days (maximum daily dose 200 mg)	*Yersinia enterocolitis*
Erythromycin	30-50 mg/kg/day in two to four divided doses PO for 5 to 7 days (maximum daily dose 2 g)	*C. jejuni*
Metronidazole	Amebiasis: 30-50 mg/kg/day in three divided doses for 7 to 10 days *Clostridium difficile:* 30 mg/kg/day in four divided doses for 7 to 14 days Giardiasis: 15 mg/kg/day three times a day for 5 to 7 days	*C. difficile* (first-line drug), *Entamoeba histolytica, Giardia lamblia, C. jejuni, E. coli* O157:H7
Tetracycline	>8 years old: 25-50 mg/kg/day in four divided doses PO for 7 to 10 days (maximum dose 3 g)	*Y. enterocolitis*

Drug	Dosage	Indication
Trimethoprim-sulfamethoxazole (TMP-SMX)	Cyclosporiasis: 10 mg/kg/day in two divided doses for 7 to 10 days Shigellosis: Not recommended	*Y. enterocolitis, Salmonella, Shigella, E. coli* O157:H7, *Cyclospora cayetanensis*
Vancomycin	40 mg/kg/day in four divided doses PO for 7 to 10 days (maximum 500 mg daily dose)	*C. difficile*

Data from Ahmed Bhutta Z: Acute gastroenteritis in children. In Kliegman RM, Behrman RE, Jenson HB, et al: *Nelson textbook of pediatrics,* ed 18, Philadelphia, 2011; Schleiss MR, Chen SF: Principles of antiparasitic therapy. In Kliegman RM, Behrman RE, Jenson HB, et al: *Nelson textbook of pediatrics,* ed 19, Philadelphia, 2011; Red book: *2012 report of the committee on infectious diseases,* ed 29, Elk Grove Village, IL, 2012, American Academy of Pediatrics.

- Treat any related conditions, such as sepsis and cardiovascular collapse.

Some adjunct medications and treatments have received wider use in countries outside of the United States and show efficacy in some studies. Some of these include:

- Antidiarrheals (antimotility agents or adsorbents) are not generally recommended (Bell, 2010). However, a review of literature demonstrated that loperamide in children older than 3 years old is safe and decreases the duration and frequency of diarrhea compared with placebo. Children younger than 3 years old and those who are malnourished, those with moderate or severe dehydration, those who are systemically ill, or those who have bloody diarrhea should not be treated with this drug (Li et al, 2008). Some over-the-counter products intended for diarrhea contain salicylates (e.g., Pepto-Bismol), and there is concern for Reye syndrome.
- Probiotics: *Lactobacillus casei* strain GG or *S. boulardii* (a yeast) given early in a viral diarrheal illness or antibiotic-associated diarrhea can both treat diarrhea (decrease duration by about 25 hours) (Allen et al, 2010) and ameliorate the risk of antibiotic-associated diarrhea (Johnston et al, 2007). Exact doses are undetermined, but Jones (2010) cites studies suggesting at least more than 5 billion colony-forming units (CFUs) per day.
- Dioctahedral smectite, adsorbent clay, is used in many countries to protect the intestinal mucosa by absorbing viruses, bacteria, and bacterial toxins; there are few reported side effects. Studies have shown that smectite can reduce the duration of diarrhea (Piescik-Lech et al, 2013). Its use is not routinely recommended in the United States.
- Oral enteric peppermint oil capsules have been studied for use with diarrhea, cramping, and bloating, especially when related to IBS. It may produce smooth muscle relaxation,

slow food transit through the intestines, and help with general symptom relief; its efficacy is still debated. Essential peppermint oil *(Mentha piperita)* aromatherapy can be used for abdominal pain and relaxation (Wall et al, 2014). See Chapter 43 for complementary medicine therapies for diarrhea.

- Zinc is commonly prescribed to shorten the duration of acute diarrhea in children from developing countries. Patel and colleagues (2010) found that zinc was efficacious for diarrhea caused by *Klebsiella,* not necessarily for *E. coli* or parasitic infections, and was detrimental when used in infections caused by rotavirus. The optimal dose of zinc has not been established and variations may account for varying efficacy. Zinc supplementation 882might have limited effect if the child is not zinc deficient (Patro et al, 2010). It is added to ORS solutions (along with prebiotics) in many developing countries (Passariello et al, 2011).

Intussusception

Intussusception involves a section of intestine being pulled antegrade into adjacent intestine with the proximal bowel trapped in the distal segment. The invagination of bowel begins proximal to the ileocecal valve and is usually ileocolic, but it can be ileoileal or colocolic. Intussusception is
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thought to be the most frequent reason for intestinal obstruction in children. Intussusception most commonly occurs between 5 and 10 months of age and is also the most common cause of intestinal obstruction in children 3 months to 6 years old; 80% of the cases occur before 2 years of age. In younger infants, intussusception is generally idiopathic and responds to nonoperative approaches. In some children, there is a known medical predisposing factor, such as polyps, Meckel diverticulum, Henoch-Schönlein purpura, constipation, lymphomas, lipomas, parasites, rotavirus, adenovirus, and foreign bodies. Intussusception may also be a complication of CF. Children older than 3 years are more likely to have a lead point caused by polyps, lymphoma, Meckel diverticulum, or Henoch-Schönlein purpura; therefore, a cause must be investigated. The currently approved rotavirus vaccines have not been associated with an increased risk of intussusception (Kennedy and Liacouras, 2011).

