Chapter e138: Parasitic Diseases

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KEY CONCEPTS

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1. Single-dose tinidazole is the preferred treatment for giardiasis treatment.
2. HIV-infected patients with cryptosporidiosis must receive antiretroviral therapy as the mainstay of therapy in addition to antiparasitic therapy.
3. *Entamoeba histolytica*-specific immunoassays are required to diagnose amebiasis because stool sample microscopy does not distinguish between *E. histolytica* and the nonpathogenic *Entamoeba*.
4. Metronidazole and tinidazole are tissue-acting agents against *Entamoeba*, whereas paromomycin and iodoquinol are luminal amebicides.
5. Benznidazole is recommended for treatment of Chagas disease in all patients without established cardiomyopathy.
6. Atovaquone and azithromycin combination therapy is recommended for treatment of babesiosis.
7. Patients with noncalcified parenchymal neurocysticercosis should initially receive symptomatic therapy with corticosteroids and antiepileptic drugs followed by antihelminthic therapy.
8. For head lice, either nonprescription 1% permethrin or pyrethrins plus piperonyl butoxide topical preparations are agents of choice unless local resistance to these agents is documented.
9. A single application of 5% permethrin results in cure rates in more than 90% of subjects with scabies at 14 and 28 days, but a second dose should be applied 1 week later because its ovicidal efficacy remains unclear.
10. Chemoprophylaxis with non-chloroquine antimalarial drugs such as atovaquone-proguanil and doxycycline retain effectiveness in areas where chloroquine-resistant *Plasmodium falciparum* exposure is likely.

BEYOND THE BOOK

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Review the figures depicting the life cycle of each of the following parasites on the Centers for Disease Control and Prevention (CDC) Website. Identify the primary way in which each parasite enters the human host and propose at least one strategy to prevent infection from that parasite. The parasites below are listed in order of least to most complex life cycle.

Head Lice (https://www.cdc.gov/parasites/lice/head/biology.html)

Giardiasis (https://www.cdc.gov/parasites/giardia/pathogen.html)

Cryptosporidiosis (https://www.cdc.gov/parasites/crypto/pathogen.html)

Cysticercosis (https://www.cdc.gov/parasites/cysticercosis/biology.html)

Chagas Disease (https://www.cdc.gov/parasites/chagas/biology.html)

Malaria (https://www.cdc.gov/dpdx/malaria/)

This activity is intended to help learners propose risk factors for parasitic infections and nonpharmacologic measures that can be implemented to prevent disease transmission.

INTRODUCTION

Parasitic diseases remain a significant global health problem causing approximately 1 million deaths per year and affecting more than 1.7 billion people worldwide.[1-4] In the United States, immunocompromised patients, ethnic/racial minorities, immigrants, those with recent travel to developing regions, individuals living in poor sanitary conditions, and people who lack access to basic healthcare services appear to be at the highest risk for developing parasitic diseases.[5,6] However, people in every income and social strata can become infected. In fact, the CDC has referred to five diseases as neglected parasitic infections and has prioritized these for increased public health action.[6] They include Chagas disease, cysticercosis, toxocariasis, toxoplasmosis, and trichomoniasis.

Host–Parasite Relationship

General prevention and treatment principles of parasitic infections are based on the host–parasite relationship. *Symbiosis* describes an essential biological relationship between two species. *Parasitism* is a symbiotic relationship in which one species (the host) is injured through the activities of the other (the parasite). The life cycle of a parasite may occur solely in human hosts or in one or more hosts before it causes human disease. *Definitive hosts* are those in which parasites undergo sexual reproduction; whereas *intermediate hosts* allow larval or asexual stages of development to occur. Determining what part of a parasite's life cycle occurs in human hosts is important for antiparasitic drug development.

Vectors, which may also serve as definitive or intermediate hosts, are responsible for transferring a parasite to another host. An example would be the *Anopheles* mosquito that harbors and supports reproduction of the parasite *Plasmodium*. In turn, the infected mosquito can transmit the malaria-causing parasite to a human host through a bite. Reducing human exposure to those vectors responsible for human disease becomes an important nonpharmacologic public health strategy for reducing the incidence of parasitic diseases worldwide. *Reservoir hosts* are those that harbor parasites that cause disease in other hosts. For example, some mammals serve as reservoir hosts for *Trypanosoma cruzi*; while the intermediate host and vector for this parasite is primarily a family of triatomine bugs. Parasites that use a variety of reservoir hosts are more difficult to eradicate because they can utilize different hosts in their life cycle.

Classification of Parasitic Infection Types

Pathogenic parasites may be divided into three general categories based on their ability to cause clinical disease in humans (protozoa, helminths, and ectoparasites). Protozoa are unicellular microscopic eukaryotes that can survive and replicate within a human host. These parasites can be further classified based on transmission as either intestinal protozoa (eg, *Giardia, Cryptosporidium,* and *Entamoeba*) or blood and tissue protozoa (eg,

Plasmodium, Trypanosoma, and Babesia). Helminths or worms are large complex multicellular organisms with life cycles that include an egg, larval, and adult stage. These parasites often complete the egg or larval stage outside the human host and ingestion of the organism at these stages leads to infection. Helminths can be further divided into either nematodes (roundworms) or platyhelminths (flatworms). Roundworm infection can occur in the gut (eg, adult stage of *Strongyloides*) or affect organs (eg, *Toxocara* larvae). Both cestodes (tapeworms such as *Taenia solium*) and trematodes (flukes) are considered flatworms, which are helminths that lack a central digestive body cavity. Medically important arthropods such as lice and mites are considered ectoparasites because these blood-feeding invertebrates can infest the skin and hair. Rather than causing infestations, some ectoparasitic arthropods such as the tick cause significant disease by acting as a vector for transmitting infectious pathogens to the human host. Overall, the extent of harm a parasite inflicts on a human host depends on factors such as parasite load, host nutritional status, and host immune status. As such, drug therapy selection depends not only on parasite characteristics but on these host factors also. This chapter discusses the major parasitic diseases including protozoan disease (giardiasis, cryptosporidiosis, amebiasis, Chagas disease, malaria, and babesiosis), helminthic infections (toxocariasis and cysticercosis), and ectoparasitic infestations (lice and scabies).

PROTOZOAN DISEASES

Giardiasis

Epidemiology and Etiology

Giardia lamblia (also known as *Giardia intestinalis* and *Giardia duodenalis*) is the most frequently identified parasitic cause of diarrhea in US patients. During 2012 to 2017, there were 111 giardiasis outbreaks, including 760 cases, reported to CDC from 26 states mostly affecting those in the northwestern and northeastern states.[7] It is most frequently reported in children between ages 1 and 4 years and peak illness occurs in late summer, possibly due to increased contact with contaminated water during the summer months or decreased immunity in children.[8,9]

Pathophysiology and Clinical Presentation

G. lamblia has two life-cycle stages: the cyst and the trophozoite. Human host infection starts with ingestion of *G. lamblia* cysts in fecally contaminated water or food. Following ingestion of as few as 10 cysts, which are moderately tolerant to chlorinated water and low gastric pH, each cyst releases two trophozoites. The pear-shaped trophozoite of *G. lamblia* has four pairs of flagella with two nuclei that lie in the area of the sucking disk, giving this protozoan a characteristic face-like image. The flagellated trophozoites colonize the mucosal tract and asexual replication of these trophozoites leads to localized edema, flattening of the villi, persistent diarrhea, and subsequent nutrient malabsorption.[10] Lactose intolerance precipitated by giardiasis and iron deficiency can persist after parasitic eradication. In addition, those infected may shed 10^8 to 10^9 cysts in their stool per day for weeks after initial infection, which further increases the risk for disease spread.

Primary risk factors for diarrhea due to *Giardia* include ingestion of contaminated untreated water, swimming, occupational exposure to infected human waste, and sexual activity that may involve fecal contact.[11]The primary modes of transmission in the United States are water exposure (26%), person-to-person contact (25%), and contaminated food (5%).[7] In countries where giardiasis is endemic, infection risk and diarrhea severity may increase among immunocompromised human immunodeficiency virus (HIV)–infected adults. A giardiasis diagnosis in a patient with diarrhea should only be suspected in patients with the aforementioned risk factors who also fit the epidemiologic profile of infected patients (Table e138-1). In the absence of these specific exposures, more prevalent alternative etiologies of community-acquired infectious diarrhea such as enteric viruses or *Clostridioides difficile* should be investigated before parasitic causes are considered.[12,13]

TABLE e138-1

Clinical Presentation of Intestinal Protozoan Diseases

Giardiasis	Cryptosporidiosis	Amebiasis
Acute	Immunocompetent	Intestinal disease
Diarrhea: foul-smelling, copious, light-colored, fatty stools Cramp-like abdominal pain, bloating, and flatulence Malaise, anorexia, nausea, and belching	Diarrhea: profuse, watery, nonbloody Abdominal pain, fever, and vomiting Malaise, anorexia, joint pain, headache	Diarrhea: bloody (heme-positive in 100% of cases) with mucus Vague abdominal discomfort to severe abdominal cramps, flatulence Eosinophilia is usually absent, although moderate leukocytosis is not unusual
Chronic	Immunocompromised	Amebic liver abscess
Periods of diarrhea alternating with constipation Weight loss, lactose intolerance, vitamin B_{12}, and fat-soluble vitamin deficiencies	Diarrhea: cholera-like large amounts of watery diarrhea, weight loss, malabsorption Biliary, respiratory, or pancreatic dissemination	High fever, rigors, and profuse sweating, significant leukocytosis with left shift, and elevated alkaline phosphatase Right upper quadrant pain, hepatomegaly, and liver tenderness with referred pain to left or right shoulder

Data from References 12–15.

Giardia diagnosis may be made by enzyme immunoassays (EIA) or nucleic acid amplification testing (NAAT) of collected stool because these are 85% to 98% sensitive, 90% to 100% specific, rapid, reproducible, cost-effective, and do not require a trained microscopist.[12,14] Where these methods are unavailable, three stool specimens collected on separate days during the acute diarrheal phase for ova and parasites will yield up to 90% of the parasites if reviewed by an experienced microscopist.[14] Fresh stool specimens may show the trophozoites, whereas preserved specimens usually yield the cysts. Public health authorities should be notified once a giardiasis diagnosis is confirmed as this parasitic infection is designated as “Notifiable at the National Level” by the CDC.

