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ECHINOCOCCOSIS

Paul Cantey, Rebecca Chancey, Sharon Roy

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INFECTIOUS AGENTS: *Echinococcus multilocularis* (alveolar echinococcosis) *Echinococcus granulosus* (cystic echinococcosis)	
ENDEMICITY	Alveolar echinococcosis: primarily in northern latitudes of North America, Asia, and Europe where canids ingest the rodent intermediate host Cystic echinococcosis: worldwide where canids ingest the organs of livestock
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Immigrants and refugees Long-term travelers
PREVENTION METHODS	Avoid canids in affected areas Avoid drinking untreated water Avoid eating food cooked by someone who does not use good hand hygiene Practice good hand hygiene
DIAGNOSTIC SUPPORT	Serologic testing: CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENTS

Echinococcosis is caused by cestode parasites of the genus *Echinococcus*, including *E. multilocularis*, *E. granulosus*, and others.

TRANSMISSION

Humans become infected through ingestion of *Echinococcus* eggs shed in the feces of infected definitive hosts, including foxes and other canids for *E. multilocularis*, or dogs and other canids for *E. granulosus*. Ingestion can occur through hand-to-mouth transfer of eggs or by consuming fecally contaminated food, water, or soil.

EPIDEMIOLOGY

The 2 main forms of echinococcosis in humans are alveolar echinococcosis (AE), caused by *E. multilocularis*, and cystic echinococcosis (CE), caused by *E. granulosus* and other species. Rarer forms, referred to as neotropical echinococcosis

(NE), are caused by *E. vogeli* and *E. oligarthrus*. AE occurs in the northern hemisphere, in parts of North America and Eurasia. CE occurs in parts of Africa, the Americas (including South America [foci within Peru]), Australia, and Eurasia, including in pastoral and rangeland areas, where transmission often is maintained by dog-sheep-dog cycles. NE occurs in rural settlements near tropical forests in Central and South America. Although indigenous human cases of AE and CE have been reported in the United States, most US cases of echinococcosis have been imported.

CLINICAL PRESENTATION

People with AE and CE could remain asymptomatic for years. The nature and severity of the clinical manifestations depend in part on the location, size, and other characteristics of the lesions that develop and the associated complications. AE usually affects the liver; direct extension to and destruction of contiguous tissues can occur, as can metastatic lesions. In CE, lesions are cystic (referred to as hydatid cysts) and most commonly develop in the liver; the next most common site is the lungs, but cysts can develop in other organ systems. NE is rare; the polycystic form can be clinically similar to AE.

DIAGNOSIS

A presumptive diagnosis can be based on a combination of the person's exposure history and imaging studies (e.g., an ultrasound or CT scan). Lesions might be found incidentally in asymptomatic people. Serologic testing also can be helpful and is available through the Parasitic Diseases Branch at the Centers for Disease Control and Prevention (CDC). Instructions on how to submit a serum specimen for testing can be found at www.cdc.gov/laboratory/specimen-submission/index.html. For assistance with parasitological diagnosis, submit a request to the Division of Parasitic Diseases and Malaria DPDx (www.cdc.gov/dpdx/dxassistance.html).

TREATMENT

For AE, treatment strategies include complete surgical removal of infected tissue (if resectable) and long-term benzimidazole therapy; untreated AE progresses and ultimately leads to death. For CE, the World Health Organization has developed an image-based staging system that facilitates selecting among potential case-management strategies, including observation without treatment, percutaneous approaches, surgical resection, and drug treatment. Treatment of NE might involve surgical treatment or benzimidazole therapy; the role of percutaneous treatment is unclear. Clinicians can consult CDC to obtain more information about diagnosis and treatment (CDC Parasitic Diseases Inquiries: 404-718-4745 or parasites@cdc.gov).

PREVENTION

To reduce the risk for echinococcosis, travelers should avoid contact with dogs and wild canids in endemic areas; should not drink untreated water from canals, lakes, rivers, or streams; and should follow food and water precautions (see Sec. 2, Ch. 8, Food & Water Precautions). In addition, travelers should practice good hand hygiene after handling dogs and during food preparation in affected areas.

CDC website: www.cdc.gov/parasites/echinococcosis

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ENTEROBIASIS / PINWORM

Rebecca Chancey, Mary Kamb

INFECTIOUS AGENT: *Enterobius vermicularis*	
ENDEMICITY	Worldwide
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Children People who take care of infected children
PREVENTION METHODS	Avoid handling contaminated bed linen and clothing Practice good hand hygiene, especially after using the toilet or changing diapers and before handling food
DIAGNOSTIC SUPPORT	Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENT

Enterobiasis is caused by the intestinal nematode (roundworm) *Enterobius vermicularis*.

TRANSMISSION

People become infected, usually unknowingly, by ingesting infective pinworm eggs. Person-to-person transmission of infective pinworm eggs occurs through the fecal–oral route (including self-inoculation) by contaminated hands or eating contaminated food (rarely), or indirectly by handling bedding, clothing, or other articles contaminated by eggs. Because of their small size, pinworm eggs can become airborne, suggesting inhalation from air and dust could be another transmission route.

EPIDEMIOLOGY

Pinworm is endemic worldwide and commonly clusters within families. Infections are typically in preschool- and school-age children, people who care for young children, and people who are institutionalized. Based on limited data, travelers could be exposed in crowded conditions with infected people or through contaminated bedding.

CLINICAL PRESENTATION

The incubation period is usually 1–2 months; successive reinfections might be needed before symptoms appear. The most common symptom is perianal itching, which can be severe, causing sleep disturbances and irritability. Secondary infection of irritated skin also can occur. Adult worms can migrate from the anal area to the urethra, vagina, vulva, or other sites. Appendicitis and enuresis are reported as possible associated conditions.

DIAGNOSIS

Adult worms might be visible near the anus 2–3 hours after the infected person is asleep. Visual inspection of undergarments or bedding also might reveal pinworms. For microscopic identification, pinworm eggs can be collected by touching transparent tape to the affected person's anal area immediately after awakening and before washing, ideally on 3 consecutive mornings. Eggs also might be found in samples taken from under fingernails before handwashing. Examining stool samples is not recommended because pinworm eggs are sparse. Diagnostic assistance is available through the Centers for Disease Control and Prevention (CDC)'s DPDx laboratory in the Division of Parasitic Diseases and Malaria (www.cdc.gov/DPDx).

TREATMENT

Drugs of choice are albendazole, pyrantel pamoate, or mebendazole given as a single, initial dose, followed by a second dose of the same drug 2 weeks later to eliminate possible reinfection. Pyrantel pamoate is available without

prescription in the United States. Mebendazole is available in the United States only through compounding pharmacies. Simultaneous treatment of all household members is warranted if >1 person is infected, or infection recurs. Offer treatment to exposed sexual partners.

PREVENTION

Careful hand hygiene is the most effective prevention method. During treatment, change bed linens and underclothing of infected children first thing in the morning. Advise patients and families to collect linens and clothing carefully to avoid contaminating the environment (e.g., not shaking out the clothing or linens), and then laundering promptly in hot (>40° C) water and drying in a hot dryer to kill any eggs that might be present. To prevent transmission or reinfection, counsel infected people to bathe (shower or stand-up baths) in the morning and change underwear daily and bed clothes frequently, including after treatment and preferably after bathing. Infected people should also practice personal hygiene measures, including washing hands with soap and water before eating or preparing food, keeping fingernails short, avoiding scratching the perianal region, and avoiding nail biting.

CDC website: www.cdc.gov/parasites/pinworm

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FILARIASIS, LYMPHATIC

Mary Kamb, Sharon Roy

INFECTIOUS AGENTS: *Wuchereria bancrofti*, *Brugia malayi*, and *B. timori*	
ENDEMICITY	Africa: Sub-Saharan Africa and Egypt Americas: Northeastern coast of Brazil; parts of Guyana, Haiti, and the Dominican Republic Asia and the Pacific: southern and southeast Asia; southwestern Pacific Islands
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Immigrants and refugees from endemic areas Long-term travelers
PREVENTION METHODS	Avoid insect bites
DIAGNOSTIC SUPPORT	Serologic testing: National Institutes of Health Laboratory of Parasitic Diseases (301-496-5398) or CDC's Parasitic Disease Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov)

INFECTIOUS AGENT

Lymphatic filariasis is caused by 3 species of filarial nematodes, *Wuchereria bancrofti*, *Brugia malayi*, and *B. timori*.

TRANSMISSION

Infective larvae can be transmitted by both day- and night-biting mosquitoes; vectors include species from several genera, including *Aedes*, *Anopheles*, *Coquillettidia*, *Culex*, and *Mansonia*. Transmission occurs in rural, urban, and semiurban settings.

EPIDEMIOLOGY

Once widespread in Africa and Asia, and swaths of Latin America and the Pacific, sustained elimination efforts based on mass drug administration have greatly reduced the global prevalence of parasites that cause lymphatic filariasis. Currently, infections occur in parts of Africa (Egypt, sub-Saharan Africa); Asia (southeast Asia, the Indian subcontinent); and some southwestern Pacific Islands. In the Americas, focal distribution has been reported on the northeastern coast of Brazil, in Guyana, and on the island of Hispaniola (Dominican Republic, Haiti). Most infections in the United States occur in immigrants and refugees.

Because multiple exposures (bites from infected mosquitoes) over time are usually required for infection, travelers are at low risk for this disease. Infections have, however, been documented in long-term travelers (usually people living many months–years in endemic countries) and in visitors to areas with highly efficient mosquito vectors (e.g., *Aedes* in the Pacific) with as little as 1 month of exposure.

CLINICAL PRESENTATION

Infective filarial larvae grow into adult worms that inhabit the human lymphatic and subcutaneous tissues. Infections can be asymptomatic (subclinical) or associated with acute and chronic clinical manifestations involving moderate to severe lymphedema of the arm, breast, leg, penis, or scrotum. In people with lymphedema, episodes of acute secondary infections can involve painful swelling of an affected limb, fever, or chills; repeated episodes can hasten the progression of lymphedema to its advanced stage, known as elephantiasis.

Tropical pulmonary eosinophilia (TPE) syndrome is a potentially serious, progressive lung disease characterized by fever and nocturnal cough, wheezing, or both, which results from immune hyper-responsiveness to microfilariae in the pulmonary capillaries. Most cases of TPE have been reported in long-term residents from Asia, often men aged 20–40 years.

