Infectious Diseases

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PUBLIC HEALTH CONSIDERATIONS: PREVENTION OF INFECTIOUS DISEASES

Infection Control and Prevention

Childcare Centers

- Immunization: Required for all enrollees and staff
- Assist children with toileting and hand hygiene
  - Hand washing with soap and water, alcohol-based antiseptic is acceptable if > 24 months old
  - Careful food preparation and diaper changing
  - Disinfecting environmental surfaces prevents diarrheal diseases
  - Respiratory etiquette (sneeze or cough into elbow)
- Exclusion and return policies:
  - Use gloves when contacting body fluids
  - Do not exclude because of lice, ringworm, conjunctivitis without fever or behavior change, rash without fever

Common organisms in childcare centers

- *Shigella* infection
  - Transmitted from infected feces (person-to-person contact)
  - Do: Stool bacterial cultures for any symptomatic contact
  - Know: If *Shigella* infections are confirmed, administer appropriate antibacterial treatment
  - Return to childcare center if diarrhea has resolved and stool culture is negative
- Nontyphoidal *Salmonella* species
  - No antibiotic is required except:
    - Infants younger than 3 months of age
    - Immunocompromised host
  - Infected individuals should be excluded from childcare until symptoms resolve
- *Salmonella* serotype Typhi
  - Treatment is indicated for infected individuals
  - Return to childcare center
    - 5 years of age or younger: 48 h after antibiotic treatment
    - Older than 5 years: 24 h after the diarrhea has resolved
- Other risk of infection: e.g., *Giardia*; rotavirus; cryptosporidiosis; respiratory syncytial virus (RSV); parainfluenza virus; adeno,

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O. I. Naga (ed.), *Pediatric Board Study Guide*, https://doi.org/10.1007/978-3-030-21267-4_9

rhino, and corona viruses; *Haemophilus influenzae*, *pneumococcal*, hepatitis A, and cytomegalovirus infections

Hospital and Office

- Standard precautions are indicated in the care of all patients including:
  - Hand hygiene before and after each patient contact
  - Protective equipment when needed

Preventive methods

- Alcohol-based products preferred because of their superior activity and adherence
- Soap and water are preferred when hands are visibly soiled or exposed to a spore-forming organism (*Clostridium difficile* is the most common), or for norovirus
- Gloves, isolation gowns, masks, and goggles for any exposure to body fluids, contaminated materials, and sharps
- Strict aseptic technique for all invasive procedures and for catheter care
- Separate well and sick children areas in medical offices

Examples of infections and agents requiring transmission-based precautions

- Contact precautions, e.g., RSV, *C. difficile*, other infectious diarrhea, and *Staphylococcus aureus*
  - Gloves and gowns are required when there is direct patient contact
- Droplet precautions, e.g., influenza, *Neisseria meningitidis*, mumps, and *Bordetella pertussis*
  - Use of a surgical mask is required
  - A single room is preferred
  - Remember all office and hospital staff should receive an annual influenza immunization
- Airborne precautions, e.g., *Mycobacterium tuberculosis*, measles, varicella (with contact precautions), severe acute respiratory syndrome (SARS)
  - Negative pressure airborne infection isolation room
  - Room air needs 6–12 changes per hour or recirculation through a high-efficiency particulate air (HEPA) filter
  - Certified N95 fine particle respirator mask or similar sealing mask

Prevention of Infection Through Breastfeeding

- Exclusive breastfeeding for the first 4–6 months is recommended by American Academy of Pediatrics (AAP)
- Interrupt breastfeeding for:
  - Breast abscess or cellulitis with direct contact with infant's mouth; can continue on other side
  - Women with tuberculosis (for first 2 weeks of treatment, then acceptable)
  - Maternal HIV (except in resource-limited settings)
  - Maternal human T cell lymphotropic virus (HTLV) types 1 or 2
- Do not interrupt for maternal hepatitis B

Immunologic characteristics of breast milk

- Postpartum colostrum contains high concentrations of antibodies and other infection-protective elements
- The actual antibodies against specific microbial agents present in an individual woman's milk depends on her exposure and response to the particular agents
- Lactoferrin: Limits bacterial growth by iron chelation
- Lysozyme: Bacterial cell wall lysis
- Lactalbumin: Enhances *Bifidobacterium* growth and modulates immune system
- Casein: Limits adhesion of bacteria and facilitates the growth of *Bifidobacterium*
- Carbohydrates: Enhance the growth of probiotics
- Lipids: Lytic effect on many viruses and are active against *Giardia*

Absolute contraindication of breastfeeding

- Maternal HIV infection (except in resource-limited settings)
- HTLV1 and HTLV2
- Tuberculosis (active, untreated pulmonary tuberculosis, until effective maternal treatment for the initial 2 weeks or the infant is receiving isoniazid)
- Herpes simplex virus (HSV) infection on a breast (until the lesions are cleared)
- Breast abscess or cellulitis with direct contact with infant's mouth; can continue on other side

Prevention of Vector-Borne Disease

- Chemoprophylaxis before traveling to endemic areas, e.g., atovaquone/proguanil for malaria should be given before traveling to endemic areas
- Use mosquito netting (bed-net) during sleep in tropical areas
- Use protective clothing
- Repellents, e.g., DEET (> 20%) applied to children should be used to prevent tick and mosquito bites
  - Insecticide should not be applied to children's hands because of risk of ingestion
- Use of occlusive clothing to prevent mosquito and tick bites is effective
- Remove tick from skin immediately, then wash with soap and water
- Keep pets tick-free
- Immunization against disease (e.g., yellow fever, typhoid, cholera, Japanese encephalitis, meningococcus, rabies if high risk) when traveling to endemic area at least 2 weeks before departure

Recreational Water Use

- Exposure to contaminated water can cause diarrhea and other infections, e.g., swimmer's ear
- *Cryptosporidium* is most common cause of recreational water-associated outbreaks; *Giardi*a is second, also *Shigella* is another cause
- Regularly test home pools for pH, free chlorine, or bromine
- People with diarrhea should not participate in recreational water activities
- Children with diarrhea should avoid swimming for 2 weeks after cessation of diarrhea (for *Cryptosporidium*)
- Avoid water ingestion
- Clean the child with soap and water before swimming
- Change diapers in the bathroom

Antimicrobial Resistance

- Use of antimicrobials is the most important factor that leads to antimicrobial resistance, including in patients and in agriculture
- Diseases for which antibiotics are not appropriate: Nonspecific cough, bronchitis, viral pharyngitis, common cold

Infections in Immunocompromised Hosts

Malnutrition

- Malnutrition increases susceptibility to infections; repeat or chronic infections contribute to malnutrition. A vicious cycle
- Malnutrition increases severity of disease and risk of poor outcomes
- Malnutrition increases risk of bacterial versus viral diarrhea
- Malnutrition increases risk of pneumonia

Central nervous system (CNS) diseases

- Infants have immature hypothalamic thermoregulatory system and lack a central "control" of temperature, making their body temperature more susceptible to environmental temperature
- Infants with CNS infection affecting thermoregulatory system may present with hypothermia

Asplenia

- Example: Sickle cell anemia, congenital or surgical asplenia
- Increased risk for bacteremia and meningitis due to encapsulated organisms like *Streptococcus pneumoniae, H. influenzae* type b (Hib), and *N. meningitidis*
- Consider daily antimicrobial prophylaxis (especially for sickle cell disease)
- Special vaccine consideration for asplenia:
  - Pneumococcal conjugate (PCV13) and polysaccharide (PPSV23) vaccines are indicated
  - Following PCV13 series, PPSV23 should be given at 24 months of age and 5 years later
  - Meningococcal conjugate vaccine (MCV) should be given at 2 months of age (MenACWY-CRM, e.g., Menveo). Revaccinate 3 years later and then every 5 years.
  - (MenACWY-D, e.g., Menactra) cannot be given before 2 years of age

Malignancy

- Fever and neutropenia (absolute neutrophil count [ANC] < 500) increase the risk of bacterial infection. Investigate with blood and urine cultures, consider chest radiograph, and treat with antibiotic for Gram-positive and Gram-negative coverage (cefepime or piperacillin/tazobactam). Consider adding vancomycin if methicillin-resistant *S. aureus* (MRSA) colonized or if skin/soft tissue infection or sepsis present.
- Major infections in patients with cancer include: bacteremia due to intestinal translocation, invasive fungal infections including *Candida* and *Aspergillus*, *Pneumocystis jiroveci* pneumonia.

Burn injury

- Burn wounds are susceptible to infection with Gram-positive and Gram-negative bacteria, yeast, and viruses (HSV, varicella-zoster virus [VZV])

Indwelling central lines

- Central line-associated bloodstream infections (CLABSI) are a common complication. Obtain culture from central line **and** periphery, then begin vancomycin + cefepime or piperacillin/tazobactam
- If MRSA or methicillin-sensitive *S. aureus* (MSSA), remove the line and continue treatment.

VIRAL INFECTIONS

Cytomegalovirus (CMV)

Background

- CMV is a double-stranded DNA virus and a member of the *Herpesviridae* family
- At least 60% of the US population has been exposed to CMV
- CMV usually causes an asymptomatic infection; afterward, it remains latent throughout life and may reactivate

Mode of transmission and period of communicability

- Vertical transmission
  - CMV can be maternally transmitted: (1) transplacentally in utero, (2) at birth through infected maternal genital tract, and (3) postnatally by ingestion of CMV-positive human milk or transfusion
  - Risk decreased by the use of pasteurized human milk or freezing human milk
- Horizontal transmission
  - Exposure to CMV can occur from almost all body fluids, including:
    - Urine, saliva, and tears
    - Genital secretions, blood transfusion, and transplanted organs
  - Toddlers infected postnatally with CMV shed the virus in their urine for a mean of 18 months (range 6–40 months)
  - Healthy adults infected with CMV will shed the virus for up to several weeks

  - Shedding of CMV in toddlers in childcare centers can be as high as 70%
- Transfusion and transplantation
  - Can be eliminated by CMV-negative donors
  - Filtration to remove white blood cells (WBCs)
  - Latent form in tissue and WBCs can be reactivated many years later

Congenital CMV infection
- Microcephaly
- Periventricular calcifications (intracerebral)
- Chorioretinitis, strabismus, microphthalmia, and optic nerve atrophy
- Hypotonia, poor feeding, ventriculomegaly, cerebellar hypoplasia
- Intrauterine growth restriction
- Prematurity
- Jaundice
- Hepatosplenomegaly
- Thrombocytopenia; petechiae and purpura
- Later in childhood 7–15% will develop progressive sensorineural hearing loss
- Developmental delays

Diagnosis
- Perinatally or postnatally:
  - Confirmed by detection of the virus in urine, blood, saliva or CSF by culture or polymerase chain reaction (PCR)
  - Congenital CMV: If diagnosed in first 3 weeks of life
- Immunocompromised host:
  - Test for pp65 antigen (CMV antigenemia assay) or quantitative DNA in blood or plasma

Treatment
- Congenital CMV
  - Treatment modestly improves hearing and neurodevelopmental outcomes for infants
  - CNS disease is treated with oral valganciclovir (or IV ganciclovir) for 6 months
- CMV retinitis in HIV
  - Ganciclovir and valganciclovir are indicated for induction and maintenance therapy
- CMV pneumonitis in bone marrow or stem cell transplant patients
  - Ganciclovir plus CMV immune globulin are used together

Herpes Family Viruses (DNA Viruses)

- Epstein–Barr virus (EBV)
- HSV1, HSV2
- CMV
- VZV
- Human herpesvirus type 6 (HHV-6), aka sixth disease
- Human herpesvirus type 7 (HHV-7)
- HHV-6 and HHV-7 can both cause exanthema subitum, aka roseola
- Human herpesvirus type 8 (HHV-8, aka Kaposi sarcoma-associated herpesvirus)

Epstein–Barr Virus (EBV)

Background
- EBV or human herpesvirus-4 is a gammaherpesvirus that infects more than 95% of the world's population
- Mode of transmission primarily by oral contact with saliva
  - EBV is shed in saliva at high concentrations for more than 6 months following acute infection and intermittently at lower concentrations for life
  - Young children directly or through handling toys
  - Adolescents due to close contact such as kissing

Clinical presentation
- EBV infection in healthy person; infectious mononucleosis (EBV is the most common cause)
  - Fever
  - Exudative pharyngitis (similar to streptococcal pharyngitis but more painful)
  - Cervical lymphadenopathy, commonly anterior, and posterior cervical lymph node (may compromise the airway)

  - Splenomegaly (90%); 2–3 cm below the left costal margin is typical
  - Hepatomegaly (10%)
  - Fatigue and malaise
  - Rash
  - Typically a benign, self-limited illness in healthy persons, but can cause fatal disseminated infection even in healthy hosts
- EBV infection in immunocompromised persons (transplant, HIV)
  - Fatal disseminated infection
  - Nonmalignant EBV-associated proliferations, e.g., virus-associated hemophagocytic syndrome
  - Post-transplant lymphoproliferative disorders
  - X-linked lymphoproliferative syndrome
  - Nasopharyngeal carcinoma, Burkitt lymphoma, Hodgkin disease, non-Hodgkin lymphoma, gastric carcinoma

Diagnosis

- Heterophile antibody test (monospot)
  - Not recommended for children younger than 5 years of age as the result is not specific for acute mononucleosis
  - Helpful for older children and adolescents with mono signs and symptoms
- EBV viral capsid antigen (VCA) immunoglobulin (Ig) M and IgG serology to distinguish acute from past infection
  - No previous infection: Negative VCA IgG, negative VCA IgM
  - Acute infection: Positive VCA IgG, positive VCA IgM
  - Recent infection: Positive VCA IgG, +/– VCA IgM, positive early antigen
  - Past infection: Positive IgG, negative VCA IgM, negative early antigen, positive nuclear antigen

Management

- Ampicillin or amoxicillin may cause morbilliform rash
- Decrease immunosuppressive therapy in transplant patients if possible
- Short courses of corticosteroids for fewer than 2 weeks can be given in the following cases:
  - Tonsillar inflammation with impending upper airway obstruction
  - Massive splenomegaly
  - Myocarditis
  - Hemolytic anemia
  - Hemophagocytic lymphohistiocytosis (HLH)

Complications

- Splenomegaly:
  - Avoid strenuous activity and contact sports for 21 days after onset, then limited noncontact aerobic activity if no overt splenomegaly
  - Contact sports allowed 4–6 weeks after onset if no splenomegaly
  - Fatigue may persist for 3–6 months or longer

Herpes Simplex Virus 1 and 2 (HSV1 and HSV2)

- Characterized by neurovirulence, latency, and reactivation in the area supplied by the ganglia in which latency was established
- Reactivation induced by various stimuli (e.g., fever, trauma, emotional stress, sunlight, and menstruation)
- Spread by direct contact with lesions or infective secretions

Epidemiology

- Neonatal:
  - Exposure during passage through birth canal or ascending infection through ruptured or apparently intact membranes

  - Risk greatest with maternal primary infection near time of delivery (25–60%) versus 2% risk if recurrent maternal infection
  - Most neonatal HSV cases born to mothers with no HSV symptoms
- Children and adolescents:
  - Shed virus for > 1 week with primary genital infection (high viral concentration)
  - Shed virus for 3–4 days with recurrent infection
  - Reactivation without symptoms is common
  - Incubation period is 2 days–2 weeks

Clinical manifestations

- Neonatal (3 forms that may overlap):
  - 25%: Disseminated disease affecting mostly liver, lungs, and CNS; "sepsis" clinical picture
  - 30%: CNS disease "meningoencephalitis"
  - 45%: Skin, eye, and mouth (SEM) disease
- Children and adolescents:
  - Most primary HSV is asymptomatic; reactivation is also mostly asymptomatic
  - Gingivostomatitis is the most common clinical manifestation; usually HSV1, associated with fever, irritability, submandibular lymphadenopathy and ulcerative gums and buccal mucosa. May recur as "fever blister" or "cold sore"
  - Genital herpes: Genital vesicles or ulcers of genitalia and/or perineum, HSV1 or HSV2. Immunocompromised may have more recurrence
  - Eczema herpeticum occurs when patients with atopic dermatitis are infected with HSV, having ulcerative and/or vesicular areas on top of eczematous lesions
  - Encephalitis results from primary or recurrent HSV, with fever, altered mental status, seizures. Magnetic resonance imaging (MRI) may show temporal lobe abnormalities. CSF may show increased red blood cells, but not if early in disease course
  - Aseptic meningitis is usually mild and associated with HSV2

Herpetic Whitlow (Fig. 9.1)

- Due to autoinoculation of HSV
- Vesiculoulcerative lesions affect the pulp of the distal phalanx of the finger associated with deep-seated swelling and erythema
- Oral antiviral medications are optional and are used in extensive disease

Herpes Gladiatorum (Fig. 9.2)

- Herpes gladiatorum occurs in contact sports, e.g., wrestling and boxing

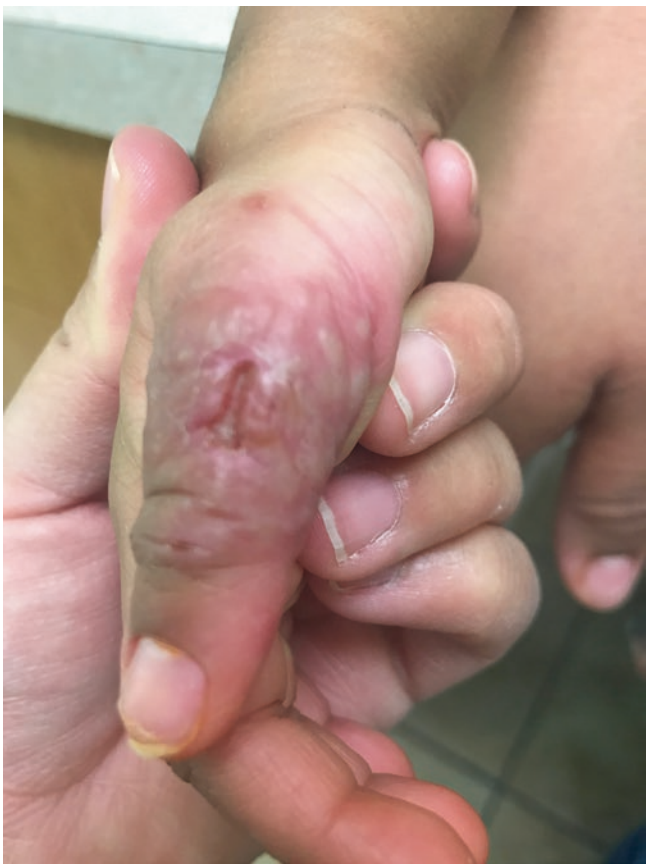

Fig. 9.1 Herpetic whitlow: Herpetic Whitlow infection in a 2-year-old with vesicular lesions, ulcer, and surrounding erythema involving the base of the thumb

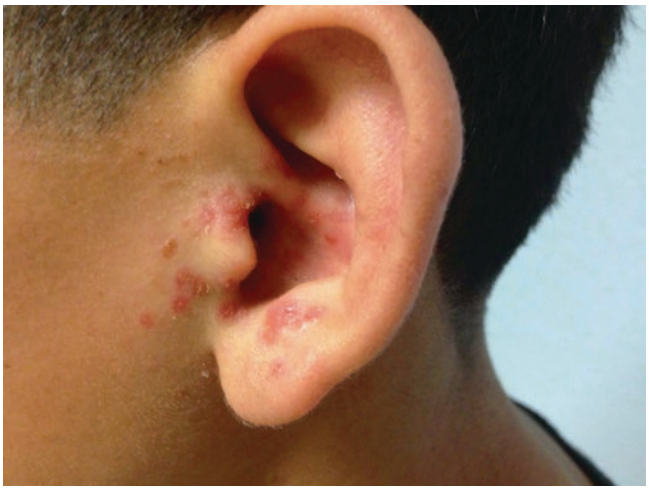

Fig. 9.2 Herpes gladiatorum: 16-year-old boy wrestling player presents with painful blisters in the left ear

- Most commonly affects exposed areas, e.g., face and upper extremities
- Patients should avoid contact sports during outbreaks until the culture or PCR results are negative
- Suppressive therapy is likely to be effective, but data about such therapy are insufficient

Treatment

- Antivirals: Acyclovir, valacyclovir, famciclovir
- Neonatal: IV acyclovir for 14 days (SEM disease) or 21 days (disseminated disease or CNS disease); begin therapy before test results return
  - All infants with any type of HSV should have ophthalmologic assessment
  - Repeat lumbar puncture near end of therapy for HSV CNS disease and continue treatment if positive
  - Oral acyclovir suppressive therapy indicated for 6 months
- Genital, primary: Oral acyclovir for 7–10 days
- Genital, recurrent: Same as primary; can be used routinely or at start of an episode
- Mucocutaneous, immunocompromised: IV acyclovir
- Mucocutaneous, healthy host: May benefit from therapy, oral acyclovir for 5–7 days
- CNS encephalitis: IV acyclovir for 21 days

Varicella-Zoster Virus (VZV): Chickenpox and Shingles

Background and epidemiology

- VZV is herpesvirus family member
- Incubation period is 2 weeks
- Contagious 1–2 days before rash until all lesions are crusted over
- Spreading via airborne or direct contact with mucosa of upper respiratory tract or conjunctiva, and transplacental passage
- VZV is the cause of varicella (chickenpox) and herpes zoster (shingles)
- Varicella is more contagious than zoster
- Immunity to varicella is lifelong; reactivation as zoster infection is possible
- Immunocompromised at higher risk for severe disease and disseminated infection

Clinical presentation

Varicella (Chickenpox)

- The prodrome: low-grade fevers, headaches, and malaise
- Skin lesions initially appear on the face and trunk
- Lesions start as red macules and pass through stages of papules, vesicles with central umbilication, pustules, and then crust over
- The vesicle on the erythematous base of a lesion leads to its description as a "pearl" or "dewdrop on a rose petal"
- Lesions predominate in central skin areas and proximal upper extremities with relative sparing of distal and lower extremities
- Chickenpox generally is a benign self-limited illness, and is more severe in adults, adolescents, and infants compared to older children

- Complications include bacterial superinfection, especially with *Streptococcus pyogenes,* which can progress to cellulitis, myositis, and sepsis
- Pneumonia (major cause of morbidity and mortality), hepatitis, and thrombocytopenia are also possible
- Immunocompromised patients may experience visceral dissemination, encephalitis, hepatitis
- Neonates whose mothers develop varicella 5 days to 2 weeks before delivery have increased risk of death due to diminished maternal antibodies

Herpes zoster (shingles)

- Latency establishes in sensory ganglia infected during primary VZV or vaccination
- Shingles classically is a unilateral rash consisting of grouped vesicles on an erythematous base, covering 1–3 adjacent dermatomes, often accompanied by pain and pruritus (Fig. 9.3)
- Postherpetic neuralgia, pain after rash resolves, is uncommon in pediatrics

Treatment of VZV

- Healthy host: Keep fingernails short, topical calamine for itching, acetaminophen for fever, avoid salicylates due to risk of Reye's syndrome
- Immunocompromised host: IV acyclovir within 24 h of rash onset
- Unvaccinated > 12 years old, chronic skin or lung disorders: Acyclovir or valacyclovir

Prevention in immunocompromised exposure

- VariZIG (varicella-zoster immune globulin) or IVIG within 4 days (ideal) and up to 10 days post-exposure. Isolate for 28 days after exposure
- Alternative is oral acyclovir or valacyclovir starting 7 days after exposure. Isolate for 21 days after exposure

General prevention

- Children can return to school if all lesions are crusted
- Airborne isolation for hospitalized patients with varicella
- Cover skin lesions for patients with herpes zoster
- Immunize all persons who lack evidence of immunity
- Immunize exposed, unvaccinated persons from 3 to 5 days post-exposure

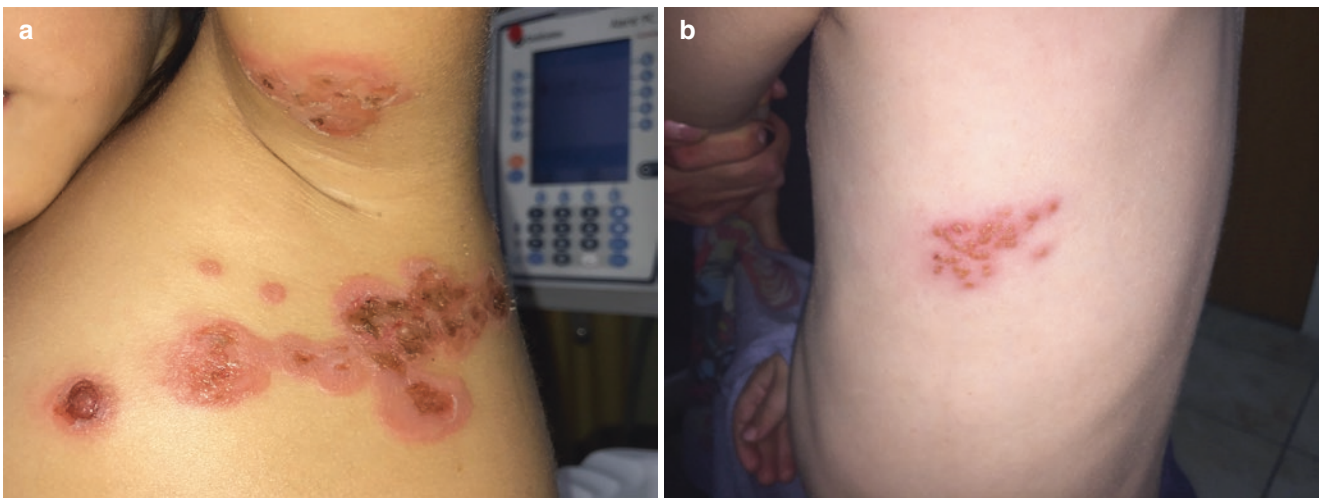

Fig. 9.3 (**a**) 2-year-old girl with painful herpes zoster rash (shingles). (**b**) 4-year-old boy with herpes zoster (shingles)