Clinical Findings

History

- The classic triad for intussusception, intermittent colicky (crampy) abdominal pain, vomiting, and bloody mucous stools, are present in fewer than 15% of cases (Kennedy and Liacouras, 2011):
- Paroxysmal, episodic abdominal pain with vomiting every 5 to 30

minutes. Vomiting is nonbilious initially. Some children do not have any pain.
- Screaming with drawing up of the legs with periods of calm, sleeping, or lethargy between episodes.
- Stool, possibly diarrhea in nature, with blood ("currant jelly").
- A history of a URI is common.
- Lethargy is a common presenting symptom.
- Fever may or may not be present; can be a late sign of transmural gangrene and infarction.
- Severe prostration is possible.

Physical Examination

- Observe the baby's appearance and behavior over a period of time; often the child appears glassy-eyed and groggy between episodes, almost as if sedated.
- A sausage-like mass may be felt in the RUQ of the abdomen with emptiness in the RLQ (Dance sign); observe the infant when quiet between spasms.
- The abdomen is often distended and tender to palpation.
- Grossly bloody or guaiac-positive stools.

Diagnostic Studies

- An abdominal flat-plate radiograph can appear normal, especially early in the course and reveal intussusceptions in only about 60% of cases (Fig. 33-5). A plain radiograph may show sparse or no intestinal gas or stool in the ascending colon with air-fluid levels and distension in the small bowel only.

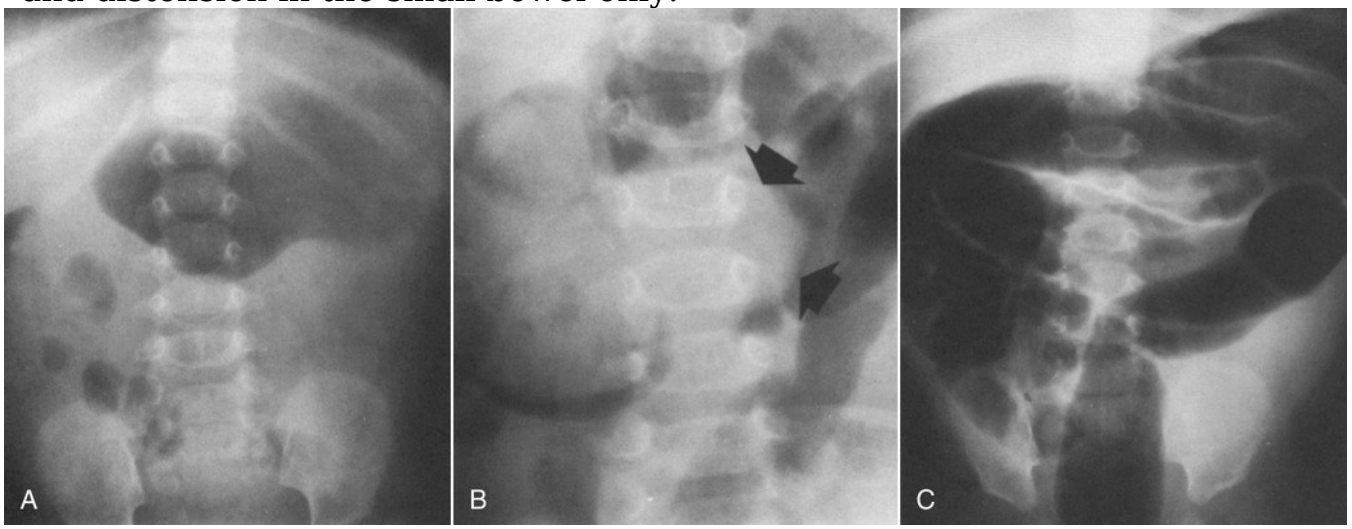

FIGURE 33-5 Intussusception. **A,** Plain abdominal radiograph demonstrating a gas-filled stomach and relatively little gas in the distal end of the bowel. This baby had typical clinical features of intussusception and a palpable upper abdominal mass. Therefore, an enema with air was performed. **B,** The intussusception *(arrows)* is outlined by air. **C,** Reduction is proved by air refluxing into loops of small bowel. (From Burg FD, Ingelfinger JR, Wald ER, editors: *Gellis and Kagan's current pediatric therapy*, ed 15, Philadelphia, 1999, Saunders.)

- Abdominal ultrasound is very accurate in detecting intussusception and is the test of choice (Ross and LeLeiko, 2010). It shows “target sign” and the “pseudo kidney” sign and can also be used to evaluate resolution following air contrast enema.
- An air contrast enema is both diagnostic and a treatment modality.

Differential Diagnosis

The differential diagnosis includes incarcerated hernia, testicular torsion, acute gastroenteritis, appendicitis, colic, and intestinal obstruction.

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Management

- Emergency management and consultation with a pediatric radiologist and a pediatric surgeon is recommended..
- Rehydration and stabilization of fluid status; gastric decompression.
- Radiologic reduction using a therapeutic air contrast enema under fluoroscopy is the gold standard.
- Surgery is necessary if perforation, peritonitis, or hypovolemic shock is suspected or radiologic reduction fails.
- IV antibiotics are often administered to cover potential intestinal perforation.
- A period of observation following radiologic reduction is recommended (12 to 18 hours); clear discharge instructions to return with any recurrence of symptoms are required, and close phone follow-up for up to 72 hours is prudent.

Complications

Swelling, hemorrhage, incarceration, and necrosis of the bowel requiring bowel resection may occur.. Perforation, sepsis, shock, and re-intussusception (reported to typically be less than 10%, usually within 72 hours of radiologic reduction but can occur up to 36 months later) can all occur. Recurrence is associated with the lead points described earlier.