DIAGNOSIS

In symptomatic people with plausible exposure based on epidemiology, diagnosis can be made by microscopic detection of characteristic microfilariae on a thick blood film made from an appropriately timed sample collection. Microfilariae are usually not detected in patients with TPE.

Filarial antibody tests that detect elevated IgG and IgG4 can be useful, especially when microfilariae are not detected. Serologic assays are available through the National Institutes of Health (301-496-5398) or Centers for Disease Control and Prevention (CDC; www.cdc.gov/dpdx; 404-718-4745; parasites@cdc.gov). PCR tests exist in some research settings but are not yet commercially available. Ultrasound and lymphoscintigraphy can be used to detect presence of motile adult worms in lymphatic vessels, known as filarial dance sign.

TREATMENT

Diethylcarbamazine (DEC) is the drug of choice for lymphatic filariasis, regardless of the causative parasite species. Although no longer approved for use in the United States by the US Food and Drug Administration and not commercially available, DEC can be obtained under an investigational new drug protocol from the CDC Drug Service (M–F, 8 a.m.–4:30 p.m. Eastern, 404-639-3670; after hours/weekends/holidays, 770-488-7100; drugservice@cdc.gov).

Before initiating DEC treatment for lymphatic filariasis, first rule out co-infection with *Onchocerca volvulus* in at-risk patients (see Sec. 5, Part 3, Ch. 17, Onchocerciasis / River Blindness). DEC use is contraindicated in patients with *O. volvulus* infection due to the potential for causing a severe allergic response (Mazzotti reaction) that especially affects the eyes and skin. In addition, DEC must be used with extreme caution in patients with loiasis (*Loa loa* infection) due to

possible life-threatening side effects in people with high circulating microfilariae loads.

People with lymphedema and hydrocele can benefit from lymphedema management and, in the case of hydrocele, surgical repair. Evidence suggests that a 4–8-week course of doxycycline (200 mg daily) can both sterilize adult worms and improve lymphatic pathologic features.

PREVENTION

No vaccines or drugs to prevent infection are available. Travelers should avoid mosquito bites (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

CDC website: www.cdc.gov/parasites/lymphaticfilariasis

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FLUKES, LIVER

Sharon Roy, Paul Cantey

INFECTIOUS AGENTS: *Clonorchis*, *Fasciola* spp., and *Opisthorchis* spp.	
ENDEMICITY	*Clonorchis*: primarily East Asia *Fasciola* spp.: Worldwide *Opisthorchis* spp.: Regional
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	All travelers Expatriates and long-term travelers living in endemic areas
PREVENTION METHODS	Follow safe food and water precautions Avoid eating raw or undercooked crab, crayfish, or fish in areas where flukes are endemic Avoid eating watercress or other greens that might have been washed with water contaminated with fluke larvae
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; or for serologic testing for *Fasciola* spp., contact CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) For *Clonorchis* and *Opisthorchis* spp. ova and parasite testing, contact Parasitological diagnosis DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENTS

Liver flukes are trematode flatworms, including *Clonorchis sinensis*; *Fasciola hepatica* and *F. gigantica*; *Opisthorchis felineus* and *O. viverrini*.

TRANSMISSION

Reservoir hosts for *Clonorchis* and *Opisthorchis* spp. are cats, dogs, and other fish-eating mammals, and human infection generally occurs by ingestion of raw or undercooked (e.g., pickled, salted, or smoked) freshwater fish. *Fasciola* spp. cause liver disease in cattle and sheep (definitive hosts) but can be transmitted to humans who consume watercress or other aquatic, freshwater plants contaminated with infective metacercariae, or who drink contaminated water.

EPIDEMIOLOGY

C. sinensis is found mainly in eastern Asia, including China, Korea, eastern Russia, Taiwan, and northern Vietnam; it was previously endemic in Japan, although the last human case there was reported in 1991. *F. hepatica* has worldwide distribution, especially in areas where cattle or sheep are raised. *F. gigantica* has a more limited distribution in parts of Africa and Asia. *O. felineus* is found mainly in eastern Europe and through central Asia to Siberia, including the Baltic countries, Belarus, Italy, Germany, Greece, Kazakhstan, Moldova, Poland, Romania, Russia, and the Ukraine. *O. viverrini* is found mainly in Burma (Myanmar), northeastern Cambodia, Laos, Thailand, and central and southern Vietnam.

Worldwide, men are more commonly infected with *Clonorchis* and *Opisthorchis* spp. than women; slightly more women are infected with *Fasciola* spp. than men. For fascioliasis, prevalence is greater during childhood and decreases somewhat in adulthood. For clonorchiasis and opisthorchiasis, prevalence increases during childhood, reaching a maximum prevalence at middle age, with a slight decrease in prevalence in older age.

Travelers to liver fluke–endemic areas can become infected by ingesting contaminated foods. The risk for infection increases with increasing exposure (i.e., ingestion of infective metacercariae on raw and inadequately washed plants), which is greater for people residing for long periods in known endemic areas (e.g., expatriates, immigrants, long-term travelers, refugees).

CLINICAL PRESENTATION

Clonorchiasis & Opisthorchiasis

Clonorchiasis and opisthorchiasis symptoms are related to worm burden and involve both the gallbladder and liver. Most low-intensity infections are asymptomatic or show only mild symptoms. Patients with high-intensity infections might show nonspecific signs and symptoms, which can include diarrhea, eosinophilia, fatigue, fever, nausea, and indigestion. They also could have abdominal pain, particularly in the right upper quadrant; intermittent colicky pain associated with worms obstructing the gallbladder; jaundice; and an enlarged or tender liver.

Generally, patients infected with *O. felineus* are more symptomatic in the acute phase than those infected with *O. viverrini* or *Clonorchis* spp. Chronic infections, at about 30 days postinfection, can result in various complications, including cholelithiasis, cholangitis, and cholecystitis. Liver abscesses and pancreatitis also have been linked to chronic clonorchiasis, as has developmental delay in children with high-intensity infections. Chronic *Clonorchis* and *Opisthorcis viverrini* from protracted episodes of reinfection over time are associated with the development of cholangiocarcinoma (CCA). Multiple nonparasitic risk factors for CCA exist, however, and liver fluke infections are very rarely associated with cases of CCA in the United States.

Fascioliasis

The acute phase of fascioliasis (also known as the migratory, invasive, or hepatic phase) can last up to 3–4 months. Although most infected people have low-intensity infections and are asymptomatic during the acute phase, ≈17.5% of patients with high-intensity infections can experience clinical manifestations, including abdominal pain and other gastrointestinal symptoms, marked eosinophilia, fever, respiratory symptoms (e.g., cough), and urticaria.

The chronic (biliary) phase begins 6 months after infection when immature worms (larval flukes) reach the bile ducts, mature into adult worms (which can live ≥10 years), and start to produce eggs. The clinical manifestations, if any, during the chronic phase reflect biliary tract disease (e.g., biliary tract obstruction, cholangitis, cholecystitis) or pancreatitis.

DIAGNOSIS

The primary mode of diagnosis of fascioliasis and liver flukes is detection of eggs in stool, or in duodenal or biliary aspirates. Distinguishing *Fasciola* eggs from those of *Fasciolopsis buski* can be difficult. *Fasciolopsis buski* is an intestinal fluke that requires a different treatment than *Fasciola*. In fascioliasis, egg production does not occur until ≥3–4 months after exposure; thus, serologic testing can be useful for fascioliasis diagnosis during the acute phase because parasite antibodies might be detectable in 2–4 weeks. Serology also can be useful during the chronic phase if egg production is intermittent or low.

Serologic testing for fascioliasis is available through the Centers for Disease Control and Prevention (CDC). Instructions for submitting specimens for testing at CDC can be found at www.cdc.gov/laboratory/specimen-submission/index.html; see the test directory for specific instructions on how to request *Fasciola* serology. Further information about diagnosis and management of the different liver flukes is available at www.cdc.gov/parasites, by emailing parasites@cdc.gov, or by calling 404-718-4745. No serologic tests are available in the United States for clonorchiasis or opisthorciasis. Imaging studies (e.g., CT, MRI, ultrasonography) of the hepatobiliary tract, can be helpful for the diagnosis of liver flukes of all species.

TREATMENT

First-line treatment of fascioliasis is with triclabendazole, approved for use in the United States by the Food and Drug Administration in 2019. Health care providers should contact the AllCare Plus Pharmacy at 888-774-7327 to order triclabendazole. AllCare will need the patient's name, address, telephone number, date of birth, weight, and clinical information; the pharmacy will arrange for free shipping of the drug to the patient. Nitazoxanide therapy might be helpful in some patients with fascioliasis.

First-line treatment for clonorchiasis and opisthorchiasis is praziquantel. Albendazole is an alternative drug for treatment of *Clonorchis* or *Opisthorchis*. In patients with biliary tract obstruction due to liver flukes of any of the species, removal of adult flukes (e.g., via endoscopic retrograde cholangiopancreatography) might be indicated.

PREVENTION

Travelers can prevent *Fasciola* infection by avoiding ingestion of uncooked, aquatic freshwater plants, including watercress, especially from endemic grazing areas. These include plants used in local dishes, appetizers, beverages, condiments, and juices. Additionally, travelers should avoid drinking water from untreated natural sources, particularly those frequented by livestock. Infection with other liver flukes can be prevented by avoiding ingestion of raw or undercooked, pickled, salted, or smoked freshwater fish in endemic areas (See Sec. 2, Ch. 8, Food & Water Precautions).

CDC website: www.cdc.gov/parasites/fasciola; www.cdc.gov/parasites/opisthorchis; www.cdc.gov/parasites/clonorchis

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FLUKES, LUNG

Susan Montgomery

INFECTIOUS AGENT: *Paragonimus* spp.	
ENDEMICITY	Africa The Americas East Asia (China, Japan, Korea) Southeast Asia
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventurous eaters
PREVENTION METHODS	Practice safe food precautions Avoid raw or undercooked freshwater crab or crawfish
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; or contact CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENTS

Paragonimiasis is caused by helminth parasites in the genus *Paragonimus*, especially *Paragonimus westermani*.