- Discharge or isolate exposed patients without evidence of immunity
- VariZIG given to the baby born to mother who develops illness from 5 days before until 2 days after birth
- IV acyclovir is indicated for varicella infection in infants born to mothers who experience chickenpox from 5 days before until 2 days after delivery

Human Herpesvirus Type 6 (HHV-6)

Including Roseola Infantum (Exanthem Subitum)

Background

- Commonly affects children ages 6–18 months old

Clinical presentation (Fig. 9.4)

- Typically, a nonspecific febrile illness without rash
- Very high fever for 3–7 days, followed by maculopapular rash in 20% after fever resolves; rash can last hours to days
- They may have lymphadenopathy, vomiting, diarrhea, febrile seizure, or respiratory symptoms

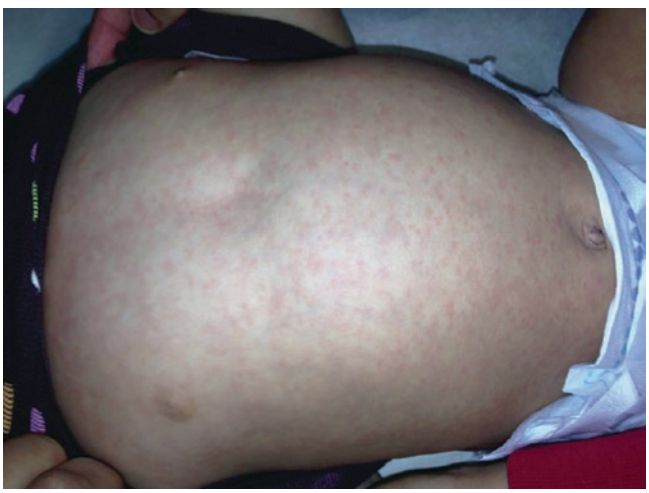

Fig. 9.4 Roseola infantum: 9-month-old boy afebrile presents with small, pale pink papules and blanchable, maculopapular exanthem, had high fever for 3 days before the rash

- 10 to 15% of children with primary HHV-6 will have febrile seizures
- Primary infection establishes latency that may reactivate (all herpes viruses)
- Immunocompromised may develop bone marrow suppression, graft rejection, pneumonia, encephalitis, hepatitis
- Incubation is 9–10 days

Management

- Mainly supportive for healthy host
- For immunocompromised, may consider ganciclovir, valganciclovir, or foscarnet

Human herpesvirus-7 (HHV-7)

- Childhood febrile illness, also causes exanthem subitum (roseola)
- Most infections are asymptomatic
- Like HHV-6, establishes latency that may reactivate
- 85% of healthy adults have evidence of past infection

Human herpesvirus-8 (HHV-8)

- Kaposi sarcoma
- A trigger for hemophagocytic lymphohistiocytosis (HLH)
- Multicentric Castleman disease

Other DNA Viruses

- Parvovirus B19
- Adenovirus

Parvovirus B19

Erythema Infectiosum/Fifth Disease

Background

- Incubation period 4–14 days
- Mode of transmission: Respiratory secretions

Clinical presentation

- *Erythema infectiosum*
  - Mild constitutional symptoms, e.g., fever, malaise, myalgia, and headache

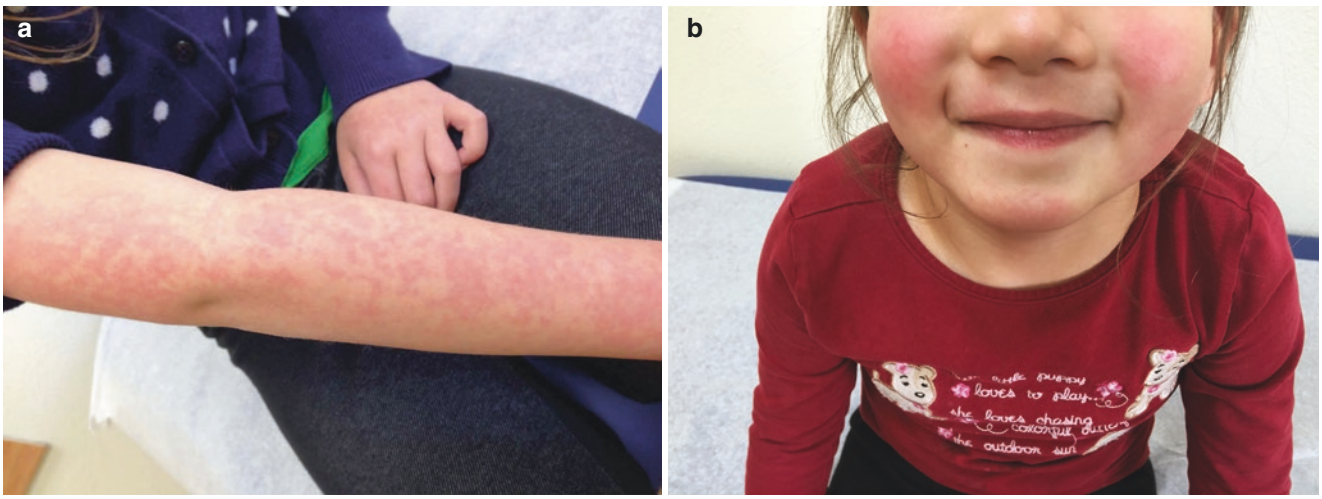

Fig. 9.5 (**a**) *Erythema infectiosum*: Erythematous maculopapular rash on the arm, which fades into a classic lacelike reticular pattern as confluent areas clear. (**b**) Classic slapped-cheek appearance of fifth disease

  - Bright red facial rash (slapped cheek appearance [Fig. 9.5])
  - Circumoral pallor
  - Lacy maculopapular rash lasting for 2–4 days begins on the trunk and moves to extremities (Fig. 9.5)
  - Rash may be pruritic, does not desquamate, and may recur with bathing or exercise
  - Arthritis or arthralgia may occur
- Mild respiratory illness without rash
- Purpuric rash in a gloves and socks distribution
- Polyarthropathy syndrome (mostly adults)
- Chronic erythroid hypoplasia and severe anemia (HIV, immunodeficient)
- Aplastic crisis for 7–10 days
  - Occurs in persons with hemolytic disease such as sickle cell anemia, spherocytosis, and thalassemia
  - Transient low to zero reticulocytes, leukopenia
- Hepatitis and myocarditis (rare)
- Hydrops fetalis
  - 2 to 6% risk of fetal death if occurs during pregnancy; increased risk earlier in pregnancy
- Can be asymptomatic or subclinical

Remember

- Rash is not infectious, and children can go to school without restrictions

Adenovirus

Background

- Mode of transmission:
  - Person to person through contact with conjunctival and respiratory secretions
  - Fecal–oral transmission and via fomites
- Outbreaks usually are concentrated in winter, spring, and early summer; otherwise all year round
- Persist in environment and resist disinfectants
- Incubation period:
  - Respiratory infections from 2 to 14 days
  - GI disease from 3 to 10 days

Clinical presentation

- Upper respiratory tract infection:
  - Nonspecific febrile illness
  - Otitis media
  - Pharyngitis
  - Exudative tonsillitis
  - Pneumonia

- Follicular conjunctivitis (clinically similar to enterovirus conjunctivitis)
- Gastroenteritis
- Hemorrhagic cystitis
- Pharyngoconjunctival fever:
  - Fever, tonsillitis (sometimes suppurative)
  - Follicular conjunctivitis, coryza, and diarrhea
  - Cervical and preauricular lymphadenopathy is common
  - Generalized rash in association with fever, conjunctivitis, and pharyngitis can be mistaken for Kawasaki disease

Laboratory

- PCR (preferred), antigen detection, and viral culture
- Persistent and intermittent shedding complicates diagnostics

Management

- Supportive treatment in healthy host
- Consider cidofovir in immunocompromised with severe disease

Respiratory viruses

- Influenza
- Parainfluenza
- Respiratory syncytial virus
- Human metapneumovirus
- Rhinovirus
- Coronavirus

Influenza Virus

Background and epidemiology

- Influenza is an orthomyxovirus
- Types: A, B, and C. Types A and B are responsible for epidemic disease in humans
  - Influenza A viruses found in humans are H1N1 and H3N2
  - Some strains are more virulent, causing more severe disease than others
  - Frequent antigenic change, or antigenic drift:
    - Point mutations causing minor antigen changes, leads to new influenza virus strains that cause seasonal epidemics in winter
    - Reason for constant reformulation of influenza vaccine to include new virus strains
  - Occasional antigenic shift:
    - Mutations causing major antigen changes, leads to new influenza virus subtypes that contain a new hemagglutinin (HA) or neuraminidase (NA), causing pandemics
    - Most recent pandemic: 2009–2010 caused by influenza A (H1N1)
- Mode of transmission
  - Large-particle respiratory droplet between individuals (cough, sneeze)
  - Contact with contaminated surfaces; fingers then touch face
  - Incubation period is 1–4 days
- Most outbreaks occur in schools
- Hospitalization rates are highest in children < 2 years and elderly > 65 years

Clinical presentation

- Fever, malaise, myalgia, headache, nonproductive cough, sore throat, and rhinitis
- Children may also develop croup or bronchiolitis
- Younger children may have febrile seizures or sepsis-like symptoms
- Uncomplicated influenza disease typically resolves within 3–7 days

Complications

- Primary viral pneumonia
- Secondary bacterial infections such as pneumonia (*S. aureus* and *S. pneumoniae*)
- Sinusitis and otitis media
- Encephalitis
- Underlying medical conditions such as asthma, diabetes, sickle cell, immunosuppression, neurologic disorders, or congenital

heart disease increase risk for complications, including hospitalization

Diagnosis

- Reverse transcription-PCR and multiplex PCR (testing for multiple respiratory viruses at once)
- Rapid antigen-detection tests, immunofluorescence
- Nasopharyngeal (NP) swab specimens have highest yield
- For hospitalized patients with lower respiratory tract disease, obtain endotracheal or bronchoalveolar lavage (BAL) specimen even if NP negative

AAP immunization guidelines

- Annual vaccination of all children ages 6 months through 18 years before the start of influenza season
- Regardless of seasonal epidemiology, children 6 months through 8 years of age who previously have not been immunized against influenza require two doses of trivalent or quadrivalent inactivated influenza vaccine or live-attenuated influenza vaccine (LAIV) administered at least 4 weeks apart to produce a satisfactory antibody response
- Children > 9 years and those who have received two doses in a previous year receive a single dose annually
- Special emphasis for those with underlying medical conditions, including asthma, hemodynamically significant cardiac disease, HIV, persons on aspirin therapy, sickle cell, diabetes, renal disease, pregnancy
- Egg allergy is not a contraindication to influenza vaccine! (but was in the past….)

Treatment

- Prophylaxis with oseltamivir or zanamivir can be given at the same time as immunization and should be considered for immunosuppressed, unimmunized, close contacts of persons at high risk for complications, and for all when seasonal vaccine does not match circulating strains
- Children who have influenza and are at high risk for complications, regardless of the severity of their illness
- Healthy children who have moderate-to-severe illness
- Three antivirals used in pediatrics:
  - Oseltamivir is administered orally, approved for > 2 weeks old; most common adverse effects are nausea and vomiting, although neuropsychiatric events have been reported
  - Zanamivir is inhaled, approved for treatment (age > 7) and prophylaxis (age > 5)
  - Baloxavir in children ≥ 12 years administered as a single oral dose
- Adamantanes (amantadine and rimantadine) no longer recommended due to resistance

Avian Influenza H5N1

Background

- Reported cases were in south Asia, Iraq, Turkey, and Egypt
- Highly pathogenic strain in birds and poultry
- Not a human strain

Mode of transmission

- Humans who have close contact with infected birds or poultry
- Visiting market selling live infected birds

Clinical presentation

- Severe lower respiratory disease in infected persons

Prevention

- H5N1-specific vaccine (developed and approved)
- Avoid visiting markets where live birds are sold
- Thorough cooking inactivates the virus, but avoidance of poultry if there a concern is more appropriate

Parainfluenza Virus (PV)

Background and epidemiology

- Parainfluenza viruses are paramyxoviruses distinct from the influenza family
- Previous infection does not confer immunity, so reinfection can occur
- Transmitted via contact with NP secretions and respiratory droplets and fomites
- Seasonal patterns of transmission: PV1 and PV2 occur in fall, PV3 occurs in spring, and PV4 occurs year-round
- Children shed virus for 1 week before symptoms and for 1–3 weeks after symptoms resolve
- Incubation period is 2–6 days

Clinical manifestation

- May cause clinical syndrome similar to influenza
- Major cause of laryngotracheobronchitis (croup) in children (see "Respiratory" section)
- Can also cause pneumonia, bronchiolitis, and otitis media
- Most parainfluenza infections are self-limited, but immunocompromised can have severe pneumonia and disseminated disease

Treatment

- Supportive care, as most infection is self-limited
- Corticosteroids lessen severity, complications, and need for hospitalization
- Nebulized racemic epinephrine for severe croup with significant inspiratory/expiratory stridor and retractions

Respiratory Syncytial Virus (RSV)

- Infection with RSV, the most common cause of bronchiolitis (See Chap. 20 "Pulmonology")

Prevention

- Palivizumab: Humanized monoclonal immunoglobulin, recombinant DNA technology
  - Reduces risk of lower tract disease in high-risk children
  - Administered every 30 days during RSV season (max 5 doses/season)
  - Considered for first 1–2 years of life
  - Indicated for:
    1. Preterm infants with chronic lung disease
    2. Infants with hemodynamically significant congenital heart disease
    3. Preterm infants < 29 weeks gestational age
    4. Anatomic pulmonary abnormalities or neuromuscular disorder
    5. Profoundly immunocompromised children

Human Metapneumovirus

Background and epidemiology

- Humans are the only source
- Spread via contact with infected secretions
- A leading cause of bronchiolitis in infants
- Overlap with RSV season (winter–spring)

Clinical presentation

- Bronchiolitis indistinguishable from RSV bronchiolitis
- Can also cause pneumonia, croup, upper respiratory infection
- Secondary bacterial infection with *S. pneumoniae* can occur
- Severe disease in immunosuppressed and history of preterm delivery
- Most children have one human metapneumovirus infection before 5 years of age

Treatment

- Supportive

Rhinoviruses

Background and epidemiology

- The most common cause of common cold (25–80% of cases)
- The common cold is an acute respiratory tract infection characterized by mild coryzal symp-

toms, rhinorrhea, nasal obstruction, and sneezing
- The most common viral trigger for asthma exacerbation
- About 200 antigenically distinct viruses from 8 different genera can cause common cold (66–75%)
- Children typically have 2 episodes/year; adults have 1 episode/year

Clinical features
- Pharyngitis, nasal congestion, and discharge that goes from clear to mucopurulent
- Malaise, headache, myalgia, cough, fever
- Symptoms peak at 3–4 days and last 7 days
- Can cause otitis media, bronchiolitis, and pneumonia

Testing
- Not useful clinically
- PCR preferred, usually paired with enterovirus PCR due to genetically conserved regions

GI Viral Infection

- Norovirus (Norwalk virus) and Sapovirus
- Rotavirus

Norovirus and Sapovirus

Background and epidemiology
- Norovirus, formerly referred to as Norwalk virus, is the most common cause of epidemic nonbacterial gastroenteritis in the world
- Norovirus is the leading cause of viral gastroenteritis cases in the USA, after rotavirus vaccine introduction
- Norovirus causes death in young children and the elderly
- Sapoviruses also cause outbreaks
- Outbreaks of both occur in crowded areas (schools, long-term care facilities, cruise ships)
- Transmission is fecal–oral or vomitus–oral, contaminated food/water, contaminated surfaces, airborne transmission of vomitus documented
- Highly resistant to environmental decontamination, including alcohol hand cleansers
- Incubation period is 12–48 h
- Shedding may last 4 weeks in healthy host, and > 6 months in immunocompromised

Clinical presentation
- Abrupt onset of nausea and vomiting (profuse, nonbloody, nonbilious) more common in adults
- Watery diarrhea (non-bloody) may be the only symptom in children
- Abdominal cramps
- Headaches
- Low-grade fever is common
- Myalgias and malaise
- Chronic gastroenteritis in immunocompromised
- Symptoms last 24–48 h, longer in children, immunocompromised, and elderly

Rotavirus

Background and epidemiology
- Causes severe acute gastroenteritis
- Shed in stool days before and after clinical illness
- Transmitted fecal–oral, possibly respiratory
- Late winter to early spring transmission
- Stable in environment for weeks to months
- Rotavirus was most common viral cause of acute gastroenteritis until vaccine introduction that reduced hospitalizations by 75% for children < 5 years

Clinical presentation
- Acute onset vomiting, then 24 h later severe watery diarrhea
- Up to 33% have high fever
- First infection is more severe
- Causes dehydration, electrolyte imbalance, and metabolic acidosis
- Symptoms last 3–7 days

- Immunocompromised may have severe, prolonged, and fatal symptoms

Diagnosis

- Antigen assay testing (enzyme immunoassay, chromatographic immunoassay, latex agglutination)

RNA Viruses

- Enterovirus
- HIV
- Measles
- Mumps
- Rubella
- Rabies
- Arboviruses

Enteroviruses (Non-polio Viruses and Poliomyelitis)

Non-polio Viruses (Echovirus, Coxsackievirus, and Numbered Enteroviruses)

Background and epidemiology

- More common in the summer and fall
- Humans are the only known reservoir for human enteroviruses
- Enteroviruses transmitted by the fecal–oral route and respiratory route
- Survive in environment for long periods
- Outbreaks can occur
- Most severe disease in infants and young children
- Viral shedding in stool (weeks to months) and respiratory secretions (1–3 weeks)

Clinical manifestations

- Meningitis/encephalitis
  - Enterovirus is the most common cause of meningitis in pediatrics (bacterial or viral)
  - Meningitis commonly caused by echovirus
  - Common in older children
  - Fever, headache, photophobia, and nuchal rigidity, CSF pleocytosis
  - Severe complications: Seizure, hemiparesis, hearing loss, and mental deterioration
  - No signs of toxicity (hypotension, hypoperfusion) as in bacterial meningitis
  - Best diagnostic test: CSF enterovirus PCR
- Herpangina
  - Caused by many enteroviruses, including coxsackievirus type A
  - Sudden onset of high fever in children 3–10 years of age, and can be associated with vomiting, malaise, myalgia, and backache
  - Poor intake, drooling, sore throat, dysphagia, and dehydration may occur
  - Oral lesions:
    - One or more small tender papular pinpoint vesicular lesions, on erythematous base on anterior pillars of the fauces, soft palate, uvula, tonsils, and tongue, then ulcerate in 3–4 days
- Hand, foot, and mouth disease (Fig. 9.6)
  - Mostly caused by coxsackie A16 and enterovirus 71
  - Fever (may be present)
  - Oral vesicles and ulcers on buccal mucosa and tongue
  - Painful erythematous vesicles on hands and feet; it may affect the groin and buttocks
  - Usually last for 7–10 days
  - Most common complication is dehydration due to odynophagia
- Acute hemorrhagic conjunctivitis (similar to adenovirus conjunctivitis)
  - Subconjunctival hemorrhage
  - Swelling, redness, and tearing of the eye
  - Resolves spontaneously within 7 days
- Myocarditis/pericarditis
  - Commonly caused by coxsackievirus B or echovirus
  - Common symptoms: Shortness of breath, chest pain, fever, and weakness
- Congenital and neonatal infection
  - Sepsis-like syndrome associated with maternal enterovirus infection and lack of maternal immunity

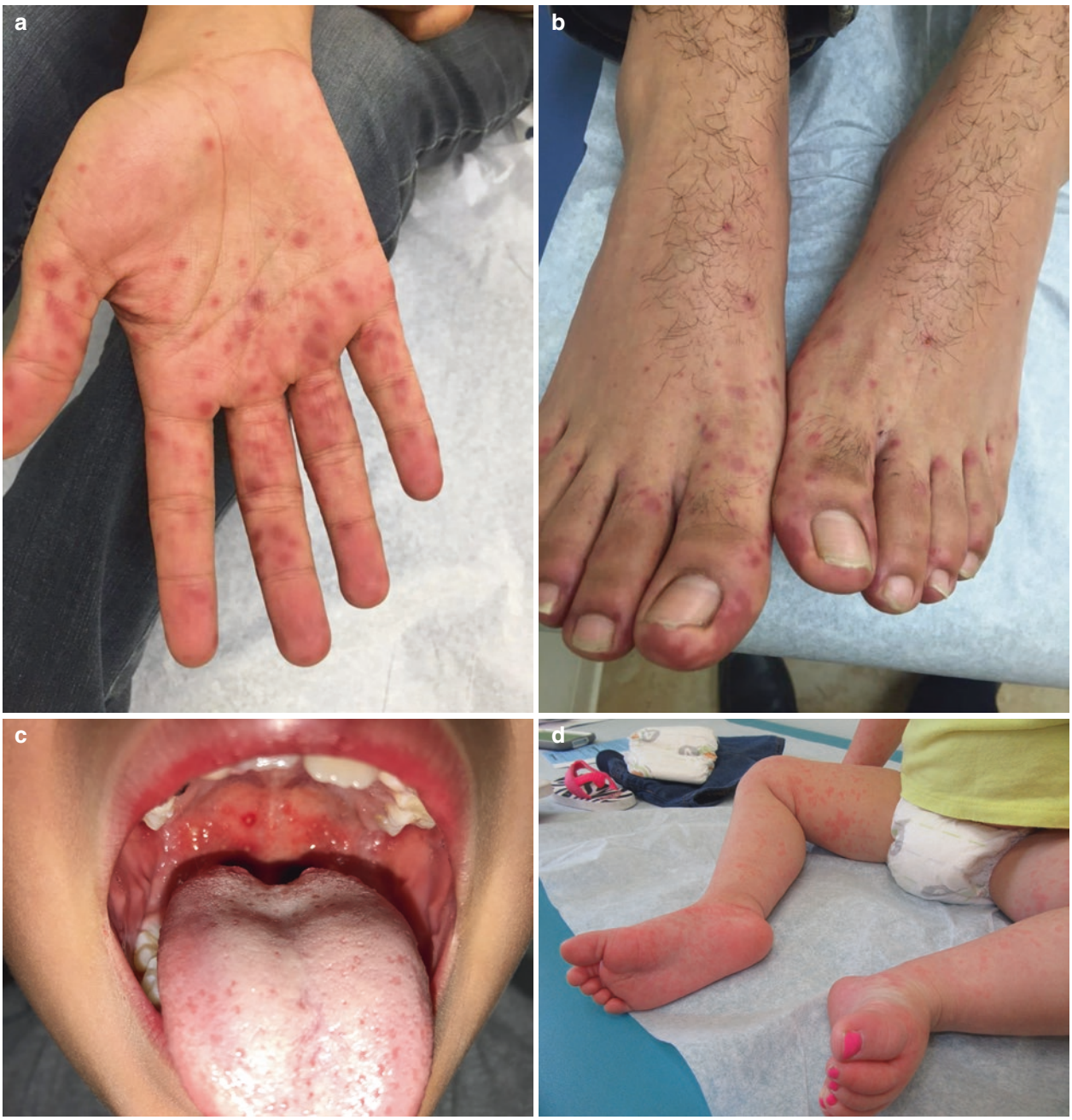

Fig. 9.6 Hand, foot, and mouth disease. (**a**) Tender macules in the hand. (**b**) Tender macules and vesicles in both feet. (**c**) Multiple painful vesicles on the hard palate. (**d**) Erythematous macules all over the body and feet in an 18-month-old who has fever and oral ulcers

  - Can range from mild febrile infection to encephalitis and negative bacterial culture
  - Can cause hepatic necrosis

Diagnosis

- PCR from rectal swab, stool, throat, nasopharynx, conjunctiva, trachea, blood, urine, tissue biopsy, and CSF
- Most respiratory panels with multiplex PCR do not distinguish enterovirus from rhinovirus due to genetic similarity and testing for a shared, conserved region in genome
- Enterovirus 71 often has negative PCR testing

Treatment

- Supportive, and IVIG can be considered for immunocompromised to reduce illness and duration of shedding

Poliomyelitis

Background and epidemiology

- Humans are the only reservoirs
- Three serotypes: Types 1, 2, and 3; type 2 eradicated globally; type 3 not seen since 2012; only type 1 is currently circulating
- Paralytic disease caused by wild type or live, oral vaccine virus
- Stable in liquid environment (pools, ponds, etc.)
- After illness, virus persists in throat (1–2 weeks) and GI tract (3–6 weeks)
- Incubation period 3–6 days; paralysis occurs 1–3 weeks after exposure

Clinical presentation

- Asymptomatic infection in 70%
- Fever and sore throat in 25%
- Aseptic meningitis in 1–5%
- Flaccid paralysis in a descending manner without reflexes in < 1%
  - Follows febrile illness
  - Symmetric paralysis affecting proximal muscles
  - Cranial nerve and diaphragm/intercostal muscle involvement may affect respiration
  - 33% recover
- Affects anterior horn cells in the spinal cord

Diagnosis

- Cell culture of pharynx, stool, and CSF obtained as early as possible

Treatment

- Supportive

Human Immunodeficiency Virus (HIV)

Background

- HIV is RNA virus
- Highest infectivity due to the very high (3–4 weeks) initial viremia
- Nearly all patients seroconvert within 6 months of acquiring the infection

Mode of transmission

- Transmitted by two principal modes in the pediatric age group:
- Mother-to-child
  - Transplacental transfer
  - Exposure to maternal blood, amniotic fluid, and cervicovaginal secretions during delivery
  - Postpartum through breastfeeding
- Behavioral (risk behavior in adolescent either unprotected sex or injection drugs)
- Other transmission modes include needle-stick injury, mucous membrane exposure, and transfusion