Celiac Dz

Malabsorption syndromes can be caused by many different genetic, congenital, and acquired conditions and usually lead to an initial decrease in weight followed by a deceleration in height velocity. This section discusses celiac disease, 864lactose intolerance, and cow's-milk protein intolerance (CMPI).

Celiac disease is an immune-mediated systemic disorder triggered by dietary exposure to wheat gluten and related proteins in barley and rye. It is

characterized by the presence of a variable combination of gluten-dependent clinical manifestations, celiac disease–specific antibodies, HLA-DQ2.5 or HLA-DQ8 haplotypes, and enteropathy. This disease frequently co-occurs with other autoimmune diseases: diabetes mellitus type 1, autoimmune thyroiditis, autoimmune liver disease, IgA nephropathy, and juvenile chronic arthritis (Mubarak et al, 2012). A number of conditions or variables may contribute to the development of celiac disease. It is suggested that demographic changes, such as immigration from developing to developed countries, increase exposure to gluten and an increased incidence of celiac disease follows (Scanlon and Murray, 2011). Celiac disease is greater among infants born by cesarean section; the development of enteric homeostasis in the newborn period may be altered, increasing susceptibility (Decker et al, 2010). Parent reported gastroenteritis occurring at the time gluten was introduced into the child's diet does not appear to be associated with celiac disease (Welander et al, 2010). Celiac disease has a worldwide distribution with overall prevalence of 1% (Mustalahti et al, 2010). The most typical presentation occurs between 6 months and 2 years old.

Juvenile Idiopathic Arthritis (Juvenile RA)

JIA, formerly known as *juvenile rheumatoid arthritis (JRA)*, now encompasses several disorders that have a common feature of arthritis (e.g., enthesitis-related arthritis and psoriatic arthritis) and had not been identified under the nomenclature of JRA (Wu et al, 2011). The diagnosis of JIA requires a persistent arthritis for more than 6 weeks in a pediatric patient younger than 16 years old. Table 25-1 shows the most current classification system.

TABLE 25-1

Juvenile Idiopathic Arthritis Subtypes and Clinical Joint Characteristics

Juvenile Idiopathic Arthritis Subtype	Clinical Joint Characteristics
Oligoarticular	Four or less joints with persistent disease never having more than progressing to more than four joints within the first 6 months
Polyarticular (RF negative)	Five or more joints with symmetrical involvement
Polyarticular (RF positive)	Symmetric involvement of both small and large joints with erosive

Systemic	Either polyarticular or oligoarticular disease
Enthesitis-related arthritis	Weight-bearing joints involved especially hip and intertarsal joint nature or sacroiliac joint involvement
Psoriatic arthritis	Asymmetric or symmetric small or large joints
Undifferentiated	

RF, Rheumatoid factor.

The underlying cause of most forms of JIA is unclear; however, it is a heterogenous disorder. It is likely environmentally induced in genetically predisposed individual. Human leukocytic antigen (HLA) class I and II alleles have been associated with JIA (Gowdie and Tse, 2012). This linkage points to the involvement of T cells and antigen presentation in the pathophysiology of the disease. An environmental trigger, such as infection or trauma, is also important in the pathogenetic process in JIA. The trigger results in an uncontrolled adaptive and innate response toward the self-antigen, the autoimmune reaction. The presence of autoantigens from cartilage and joint tissue leads to activation of the T cells and results in release of proinflammatory cytokines (Gowdie and Tse, 2012). In contrast, systemic juvenile idiopathic arthritis (SJIA), which does not have HLA gene association, may be the result of an autoinflammatory response from the innate immune system. SJIA is postulated to be the result of uncontrolled activity of the innate immune system, because this type of JIA disease is not associated with

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autoantibodies but rather uncontrolled activity of the phagocytes, including neutrophils, monocytes, and macrophages. The difference in the pathogenic processes may explain the differences in the clinical presentation of the disease.

In oligoarticular and rheumatoid factor (RF)-positive polyarticular JIA, there is autoimmunity with involvement of the adaptive immune system. The presence of positive ANAs and RF is associated with HLA genes. The humoral response is responsible for the release of autoantibodies (especially ANAs), an increase in serum immunoglobulins, and the formation of circulating immune complexes and complement activation. The cell-mediated reaction is associated with a T-lymphocyte response that plays a key role in cytokine production, resulting in the release of tumor necrosis

factor alpha (TNF-α), IL-1, and IL-6. B lymphocytes are activated by T-helper cells and produce autoantibodies that link to self-antigens. The B lymphocytes infiltrate the synovium with the end result of nonsuppurative chronic inflammation of the synovium that can lead to articular cartilage and joint structure erosion.

The chronic arthritides of childhood present unique challenges to the child, family, and the pediatric provider. Approximately 1 in 1000 children are affected with oligoarticular JIA, the most common arthritic subtype. Certain histocompatibility complex antigens are more prevalent in the JIA population. Cytokine production, proliferation of macrophage-like synoviocytes, infiltration with neutrophils and T lymphocytes, and autoimmunity are thought to be the major pathologic processes causing chronic joint inflammation.

The rate of JIA is significantly higher in girls than in boys, typically in oligoarticular and pauciarticular JIA. The female to male ratio in systemic onset is equal. The approximate percentage of occurrence and age breakdown for each of the subtypes follows: systemic (10%) occurs at any age; polyarticular (40%) has a late (6 to 12 years old) or early childhood (1 to 4 years old) onset; and oligoarticular (50%) has a late or early onset. Adolescents tend to have more RF-positive disease (Wu et al, 2011).