TRANSMISSION

Lung fluke infections are transmitted by eating raw or undercooked, pickled, or salted freshwater crab or crawfish infected with the immature form of the parasite. Ingested larval stages of the parasite are released when the infected crustacean is digested and then migrates from the intestines to other parts of the body. Most end up in the lungs, where they develop into adults and produce eggs. Human infections can persist for 20 years.

EPIDEMIOLOGY

Human disease is caused by ≥15 species of *Paragonimus*, which vary by geographic area and definitive host. *Paragonimus* species are found in western Africa, the Americas, and Asia. *P. westermani*, the most common cause of human disease, occurs predominantly in eastern and southern Asia.

CLINICAL PRESENTATION

Patients with *Paragonimus* infection can present with an acute syndrome within 2 days to 2 weeks after ingestion. Infections of longer duration can present with signs and symptoms like tuberculosis, with shortness of breath, cough, and hemoptysis. Extrapulmonary infections can occur and cause serious disease when the central nervous system is involved. Infections are usually associated with eosinophilia, especially during the larval migration stage.

DIAGNOSIS

Refer travelers to an infectious disease specialist if there is clinical suspicion of a lung fluke infection. Diagnosis is usually made by identifying eggs in stool or sputum. Serologic testing for *P. westermani*–specific antibodies can be helpful, especially for diagnosis of extrapulmonary infection; depending on the serologic assay, this testing can detect infections with other *Paragonimus* species because of differing levels of cross-reactivity among species.

Clinicians can obtain diagnostic assistance and confirmatory testing from the Centers for Disease Control and Prevention (CDC)'s Division of Parasitic Diseases and Malaria

DPDx laboratory (dpdx@cdc.gov), and from the Parasitic Diseases Hotline for Healthcare Providers (404-718-4745; parasites@cdc.gov).

TREATMENT

Treatment is with praziquantel; triclabendazole is an alternative.

PREVENTION

Travelers should avoid eating raw or undercooked freshwater crab or crawfish.

CDC website: www.cdc.gov/parasites/paragonimus/

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GIARDIASIS

Katharine Benedict, Dawn Roellig

INFECTIOUS AGENT: *Giardia duodenalis*	
ENDEMICITY	Worldwide
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventure tourists Children Humanitarian aid workers Immigrants and refugees Long-term travelers and expatriates
PREVENTION METHODS	Follow safe food and water safety precautions Minimize fecal–oral exposures during sexual activity Practice good hand hygiene
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing

INFECTIOUS AGENT

Giardiasis is an illness caused by the anaerobic protozoan parasite *Giardia duodenalis* (formerly known as *G. lamblia* or *G. intestinalis*).

TRANSMISSION

Giardia is transmitted via the fecal–oral route. Its low infectious dose, protracted communicability, and moderate chlorine tolerance make *Giardia* ideally suited for transmission through drinking and recreational water. Transmission also occurs through contact with feces (e.g., when providing direct patient care or during sexual activity), eating contaminated food, or contact with fecally contaminated surfaces.

EPIDEMIOLOGY

Giardia is endemic worldwide, including in the United States. Based on GeoSentinel Global Surveillance Network data from 2000–2012, *Giardia*-related acute diarrhea was a top 10 diagnosis in ill US travelers returning from destinations

in Africa (North Africa and sub-Saharan Africa), the Americas (the Caribbean, Central America, and South America), Asia (South-Central Asia), Eastern Europe, and the Middle East. The risk for infection increases with duration of travel and travel within areas that have poor sanitation. Backpackers or campers who drink untreated water from lakes or rivers are also more likely to be infected. *Giardia* is commonly identified in routine screening of refugees and internationally adopted children, although many are asymptomatic.

CLINICAL PRESENTATION

Many infected people are asymptomatic; if symptoms develop, they typically develop 1–2 weeks after exposure and generally resolve within 2–4 weeks. Symptoms include abdominal cramps, anorexia, bloating, diarrhea (often with foul-smelling, greasy stools), flatulence, and nausea. Patients usually present with a history of gradual onset of 2–5 loose stools per day and increasing fatigue. Sometimes upper gastrointestinal symptoms are prominent. Weight loss can occur over time. Fever and vomiting are uncommon. Reactive arthritis, irritable bowel syndrome, and other chronic symptoms sometimes occur after infection with *Giardia* (see Sec. 11, Ch. 7, Persistent Diarrhea in Returned Travelers). In children, severe giardiasis can cause development delay, failure to thrive, malnutrition, and stunted growth.

DIAGNOSIS

Giardia cysts or trophozoites are not seen consistently in the stools of infected patients. Diagnostic sensitivity can be increased by examining ≤3 stool specimens over several days. New molecular enteric panel assays generally include *Giardia* as a target pathogen. Diagnostic techniques include microscopy with direct fluorescent antibody testing (considered the gold standard), microscopy with trichrome staining, enzyme immunoassay kits, rapid immunochromatographic cartridge assays, and molecular assays. Only molecular testing (e.g., DNA sequencing) can identify the genotypes and subtypes of *Giardia*. Retesting is recommended only if symptoms persist after treatment.

Health care professionals seeking laboratory support should consult their usual diagnostic laboratory with questions about appropriate testing. If testing beyond the capacity of the diagnostic laboratory is warranted, the diagnostic laboratory should reach out to public health officials (state or county as appropriate) for information and guidance on specimen submission, including submission to the Centers for Disease Control and Prevention (CDC), if appropriate.

TREATMENT

Effective treatments include metronidazole, tinidazole, and nitazoxanide. Alternative treatments include furozolidone, paromomycin, and quinacrine. Because a definitive diagnosis is difficult, empiric treatment can be used in patients with the appropriate history and typical symptoms.

PREVENTION

Travelers should follow safe water precautions, use appropriate sanitation, and practice good handwashing to avoid giardiasis. Travelers also should avoid drinking water and recreational water that could be contaminated. If the safety of drinking water is in doubt (e.g., during travel to a location with poor sanitation or lack of water treatment systems), travelers should follow recommended safe water precautions, including drinking commercially bottled water from an unopened factory-sealed container, or treating the water to make it safe for drinking. For more details, see Sec. 2, Ch. 8, Food & Water Precautions, and Sec. 2, Ch. 9, Water Disinfection.

Instruct travelers to avoid swallowing or drinking untreated water (even small amounts) from lakes, the ocean, ponds, rivers, springs, streams, or shallow wells. Travelers also should avoid swallowing water when swimming or recreating in hot tubs, interactive fountains, and swimming pools.

Travelers should wash hands frequently with soap and clean, running water for ≥20 seconds, rubbing hands together to make a lather, and making certain to lather backs of hands and between fingers and to scrub under nails. Travelers should especially wash hands before, during, and after preparing food; before eating; before and after caring for someone who is sick; after using the toilet, changing diapers, or cleaning a child who has used the toilet; and after touching an animal, animal waste, or animal environments.

In addition, travelers should prevent contact and contamination with feces during sex by using

a barrier during oral–anal sex, and washing hands immediately after handling a condom used during anal sex and after touching the anus or rectal area of sexual partner(s).

In the United States, giardiasis is a nationally notifiable disease. State health departments should report outbreaks of giardiasis affecting multiple people to the CDC. Clinicians should inform local, state, and federal health authorities about cases of giardiasis so that appropriate public health responses can be taken to help control the spread of this disease.

CDC websites: www.cdc.gov/parasites/giardia; www.cdc.gov/healthywater/surveillance/nndss.html

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HELMINTHS, SOIL-TRANSMITTED

Mary Kamb, Sharon Roy

INFECTIOUS AGENTS:
Ascaris lumbricoides (roundworm)
Ancylostoma duodenale and *Necator americanus* (hookworm)
Trichuris trichiura (whipworm)

ENDEMICITY	Worldwide
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	All travelers Immigrants and refugees from endemic countries
PREVENTION METHODS	Avoid contact with contaminated soil Follow safe food and water precautions Practice good hand hygiene Wear shoes
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; or for clinical consultation, contact CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENTS

Ascaris lumbricoides (*Ascaris* or roundworm), *Ancylostoma duodenale* (hookworm), *Necator americanus* (hookworm), and *Trichuris trichiura* (whipworm) are helminths (parasitic worms) that infect the intestine. Due to the role of contaminated soil in their transmission, this group of nematode worms are known as soil-transmitted helminths (STH). *Strongyloides stercoralis* (threadworm) is sometimes included in the STH (see Sec. 5, Part 3, Ch. 21, Strongyloidiasis).

TRANSMISSION

STH are transmitted through ingestion of the tiny, infectious eggs of *Ascaris*, whipworm, and some hookworm, and through skin transmission for hookworm. People of all ages can become infected. Adult female worms produce thousands of eggs daily that are passed in feces and, if conditions allow, deposited in soil. Once in soil, infective larvae of *Ascaris* and whipworms develop in the fertile eggs and, if ingested by a human host, hatch and develop into adult worms over several months. Hookworm eggs are not infective—the eggs hatch and release larvae that must mature in soil before they become infective. Hookworm infection usually occurs when larvae penetrate the skin of people walking barefoot on contaminated soil; *Ancylostoma duodenale* also can be transmitted when larvae are ingested. Occasionally, human infection with *Ascaris suum* (pig roundworm) can occur due to ingestion of infectious eggs shed in pig feces.

EPIDEMIOLOGY

Globally, ≈2 billion people are infected with ≥1 STH, which together account for most parasitic disease burden worldwide. STH have widespread global distribution and are endemic in countries with tropical or subtropical climates and where sanitation is poor, human feces are used as fertilizer ("night soil"), or water supplies are contaminated. Although all travelers to endemic countries have some risk for STH infection, risk increases for long-term travelers and expatriates going to countries with poor general sanitation. Travelers can minimize risk by taking preventive measures.

Historically, STH infections were common in people living in US states where warm, moist climate and lack of sanitation enabled transmission; current prevalence of infection in those areas is unknown. Most reported infections in the United States are among immigrant and refugee populations. Since the introduction of predeparture treatment, stool testing for STH is unnecessary for most refugees. Because *Ascaris*, whipworm, and hookworm do not multiply in hosts (as opposed to threadworm), reinfection occurs only as a result of additional exposure to the infective-stage larvae.