Patient Care Process for Giardiasis

Collect

- Patient characteristics: age, recent fluid intake, and description of diarrheal illness (eg, duration, stool appearance)
- Patient medical history: immunocompromising conditions
- Social history: alcohol use, recent travel, animal contact, and other high-risk activities (see Table e138-1)
- Current medications: recent antibiotics, nonprescription laxatives, antidiarrheal medications
- Objective data
  - Vital signs: temperature, blood pressure, heart rate, respiratory rate, height, weight
  - Physical exam: mucous membrane inspection, skin turgor, abdominal exam, appearance of stool
  - Labs: chemistry panel, urine output, hemoglobin, platelets
  - Diagnostic stool sample evaluation

Assess

- Dehydration (acute), malnutrition, and vitamin deficiencies (chronic)
- Alternative etiologies based on clinical presentation and risk factors (eg, *Clostridioides difficile, Cryptosporidium*)
- Medication adherence and preference for tablets versus liquid formulation
- Likelihood of outbreak based on probable source of *Giardia* infection (eg, swimming pool, well water)

Plan*

- Nonpharmacologic therapy including oral rehydration and hand hygiene
- Drug therapy regimen including fluid therapy, electrolyte replenishment, and specific anti-infective, dose, route, frequency, and duration (see Table e138-2)
- Monitoring parameters including efficacy (eg, diarrhea resolution, volume status, electrolyte balance, urine output, serum creatinine) and safety (eg, metallic taste, nausea)
- Patient education (eg, risk factor avoidance, hand hygiene, purpose of treatment, drug-specific information including antidiarrheal medication avoidance)
- Self-monitoring for resolution of diarrhea and rehydration

Implement

- Provide patient education regarding all elements of treatment plan
- Patient or caregiver to ensure additional sick contacts with diarrhea seek care
- Report confirmed giardiasis case to public health officials

Follow-up: Monitor and Evaluate

- Resolution of diarrhea within 4 to 7 days following completion of anti-infective regimen
- Presence of adverse effects (eg, metallic taste, nausea)

- Avoid recreational water venues for two or more weeks following symptom resolution

Collaborate with patients, caregivers, and other healthcare professionals.

Treatment

Only patients with confirmed giardiasis should receive antiparasitic therapy. Since the primary clinical manifestation of giardiasis is prolonged diarrhea, clinicians must ensure patients receive adequate oral or intravenous fluids to maintain hydration, correct electrolyte abnormalities, and provide oral, enteral, or parenteral nutrition in severe cases. The antimotility agent loperamide and the antisecretory agent bismuth subsalicylate are available without a prescription, but should be avoided in children less than 18 years of age, immunocompromised patients, those with suspected toxic megacolon, or individuals with febrile diarrhea that may be due to a non-*Giardia* etiology.[12,13] The primary differences between recommended antiparasitic regimens for giardiasis are approved age for use, frequency of administration, duration of therapy, and commercially-available formulations (Table e138-2). Nitazoxanide and tinidazole are the only Food and Drug Administration (FDA)–approved medications for giardiasis. While the FDA has not approved metronidazole for this indication, it has been widely accepted as the mainstay of giardiasis therapy for the past 50 years.

TABLE e138-2

Treatment of Protozoan Diseases

	Adults	Children
Giardiasis[16,17]		
Tinidazole	2 g × single oral dose with food	≥3 years: 50 mg/kg orally × 1 dose with food (maximum 2 g)
Nitazoxanide	500 mg orally every 12 hours with food × 3 days	1-3 years: 100 mg orally every 12 hours with food × 3 days 4-11 years: 200 mg orally every 12 hours with food × 3 days ≥12 years: 500 mg orally every 12 hours with food × 3 days
Metronidazole	250 mg orally every 8 hours x 5 days	5 mg/kg orally every 8 hours x 5-7 days (maximum 250 mg dose)
Albendazole	400 mg orally once daily x 5 days	> 2 years: 10 mg/kg orally once daily x 5 days (maximum 400 mg dose)
Cryptosporidiosis[20,21]		
Nitazoxanide	Same as giardiasis dosing recommendations above for both adults and children	
Amebiasis[25–27]		
Asymptomatic Cyst Passer		
Paromomycin	8-12 mg/kg orally every 8 hours × 7 days	8-12 mg/kg orally every 8 hours × 7 days
Iodoquinol	650 mg orally every 8 hours × 20 days	10-13 mg/kg orally every 8 hours × 20 days (maximum 2 g/day)

Intestinal/Amebic Liver Abscess		
Metronidazole	750 mg orally or IV every 8 hours × 7-10 days	17 mg/kg orally or iv every 8 hours × 7-10 days (maximum 750 mg/dose)
Tinidazole	2 g daily × 3-5 days	≥3 years: 50 mg/kg daily × 3-5 days (maximum 2 g/dose)
	Each regimen for intestinal amebiasis/amebic liver abscess should be followed by a luminal agent	
Chagas disease[35–37]		
Benznidazole	2.5-4 mg/kg orally twice daily × 60 days (maximum 300 mg per dose)	2.5 - 4 mg/kg orally twice daily × 60 days (maximum 200 mg/dose)
Nifurtimox (CDC IND protocol only)	2-2.5 mg/kg orally every 6 hours × 90 days	≤10 years: 3.75-5 mg/kg orally every 6 hours × 90 days 11-16 years: 3.125-3.75 mg/kg orally every 6 hours × 90 days

Two clinical practice guidelines list nitazoxanide and tinidazole as a first-choice or preferred agent and metronidazole as an alternative regimen for giardiasis.[13,15] Efficacy at 1 to 4 weeks is 85% to 90% for tinidazole, 85% to 95% for metronidazole, 63% to 78% for nitazoxanide, and 69% to 86% for albendazole.[16] Albendazole has similar or lower efficacy than metronidazole.[16] Given the ease of use emerging evidence for greater efficacy, single-dose tinidazole is the preferred treatment for giardiasis. Metronidazole and tinidazole recipients most commonly report metallic taste and nausea as an adverse effect. Metronidazole has been used in the second and third trimesters of pregnancy. Paromomycin, an oral aminoglycoside, given at 25 to 35 mg/kg/day in three divided oral doses for 1 week is an alternative agent that can be given in all pregnancy trimesters because it is not systemically absorbed.

Evaluation of Therapeutic Outcomes

Patients should be assessed to achieve euvolemia if dehydrated and electrolyte balance should be restored. Diarrhea should stop within 3 to 6 days following treatment. While cyst excretion should also cease within days, patients should be advised to avoid recreational water venues for at least 2 weeks following resolution of diarrhea. During this time, patients should also follow strict hand hygiene and receive counseling on risk factor avoidance. Intestinal dysfunction (manifested as increased transit time) and radiologic changes (irregular thickening of the folds in the upper small intestine) may persist for months. Patients who fail initial therapy should preferably be treated with a drug from a different class.

Cryptosporidiosis

Epidemiology and Etiology

The protozoa genus *Cryptosporidium* is the leading cause of waterborne outbreaks of gastrointestinal illness in the United States and a major cause of mortality due to diarrhea in children under five, globally.[11,24,25] Between 2009 and 2017, there were 7,465 cases, 287 hospitalizations, and one death reported in the United States.[26] *C. hominis, C. parvum, and C. meleagridis* cause the majority of human cryptosporidiosis cases that lead to infectious diarrhea, but infection with many other *Cryptosporidium* species has been documented. Like giardiasis, the incidence rate of diarrheal illness due to *Cryptosporidium* is highest in children ages one through four and occurs primarily in the summer when increased exposure to recreational water occurs.

Pathophysiology and Clinical Presentation

The *Cryptosporodium* life cycle that occurs in the human host is more complex than *Giardia,* but transmission and infection principles remain similar.

Like giardiasis, host infection occurs when *Cryptosporidium* oocysts, which have an outer shell that allows them to be extremely tolerant to chlorinated water, are ingested from water or food that is contaminated with fecal matter. In the case of *Cryptosporidium,* the oocysts can remain viable >7 days in recreational pools.[11,26] After oral oocyst ingestion, nonflagellated sporozoites are released and infect the host's intestinal mucosa. Unlike *Giardia, Cryptosporodium* parasites undergo both sexual and asexual reproduction. Replicating parasites cause mucosal cell apoptosis, blunting of villi, diarrhea with chloride secretion, and impaired glucose and nutrient absorption.[10] Because the host immune response limits the severity of infection, symptomatic disease is mostly recognized in children or immunocompromised hosts. Watery diarrhea is the most common presentation and may be accompanied with abdominal cramps, nausea, vomiting, and fever. Prolonged infection causes malnutrition, inadequate nutrient absorption, and dehydration. Villous atrophy results in loss of enzymes such as lactase. Extraintestinal complications such as acalculous cholecystitis, sclerosing cholangitis, pancreatitis secondary to papillary stenosis, and pulmonary cryptosporidiosis may occur in immunocompromised patients.[27] The oocysts that develop following fertilization may sporulate in the host causing autoinfection or may be excreted in the stool allowing for transmission to other hosts following ingestion of less than 10 oocysts. Infected patients may shed infectious oocysts up to 2 weeks after diarrhea resolution.

The same risk factors for diarrhea due to *Giardia* should be present before suspecting cryptosporidiosis (Table e138-1). In addition to these risk factors, testing for *Cryptosporidium* infection is recommended in those with foodborne exposures including consumption of unpasteurized dairy products or contaminated fruits and vegetables and in immunocompromised patients such as those with acquired immunodeficiency syndrome. In patients with diarrhea lasting more than 1 to 2 weeks in whom common alternative etiologies have been excluded, a cryptosporidiosis diagnosis may be made by performing a *Cryptosporidium* direct fluorescent immunoassay, EIA, or NAAT on a collected stool sample. As several species of *Cryptosporidium* may cause human infection and each appear morphologically similar under microscopy, these methods are preferred for diagnosis because these point-of-care tests are rapid, widely available, and have high specificity and sensitivity of approximately 90%.[12-14] Cryptosporidiosis is also designated as "Notifiable at the National Level" by the CDC and should be reported to appropriate public health officials.

Treatment

Cryptosporidiosis treatment options are limited at present.[28] Correction of fluid and electrolyte abnormalities remains essential. Due to loss of villous glucose-stimulated sodium pumps, glutamine supplementation may enhance sodium absorption via glutamine-stimulated sodium pumps. Guidelines for treating cryptosporidiosis in HIV-infected adults recommend antimotility agents such as tincture of opium, which may be more effective than loperamide.[17] However, antimotility agents should be used with caution in young children.[15] Moreover, patients should avoid lactose-containing products such as milk.

2 Only nitazoxanide is FDA-approved for cryptosporidiosis and its efficacy is suboptimal in HIV-infected patients. Although nitazoxanide dosing for cryptosporidiosis in non-HIV infected patients is the same as giardiasis treatment (Table e138-2), HIV guidelines recommend considering nitazoxanide 500 to 1,000 mg orally twice daily with food for 14 days in adults. For children living with HIV, the recommended dosing is the same as giardiasis with a recommended duration of treatment of 3 to 14 days. Nitazoxanide is effective in adults and children without HIV including a decrease in mortality in malnourished children.[13] However, only 33% of patients had diarrhea resolution compared to placebo. No improvement was observed in HIV-infected patients who received nitazoxanide who did not also receive effective antiretroviral therapy. As a result, it is imperative that HIV-infected patients with cryptosporidiosis receive antiretroviral therapy as the mainstay of therapy in addition to antiparasitic therapy.[13,15,17] Other drugs such as paromomycin, azithromycin, rifaximin, rifabutin, and protease inhibitors may have activity against *Cryptosporidium*, but lack robust clinical data. HIV guidelines recommend 14 to 21 days of paromomycin 500 mg orally four times a day as an alternative to nitazoxanide in adults only.