Clinical presentation

- During the "window" period:
  - Infected person has a negative HIV antibody test result, but HIV RNA testing results are usually positive
- Acute retroviral syndrome, characterized by:
  - Fever, lymphadenopathy, rash, myalgia, arthralgia, headache, diarrhea, oral ulcers, leukopenia, thrombocytopenia, and transaminitis
- Red flags for HIV infection
  - Thrush in apparently healthy child or adolescent
  - Invasive candidal infections
  - Recurrent severe infections
  - Lymphadenopathy and/or hepatosplenomegaly
  - Failure to thrive

- Parotid enlargement
- Opportunistic infections
  - *Pneumocystis jiroveci* pneumonia
  - *Mycobacterium avium* complex
  - Cytomegalovirus
  - *Toxoplasma gondii*
  - Human viscerotropic leishmaniasis

Diagnosis: Perinatal and postnatal infection

- Preferred overall test in infants and children < 18 months is HIV DNA PCR; highly specific by 2 weeks of age
  - 55% sensitivity at birth that increases to 100% by age 3 months
- Preferred test for HIV-1 infection is HIV RNA PCR because of greater clinical experience
- Some use both to obtain viral load and confirmation
- Maternal antibody transfer can complicate diagnostics
- In HIV exposed, test at delivery, 2–3 weeks, 1–2 months, and 4–6 months
- Presumed negative in children < 18 months if: Two negative HIV DNA or RNA tests from separate specimens at > 2 weeks of age, one negative HIV DNA or RNA test from > 8 weeks of age, or one negative HIV antibody test at > 6 months of age and no clinical or laboratory evidence of infection
- Definitive negative in non-breastfed < 12 months: At least 2 negative HIV DNA or RNA virologic tests from separate specimens at > 1 month and > 4 months, at least 2 negative HIV antibody tests from separate specimens at > 6 months and no clinical or laboratory evidence of infection

Diagnosis: Adult and adolescent infection

- Conduct initial serology, followed by confirmatory serology testing
- For initial serology testing:
  - Antibodies to HIV-1/HIV-2 and HIV-1 p24 antigen (fourth generation)
  - Antibodies to either HIV-1 and HIV-2 (third generation)
- For confirmatory serology testing:
  - Differential antibody testing to HIV-1 and HIV-2
  - HIV-1 Western blot and HIV-1 indirect immunofluorescence assay

Evaluation of HIV positive children

- CD4 percentage and absolute cell counts
- Plasma HIV RNA concentration (viral load)
- HIV genotype to assess for baseline resistance and mutations
- Complete blood count with differential count
- Serum chemistries with liver and renal function tests
- Lipid profile and urinalysis
- For children younger than 5 years of age, CD4 percentage is the preferred test for monitoring immune status
- Screening for hepatitis B, hepatitis C, and tuberculosis is recommended for all HIV positive patients

Treatment of HIV

- Triple-drug combination antiretroviral therapy effectively controls HIV infection

Prevention

- Breastfeeding is contraindicated in HIV positive mothers
- All exposed infants should receive 6 weeks of zidovudine
- Condoms and abstinence are the best forms of preventing sexual transmission of AIDS
- Cesarean delivery and treatment of HIV-positive mothers (especially with high viral load) decreases the risk of transmission of HIV to their infants
- Immunization of infants and children
  - Immunization schedule for HIV-exposed children is the same as for their healthy peers, with only a few exceptions:
    - Patients who have severely symptomatic illness
    - Patient with CD4 percentage of less than 15% or CD4 counts of less than 200 cells/mm^3 should not receive MMR, varicella vaccines, or other live vaccines

- Annual influenza immunization is recommended for all children older than age 6 months, but only the killed vaccine

Measles Virus

Background

- Mode of transmission: Respiratory droplets (airborne)
- Infectious for 3–4 days before the onset of morbilliform rash and 4 days after the exanthem

Diagnosis

- PCR testing, IgM detection, 4-fold rise in IgG serology, cell culture
- IgM detection is preferred test

Clinical presentation

- High fever plus coryza, cough, conjunctivitis
- Rash develops next: Erythematous, morbilliform, maculopapular rash spread from face downward and disappears the same way
- Koplik spots (white spots on oral mucosa) during prodrome
- Complications in young children and immunocompromised include otitis media, bronchopneumonia, croup, diarrhea, and death
- Death is also more common with severe malnutrition
- Severe complication: Acute encephalitis with permanent brain damage

Control and prevention

- Vaccinate non-immunes within 72 h of exposure
- Immune globulin within 6 days of exposure for non-immunes if vaccination not possible, including pregnant women, severe primary immunodeficiency, bone marrow or solid organ transplant recipient, acute lymphoblastic leukemia, HIV AIDS with severe immunosuppression, and infants whose mothers received immunomodulatory drugs during pregnancy
- HIV on antiretroviral therapy and documented measles vaccination × 2: Treat as immune
- Vaccinate all health-care personnel

Mumps

Background

- An acute, self-limited, systemic viral illness characterized by the swelling of one or more of the salivary glands, typically the parotid glands

Mode of transmission

- Contact to respiratory secretions
- Incubation period is 16–18 days

Clinical presentation

- Symptoms in the patient's history consist mostly of fever, headache, and malaise
- Within 24 h, patients may report ear pain localized near the lobe of the ear and aggravated by a chewing movement of the jaw
- Unilateral or bilateral parotid swelling (Fig. 9.7)
- Orchitis may occur after puberty; rarely causes sterility

Complications

- Rare: Arthritis, thyroiditis, glomerulonephritis, myocarditis, transverse myelitis, encephalitis, oophoritis, permanent hearing impairment

Diagnosis (Table 9.1)

- PCR from buccal swabs, throat washings, saliva, or CSF
- Viral cell culture
- Serology

Treatment

- Supportive care only
- School exclusion for 5 days from onset of parotid gland swelling

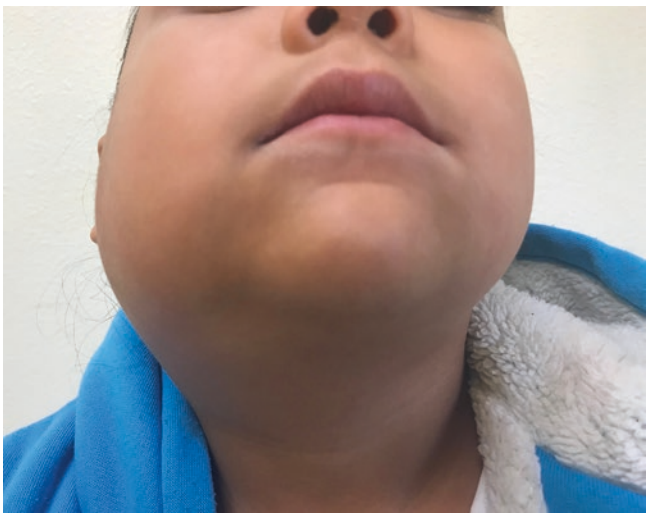

Fig. 9.7 Child with unilateral parotitis

Table 9.1 Differences between viral and bacterial parotitis

Viral parotitis (mumps)	Bacterial parotitis
Well-appearing	Toxic-appearing or ill-looking
No fever or low-grade fever	High fever
Mild tenderness	Moderate or severe tenderness
Normal labs, positive mumps IgM	Leukocytosis, shift to the left, high CRP

IgM Immunoglobulin M, *CRP* C-reactive protein

- Unimmunized children should stay out of school for 26 days after onset of parotitis in the last person with mumps in the affected school.

Rubella Virus

Epidemiology

- Transmitted via direct or droplet contact with respiratory secretions
- Peak incidence from winter to spring
- 25 to 50% asymptomatic
- Lifelong immunity
- Can transmit 3 days before to 7 days after rash appears
- Infants with congenital rubella may shed for 1 year in nasopharyngeal secretions and urine
- The USA has not experienced rubella transmission since 2004; imported cases occur
- The Americas have not experienced rubella transmission since 2009
- Incubation period: 16–18 days

Clinical presentation

- Congenital rubella syndrome
  - Constellation of congenital anomalies
    - Ophthalmologic (cataracts, microphthalmos, congenital glaucoma)
    - Cardiac (patent ductus arteriosus, peripheral pulmonary artery stenosis)
    - Auditory (hearing impairment)
    - Neurologic (meningoencephalitis, microcephaly, mental retardation, autism)
  - Neonates will have growth restriction, interstitial pneumonitis, hepatosplenomegaly, thrombocytopenia, and dermal erythropoiesis that manifests as "blueberry muffin" rash
  - Neonates may also have metaphyseal lucencies (also seen in vitamin D intoxication/hypercalcemia, rickets, scurvy, arsenic and heavy metal poisoning, leukemia, congenital syphilis, sickle cell disease, congenital hypothyroidism)
  - Increased risk of congenital defects if fetal infection occurs early in pregnancy
- Postnatal rubella
  - Subclinical or mild disease
  - Erythematous maculopapular rash
  - Forchheimer spots: Rose-colored spot on soft palate
  - Lymphadenopathy (posterior auricular or suboccipital nodes)
  - Conjunctivitis
  - Adolescent females susceptible to transient arthralgia and arthritis
  - Rare complications: Encephalitis, thrombocytopenia
- Infants with congenital rubella may shed the virus from the nasal mucosa > 1 year to susceptible contact

Rabies Virus

Background

- RNA virus classified in the *Rhabdoviridae* family
- Usually transmitted by bats and carnivores, e.g., raccoons, foxes, and coyotes
- Almost never transmitted by squirrels, chipmunks, rats, mice, rabbits, and guinea pigs

Clinical presentation

- Anxiety
- Dysphagia
- Seizures
- Encephalitis
- In most cases, progress to death

Treatment

- Prompt local flushing and cleaning the wound with soap and water
- Passive and active immunization for:
  - All persons bitten by bats, carnivores, e.g., raccoon, foxes, and coyotes
  - Open wound or scratch contaminated with saliva of infected animals or human
- No prophylaxis if domestic dog, cat or ferret that can be observed for 10 days
- Domestic animals that may be infected should be euthanized and tested
- The need for tetanus and local wound care should be considered

Passive and active immunization should be started as soon as possible

- Human rabies immunoglobulin (passive)
- Rabies vaccine (active)
- Both should be given together
- Human rabies immunoglobulin: As much as possible of the dose should be infiltrated directly to wound, the remainder of the dose should be given intramuscularly (IM)
- Rabies vaccine should be given IM in opposite arm or thigh, the first dose immediately after exposure then repeated at days 3, 7, and 14. Immunocompromised persons get an additional dose at day 28

Arboviruses (Arthropod-Borne Viruses)

- West Nile virus (WNV)
- Dengue fever

West Nile Virus

Background and epidemiology

- The most common neuroinvasive arboviral disease in the USA
- Transmitted to humans by *Culex* mosquitoes
- Transmission occurs from summer to fall
- California, North and South Dakota, Nebraska and Illinois were the most common locations in 2018
- Incubation 2–6 days
- Humans also infected via transfusion and organ transplant

Clinical presentation

- Most cases are asymptomatic (70–80%)
- May present with fever and flu-like symptoms
- Fever, headache, myalgia, arthralgia, vomiting, diarrhea, transient rash
- < 1% have neuroinvasive disease: Meningitis, encephalitis, acute flaccid myelitis
- WNV encephalitis: Altered mental status, seizures, paresis, nerve palsies, or coma in more severe cases
- Most recover completely but can take months

Diagnosis

- Anti-WNV IgM in serum or CSF may take a week to turn positive

Treatment

- Supportive

Dengue Fever

Background and epidemiology

- Arbovirus transmitted by *Aedes* mosquitoes
- History of travel to endemic area

- Endemic in Asia, Africa, Latin America, and Puerto Rico
- Transmission has occurred in Hawaii, Florida, and Texas
- Incubation period is 3–14 days

Clinical presentation

- Can be asymptomatic
- Febrile illness lasting 2–7 days: Pain in muscles, joints and bones, headache; retro-orbital pain, facial erythema, injected oropharynx, macular or maculopapular rash, leukopenia, petechiae
- Critical phase: 24–48 h with plasma leakage
- Convalescent phase: Improvement and stabilization
- Severe dengue (dengue hemorrhagic fever or dengue shock syndrome) occurs in 5% and can be deadly
- Increased risk for severe dengue with subsequent infection

Laboratory

- During febrile phase, diagnose with PCR for viral DNA or immunoassay for nonstructural protein 1 (NS-1)
- From 3 to 5 days after onset, can test for anti-dengue IgM
- Leukopenia, thrombocytopenia, and modest elevation of liver enzymes

Treatment

- Supportive

Human Papillomavirus (HPV)

Background and epidemiology

- Most adults will be infected at some time
- School-age children acquire nongenital hand and foot warts through minor skin trauma
- Genital transmission occurs skin-to-skin
- HPV causes most vulvar, vaginal, penile, and anal cancers; 70% of oropharyngeal cancers
- Rare transmission to infant during delivery
- Incubation period is months to years
- Oncogenic strains 16 and 18 are responsible for two thirds of all cervical cancers
- Nononcogenic HPV type 6 and 11 are responsible for > 90% of anogenital warts

Clinical features

- Most infections are subclinical
- Skin warts are generally painless; plantar warts can be painful
- Anogenital warts (*condylomata acuminata*) have cauliflower-like surface and can occur in groups
- Invasive cancers linked to HPV include the following locations: Oropharynx, penis, anus, cervix, vagina, and vulva
- Squamous intraepithelial lesions can be low or high grade due to persistent HPV
- Cervical intraepithelial neoplasia (CIN) is precancerous and linked to HPV
- Adenocarcinoma in situ is another endocervical precancer

Immunization

- 2 doses before 15th birthday
- Only 9-valent vaccine available in USA since 2017

BACTERIAL PATHOGENS

Gram-Positive Bacteria

S. aureus

Background and epidemiology

- *S. aureus* is the most common cause of skin and soft tissue infection and musculoskeletal infection in healthy children
- Second leading cause of healthcare-associated bacteremia (coagulase-negative staphylococci is first)
- Leading cause of secondary bacterial pneumonia in children
- Most common cause of healthcare-associated surgical site infections
- Coagulase positive
- Grapelike clusters (Fig. 9.8)

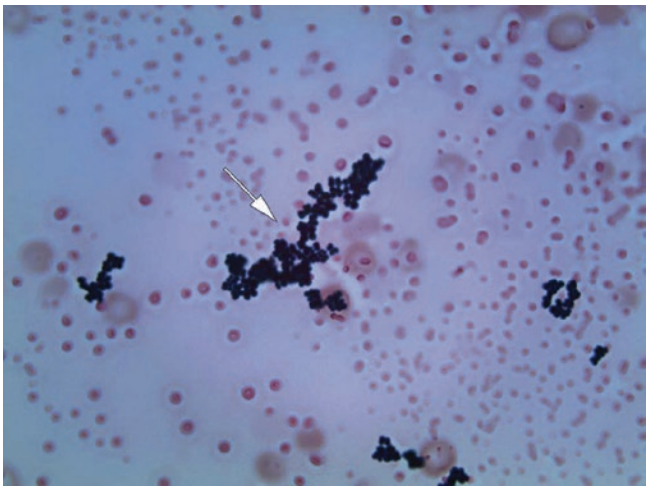

Fig. 9.8 *Staphylococci* in blood culture (Gram stain, original magnification × 1000). The bacteria are Gram-positive cocci and grow in pairs, tetrads, and clusters (*arrow*). (Courtesy of M. Nawar Hakim, MD, Department of Pathology, Texas Tech University Health Sciences Center, El Paso, Texas, USA)

- *S. aureus* colonizes the nares and skin in 30–50% of children
- Transmitted by direct contact and indirectly from other patients in hospital settings
- Can spray short distances into the air
- "Vancomycin-intermediately susceptible *S. aureus*" related to repeat vancomycin use in individuals. Vancomycin-resistant *S. aureus* rare
- Incubation period can be 12 h for postoperative toxic shock syndrome

Common staphylococcal infections

- Bullous and crusted impetigo
- Skin and soft tissue or lymph node infection
- If the organism seeds the bloodstream, dissemination to joints, bones, kidney, liver, muscles, lungs, and heart valves may occur, causing substantial morbidity and potential mortality
- *S. aureus* is the most common cause of osteomyelitis, including sickle cell disease patients (who are also at increased risk for *Salmonella* osteomyelitis)
- Children with cyanotic congenital heart disease are at high risk of staphylococcal brain abscess
- Children who undergo neurosurgical procedures, especially shunt revisions, are at high risk for staphylococcal infection
- Indwelling bloodstream catheters can be associated with staphylococcal infection and must be removed if the patient develops symptoms or positive culture

Folliculitis/Furunculosis/Carbunculosis (Fig. 9.9)

Background

- Folliculitis: Superficial inflammation centered around a follicle
- Furuncles: Bacterial folliculitis of a single follicle that involves a deeper portion of the follicle
- Carbuncle: Bacterial folliculitis that involves the deeper portion of several contiguous follicles
- Bacterial folliculitis most often caused by *S. aureus*.
- Hot tub folliculitis is usually caused by Gram-negative bacteria (most *often P. aeruginosa;* self-limited)
- Usually the child looks healthy and does not appear ill
- Abscess (< 5 cm) drainage alone is curative without antibiotics and should be performed along with a request for culture

Management of skin and soft tissue infections

- Indication for antibiotics
  - The child has high fever or other systemic symptom
  - The abscess is larger than 5 cm
  - Located in a critical location or in an area difficult to drain
  - Signs and symptoms persist following incision and drainage
- Common oral anti-staphylococcal antibiotics
  - Trimethoprim–sulfamethoxazole (TMP-SMX) effective against most MRSA
  - Cephalexin remains a good empiric choice for MSSA and group A *Streptococcus* (GAS) infections

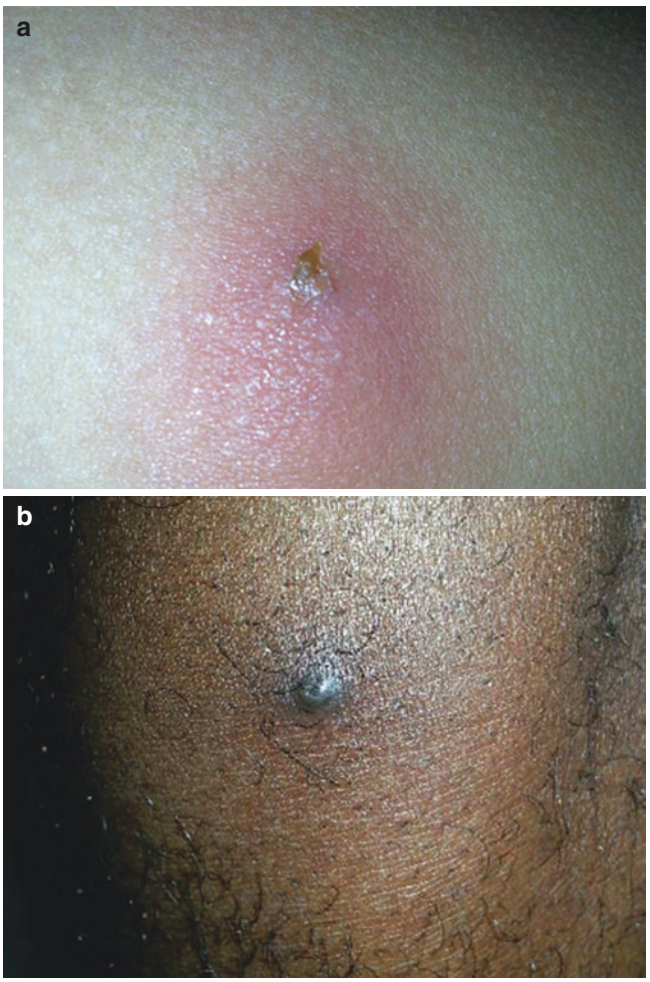

Fig. 9.9 (**a**) Furuncle: Erythematous tender papulonodule with central punctum with point of fluctuant. (**b**) Folliculitis: Superficial inflammation centered around a follicle, tender to touch

  - Clindamycin
  - Doxycycline (in children older than 8 years of age)
  - Linezolid (for resistant MRSA infections not susceptible to TMP-SMX or clindamycin)
- Recurrent staphylococcal skin infections recommendations
  - Enhanced hygiene and environmental cleaning
  - Treatment for anyone in the family who has active disease
  - Nasal and perianal mupirocin
  - Skin decolonization (chlorhexidine and/or bleach baths)
  - Treatment with antibiotic-based decolonization regimens (usually rifampin plus an additional agent) in selected cases

Toxic Shock Syndrome (TSS)

Background

- Production of toxic shock syndrome toxin-1 (TSST-1)
- Can be caused by *S. aureus or S. pyogenes* (aka group A *Streptococcus* or GAS)

Risk factors

- Tampon
- Surgical implants
- Invasive staphylococcal disease, including pneumonia and skeletal infection
- Nasal packing
- Progressive skin infection in cases caused by *S. pyogenes*

Clinical presentation

- Fever
- Vomiting
- Hypotension (abrupt onset)
- Hypocalcemia
- Watery diarrhea
- Myalgia
- Strawberry tongue
- Conjunctival hyperemia
- Rash with hand and foot desquamation
- Blood culture is usually negative if the cause is *S. aureus*
- Blood culture is usually positive if the cause is *S. pyogenes*

Treatment

- Vancomycin + clindamycin (stops toxin production) + nafcillin or oxacillin, pending culture results
- In cases of tampon-associated TSS, must be removed immediately and the recommended length of therapy is 10–14 days
- IV fluids and routine management of shock; consider IVIG for refractory shock

- Do not treat hypocalcemia unless symptomatic or electrocardiogram changes
- Anytime there is a postsurgical toxic shock, any device implanted during surgery must be removed immediately

Staphylococcal Scalded Skin Syndrome (SSSS)

Background
- SSSS (aka Ritter disease of the newborn)
- Ritter disease and staphylococcal epidermal necrolysis encompass a spectrum of superficial blistering skin disorders caused by exfoliative toxins of some strains of *S. aureus*
- SSSS differs from bullous impetigo; the exfoliative toxins are restricted to the area of infection in bullous impetigo, and bacteria can be cultured from the blister contents
- Exfoliative toxins cause separation of the epidermis beneath the granular cell layer. Bullae and diffuse sheetlike desquamation occurs
- Exotoxin is a protein and is classified as either type A or B. Most are type A

Clinical presentation
- Fever, malaise, and irritability
- Most of the patients do not appear severely ill
- Tenderness to palpation
- Dehydration may be present and can be significant
- Nikolsky sign (gentle stroking of the skin causes the skin to separate at the epidermis)
- Bacteremia may or may not present

Diagnosis
- Blood cultures are usually negative in children (but positive in bullous impetigo) and is usually positive in adults
- A chest radiograph should be considered to rule out pneumonia as the original focus of infection
- A biopsy of the affected area will demonstrate separation of the epidermis at the granular layer

Management
- Fluid rehydration is initiated with lactated Ringer solution at 20 mL/kg initial bolus
- Repeat the initial bolus, as clinically indicated, followed by maintenance therapy with consideration for fluid losses from exfoliation of skin being similar to a burn patient
- Prompt treatment with parenteral anti-staphylococcal antibiotics is essential

S. aureus Food Poisoning

Background
- The most common cause of food poisoning in the USA
- Eating contaminated food containing preformed enterotoxin
- Usually associated with meat, baked food filled with cream, and mayonnaise
- Incubation period < 4–6 h

Clinical presentation
- Nausea, vomiting, and abdominal cramps in few hours after exposure to contaminated food
- Fever may be present
- Some children can have severe dehydration

Management
- Hydration
- No antibiotic required

Staphylococcal, Coagulase-Negative

Background
- *Staphylococcus epidermidis* and *Staphylococcus saprophyticus* are examples of coagulase-negative staphylococci

- *S. epidermidis* is methicillin-resistant in most cases
- *S. epidermidis* is the most common cause of catheter-related bacteremia
- Catheter becomes contaminated when passing through the skin
- *S. epidermidis* is a common contaminant in the blood cultures

Common source of infection

- Skin, mucous membrane
- Nosocomial infection
- IV catheter
- Ventriculoperitoneal shunts
- Prosthetic devices, e.g., heart valves, joints, and pacemakers
- Bone marrow transplant
- Premature infants (intravascular catheter)

Management

- Removal of the foreign body may be necessary to clear the infection
- In neonatal intensive care unit (NICU), positive culture must be initially treated if suspicious of infection
- Draw two cultures from two different sites. To be considered positive, both cultures should be positive within 24 h.
- Vancomycin is the drug of choice

Methicillin-Sensitive *S. aureus* (MSSA)

Background

- Most of *S. aureus* strains produce beta-lactamase enzyme and are resistant to penicillin and ampicillin

Drug of choice

- Nafcillin or oxacillin (+ rifampin if indwelling foreign body)
- Treat for 3–4 days for bacteremia

Alternative drugs

- Cefazolin
- Clindamycin
- Vancomycin
- Ampicillin + sulbactam

Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Background

- MRSA strains are resistant to all beta-lactamase resistant (BLR) beta-lactam and cephalosporin antimicrobials and other antimicrobial agents

Drug of choice in MRSA cases (oxacillin MIC, 4 ≥ µg/mL)

- Vancomycin ± gentamicin or ± rifampin (multidrug resistance)
- For example, endocarditis, septicemia, and CNS infection (combination therapy is recommended)
- Alternative drugs in MRSA cases (multidrug resistance)
  - Trimethoprim–sulfamethoxazole
  - Linezolid
  - Quinupristin/dalfopristin
  - Daptomycin
  - Treat for 7–9 days for bacteremia

Community (not multidrug resistance)

- Vancomycin ± gentamicin (or ± rifampin) for life-threatening infections, e.g., endocarditis
- Clindamycin (if strain susceptible) for pneumonia, septic arthritis, osteomyelitis, skin, or soft tissue infection
- TMP-SMX for skin or soft tissue infections
- Daptomycin for vancomycin-intermediately susceptible *S. aureus*

S. pneumonia (Pneumococcal Infection)

Background and epidemiology

- *S. pneumoniae* is a Gram-positive, catalase-negative, alpha-hemolytic bacterium
- The bacteria are Gram-positive diplococci (Fig. 9.10)
- Introduction of pneumococcal conjugate vaccines (PCV7 and PCV13) significantly reduce invasive pneumococcal disease in children
- Nasopharyngeal carriage rates are 21% for industrialized countries to 90% in resource-limited settings
- Transmission is person-to-person via respiratory droplets, occurring with viral upper respiratory infections
- More common in winter
- Incubation period is 1–3 days

Risks of invasive pneumococcal disease

- The highest age-specific attack rates occur during the first 2 years of life
- Children who have sickle cell disease
- Children who have asplenia
- Congenital immune deficiencies

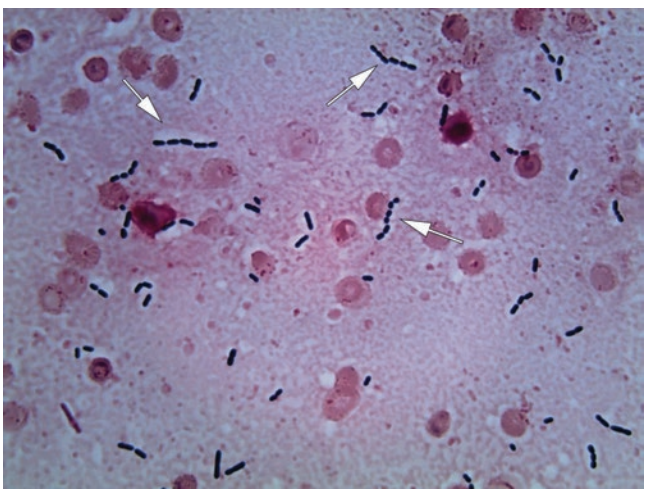

Fig. 9.10 *Streptococcus pneumoniae* (pneumococci) in blood culture (Gram stain, original magnification × 1000). The bacteria are Gram-positive diplococci (*arrows*). They are often lancet-shaped. (Courtesy of M. Nawar Hakim, MD, Department of Pathology, Texas Tech University Health Sciences Center, El Paso, Texas, USA)

- Immunosuppressive medications or bone marrow transplants also are at increased risk
- CSF leaks, e.g., neurosurgical procedures or skull fractures
- Cochlear implants
- Chronic heart or lung disease
- Diabetics

Clinical manifestations

- Common pneumococcal infections include:
  - Acute otitis media
  - Sinusitis
  - Pneumonia
  - Bacteremia (most common manifestation of invasive pneumococcal disease)
  - Meningitis (leading cause of meningitis)
- Pneumonia
  - *S. pneumoniae* is the most common bacterial cause of community-acquired pneumonia in both children and adults
  - High fever and ill-appearing
  - Cough and tachypnea
  - Respiratory distress
  - Crackles
  - Diminished breath sounds
  - Lobar consolidation may be noted on chest radiography in older children
  - Know: Infants and young children may have bronchopneumonia with a scattered distribution of parenchymal consolidation
  - Pleural fluid may be evident in some patients

Diagnosis

- Culture from blood or normally sterile body fluids such as CSF, pleural, synovial, or middle ear fluid
- PCR on blood or CSF specimen
- Positive results should have antimicrobial susceptibility testing for penicillin, cefotaxime or ceftriaxone, and clindamycin.