CLINICAL PRESENTATION

Most STH infections are asymptomatic, especially when few worms are present. With *Ascaris*, pulmonary symptoms (Löffler syndrome) associated with marked eosinophilia and fever occur in a few patients when larvae pass through the lungs. Heavy roundworm infection also can cause intestinal discomfort, impaired nutritional status, and obstruction. Hookworm infection can lead to anemia due to blood loss and chronic protein deficiency, particularly in children. Whipworm infection can cause chronic abdominal pain, blood loss, diarrhea, dysentery, and rectal prolapse. Travelers rarely develop these more severe manifestations, however, which generally are associated with high worm burdens in indigenous populations.

DIAGNOSIS

Diagnosis is through detection of characteristic eggs using standard microscopy to examine fresh stool specimens. Stool concentration methods (e.g., Kato-Katz, McMaster, or FLOTAC techniques) can improve diagnostic yield. Collecting and testing 3 stool specimens on 3 separate days also improves detection because of variable shedding.

In returning travelers, parasitic eggs might not appear in stool for several months after exposure or symptom onset, because after infection female worms do not produce eggs for ≥40 days for *Ascaris* and ≥70 days for whipworm or hookworm. Serology to detect STH antibodies is not available in the United States. PCR testing is more sensitive and specific than microscopy, but tests are generally still unavailable commercially.

Co-infection with ≥1 STH or other parasitic worms common in some endemic areas can make diagnosis challenging. Request assistance with parasitological diagnosis through DPDx (www.cdc.gov/DPDx). Clinical consultations are available through the Parasitic Diseases Branch of the Centers for Disease Control and Prevention (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov).

TREATMENT

Treatment of intestinal ascariasis consists of anthelminthic therapy, which effectively reduces morbidity but does not prevent reinfection. The drugs used most often to treat hookworm and *Ascaris* are albendazole and mebendazole, and for whipworm a combination of albendazole plus ivermectin. These drugs are safe for children but should be avoided or used with caution in pregnant or lactating people.

PREVENTION

No vaccines or drugs are available to prevent STH infection. Travelers can minimize infection risk by using preventive measures aimed at reducing ingestion or exposure to soil contaminated with human feces. Preventive measures include careful hand hygiene; washing, peeling, and cooking raw vegetables and fruit; and boiling or treating water (see Sec. 2, Ch. 8, Food & Water Precautions, and Sec. 2, Ch. 9, Water Disinfection). To avoid hookworm infection, travelers should avoid walking barefoot in areas where hookworm is common or where soil might be contaminated by human feces.

CDC website: www.cdc.gov/parasites/sth

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LEISHMANIASIS, CUTANEOUS

Mary Kamb, Sharon Roy, Paul Cantey

INFECTIOUS AGENTS: >20 *Leishmania* spp.	
ENDEMICITY	Eastern Hemisphere: Africa, Asia, southern Europe, Middle East Western Hemisphere: Central and South America
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Any traveler or migrant exposed to the vector
PREVENTION METHODS	Avoid insect bites
DIAGNOSTIC SUPPORT	A clinical laboratory certified in high complexity testing; or for tissue diagnostic techniques, contact CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENT

Leishmaniasis is caused by obligate intracellular protozoan parasites; >20 *Leishmania* species cause cutaneous leishmaniasis (CL). Leishmaniasis has different forms, including visceral leishmaniasis (the most severe form), but CL is the most common form. An aggressive form of CL, mucosal leishmaniasis (ML), affects mucosal areas.

TRANSMISSION

Leishmania parasites that cause CL are transmitted through the bites of infected female phlebotomine sand flies. CL also can occur after accidental occupational (laboratory) exposures to *Leishmania* parasites. Transmission risk is greatest from dusk to dawn because sand flies typically feed (bite) at night and during twilight hours. Although sand flies are less active during the hottest part of the day, they can bite if they are disturbed, for instance when people brush against tree trunks or other sites where sand flies are resting. Vector activity might easily be overlooked because sand flies are small and silent, and their bites can go unnoticed. Travelers with potentially increased risk for CL include adventure travelers, bird watchers, construction workers, ecotourists, military personnel, missionaries, Peace Corps volunteers, and people doing research or humanitarian work outdoors at night or twilight. Even short-term travelers in leishmaniasis-endemic areas have developed CL, however. Immigrants and refugees from endemic areas also might present with CL.

EPIDEMIOLOGY

As of 2017, CL was reported to be endemic in 87 countries on 6 continents, with an estimated annual prevalence of 4.13 million, including 700,000 new cases globally. The ecologic settings for leishmaniasis transmission range from rainforests to arid regions.

In the Eastern Hemisphere, CL is found in Africa, particularly the tropical region and North Africa; Asia, particularly central and southwest Asia; southern Europe, including southern France, Greece, Italy, Portugal, Spain, and the Mediterranean islands; and some countries of the Middle East. In the Western Hemisphere, CL is found in parts of Mexico, all countries of Central America, and most of South America. Endemic transmission in the United States has been identified in Texas, especially among people living in areas bordering northeastern Mexico, and in neighboring Oklahoma. CL is not found in Canada, Chile, or Uruguay.

GeoSentinel Surveillance from 1997–2017 indicated that among patients examined at specialized travel or tropical medicine clinics on 6 continents, including North America, and who had laboratory-confirmed diagnoses, common source countries for travel-associated CL were Bolivia; countries in the Amazon Basin, including Brazil, Colombia, Ecuador, and Peru; Costa Rica; El Salvador; and Israel. Among immigrants, common source countries were Afghanistan and Syria. Cases of CL in US service personnel have reflected military activities (e.g., in Afghanistan and Iraq). CL is usually more common in rural than urban areas but is found in some peri-urban and urban areas (e.g., in Kabul, Afghanistan).

CLINICAL PRESENTATION

CL can present with a broad variety of dermatologic manifestations ranging from small and localized skin lesions to large nodules or plaques covering multiple body surfaces; ≈10% of infections are asymptomatic. The clinical spectrum can mimic other skin conditions (e.g., leprosy, squamous cell cancer, fungal or other skin infections).

CL is characterized by skin lesions, which can be closed or open sores, that typically develop on exposed areas of the skin within several weeks or months after infection. In some people, however, the sores first appear months or years later, often in the context of trauma (e.g., skin wounds, surgery). The sores can change in appearance and size over time. Sores typically progress from small, erythematous papules or nodular plaques to open sores with a raised border and central crater (ulcer), which can be covered with crust or scales. Lesions usually are painless but can be painful if superinfected with bacteria. Satellite lesions, regional lymphadenopathy, and nodular lymphangitis can occur. Even without treatment, most sores eventually heal; they can last for months or years, however, and typically result in scarring.

Mucosal Leishmaniasis

Some *Leishmania* species in Central and South America are a potential concern because parasites might spread from the skin to the mucosal surfaces of the nose or mouth and cause sores in these areas. ML might not be apparent until years after the original skin sores appear to have healed. Although ML is uncommon, it has occurred in travelers and expatriates, including in people whose cases of CL were not treated or were treated inadequately. The initial clinical manifestations typically involve the nose, with bleeding, chronic stuffiness, and inflamed mucosa or sores; less often the mouth or larynx are involved, manifesting as a brassy cough or hoarseness.

In advanced cases, ulcerative destruction of the mouth, nose, larynx, and pharynx (e.g., perforation of the nasal septum, or laryngeal or tracheal damage) can occur. Thus, any patient with CL caused by a *Viannia* subgenus from the Western Hemisphere, regardless of symptoms, should undergo a careful examination of mucosal surfaces, including the vocal cords and oronasal pharynx, along with biopsy of any abnormal-appearing tissue, to avoid missing ML cases. Although most commonly associated with species of *Leishmania* found in the Western Hemisphere, ML has been documented on rare occasions with species of *Leishmania* found in various countries of the Eastern Hemisphere.

DIAGNOSIS

Consider CL in people with chronic, nonhealing skin lesions who have been in areas where leishmaniasis is found. Clinical signs and symptoms are not sufficiently specific to differentiate CL from other conditions. Obtain an explicit travel history, including, if possible, questioning fellow travelers about similar lesions. Obtain information about duration and progression of symptoms, whether the lesions are painful, prior treatment, and current medications (e.g., immunosuppressive agents); photographs are helpful to assess lesions over time. Conduct a careful physical examination including evaluation of skin, lymph nodes, and mucosal surfaces; referral to a specialist able to conduct an endoscopic laryngeal examination might be warranted if ML is suspected.

Laboratory confirmation of the diagnosis is achieved by detecting *Leishmania* parasites or DNA in infected tissue through light-microscopic examination of stained specimens, culture techniques, or molecular methods (e.g., PCR); conducting all 3 tests maximizes diagnostic yield. The Centers for Disease Control and Prevention (CDC) can assist in all aspects of the diagnostic evaluation. Because different *Leishmania* species have different management implications, species identification through molecular testing is important, particularly if >1 species is endemic to areas where the patient traveled.

Serologic testing generally is not useful for CL because the assays are insensitive and cannot distinguish between active and past infection. For consultative services, including collection and packaging of samples for molecular testing, contact CDC Parasitic Diseases Inquiries (404-718-4745; parasites@cdc.gov) or see www.cdc.gov/dpdx.

TREATMENT

The primary goal of treatment is to prevent morbidity. Individualize decisions about whether and how to treat CL, including whether to use a systemic (oral or parenteral) medication rather than a local or topical approach. Treat all cases of ML with systemic therapy. Clinicians can consult with CDC staff about the relative merits of various approaches to treat CL and ML (see the Diagnosis section for contact information). The response to a particular regimen can vary not only among *Leishmania* species but also for the same species in different geographic regions.

The oral agent miltefosine is approved by the US Food and Drug Administration (FDA) to treat CL caused by 3 Western Hemisphere species of the *Viannia* subgenus: *Leishmania* (*V.*) *braziliensis*, *L.* (*V.*) *guyanensis*, and *L.* (*V.*) *panamensis*, as well as for ML caused by *L.* (*V.*) *braziliensis*, in adults and adolescents ≥12 years old who weigh ≥30 kg and are not pregnant or breastfeeding during therapy or for 5 months after treatment. Various parenteral options, including liposomal amphotericin B, are commercially available, although not FDA-approved to treat CL or ML. The pentavalent antimonial compound sodium stibogluconate

(Pentostam) is no longer available through the CDC Drug Service.