Evaluation of Therapeutic Outcomes

Rehydration, correction of electrolyte abnormalities, restoration of nutritional deficiencies, and resolution of diarrhea are key therapeutic outcomes. To avoid further transmission to others, it is important for patients to avoid recreational waters for at least 2 weeks after symptom resolution.[29] Antiparasitic therapy alone is not curative in immunosuppressed patients. As such, HIV-infected patients should be started on antiretrovirals and CD4+ T-cell counts may be followed. All patients, especially those with HIV and CD4+ T-cell counts less than 200 cells/μL (200×10^6/L), should be counseled on risk reduction by avoiding direct contact with stool from pets, maintaining good hand hygiene, refraining from drinking untreated water, and staying away from swimming in freshwater or public recreational water facilities. When traveling to developing countries, using tap water to brush teeth or to wash raw fruits or vegetables should be avoided. Boiling water for at least 1 minute or using bottled water is recommended.

Amebiasis

Epidemiology and Etiology

Amebiasis is caused by the enteric protozoan pathogen *Entamoeba histolytica*. Morphologically, there are three species of Entamoeba that are indistinguishable from *E. histolytica: E.dispar, E. moshkovskii,* and *E. Bangladeshi. E. dispar* and *E. bangladeshi* are associated with an asymptomatic carrier state and do not typically cause disease in the human host.[30] *E. moshkovskii*, however, has been associated with noninvasive diarrhea in children and experimentally induced colitis in mice. Amebiasis caused an estimated 15,400 deaths and represented approximately 3% of all deaths due to diarrheal illness in 2015.[24,31-33] In Asia and Africa, amebiasis was among the top seven pathogens causing dysentery among children <5 years of age.[34] In the United States, amebiasis accounts for approximately 1.4 million hospitalizations and five deaths per year and most commonly affects young Hispanic men living in southwestern states along the Mexican border.[31-33] In the United States, *E. histolytica* is classified as a biodefense research category B because of its low infective dose, resistance to chlorine and environmental stability.[35] These characteristics have also resulted in outbreaks from consumption of contaminated municipal water.[35]

Pathophysiology and Clinical Presentation

As was described with other enteric protozoa, oral ingestion of mature *E. histolytica* cysts from fecal material initiates the parasitic host invasion cycle. Excystation occurs in the small intestine and released trophozoites migrate to the colon. *E. histolytica* trophozoites reproduce in the same manner as *G. lamblia.* In 90% of cases trophozoites convert to cysts, which are shed in the host's stool. This results in asymptomatic disease, but allows the human host to serve as an important reservoir for *E. histolytica* transmission. In 10% to 20% of cases, *E. histolytica* trophozoites will invade mucosal cells of colonic epithelium and produce necrotizing ulcers in the submucosa, which leads to abdominal pain with bloody, mucoid diarrhea.[10] Invasion into the bowel wall gives access to the portal circulation and enables hematogenous spread to the liver where they may form abscesses and periportal fibrosis. Extrahepatic extension to the chest is the second most common extra-abdominal manifestation of disease and typically involves direct extension of a hepatic abscess into the thoracic space. Pericardial disease can occur from rupture of a left hepatic lobe abscess or from extension from a pleural abscess.[37] Hematogenous spread to the brain occurs in up to 4.7% of patients with amebic liver abscesses (ALAs).[38]

3 *E. histolytica* is endemic in resource-limited countries and at-risk individuals include immigrants, persons with recent travel to endemic countries, men who have sex with men, and individuals with and history of oral-anal contact.[13,33] Clinicians should suspect amebiasis in patients with these risk factors who develop dysentery, colitis, or intestinal perforation with or without liver abscesses (Table e138-1). Stool sample analysis is insensitive and does not distinguish between *E. histolytica* and the nonpathogenic Entamoeba. As a result, *E. histolytica*-specific antigens and real-time polymerase chain reaction (PCR) tests are the preferred diagnostic platforms to diagnose acute amebiasis.[13,14] The FDA has approved a stool antigen detection test with a sensitivity and specificity of 98% and 100%, respectively, while other available stool EIAs have sensitivities and specificities that range from 93% to 100% for diagnosis of intestinal disease.[14,39] PCR testing, considered the gold standard for diagnosis, has the best sensitivity and is available through various FDA-cleared gastrointestinal panels.[40] It has excellent sensitivity in the evaluation of ALA, identifying *E. hystolitica* in 20 of 23 hepatic samples obtained from patients with ALA.[41] Additionally, serum-based EIAs and antibody detection tests have sensitivities greater than 92% and specificities that range from 80% to 100% for extraintestinal disease. Endoscopy with biopsy may provide more definitive diagnosis and help evaluate for other infectious and non-infectious etiologies of colitis such as tuberculosis and inflammatory bowel disease when stool diagnostic testing has been inconclusive. When ALA is suspected from initial physical examination and history, various imaging modalities are available to aid in diagnosis, such as liver ultrasound, abdominal computed tomography (CT), and magnetic resonance imaging (MRI). Leukocytosis and an elevated alkaline phosphatase concentration are common findings in patie. In rare instances, needle aspiration of the hepatic abscess may be attempted using ultrasound guidance to assist with diagnosis.[14]

Treatment

Recommended treatment regimens depend on the category of amebiasis: asymptomatic cyst passers, intestinal amebiasis, and ALA (Table e138-2). Rehydration with clean water, electrolyte replacement, and nutritional support are essential adjunctive treatment modalities. Percutaneous drainage may be required for management of hepatic abscesses greater than 5 to 10 cm, abscesses involving the left hepatic lobe or pericardium and if there is no clinical response to drug therapy within 5 to 7 days. Most regimens require a combination of drugs administered concurrently or sequentially.

4 Metronidazole and tinidazole are tissue-acting agents, whereas paromomycin and iodoquinol are luminal amebicides. A systemic agent may be so well absorbed that only small amounts of the drug stay in the bowel, which might prove ineffective as a luminal agent. A luminal-acting agent, on the other hand, may be too poorly absorbed to be effective in the tissue. In the asymptomatic cyst passer, it is necessary to eradicate the causative agent from the lumen to prevent intestinal amebiasis or the development of ALA.

Asymptomatic cyst passers and patients with mild intestinal amebiasis should receive one of the following luminal agents: paromomycin or iodoquinol.[18,19] Paromomycin is the preferred luminal agent in pregnant patients. Patients with severe intestinal disease or liver abscess should receive metronidazole or tinidazole followed by a course of one of the luminal agents.[20]

Evaluation of Therapeutic Outcomes

Most patients with either intestinal amebiasis or colitis will respond in 3 to 5 days with amelioration of symptoms. Patients with liver abscesses may take up to 7 to 10 days to respond. Patients not responding during this period may require aspiration of abscesses or exploratory laparotomy. Serial liver scans have demonstrated healing of liver abscesses over 4 to 8 months after adequate therapy.

Travelers and tourists visiting an epidemic area should avoid local tap water, ice, salads, and unpeeled fruits. Travel kits for water decontamination are available for purchase, but boiled water is safest. An alternative or additional measure may be to carry a portable water purifier. Because food handlers may be a source of amebiasis, travelers should avoid eating at food stalls and open markets.

Chagas Disease (American Trypanosomiasis)

Epidemiology and Etiology

Trypanosoma brucei gambiense, *T. brucei*, and *T. brucei rhodesiense* are tissue protozoan parasites that cause African trypanosomiasis (sleeping sickness) and *T. cruzi* is the agent that causes American trypanosomiasis (Chagas disease). Further discussion of this subject will focus on American trypanosomiasis. Chagas disease is considered a neglected parasitic infection by the CDC. Over 180,000 new cases of Chagas disease occurred globally with over 7,000 deaths in 2016.[1,3] Six to 10 million people are affected globally and about 300,000 infected patients reside in the United States.[42-44] The majority of *T. cruzi* infections occur in Latin America where over 5.7 million patients were infected in 2010 with over 15% from Mexico and 42% from Brazil and Argentina.[45,46] Immigrants from El Salvador and Mexico are at highest risk for Chagas disease in the United States and the most prevalent number of cases occur in California (greater than 70,000), Texas (almost 37,000), Florida (greater than 18,000), and New York (almost 17,500).[42,44,47]

Pathophysiology and Clinical Presentation

The two major life cycle forms of *T. cruzi* include the nondividing motile flagellated trypomastigote and the nonmotile intracellular amastigote, which undergoes asexual binary fission.[48] *T. cruzi* is considered a blood or tissue protozoan and is transmitted to the human host by the reduviid bug or kissing bug species (*Triatoma, Rhodnius, and Panstrongylus*) that live in wall cracks of houses in rural areas of North, Central, and South America, and less commonly via transfusion, organ transplant, contaminated food or drink, and vertical transmission.[17,48] The reduviid bug vector becomes infected after sucking blood from animals (eg, opossums, dogs, and cats) or humans infected with circulating trypomastigotes at night.[48] The infected vector takes a blood meal from a human host and releases fecal trypomastigotes, which enter the host near the bite wound. The bite may cause intense itching and may result in a chagoma, which is a painful erythematous subcutaneous nodule that forms at the bite site.[10,48] If trypomastigotes enter the host through ocular mucosa, a unilateral conjunctivitis known as Romaña's sign appears. Once inside the host, trypomastigotes transform into intracellular amastigotes. Intracellular amastigotes replicate and transform back into trypomastigotes, which then enter the bloodstream following cell rupture and cause infection in other host tissues. The incubation period is 1 to 2 weeks. Acute phase of the infection generally presents with mild and nonspecific (eg, fever, malaise, hepatosplenomegaly) symptoms and rarely (<1%) patients develop severe and life-threatening symptoms as a result of meningoencephalitis or myocarditis.[49] After 8 to 10 weeks of persistent *T. cruzi* parasitemia, untreated patients develop chronic complications of Chagas disease and serve as a reservoir host that transmits *T. cruzi* to reduviid bugs that bite the infected host.