Clinical Findings

History

The major complaints in all forms of JIA are from the arthritis characterized by:

- Pain—generally a mild to moderate aching
- Joint stiffness—worse in the morning and after rest; arthralgia may occur during the day
- Joint effusion and warmth

Systemic symptoms are found more commonly in systemic and polyarticular subtypes and include anemia, anorexia, fever, fatigue, lymphadenopathy, salmon-colored rash (SJIA), and weight loss. Growth abnormalities can result in localized growth disturbances, including premature fusion of the epiphyses, bony overgrowth (rheumatoid nodules), and limb-length discrepancies.

Physical Examination

Associated features are:

- Non-migratory monoarticular or polyarticular involvement of large or proximal interphalangeal joints for more than 3 months
- Systemic manifestations—fever, salmon-colored rashes, leukocytosis, serositis, lymphadenopathy, and rheumatoid nodules

Less commonly seen are ocular disease (e.g., iridocyclitis, iritis, or uveitis), pleuritis, pericarditis, anemia of chronic disease, fatigue,

and growth failure, or leg-length discrepancy if the arthritis is unilateral.

Key physical findings are:

- Swelling of the joint with effusion or thickening of synovial membrane, or both, noted on palpation of the joint line
- Heat over inflamed joint and tenderness along joint line
- Loss of joint range of motion and function; child typically holds the affected joints in slight flexion and may walk with limp
- Uveitis may be present with ciliary injection and decreased vision. However, it is usually asymptomatic.

There are five major types of JIA (Gowdie and Tse, 2012):

1. Oligoarticular pattern: This type of JIA involves four or less joints, typically the weight-bearing joints within the first 6 months of diagnosis. The diagnosis is classified as persistent or extended disease, depending on the number of joints involved. About 50% progress to extended disease where there is involvement of four or more joints after the first 6 months of disease. This involvement primarily is in larger or medium joints, such as the knee, ankle, wrists, and elbow; however, systemic symptoms are rare. The synovitis may be mild and painless with asymmetric joint involvement and unremarkable laboratory values. Uveitis occurs in 30% especially if the child has a positive ANA (Gowdie and Tse, 2012).
2. Polyarticular pattern: This involves five or more joints and is divided into RF-negative and RF-positive disease. Involved joints can be large or small with an acute or insidious onset. RF-negative ANA positive polyarticular JIA is difficult to distinguish from extended oligoarticular pattern disease. Using the number of joints involved and the timing of onset of the arthritis can be helpful. In contrast, RF-positive disease can have chronic pain and symmetric joint swelling, low-grade fever, fatigue, nodules, and anemia of chronic disease. An acute form of uveitis occurs in this subtype. Polyarticular JIA typically involves small joints of the hands, feet, ankles, wrists, knees, and can also involve the cervical spine. Adolescents with this type differ from those with early onset in that they exhibit a positive RF. Adolescents who develop late-onset polyarticular JIA have a course similar to the adult entity. Both forms of the disease are more common in females.
3. SJIA: This is characterized by arthritis in one or more joints for 6 weeks' duration in a child younger than 16 years old with a fever of at least 2 weeks' duration with

at least 3 days of daily fever. In addition, there is also a fleeting

erythematous rash, lymphadenopathy, hepatomegaly, splenomegaly, and serositis (Ringold et al, 2013). Myocarditis with pericardial effusion occurs in approximately 10%. RF is rarely positive and the ANA is only positive in 5% to 10%; however, there may be anemia, thrombocytosis, increased acute phase reactants, and elevated transaminase levels. About 10% of children with SJIA develop a life-threatening macrophage activation syndrome (MAS) with fever, organomegaly, cytopenia, hyperferritinemia (acute phase reactant), hypertriglyceridemia, coagulopathy, and hypofibrinogenemia.

4. Enthesitis-related JIA: This typically entails arthritis of the lower limbs especially the hip and intertarsal joints with the sacroiliac joints involved later in the disease. Enthesitis involves inflammation at the insertion of tendons, ligaments, or joint capsules and is characterized by swelling, tenderness, and warmth. Enthesitis may present with joint or foot pain. There is a risk of anklyosing spondylitis 10 to 15 years later. It tends to occur in late childhood and adolescence and acute symptomatic uveitis occurs in about 7%.
5. Psoriatic arthritis: This is more common between the ages of 2 and 4 and again between 9 to 11 years old. There is usually a family history of psoriasis, or the child has psoriasis; however, the arthritis can precede the psoriasis by years. There can be dactylitis or a sausage-like swelling of the digits; involvement in the small digits is not uncommon.

Diagnostic Studies

JIA is a diagnosis of exclusion. The diagnosis is based on physical findings and history of arthritis lasting for 6 weeks or longer. There is no diagnostic laboratory test for JIA. Most children with oligoarticular arthritis have negative laboratory markers. Those with polyarticular and systemic-onset typically have elevated acute-phase reactants and anemia of chronic disease. A positive result for RF by latex fixation may be present, but a positive RF occurs in less than 10% of children with JIA and rarely in those with SJIA. ANA may be present in up to 50% of children with oligoarticular disease. A positive ANA helps identify children at higher risk for uveitis. The anti-CCP antibody test can be added to the initial workup of JIA, because citrullinated residues are part of the essential antigenic components that are recognized by autoantibodies in rheumatoid arthritis (Mehta, 2012). The anti-CCP antibodies are associated with more aggressive disease and may be present before the onset of symptoms. The anti-CCP antibody is highly specific, but its precise role has not been established because it is found primarily in children with polyarticular JIA (Mehta, 2012). Useful laboratory

tests include a complete blood count (CBC) (to exclude leukemia); ESR, CRP, Lyme titers, and liver function tests. The results may reveal lymphopenia, anemia, elevated transaminases, and hypoalbuminemia; however, laboratory studies may be normal in these children. Imaging studies (MRI) can help in managing joint pathologic conditions. Analysis of synovial fluid is not helpful in the diagnosis of JIA.