PREVENTION

No vaccines or drugs to prevent infection are available. Travelers can reduce the risk for CL by using personal protective measures to avoid sand fly contact and sand fly bites (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods). Advise travelers to avoid outdoor activities, to the extent possible, especially from dusk to dawn when sand flies are the most active; wear protective clothing and apply insect repellent to exposed skin and under the edges of clothing (e.g., shirt sleeves, pant legs) according to the manufacturer's instructions; and sleep in air-conditioned or well-screened areas. Spraying sleeping quarters with insecticide might provide some protection, and fans or ventilators might inhibit the movement of sand flies, which are weak fliers.

Sand flies are small (≈2–3 mm, <1/8 inch) and can pass through the holes in ordinary mosquito nets. Although fine mesh nets are available, these can be uncomfortable in hot climates. The effectiveness of mosquito nets can be enhanced by treating with a pyrethroid-containing (i.e., permethrin) insecticide. The same treatment can be applied to bed sheets and clothing, curtains, and window screens.

CDC website: www.cdc.gov/parasites/leishmaniasis

5

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LEISHMANIASIS, VISCERAL

Rebecca Chancey, Sharon Roy, Paul Cantey

INFECTIOUS AGENTS: *Leishmania* spp.	
ENDEMICITY	Eastern Hemisphere: East Africa, southwest Asia, southern Europe, Middle East Western Hemisphere: Brazil, Latin America
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventure tourists Humanitarian aid workers Immigrants and refugees Long-term travelers and expatriates
PREVENTION METHODS	Avoid insect bites Avoid outdoor activities when sand flies are most active (especially from dusk to dawn)
DIAGNOSTIC SUPPORT	A clinical laboratory certified in high complexity testing; or for clinical consultation, CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENTS

Visceral leishmaniasis (VL) is caused by obligate intracellular protozoan parasites, primarily *Leishmania infantum* (considered synonymous with *L. chagasi*) and *L. donovani*. Leishmaniasis has several different forms. VL affects some of the internal organs of the body (e.g., bone marrow, liver, spleen).

TRANSMISSION

The parasites that cause VL are transmitted through the bite of infected female phlebotomine sand flies. Congenital transmission and parenteral transmission through blood transfusions and needle sharing have been reported.

EPIDEMIOLOGY

Leishmaniasis is a parasitic disease found in parts of the tropics, subtropics, and southern Europe. VL is usually more common in rural than urban areas, but it is found in some peri-urban areas (e.g., in northeastern Brazil). In the Eastern Hemisphere, VL is found in Africa, particularly East Africa; parts of Asia, particularly the Indian subcontinent and central and southwest Asia; southern Europe; and the Middle East. In the Western Hemisphere, most cases occur in Brazil; some cases occur in scattered foci elsewhere in Latin America. Overall, VL is found in focal areas of >70 countries; most (>90%) cases occur on the Indian subcontinent, in Bangladesh, India, and Nepal; countries in East Africa, including Ethiopia, Kenya, Somalia, South Sudan, and Sudan; and in Brazil. More information is available at https://apps.who.int/gho/data/node.main.NTDLEISHVNUM?lang=en.

The geographic distribution of VL cases evaluated in the United States and other countries reflects travel and immigration patterns. Although uncommon in most US travelers and expatriates, VL can occur in travelers returning from visits to endemic regions in European countries (e.g., France, Greece, Italy, Macedonia, and Spain) and among military personnel returning from the Middle East. Cases have been documented in short-term travelers to the Camino de Santiago in northern Spain and endemic areas of southern France, and in longer-term travelers (e.g., expatriates, deployed soldiers) to the Mediterranean region and Middle East.

CLINICAL PRESENTATION

Among symptomatic people, the incubation period typically ranges from weeks to months. Illness onset can be abrupt or gradual. Stereotypical clinical manifestations of VL include fever, hepatosplenomegaly (especially splenomegaly), night sweats, and weight loss; lymphadenopathy can occur. Laboratory findings characteristic of VL include pancytopenia (anemia, leukopenia, thrombocytopenia), high total protein, low albumin, and hypergammaglobulinemia. If untreated, severe (advanced) cases of VL typically are fatal. Latent infection can clinically manifest years to decades after exposure in people who become immunocompromised through HIV infection, biologic immunomodulatory therapy, or immunosuppressive therapy.

DIAGNOSIS

Consider VL in the differential diagnosis of people with a relevant travel history even in the distant past, and a persistent, unexplained febrile illness, especially if accompanied by other suggestive manifestations (e.g., pancytopenia or splenomegaly). Hemophagocytic lymphohistiocytosis (HLH) could be a complication and should prompt clinicians to consider VL in patients with the appropriate travel history.

Laboratory confirmation of the diagnosis is achieved by detecting *Leishmania* parasites or DNA in infected blood, bone marrow, liver, or lymph nodes through light-microscopic examination of stained specimens, molecular methods, or tissue culture techniques. Serologic testing can provide supportive evidence for the diagnosis.

The Centers for Disease Control and Prevention (CDC) can assist in all aspects of the diagnostic evaluation, including species identification. Information on specimen collection and diagnosis of leishmaniasis is available at www.cdc.gov/parasites/leishmaniasis/resources/pdf/cdc_diagnosis_guide_leishmaniasis_2016.pdf. For consultative services, contact CDC Parasitic Diseases Inquiries (404-718-4745; parasites@cdc.gov), or see www.cdc.gov/dpdx.

TREATMENT

Refer people with VL to an infectious disease or tropical medicine specialist who can help direct care and provide individualized treatment. CDC staff can discuss the relative merits of various approaches (see the Diagnosis section of this chapter for contact information). Risk for relapse and treatment failure is greater in patients with HIV, but also might occur rarely in immunocompetent patients.

Liposomal amphotericin B (AmBisome) is approved by the US Food and Drug Administration (FDA) to treat VL and is generally the drug of choice for US patients. The oral agent miltefosine is approved by the FDA to treat VL in patients infected with *L. donovani* who are ≥12 years old, who weigh ≥30 kg, and who are not pregnant or breastfeeding during therapy or for 5 months after treatment; the drug is available in the United States via www.profounda.com. Pentavalent antimonials (e.g., meglumine antimoniate, sodium stibogluconate [Pentostam]) are used in endemic areas, except for India, where developing resistance is a concern. Pentavalent antimonial drugs are currently not FDA approved and not available for use in the United States; Pentostam is no longer available through the CDC Drug Service.

PREVENTION

No vaccines or drugs to prevent infection are available. Preventive measures are aimed at reducing contact with sand flies and avoiding sand fly bites (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods, and Sec. 5, Part 3, Ch. 14, Cutaneous Leishmaniasis). Preventive measures include minimizing outdoor activities, to the extent possible, especially from dusk to dawn when sand flies generally are most active; wearing protective clothing; applying insect repellent to exposed skin; using bed nets treated with a pyrethroid-containing insecticide; and spraying dwellings with residual-action insecticides.

CDC website: www.cdc.gov/parasites/leishmaniasis

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MALARIA

Kathrine Tan, Francisca Abanyie

INFECTIOUS AGENT: *Plasmodium* spp.	
ENDEMICITY	Multiple countries in Africa, the Americas, and Asia
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Children Long-term travelers and expatriates Pregnant travelers Tourists, business travelers, and missionaries Travelers visiting friends and relatives in areas with malaria
PREVENTION METHODS	Avoid insect bites Use malaria chemoprophylaxis
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; state health department; or contact CDC's Malaria Hotline: ▪ 770-488-7788 (M–F 9 a.m.–5 p.m. Eastern) ▪ 770-488-7100 (after hours) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENT

Malaria in humans is caused by protozoan parasites of the genus *Plasmodium*, including *Plasmodium falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*. In addition, zoonotic forms have been documented as causes of human infections and some deaths, especially *P. knowlesi*, a parasite of Old World (Eastern Hemisphere) monkeys, in Southeast Asia.

TRANSMISSION

Plasmodium species are transmitted by the bite of an infective female *Anopheles* mosquito.

Occasionally, transmission occurs by blood transfusion, needle sharing, nosocomially, organ transplantation, or vertically from mother to fetus. Malaria transmission occurs in large areas of Africa, Latin America, and parts of the Caribbean, Eastern Europe, the South Pacific, and in Asia including South Asia, Southeast Asia, and the Middle East (Map 5-12, Map 5-13, and Map 5-14).

EPIDEMIOLOGY

Malaria is a major international public health problem. According to the World Health Organization (WHO) World Malaria Report 2019, >90 countries reported ≈228 million infections and ≈405,000 deaths in 2018. Travelers going to malaria-endemic countries are at risk of contracting the disease, and almost all the ≈2,000 cases of malaria that occur each year in the United States are imported.

The risk of acquiring malaria differs substantially from traveler to traveler and from region to region, even within a single country. This variability is a function of the intensity of transmission within the various regions and the itinerary, duration, season, and type of travel. Risk also varies by travelers' adherence to mosquito precautions and prophylaxis recommendations. In 2016, 2,078 cases of malaria (including 7 deaths) were diagnosed in the United States and its territories and were reported to the Centers for Disease Control and Prevention (CDC). Of cases for which country of acquisition was known, 85% were acquired in Africa, 9% in Asia, 5% in the Caribbean and the Americas, and 1% in Oceania or the Eastern Mediterranean. Of US residents with malaria who reported a reason for travel, 69% were visiting friends and relatives.

Information about malaria transmission in specific countries is derived from various sources, including WHO (see Sec. 2, Ch. 5, Yellow Fever Vaccine & Malaria Prevention Information, by Country). The information presented here was accurate at the time of publication; the risk for malaria can change rapidly and from year to year, however, because of changes in local weather conditions, mosquito vector density, and prevalence of infection. Updated information can be found on the CDC website at www.cdc.gov/malaria.

CLINICAL PRESENTATION

Malaria is characterized by fever and influenza-like symptoms, including chills, headache, myalgias, and malaise; symptoms can occur intermittently. In severe disease, acute kidney injury, acute respiratory distress syndrome, mental confusion, seizures, coma, and death can occur. Malaria symptoms can develop as early as 7 days after being bitten by an infectious mosquito in a malaria-endemic area and as late as several months or more after exposure. Suspected or confirmed malaria, especially *P. falciparum*, is a medical emergency requiring urgent intervention, because clinical deterioration can occur rapidly and unpredictably. See Box 5-10 for frequently asked clinical questions.