In chronic trypanosomiasis, 20% to 30% of patients present with cardiomyopathy and heart failure (see Table e138-1).[48] Electrocardiograms (ECGs) are usually abnormal, demonstrating extrasystoles, first-degree heart block, right bundle-branch block, and other serious conduction disturbances.[44,50]

Degeneration of the autonomic ganglia in the smooth muscle of the esophagus and colon leads to uncoordinated peristalsis. The end result of chronic *T. cruzi* parasitemia and tissue invasion is "megasyndromes" of affected organs.[48,50] Penetration of the central nervous system (CNS) results in meningoencephalitis, strokes, seizures, and focal paralysis. In HIV coinfected patients, meningoencephalitis is the most common manifestation.[17]

T. cruzi exposure history is essential in risk-stratifying patients during initial diagnostic workup and clinicians should aim to diagnose Chagas disease early before cardiac complications occur. At least two positive serologic tests using the indirect hemagglutination assay (IHA), immunofluorescent antibody test (IFA), or enzyme-linked immunosorbent assay (ELISA) is diagnostic for the disease. A PCR test has also been most useful in monitoring for early treatment failure as opposed to an initial diagnosis.[48] Once a diagnosis is made, baseline ECG, chest X-ray, and echocardiograph are recommended along with serial evaluation based on clinical findings.[44]

Treatment

5 Benznidazole is the only FDA-approved treatment for Chagas disease. While a 60-day benznidazole course is only indicated in children from 2 to 12 years of age, all patients with acute, early chronic, and reactivated Chagas disease should receive treatment except patients with established cardiomyopathy.[44] For adults weighing >60 kg, a longer duration of treatment may be needed and optimal duration of therapy is unknown for HIV coinfected patients.[17,44] Antitrypanosomal therapy is generally not recommended for pregnant patients due to concerns for toxicity and limited experience.[48] While treatment results in serologic or PCR conversion, the incidence of progressive cardiac complications remains unchanged.[21,22] Side effects of benznidazole include neuropathy, rash, and granulocytopenia, which may lead to discontinuation in up to 30% of patients. Approximately 30% to 50% of benznidazole-recipients experience allergic dermatitis, which can be managed with antihistamines, corticosteroids, or both.[48] Nifurtimox, the only alternative *T. cruzi* infection treatment option, is only available under a CDC investigational protocol and should be reserved for benznidazole treatment failures. Also, up to 75% of nifurtimox recipients discontinue therapy due to adverse effects, which include gastrointestinal disturbances (anorexia, nausea, vomiting), CNS toxicity (headache, vertigo, insomnia), myalgias, and peripheral neuropathy.[23] Lastly, allopurinol monotherapy and triazoles such as posaconazole as monotherapy or in combination with antitrypanosomal agents were ineffective for treatment of Chagas disease and should be avoided.[51,52]

Evaluation of Therapeutic Outcomes

Unfortunately, reliable tests of cure are currently unavailable because serologic markers used to diagnose Chagas disease may remain positive for years after completion of therapy. Instead, early visits evaluating for clinical progression is recommended followed by annual serologic testing. Quantitative PCR results may become a useful way to monitor for early treatment failure, but is an unreliable surrogate marker for visceral complications.[22] Patients should receive at least annual 12-lead ECG evaluations regardless of the extent of cardiac involvement on presentation.[44,48] Primary preventative measures involve vector control and there is no vaccine available.[53]

Malaria

Epidemiology and Etiology

Malaria is the most devastating disease in terms of human suffering and economics. In 2019, there were 229 million cases and 409,000 deaths reported by the World Health Organization (WHO). Although this is a decline from 720,000 deaths reported in 2016, this remains the third leading cause of death in children under the age of 5 accounting for 274,00 malaria deaths in 2019.[54] Fortunately, malaria incidence and the death rates have declined in recent years, yet still nearly half the world's population remains at risk for malaria.[1,2,54] In the United States, over 99% of malaria cases are imported and malaria remains the most common cause of hospitalization due to travel-associated disease.[55] In 2017, 2,161 cases of malaria were reported to the CDC, representing the highest number of cases in the United States since 1971 and 86% of the cases were from Africa. Overall, 70.5% of all cases were due to *Plasmodium falciparum*, 14.4% of cases were classified as severe, and seven patients died.[56] Despite chemoprophylaxis and mosquito avoidance measures recommended to those who travel to endemic regions, in 2017 only 28.4% of the cases with chemoprophylaxis data, reported taking chemoprophylaxis.[56]

The four predominant *Plasmodia* species that cause malaria include *P. falciparum, P. vivax, P. malariae,* and *P. ovale. P. knowlesi* is now recognized as

a fifth human pathogen causing significant disease in Malaysia.[57] These blood and tissue protozoa are transmitted by the bite of an infected *Anopheles* mosquito—the malaria vector. *P. vivax* is more prevalent in India, Pakistan, Bangladesh, Sri Lanka, and Central America, whereas *P. falciparum* is predominant in Africa, Haiti, Dominican Republic, the Amazon region of South America, and New Guinea.[58] Most of the infections with *P. ovale* are mixed infections and occur predominantly in Africa and also in parts of Asia and Oceania.[66] The distribution of *P. malariae* is worldwide.[40] Determining species' geographic distribution is important for choosing chemoprophylaxis and empiric treatment regimens.

Pathophysiology and Clinical Presentation

Plasmodium sporozoites (tissue protozoa) enter the host bloodstream following the bite of an infected female *Anopheles* mosquito. The sporozoites invade parenchymal hepatocytes, multiply in stages referred to as *exoerythrocytic stages*, and become hepatic vegetative forms or schizonts. Schizonts rupture to release thousands of daughter cells, or merozoites (blood protozoa), that then infect erythrocytes.[10] Merozoites within erythrocytes undergo asexual reproduction, develop into ring forms, trophozoites, schizonts, and finally, merozoites, which then invade other erythrocytes. The erythrocytic phase causes extensive hemolysis, which results in anemia and splenomegaly.

Clinical presentation of malaria differs based on the infecting species (Table e138-3). *P. vivax* and *P. ovale* can exist in the liver in the latent exoerythrocytic form (hypnozoites) for extended periods and, therefore, infected subjects can experience relapses. *P. falciparum* and *P. malariae* remain in the exoerythrocytic stage in the liver for about 4 weeks before invading erythrocytes.[58,59] *P. malariae* is implicated in immune-mediated glomerulonephritis and nephrotic syndrome. *P. falciparum* infection causes serious complications for several reasons. This species can invade erythrocytes of all ages causing high levels of parasitemia and the parasites can sequester in capillaries and postcapillary vessels of organs such as the brain and the kidney.[58,59] Tissue hypoxia from anemia, together with *P. falciparum*-parasitized red blood cell adherence to endothelial cells in capillaries, likely contribute to extensive vascular disease and severe metabolic effects. Children younger than 5 years old and pregnant women are at high risk for severe complications from falciparum malaria.[60] *P. knowlesi* appears identical to *P. malariae* on blood smear, but clinically causes more severe disease. *P. knowlesi* replicates every 24 hours causing daily fever spikes and hyperparasitemia. Severe cases have been associated with metabolic acidosis, hepatorenal dysfunction, respiratory distress, severe anemia, and refractory hypotension.[57]

TABLE e138-3

Clinical Presentation of Malaria

Initial presentation Nonspecific fever, chills, rigors, diaphoresis, malaise, vomiting, orthostatic hypotension, electrolyte abnormalities
Erythrocytic phase Prodrome: headache, anorexia, malaise, fatigue, and myalgia Nonspecific complaints such as abdominal pain, diarrhea, chest pain, and arthralgia Paroxysm: high fever, chills, and rigor Cold phase: severe pallor and cyanosis of the lips Hot phase: fever between 40.5°C (104.9°F) and 41°C (105.8°F) Sweating phase: Follows hot phase by 2-6 hours where fever resolves Marked fatigue and drowsiness, warm, dry skin, tachycardia, cough, severe headache, nausea, vomiting, abdominal pain, diarrhea, and delirium Lactic acidosis and hypoglycemia (with falciparum malaria) Anemia and splenomegaly
P. falciparum infections Hypoglycemia, acute renal failure, pulmonary edema, severe anemia, thrombocytopenia, high-output heart failure, cerebral congestion, seizures and coma, and adult respiratory syndrome

Data from References 49,58.

Effective malaria management is predicated on rapid diagnosis. Point-of-care rapid antigen detection tests that require finger-prick blood are widely available. These tests detect *P. falciparum* histidine-rich protein 2, *Plasmodium*-specific lactate dehydrogenase, or aldolase antigens, but generally require confirmatory testing because they may lack adequate sensitivity in detecting non-*falciparum* infections or those with low-level parasitemia.[61,62] The FDA has approved the ID-Fluorescent in situ hybridization Plasmodium Genus Test Kit, a qualitative test for detection of malaria parasites in blood smears that has an overall sensitivity of 95% for detection of *P. falciparum* and 90% sensitivity for identification of *P. vivax*.[63] NAATs are also available at various CLIA accredited laboratories, but may be expensive, unavailable, and follow-up microscopy is recommended to quantify parasitemia.[61] As such, microscopy remains the gold standard for malaria diagnosis. To ensure a positive diagnosis, thick and thin blood smears should be obtained every 12 to 24 hours for three consecutive days. Confirmed malaria cases should be reported to appropriate public health authorities.

Chemoprophylaxis and Prevention

6 Along with nonpharmacologic measures to avoid mosquito bites (diethyltoluamide- or picaridin-containing repellant use, full-coverage clothing, window screens, insecticide-impregnated nets, and air-conditioned rooms), chemoprophylaxis is recommended for all those travelling to areas where malaria exposure is possible. Specific antimalarial recommendations vary depending on local susceptibility patterns and can be found in the CDC Yellow Book or on the CDC Website. Of note, approximately 95% of US residents who traveled to an endemic region and were reported to have developed malaria upon return did not adhere to or did not take a CDC-recommended chemoprophylaxis regimen.[64] Clinicians have increasingly prescribed non-chloroquine antimalarial drugs such as atovaquone-proguanil and doxycycline for chemoprophylaxis because these regimens retain effectiveness in areas where chloroquine-resistant *P. falciparum* exposure is likely (Table e138-4). Antimalarial drugs that lack activity against the liver stage or preerythrocytic stage of infection must be given during and at least 4 weeks after leaving an endemic area.

TABLE e138-4

Chemoprophylaxis of Malaria

	Adults	Children	Notes
Chloroquine-susceptible area			
Chloroquine	300 mg base orally once weekly	5 mg/kg base orally once weekly (max 300 mg/dose)	Begin 1-2 weeks before travel. Continue 4 weeks after leaving.
Hydroxychloroquine	310 mg base orally once weekly	5 mg/kg base orally once weekly (max 310 mg/dose)	
Mefloquine	228 mg base orally once weekly	≤9 kg: 4.6 mg/kg base orally once weekly 9-19 kg: ¼ tablet orally once weekly 19-30 kg: ½ tablet orally once weekly 30-45 kg: ¾ tablet orally once weekly >45 kg: 1 tablet orally once weekly	Begin ≥2 weeks before travel. Continue 4 weeks after leaving. Contraindicated in those with psychiatric disorders. Caution in those with cardiac conduction abnormalities.
Chloroquine-resistant area			
Atovaquone-progaunil Adult tablet: 250 mg/100 mg Pedi tablet: 62.5 mg/25 mg	1-adult tablet orally daily	5-8 kg: ½ pediatric tablet orally daily 8-10 kg: ¾ pediatric tablet orally daily 10-20 kg: 1-pediatric tablet orally daily 20-30 kg: 2-pediatric tablets orally daily	Begin 1-2 days before travel. Continue 7 days after leaving. Contraindicated in those with a CrCl <30 mL/min (0.5 mL/s).