Treatment

- **Outpatient otitis media:** Amoxicillin (80–90 mg/kg/day for < 6 months and 6–23 months with bilateral disease) with watch and wait 48–72 h for older children

and nonsevere disease. Treat 10 days for severe disease. Treat 5–7 days for > 6 years for mild or moderate disease. Alternate therapies include amoxicillin-clavulanate, cefdinir, cefpodoxime or cefuroxime or IM ceftriaxone × 3 doses. Same dosages for sinusitis if bacterial sinusitis diagnosed. If penicillin allergic type I (anaphylaxis), use clindamycin or levofloxacin

- **Outpatient pneumonia:** Amoxicillin (90 mg/kg/day)
- **Inpatient pneumonia**: Parenteral ampicillin. Alternatives: Cefotaxime and ceftriaxone
- **Pneumococcal meningitis:** Due to antibiotic resistance concerns, treatment of proven or suspected cases mandates empiric therapy with **cefotaxime or ceftriaxone plus vancomycin** while awaiting susceptibility results. Discontinue vancomycin if susceptible to penicillin, cefotaxime, or ceftriaxone
- **Other invasive pneumococcal infections, inpatient:** Same as for pneumococcal meningitis

Streptococcus pyogenes

- Group A Streptococcus (GAS) is a Gram-positive bacterium that grows in chains (Fig. 9.11)

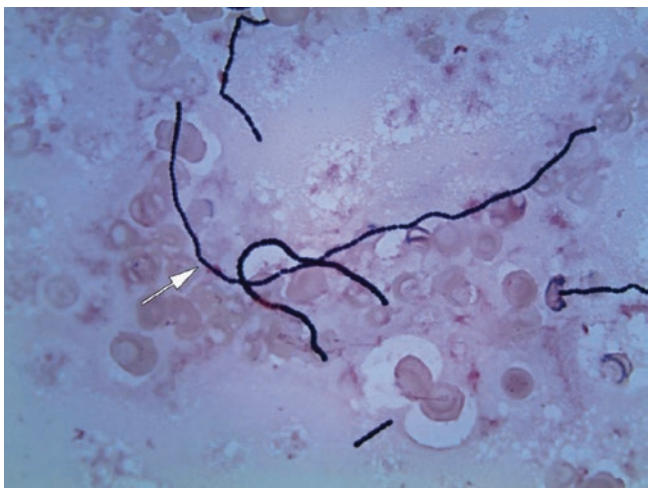

Fig. 9.11 Streptococci in blood culture (Gram stain, original magnification × 1000). The bacteria are Gram-positive cocci and grow in chains (*arrow*). (Courtesy of M. Nawar Hakim, MD, Department of Pathology, Texas Tech University Health Sciences Center, El Paso, Texas, USA)

Group A Beta-Hemolytic Streptococcus (GAS) Pharyngitis

Background and epidemiology

- Causes pharyngitis and impetigo
- Pharyngitis: Transmits via contact with respiratory tract secretions of infected person
- Impetigo: Transmits via direct contact from another person
- Increased risk for pharyngitis and impetigo with crowding
- Most often in schools, childcare centers, contact sports
- Some are chronic pharyngeal carriers
- Increased risk of invasive GAS infection in infants and elderly
- Like *S. aureus*, can cause TSS
- Rheumatic fever can develop in about 3% of untreated patients with GAS pharyngitis
- Incubation period for GAS pharyngitis is 2–5 days; for GAS impetigo is 7–10 days
- For TSS, can occur 14 h after inoculation of organism (e.g., trauma)

Clinical presentation

- Sore throat, fever, headache, and abdominal pain the most classic presentation
- Nausea and vomiting may occur
- Pharyngeal erythema and palatal petechiae (Fig. 9.12)
- Inflammation of the uvula
- Anterior cervical lymphadenopathy
- Tonsillar exudates may or may not be present

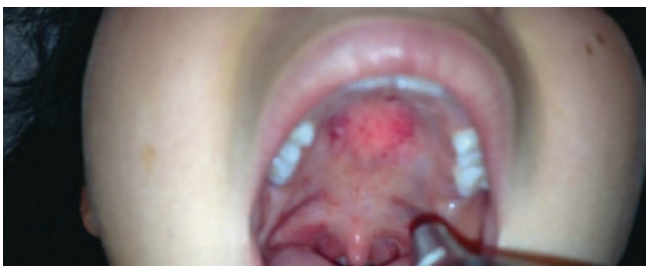

Fig. 9.12 Streptococcal pharyngitis: Palatal petechiae, rapid strep was positive in this patient

Diagnosis

- Rapid antigen detection test is highly recommended to decrease overuse of antibiotics
- Testing of asymptomatic household contacts not recommended except when contacts are at increased risk of developing sequelae of GAS infection, e.g., rheumatic fever, post-streptococcal glomerulonephritis, or TSS
- If rapid antigen detection test (RADT) positive, treat (specificity of 95%)
- If RADT is negative, do throat culture (sensitivity of 65–90%)
- Treatment of GAS sore throat as long as 9 days after the onset of symptoms still effectively prevents rheumatic fever; initiation of antibiotics is seldom of urgent importance

Treatment

- Reduces complications
- Decreases the duration of infection
- Reduces transmission to others
- Oral penicillin VK (250–500 mg twice to three times a day for 10 days) is the antibiotic treatment of choice for GAS pharyngitis
- Amoxicillin (50 mg/kg, maximum 1 g, once daily for 10 days) often is used instead of oral penicillin because of its more palatable liquid formulation
- Cephalosporins or macrolides may be used as first-line therapy in patients allergic to beta-lactam antibiotics but otherwise are not recommended as first-line therapy
- IM benzathine penicillin G 600,000 U for children who weigh < 27 kg and 1.2 million U for heavier children as a single dose (if adherence is a problem but is painful)
- Know: Treatment is indicated if a GAS carrier develops an acute illness consistent with GAS pharyngitis

Treatment to eradicate GAS carriage indications

- History of acute rheumatic fever
- Close contact who has a history of rheumatic fever
- Families experiencing repeated episodes of GAS pharyngitis
- Eradication regimens include clindamycin, cephalosporins, amoxicillin–clavulanate

Scarlet Fever (Scarlatina)

Background

- Syndrome characterized by exudative pharyngitis, fever, and scarlatiniform rash
- Caused by toxin-producing GAS found in secretions and discharge from the nose, ears, throat, and skin

Clinical presentation

- Fever may be present
- Patient usually appears moderately ill
- On day 1 or 2, the tongue is heavily coated with a white membrane through which edematous red papillae protrude (classic appearance of white strawberry tongue) (Fig. 9.13)
- By day 4 or 5, the white membrane sloughs off, revealing a shiny red tongue with prominent papillae (red strawberry tongue)
- Red, edematous, exudative tonsillitis

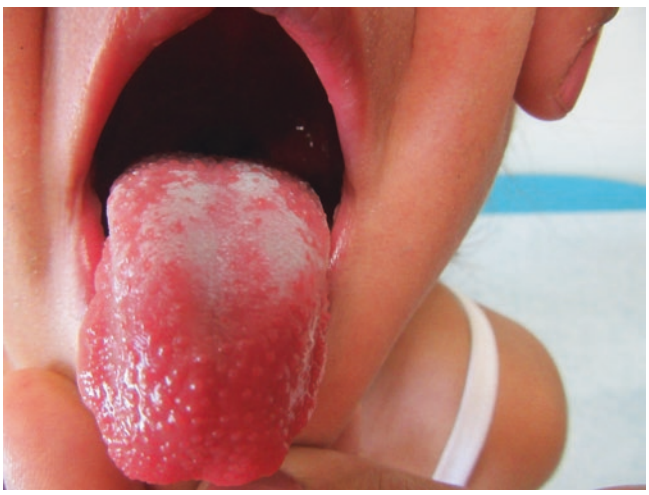

Fig. 9.13 Strawberry tongue with white coat in a child with scarlet fever

- Diffuse, erythematous, blanching, fine papular rash that resembles sandpaper on palpation (Fig. 9.14)
- The rash is prominent especially in the flexor skin creases of the antecubital fossa and axillae (Pastia lines, which are pathognomonic for scarlet fever)
- Circumoral pallor
- Desquamation after the rash starts to fade (usually the rash lasts about 1 week)

Diagnosis

- Throat culture or rapid streptococcal test
- Anti-deoxyribonuclease B and antistreptolysin O titers (anti-DNase B and ASO, antibodies to streptococcal extracellular products)

Management

- Penicillin remains the drug of choice (documented cases of penicillin-resistant group A streptococcal infections still do not exist)
- First-generation cephalosporin may be an effective alternative

Streptococcosis

- Occurs in children younger than 3 years
- Young infants may not present with classic pharyngitis
- Low-grade fever
- Thick purulent nasal discharge
- Poor feeding
- Anterior cervical lymphadenopathy
- Some patients may be toxic with high fever, malaise, headache, and severe pain upon swallowing

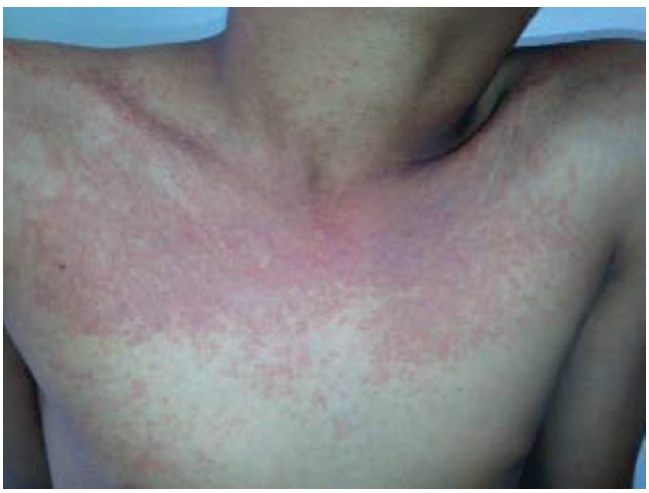

Fig. 9.14 Scarlet fever: Fine erythematous punctate eruption with dry, rough texture to the skin that resembles the feel of coarse sandpaper and scarlet macules overlying the generalized erythema

Impetigo

Background

- GAS impetigo is a superficial bacterial skin infection (small percentage)
- In North America the etiologic agent is primarily *S. aureus*

Clinical presentation

- Common (i.e., crusted or nonbullous) impetigo: Initial lesion is a superficial papulovesicular lesion that ruptures easily
- The lesion becomes purulent and covered with an amber-colored crust (Fig. 9.15)
- Bullous impetigo: Superficial fragile bullae containing serous fluid or pus form and then

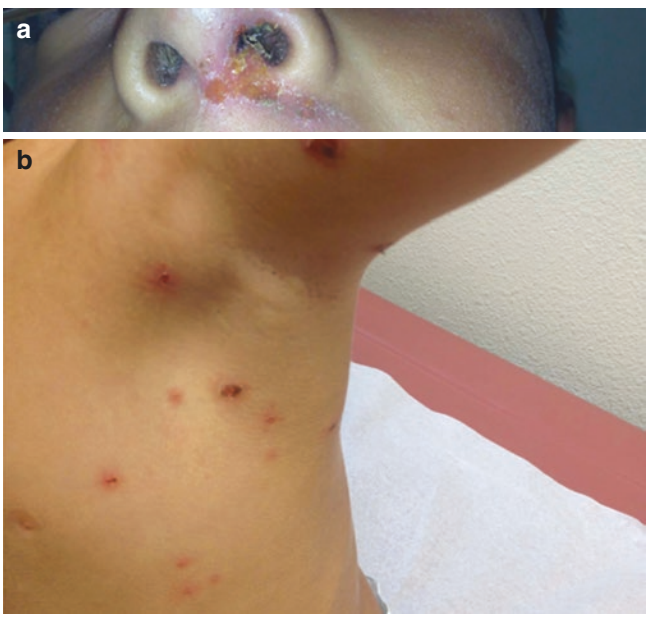

Fig. 9.15 (**a**) Impetigo: Honey-crusted lesions under the nostril and on the cheek. (**b**) Impetigo: Honey-crusted lesions on the arm and trunk

rupture to form round, very erythematous erosions
- The lesions usually located in exposed areas, especially the face and extremities
- Lesions usually often spread due to autoinoculation

Treatment
- Topical mupirocin or retapamulin for localized lesions
- Multiple localized lesions may require systemic treatment such as cephalexin or clindamycin that covers both GAS and staphylococcal infections
- Should not go back to school until at least 12 h after beginning appropriate antimicrobial
- Patient should avoid close contact with other children if possible

Perianal Bacterial Dermatitis (Formerly Called Perianal Streptococcal Dermatitis)

Background
- May be caused by *S. pyogenes* (GAS) or *S. aureus*, occurring in children 6 months–10 years
- Often misdiagnosed and treated inappropriately
- Early antibiotic treatment results in dramatic and rapid improvement in symptoms

Clinical presentation
- Perianal rash, itching, and rectal pain; blood-streaked stools may also be seen in one-third of patients
- Bright red, sharply demarcated rash around the anal area (Fig. 9.16)

Diagnosis
- A rapid streptococcal test of suspicious areas can confirm the diagnosis if etiology is GAS (vast majority of cases)
- Routine skin culture is an alternative diagnostic aid

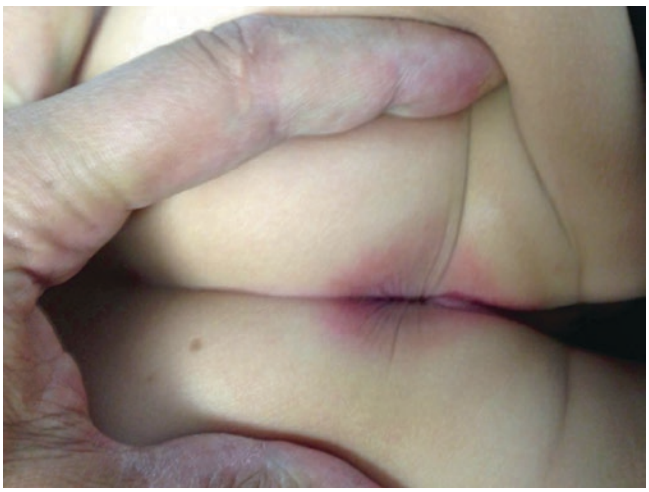

Fig. 9.16 Perianal bacterial dermatitis: 4-year-old presents with rectal pain, itchiness, and discomfort when sitting; physical exam shows bright red, sharply demarcated rash around the anal area. Strep test was positive

Management
- Treatment with empiric oral cephalexin is effective for most staph and strep; if rapid strep is positive, can use oral penicillin or amoxicillin
- Topical mupirocin three times per day for 10 days
- Follow-up is necessary because recurrences are common

Erysipelas GAS

Clinical presentation
- Erythema and edema
- Sharply defined and elevated border tender to palpation
- Systemic signs such as fever are often present
- Lymphangitis may occur

Management
- Systemic antibiotic therapy is required
- Parenteral antibiotics may be needed, especially in immunocompromised patients

Streptococcal Toxic Shock Syndrome

Background

- GAS TSS is a form of invasive GAS disease associated with the acute onset of shock and organ failure

Risk factors

- Injuries resulting in bruising or muscle strain
- Surgical procedures
- Varicella infection
- NSAID use
- Streptococcal exotoxins that act as superantigens cause release of cytokines leading to capillary leak, leading to hypotension and organ damage

Clinical presentation

- Fever
- Abrupt onset of severe pain, often associated with a preceding soft-tissue infection, e.g., cellulitis or osteomyelitis
- Know: Patient may be normotensive initially, but hypotension develops quickly
- Erythroderma, a generalized erythematous macular rash, may develop

Diagnosis

- Leukocytosis with immature neutrophils
- Elevated serum creatinine values
- Hypoalbuminemia
- Hypocalcemia
- Elevated creatine kinase concentration
- Myoglobinuria, hemoglobinuria
- Positive blood cultures
- Diagnosis of GAS TSS requires isolation of GAS, e.g., blood or CSF

Treatment for GAS TSS

- Aggressive fluid replacement is essential to maintain adequate perfusion to prevent end-organ damage
- Vasopressors also may be required
- Immediate surgical exploration and debridement are necessary, and repeated resections may be required
- Empiric therapy with broad-spectrum IV antibiotics to cover both streptococcal and staphylococcal infections, e.g., clindamycin IV plus penicillin G IV
- Immune globulin intravenous (IGIV) also may be used as adjunctive therapy

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus Infections (PANDAS)

Background

- PANDAS describes a group of neuropsychiatric disorders, in particular, obsessive compulsive disorder (OCD), tic disorders, and Tourette syndrome, that are exacerbated by GAS infection
- Diagnostic criteria for PANDAS include:
  - Tourette syndrome; abrupt onset in childhood
  - Relationship between GAS infection and episodic symptoms confirmed by RADT, throat culture, skin culture, or serologic testing
  - Evaluation for GAS infection should be considered in children who present with the abrupt onset of OCD or tic disorder

Management

- Treatment of the GAS infection and neuropsychiatric therapy
- Behavioral therapy and pharmacological therapies, including:
  - Selective serotonin reuptake inhibitors (SSRIs) for OCD
  - Clonidine for tics

Necrotizing Fasciitis

Background

- A form of invasive bacterial disease that is often polymicrobial. This infection is characterized by extensive local necrosis of subcutaneous soft tissues

- Typically caused by GAS and/or mixed aerobic and anaerobic flora, including *Clostridium, Staphylococcus.* Salt water necrotizing fasciitis contains *Vibrio species*. Freshwater necrotizing fasciitis contains *Aeromonas*

Clinical presentation
- Fever, hypotension, malaise, and myalgias
- Rapidly increasing pain; erythematous skin that progresses to blisters, bullae, and crepitus with subcutaneous gas

Laboratory findings
- Leukocytosis with a predominance of neutrophils
- Elevated creatine kinase, lactate, and creatinine values
- Positive wound cultures

Diagnosis
- Diagnosis is clinical and requires a high degree of suspicion because of the rapid progression of infection

Treatment
- Early and aggressive surgical exploration and debridement
- Triple antibiotic therapy with IV penicillin G, clindamycin, and an aminoglycoside is recommended
- Hemodynamic support if GAS TSS is present
- Repeat surgery is necessary until all necrotic tissue has been removed
- Antibiotic therapy should continue for several days after completion of surgical debridement and may include penicillin G, vancomycin, metronidazole, or imipenem/meropenem

Listeria monocytogenes

Background
- Aerobic Gram-positive bacillus
- Rare disease with case fatality of 16–20%
- Mode of transmission is mostly foodborne
  - Unpasteurized milk and soft cheeses
  - Undercooked poultry
  - Deli-style, prepared meats
  - Asymptomatic vagina carrier in pregnant women

Clinical presentation
- Neonatal early onset infection < 7 days causes preterm birth, sepsis, or pneumonia with 14–56% fatality. Characteristic *granulomatosis infantisepticum* rash with papules
- Neonatal late onset infection > 7 days causes meningitis with 25% fatality

Treatment
- Ampicillin and aminoglycoside

Corynebacterium diphtheriae

Background
- Gram-positive pleomorphic bacillus
- Humans are reservoirs
- Rare due to immunization

Clinical presentation
- Low-grade fever
- Sore throat
- Malaise
- Difficulty swallowing
- Bilateral cervical lymphadenopathy ("bull neck")
- Grayish exudates over mucous membrane
- Bleeding after attempting to remove the membrane
- Diphtheria toxins can cause myocarditis, necrosis, and peripheral neuritis

Treatment
- If diphtheria is suspected, antitoxin (equine hyperimmune antiserum IV) should be started immediately to neutralize the toxins. Administer erythromycin for 14 days also.
- Know: Close contacts should receive single IM dose of penicillin G benzathine or oral erythromycin regardless of their immunization status.