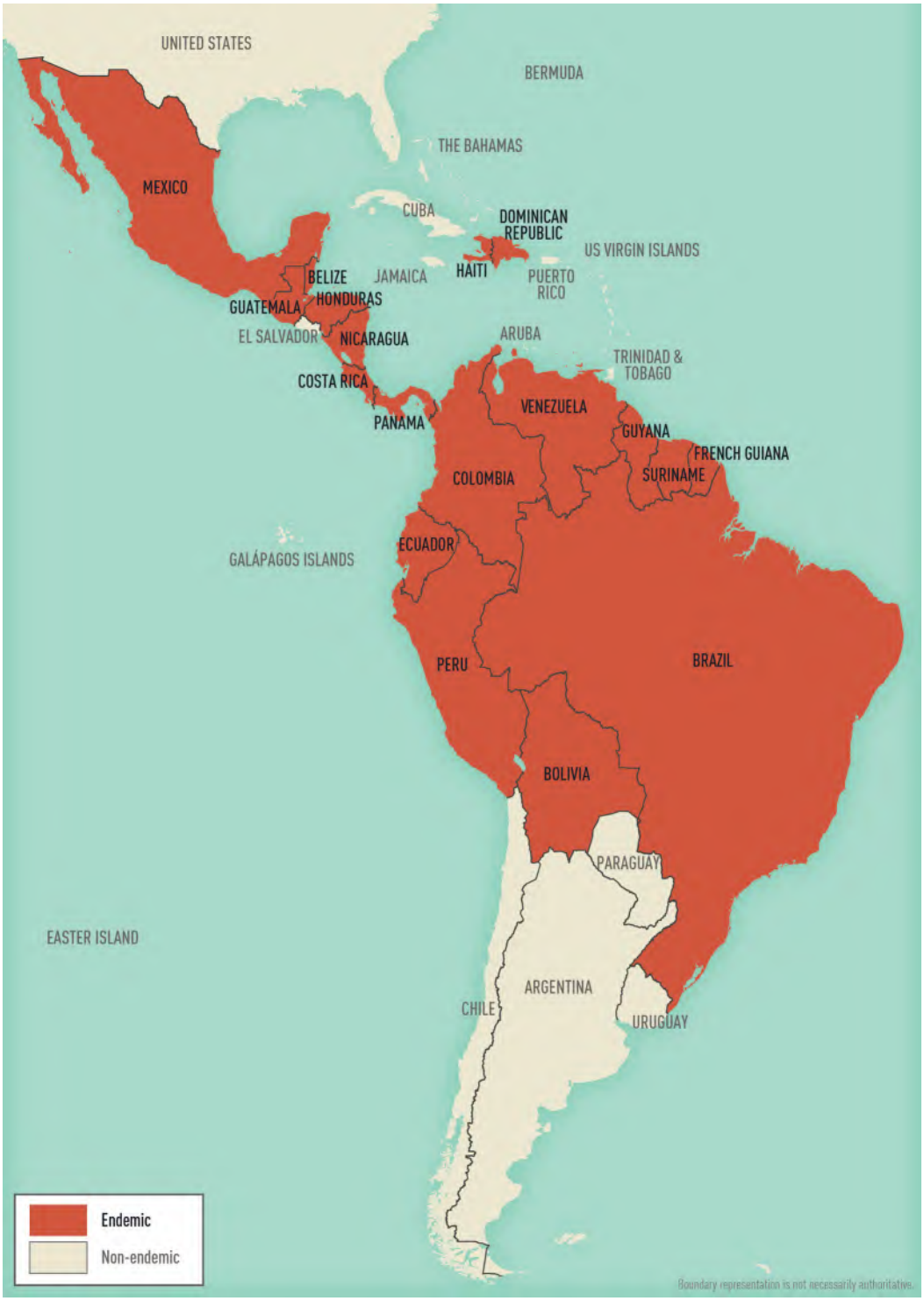
DIAGNOSIS

Travelers with symptoms of malaria should seek medical evaluation as soon as possible, even if still traveling. Consider malaria in any patient with a febrile illness who has recently returned from a malaria-endemic country. Diagnostic assistance is available from state public health laboratories or CDC (www.cdc.gov/dpdx/dxassistance.html). The CDC malaria laboratory can assist in speciating malaria by blood smear microscopy, or confirm species by PCR testing. The CDC laboratory also can assess malaria parasites for mutations that confer resistance to medications. Serologic testing, used in certain situations (e.g., case investigations), can also be done by CDC laboratories (www.cdc.gov/dpdx/dxassistance.html).

In the United States, malaria is a notifiable disease. Health care providers must report cases of malaria diagnosed via microscopy or PCR in the United States and its territories to local or state health departments. More information on reporting malaria can be found at www.cdc.gov/malaria/report.html.

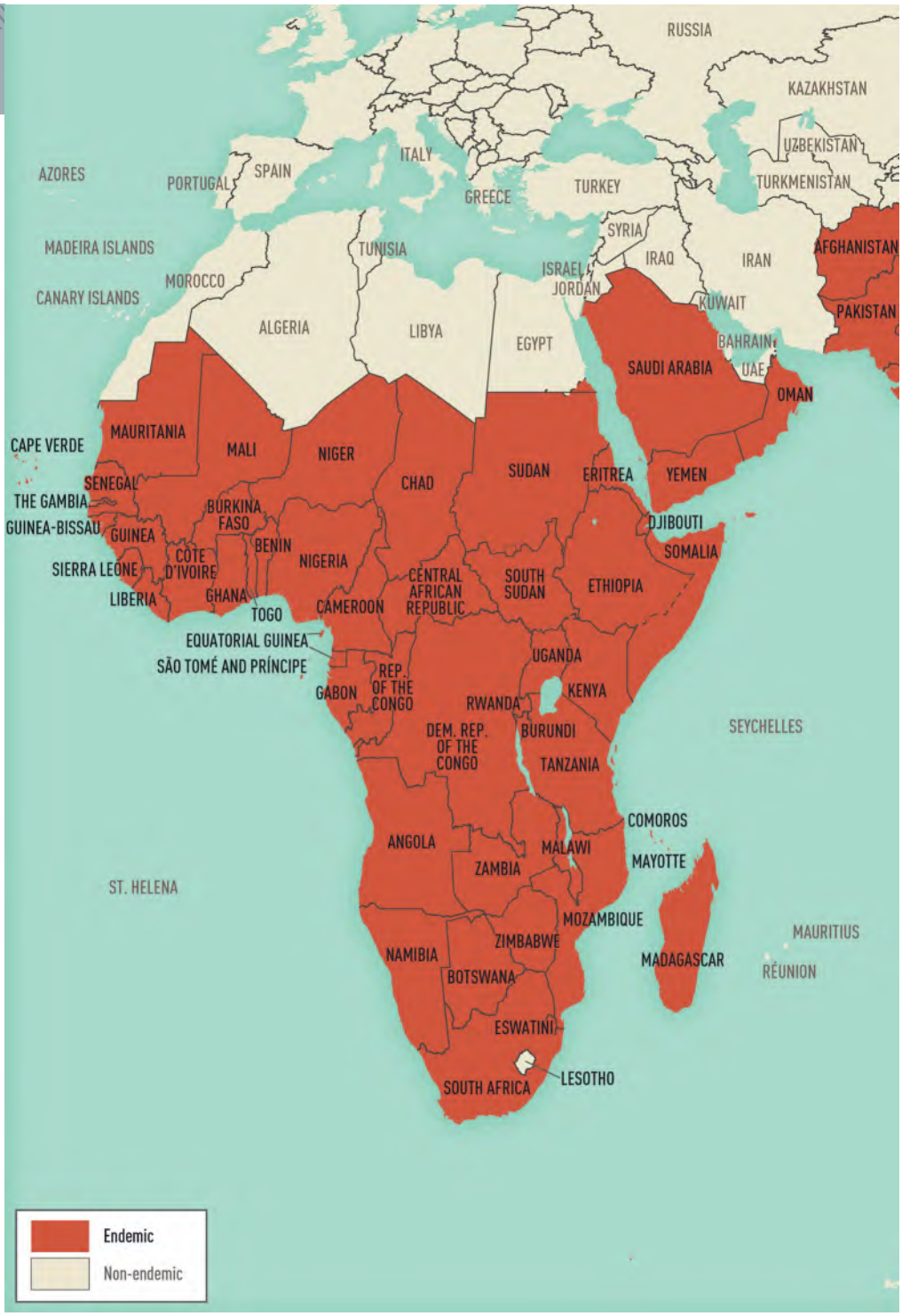
Blood Smear Microscopy

Blood smear microscopy remains the most important method for malaria diagnosis. Microscopy can provide immediate information about the presence of parasites, allow quantification of the density of the infection, and allow determination of the species of the malaria parasite—all of which are necessary for providing