		30-40 kg: 3-pediatric tablets orally daily >40 kg: 1-adult tablet orally daily	
Doxycycline	100 mg orally daily	≥8 years: 2.2 mg/kg orally daily (max 100 mg/dose)	Begin 1-2 days before travel. Continue 4 weeks after leaving. Contraindicated in pregnancy.
P. vivax endemic areas			
Primaquine	30 mg base orally once daily	0.5 mg/kg base orally daily (max 30 mg/dose)	Begin 1-2 days before travel. Continue 7 days after leaving. Contraindicated in G6PD deficiency and pregnancy.
Tafenoquine	200 mg (2 tablets) orally daily × 3 days before travel 200 mg (2 tablets) orally weekly during travel 200 mg (2 tablets) orally once 1 week after travel	Only indicated for patients ≥18 years	May be used as prophylaxis against all *Plasmodium* species including those found in chloroquine-susceptible and chloroquine-resistant areas. Contraindicated in G6PD deficiency and pregnancy.

Data from References 40,41,45.

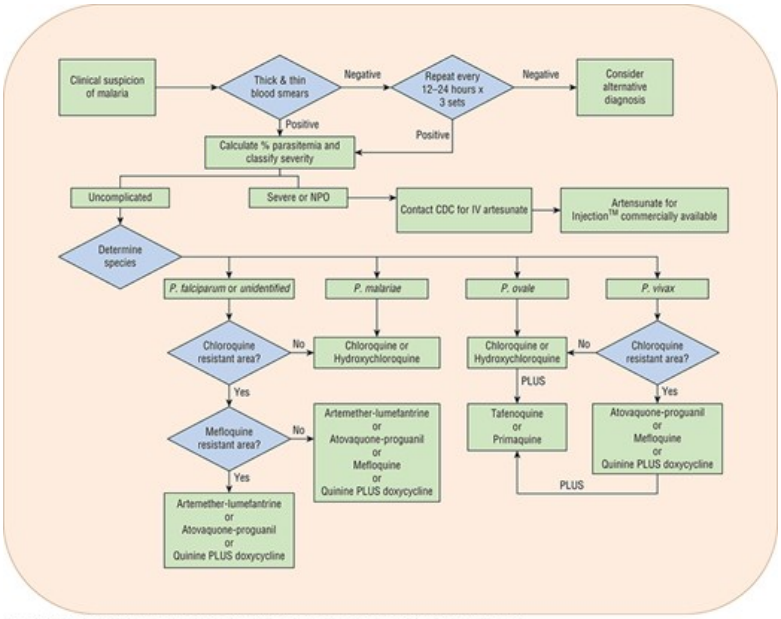
Treatment

A rapid malaria diagnosis, especially of *P. falciparum*, is essential because antimalarial therapy given within 48 to 72 hours can decrease risks of high-mortality complications such as hypoglycemia, pulmonary edema, and renal failure. Malaria treatment has changed in recent years with the availability of artemisinin-based antimalarials (Fig. e138-1). Artesunate and artemether-lumefantrine are approved for use in the United States. Artesunate for Injection™ has been approved by the FDA and is now commercially available, however, until it is fully distributed across United States, the CDC will continue to distribute artesunate under its investigational new drug (IND) protocol when artesunate is not available within 24 hours of a clinician requesting the drug. The CDC will monitor the availability of Artesunate for Injection™ and will provide updates prior to stopping the IND program.[65,66] Other artemisinin-based antimalarial drugs found worldwide include dihydroartemisinin-piperaquine, artesunate-amodiaquine, and artesunate-pyronaridine.[58,59]

FIGURE e138-1

Malaria treatment algorithm.

Data from References 40,41,47.



Severe malaria is defined as those patients with a confirmed malaria diagnosis who also have one of the following: impaired consciousness, severe normocytic anemia (hemoglobin less than 7 g/dL [70 g/L; 4.34 mmol/L]), acute kidney injury, pulmonary edema or acute respiratory distress syndrome, septic shock, disseminated intravascular coagulation or spontaneous bleeding, acidosis, jaundice, seizures, or parasitemia of more than 5%.[67] In the past, those patients with severe illness including *P. falciparum* have received parenteral quinidine as the drug of choice, but evidence from randomized controlled trials support the superiority of artesunate over quinidine.[68] Furthermore, intravenous quinidine has been discontinued and is no longer available in the United States. As such, artesunate is the drug of choice for the treatment of severe malaria. While waiting for artesunate delivery, if not locally available, clinicians may opt to give a single dose of artemether-lumafantrine, atovaquone-proguanil, or quinine via a nasogastric tube.

In uncomplicated malaria, options include artemether-lumefantrine, atovaquone-progaunil, quinine plus doxycycline, quinine plus clindamycin, chloroquine, or hydroxychloroquine depending on the infecting species and likelihood of chloroquine resistance. Patients with *P. vivax* and *P. ovale* infections should also be given an 8-aminoquinoline such as tafenoquine or primaquine to eradicate dormant hypnozoites found in the liver (radical cure). Dosing regimens can be found in Table e138-5.

TABLE e138-5

Recommended Doses for Malaria Treatment

	Adults	Children	Notes
Severe malaria			
Artesunate	2.4 mg/kg IV × 1, then at 12, 24, and 48 hours (may continue once daily if necessary)		Artesunate is available as Artensunate for Injection™ but if it cannot be obtained within 24 hours, it is available under CDC IND protocol at 770-488-7788 or 770-488-7100
Uncomplicated *P.*			

falciparum or chloroquine-resistant			
Artemether-lumafantrine Tablet: 20 mg/120 mg	4 tablets orally twice daily × 3 days	5-15 kg: 1 tablet orally twice daily × 3 days 15-25 kg: 2 tablets orally twice daily × 3 days 25-35 kg: 3 tablets orally twice daily × 3 days ≥35 kg: 4 tablets orally twice daily × 3 days	Second dose should be taken 8 hours after initial dose. Take with food or milk. Equal recommendation given in 2013 malaria guidelines to atovaquone- and quinine-based regimens.
Atovaquone-proguanil Adult tablet: 250 mg/100 mg Pedi tablet: 62.5 mg/25 mg	4 adult tabs orally daily × 3 days	5-8 kg: 2-pediatric tablets orally daily × 3 days 8-10 kg: 3-pediatric tablets orally daily × 3 days 10-20 kg: 1-adult tablet orally daily × 3 days 20-30 kg: 2-adult tablets orally daily × 3 days 30-40 kg: 3-adult tablets orally daily × 3 days >40 kg: 4-adult tablets orally daily × 3 days	Take with food or milk. Equal recommendation given in 2013 malaria guidelines to artemisinin- and quinine-based regimens.
Quinine sulfate plus: either doxycycline or clindamycin	542 mg base orally three times daily × 3-7 days 100 mg orally twice daily × 7 days 6.7 mg/kg/orally three times × 7 days	8.3 mg/kg base orally three times daily × 3-7 days ≥8 years: 2.2 mg/kg orally twice daily × 7 days 6.7 mg/kg/orally three times daily × 7 days	Equal recommendation given in 2013 malaria guidelines to artemisinin- and atovaquone-based regimens.
Mefloquine	648 mg base orally × 1, then 456 mg base orally 6-12 hours later	13.7 mg/kg base orally × 1, then 9.1 mg/kg base orally given 6-12 hours later	High rate of severe neuropsychiatric reactions.

Uncomplicated chloroquine-susceptible malaria			
Chloroquine	600 mg base orally × 1, then 300 mg base orally at 6, 24, 48 hours	10 mg/kg base orally × 1, then 5 mg/kg base orally at 6, 24, 48 hours	May also use the above-mentioned regimens.
Hydroxychloroquine	620 mg base orally × 1, then 310 mg base orally at 6, 24, 48 hours	10 mg/kg base orally × 1, then 5 mg/kg base orally at 6, 24, 48 hours	May also use the above-mentioned regimens.
P. vivax or P. ovale malaria			
Tafenoquine	300 mg (2 tablets) × 1 dose	Only indicated in patients ≥16 years	Add to above regimens to eradicate dormant liver hypnozoites; contraindicated in G6PD deficiency; FDA-approved for radical cure of *P. vivax* (not *P. ovale*)
Primaquine	30 mg base orally daily × 14 days	0.5 mg/kg base orally daily × 14 days	Add to the above regimens to eradicate dormant liver hypnozoites; contraindicated in G6PD deficiency.

Data from References 40,41,47.

Evaluation of Therapeutic Outcomes

The CDC recommends checking blood smears every 12 to 24 hours to assess for an appropriate response to therapy. For severe infection, blood smears should be studied until clearance of parasitemia is documented. Hypoglycemia that is associated with *P. falciparum* should be checked and corrected with dextrose infusions. Once the parasite count is <1% and the patient can tolerate oral therapy, the patient should receive a full-treatment course with one of the recommended regimens (artemether-lumefantrine, atovaquone-proguanil or quinine plus doxycycline or clindamycin).[58,59] Patients treated with IV artesunate for severe malaria should be monitored weekly for up to 4 weeks for evidence of hemolytic anemia by checking weekly hemoglobin, reticulocyte count, lactate dehydrogenase, and total bilirubin. Cases of delayed-post artemisinin hemolytic anemia should be reported.[67] Increasing incidence of artemisinin-resistant and chloroquine-resistant malaria found in Western Cambodia, Thailand, and Myanmar present a great threat to malaria control. Malaria does not produce immunity in patients. While research is being conducted to develop a malaria vaccine, a licensed vaccine remains unavailable.

Babesia

Babesiosis is caused by the species, Babesia, an intraerythrocytic protozoa transmitted by hard-bodied ticks. There are several species that infect humans throughout the world, including *Babesia microti, Babesia duncani*, and *Babesia divergens* in the United States.[69] There are over 2,000 cases of babesiosis reported to the CDC annually mostly attributed to the species, *B. microti*. Infection typically occurs not only from the bite of a *B. microti*–

infected Ixodes scapularis tick, but can also be transmitted through blood transfusion, organ transplantation, and perinatally. *B. microti* has become a leading pathogen in transfusion-associated infections in the United States, responsible for death in 20% of blood recipients infected with babesia. This has led to recommendations to screen the blood supply for *Babesia spp.* in babesiosis endemic states.