Enterococcus

Background
- Gram-positive cocci
- Normal inhabitant of the GI tract
- *Enterococcus faecalis* and *Enterococcus faecium*
- Most neonatal enterococcal infections are nosocomial and occur after 2nd week of life, usually with bacteremia due to line infection or necrotizing enterocolitis (common symptoms in neonates include, fever, bradycardia, apnea, and abdominal distention)

Associated infections
- Bacteremia in neonates
- Catheter-associated bacteremia
- Endocarditis
- Intra-abdominal abscess
- UTI

Antibiotics
- Resistant to all cephalosporins and vancomycin
- *E. faecalis* is susceptible to ampicillin
- *E. faecium* is resistant to ampicillin. Treat with vancomycin pending susceptibility results unless vancomycin-resistant *enterococcus* (VRE), which requires linezolid
- Sensitivity testing is imperative because of resistance
- Sensitive enterococcal sepsis or endocarditis must be treated with penicillin, ampicillin, or vancomycin + gentamicin

Bacillus anthracis

Background
- Large positive rods (bacilli) that cause anthrax
- Types of anthrax: Cutaneous anthrax, pulmonic, and GI
- Inoculation occurs from handling contaminated substance, e.g., wool, and in cases of bioterrorism, via mail

Clinical presentation
- Painless papules and ulcers
- Painless black eschar with painless swelling and induration

Treatment
- Penicillin G or quinolones, e.g., ciprofloxacin

Bacillus cereus

Background
- Soil-dwelling, Gram-positive rods, beta hemolytic bacterium
- Produces GI symptoms due to enterotoxin production in vivo in the GI tract

Clinical presentation
- Vomiting with incubation period 1–6 h (the emetic form is commonly associated with fried rice left at room temperature)
- Diarrhea with incubation period 8–16 h
- Eye infection after traumatic eye injuries in contact lens wearers

Diagnosis
- Usually clinical
- *B. cereus* spores in stool
- Isolated toxins from suspected food items

Treatment
- Self-limited and requires no antibiotics

Arcanobacterium haemolyticum

Background
- *A. haemolyticum* can be mistaken with strep pharyngitis or scarlet fever
- Gram-positive bacillus
- Grows slowly as small colonies with narrow bands of hemolysis on blood-enriched agar
- Growth enhanced by culture on rabbit or human blood with incubation in 5% CO2

Clinical presentation
- Common in teenagers and young adults
- 0.5–3% of acute pharyngitis
- Except for absence of palatal petechiae and strawberry tongue, the disease indistinguishable from that caused by group A *Streptococcus*
- Fever
- Pharyngeal exudates
- Cervical lymphadenopathy
- Scarlatiniform or maculopapular pruritic rash in 50% of cases; usually spares the palms and soles

Treatment
- Macrolides: Erythromycin or azithromycin

ANAEROBES

Clostridium botulinum

Background
- *C. botulinum* is an anaerobic Gram-positive rod that survives in soil and marine sediment by forming spores
- Human botulism is caused by neurotoxins A, B, E, and, occasionally, F

Infant Botulism

- Ingestion of honey or exposure to contaminated soils increases the risk
- Age between 3 weeks and 6 months
- Symptoms develop 3–30 days from the time of exposure

Clinical presentation
- Constipation usually the initial finding
- Feeding difficulty is a common presenting symptom
- Hypotonia
- Increased drooling
- Weak cry
- Truncal weakness
- Cranial nerve palsies
- Generalized weakness with ventilatory failure

Diagnosis
- Stool toxin detection

Treatment
- Botulism immune globulin (BIG) IV should be started as early as possible if clinically suspected
- Antibiotics (gentamicin) can potentiate toxin paralytic effect

Foodborne Botulism

Background
- Most common source is home canned food
- Symptoms develop 12–36 h after toxin ingestion
- Wound botulism is similar, except the incubation period between 4 and 14 days

Clinical presentation
- Initial symptoms: Dry mouth, nausea, and diarrhea
- Bilateral cranial nerve palsies
- Eye diplopia and blurring vision
- Dysphagia
- Upper extremity weakness
- Respiratory dysfunction
- Lower extremity dysfunction

Treatment of botulism in older patients
- Equine trivalent antitoxin (types A, B, and E)
- Wound debridement for wound botulism is recommended

Clostridium perfringens

Background
- Gram-positive, rod- shaped, anaerobic, spore-forming bacterium
- Spores found in raw meat and poultry
- Incubation period 8–12 h

Clinical presentation
- Sudden onset of diarrhea
- Crampy abdominal pain

Management
- Resolves within 24 h
- Rehydration

Clostridium tetani

Background
- *C. tetani,* an obligate anaerobic Gram-positive bacillus, is the pathogen responsible for tetanus
- Nonencapsulated and forms spores that resist heat, desiccation, and disinfectants
- Contaminated deep puncture wounds, open wounds, soil, and animals (wool) containing spores are the most common sources of this bacteria

Neonatal tetanus
- Contaminated umbilical cord is a common source of infection
- Poor feeding (poor suck and swallowing due to muscle spasm)
- Constant crying
- Decreased movement
- Spasm and rigidity

Generalized tetanus
- Trismus (lockjaw)
- Sardonic smile (*risus sardonicus*)
- Severe muscle spasm
- Opisthotonos (severe hyperextension)
- Laryngeal spasm can lead to airway obstruction and death
- Tetanic seizure is severe; tonic contractions with high fever
- Diagnosis is always clinical

Treatment
- Human tetanus immune globulin immediately
- Penicillin G or metronidazole
- Muscle relaxants

Prevention of tetanus
- Routine immunization with DTaP and Tdap

Prevention in wound injuries guideline
- Tetanus vaccine +/− tetanus immunoglobulin (TIG)
  - Dirty wound, immunization is unknown or less than three tetanus shots: Give TIG + tetanus vaccine
  - Dirty wound, immunized > 5 years and < 10 years: Immunize, no TIG
  - Dirty wound, immunized < 5 years: No treatment
  - Clean wound, immunized < 10 years: No treatment
  - Clean wound, immunized > 10 years: Immunize, no TIG

Clostridium difficile

Background
- Gram-positive anaerobes
- Colonization
  - Around 50% of infants younger than 1 year are colonized
  - Carriage decreases by 1–5% by 2 years of age
- Risk factors:
  - Having infected roommate or having symptomatic patient in the same ward
  - Antibiotics, e.g., beta-lactams drugs, clindamycin, and macrolides
  - Underlying bowel disease or surgeries
- Symptomatic disease is due to toxins A and B produced by the organism

Clinical presentation
- Asymptomatic colonization is common in infants and young children
- Watery diarrhea

- Abdominal cramps
- Abdominal tenderness
- In severe cases:
  - Systemic toxicity
  - Bloody diarrhea
  - Toxic megacolon, perforation, or even death are complications of pseudomembranous colitis

Diagnosis

- Documenting toxin A and B in stool using PCR or nucleic acid amplification tests (NAATs) (for toxin genes)
- Endoscopic findings of pseudomembranous enterocolitis
- Young children < 2 years are commonly colonized with *C. difficile*

Treatment

- Initial episode, non-severe: Oral metronidazole
- Oral vancomycin with or without metronidazole can be used in severe cases
- Recurrence: Oral vancomycin can be used alone or with rifaximin, or fecal microbiota transplantation

Prevention

- Hand washing with water and soap
- Know: Alcohol-based product are not effective against the organism
- Diluted bleach solution is the best for decontamination of surfaces
- Limit antibiotic use
- Infected children should be excluded from childcare facility for the duration of diarrhea

GRAM-NEGATIVE BACTERIA

Gram-Negative Anaerobes

- Bacteroides
- Fusobacterium anaerobes
- **Causes a variety of clinical manifestations depending on the location**
  - Head and neck
    - Retropharyngeal abscess
    - Peritonsillar abscess
    - Dental abscess
    - Ludwig angina
  - CNS
    - Brain abscess
    - Subdural and epidural empyema
  - Lung
    - Aspiration pneumonia
    - Lung abscess
    - Pleural empyema
  - Abdomen
    - Peritonitis
    - Appendicitis
    - Intra-abdominal abscess
  - Skin and soft tissue
    - Infected bite wound
    - Necrotizing fasciitis
    - Cellulitis
  - Antibiotics with anaerobic activity
    - Clindamycin
    - Penicillin
    - Ampicillin–sulbactam
    - Amoxicillin–clavulanic acid
    - Metronidazole

Campylobacter Species

Background and epidemiology

- *Campylobacter jejuni* (Gram-negative motile bacilli)
- One of the most common agents associated with bacterial gastroenteritis
- Common sources: Uncooked poultry (chicken and turkey), unpasteurized milk, dogs and cats
- Incubation period: 2–5 days

Clinical presentation

- Bloody diarrhea
- Abdominal pain (may mimic inflammatory bowel disease in severe cases)
- Tenesmus
- Fever

Diagnosis
- Stool culture in a selective media at temperature 42 °C incubated in gas mixture O2 and CO2

Treatment
- Azithromycin and erythromycin shorten illness duration and prevent relapse

Chlamydia pneumoniae

Background and epidemiology
- Transmitted from one person to another via respiratory secretions
- 50% of adults have antibody evidence of exposure

Clinical presentation
- Patient may be asymptomatic or mildly to moderately ill
- Illness is usually prolonged with cough persisting for 2–6 weeks
- Pneumonia and pulmonary rales
- Acute bronchitis and bronchospasm
- Less commonly: Nonexudative pharyngitis, laryngitis, otitis media, and sinusitis

Diagnosis
- Fourfold increase in IgG titer from acute to convalescent
- IgM titer of ≥ 1:16
- Cross-reactivity and persistent antibody makes diagnosis problematic

Treatment
- Macrolides, doxycycline, or tetracycline

Chlamydophila psittaci

Background
- *C. psittaci* is obligate intracellular bacterial pathogen
- Birds are major reservoir of *C. psittaci*, e.g., parakeets and parrots
- Animals such as goats and cows may become infected

Clinical presentation (psittacosis)
- Fever
- Nonproductive cough
- Headache
- Malaise
- Extensive interstitial pneumonia can occur
- Pericarditis, hepatitis, and encephalitis (rare)

Diagnosis
- Serology, nucleic acid amplification tests, PCR

Treatment
- Doxycycline preferred therapy, including children < 8 years
- Macrolides for pregnant women

Conjunctivitis Due to *Chlamydia trachomatis*

Background and epidemiology
- The most frequently identified infectious cause of neonatal conjunctivitis
- Transmitted perinatally from infected mothers

Clinical presentation
- The symptoms typically develop 5–14 days after birth
- Conjunctival edema
- Hyperemia
- Watery-to-mucopurulent discharge
- A pseudomembrane may form and bloody discharge may be present if infection is prolonged

Management
- Oral erythromycin × 14 days or azithromycin × 3 days
- Know: Topical prophylaxis with erythromycin or silver nitrate given to all infants to prevent neonatal gonococcal conjunctivitis is *ineffective* against chlamydial conjunctivitis. Suctioning may increase comfort and improve feeding.

Pneumonia Due to *C. trachomatis*

Background

- Small, Gram-negative, obligate intracellular organisms
- Transmitted to the infant from the birth canal
- Generally presents as a subacute infection 2–19 weeks after birth

Clinical presentation

- Rhinorrhea, congestion, or conjunctivitis
- Tachypnea
- Staccato cough
- Crackles (rales)
- Wheezing (rare)
- Preterm infants may have episodes of apnea

Diagnosis

- Chest radiography reveals infiltrates and hyperinflation
- Laboratory testing may reveal:
  - Peripheral eosinophilia
  - Elevated serum immunoglobulins
- A positive NP direct fluorescent antibody (DFA) test or culture is considered diagnostic

Treatment

- Antibiotic treatment should be started presumptively on clinical grounds
- Same antibiotic regimens as for neonatal conjunctivitis
- If untreated, symptoms can last for months and include persistent hypoxemia
- Remember: Diagnosis of chlamydial pneumonia in an infant necessitates treatment of the infant's mother and her sexual partner

Chlamydia Genitourinary Tract Infection

Background

- Sexual transmission

Clinical presentation

- Females: Vaginitis in prepubertal girls, urethritis, cervicitis, endometritis, salpingitis, proctitis, and perihepatitis (Fitz–Hugh–Curtis syndrome). Can progress to pelvic inflammatory disease
- Males: Urethritis, epididymitis, and proctitis
- Reiter syndrome (arthritis, urethritis, bilateral conjunctivitis)
- *Lymphogranuloma venereum* (LGV): Ulcerative lesion on genitalia followed by tender, unilateral lymphadenopathy

Diagnosis

- NAATs of vaginal, endocervical, and male intraurethral specimens; urine specimens

Treatment

- Doxycycline 100 mg per os BID for 7 days
- Azithromycin single dose 1 g

Trachoma

Background

- Chronic keratoconjunctivitis caused by the obligate intracellular bacterium *C. trachomatis*
- Disease transmission occurs primarily between children and the women who care for them
- Trachoma is the most common infectious cause of blindness worldwide

Clinical presentation

- Chronic follicular keratoconjunctivitis with corneal neovascularization resulting from untreated or chronic infection
- Blindness occurs in up to 15% of those infected
- Trachoma rarely occurs in the USA

Diagnosis

- Clinical diagnosis and NAATs can confirm the causative agent
- The cicatricial phase has unique clinical features (eyelid scarring, eyelid buckling, lashes

rubbing on eye), which lead to definitive diagnosis in most cases

Treatment
- Azithromycin single dose 20 mg/kg

Neisseria gonorrhoeae (Gonococcal Infections)

Background
- *N. gonorrhoeae* is a Gram-negative diplococcus
- Gonococcal infection is the second most common bacterial disease in the USA classified as nationally reportable and notifiable
- Highest prevalence in youth, especially females between 15 and 19 years of age
- The incubation period is 2–7 days
- A child abuse evaluation must be performed in any prepubertal case

Neonatal conjunctivitis
- Conjunctivitis due to mucosal transmission during vaginal delivery
- Topical antibiotics (erythromycin, silver nitrate, or tetracycline) to the eyes of a newborn within 1 h of birth can prevent the infection
- Treatment is ceftriaxone 125 mg IM × 1

Gonococcal pharyngitis
- Genital–oral activity is the major risk
- Infection is asymptomatic in most cases
- Patients who have gonococcal pharyngitis have a significant public health impact
- Gonococcal pharyngitis patients at risk for developing disseminated gonococcal infection (DGI)
- Pharyngeal infection clears spontaneously within 12 weeks
- Treatment is ceftriaxone 250 mg IM × 1

Gonococcal urethritis
- Dysuria and a mucopurulent penile discharge
- May be coinfected with other sexually transmitted organisms, most commonly, *C. trachomatis*
- Positive leukocyte esterase usually seen in urine specimen
- Diagnosis of gonococcal urethritis with NAATs
- Presence of intracellular diplococci in urethral discharge
- Treatment is ceftriaxone 250 mg IM × 1 plus azithromycin 1 g × 1

Epididymitis (gonococcus)
- Dysuria and a mucopurulent discharge
- Scrotal edema with scrotal, inguinal, or flank pain
- Urinalysis may demonstrate WBCs
- In most cases this infection is transmitted sexually and may be an extension of urethritis

Gonococcal proctitis
- Most cases of proctitis due to *N. gonorrhoeae* occur in homosexual males
- Clinical presentation
  - Anal discharge
  - Rectal bleeding
  - Anorectal pain
  - Tenesmus
  - Constipation

Disseminated gonococcal infection (DGI)
- DGI infection occurs in 0.5–3% of people infected with *N. gonorrhoeae*
- DGI usually causes an asymptomatic genital infection
- Migratory arthritis (wrist, ankle, and knee) are the most common locations
- Dermatitis
- Tenosynovitis
- Fever and chills may occur
- Elevated WBC count
- DGI occurs more commonly in females

Screening methods for infection *N. gonorrhoeae* and *Chlamydia*

- Culture is the gold standard for diagnosing *C. trachomatis*
- Standard collection sites include the endocervix, male and female urethra, nasopharynx, conjunctiva, vagina, and rectum
- NAATs amplify nucleic acid sequences specific for the organism of interest
- The ease of urine collection, together with the high sensitivity of NAATs, has made these tests the preferred method for screening
- The presence of Gram-negative intracellular diplococci on microscopy suggests the diagnosis of gonococcal infection

N. meningitidis (Meningococcal Infections)

Background

- Aerobic Gram-negative diplococcus *N. meningitidis*
- Natural commensal organism living in the nasopharynx of humans
- Children younger than 2 years of age have a nearly fivefold greater risk of contracting meningococcal disease than the general adult population
- Risk of transmission: Crowded living conditions, e.g., college dormitories, military barracks

Clues to investigate for invasive meningococcal infection

- Rash
  - Any rash appearing in the context of a sudden febrile illness should raise concern
  - Meningococcal rash is typically present within 24 h of any symptomatology
  - Petechiae may be intraoral or conjunctival or be hidden in skinfolds
  - Early rash may not be petechial
- True rigors
  - Shaking chills that cannot be stopped voluntarily
  - Prolonged (10–20 min)
- Neck pain
  - Severe pain in the neck, back, or extremities
  - May manifest in younger children as refusal to walk
  - Meningismus: In patients older than 3 years, the classic signs of Kernig and Brudzinski may be elicited
- Vomiting
  - May be associated with headache or abdominal pain without diarrhea
- Cushing triad:
  - Bradycardia
  - Hypertension
  - Respiratory depression
- Purpura fulminans (meningococcemia)
  - Aggressive spread of purpura to large areas with ischemic necrosis
  - Sudden drops in blood pressure
  - Acute adrenal hemorrhage (Waterhouse–Friderichsen syndrome)

Diagnosis

- Culture of the organism from a normally sterile site is the gold standard for bacteriological diagnosis
- CSF study:
  - CSF WBC counts are elevated in most patients who have meningitis
  - CSF WBC counts are low or even normal if the disease is severe and rapidly progressive
  - Markedly low glucose and elevated protein values are associated with the diagnosis of meningitis
- All patients with meningococcal disease or meningitis must be tested for CH50 or CH100 assay (20% of children with meningococcal disease will end having a complement deficiency)

Management

- Know: Antibiotics and fluids should not be delayed
- Penicillin is effective treatment for both severe meningococcal septicemia (SMS) and meningococcal meningitis if the diagnosis is certain
- Broad-spectrum antibiotics effective against *N. meningitidis* and other potential pathogens are indicated (e.g., ceftriaxone, cefotaxime, and vancomycin)
- Emergency care evaluation and preferably transported via emergency medical services to allow for prompt delivery of IV fluids and airway management if the condition is suspected
- Large isotonic fluid boluses (20 mL/kg) over the first 5 min
- Inotropic/vasoactive agent such as dopamine or dobutamine
- Hydrocortisone may be beneficial in children respond poorly to vasopressors

Prevention and indications for meningococcal vaccines

- MenACWY vaccine is routinely recommended at 11–12 years of age; 2 vaccines licensed for children and adults, 1 dose
  - Can give as young as 2 months as a 4-dose series for high risk (complement deficiency, asplenia, HIV, travel to endemic area)
- MenB vaccine is optional and preferred for 16–18 years of age, 2-dose series
  - Can give as young as 10 years for high risk (complement deficiency, asplenia, outbreak, lab workers); 2- or 3-dose series for high risk
- Antibiotic prophylaxis, e.g., rifampin, ciprofloxacin, azithromycin, or ceftriaxone should be used for contacts:
  - Childcare contact
  - Direct exposure to oral secretions of individuals with meningococcal disease (such as personnel providing mouth-to-mouth resuscitation)

Haemophilus influenzae

Background

- Pleomorphic Gram-negative coccobacillus spread via respiratory tract secretions
- Formerly the most common cause of meningitis and serious bacteremia in children
- Introduction of the *H. influenzae* vaccine quickly reduced the incidence of encapsulated *H. influenzae* type b
- Nontypeable strains are still responsible for a large number of mucosal infections, including conjunctivitis, otitis media, sinusitis, and bronchitis

Bacterial meningitis

- Peak age is less than 1 year
- Mortality rate around 5%
- Common complications include: Subdural empyema, brain infarct, cerebritis, ventriculitis, brain abscess, and hydrocephalus
- Long-term sequelae occur in 15–30% of survivors with sensorineural hearing loss; others include language disorders, intellectual disability, and developmental delay
- Dexamethasone before or with antibiotics such as ceftriaxone or cefotaxime to prevent hearing loss and neurologic sequelae

Epiglottitis

- Hib was the predominant organism (> 90%) in pediatric epiglottitis before vaccine introduction. Since that time, other bacteria, including *S. pneumoniae*, GAS, *S. aureus*, and *Moraxella catarrhalis,* can cause epiglottitis
- Occurs primarily in children aged 2–7 years.
- The clinical triad of drooling, dysphagia, and distress is the classic presentation
- Fever with associated respiratory distress or air hunger occurs in most patients
- Treatment in patients with epiglottitis is directed toward relieving the airway obstruction and eradicating the infectious agent

- Optimally, initial treatment is provided by a pediatric anesthesiologist and either a pediatric surgeon or a pediatric otolaryngologist

Buccal infections

- Buccal cellulitis previously was always caused by *H. influenzae* infection before the vaccine
- Always associated with bacteremia if present
- Present with palpable cellulitis on both checks, purplish in color, and child looks very toxic

Periorbital cellulitis

- Previously *H. influenzae* was a common cause, now *S. pneumoniae* bacteria is the most common etiology associated with sinusitis
- Minor trauma or insect bite of the eyelid usually associated with preseptal cellulitis due to *S. aureus* or a Group A *Streptococcus*

Pyogenic arthritis

- *H. influenzae* was the most common cause of septic arthritis in children less than 2 years of age before Hib vaccine

Occult bacteremia

- Occult bacteremia with *H. influenzae* will result in in 30–50% developing meningitis or other deep or focal infection from occult bacteremia
- All occult bacteremia from *H. influenzae* has to be treated immediately

Pneumonia

- Pneumonia from *H. influenzae* used to cause about one-third of bacterial pneumonia before Hib vaccine and was associated with pleural effusion and positive blood culture in most cases

Treatment (in patient with life-threatening illness)

- Remember: The organism produces beta lactamase, which makes amoxicillin ineffective
- Cefotaxime or ceftriaxone is the antimicrobial of choice
- Meropenem or chloramphenicol is another option
- Amoxicillin is the drug of choice for noninvasive diseases such as otitis media or sinusitis; if amoxicillin fails, uses antibiotics against beta-lactamase-producing strains, e.g., nontypeable *H. influenzae* including amoxicillin/clavulanate, TMP-SMX, azithromycin, cefuroxime axetil, cefixime, and cefpodoxime.

Rifampin antibiotic prophylaxis for contact with invasive Hib infection

- All members of household who did not receive immunization
- Less than 4 years with incomplete immunization
- Younger than 12 months who did not complete primary Hib immunization
- Immunocompromised child
- Nursery school and childcare center if two or more cases within 60 days (outbreak)

Mycoplasma pneumonia

Background

- *M. pneumoniae* is the leading cause of pneumonia in school age children and young adults
- Infection is prevalent in persons living in group setting
- Incubation period is 2–3 weeks

Clinical presentation

- Pulmonary manifestations
  - Nonproductive cough
  - Chills
  - Scattered rales
  - Skin rash
  - Bilateral infiltrate on chest radiograph
- Extrapulmonary manifestations
  - Pharyngitis
  - Rash
  - Stevens–Johnson syndrome

- Hemolytic anemia
- Arthritis
- CNS disease (encephalitis; cranial nerve palsy, especially CN III)

Testing for mycoplasma

- Mycoplasma DNA PCR nasal washing
- IgG and IgM serology or cold agglutinin

Treatment

- Mycoplasma lacks the cell wall and beta lactams are not effective
- Azithromycin is the drug of choice

Pasteurella multocida

Background

- Small Gram-negative coccobacilli; normal oral flora in animals, e.g., dogs and cats
- Dog or cat bite is a common risk

Clinical presentation

- Erythema, tenderness, and edema usually develop rapidly within 24 h
- Regional lymphadenopathy and fever may occur
- Infection that occurs days after the bite is usually caused by *S. aureus*

Treatment

- Clean wound with soap and water
- Treatment should cover potential pathogens, e.g., *P. multocida, S. aureus*, and anaerobes
- Administration of antibiotic within 8–12 h of injury may decrease the risk of infection
- Penicillin is the drug of choice for *P. multocida* alone
- Amoxicillin–clavulanate is the drug of choice for suspected polymicrobial wounds, including cat bites
- Clindamycin + TMP-SMX is appropriate for children allergic to penicillin

Bordetella pertussis

Background

- Small Gram-negative coccobacillus that infects only humans
- Spreads by aerosol droplets expelled while coughing or sneezing in proximity to others
- Incubation period of 7–10 days

Clinical presentation

- Catarrhal phase
  - Lasts from 1 to 2 weeks
  - Mild fever
  - Cough
  - The cough worsens as the patient progresses to the paroxysmal phase
- Paroxysmal phase
  - Lasts from 2 to 6 weeks
  - Rapid fire or staccato cough
  - 5 to 10 uninterrupted coughs occur in succession, followed by a "whoop" as the patient rapidly draws in a breath
  - May occur several times per hour
  - Can be associated with cyanosis, salivation, lacrimation, and post tussive emesis
  - Despite the severe spells, patients often appear relatively well between episodes
  - Whoop is usually absent in infants less than 6 months of age
  - Gasping, gagging, and apnea can occur
- Convalescent phase
  - Decreasing frequency and severity of the coughing episodes
  - Lasts from weeks to months

Complications of pertussis

- Pertussis is most severe in infants < 6 months
- Apnea
- Pneumonia
- Seizures
- Encephalopathy
- Death

Thoracic pressure-related complications
- Pneumothorax or pneumomediastinum
- Subcutaneous emphysema
- Superficial petechial hemorrhage
- Rib fracture
- Rectal prolapse
- Intracranial hemorrhage

Diagnosis
- PCR of NP specimen collected with Dacron swab is diagnostic test of choice
- PCR remains positive late in the course of the illness
- Leukocytosis as high as 60,000 can be seen due to absolute lymphocytosis

Management
- Infants afflicted with pertussis often require hospitalization for fluid, nutritional, and respiratory support
- If left untreated, most individuals will clear *B. pertussis* spontaneously from the nasopharynx within 2 to 4 weeks of infection
- Antibiotics can shorten the course and attenuate the severity of pertussis if started early and can shorten the period of contagiousness
- Once the paroxysmal phase begins, antibiotics are not effective in altering the course of the disease
- Excluded from school for 21 days if untreated, or for 5 days while taking antibiotic
- Azithromycin is the drug of choice:
  - Infant less than 6 months: 10 mg/kg per day as a single dose for 5 days
  - Older infants and children: 10 mg/kg as a single dose on day 1 then 5 mg/kg per day as a single dose on days 2–5

Prophylaxis to close contacts is the same as the treatment
- Infants less than 1 year
- Pregnant women
- Immunocompromised
- Underlying lung disease

Immunization
- Because immunity to pertussis from the DTaP series wanes over time, a booster dose is recommended at age 11–12 years

Brucellosis

Background
- Brucellosis is a zoonotic infection caused by the bacterial genus *Brucella*
- Brucellosis caused by Gram-negative bacillus
- The bacteria are transmitted from animals to humans by ingestion of unpasteurized milk or cheese, direct contact with an infected animal, or inhalation of aerosols
  - *B. melitensis* (from sheep; highest pathogenicity)
  - *B. suis* (from pigs; high pathogenicity)
  - *B. abortus* (from cattle; moderate pathogenicity)
  - *B. canis* (from dogs; moderate pathogenicity)

Clues to *Brucella* infection
- Fever of unknown origin
- Culture negative endocarditis
- Individuals at greatest risk for brucellosis are those exposed to goats, sheep, cows, camels, pigs, reindeer, rabbits, or hares, both in areas of endemic disease and in areas where the disease is not endemic
- Bone/joint inflammation
- Orchitis
- Hepatic abscess
- CNS symptoms

Diagnosis
- Elevated liver enzymes is a common finding
- Blood culture (alert laboratory if suspecting *Brucella*, as lab staff easily infected)
- Serology is most commonly used
- PCR in development

Treatment

- Children > 8: doxycycline + rifampin for 6 weeks
- Children < 8: TMP/SMX + rifampin for 6 weeks
- Add gentamicin for serious infection or complications

Bartonella henselae

Cat-Scratch Disease

Background

- *B. henselae* is Gram-negative rod or bacilli with a polar flagellum
- Kittens or cats less than 1 year old are most common source, also dogs
- Transmission can occur by petting alone with subsequent self-inoculation via a mucous membrane, skin break, or conjunctiva
- Clue for the diagnosis: Contact with cats and lymphadenopathy