Differential Diagnosis

The various causes of monoarticular arthritis are part of the differential diagnosis. However, Lyme disease must be excluded and other differentials, including tumors, leukemia, cancer, bacterial infections, toxic synovitis, rheumatic fever, SLE, spondyloarthropathies, inflammatory bowel disease, septic arthritis, and chondromalacia patellae, need to be carefully considered.

Management

A specialist in pediatric rheumatology should follow children with severe involvement. Ophthalmology referral and evaluation is critical in a child with a positive ANA. Uveitis needs immediate ophthalmologic management.. It is most common in oligoarticular JIA and is highly associated with a positive ANA. Other pediatric subspecialists, such as orthopedists, pain management specialists, and cardiologists, may be consulted as needed. Therapy depends on the degree of local or systemic involvement.

The main treatment goals are to suppress inflammation, preserve and maximize joint function, prevent joint deformities, and prevent blindness. Drug therapy is used to control the inflammation responsible for tissue injury with the goal of preventing permanent tissue changes, which is not always possible. Aggressive early treatment to induce a remission is a key consideration in JIA management in order to prevent deformity and improve outcomes and is now the goal of the practice guidelines for both polyarticular JIA and SJIA (Ringold et al, 2013, 2014). Aspirin therapy has largely been replaced with the use of nonsteroidal anti-inflammatory drugs (NSAIDs). Pharmacologic agents commonly used in the management of JIA include the following (Gowdie and Tse, 2012):

- NSAIDs: Children with oligoarthritis generally respond well to NSAIDs (Taketomo et al, 2014).
- Ibuprofen: 30 to 40 mg/kg/day three to four divided doses (maximum single dose is 800 mg; maximum daily dose 2400 mg/day)
- Tolmetin: 20 to 30 mg/kg/day divided in three to four doses (maximum dose is 1800 mg/day)
- Naproxen: 10 mg/kg/day in two divided doses (maximum dose is

1000 mg/day)
- Indomethacin: Older than 2 years old, 1 to 2 mg/kg/day divided in two to four doses (maximum dose is 4 mg/kg/day); adults, 25 to 50 mg/dose two or three times/day (maximum dose is 200 mg/day)
- Celecoxib: Older than 2 years old and adolescents (≥10 kg to ≤25 kg), 50 mg twice daily; >25 kg, 100 mg twice daily
- Oral, parenteral, intraarticular corticosteroids:
- Systemic arthritis: Can be used for 2 weeks as initial therapy for SJIA with involvement of more than four joints and a physician global assessment (using the Provider global assessment tool of disease activity) of

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less than 5 or a Provider global score of more than 5 without care about active joint involvement. Corticosteroids can be used as bridging therapy until other medications take effect (Ringold et al, 2013)
- All the other types of arthritis: Prednisone in the lowest possible dose with optional intraarticular steroid injection (Ringold et al, 2014)
- Disease-modifying antirheumatic drugs (DMARDs): Recent published guidelines vary related to the initiation of these agents depending on type of arthritis, joint involvement, and MD global assessment of functioning
- Nonbiologic DMARD treatment: methotrexate, sulfasalazine, leflunomide (managed by pediatric rheumatologist)
- Biologic DMARD treatment (managed by pediatric rheumatologist)
- Short-acting agents: Anti-IL-1 anakinra is the first-line agent for SJIA with significant joint involvement and poor global functioning (Sterba and Sterba, 2013).
- Long-acting agents: Rilonacept, canakinumab, and tocilizumab have long-acting activity (Sterba and Sterba, 2013). Rilonacept is a recombinant fusion protein with high affinity for IL-1β, IL-1α, and IL-1 receptors and a half-life of 8.6 days. Canakinumab is a humanized monoclonal antibody effective against IL-β with a half-life of 28 days. Tocilizumab is effective against IL-6 (Sterba and Sterba, 2013).
- TNF-α agents: For example, etanercept (Enbrel, infliximab (Remicade), and adalimumab (Humira) soak up tumor necrosis factor, an immune-system protein, and block the inflammatory cascade. Methotrexate or anakinra is used in severe forms of JIA.
- Intraarticular corticosteroid injections are used if there is severe

joint involvement.
- Pharmacologic therapy for uveitis is given as indicated by an ophthalmologist. Females with ANA-positive oligoarticular JIA are at high risk for uveitis and require slit-lamp examination every 3 to 4 months. The uveitis often does not correspond to the severity of the arthritis (i.e., uveitis may be present despite quiescent arthritis).
- Physical therapy—range of motion muscle-strengthening exercises and heat treatments—is used for joint involvement; occupational therapy is beneficial. Rest and splinting are used if indicated.
- Ophthalmologic follow-up every 3 months for 4 years (even if the arthritis has resolved) for all ANA-positive JIA children. They have a greater risk of uveitis that may not be clinically apparent but can lead to blindness if not detected and treated.

Complications and Prognosis

Systemic involvement can include iridocyclitis, uveitis, pleuritis, pericarditis, anemia, fatigue, and hepatitis. Residual joint damage caused by granulation of tissue in the joint space can occur. Children most likely to develop permanent crippling disability include those with hip involvement, unremitting synovitis, or positive-RF test.