Cases typically present with fever, fatigue, chills, night sweats, and anorexia. Severe babesiosis may cause severe anemia, acute respiratory distress syndrome, disseminated intravascular coagulation, liver failure, heart failure, and shock and requires close monitoring and hospitalization. About half of the babesiosis cases reported to the CDC between 2011 and 2015, for which clinical data was available, resulted in hospitalization and nearly one-third had one or more complications.[70] While the diagnosis is clinical and based on epidemiological risk factors, confirmation of acute babesiosis is based on peripheral blood smear examination or PCR.[69] Thick and thin blood smears should be prepared and examined by experienced personnel. Although the number of microscopic fields has not been standardized, evaluation of over 200 hundred oil immersion fields will increase sensitivity. Trophozoites may resemble malaria, but identification of merozoites organized in tetrads, the Maltese cross forms, are pathognomonic for babesiosis. Microscopy provides fast results, but PCR can be useful when laboratory personnel are inexperienced or there is low level of parasitemia. Antibody testing is available, but not recommended for diagnosis of acute babesiosis.[74]

Treatment

Asymptomatic carriers of *Babesia spp.* do not require treatment as they typically clear the infection within 1 year, unless parasites are seen on thin blood smear for more than a month. The preferred treatment regimen for babesiosis is the combination of atovaquone and azithromycin for 7 to 10 days, often extended in immunocompromised patients (at least 6 weeks for highly immunocompromised patients).[69] Mild to moderate disease can be treated with oral regimens whereas hospitalized patients with severe disease will require IV regimens initially and can be transitioned to oral therapy (Table e138-6). The combination of clindamycin and quinine is an alternative treatment due to poor tolerability of quinine leading to low adherence. Patients with high-grade parasitemia (>10%) or who have severe manifestations may be considered for exchange transfusion. Consultation with infectious diseases and transfusion specialists is recommended. Daily monitoring parameters include hematocrit, platelet count, liver enzymes, renal function and parasitemia levels until symptoms abate and parasitemia is reduced to <4%. Symptoms typically improve within 2 days of initiation of therapy and resolve within 1 to 2 weeks. However, fatigue and low-grade parasitemia may persist for a few months, but do not imply treatment failure (see Table e138-6).

TABLE e138-6

Treatment of Babesiosis

Patient Category	Adult	Children
Mild-to-moderate babesiosis	Preferred: Atovaquone 750 mg orally twice daily with food plus azithromycin 500 mg orally on day 1, then 250 mg once daily for 7-10 days Alternative: Clindamycin 600 mg orally every 8 hours plus quinine sulfate 542 mg base orally every 6-8 hours for 7-10 days	Preferred: Atovaquone 20 mg/kg (maximum 750 mg) orally twice daily plus azithromycin 10 mg/kg (maximum 500 mg) orally on day 1, then 5 mg/kg (maximum 250 mg) once daily for 7-10 days Alternative: Clindamycin 7-10 mg/kg (maximum 600 mg) orally every 8 hours plus quinine sulfate 6 mg base/kg (maximum 542 mg base) orally every 6-8 hours for 7-10 days
Severe babesiosis (hospitalized)	Preferred: Atovaquone 750 mg orally twice daily plus azithromycin 500-1,000 mg intravenously once daily until symptoms abate, then convert to oral step-down therapy Alternative: Clindamycin 600 mg intravenously every 6 hours plus quinine sulfate 542 mg base orally every 6-8 hours until symptoms abate, then convert to oral step-down therapy	Preferred: Atovaquone 20 mg/kg (maximum 750 mg) orally twice daily plus azithromycin 10 mg/kg (maximum 500 mg) intravenously once daily until symptoms abate, then convert to oral step-down therapy Alternative: Clindamycin 7-10 mg/kg (maximum 600 mg) intravenously plus quinine sulfate 6 mg base/kg (maximum 542 mg base) orally every 6-8 hours until symptoms abate, then convert to oral step-down therapy
Step-down therapy for hospitalized patients	Preferred: Atovaquone 750 mg orally twice daily plus azithromycin 250-500 mg orally once daily to complete a total of 7-10 days; azithromycin 500-1000 mg should be considered for immunocompromised patients Alternative: Clindamycin 600 mg orally every 8 hours plus quinine sulfate 542 mg base orally every 6-8 hours to complete a total of 7-10 days	Preferred: Atovaquone 20 mg/kg (maximum 750 mg) orally twice daily plus azithromycin 10 mg/kg (maximum 500 mg) orally once daily to complete a total of 7-10 days Alternative: Clindamycin 7-10 mg/kg (maximum 600 mg) orally every 8 hours plus quinine sulfate 6 mg base/kg (maximum 542 mg base) orally every 6-8 hours to complete a total of 7-10 days

HELMINTHIC DISEASES

Endemic helminthic infections are uncommon in the United States, but the infection prevalence may be as high as 1.5 billion in Asia, Latin America, the Caribbean, and Sub-Saharan Africa.[1] In the United States, helminth infections are most often imported, but may be acquired locally from exposure to domestic or wild animals, improperly prepared food, or as a consequence of poverty and poor sanitation.[71] Most intestinal helminthic infections may not be associated with clearly defined manifestation of disease, but they can cause significant pathology. One factor that determines the pathogenicity of helminths is their population density. Light infections may be fairly well tolerated, whereas high populations of intestinal helminths can result in predictable disease presentations. Certain conditions and drugs (fever, corticosteroids, and anesthesia) can cause atypical location of worms.

Cysticercosis and Neurocysticercosis

Epidemiology and Etiology

Cysticercosis is considered a neglected parasitic infection by the CDC and is caused by the larval form of the tapeworm (cestode) *Taenia solium*. From 2003 to 2012, 18,600 neurocysticercosis-related hospitalizations were documented in the United States.[72] In disease-endemic countries, neurocysticercosis is the leading cause of acquired epilepsy.[73,74] The prevalence of neurocysticercosis in patients presenting to US emergency departments with seizures is estimated to be approximately 2%.[75] In the United States, the highest incidence of cysticercosis has been reported in

immigrants from Mexico.[75] Comprehensive US epidemiologic data is scarce because cysticercosis is only a reportable disease in Arizona, California, New Mexico, Oregon, and Texas.

Pathophysiology and Clinical Presentation

Cysticercosis occurs from consumption of *Taenia solium* eggs that have been excreted from a *T. solium* tapeworm carrier. Intestinal tapeworm infection is a result of ingestion of poorly cooked pork that contains larvae or cysticerci. Cysticerci mature into adult tapeworms and attach to the small intestine via the scolex. The adult tapeworm produces approximately 1,000 proglottids that detach, migrate to the anus, and pass in the stool. Gravid proglottids release approximately 50,000 eggs in the feces.[76] Cysticercosis is a systemic disease caused by the larva of *T. solium* (oncosphere) and is usually acquired by ingestion of eggs in fecal-contaminated food or by autoinfection. The larvae penetrate the bowel and migrate through the bloodstream to infect different organs including the CNS (neurocysticercosis).[73,74] The larvae mature in about 8 weeks and remain as semitransparent, oval-shaped, fluid-filled cystin tissues. Cysticercosis in most tissues may not produce major symptoms and usually manifest as subcutaneous nodules, primarily in the arms, legs, and chest.

The most serious complication of cysticercosis is invasion of the CNS, which results in neurocysticercosis. Neurocysticercosis can cause obstructive hydrocephalus, strokes, and seizures. Epileptic seizures (50%-80%) may be the presenting symptoms in patients with neurocysticercosis.[76] Clinical presentation, primarily seizure history, together with radiographic demonstration (computed tomography and MRI) of the cysticerci within cysts in the CNS, is diagnostic for neurocysticercosis.[50] Serologic diagnosis is made by the use of an enzyme-linked immune transfer blot assay, which is considered highly sensitive and specific for cysticercosis.[77] Treatment recommendations are based on the location and appearance of the cysts on neuroimaging.

Treatment

Only neurocysticercosis is treated. The four approaches to neurocysticercosis management include surgery, symptomatic relief with corticosteroids, antiepileptic drug therapy, and antihelminthic therapy (Table e138-7). Antiparasitic therapy is often delayed until the patient's CNS symptoms are treated since antiparasitic drugs can worsen symptoms by inducing an inflammatory response. Fundoscopy should be performed in patients with potential hydrocephalus or cerebral edema and to exclude intraocular cysterci. Antihelminthic therapy is contraindicated in those with intraocular cysticerci due to risk of blindness with treatment. Patients with noncalcified parenchymal neurocysticercosis should initially receive symptomatic therapy with corticosteroids and antiepileptic drugs followed by antihelminthic therapy.[52] Albendazole with or without praziquantel is recommended based on how the patient is classified. Surgical management is often required for treatment of intraventricular neurocysticercosis.

TABLE e138-7

Treatment of Neurocysticercosis

	Corticosteroid Therapy	Antihelminthic Therapy
Parenchymal		
Nonviable calcified cysts +/− surrounding edema	Not routinely recommended	Not recommended
Single cystic or nodular enhancing lesion	Prednisone 1-2 mg/kg/day orally × 5-10 days	Albendazole 15 mg/kg/day orally divided into 2 doses × 7-14 days (maximum dose = 400 mg twice daily)
1-2 viable cysts seen as vesicular enhancing lesions +/− visible scolex	Dexamethasone 8 mg/day orally × 28 days; then taper down over 14 days	Albendazole 15 mg/kg/day orally divided into 2 doses × 10-14 days (maximum dose = 600 mg twice daily)
3 or more viable cysts seen as vesicular enhancing lesions +/− visible scolex	Dexamethasone 8 mg/day orally × 28 days; then taper down over 14 days	Albendazole 15 mg/kg/day orally divided into 2 doses × 10-14 days (maximum dose = 600 mg twice daily) ---**PLUS**--- Praziquantel 50 mg/kg/day orally divided into 3 doses × 10-14 days
Extraparenchymal		
Intraventricular cysts when surgical removal is contraindicated and a ventriculoperitoneal shunt is placed	Dexamethasone 8 mg/day orally × 14-28 days ---**OR**--- Prednisone 1-2 mg/kg/day orally × 14-28 days	Albendazole 15 mg/kg/day orally divided into 2 doses × 14 days (maximum dose = 400 mg twice daily)
Subarachnoid cysts in Sylvian fissure, basilar cisterns, or interhemispheric spaces	Following hydrocephalus management given 3-4 days before and throughout the duration of antihelminthic therapy: Prednisone 1 mg/kg/day orally ---**OR**--- Dexamethasone 0.2-0.4 mg/kg/day orally or IV	Albendazole 15 mg/kg/day orally divided into 2 doses (maximum dose = 600 mg twice daily) ---**OR**--- Albendazole 15 mg/kg/day orally divided into 2 doses (maximum dose = 600 mg twice daily) ---**PLUS**--- Praziquantel 50 mg/kg/day orally divided into 3 doses Duration of therapy is prolonged and depends on clinical and radiological response. Consultation with subject matter.

Data from References 73,75,78.

Evaluation of Therapeutic Outcomes

Weekly serum transaminases and a complete blood count with differential should be monitored for 2 to 4 weeks following the initiation of albendazole to evaluate for hepatoxicity and leukopenia. For patients with noncalcified parenchymal neurocysticercosis, an MRI should be performed every 6 months to monitor for resolution of cystic lesions. Household contacts should be screened for *T. solium* carriage if the affected patient acquired neurocysticercosis from a nonendemic area or the affected patient does not report a history of having eaten undercooked pork.

Toxocariasis

Epidemiology and Etiology

Toxocariasis is a neglected parasitic disease that is caused by the nematode (canine roundworm) *Toxocara canis* and less commonly from the feline roundworm *T. cati.* Since it is a zoonotic parasite, most cases occur in children with exposure to playgrounds and sandboxes contaminated with dog and cat feces. Children who have dogs and cats as household pets are also at increased risk of disease. The reported United States *Toxocara* seroprevalence rates were approximately 5% using the National Health and Nutrition Examination Survey (NHANES III) data from 2011 to 2014, which is a decrease from previous estimates at around 12%.[78,79] The highest risk patient populations remain non-White, males, and lower socioeconomic status.