Clinical presentation

- Regional lymphadenopathy (cervical and axillary are common locations) (Fig. 9.17)
  - Usually large and may be tender, warm, and erythematous
  - Suppuration can occur in 30% of cases
  - Node may remain enlarged for several months
  - Papule at the site of scratch may precede the development of lymphadenopathy
- Parinaud oculoglandular syndrome:
  - Painless nonpurulent conjunctivitis
  - Ipsilateral preauricular lymphadenopathy
- Other clinical presentations
  - Fever of unknown origin
  - Hepatic splenic microabscesses
  - Painful osteolytic lesions
- Patients may recall being scratched, licked, or bitten by a cat in the previous 2–8 weeks
- Fever, anorexia, headache, sore throat, or arthralgia may occur

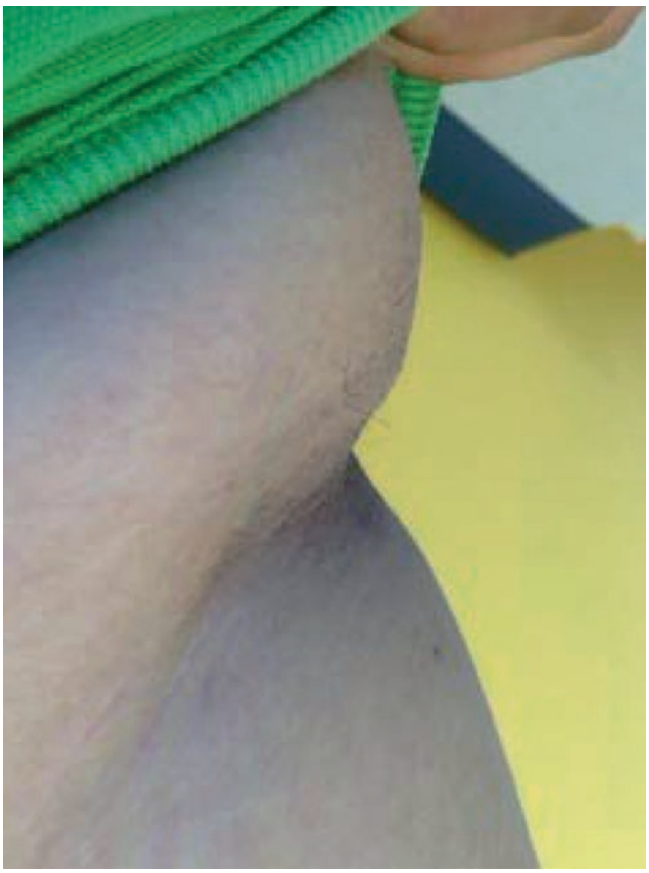

Fig. 9.17 14-year-old female with large tender axillary lymphadenopathy, she has kittens at home

- Lymphadenopathy remains regional and typically resolves within 2–4 months but may last up to 6–12 months

Diagnosis

- Indirect fluorescence assay (IFA) testing and enzyme-linked immunoassay (ELISA) are used to detect serum antibody to *B. henselae*
- An antibody titer that exceeds 1:64 suggests recent *Bartonella* infection
- Lymph node biopsy generally is not indicated in typical cases

Treatment

- Cat-scratch disease is self-limited
- Use of azithromycin can decrease lymph node size faster than natural course

- Doxycycline or rifampin may also treat
- Immunocompromised should receive antibiotics

Surgical treatment

- Remember: Incision and drainage are not recommended (risk of sinus tract and persistent drainage)
- Aspiration will be diagnostic and therapeutic; repeated aspirations may be performed if pus reaccumulates and pain recurs

Citrobacter

- Cause brain abscess in neonates
- Order computed tomography (CT) or MRI if CSF grow
- *Citrobacter* otherwise is very rare disease

Klebsiella

- A rare cause of pneumonia and meningitis
- Can cause UTIs but is less common than *E. coli*
- Most *Klebsiella* are resistant to ampicillin

Pseudomonas Species

Background

- Gram-negative organism
- Found in the soil and freshwater
- Gains entry through hair follicles or via skin breaks

Risk factors

- Cystic fibrosis (see Chap. 20 "Pulmonology")
- Associated with progressive deterioration of pulmonary function
- Associated with hot tub folliculitis
- Ocular infection from contaminated lenses
- Puncture wound osteomyelitis
- In immunocompromised patients, e.g., ecthyma gangrenosum
- Hospitalized and debilitated patients
- Burn wounds
- Ventilator-associated pneumonia

Clinical presentation according to the site of infection

- *Pseudomonas* keywords
  - Nail-puncture wound through tennis shoes
  - IV drug abuse, with endocarditis or osteomyelitis
  - Diabetes with otitis media
  - Leukemia with ecthyma gangrenosum
- Hot tub folliculitis
  - Clinical presentation:
    - The rash onset is usually 8 h to 5 days after exposure to contaminated water
    - Erythematous pruritic macules that progress to papules and pustules
    - Rash usually spares face, neck, soles, and palms
    - Usually confused with insect bites (history is important)
    - Rash clears spontaneously within 2–10 days
  - Self-limited, require no antibiotics
  - Acetic acid 5% compresses for 20 min twice a day for 4 days for symptomatic relief

Antimicrobial therapy

- Piperacillin/tazobactam (Zosyn)
- Ceftazidime (third generation)
- Cefepime (fourth generation)
- Carbapenems (meropenem, imipenem)
- Aminoglycosides (gentamicin)
- Aztreonam
- Certain fluoroquinolones (ciprofloxacin, levofloxacin)

Nontyphoidal Salmonellosis

Background

- Gram-negative bacilli that are usually motile bacteria
- A common cause of diarrhea
- Incubation period 6–72 h

Mode of transmission
- Contaminated poultry, beef, eggs, fruits, vegetables, bakery, and dairy products
- Turtles, iguana, and exotic reptiles

Clinical presentation
- Can be asymptomatic
- Most common presentation is gastroenteritis
- Abrupt onset of fever, nausea, and vomiting
- Abdominal cramps
- Moderate-to-severe watery diarrhea most common manifestation

Diagnosis
- Stool may show leukocytes, mucus, and blood
- CBC; leukocytosis and shift to the left
- After symptoms the patient can be a carrier for 4–5 weeks

Indication of antibiotic therapy
- In infants less than 3 months
- Infant < 12 months with temperature > 39 °C
- Hemoglobinopathies, e.g., sickle cell anemia, HIV, and neoplastic diseases
- Immunocompromised patients at any age

Typhoid Fever

Background
- *Salmonella enterica* serovar Typhi (*S.* Typhi)
- Mode of transmission
  - Poor sanitation and overcrowding
  - Spread by fecal–oral contamination of food or water by individuals who are carriers for *S.* Typhi in either stool or urine
  - Typhoid is endemic in many developing areas

Clinical presentation
- Fever "can exceed 104 °F (40 °C)"
- Malaise
- Chills
- Headache, anorexia, myalgias, and dry cough may be seen
- Abdominal pain is common
- Diarrhea is more likely in children
- Abdominal tenderness, hepatosplenomegaly, and a coated tongue
- Rose spots (pink, blanchable maculopapular lesions that are 2–4 mm in diameter) are seen on the torso and abdomen
- Know: Neonatal typhoid generally presents within 3 days of birth with fever, emesis, diarrhea, abdominal distention, pronounced hepatomegaly, jaundice, and (sometimes) seizures
- Know: Absence of abdominal or intestinal changes is not typical of typhoid

Diagnosis
- Blood cultures are the mainstay of diagnosis, positive in 50% of those with the disease
- Stool culture may increase yield

Treatment
- Treatment includes:
  - Hydration and correction of fluid–electrolyte imbalance
  - Antipyretics and antibiotics
- The choice of antibiotic, route, and duration depends on the host, site of infection, and sensitivities of the organism
- IV cefotaxime or ceftriaxone for 14 days is appropriate
- Multidrug resistant (MDR) strains, including resistance to ampicillin, TMP-SMX, cephalosporins, carbapenems, and fluoroquinolones have emerged mostly from Asia. Only azithromycin works for these MDR strains
- For severe typhoid with obtundation, stupor, coma, or shock:
  - Two-day course of IV dexamethasone may be life-saving

Shigella

Background
- *Shigella* is a Gram-negative bacillus
- *S. dysenteriae and S. flexneri* usually cause bloody diarrhea

- *S. sonnei and S. boydii* usually cause watery diarrhea
- Ingestion of as few as 10 organisms can cause diarrhea
- Incubation period is 2–4 days
- Outbreak can occur in childcare centers

Mode of transmission
- Person to person
- Fecal–oral
- Anal–oral
- House flies
- Contaminated fomites

Clinical presentation
- Ranges from mild diarrhea to life-threatening dysentery
- Fever
- Abdominal camps
- High-volume watery stools
- Small-volume bloody stool may follow 24–48 h later
- Blood-mucoid stool is a common presentation
- Rectal prolapse occurs in 5–8%

Complications
- Hemolytic-uremic syndrome
- Seizures
- Colonic perforation
- Toxic encephalopathy

Diagnosis
- Stool culture is diagnostic
- Stool study with large number of neutrophils is suggestive but not specific
- Peripheral WBCs are usually elevated; bandemia is very common

Treatment
- Most infections with *S. sonnei* are self-limited and do not warrant antibiotics
- Antimicrobial therapy is recommended for immunocompromised patients with shigellosis
- Antimicrobial therapy for 5 days will shorten the duration and eradicate the organism from stool
- Antimicrobial resistance testing guides therapy
- Empiric ceftriaxone, ciprofloxacin or azithromycin are usually effective
- If there is an alternative to ciprofloxacin, it is not recommended for those less than 18 years

Childcare center
- Once *Shigella* is identified in a childcare center or household, all symptomatic individuals in these environments should be cultured for *Shigella*
- Anyone found to have *Shigella* cannot return to the care center until the diarrhea has stopped and stool culture test is negative

Escherichia coli

Background
- *E. coli* is a Gram-negative, lactose fermenting, motile rod, belonging to the *Enterobacteriaceae*
- *E. coli* is one of the most frequent causes of many common bacterial infections, including cholecystitis, bacteremia, cholangitis, UTI, and traveler's diarrhea; and other clinical infections such as neonatal meningitis and pneumonia

Acute bacterial meningitis
- The vast majority of neonatal meningitis cases are caused by *E. coli* and group B streptococcal infections
- Pregnant women are at a higher risk of colonization with the K1 capsular antigen strain of *E. coli*, which is commonly observed in neonatal sepsis
- Low-birth weight and a positive CSF culture result portend a poor outcome
- Most survivors have subsequent neurologic or developmental abnormalities

Pneumonia

- *E. coli* respiratory tract infections are uncommon and are almost always associated with *E. coli* UTI

Intra-abdominal infections

- *E. coli* intra-abdominal infections often result from a perforated viscus (e.g., appendix, diverticulum) or may be associated with intra-abdominal abscess, cholecystitis, and ascending cholangitis
- They can be observed in the postoperative period after anastomotic disruption. Abscesses are often polymicrobial
- *E. coli* is one of the more common Gram-negative bacilli observed together with anaerobes

Enteric infections

- Enterotoxigenic *E. coli* (ETEC) is a cause of traveler's diarrhea; azithromycin is the drug of choice; infants < 3 months can receive a third generation cephalosporin
- Enteropathogenic *E. coli* (EPEC) is a cause of childhood diarrhea; can be treated with TMP-SMX
- *Enteroinvasive E. coli* (EIEC) causes a *Shigella*-like dysentery
- Enteroaggregative *E. coli* (EAEC) is primarily associated with persistent diarrhea in children in developing countries, and enteroadherent *E. coli* (EAEC) is a cause of childhood diarrhea and traveler's diarrhea in Mexico and North Africa
- Enterohemorrhagic *E. coli* (EHEC) causes hemorrhagic colitis or hemolytic-uremic syndrome (HUS)
- Strains of STEC serotype O157:H7 have caused numerous outbreaks and sporadic cases of bloody diarrhea and HUS

Urinary tract infections

- The urinary tract is the most common site of *E. coli* infection, and more than 90% of all uncomplicated UTIs are caused by *E. coli* infection
- The recurrence rate after a first *E. coli* infection is 44% over 12 months
- *E. coli* UTIs are caused by uropathogenic strains of *E. coli*
- *E. coli* causes a wide range of UTIs, including uncomplicated urethritis, cystitis, pyelonephritis, and urosepsis

Other miscellaneous *E. coli* infections

- Septic arthritis
- Endocarditis
- Soft tissue infections especially in patients with diabetes

E. coli (O157:H7)

Background

- Gram-negative rods
- Occurs in all ages
- Transmitted via ingestion of contaminated food (e.g., ground beef) or infected feces
- The disease linked to eating undercooked beef and unpasteurized milk or apple juice
- Produces Shiga toxins; the most virulent strain
- The incidence of *E. coli* O157:H7 > *Shigella*

Clinical presentation

- Usually begins as nonbloody diarrhea then becomes bloody
- Severe abdominal pain is common
- Fever in one-third of the cases
- May progress to hemorrhagic colitis in severe cases
- HUS may occur

Management

- No antibiotic is proven effective, and antibiotic use may increase risk of HUS
- Do not treat with antibiotics in most cases
- Do not use antimotility agents

Yersinia enterocolitica

Background
- Small Gram-negative coccobacillus
- It produces entero and endotoxins
- Pigs are commonly infected
- Ingestion of raw or improperly prepared food, such as pork (pork intestine or chitterlings), contaminated unpasteurized milk, and water

Clinical presentation
- Blood and mucus in stool
- Fever
- Right lower quadrant pain
- Leukocytosis
- Mimics appendicitis

Treatment
- No treatment for isolated intestinal infection
- If < 6 months old, extraintestinal manifestation, sepsis, or immunocompromised, then antibiotic is indicated
- Cefotaxime or ceftriaxone

Francisella tularensis

Background
- Gram-negative pleomorphic bacillus that causes tularemia or "rabbit fever"
- Found in many animals, especially rabbits
- Transmitted by ticks and blood-sucking flies
- Organism can be ingested or inhaled
- Prevalent in the Southwest desert; Arkansas, Missouri, and Oklahoma

Clinical presentation
- Fever, chills, myalgias, and arthralgias
- Irregular ulcers at the site of inoculation
- Lymphadenopathy that suppurates and forms an ulcer
- Oculoglandular tularemia (unilateral conjunctivitis, corneal ulceration)
- Pneumonic tularemia (dry cough, dyspnea, and pleuritic-type chest pain)
- Typhoidal tularemia (fever, chills, myalgias, malaise, and weight loss)

Diagnosis
- Serology, e.g., ELISA or PCR

Treatment
- Gentamicin or streptomycin for 10 days

Prevention
- Avoid tick-infested areas, check clothing for ticks, and use tick repellents
- Avoid exposure to dead or wild mammals and wear gloves if such exposure is necessary; hands should be thoroughly washed afterward

Rocky Mountain Spotted Fever (RMSF)

Background and epidemiology
- Tickborne rickettsial disease
- Transmitted by the American dog tick (*Dermacentor variabilis*) east of the Rocky Mountains and Pacific coast
- Spread by Rocky Mountain wood tick (*D. andersoni*) in Rocky Mountain region
- Spread by Brown dog tick (*Rhipicephalus sanguineus*) worldwide
- Caused *by Rickettsia rickettsii*
- Peak transmission in summer

Clinical features
- Early illness (days 1–4)
  - Fever
  - Malaise
  - Headache
  - Abdominal pain
  - Myalgias
  - Rash appears 2–4 days after fever; 10–15% do not have rash
  - Maculopapular rash starts at the wrists and ankles, spreads centrally to palms and soles
  - Rash becomes petechial and purpuric

- Late illness
  - Altered mental status
  - Pulmonary edema, acute respiratory distress syndrome (ARDS)
  - Multiorgan failure (CNS, kidney)

Laboratory

- Serology testing: Indirect fluorescent antibody (IFA) for IgG at presentation and 2–4 weeks later. Frequently negative during 1st week of illness
- PCR blood may be helpful if positive but does not rule out infection, as the organism is intracellular

Treatment

- Start treatment before testing results return; can be fatal within days
- Doxycycline is the treatment of choice even in children < 8 years
- Antibiotic is given for at least 5–7 days and at least 3 days after fever resolves
- Best outcome when treatment started within 5 days of illness

Complications

- Vasculitis
- Disseminated intravascular coagulation (DIC)
- Death

Ehrlichiosis

Background and epidemiology

- Gram-negative cocci
- Transmitted by:
  - Lone star tick (*Amblyomma americanum*) in South Central and Eastern United States. Also transmits for tularemia and southern tick associated rash illness (STARI)
  - Blacklegged tick (*Ixodes scapularis*) in Eastern United States. Also transmits for anaplasmosis, Lyme disease, and babesiosis
- Can transmit via blood transfusion and organ transplantation
- Peak transmission in summer
- Incubation period is 5–14 days

Clinical presentation

- Similar to RMSF with early and late illness (Table 9.2)
- Maculopapular rash sparing the face that may spread to palms/soles; appears in 60% of children 5 days after fever begins

Laboratory findings

- Leukopenia
- Neutropenia
- Thrombocytopenia
- Hyponatremia
- Elevated liver enzymes

Treatment

- Drug of choice is doxycycline, including children < 8 years

Borrelia burgdorferi

Lyme Disease

Background

- Tick-borne infection caused by spirochete *B. burgdorferi*
- Transmitted by *Ixodes* species ticks in the nymphal stage
- Commonly seen in spring and summer

Table 9.2 Difference between Rocky Mountain spotted fever and ehrlichiosis

Difference	Rocky Mountain spotted fever	Ehrlichiosis
Mode of transmission	Tick	Tick
Rash	Very common, including on palms and soles	60% of children
Neutropenia	Less common	More common
Thrombocytopenia	Yes	Yes
Anemia	Present in ~15%	Occurs in 50% later in illness
Hyponatremia	Yes	Yes
Liver enzymes	May be elevated	Usually elevated
Treatment	Doxycycline	Doxycycline

- Common regions in the USA: Northeast to Mid-Atlantic (> 90%), upper Midwest (Wisconsin and Minnesota), West Coast (California)
- Incubation period: 11 days

Early localized disease stage I

- Erythema migrans (pathognomonic skin lesion) either bullseye or clear center
- Myalgia
- Arthralgia
- Mild fever

Early disseminated disease stage II (weeks to months later)

- Multiple erythema migrans lesions
- Meningitis (lymphocytic)
- Cranial nerve palsies, e.g., Bell palsy
- Peripheral neuropathy, e.g., foot drop
- Heart block: first, second, or third degree

Late disseminated disease stage III

- Arthritis
- Oligo-migratory arthritis
- Remember: Lyme disease can be confused with juvenile idiopathic arthritis (JIA)

Diagnosis

- Erythema migrans is pathognomonic and is an early lesion; antibodies not developed yet
  - No need to test. Treat based on clinical diagnosis
- Serologic testing indicated to confirm early and late disseminated disease. Two-tiered testing:
  - Initial test is highly sensitive enzyme immunoassay assay (EIA). If positive, then
  - Western blot test, considered positive if *either*
    - 2 IgM bands positive, *or*
    - 5 IgG bands positive

Treatment

- Early localized: Doxycycline for 10 days (amoxicillin for 14 days if < 8 years)
- Isolated facial palsy: Doxycycline for 14 days
- AV block or meningitis: Doxycycline or ceftriaxone for 14 days
- Arthritis: Doxycycline for 28 days (amoxicillin for 28 days if < 8 years)

Treponema pallidum

Background

- *T. pallidum* is spirochete mobile bacteria
- Mode of transmission:
  - Sexual contact
  - Transplacental (congenital)
  - Exposure to infected blood or tissue

Clinical presentation

- Congenital syphilis
  - Stillbirth, hydrops, preterm, or asymptomatic
  - Hepatosplenomegaly
  - Snuffles (nasal secretions)
  - Lymphadenopathy
  - Mucocutaneous lesions
  - Pneumonia
  - Bone findings: Osteochondritis and periostitis
  - Maculopapular rash prominent on hands and feet that are highly infective
  - Late manifestations: Interstitial keratitis, deafness, Hutchinson teeth (peg-shaped incisors), anterior bowing of shins, frontal bossing, mulberry molars, saddle nose
- Primary syphilis
  - Genital chancre 3 weeks after exposure
  - Painless papule that then become painless ulcer, which is very contagious
- Secondary syphilis 2–10 weeks after the chancre heals
  - Maculopapular rash involving palms and soles
  - *Condyloma lata* (wart-like plaques around the anus or the vagina confused with *condyloma acuminata* seen in HPV)
  - Generalized lymphadenopathy
- Tertiary syphilis (symptomatic late syphilis 15–30 years after initial infection)
  - Cardiovascular, CNS, gummatous lesions

Diagnosis and treatment

- Screening methods:
  - Rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) test correlate with disease activity
  - Other infections and autoimmune diseases can cause false positive RPR or VDRL
- Fluorescent treponemal antibody absorption (FTA-ABS) test confirms the diagnosis, and this test remains positive for life
- Congenital syphilis:
  - Unlikely: No evaluation or treatment. Maternal titer low/negative and history of adequate treatment, normal infant physical exam, and infant titer < 4-fold the maternal titer
  - Less likely: Benzathine penicillin G single dose, no evaluation. Maternal history of adequate treatment > 4 weeks before delivery, normal infant physical exam, and infant titer < 4-fold the maternal titer
  - Possible: Aqueous crystalline penicillin G for 10 days; analysis of CSF, CBC, long bone radiographs: Mother not treated adequately or treated < 4 weeks before delivery, normal infant physical exam, and infant titer < 4-fold the maternal titer
  - Proven/highly probable: Aqueous crystalline penicillin G for 10 days; analysis of CSF, CBC, chest and long bone radiographs; transaminase; neuroimaging; ophthalmologic exam. Mother not treated adequately or treated < 4 weeks before delivery, or abnormal infant physical exam, or infant titer 4-fold higher than maternal titer
- Treatment with penicillin for acquired syphilis, with doxycycline or tetracycline if allergic to penicillin

Mycobacterium tuberculosis

Background

- *M. tuberculosis*, a tubercle bacillus, is the causative agent of tuberculosis (TB)
- Mycobacteria, such as *M. tuberculosis,* are aerobic, non-spore-forming, non-motile, facultative, curved intracellular rods measuring 0.2–0.5 μm by 2–4 μm
- Retains many stains after decolorization with acid-alcohol, which is the basis of the acid-fast stains used for pathologic identification
- TB spreads most commonly via airborne transmission
- TB is unlikely to spread from child < 4 years of age due to limited tussive force
- TB is likely to spread from infected adults to children (usually household or childcare center)

Risk factors

- Foreign-born individuals in the USA have TB rates 9.5 times higher than those of persons born in the USA
- HIV infection, treatment with TNF-alpha antagonists such as infliximab and etanercept, and other immunocompromising conditions
- Recent latent tuberculosis infection (LTBI)
- IV drug use
- Certain medical conditions such as diabetes and renal failure
- Incubation period from exposure to positive test is 2–10 weeks

Clinical presentation

- Only 5–10% of children older than 3 years of age who have untreated LTBI progress to disease
- Most LTBI progress to disease within 1–2 years of initial infection
- The most common site of infection is the lung (up to 80%)
- **Pulmonary disease**
  - Infants and adolescents are more likely to be symptomatic than 5 to 10-year-old children
  - Cough (usually last 3 weeks or longer)
  - Hemoptysis
  - Low-grade fever
  - Weight loss (rare)
  - Night sweats

  - Loss of appetite
  - Hilar or mediastinal adenopathy may be seen
  - Cavity lesions
- **Superficial lymphadenopathy**
  - The most common extrapulmonary form of TB
  - Children who have TB lymphadenopathy tend to be older than those who have non-tuberculous mycobacterial lymphadenopathy
  - Common locations: Anterior cervical, followed by posterior triangle, submandibular, and supraclavicular
  - Lymph nodes usually measure 2–4 cm and lack the classic inflammatory findings of pyogenic nodes
  - There may be overlying violaceous skin discoloration
  - Surgical node excision is not curative but may be necessary to establish the diagnosis
  - Most children respond well to a 6-month course of multidrug therapy, but occasionally therapy must be extended to 9 months, based on clinical response
- **CNS disease**
  - Tuberculomas, occurring in 5% of children who have CNS TB, appear as single rim-enhancing lesions ranging from 1 to 5 cm
  - In TB meningitis, CSF analysis typically demonstrates lymphocytes, a low-glucose concentration, and a high-protein value
  - The most common findings on CNS imaging:
    - Hydrocephalus and basilar enhancement
    - Vascular lesions involving the basal ganglia and midbrain also are common
  - TB should be considered in cases of childhood stroke
- **Pleural TB**
  - Seen more in older child and adolescent
  - Can occur in isolation or concomitantly with pulmonary parenchymal disease
  - Symptoms include chest pain, fever, cough, dyspnea, and anorexia. Auscultatory findings mimic those of bacterial pneumonia
  - Most children have positive tuberculin skin test (TST) results
  - Effusions are more common on the right and rarely bilateral
  - The pleural fluid is exudative and lymphocytic
  - A 6-month course of therapy is recommended
- **Miliary tuberculosis**
  - Due to lymphohematogenous spread, it is a disease of the young or immunocompromised children
  - Miliary disease can present shortly after primary infection
  - Multiorgan involvement is common
  - Clinical presentation:
    - Pyrexia
    - Hepatomegaly and splenomegaly
  - TST is insensitive because disseminated disease can produce TST anergy
  - AFB culture from gastric aspirates can have a yield as high as 50%
  - A prolonged course of therapy (9–12 months) should be administered to patients who have disseminated disease
- **Skeletal TB**
  - The most common manifestations of skeletal disease are:
    - Spondylitis
    - Arthritis
    - Osteomyelitis
  - Most patients are in the second decade of life
  - Spinal involvement (Pott disease), which can affect even young children
  - Skeletal lesions can develop more than 10 years after initial infection
  - MRI is the preferred imaging choice because it can demonstrate lesions months before plain radiographs
  - Chest radiographs are positive in 50% of children who have skeletal TB
  - TST results are usually positive
- **Other forms of TB include:**
  - Abdominal
  - Renal
  - Cutaneous disease

TB testing

- Cultures can be obtained by sequential sputum sampling or by gastric aspiration of early morning secretions in the younger child
- The bacillus grows slowly
  - 6 to 8 weeks to grow on Lowenstein–Jensen media
  - 2 to 3 weeks to grow in liquid media
- AFB stains include Kinyoun, auramine–rhodamine (Truant), and Ziehl–Neelsen
- Tuberculin skin test (TST) (Table 9.3)
  - Measured in millimeters of induration (not erythema)
  - Reading is 48–72 h after placement
  - Preferred for children < 2 years
  - Know: If a child returns for TST interpretation after 72 h and has induration meeting the criteria for positivity, the test is considered positive.