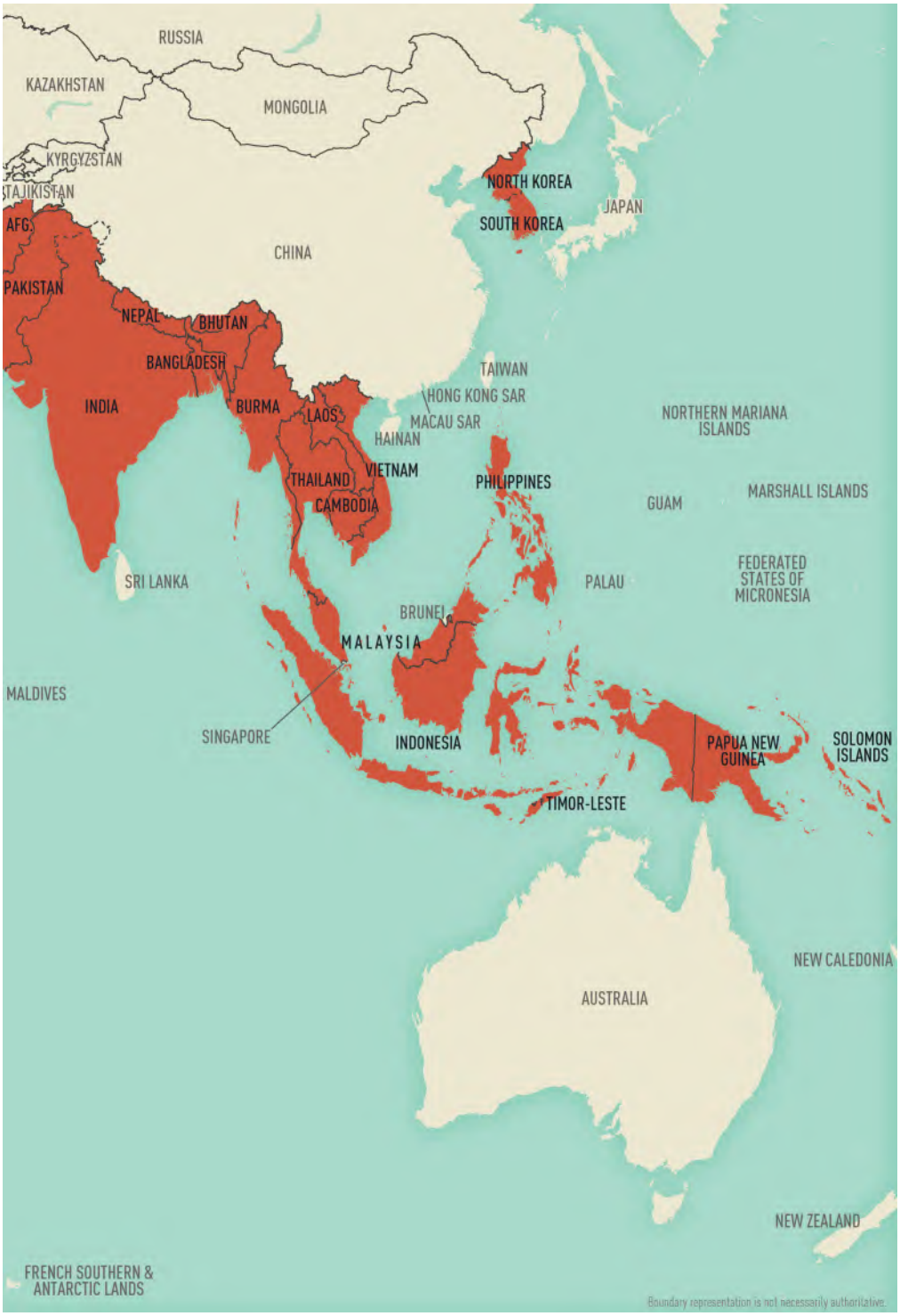
MAP 5-12 Malaria-endemic destinations in the Americas & the Caribbean

Malaria-endemic destinations are labeled using black font; destinations not endemic for malaria are labeled using gray font. Countries with areas endemic for malaria are shaded completely even if transmission occurs only in a small part of the country. For more specific within-country malaria transmission information, see Section 2, Yellow Fever Vaccine & Malaria Prevention Information, by Country.



MAP 5-13 Malaria-endemic destinations in Africa & the Middle East

Malaria-endemic destinations are labeled using black font; destinations not endemic for malaria are labeled using gray font. Countries with areas endemic for malaria are shaded completely even if transmission occurs only in a small part of the country. For more specific within-country malaria transmission information, see Section 2, Yellow Fever Vaccine & Malaria Prevention Information, by Country.



MAP 5-14 Malaria-endemic destinations in Asia & Oceania

Malaria-endemic destinations are labeled using black font; destinations not endemic for malaria are labeled using gray font. Countries with areas endemic for malaria are shaded completely even if transmission occurs only in a small part of the country. For more specific within-country malaria transmission information, see Section 2, Yellow Fever Vaccine & Malaria Prevention Information, by Country.

BOX 5-10 Frequently asked clinical questions

HOW DO I ADDRESS CONCERNS ABOUT SIDE EFFECTS FROM PROPHYLAXIS?

- Prophylaxis can be started earlier if the traveler has concerns about tolerating a particular medication. For example, mefloquine can be started 3–4 weeks in advance to allow potential adverse events to occur before travel. If unacceptable side effects develop, the clinician has time to change the medication before the traveler's departure.
- The drugs used for antimalarial prophylaxis are generally well tolerated. Side effects can occur, however. Minor side effects usually do not require stopping the drug. Clinicians should determine if symptoms are related to the medicine and make a medication change if needed.

WHAT SHOULD A TRAVELER DO IF THEY MISS A DOSE OF PROPHYLAXIS?

- Compared with drugs with short half-lives, which are taken daily, drugs with longer half-lives, which are taken weekly, offer the advantage of a wider margin of error if the traveler is late with a dose.
- For a weekly drug, prophylactic blood levels can remain adequate if the dose is only 1–2 days late. If this is the case, the traveler can take a dose as soon as possible, then resume weekly doses on the originally scheduled day. If the traveler is >2 days late, blood levels might not be adequate. The traveler should take a dose as soon as possible. The weekly doses should resume at this new day of the week (the next dose is 1 week later, then weekly thereafter).
- For a daily drug, if the traveler is 1–2 days late, protective blood levels are less likely to be maintained. The traveler should take a dose as soon as possible and resume the daily schedule at the new time of day.

WHAT HAPPENS IF TOO HIGH A DOSE OF PROPHYLAXIS IS TAKEN?

- Overdose of antimalarial drugs, particularly chloroquine, can be fatal. Medications should be stored in childproof containers out of reach of infants and children.

ISN'T MALARIA A TREATABLE DISEASE? WHY NOT CARRY A TREATMENT DOSE OF ANTIMALARIALS INSTEAD OF TAKING MALARIA PROPHYLAXIS?

- Malaria could be fatal even when treated, which is why prevention is always preferable to treating infections after they occur.

WHAT SHOULD BE DONE IF FEVER DEVELOPS WHILE TRAVELING IN A MALARIA-ENDEMIC AREA?

- Malaria and other potentially life-threatening infections acquired during travel could be fatal if treatment is delayed. Travelers should promptly seek medical help and continue to take malaria prophylaxis while in the malaria-endemic area.

WHAT SHOULD BE DONE IF A TRAVELER WHO TOOK MALARIA PROPHYLAXIS DEVELOPS FEVER AFTER RETURNING FROM THEIR TRIP?

- Malaria prophylaxis, while highly effective, is not 100% effective. Travelers should be advised to seek medical care immediately if fever develops, report their travel history, get tested for malaria, and get treated promptly if infection is confirmed.
- Malaria smear or a rapid diagnostic test must be performed, and results obtained immediately (within a few hours). These tests should not be sent out to reference laboratories that take days to weeks to return results. Empiric treatment with antimalarial drugs is not recommended because the malaria smear provides critical information for appropriate treatment. If a patient has an illness suggestive of severe malaria and a compatible travel history in an area where malaria transmission occurs, and malaria testing is not immediately available, start treatment as soon as possible, even before the diagnosis is established. CDC recommendations for malaria treatment can be found at www.cdc.gov/malaria/diagnosis_treatment/treatment.html.

the most appropriate treatment. Tests should be performed immediately when ordered by a health care provider, and microscopy results should be available as soon as possible, ≤24 hours of the patient's presentation. Assistance with speciation of malaria on smears is available from state health departments or CDC (www.cdc.gov/dpdx/dxassistance.html).

In resource-limited settings, and particularly in sub-Saharan Africa, overdiagnosis and the rate of false-positive microscopy for malaria can be high; warn travelers that a local diagnosis of malaria could be incorrect. In such cases, acutely ill travelers should seek the best available medical services and continue their prophylaxis regimen until they have a definitive diagnosis.

Rapid Diagnostic Testing

Rapid diagnostic tests (RDTs) for malaria detect antigens derived from malaria parasites. Malaria RDTs are immunochromatographic tests that most often use a dipstick or cassette format and provide results in 2–15 minutes. RDTs offer a useful alternative to microscopy in situations where reliable microscopic diagnosis is not immediately available. Although RDTs can detect malaria antigens within minutes, they have several limitations. RDTs cannot distinguish between all *Plasmodium* species that affect humans, they might be less sensitive than expert microscopy or PCR for diagnosis, they cannot quantify parasitemia, and an RDT-positive test result might persist for days or weeks after an infection has been treated and cleared. Thus, RDTs are not useful for assessing response to therapy. Furthermore, in some areas, mutations are increasingly being observed in malaria parasites, resulting in an absence of the malaria antigen usually detected by many RDTs, including the only RDT used in the United States. The absence of this parasite antigen in peripheral blood can lead to false-negative RDT test results.

Both positive and negative RDT results must always be confirmed by microscopy. Microscopy confirmation of the RDT result should occur as soon as possible, because the information on the presence, density, and parasite species is critical for optimal management of malaria. The US Food and Drug Administration (FDA) has approved an RDT (the BinaxNOW Malaria test) for hospital and commercial laboratory use; the test is not approved for use by clinicians or patients. Laboratories that do not provide in-house, on-the-spot microscopy services should maintain a stock of malaria RDTs so that they will be able to perform immediate malaria diagnostic testing when needed.

PCR Testing

PCR tests also are available to detect malaria parasites. These tests are more sensitive than routine microscopy, but results are not usually available as quickly as microscopy results, thus limiting the utility of PCR for acute diagnosis and initial clinical management. Use of PCR testing is encouraged to confirm the species of malaria parasite and detect mixed infections.

TREATMENT

Malaria can be treated effectively if treatment begins early in the disease; delaying therapy, however, can have serious or even fatal consequences. Specific treatment options depend on the species of malaria, the severity of infection, the likelihood of drug resistance (based on where the infection was acquired), the patient's age, and whether the patient is pregnant or breastfeeding.

Detailed CDC recommendations for malaria treatment can be found at www.cdc.gov/malaria/diagnosis_treatment/treatment.html. For assistance with the diagnosis or treatment of malaria, call the CDC Malaria Hotline (770-488-7788 or toll-free at 855-856-4713) from 9 a.m. to 5 p.m. Eastern Time. After hours, on weekends, or on holidays, call the CDC Emergency Operations Center at 770-488-7100 and ask the operator to contact the subject matter expert on call for the Malaria Branch. In addition, consult a clinician specializing in travel or tropical medicine or infectious diseases.