The course of the disease is variable, and there is no curative treatment. Again, early aggressive treatment is critical; therefore, referral to a specialist is important.. After an initial episode, the child may never have another episode, or the disease may go into remission and recur months or years later. The disease process of JIA wanes with age and completely subsides in 85% of children; however, systemic onset, a positive RF, poor response to therapy, and the radiologic evidence of erosion are associated with a poor prognosis. Onset of disease in the teenage years is related to progression to adult rheumatoid disease.

Febrile Seizures

Febrile seizures are the most common type of seizures in children. They are brief, generalized, clonic or tonic-clonic in nature, and can be either simple or complex. A concurrent illness is present with rapid fever rise to at least more than 102.2° F (39° C), but the fever is not necessarily that high at the time of the seizure. It is conjectured that these seizures may be related to peak temperature reached during the febrile episode. Minimal postictal

confusion is associated with febrile seizures. Simple febrile seizures last less than 15 minutes and may recur during the same febrile illness period. Complex febrile seizures last longer than 15 minutes, can recur on the same day, and can have focal attributes (even during the postictal phase). Febrile SE is uncommon, rarely stops spontaneously, is fairly resistant to medications, and can persist for a long period of time. Most children in febrile SE require one or more medications to end the seizure. A report found that reducing the time from seizure onset to anticonvulsant medication administration was key to reducing the seizure duration during an episode (Seinfeld et al, 2014).

The etiology of febrile seizures is unclear and by definition excludes seizures that are caused by intracranial illness or are related to an underlying CNS problem. The risk is higher in children with a family medical history for febrile seizures or in those with predisposing factors (e.g., neonatal intensive care unit [NICU] stay more than 30 days, developmental delay, day care attendance).

The age range associated with febrile seizures is 6 months to 60 months. Male gender is a minor risk factor as is a lower sodium level. Approximately 2% to 5% of neurologically healthy infants and young children experience at least one simple febrile seizure with about 30% of this group experiencing a second episode (Mikati, 2011).

Clinical Findings

History.

Include the following:

- Description of seizure duration, type (generalized or focal), frequency in 24 hours
- Relationship of the seizure to a febrile episode and level of temperature
- Any abnormal neurologic findings noted before the seizure (is not consistent with a febrile seizure)
- Family history of afebrile or febrile seizures
- Maternal smoking in the perinatal period
- Prematurity or neonatal hospitalizations for more than 28 days
- Parents' perception of development of child

Physical Examination.

The physical examination is the same as that described earlier for seizures.

Diagnostic Studies.

Diagnostic studies include the following:

- A lumbar puncture may be done in infants younger than 12 months old and who may also have used an antibiotic prior to seizure onset, and/or in those who have signs of meningeal irritation.
- Blood glucose in all children.
- CBC, calcium, electrolytes, and urinalysis are optional but frequently included.
- EEG if neurologic signs are present or seizure was atypical.
- MRI for complex febrile seizure features or if any doubt exists about the diagnosis.

Differential Diagnosis

Consider sepsis, meningitis, metabolic or toxic encephalopathies, hypoglycemia, anoxia, trauma, tumor, and hemorrhage. Febrile delirium and febrile shivering can be confused with seizures. Breath-holding spells can mimic febrile seizures; however, the former are always related to crying or tantrums. Febrile seizures come at unpredictable times during sleep, eating, play, or other generally calm times and are related to the onset of an illness. Epileptic seizures occur without concurrent illness and at unpredictable times.

Management

- Protect the airway, breathing, and circulation if the seizure is still occurring. Place the child in a side-lying position to prevent aspiration or airway obstruction.
- Do not put anything into the child's mouth during the seizure.
- Time the duration of the seizure and observe whether it is focal or generalized.
- Reduce the fever with acetaminophen or ibuprofen (oral or suppository) after the seizure has stopped, although the use of antipyretics will not necessarily prevent another febrile seizure.
- The child should be seen shortly after the seizure. Advise transport to an emergency center if the seizure lasts more than 10 minutes.
- Most medical providers agree that anticonvulsants are not recommended for febrile seizures, but they may be considered if the child has abnormal neurologic findings or developmental delays; the initial seizure was

complex febrile, *and* there is a family history of afebrile seizures; 683or if the child has recurrent, prolonged simple febrile seizures.

Prophylaxis for Recurrent Febrile Seizures

Prolonged anticonvulsant prophylaxis is not recommended. In the rare instance that prophylaxis is indicated, diazepam by mouth 0.33 mg/kg every 8 hours (1 mg/kg/24 hours) can be given over the course of the febrile illness (usually for 2 to 3 days). Another approach is to use rectal diazepam in a gel form (dosed at 0.5 mg/kg for children 2 to 5 years of age) at the time of a seizure; this will prevent recurrence for approximately 12 hours. Side effects of diazepam include transient ataxia, lethargy, and irritability that can be decreased by adjusting the dosage.

Antipyretics can reduce the discomfort associated with a fever but do not alter the risk of having another febrile seizure. The thought as to why antipyretics are not helpful as prophylactic agents involves the mechanism implicated in a simple febrile seizure which likely takes place when the temperature is either rising or falling (Mikati, 2011).

Education

The family should receive information about febrile seizures, their risks, and their management. Education should include information explaining the febrile seizure, reassurance that no long-term consequences are associated with febrile seizures, information that febrile seizures recur in some children and that nothing can be done to prevent the seizures, and first-aid information in case another seizure occurs at some time. The decision to use prophylaxis is up to the parents and the PCP on a case-by-case basis. A follow-up phone call after the event is useful.