Table 9.3 Positive tuberculin test reaction results in infants, children, and adolescents

Induration of 5 mm or more	Induration 10 mm or more	Induration more than 15 mm
Children in close contact with known or suspected contagious people with tuberculosis	Children < 4 years of age	Children 4 years of age or older without any risk
Children with suspected tuberculosis either clinically or on chest radiograph	Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes, renal failure, malnutrition	
Children receiving immunosuppressive therapy or with immunosuppressive conditions, including HIV	Children born in, or who travel to, high-prevalence countries	
	Children exposed to adults in high-risk categories	

  - A negative result never eliminates the possibility of TB disease because many disseminated forms of TB, including TB meningitis, can induce TST anergy
- False-negative TST results:
  - Recent measles infection or vaccination
  - High-dose corticosteroid treatment, irradiation
  - Immunosuppressive therapy
  - Immunocompromising medical conditions
  - Disseminated tuberculosis
- False-positive TST result:
  - Primarily in children exposed to nontuberculous (environmental) mycobacteria
  - Children recently received a bacillus Calmette–Guérin vaccine
  - A boosting phenomenon: Children received multiple sequential TSTs
  - First screen for exposure risk by history before testing. Do not test all children routinely
- Bacillus Calmette–Guérin (BCG) vaccine
  - TST can be interpreted normally in a child who received a single dose of BCG vaccine as a young child
  - Having received BCG as an infant may not explain a positive skin test result later in life
  - The assumption that BCG receipt is the cause of a positive TST could lead to a lack of treatment for high-risk children who potentially could benefit from LTBI therapy
- Whole blood interferon-gamma release assays (IGRAs) have several potential advantages:
  - Only one office visit is required
  - There is no risk of the boosting phenomenon
  - More specificity for LTBI because the antigens in the IGRAs is shared less commonly with nontuberculous mycobacteria and are not found on BCG
- Chest radiographs
  - Children who have LTBI usually have normal-appearing chest radiographs

  - An isolated calcified lesion in a child who has a positive TST result can be treated as LTBI
  - The most common abnormal radiographic finding is hilar or mediastinal adenopathy
  - Other findings can include infiltrates, atelectasis, pleural effusions, cavities, or miliary disease
- TB exposure:
  - Children younger than 4 years of age and immunocompromised children
  - Should begin isoniazid (INH), pending results of repeat testing
  - If the second test result is negative, medication can be discontinued
  - Children experiencing TB exposure who are older than age 4 years and immunocompetent can be observed off medications, pending the second test result in 2–3 months

Latent TB infection (LTBI)

- The child demonstrating a positive skin test result should be treated for LTBI to decrease the risk of disease progression later in life
- The mainstay of therapy for LTBI is 12 weeks of daily INH and weekly rifampin
- An alternative is 4 months of daily rifampin (for INH intolerant or resistance)

Treatment of TB

- The standard initial regimen for pulmonary and extrapulmonary TB:
  - INH, rifampin, pyrazinamide (PZA), and ethambutol
  - INH and rifampin are administered for 6 months, and PZA and ethambutol are stopped after the first 2 months
- Exceptions: Treating children who have TB meningitis, where treatment courses of 7–12 months often are used

Side effects of antituberculous medications

- INH, rifampin, and PZA are all hepatotoxic
- Ethambutol can rarely cause optic neuritis (decreased color perception is the first sign of deterioration)
- Pyridoxine supplementation indicated for exclusively breastfed infants, nutritional deficiencies, symptomatic HIV, and pregnant females

Challenging clinical scenarios

- Adult in the household has infectious TB
  - All children in the household should have chest radiographs and TSTs performed
  - Children younger than 4 years of age should be started empirically on INH and rifampin until the TST is repeated in 2–3 months
  - If the second TST result is negative and the child is immunocompetent, medication can be discontinued
  - If the TST result is positive or the child is immunocompromised, INH and rifampin should be continued
- Infant whose mother has TB
  - The TST is helpful only if the result is positive, which is very rare
  - If the mother has a positive TST result and negative chest radiograph (LTBI), the child needs no evaluation
  - If the mother has radiographic features consistent with TB, the neonate requires evaluation for congenital TB
  - If the infant does not have congenital TB, he or she should be separated from the mother until the infant is receiving INH and pyridoxine (if the mother is breastfeeding) and the mother is receiving appropriate multidrug therapy
  - Once the infant is receiving INH, separation is unnecessary, and breastfeeding should be encouraged unless INH resistance is suspected
- Health-care workers (HCWs)
  - If positive TST results, they should receive chest radiographs

  - If the chest radiograph is negative, the HCW may be offered therapy for LTBI after weighing the risks and benefits of latent TB treatment in adults
  - If the chest radiograph is positive, the HCW needs to be evaluated further

Follow-up

- Children who have TB disease should be seen monthly while receiving therapy to document medication tolerance and adherence, weight gain, and achievement of appropriate milestones

Mycobacterium Avium-Intracellulare

Background

- Mycobacterium avium-intracellulare complex is the most common cause of nontuberculous disease in children
- Caused by two types of bacteria: *Mycobacterium avium* and *Mycobacterium intracellulare*
- Usually occurs in children with impaired cell immunity, including very young children < 5 years old
- Organisms are ubiquitous in soil

Clinical presentation

- Cervical lymphadenitis
  - Overlying skin is usually pink to violaceous
  - Usually unilateral
  - Increase in size over several weeks
- Cutaneous infections
- Ear infections
- Disseminated and pulmonary infections (high fever, night sweats, weight loss, lymphadenopathy, abdominal pain, diarrhea, and anemia) can occur in immunocompromised

Management

- Complete resection of infected lymph node is diagnostic and curative. Antibiotics are not necessary!
- Azithromycin or clarithromycin in combination with ethambutol or rifampin if cannot be resected

FUNGAL INFECTIONS

Candida Species

- *Candida albicans* is the most commonly isolated species, and causes infections (Candidiasis or thrush)
- Systemic infections of the bloodstream and major organs (invasive candidiasis or candidemia, particularly in immunocompromised patients)
- *Candida* appears as budding yeast cells and pseudohyphae (Fig. 9.18)

Oral Thrush

Background

- Common in the first 6 postnatal months
- Possibly due to infants' immunologic immaturity

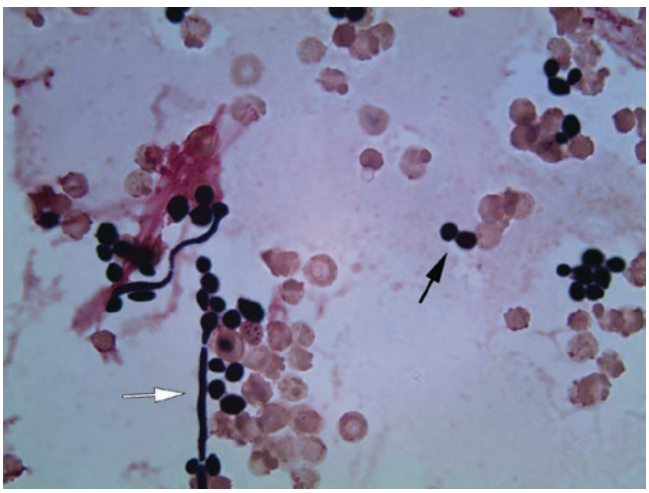

Fig. 9.18 *Candida albicans* in blood culture (Gram stain, original magnification × 1000). Budding yeast cells (blastoconidia, *black arrow*) and pseudohyphae (*white arrow*). (Courtesy of M. Nawar Hakim, MD, Department of Pathology, Texas Tech University Health Sciences Center, El Paso, Texas, USA)

Infection sources

- Contaminated bottle nipples, pacifier, or dropper, e.g., vitamin dropper
- Infected mother's nipples (although the incidence is high in formula fed infants)
- Maternal vaginal colonization with *Candida*

Recognize

- Recurrent or persistent oral thrush beyond 6–12 months raises the concern of immunodeficiency, especially if associated with failure to thrive or hepatosplenomegaly

Risk of infection

- Use of inhaled steroid without adequate rinsing afterward or oral antibiotics can cause oral thrush
- Poorly controlled diabetes in adults can cause *Candida* infection; however, it is not associated with gestational diabetes

Clinical presentation

- Infants may have trouble feeding in severe cases
- Tiny focal white area that enlarge to white patches on oral mucosa (Fig. 9.19)
- If scraped with a tongue blade, lesions are difficult to remove and leave behind an inflamed base that may be painful and may bleed
- Examine the patient with diaper dermatitis for oral lesions

Treatment

- Oral nystatin
- Once-daily oral fluconazole is superior to oral nystatin for resistant thrush

Candidal Diaper Dermatitis

Clinical presentation

- Lesions consist of beefy-red plaques, often with scalloped borders
- Satellite papules and pustules may be observed surrounding the plaques (Fig. 9.20)
- Maceration is often present, especially in intertriginous areas

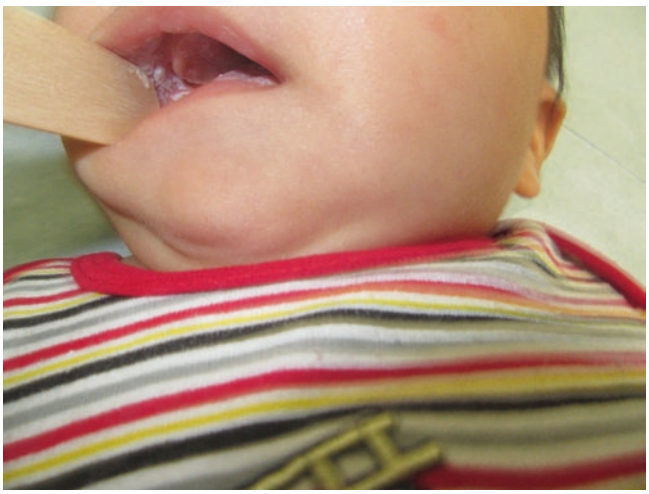

Fig. 9.19 Thrush: Tiny focal white areas that enlarge to white patches on oral mucosa; it was difficult to remove the white spots with the tongue blade

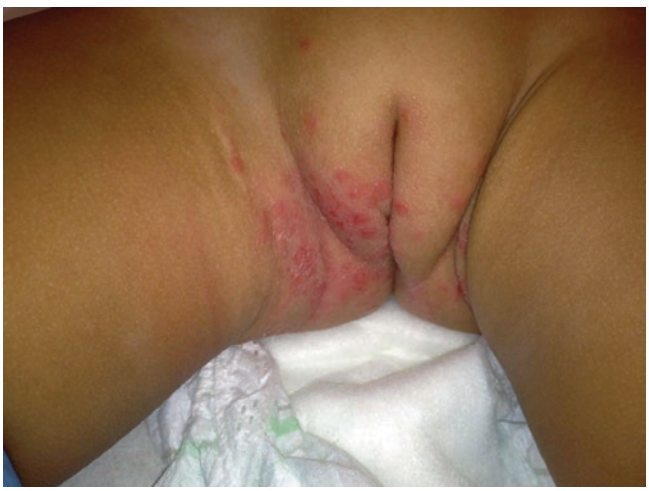

Fig. 9.20 Candidal diaper rash: Lesions consist of beefy-red plaques with satellite papules

Treatment

- Topical nystatin, miconazole, clotrimazole

Vulvovaginitis

Background

- Common in pubertal and adolescent girls
- Risk factors
  - Oral antibiotics
  - Oral contraceptive
  - Pregnancy
  - Poor hygiene
  - Diabetes

Clinical presentation
- Vulvar/vaginal erythema and itching
- White, cottage cheese-like vaginal discharge

Treatment
- Topical nystatin or clotrimazole
- Single dose of oral fluconazole for recurrent or refractory cases

Candidal Infections in Neonates

Background
- Very low-birth-weight and premature infants
- Central line-associated bloodstream infection (CLABSI): Obtain blood culture from periphery and catheter

Treatment
- Remove the catheter if CLABSI
- Parenteral micafungin or amphotericin, pending identification and sensitivity testing

Aspergillus

Background
- *Aspergillus* species consist of ubiquitous molds found in organic matter
- Most common species affecting humans are *A. fumigatus* and *A. niger*

Mode of transmission
- Inhalation of fungus spores
- Outbreaks can occur during hospital construction

Clinical presentation
- Invasive aspergillosis: Immunocompromised (neutropenia, graft-versus-host disease)
- Pulmonary, sinus, skin, intracranial
- Invasion of vasculature with erosion and hemorrhage
- Aspergillomas and otomycosis: Colonization in immunocompetent children
- Growth in cavities or cysts without invasion
- Underlying cystic fibrosis and TB
- Allergic bronchopulmonary aspergillosis: Hypersensitivity
- Wheezing, mucous plugging, fever, eosinophilia, transient lung infiltrates
- Underlying asthma or cystic fibrosis
- Allergic sinusitis
- Nasal polyps or sinus surgery
- Dark nasal discharge

Diagnosis
- Branched and septate hyphae seen on tissue or BAL
- Molecular testing is definitive
- Galactomannan assay from BAL specimen and serum

Treatment
- Invasive aspergillosis: Voriconazole
- Allergic bronchopulmonary aspergillosis: Corticosteroids

Malassezia furfur

Overview
- Can cause tinea versicolor (see Chap. 26 "Dermatology")
- Can cause neonatal infection in NICU babies receiving total parenteral nutrition (TPN) with lipids
- NICU babies with *M. furfur* may present with fever, bilateral interstitial infiltrates, and increased WBCs
- *M. furfur* requires olive oil overlay to grow

Management of infection in neonates
- Removal of catheters
- Stop lipid infusion
- Start amphotericin B or fluconazole

Histoplasmosis

Background
- Endemic areas: Ohio, Missouri, and Mississippi River valleys
- Mode of transmission
  - Inhalation of spores from bird excreta or contaminated soil
  - No person-to-person transmission

Clinical presentation
- Flu-like symptoms
- Pulmonary infiltrates
- Hilar lymphadenopathy with or without calcifications
- Erythema nodosum
- In younger children may develop progressive disseminated histoplasmosis

Treatment
- Not indicated for immunocompetent children with mild/moderate disease
- Severe or disseminated infection, especially in immunocompromised, treated with amphotericin B + steroids

Coccidioides

Coccidioidomycosis

Background
- Endemic areas
  - California, Arizona, New Mexico, and Texas
- Mode of transmission
  - Inhalation of airborne spores

Clinical presentation
- Most cases are asymptomatic
- Fever
- Cough
- Weight loss (common)
- Fatigue
- Shortness of breath
- Chills
- Erythema nodosum
- Night sweats
- Mild respiratory distress or respiratory failure in severe cases

Diagnosis
- Serology: The appearance of IgM or precipitin antibody against *Coccidioide*s is the most sensitive serologic indication of early infection
- Culture and DNA probe is the most definitive method for the diagnosis
- High index of suspicion is important in patient who travelled or underlying medical conditions
- Elevated erythrocyte sedimentation rate (ESR)
- Lymphocytosis and monocytosis
- Eosinophilia > 5%
- Chest radiograph may show consolidations and hilar lymphadenopathy

Treatment
- Not indicated for immunocompetent children with mild/moderate disease
- Severe or disseminated infection, especially in immunocompromised, treated with fluconazole or itraconazole
- High dose fluconazole for CNS infections

Blastomyces
- *Blastomyce*s causes illness similar to *Histoplasma* and *Coccidioides*
- Seen in Arkansas and Wisconsin hunters and loggers
- Outbreak occurred in children visiting Wisconsin lodge and beaver dam
- B*lastomyces* may disseminate to the skin and cause crusted skin lesions
- Bone lesions more common with blastomycosis
- Itraconazole (mild disease) or amphotericin B (severe disease) are the treatments of choice

Sporothrix schenckii
- Common in florists, as thorny plants are implicated
- Symptoms appear from 7 to 30 days after inoculation
- Present with painless papule at the site of inoculation, then ulcerates
- Secondary lesions follow along the lymphatic chain proximally
- Extracutaneous manifestation may occur, especially in immunocompromised
- Treat with itraconazole for 2–4 weeks

PROTOZOA

Giardia lamblia

Giardiasis

Background
- Giardiasis is an infection of the small intestine caused by the flagellated protozoan *Giardia intestinalis*
- Mode of transmission
  - Travelers and hikers who drink water contaminated with stool from infected animals such as beavers, muskrats, and sheep
  - Outbreaks also may occur from sewage contamination of water supplies
  - Unprotected anal sex also is a source of transmission
  - Childcare centers from fecal–oral transmission
  - Food-associated outbreaks may occur

Clinical presentation
- Most infections remain asymptomatic
- Watery diarrhea with abdominal cramping
- Nausea
- Vomiting
- Weight loss
- Flatulence

Diagnosed
- Microscopic examination of the stool for cysts or by antigen detection

Treatment
- Indicated for all symptomatic patients
- Metronidazole, a single dose of tinidazole, or nitazoxanide for 3 days
- Immunocompromised patients at increased risk for chronic giardiasis and treatment failure

Entamoeba histolytica

Background
- Amebiasis is caused by pathogenic species of Entamoeba
- Mode of transmission
  - Fecal–oral route
  - Travel to high-risk areas with poor sanitation and hygiene

Clinical presentation
- Can be asymptomatic
- Amebic dysentery or colitis
  - Bloody diarrhea with mucus
  - Tenesmus
- Hepatic abscess
  - Fever
  - Abdominal pain
  - Tender enlarged liver
  - Elevated liver enzymes
  - Elevated ESR

Diagnosis
- Serum antibody (95% detectable in invasive amebiasis)
- Stool microscopic examination
- Stool antigen
- Ultrasound if liver abscess is suspected

Treatment
- Symptomatic cases with systemic symptoms
  - Metronidazole followed by paromomycin or iodoquinol to eradicate colonization
- Asymptomatic amebiasis in nonendemic areas should be treated with a luminal agent (iodoquinol, paromomycin, or diloxanide furoate) to eradicate infection
- Amebic liver abscess cured by medical therapy without drainage

Cryptosporidiosis

Background
- Cryptosporidiosis, caused by *Cryptosporidium protozoa*
- Transmitted via fecal–oral route; childcare centers and swimming pools

Clinical presentation
- Nonbloody, watery diarrhea
- Chronic diarrhea in immunodeficient patients

- Test using DFA in stool; routine ova and parasite testing insufficient

Treatment
- Many immunocompetent patients who have cryptosporidiosis have self-limited disease and do not require therapy
- A 3-day course of nitazoxanide:
  - To reduce duration and transmission of diarrhea in children older than 1 year of age
- No swimming pool for at least 2 weeks after diarrhea ends

Toxoplasma gondii

Toxoplasmosis

Background
- Obligate intracellular protozoa
- Mode of transmission
  - Ingestion of contaminated raw or uncooked meat
  - Cat excreta
  - Organ transplants
  - Transplacental to fetus causes congenital toxoplasmosis (see Chap. 2 "Neonatology")

Clinical presentation
- Most cases are asymptomatic
- Fever
- Malaise
- Rash
- Myalgia
- Cervical lymphadenopathy (most common sign)
- Brain abscess (test for HIV)
- Chorioretinitis usually present years later (mostly congenital)

Diagnosis
- Head CT: Ring-enhanced lesion, intracerebral calcifications
- Toxoplasma IgM antibodies
- PCR

Treatment
- Infants with congenital toxoplasmosis: Pyrimethamine plus sulfadiazine and folic acid
- Pregnant females: Spiramycin

Pneumocystis jiroveci

Pneumocystis Pneumonia

Background
- Unicellular fungi that do not respond to antifungal treatment
- Mode of transmission is unknown
- Commonly seen in immunocompromised patients, e.g., HIV patients

Clinical presentation
- Subacute diffuse pneumonitis
- Dyspnea
- Tachycardia
- Hypoxemia that is exaggerated with exertion
- Nonproductive cough
- Fever

Diagnosis
- Chest radiography
  - Bilateral diffuse interstitial disease
- Low CD4
- BAL
- Lung biopsy

Treatment
- TMP-SMX
- IV pentamidine in severe cases
- Prophylaxis in immunocompromised patients
  - TMP-SMX

Plasmodium

Malaria

Background
- Intracellular protozoa
- Transmitted by mosquito bites in endemic areas of the tropics

Plasmodium falciparum

- Most severe, causing death within 48 h if untreated
- Symptoms develop 10 days after mosquito bite, longer if taking prophylaxis
- Complications
  - Cerebral malaria
  - Pulmonary edema
  - Severe anemia
  - Renal failure
  - Shock
- Treatment
  - Chloroquine sensitive (rare)
    - Chloroquine
  - Chloroquine resistant
    - Artemether–lumefantrine
    - Quinine plus doxycycline or clindamycin
    - Atovaquone–proguanil
  - Severe cases
    - IV artesunate (available from Centers for Disease Control and Prevention [CDC] only; not yet FDA-approved)
    - Quinidine gluconate IV (no longer produced for the US market as of 2019) plus doxycycline or clindamycin

P. malariae, P. vivax, and P. ovale

- Periodicity of symptoms
- Nephrotic syndrome – *P. malariae* (most benign form)
- Hypersplenism and splenic rupture – *P. vivax* and *P. ovale*
- Treatment
  - Chloroquine plus primaquine for *P. vivax,* and *P. ovale*
  - Chloroquine for *P. malariae*

Clinical presentation of malaria

- History of traveling to endemic area
- Paroxysmal fever, sweat, and rigors
- Pallor and jaundice
- Headache and myalgia
- Abdominal pain
- Vomiting and diarrhea
- In severe cases
  - Altered mental status
  - Hepatosplenomegaly
  - Anemia
  - Thrombocytopenia
  - Hypotension
  - Hypoglycemia
  - Hyperkalemia
  - Respiratory distress

Diagnosis

- Rapid diagnostic test (immunochromatographic test)
- Thick blood smear
- PCR available, but results are delayed

Prevention

- Traveling to chloroquine resistant areas, e.g., most tropical areas with malaria
  - Atovaquone–proguanil 1–2 days before and 7 days after travel, *or*
  - Doxycycline (> 8 years old) 1 week before until 4 weeks after travel
- Traveling to chloroquine sensitive areas, e.g., Central America
  - Chloroquine 1–2 weeks before and 4 weeks after, *or*
  - Atovaquone–proguanil 1–2 days before and 7 days after travel

HELMINTHIC ORGANISM

Enterobius vermicularis

Pinworm

Mode of transmission

- Person-to-person via fecal–oral route
- Eggs survive up to 3 weeks and are ingested from finger nails, bedding, and toys
- Autoinfection

Clinical presentation
- Anal and vulvar itching (more at night)
- Enuresis

Diagnosis
- Visualizing the adult worm at night on the perineum
- Transparent tape collected over three consecutive mornings under microscope low power

Treatment
- Pyrantel pamoate (over-the-counter), albendazole, mebendazole

Ascaris lumbricoides

Ascariasis

Mode of transmission
- Ingestion of eggs from contaminated soil (fecal–oral)

Clinical presentation
- Most patients are asymptomatic
- Nonspecific abdominal pain or discomfort
- Intestinal obstruction (large number of worms)
- Due to larvae migration to the liver and lung:
  - Obstructive jaundice
  - Peritonitis
  - Cough (Loeffler syndrome)

Diagnosis
- Seeing the ova on microscopic stool examination
- Seeing the adult worm itself

Treatment
- Pyrantel pamoate (over-the-counter), albendazole, mebendazole

Necator americanus

Ancylostoma duodenale

Hookworm

Background
- Found in rural, tropical, and subtropical locales
- Mode of transmission
  - Skin penetration of larvae from soil contaminated by human feces
  - Ingestion

Clinical presentation (blood sucker worms from the intestine)
- Itchiness and burning sensation
- Pharyngitis and gastroenteritis
- Failure to thrive
- Short stature
- Anemia due to chronic blood loss

Diagnosis
- Visualization of eggs in stool (may take 5–10 weeks after infection)

Treatment
- Pyrantel pamoate (over-the-counter), albendazole, mebendazole

Trichuriasis

Whipworm
- Due to infection of large intestine with *Trichuris trichiura*
- More common in the Southern United States
- Transmitted to humans by ingesting eggs
- Usually asymptomatic if only few worms
- Can cause fever, abdominal pain, weight loss, blood in stool, and rectal prolapse
- Presence of eggs in stool is diagnostic
- Treatment is with albendazole, mebendazole, or ivermectin

Trichinella spiralis

Trichinellosis

- *T. spiralis* is usually found in pork
- Symptoms depend on the worm location
- After ingestion the eggs hatch, larvae invade the duodenum and cause abdominal symptoms
- Larvae penetrate, reach bloodstream, end in muscular tissue and cause muscle pain
- If the larvae reach the heart, can cause myocarditis
- Ocular involvement: Presence of chemosis, periorbital edema, and eosinophilia usually suggest the diagnosis
- Diagnosis is confirmed by rising titers
- Treatment is with albendazole or mebendazole

Strongyloides stercoralis

Strongyloidiasis

- *S. stercoralis* is common in certain areas (Kentucky and Tennessee) of the USA
- The only helminthic organism that replicates in the body with autoinfection, and the infection may persist for decades
- Can cause pulmonary symptoms with eosinophilia and GI symptoms
- Potentially fatal in immunosuppressed patients
- Diagnosis of serial stool studies for larvae not the eggs
- Treatment: Ivermectin or albendazole