Pathophysiology and Clinical Presentation

Toxocara species infect dogs and cats and shed their eggs in feces. The eggs undergo embryonation over 1 to 4 weeks and are able to resist harsh environmental conditions to remain viable for months. Human toxocariasis occurs when humans ingest viable embryonated eggs in contaminated soil. After ingestion, *Toxocara* eggs hatch and release larvae, which disseminate and cause systemic symptoms.[80] Children may be at highest risk because of poor hand hygiene and ingestion of contaminated dirt in playgrounds and sandboxes.[81] Toxocariasis is commonly asymptomatic; the most common clinical syndromes are visceral larva migrans and ocular larva migrans. Visceral larva migrans most commonly affects children younger than 7 years old and typically causes hepatitis or pneumonitis as the larvae migrate from the intestine to the liver and lungs. A significantly higher prevalence of *T. canis* infection has been observed in those with asthma suggesting that toxocariasis may be associated with atopy.[82,83] Ocular larva migrans often is seen in older children and typically presents as unilateral vision loss. This is caused by granulomatous inflammation in response to the larvae migrating through the eye. Other manifestations include cutaneous disease, isolated eosinophilia, covert and common toxocariasis.[82,83] Leukocytosis, eosinophilia, and a positive Toxocara ELISA are typically seen with systemic disease. A Toxocara ELISA is recommended for diagnosis and a titer greater than or equal to 1:32 has a sensitivity of approximately 80% and greater than 90% specificity for diagnosing visceral toxocariasis and other forms of systemic toxocariasis.[80,81]

Treatment

The antihelminthic drugs albendazole and mebendazole are recommended for toxocariasis.[80,81] Neither drug is FDA-approved for this indication and the lack of large randomized controlled trials precludes definitive dosing and duration recommendations. Most sources recommend 5-day courses at standard doses. While the safety of albendazole in children younger than 6 years is unclear, the WHO recommends 200-mg doses for those at least 12 months of age. Mebendazole use is also limited in those younger than 2 years. Severe pulmonary, cardiac, neurologic disease and OLM should also be treated with concomitant anti-inflammatory therapy with corticosteroids, typically prednisone 0.5 to 1 mg/kg/day.[84]

ECTOPARASITES

Lice

Epidemiology and Etiology

A parasite that lives on the outside of the body of the host is called an *ectoparasite.* Three species of blood-sucking human lice belong to two genera: *Pediculus* and *Phtirus. Pediculus humanus capitis* causes head lice and *Pediculus humanus corporis* causes body lice. *Phthirus pubis* is a crab louse that causes pubic lice. These three infestations are collectively referred to as pediculosis. The human louse is detectable to the human naked eye and

measures approximately 2 to 3 mm in length. Reliable data on the prevalence of lice in the United States are unavailable, but direct and indirect costs due to head lice may be as high as $1 billion per year.[85,86] Using pediculicide sales estimates in the United States, 6 to 12 million people per year may be affected, with girls likely affected more than boys.[87,88]

Pathophysiology and Clinical Presentation

Female lice deposit eggs on the hair. The eggs (or nits) remain firmly attached to the hair, and in about 10 days, the lice hatch to form nymphs, which mature in 2 weeks. Using both their piercing mouthparts and a pumping device, the larva and adults feed on the blood of the host.[87] The body louse and head louse are essentially identical, although they live on different parts of the body. Unlike the head louse, which lives on the hair, the body louse is more frequently found on clothing of the infected host.

Pubic or crab lice are found on the hair around the genitals, although they can occur in other areas of the body (eg, eyelashes, beards, and axillae). Patients usually complain of severe pruritus from papular lesions produced by the bite of the louse. Hypersensitivity to foreign material injected by the lice can produce macular swellings and occasionally can lead to secondary bacterial infections.

Treatment

8 For head lice, the American Academy of Pediatrics recommends either nonprescription 1% permethrin or pyrethrins plus piperonyl butoxide topical preparations as agents of choice unless local resistance to these agents is documented.[85] Permethrin is a derivative of the flowers of the plant *Chrysanthemum cinerariifolium*. The term *pyrethrin* is usually applied to several esters of chrysanthemic acid and pyrethric acid. Individuals who have a history of ragweed or chrysanthemum allergy should use pyrethrins with caution. The side effects reported with permethrin products are mild and include itching, burning, stinging, and tingling. Permethrin 1% is applied to the scalp after the hair has been dried following a shampooing. The scalp should be saturated with permethrin liquid, and a towel should be wrapped around the scalp to allow the application to stay on for 10 minutes. The hair then should be rinsed thoroughly. Permethrin and pyrethrins plus piperonyl butoxide should be used with nit combs because these agents are pediculocidal, but nonovidicidal. To ensure complete eradication, especially of newly hatched lice, it may be necessary to repeat the application since these drugs are not ovicidal.

Reports of lice resistance to nonprescription products, permethrin and pyrethrins, may make prescription-only spinosad 0.9% topical suspension the drug of choice for head lice as it is more effective than permethrin.[89,90] Spinosad is a semi-synthetic fermentation product of soil *Saccharopolyspora spinosa*. Its adverse effects may include erythema and irritation of the scalp. In addition to spinosad effectiveness in permethrin-resistant lice, nit combs are unnecessary because this drug kills both lice and their ova. Widespread use of spinosad as an alternative first-line agent may be limited by its prescription-only availability and higher cost compared to nonprescription permethrin.

Other topical preparations for lice are 0.5% malathion, 5% benzyl alcohol, and 0.5% ivermectin (Table e138-8).[85,87,89,90] Lindane 1% shampoo is no longer recommended because of neurotoxicity to humans.[85,90] Although not FDA-approved for head lice infection, oral ivermectin has been evaluated for this indication and it may have superior effectiveness compared to other topical treatment options.[92] It is well tolerated and may be an option for individuals who have experienced treatment failure. All agents except ivermectin may be used during pregnancy.[93] For the relief of pruritus, a soothing lotion of calamine liniment or lotion with 0.1% menthol may be used. Other members of the family should be treated. All bedding and clothes should be sterilized by boiling or washing in the hot water cycle of the washing machine to avoid reinfections. Seams of clothes should be examined to verify that all organisms are eradicated. An ocular lubricant (eg, Refresh Lacri-Lube) applied twice daily may be used to remove crab louse infection of the eyelids.

Scabies

Epidemiology and Etiology

Scabies is caused by the itch mite *Sarcoptes scabiei*, which affects both humans and animals. Mange in domestic animals is caused by the same organism. *S. scabiei* burrows under the skin and is transmitted through direct skin-to-skin contact for 15 to 20 minutes. The worldwide prevalence of scabies was over 200 million according to the Global Burden of Disease Study 2015.[94] The burden of scabies has decreased or remained stable over the past two decades across the world except in North America where a 24% increase was observed. Children less than 5 years old are most widely affected

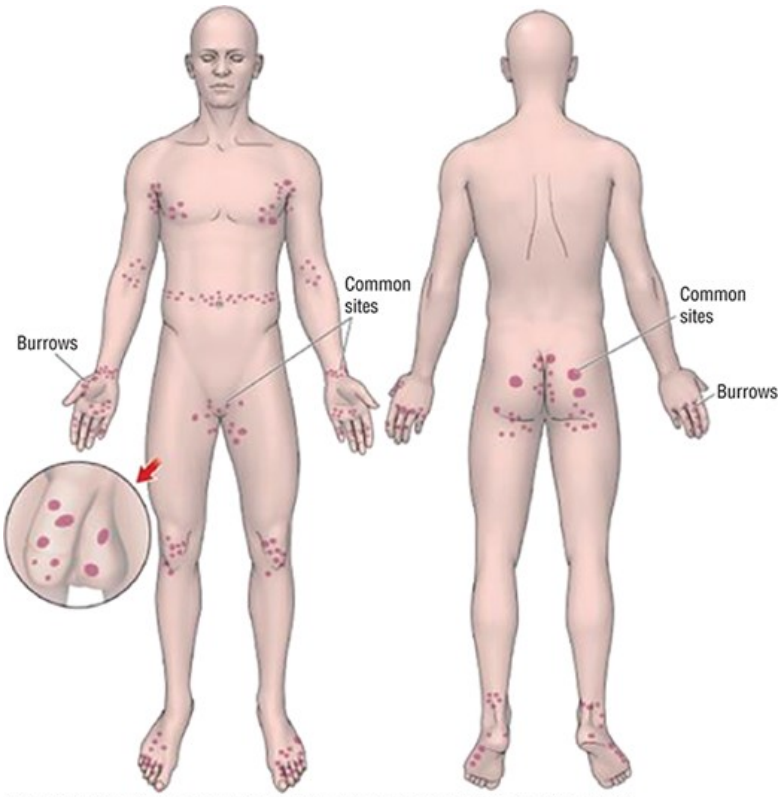
worldwide. The distribution of scabies is more evenly distributed across age groups in North America, but the majority of scabies cases continue to be diagnosed in children.[95]

Pathophysiology and Clinical Presentation

Infection usually affects the interdigital and popliteal folds, axillary folds, the umbilicus, and the scrotum (Fig. e138-2). Classic or typical scabies (scabies vulgaris) presents with severe itching and an inability to sleep and may have excoriations in the interdigital web spaces, wrists, elbows, buttocks, and groin with the face and neck unaffected. Atypical scabies include scalp scabies, crusted scabies (Norwegian scabies), and nodular scabies, all of which may occur in high-risk institutionalized or immunocompromised patients. Excoriations may lead to secondary bacterial infections, making scabies a major cause of impetigo. The diagnosis is made by looking for burrows formed by the mite and taking skin scrapings, which will demonstrate the mite on a wet mount. Typically, 10 to 15 mites may be present.

FIGURE e138-2

Scabies predilection sites.



Treatment

These infections cause a great deal of discomfort and distress to patients and families. Therefore, the goals of therapy are to eradicate the infestations rapidly, to institute symptomatic treatment, and to provide counseling and reassurance. The CDC-recommended treatment of choice remains permethrin 5% cream despite concerns of increased resistance or oral ivermectin repeated in 2 weeks.[96,98] To initiate permethrin treatment, the skin should be scrubbed thoroughly in a warm soapy bath using a soft brush to remove all scabs. The lotion is then applied to the whole body, avoiding the face, mucous membranes, and eyes. The application should be left on for 8 to 14 hours before bathing. A single application of 5% permethrin results in cure rates in greater than 90% of subjects with scabies at 14 and 28 days, but a second dose should be applied 1 week later because its ovicidal efficacy remains unclear.[96,98] All close contacts should be checked and treated appropriately.

Other agents used to treat scabies include topical crotamiton 10% (Eurax) and oral ivermectin 200 mcg/kg as a single dose, which may be repeated in 2 weeks Table e138-8.[99] Crotamiton and oral ivermectin may be used in patients who have hypersensitivity to permethrin preparations. Topical corticosteroids and antihistamines may be used to decrease pruritus. There are no nonprescription drugs approved for treatment of scabies. Retreatment can be considered 2 weeks after initial treatment for patients who are still symptomatic or when live mites are present. Crusted scabies is more difficult to treat and may require combination therapy with oral ivermectin and a topical scabicide agent.