Complications

Death or persisting motor deficits do not occur in patients with febrile seizures. No indication has been found that intellect or learning is impaired. An affected child has an increased risk for the development of epilepsy (less than 5%) if the seizure is prolonged and focal; if the child has repeated seizures with the same febrile episode; or if the child has had a prior neurologic deficit, a family history of epilepsy, or both. Two thirds of children who have had one simple febrile seizure will have no more. The younger the age at onset (younger than 18 months old) of the first febrile seizure, the lower the temperature threshold that is needed to cause the child to seize and the more likely the child is to have a recurrence.

Testicular Torsion

Testicular torsion is the result of twisting of the spermatic cord, which subsequently compromises the blood supply to the testicle. Generally, there is a 6-hour window following a testicular torsion before significant ischemic damage and alteration in spermatic morphology and formation occurs (Elder, 2011b).

Normal fixation of the testis is absent, so the testis can rotate and block lymphatic and then blood flow. Torsion can occur after physical exertion, trauma, or on arising. Torsion can occur at any age but is most common in adolescence and is uncommon before 10 years old. The left side

is twice as likely to be involved because of the longer spermatic cord.

Clinical Findings

History

- Sudden onset of unilateral scrotal pain, often associated with nausea and vomiting. The pain is unrelenting.
- History of bouts of intermittent testicular pain. Prior episodes of transient pain are reported in about half of patients.
- Minor trauma, physical exertion, or onset of acute pain on arising is possible.
- May be described as abdominal or inguinal pain by the embarrassed child.
- Fever is minimal or absent.

Physical Examination

- Ill-appearing and anxious male, resisting movement
- Gradual, progressive swelling of involved scrotum with redness, warmth, and tenderness
- The ipsilateral scrotum can be edematous, erythematous, and warm
- Testis swollen larger than opposite side, elevated, lying transversely, exquisitely painful
- Spermatic cord thickened, twisted, and tender
- Slight elevation of the testis increases pain (in epididymitis it relieves pain)
- Transillumination can reveal a solid mass
- The cremasteric reflex is absent on the side with torsion
- Neonate—hard, painless, non-transilluminating mass with edema or discolored scrotal skin

Diagnostic Studies

- UA is usually normal and pyuria and bacteriuria indicate UTI, epididymitis, or orchitis.

• Doppler ultrasound: Testicular flow scan considered if Doppler ultrasound within normal and time allows.

Differential Diagnosis

Torsion of the testicular or epididymal appendage, acute epididymitis (mild to moderate pain of gradual onset), orchitis, trauma (pain is better within an hour), hernia, hydrocele, and varicocele are included in the differential diagnosis.

Management

Testicular torsion is a surgical emergency, and identification with prompt surgical referral must occur immediately.. Occasionally manual reduction can be performed, but surgery should follow within 6 to 12 hours to prevent retorsion, preserve fertility, and prevent abscess and atrophy. Contralateral orchiopexy may be done because of a 50% occurrence of torsion in nonfixed testes. Rest and scrotal support do not provide relief.

Patient and Family Education, Prevention, and Prognosis

Testicular atrophy, abscess, or decreased fertility and loss of the testis as a result of necrosis can occur if the torsion persists more than 24 hours.

Iron deficiency	Fatigue Irritability Excess milk intake	Pallor or none	RBC hypochromic, microcytic MCV ↓ Serum iron ↓ TIBC ↑ Percentage of saturation ↓ Ferritin ↓ Blood in stool or urine Ratio of MCV/RBC >13	Correct diet Eliminate source of bleeding Ferrous SO_4 up to 6 mg/kg/day of elemental iron

Iron Deficiency Anemia

IDA is the most common nutritional disorder and hematologic condition in the world. Approximately 3% to 7% of children at age 1 year suffer from iron deficiency (Powers and Buchanan, 2014). Nine percent of adolescent girls develop iron deficiency and 2% to 3% between the ages of 12 and 19 years old develop anemia primarily due to rapid growth, heavy menses, and nutritionally inadequate diets 641(Abrams, 2014). The incidence of IDA among children in the United States has been declining slightly during the past four decades, although the prevalence remains high among children living at or below poverty level and in black and Hispanic children. Other risk factors include childhood obesity and a history of prematurity or low birth weight (Mahoney, 2015). Iron deficiency correlates with rapid increases in body size and blood volume during the first 2 years, along with diets low in iron, such as occurs with an overuse of goat's or cow's milk. The deficient iron intake is also associated with prolonged bottle-feeding.

Dietary iron is absorbed throughout the intestine but especially in the duodenum. Malabsorption of iron occurs in diseases that affect this segment of the intestine, such as celiac disease, Crohn disease, giardiasis, or resection of the proximal small intestine. Disorders causing GI blood loss such as inflammatory bowel disease, cow's milk–induced colitis, or chronic use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) also deplete iron stores and contribute to iron deficiency (Mahoney, 2015).

Anemia (Hgb level <11 g/dL) is neither a sensitive nor a specific screen for iron deficiency because about two thirds of iron-deficient children are not anemic. Conversely, the detection of anemia is not specific to iron deficiency, because two thirds of anemic children have another cause for their anemia. The minimum laboratory screening for iron deficiency is the Hgb level. Often, the simplest and most cost-effective measurement is a CBC, which includes the Hgb, Hct, MCV, and RDW. A ferritin level may also be helpful because this indicates body stores of iron, but it must be interpreted carefully because ferritin is an acute phase reactant and may be increased with inflammatory conditions (Mahoney, 2015). The American Academy of Pediatrics (AAP) Committee on Nutrition recommends universal Hgb screening for anemia at 12 months old (Baker and Greer, 2010). This screening should include an assessment of risk factors for iron deficiency and IDA (Box 27-2).