Toxocariasis

- *Toxocara canis* and *Toxocara cati* can cause visceral larva migrans
- Transmitted to humans by ingesting soil contaminated with dog or cat excreta
- In humans larvae do not develop into adult worms but rather migrate through the host tissue, causing eosinophilia
- Treatment: Albendazole or mebendazole

Cestodes (Platyhelminthes)

- Platyhelminthes include cestodes (tapeworms) and trematodes (flukes)
- Cestodes are flatworms (tapeworms)
- The pork tapeworm *Taenia solium*, present in two different ways
  - If the cysticerci are ingested, taeniasis develops and tape worm grows in the intestine
  - If contaminated food with eggs is ingested, the patient will develop cysticercosis
- Cysticerci live in CNS and the eyes and do nothing until they die
- Diagnosis of neurocysticercosis must be considered in patients with new onset seizures and history of traveling to or immigration from Mexico, Central, or South America, or who are from a household in these areas
- Treatment: Albendazole or praziquantel

Trematodes (Platyhelminthes)

- Trematodes or flukes
- *Clonorchis sinensis* is the Chinese liver fluke
- *Schistosoma haematobium* infects the bladder and causes urinary symptoms
- *Schistosoma mansoni* is a fluke found in Africa, the Middle East, and South America
- *Schistosoma japonicum* is found in Asia
- Most serious complications of Schistosomiasis is cirrhosis with esophageal varices
- Treatment: Praziquantel

FEVER

Fever Without Focus

Febrile Neonate

Background

- Difficult to distinguish between a serious bacterial infection and self-limited viral illness in this age group
- Neonates who have fever and do not appear ill have a 7% risk of having a serious bacterial infection
- Serious bacterial infections include occult bacteremia, meningitis, pneumonia, osteomyelitis, septic arthritis, enteritis, and UTI
- Late onset neonatal bacterial diseases, e.g., group B *Streptococci, E. coli*, and *Listeria monocytogenes* and perinatal herpes (HSV) infection
- If the neonate has fever recorded at home by reliable parents, the patient should be treated as febrile neonate
- If excessive clothing and blanket falsely elevate the temperature, the excessive covering should be removed and retake the temperature in 15–30 min

Management

- All febrile neonates must be hospitalized
- Full sepsis evaluation including blood, urine; CSF should be cultured
- CSF studies should include cell count, glucose, and protein level, Gram stain, cultures; HSV, and enterovirus PCR should be considered
- Blood and urine cultures warranted
- Chest radiograph may be included
- Child should receive empiric antibiotics such as cefotaxime or gentamicin + ampicillin
- Acyclovir should be included if HSV infection is suspected

Fever in 1–3-Month-Old Infants

Background

- Large majority of children with fever without localizing signs in 1–3 months age group likely viral syndrome
- Most viral diseases have distinct seasonal pattern, unlike bacteria, e.g., respiratory syncytial virus, and influenza more common during winter and enterovirus infection more common during summer and fall

Management

- Ill-appearing (toxic) febrile infants ≤ 3 months:
  - Require prompt hospitalization, immediate parenteral antibiotics after blood and CSF cultures are obtained
- Well-appearing infants 1–3 months previously healthy with no evidence of focus of infection:
  - WBCs count of 5000–15,000 cells/μL, an absolute band count of ≤ 1500 cells/μL, normal urinalysis, and negative culture (blood and urine) results are unlikely to have a serious bacterial infection
- The decision to obtain CSF studies in the well-appearing 1–3 months old infant depends on the decision to administer empiric antibiotics
- If close observation without antibiotics planned, a lumbar puncture may be deferred

Fever in 3–36 Months of Age

Background

- Approximately 30% of febrile children in the 3–36 months age group have no localizing signs of infection
- Viral infections cause most fevers in this population
- Risk factors indicating probability of occult bacteremia: Temperature ≥ 39 °C, WBC count ≥ 15,000/μL, elevated absolute neutro-

phil count, bands, ESR and C-reactive protein (CRP)
- The risk of bacteremia and/or pneumonia or pyelonephritis among infants 3–36 months of age increases as temperature (especially > 40 °C) and WBC count (especially > 25,000) increase

Management
- Toxic-appearing febrile children 3–36 months of age who do not have focal infection should be hospitalized, with prompt institution of parenteral antibiotics after blood, urine, and CSF cultures are obtained (full sepsis evaluation)
- For nontoxic-appearing infants who have temperature < 39 °C: Can be observed as outpatient with no diagnostic test or antibiotics
- For nontoxic infants who have rectal temperature ≥ 39 °C, options include obtaining a blood culture and administering empiric antibiotic therapy (ceftriaxone, a single dose 50 mg/kg not to exceed 1 g); or blood culture with no antibiotic and observing the patient within 24 h as outpatient. (Careful observation without empiric antibiotics is generally prudent)

Fever of Unknown Origin (FUO)

Background
- FUO was defined as:
  - More than 8 days' duration of illness. Temperature greater than 38.3 °C (101 °F) on several occasions
  - Failure to reach a diagnosis despite 1 week of investigation
- Patients with undiagnosed FUO (5–15% of cases) generally have a benign long-term course, especially when the fever is not accompanied by substantial weight loss or other signs of a serious underlying disease
- FUO lasting > 6 months is uncommon in children and suggests granulomatous or autoimmune disease (Table 9.4)

Table 9.4 Differential diagnosis of fever of unknown origin

Fever type	Differential diagnosis
Infectious	Viral: EBV, CMV, hepatitis, HIV, parvovirus B19
	Bacterial: tuberculosis, cat scratch, *Brucella*, *Salmonella*, meningococcemia
	Common: otitis media, sinusitis, pneumonia, UTI, osteomyelitis, septic arthritis, meningitis
	Less common: malaria, Lyme disease, endocarditis
Rheumatologic	Juvenile idiopathic arthritis, SLE, dermatomyositis
Oncologic	Leukemia, lymphoma, neuroblastoma, Ewing sarcoma, hemophagocytic lymphohistiocytosis
Autoimmune	Inflammatory bowel disease, macrophage activation syndrome
Drug related	Penicillin, cephalosporins, sulfonamides, acetaminophen
Other	Kawasaki disease, thyrotoxicosis, factitious fever

EBV Epstein-Barr virus, *CMV* cytomegalovirus, *UTI* urinary tract infection, *SLE* Systemic lupus erythematosus

Approach
- Age of the patient is helpful:
  - Children > 6 years of age often have respiratory or genitourinary tract infection, localized infection (abscess, osteomyelitis), JIA, or (rarely) leukemia
  - Adolescent patients more likely to have TB, inflammatory bowel disease, autoimmune process, or lymphoma in addition to the causes of FUO in younger children
- Exposure to wild or domestic animals, and zoonotic infection
- History of pica should be elicited; ingestion of dirt is particularly important due to infection with *T. canis* or *T. gondii*
- Physical examination is essential to find any physical clues to underlying diagnosis, e.g., lymphadenopathy, rash, joint swelling, etc.
- Laboratory determined on case-by-case basis
- ESR > 30 mm/h indicates inflammation and needs further evaluation

- ESR > 100 mm/h suggests tuberculosis, Kawasaki disease, malignancy or autoimmune disease
- Low ESR does not eliminate the possibility of infection
- CRP is another acute phase reactant that is elevated and returns to normal more rapidly than ESR
- Cultures, serologic studies, imaging studies, and biopsies, depending on the individual case

Treatment

- The ultimate treatment of FUO is tailored to the underlying diagnosis
- Empiric trials of antimicrobial agents may be dangerous and obscure the diagnosis of infective endocarditis, meningitis, parameningeal infection, and osteomyelitis
- Antipyretics for fever and relief of symptoms

CENTRAL NERVOUS SYSTEM (CNS) INFECTIONS

Encephalitis

Definition

- Inflammation of the brain

Causes

- Viral, e.g., West Nile virus and herpesvirus (most common)
- Bacteria, e.g., mycoplasma, tertiary syphilis
- Noninfectious, e.g., autoimmune
- Prion protein
- Parasitic
- Fungal
- Acute cerebellar ataxia
  - Ataxia
  - Nystagmus
  - Cerebellar dysarthria

Epidemiology

- WNV remains the most commonly encountered arboviral encephalitis agent
- California encephalitis viruses cause the greatest proportion of symptomatic pediatric infections
- Eastern equine encephalitis has the highest overall mortality rate
- The importance of local epidemiological information and seasonality cannot be ignored
- Enteroviruses are most often seen in spring and summer; arthropod-borne illnesses in the summer and fall

Clinical presentation

- Altered mental status
- Seizures
- Weakness
- Sensory disturbances
- Nonepileptic movement disorders
- Young children in absence of identifiable cause may present with:
  - Somnolence
  - Disinterest in feeding
  - Weak suck and irritability
  - Loss of head control
  - Abnormal eye movements
- Further clinical clues:
  - Fever (either acutely or in the 1–4 weeks interval before the onset of symptoms)
  - Meningeal irritation
  - Any child presenting with uncharacteristic behavior that is persistent and disproportionate to environmental and situational factors

Initial evaluation of the patient includes

- Seasonal presentation
- History of immunosuppression
- Travel history
- Recent local epidemiological information
- Presence of focal neurologic symptoms or deficits.

Investigation

- CBC
- Complete metabolic panel
- Urinalysis
- MRI or CT scan for intracranial pressure (ICP)
- Electroencephalogram (EEG)

- Enteroviral infections can produce a sepsis-like syndrome with more remarkable hematologic abnormalities
- Neonatal HSV infections sometimes produce hepatic function abnormalities and disseminated intravascular coagulation
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- Lumbar puncture if normal pressure
- Cerebrospinal spinal fluid study:
  - The lumbar puncture is the single most utilized test for the diagnosis of encephalitis
  - Increased opening pressure
  - Normal or elevated protein concentration
  - Normal glucose level
  - Pleocytosis, polymorphonuclear leukocytes; then converts to lymphocytic in many viral cases
  - Monocytic; predominance may show with progression of the disease
  - Hemorrhagic pleocytosis with HSV
  - Atypical lymphocytes with EBV
  - Mononuclear leukocytes with echovirus or varicella-zoster infection
  - PCR amplification of viral DNA
  - Pleocytosis tends to be less dramatic in parainfectious encephalitis or acute cerebellar ataxia
  - Fourfold rise in titer, especially IgM, against a suspected agent is most often considered diagnostic
- IV acyclovir while waiting for lumbar puncture, or while waiting for laboratory results, including HSV PCR
- Intracranial hypertension conservative measures
  - Head elevation
  - Hyperventilation
  - Fluid restriction
  - Mannitol is used on a limited basis

Treatment of seizure

- Benzodiazepines (midazolam, lorazepam, diazepam) in the beginning followed by loading dose of fosphenytoin, or phenobarbital II

Meningitis

Neonatal Streptococcal Meningitis

- Guillain–Barré syndrome remains the predominant neonatal meningitis pathogen
- Early-onset disease: Infants typically manifest with signs suggestive of sepsis, often with pneumonia, but less commonly with meningitis
- Late-onset disease: Infants typically are 3–4 weeks of age and present with meningitis or bacteremia

Neonatal Gram-negative meningitis

- Gram-negative bacillary meningitis is rare, *E. coli* being the most commonly isolated pathogen
- Other Gram-negative neonatal meningitis pathogens such as *Citrobacter koseri, Enterobacter sakazakii,* and *Serratia marcescens*

Neonatal herpes simplex (HSV) infection

- HSV in the newborn can present as isolated skin or mucous membrane lesions, encephalitis, or disseminated process
- HSV infection occurs most commonly in infants born to mothers who have active primary infection
- Frequently no maternal history or clinical evidence is available to alert the practitioner to this diagnosis
- The incubation period is 2 days to 2 weeks, and most infants who develop HSV CNS infection are 2–3 weeks of age

Neonatal meningitis due to Listeria

- Common sources:
  - Unpasteurized milk
  - Soft cheese
  - Prepared ready-to-eat meats
  - Undercooked poultry
  - Unwashed raw vegetables
- Can precipitate abortion and preterm delivery
- Septic appearance in the neonate is typical in cases of early onset
- Papular truncal rash has been identified

S. pneumoniae

- Pneumococcus is the leading pathogen causing bacterial meningitis in infants and young children in developed countries

N. meningitidis

- Meningococcal disease generally occurs in otherwise healthy individuals and often has a fulminant presentation with high fatality rates

Aseptic meningitis

- Enterovirus is the most common etiology
- *B. burgdorferi* in mid-Atlantic states (Lyme)
- Vasculitis in the setting of systemic lupus erythematosus or Kawasaki disease.
- Drug-induced such as ibuprofen, and IV immunoglobulin

Other causes of meningitis

- *M. tuberculosis*
- *B. burgdorferi*
- *R. rickettsii*

Clinical manifestations

- Infants younger than 1 month of age who have viral or bacterial meningitis
  - Fever
  - Hypothermia
  - Lethargy
  - Irritability
  - Poor feeding
- Signs and symptoms of increased ICP and meningeal inflammation
  - Vomiting
  - Apnea
  - Seizures can also occur
- Older children and adolescents often experience
  - Malaise
  - Myalgia
  - Headache
  - Photophobia
  - Neck stiffness
  - Anorexia
  - Nausea

Physical examination

- Altered levels of consciousness can present as irritability, somnolence, lethargy, or coma
- ICP include:
  - Papilledema
  - Diplopia
  - Unilateral or bilateral dilated pupils
  - Poorly reactive pupils
  - Bulging fontanelle in infants
  - Head circumference should always be obtained, especially in those who have an open fontanelle
- Meningismus is suggestive of meningeal irritation
- Kernig sign:
  - The patient lies supine and the thigh is flexed at a right angle to the trunk. If knee extension from this position elicits pain, the Kernig sign is positive
- Brudzinski sign:
  - The patient lies supine and flexes his or her neck
  - A positive sign occurs if the patient also reflexively flexes the lower extremities, typically at the knees
- Absence of Kernig and Brudzinski signs does not exclude meningitis
- Exanthems typical for enterovirus, borreliosis (erythema migrans), and invasive meningococcal or pneumococcal disease (petechiae and purpura) may be present

Diagnosis

- All children who are suspected of having meningitis should have their CSF examined unless lumbar puncture is contraindicated
- Contraindications of lumbar puncture include:
  - Focal neurologic deficits
  - Signs of increased ICP
  - Uncorrected coagulopathy
  - Cardiopulmonary compromise
- CT scan is performed before lumbar puncture if any sign of ICP present
- CSF findings in bacterial meningitis (Table 9.5)

Table 9.5 Cerebrospinal fluid analysis

Type of infection	White blood cells	Protein	Glucose
Bacterial meningitis	> 1000/μL	High	Low (less than half of serum)
Viral meningitis (viral)	< 500/μL	Normal	Usually normal
Tuberculosis	< 500/μL (predominant lymphocyte)	Very high	Low (less than half of serum)

  - Glucose concentration is usually less than one half of the measured serum value
  - Protein value often is greater than 100 mg/dL
  - WBC often greater than 1000/mcL, with a predominance of polymorphonuclear leukocytes
  - Gram stain is extremely helpful if positive
  - CSF culture remains the gold standard for diagnosing bacterial meningitis
- CSF finding viral meningitis
  - WBC count of 50–500/mcL
  - Neutrophil predominance is common early in the course of infection, shifting to lymphocytic predominance quickly during the illness
  - Glucose and protein concentrations frequently are normal, although the protein value can be slightly elevated. Gram stain is universally negative
  - In cases of enteroviral meningitis, enteroviral PCR can confirm the diagnosis
- Tuberculous meningitis, epidemiologic clue, high protein, and lymphocytosis
- SIADH and hyponatremia commonly occur in bacterial meningitis
- Leukopenia, thrombocytopenia, and coagulopathy may be present in meningococcal and rickettsial infections

Management

- Therapy should not be delayed if CNS infection is suspected
- Appropriate antimicrobials are required in bacterial meningitis, HSV encephalitis, Lyme meningitis, tuberculous meningitis, and rickettsial infection; in all cases, timely diagnosis and correct antimicrobial choice are critical
- If the practitioner cannot perform a lumbar puncture or there are contraindications to CSF examination, a blood culture should be obtained and antibiotics administered promptly

Drug choice and duration

- For infants
  - Ampicillin (300 mg/kg/day divided every 6 h) and cefotaxime (300 mg/kg/day divided every 6 h) is appropriate. Gentamicin can be used instead of cefotaxime
  - Acyclovir (60 mg/kg/day divided every 8 h) should be added if HSV infection is a concern
  - Vancomycin (60 mg/kg/day given every 6 h) should be added, if the Gram stain suggests pneumococcus
- Children older than 1–2 months of age
  - Vancomycin (60 mg/kg/day divided every 6 h) plus ceftriaxone (100 mg/kg/day given in one dose or divided into two doses) or cefotaxime (200–300 mg/kg/day divided every 6 h) should be used for empiric coverage
  - Once culture and susceptibility data are available, definitive therapy can be selected
- HSV meningitis
  - Neonatal HSV CNS infection typically is treated with IV acyclovir (60 mg/kg/day divided every 8 h) for 21 days
  - The dosing for non-neonates is 30 mg/kg/day divided every 8 h IV for 14–21 days
  - Follow-up CSF HSV DNA PCR should be evaluated at day 21 and the course of therapy extended if the result is still positive

Corticosteroids in bacterial meningitis

- Adjunctive treatment has reduced rates of mortality, severe hearing loss, and neurologic sequelae, significantly in adults who have community-acquired bacterial meningitis
- For children beyond the neonatal age groups, available data suggest that the use of adjunctive corticosteroids may be beneficial for Hib meningitis and could be considered in cases of pneumococcal meningitis
- The dose of dexamethasone for bacterial meningitis is 0.6 mg/kg/day divided into four doses and administered IV for 4 days. The first dose should be given before or concurrently with antibiotics

Care of the child exposed to meningitis

- Meningococcal and Hib disease create an increased risk for secondary infection in contacts
- Rifampin generally is the drug of choice for chemoprophylaxis in children

Prognosis for meningitis

- Intellectual deficits (intelligence quotient < 70), hydrocephalus, spasticity, blindness, and severe hearing loss are the most common sequelae
- Hearing loss occurs in approximately 30% of patients, can be unilateral or bilateral, and is more common in pneumococcal than meningococcal meningitis

Brain Abscess

Causes

- Chronic otitis media
- Paranasal sinus infection
- Otogenic infections, poor dental hygiene/complications from dental procedures
- Mastoiditis
- Metastatic spread, e.g., endocarditis
- Right-to-left cardiac or pulmonary shunts, especially in the presence of cyanotic congenital heart disease
- Neurosurgical procedures (VP shunt)
- Penetrating skull injury, congenital head and neck lesions
- Immunosuppression
- Commonly identified microorganisms: *Streptococci* and *Staphylococci*

Clinical presentation

- Triad of fever, headache, and focal neurologic deficit
- Headache (most common)
  - May be throbbing
  - Worsens with changes in posture or Valsalva maneuver
- Vomiting
- Drowsiness
- Confusion
- Coma
- Hemiparesis
- Papilledema

Frontal lobe abscesses

- Apathy, memory deficits
- Personality change
- Mental slowing

Cerebellar abscesses

- Nystagmus
- Defective conjugate eye movements to that side
- Ataxia
- Hypotonia

Laboratory diagnosis

- Little in the laboratory investigation of patients who have brain abscesses is specific to the diagnosis except for culture of the purulent material and antibiotic sensitivity of the responsible organism

Neuroimaging

- CT scan of the brain
  - Ill-defined
  - Low-density change within the parenchyma
  - Enhancement occurs following administration of contrast material

  - Classic ring-enhancing lesion with surrounding edema
  - Calcification is common in abscesses in neonates
- MRI

Antimicrobial therapy

- For abscesses arising as a result of sinusitis in which *Streptococci* are the most likely organisms, penicillin or cefotaxime and metronidazole
- Chronic otitis media or mastoiditis often is associated with *P. aeruginosa* and *Enterobacteriaceae*, antibiotics to treat abscesses secondary to these infections should include penicillin, metronidazole, and a third-generation cephalosporin
- Metastatic abscesses require a regimen based on the likely site of primary infection
- *S. aureus* is commonly isolated in abscess following trauma

Surgical intervention

- Provide a specimen of purulent material for bacteriologic analysis and antibiotic sensitivity testing
- Remove purulent material, thereby lowering ICP and decreasing the mass effect of the abscess
- Decompress and irrigate the ventricular system and debride the abscess in the event of its rupture into the ventricular system

Prognosis

- Brain abscess is a destructive lesion
- Neurologic sequelae: Epilepsy, motor deficits, visual field cuts, learning disability, hydrocephalus requiring VP shunt placement

PEARLS AND PITFALLS

- Monospot testing for acute mononucleosis is not indicated for children < 5 years of age because results are not reliable in young children.
- For children with multiple ulcerations of buccal mucosa and conjunctival involvement (mucous membranes) with skin rash, think erythema multiforme major (Stevens–Johnson syndrome).
- For children with ulcerations of posterior pharynx and painful papules on palms and soles, think enterovirus (especially Coxsackie virus) causing hand, foot, and mouth disease
- For a child with pharyngitis and redness of skin creases of anterior cubital fossae (Pastia lines, also called Thompson sign), think Group A Strep (strep throat).
- Egg allergy, including anaphylaxis, is not a contraindication to influenza vaccination. Only persons with a previous severe allergic reaction to flu vaccine should not receive flu vaccine.
- For returning travelers with fever, obtain malaria testing immediately and begin appropriate therapy (artemether–lumefantrine or atovaquone–proguanil for *P. falciparum*) if positive. Do not delay!
- Children < 2 years old can be colonized with *C. difficile* and may test positive for the organism. Only patients with *C. difficile* toxin production should be considered for treatment with first-line oral metronidazole.
- Patients with a classic bull's eye rash at the site of a tick bite do not require diagnostic testing. Treat for early localized Lyme disease with doxycycline (amoxicillin or cefuroxime for children < 8 years old).
- A positive blood culture for *Candid*a should be acted upon, including repeat blood culture and IV antifungal therapy with central line removal (if associated). A positive sputum culture for *Candida* may represent colonization and should be taken in the clinical context.
- Rash that begins on wrists and ankles, spreading centrally to palms/soles, is likely Rocky Mountain spotted fever. Treat with doxycycline no matter what age.
- Children who return from travel to the Middle East or Central America with ulcerative skin lesions and no systemic symptoms may have cutaneous Leishmaniasis.

- *Kingella kingae* is an etiologic agent of indolent septic arthritis or osteomyelitis in a young child. Can also cause bacteremia in infants and endocarditis in older children.
- Uncommon causes of fever in pediatrics include osteomyelitis, intraabdominal abscess, deep venous thrombosis, Still disease, recurrent fever syndromes (periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA), and familial Mediterranean fever).
- CNS complications of HIV include infection (cryptococcal meningitis, toxoplasmosis, CMV encephalitis, neurocysticercosis), lymphoma, progressive multifocal leukoencephalopathy (PML), peripheral neuropathy, and HIV encephalopathy.
- Nontuberculous mycobacteria can cause unilateral submandibular lymphadenitis with a violaceous hue in young children. Primary treatment is surgical excision, not antibiotics. Excision prevents fistula formation.
- Most mild community-acquired pneumonia can be treated as outpatient with oral amoxicillin as first-line therapy in patients who can tolerate oral fluids.
- The most common etiology for osteomyelitis *and* septic arthritis is *S. aureus*. Persons with sickle cell disease are at higher risk for *Salmonella.*
- For post-exposure rabies prophylaxis, administer rabies immune globulin at the bite site and rabies vaccine at a contralateral site on days 0, 3, 7, and 14 (four total doses of vaccine). For immunocompromised persons (HIV), a fifth dose of rabies vaccine is given on day 28.
- To avoid botulism in the 1st year of life, avoid giving infants prepared cereals that contain honey, as these may also be a potential source.
- For TB testing, can use an interferon gamma release assay (IGRA) for children > 2 years of age. Use skin testing for younger children.

Suggested Reading

American Academy of Pediatrics. *Bartonella henselae* (cat-scratch disease). In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018a. p. 244–7.

American Academy of Pediatrics. Chlamydial infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018b. p. 273–83.

American Academy of Pediatrics. Cytomegalovirus infection, varicella-zoster virus infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018c. p. 310–7. and 869–83.

American Academy of Pediatrics. Gonococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018d. p. 355–65.

American Academy of Pediatrics. Group A streptococcal infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018e. p. 616–28.

American Academy of Pediatrics. Human immunodeficiency virus infection. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018f. p. 459–76.

American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, editors. Red book: 2018–2021 report of the committee on infectious diseases. 31st ed. Itasca: American Academy of Pediatrics; 2018g. p. 829–53.

American Academy of Pediatrics Committee on Pediatric AIDS. HIV testing and prophylaxis to prevent mother-to-child transmission in the United States. Pediatrics. 2008;122(5):1127–34.

American Academy of Pediatrics, American Public Health Association, National Resource Center for Health and Safety in Child Care and Early Education. CFOC standards online database. www.nrckids.org/CFOC. Aurora: National Resource Center for Health and Safety in Child Care and Early Education; 2019. Accessed 31 Jan 2019.

Amren DP, Anderson AS, Wannamaker LW. Perianal cellulitis associated with group A streptococci. Am J Dis Child. 1966;112(6):546–52.

Chayavichitsilp P, Buckwalter JV, Krakowski AC, Friedlander SF. Herpes simplex. Pediatr Rev. 2009;30(4):119–30.

Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. Ann Emerg Med. 2010;55(5):401–7.

Fatahzadeh M, Schwartz RA. Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management. J Am Acad Dermatol. 2007;57(5):737–63.

Khazaeni LM. Ocular complications of congenital infections. NeoReviews. 2017;18(2):e100–4.

Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):21):e1474–502.