TABLE e138-8

Treatment of Ectoparasites

Drug	Ovicidal?	Resistance?	Lower Age or Weight Limit	Effectiveness	Dose
Head Lice					
Benzyl alcohol 5% lotion	No	No	6 months	75%	Apply to dry hair, leave on for 10 minutes then rinse; repeat in 7 days
Ivermectin 0.5% lotion	Partial (lice hatched from treated eggs die within 48 hours)	No	6 months	74%	Apply to dry hair and scalp, leave on for 10 minutes then rinse; one application is sufficient
Ivermectin oral tablet	Partial	No	15 kg	92%-97%	200 mcg/kg, two doses 7-10 days apart
Lindane 1% shampoo or lotion	Partial	Yes	6 months; 50 kg	70%-86%	Not recommended
Malathion 0.5% lotion	Partial	Not in the United States	6 years	80%-98%	Apply to dry hair until hair and scalp are wet, allow to dry naturally, shampoo 8-12 hours later, rinse and use a lice comb; repeat after 7-9 days only if live lice are still present
Permethrin 1% cream (OTC)	No	Yes	2 months	25%-50%	Apply to shampooed, towel-dried hair for 10 minutes, then rinse; repeat in 7 days
Pyrethrins with piperonyl butoxide shampoo (OTC)	No	Yes	2 months	62%	Apply to dry hair, leave on for 10 minutes then rinse; repeat in 7 days
Spinosad 0.9% suspension	Yes	No	6 months	85%-87%	Apply to dry hair, leave on for 10 minutes then rinse; repeat in 7 days only if live lice are present
Scabies					
Crotamiton 10% lotion	Yes	Yes	None	67%	Apply a thin layer to skin of the entire body from the neck down for 24 hours and then rinse off. Repeat application for another 24 hours.

Ivermectin oral tablet	Partial	Yes	15 kg	70%-95%	Take 200 mcg/kg orally, repeated in 2 weeks.
Lindane 1% lotion or cream	Yes	Yes	10 years	86%	Apply 1 oz of lotion or 30 g of cream in a thin layer to all areas of the body from the neck down and thoroughly washed off after 8 hours.
Permethrin 5% cream	Partial	Yes	2 months	90%-100%	Apply to all areas of the body from the neck down and wash off after 8-14 hours; apply a second dose 1 week later

Data from References 90,91,100.

ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
CNS	central nervous system
ECG	electrocardiogram
EIA	enzyme immunoassay
ELISA	enzyme-linked immunosorbent assay
FDA	Food and Drug Administration
HIV	human immunodeficiency virus
IND	investigational new drug
MRI	magnetic resonance imaging
NAAT	nucleic acid amplification testing
NHANES III	National Health and Nutrition Examination Survey
PCR	polymerase chain reaction
WHO	World Health Organization

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SELF-ASSESSMENT QUESTIONS

1. Which one of the following antiparasitic drugs may be given as a single-dose to treat a 6-year-old child with giardiasis?

   A. Albendazole

   B. Benznidazole

   C. Mebendazole

   D. Metronidazole

   E. Tinidazole

2. Which one of the following is the greatest risk factor for contracting giardiasis?

A. Drinking unpasteurized milk

B. Eating undercooked pork

C. Living near opossums

D. Playing in outdoor sandboxes

E. Swimming in contaminated water

3. Which of the following pairs matches the parasitic infection with the most effective preventative strategy?

A. Malaria; mosquito avoidance

B. Chagas disease; canine deworming

C. Cysticercosis; unpasteurized dairy avoidance

D. Amebiasis; reduviid bug control

E. Cryptosporidiosis; good hand hygiene

4. JC is a 35-year-old man with HIV infection who presents with profuse, watery, nonbloody diarrhea. He stopped taking antiretroviral therapy 5 years ago and his most recent CD4+ T-cell count is 35 cells/mm^3 (35×10^6/L). Stool samples are collected and a *Cryptosporidium* direct fluorescent antibody test returns positive. JC should receive:

A. Oral fluids and tinidazole

B. Loperamide and nitazoxanide

C. Opium tincture and metronidazole

D. Antiretroviral therapy and nitazoxanide

E. Antiretroviral therapy and metronidazole

5. Luminal agents that are recommended for patients with amebiasis who are asymptomatic cyst passers include:

A. Iodoquinol and albendazole

B. Iodoquinol and paramomycin

C. Metronidazole and paramomycin

D. Metronidazole and tinidazole

E. Tinidazole and paramomycin

6. Tissue-acting agents that are recommended for patients with ALAs include:

A. Iodoquinol and albendazole

B. Iodoquinol and paramomycin

C. Metronidazole and paramomycin

D. Metronidazole and tinidazole

E. Tinidazole and paramomycin

7. LL is a 52-year-old recent immigrant of Columbia who has been diagnosed with neurocysticercosis. *Taenia solium* cysts are found to be located in the basal meninges and in the fourth ventricles by MRI. Treatment of this patient may include surgical cyst removal, antiepileptic drugs, corticosteroids, and antihelminthic therapy. Which of these options may lead to worsening of neurocysticercosis symptoms?

   A. Phenytoin

   B. Metronidazole

   C. Dexamethasone

   D. Surgical cyst removal

   E. Albendazole and praziquantel

8. MC is a 4-year-old boy with fever, hepatosplenomegaly, abdominal pain, and wheezing who is diagnosed with toxocariasis. MC should receive:

   A. Albendazole

   B. Benznidazole

   C. Fluconazole

   D. Metronidazole

   E. Tinidazole

9. TG is a 45-year-old man traveling to Kenya in 6 months. According to the Centers for Disease Control and Prevention (CDC) Yellow Book, the relative risk for malaria is moderate and chloroquine-resistant *P. falciparum* is prevalent. His current medications include lisinopril, duloxetine, and zolpidem as needed for insomnia. A recommended malaria chemoprophylaxis regimen is:

   A. Doxycycline 100 mg orally once daily

   B. Primaquine 30 mg base orally once daily

   C. Mefloquine 228 mg base orally once weekly

   D. Hydroxychloroquine 310 mg base orally once weekly

   E. Atovaquone/proguanil 62.5 mg/25 mg orally once weekly

10. Severe falciparum malaria requires a patient to be admitted to an acute care unit and treated with:

    A. Artesunate

    B. Artemether-lumefantrine

    C. Atovaquone-proguanil

    D. Mefloquine

    E. Quinine sulfate

11. An artemisinin-based regimen that may be used to treat uncomplicated chloroquine-resistant malaria includes:

    A. Artesunate

B. Artemether-lumefantrine

C. Atovaqone-proguanil

D. Mefloquine

E. Quinine sulfate

12. RT is a 41-year-old Mexican man who has lived in California for the last 20 years and makes frequent trips to Guadalajara to visit his sisters. Two days ago, after he returned from a 3-week trip, he began complaining of fever, nausea, vomiting, and left eye swelling. He is diagnosed with Chagas disease (*Trypanosoma cruzi*). RT should receive:

A. Albendazole

B. Benznidazole

C. Metronidazole

D. Nifurtimox

E. Nitazoxanide

13. Chronic *Trypanosoma cruzi* infection or Chagas disease is likely to lead to:

A. Asthma

B. Cardiomyopathy

C. Epilepsy

D. Lactic acidosis

E. Liver failure

14. An alternative prescription-only agent for *Pediculosis capitis* (head lice) in which permethrin resistance has been documented includes:

A. Crotamiton 10% topical lotion

B. Lindane 1% shampoo or lotion

C. Spinosad 0.9% topical suspension

D. Permethrin 5% topical cream

E. Pyrethrins plus piperonyl butoxide shampoo

15. The drug regimen of choice for scabies treatment is:

A. Crotamiton 10% topical lotion

B. Lindane 1% shampoo or lotion

C. Spinosad 0.9% topical suspension

D. Permethrin 5% topical cream

E. Pyrethrins plus piperonyl butoxide shampoo

SELF-ASSESSMENT QUESTION-ANSWERS

1. **E.** Tinidazole is the only single-dose regimen available for giardiasis treatment and accumulating evidence supports tinidazole as the 5-nitroimidazole of choice (see Table e138-2).

2. **E.** Like cryptosporidiosis, the greatest risk factor for giardiasis is ingestion of fecally contaminated water containing infective cysts (see subsection "Pathophysiology and Clinical Presentation" under section "Giardiasis").

3. **A.** Malaria results after *Plasmodium* sporozoites enter the host bloodstream following the bite of an infected female *Anopheles* mosquito. Mosquito avoidance is an effective strategy (see subsection "Chemoprophylaxis and Prevention" under section "Malaria"). Other causes of parasitic diseases may be further investigated after reviewing parasitic life cycles found in the section "Beyond the Book."

4. **D.** Antiretroviral therapy is essential for an effective treatment of cryptosporidiosis with nitazoxanide (see subsection "Treatment" under section "Cryptosporidiosis" and DHHS Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents).

5. **B.** Paromomycin and iodoquinol remain in the lumen of the gastrointestinal tract and are used to eliminate *E. histolytica* cyst carriage (see Table e138-2).

6. **D.** Metronidazole and tinidazole are systemically absorbed and are used to treat amebic liver abscess (see Table e138-2).

7. **E.** Antiparasitic drugs are often delayed until CNS symptoms such as seizures are addressed because cyst destruction may lead to an acute exacerbation due to increased inflammation (see subsection "Treatment" under section "Cysticercosis and Neurocysticercosis" and Table e138-7).

8. **A.** Toxocariasis is treated with the antihelminthic drug albendazole (see subsection "Treatment" under section "Toxocariasis").

9. **A.** Either doxycycline or atovaquone-proguanil are recommended for chemoprophylaxis in chloroquine-resistant areas. The pediatric dose of atovaquone-proguanil 62.5 mg/25 mg is inappropriate for this 45-year-old man. Atovaquone-proguanil must also be given once daily (see Table e138-4).

10. **A.** Severe malaria falciparum should be treated with intravenous artusenate or intravenous quinidine gluconate (see Table e138-5 and Fig. e138-1).

11. **B.** Artemether-lumefantrine is the only oral artemisinin-based therapy listed (see Table e138-5 and Fig. e138-1).

12. **B.** Benznidazole is the only FDA-approved treatment for Chagas disease and is better tolerated than nifurtimox (see Table e138-2).

13. **B.** Early detection and treatment of Chagas disease is important because chronic infection with *T. cruzi* results in an irreversible cardiomyopathy (see subsection "Pathophysiology and Clinical Presentation" under section "Chagas Disease [American Trypanosomiasis]").

14. **C.** Topical spinosad may retain effectiveness in resistant lice and is considered to be both pediculocidal and ovicidal (see subsection "Treatment" under section "Lice").

15. **D.** Topical 5% permethrin cream remains the drug of choice for scabies (see subsection "Treatment" under section "Scabies").