Box 27-2

Risk Factors for Iron Deficiency Anemia

- History of prematurity or low birth weight

- Exposure to lead
- Exclusive breastfeeding beyond 6 months without iron supplementation
- Weaning to whole cow's milk without iron source
- Feeding problems
- Special health care needs
- Prolonged bottle use
- Low socioeconomic status
- Excessive or prolonged intake of cow's milk
- Obesity
- Hispanic or Asian descent
- Adolescent female, excessive menstrual bleeding

Screening Hgb can be performed on children younger than 1 year old when risk factors warrant it. Menstruating females may also require screening for IDA due to the monthly blood loss, rapid growth, and potentially inadequate diet. When screening for IDA or any other routine health screening recommendation, remember that screening is not just a one-time test; the effectiveness of treatment must be determined through follow-up testing. Thus after the routine 12-month Hgb/Hct testing, risk assessment for anemia should be performed at all preventive pediatric health care visits with follow-up blood testing if positive. If children are at risk for IDA, a repeat Hgb/Hct should be performed as often as indicated.

Effects of Iron Deficiency

Many studies demonstrate that iron-deficient states in the first few years of life are associated with subsequent cognitive deficits well into adulthood, although direct causality is difficult to prove. Further complicating the picture of causality is that lead poisoning is often a comorbid condition to IDA. The presence of low levels of iron facilitates intestinal absorption of lead. Lead poisoning and iron deficiency have significant effects on the developing brain. Due to these factors, lead screening is an integral part of pediatric primary care. Early in the child's life, there is critical and rapid brain development; the brain grows to 95% of its adult size by 2 years old. Nutritional deficits that result in IDA or plumbism can cause lasting damage, perhaps manifesting as diminished reading and math computational ability. A child at risk for lead exposure should typically have blood drawn to determine the level of lead at 9 to 12 months old and again at 24 months old. Additional screening should be done at 15 and 30 months old based on at-risk status. Local health departments determine the prevalence of lead

poisoning in their area and issue guidelines related to blood lead screenings for targeted children in their catchment areas (Simon et al, 2014). If the initial blood lead level is 10 mcg/dL or greater on a single visit, it is a concern for public health purposes. The United States has made great strides in reducing lead toxicity through the elimination of tetraethyl leaded gasoline, banning lead-containing solder to seal food and beverage cans, and a federal rule to limit the amount of lead allowed in paint intended for household use. An estimated 99% of lead-poisoned children are identified through screening procedures rather than through clinical recognition.

Clinical Findings

History

Conduct a detailed history for hematologic disorders mentioned at the beginning of this chapter, but keep in mind that even children with moderate to severe anemia may be asymptomatic. Some key elements to remember are:

- Infants and toddlers may be irritable and restless, but this only occurs with Hgb less than 8 g/dL and is often noticed in retrospect—after treatment. Pica (appetite for nonfood items such as paper, dirt, and clay) and pagophagia (the desire to ingest ice) may be present and is common and specific for the iron-deficient state.

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- Anorexia has been reported with Hgb levels less than 8 g/dL.
- Developmental delays (mental and motor areas) and social-emotional behavioral disturbances that may be irreversible have been reported in infants and young children; adolescents may experience cognitive impairment (Mahoney, 2015).

Physical Examination

In mild to moderate iron deficiency, few symptoms are seen, but all systems must be methodically assessed. The child may appear normal, or pallor may be present. Rarely, in anemias that develop slowly, the physical examination may reveal tachycardia or systolic murmurs and signs of congestive heart failure. If symptoms of severe anemia exist, the examination should include stool guaiac testing.

Diagnostic Studies

The two most commonly used screening tests for IDA are Hgb and Hct, with Hgb being the more direct and sensitive marker of anemia compared with Hct measurements. IDA is frequently identified in routine screenings of Hgb level via capillary sampling. Excessive squeezing of the finger for capillary sample may produce inaccurate results (lower Hct), so proper technique is essential. Venous sampling is the most reliable indicator. IDA is likely if there is a low Hgb level for age (in the range of 8 to 11 g/dL), a history of low iron intake, and no concern about other possible causes for the anemia or the possibility of another hemoglobinopathy. Table 27-9 provides laboratory cutoff values for anemia. If the age of the child and the dietary patterns are consistent with IDA and there is microcytic anemia (Hgb >9 g/dL), many clinicians begin a trial of iron supplementation for 4 to 6 weeks without further diagnostic testing and then follow the child's Hgb and reticulocyte counts. The RDW is the earliest marker of iron deficiency. Serum ferritin is low with iron deficiency (Powers and Buchanan, 2014).

Mild to moderate IDA is characterized by Hgb levels of 7 to 10 g/dL. Levels less than 4 g/dL necessitate consultation with a hematologist; and levels of 7 or less should be carefully evaluated as to whether the child needs referral to hematology.. If treatment with oral iron supplements is effective, follow-up Hgb in 1 month should reveal a minimum 1 to 2 g/dL improvement, but the reticulocyte count will increase to greater than 3% in 48 to 96 hours (Lerner and Sills, 2011).

There is a high comorbidity between IDA and lead poisoning (Pb >10 mcg/dL) because lead molecules block iron from binding to protoporphyrin by inhibiting essential mitochondrial membrane function and interfering with enzymes. In low iron states, the lack of iron results in an accumulation of erythrocyte protoporphyrin in blood.

The typical profile for IDA is:

- Microcytic, hypochromic RBCs on CBC
- Low or normal MCV; low to normal RBC number
- High RDW (>14%)
- Low ferritin
- High TIBC
- Mentzer Index greater than 13 (IDA more likely)