Travelers who decline to take prophylaxis, who choose a suboptimal drug regimen (e.g., chloroquine in an area with chloroquine-resistant *P. falciparum*), or who require a less-than-optimal drug regimen for medical reasons are at increased risk for acquiring malaria and then needing prompt treatment while abroad. Medications not used in the United States to treat malaria (e.g., halofantrine, sulfadoxine-pyrimethamine) are widely available abroad. CDC does not recommend halofantrine for treatment because of documented adverse cardiac events, including deaths. These adverse events have occurred in people with and without preexisting cardiac problems, and both in the presence and absence of other antimalarial drugs. Sulfadoxine-pyrimethamine is not recommended because of widespread drug-resistant *Plasmodium*.

Reliable Supply of Malaria Treatment

Some travelers who take effective prophylaxis but who will be in remote areas might decide, in consultation with their travel health provider, to also carry a reliable supply of a full course of an approved malaria treatment regimen. In the event a traveler carrying a reliable supply is diagnosed

with malaria, they will have immediate access to an approved treatment.

CDC recommends that the reliable supply be acquired in the United States, so clinicians can consider the traveler's other medical conditions or medications when selecting an antimalarial drug and to avoid the possibility of travelers obtaining counterfeit drugs in the local pharmacy or market, or depleting local resources. In rare instances when access to medical care is not available and the traveler develops a febrile illness consistent with malaria, the reliable supply medication can be self-administered presumptively. Advise travelers that self-treatment of a possible malarial infection is only a temporary measure, and that prompt medical evaluation is imperative.

Two malaria treatment regimens available in the United States can be prescribed as a reliable supply for self-treatment: atovaquone-proguanil and artemether-lumefantrine. To treat malaria, CDC recommends against using the same (or related) drug that has been taken for prophylaxis. For example, atovaquone-proguanil can be used as a reliable supply medication by travelers who are not taking atovaquone-proguanil for prophylaxis. See Table 5-26 for dosing recommendations.

PREVENTION

Malaria prevention consists of a combination of mosquito avoidance measures and chemoprophylaxis. Prevention measures must address all malaria species in the travel area and apply to both short-term and long-term travelers. Although highly efficacious, interventions are not 100% effective, so all febrile persons returning from malaria-endemic areas should be tested for malaria even if they took chemoprophylaxis.

Table 5-26 Reliable supply regimens for malaria treatment[1]

DRUG	ADULT DOSE	PEDIATRIC DOSE	COMMENTS
ATOVAQUONE-PROGUANIL[2] Adult tablets: ▪ Atovaquone 250 mg ▪ Proguanil 100 mg Pediatric tablets: ▪ Atovaquone 62.5 mg ▪ Proguanil 25 mg	4 adult tablets taken orally (as a single daily dose) for 3 consecutive days	Weight-based daily dose taken orally (as a single daily dose) for 3 consecutive days 5–8 kg: 2 pediatric tablets 9–10 kg: 3 pediatric tablets 11–20 kg: 1 adult tablet 21–30 kg: 2 adult tablets 31–40 kg: 3 adult tablets >41 kg: 4 adult tablets	Contraindicated in people with severe renal impairment (creatinine clearance <30 mL/min). Not recommended for people taking atovaquone-proguanil prophylaxis. Not recommended for children weighing <5 kg, or people who are pregnant or breastfeeding infants weighing <5 kg.
ARTEMETHER-LUMEFANTRINE[2] One tablet ▪ Artemether 20 mg ▪ Lumefantrine 120 mg	Weight-based treatment schedule for both adult and pediatric patients. Patients should take an initial dose, followed by a second dose 8 hours later, then 1 dose twice a day for the next 2 days (total of 6 oral doses over 3 days). 5 kg to <15 kg: 1 tablet per dose 15 kg to <25 kg: 2 tablets per dose 25 kg to <35 kg: 3 tablets per dose ≥35 kg: 4 tablets per dose		Not recommended for people taking mefloquine prophylaxis. Not recommended for children weighing <5 kg, or people breastfeeding infants weighing <5 kg.

[1]A reliable supply is a complete course of an approved malaria treatment regimen obtained in the United States before travel. A reliable supply is not counterfeit or substandard; will not interact adversely with the patient's other medicines, including malaria chemoprophylaxis; will not deplete local resources in the destination country.
[2]If used for presumptive self-treatment, patients should seek medical care as soon as possible.

Preventing malaria involves striking a balance between effectiveness and safety: ensuring that all people at risk for infection use the recommended prevention measures, and preventing rare occurrences of adverse effects. Conduct an individual risk assessment for every traveler by collecting a detailed travel itinerary, including countries, specific areas to be visited in those countries (e.g., cities, rural areas, both), types of accommodation, season, and style of travel. Modify the risk assessment depending on traveler characteristics (e.g., pregnancy, underlying health conditions) and malaria characteristics at the destination (e.g., intensity of transmission, local parasite resistance to drugs). Depending on the level of risk, it might be appropriate to recommend no specific interventions, mosquito avoidance measures only, or mosquito avoidance measures plus chemoprophylaxis.

Several factors increase a traveler's risk for malaria. Travel, even for short periods of time, to areas with intense malaria transmission can result in infection. Malaria transmission is not distributed homogeneously throughout a country, so review the exact itinerary to determine if travel will occur in highly endemic areas. In countries where malaria is seasonal, travel during peak transmission season also increases risk. Travelers going to rural areas or staying in accommodations without screens or air conditioning also will be at greater risk. The greatest risk for malaria is associated with first- and second-generation immigrants living in nonendemic countries who return to their countries of origin to visit friends and relatives (VFRs). VFR travelers might perceive themselves to be at no risk because they grew up in a malaria-endemic country and consider themselves immune to the disease. Tolerance acquired through continuous exposure to malaria is quickly lost, however; consider VFRs to have the same risk as other nonimmune travelers (see Sec. 9, Ch. 9, Visiting Friends & Relatives: VFR Travel). Also remind travelers that they could become infected even if they had malaria before, and they still need to take preventive measures.

Mosquito Avoidance Measures

Because of the nocturnal feeding habits of *Anopheles* mosquitoes, malaria transmission occurs primarily between dusk and dawn. Travelers can reduce contact with mosquitoes by remaining in enclosed air-conditioned rooms or well-screened areas, sleeping under mosquito nets (preferably insecticide-treated), using an effective insecticide spray or mosquito coils in living and sleeping areas during evening and nighttime hours, and wearing clothes that cover most of the body.

All travelers should use an effective mosquito repellent, such as those that contain DEET (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods). Repellents should be applied to exposed parts of the skin. If travelers are also wearing sunscreen, they should apply sunscreen first and insect repellent second. In addition to using a topical insect repellent, a permethrin-containing product can be applied to mosquito nets and clothing for additional protection against mosquitoes. Mosquito repellant–impregnated clothing also is available.

Chemoprophylaxis

CHOOSING A DRUG TO PREVENT MALARIA

All recommended primary prophylaxis regimens involve taking a medicine before, during, and after travel to an area with malaria. Beginning the drug before travel allows the antimalarial agent to be in the blood before the traveler is exposed to malaria parasites. In choosing a prophylaxis regimen before travel, the traveler and the travel health provider should consider several factors, including the presence of antimalarial drug resistance in the area of travel, length of travel, the patient's other medical conditions, allergy history, other medications prescribed or already being taken (to assess possible drug interactions), potential side effects, and the cost of the antimalarial. Long-term travelers, defined as people who travel for ≥6 months, have additional considerations (see Box 5-11). Table 5-27 lists some of the benefits and limitations of medicines used for malaria prophylaxis; additional information about choosing a malaria prophylaxis regimen can be found at www.cdc.gov/malaria/travelers/drugs.html.

Recommendations for drugs to prevent malaria by country of travel can be found in Sec. 2, Ch. 5, Yellow Fever Vaccine & Malaria Prevention Information, by Country. Recommended drugs for each country are listed in alphabetical order

BOX 5-11 Malaria prevention & prophylaxis considerations for the long-term traveler (travel >6 months)

CONSIDERATIONS

Malaria prevention measures are the same for both short- and long-term travelers.

Longer stays mean longer duration of exposure and increased risk of acquiring malaria.

Travelers' attention to mosquito avoidance can wane over time.

Travelers might not adhere to a lengthy course of malaria prophylaxis due to forgetfulness, fear of side effects, and the possible declining sense of risk and need over time.

Travelers might move between highly endemic or low endemic areas within a country or region.

Travelers might have a decreased sense of risk and concern about malaria after engaging in local conversations and lore, particularly regarding malaria immunity over time.

Travelers who become ill with malaria in countries with limited access and quality of health care might not receive appropriate or effective treatment.

ADDITIONAL ADVICE FOR LONG-TERM TRAVELERS

Travelers should not count on being able to obtain safe, reliable malaria prophylaxis medication abroad; strongly advise that before leaving the United States they purchase enough medication to last them for the entire duration of their travel to malaria-endemic areas.

Emphasize continued adherence to and safety of malaria prophylaxis drugs.

Develop a plan for seeking immediate care when ill with fever, including where to get promptly tested and treated for malaria.

Advise travelers to purchase travel insurance, including contingencies for medical evacuation.

Consider having a reliable supply of a treatment dose of antimalarial drugs available in case malaria is diagnosed while traveling.

and have comparable efficacy in that country. When >1 drug is recommended, Table 5-27 can help with the decision-making process. No antimalarial drug is 100% protective; therefore, travelers must combine prophylaxis with mosquito avoidance and personal protective measures (e.g., insect repellent, long sleeves, long pants, sleeping in a mosquito-free setting, using an insecticide-treated mosquito net).

MEDICATIONS USED FOR PROPHYLAXIS

ATOVAQUONE-PROGUANIL

Atovaquone-proguanil (Malarone) is a fixed combination of the drugs atovaquone and proguanil. Prophylaxis should begin 1–2 days before travel to malaria-endemic areas; the medication should then be taken daily, at the same time each day, while in the malaria-endemic areas, and daily for 7 days after leaving the endemic areas (see Table 5-28 for recommended dosages). Atovaquone-proguanil is well tolerated, and side effects are rare. The most common adverse effects reported in people using atovaquone-proguanil for prophylaxis or treatment are abdominal pain, nausea, vomiting, and headache.

Atovaquone-proguanil is not recommended for prophylaxis in children weighing <5 kg (11 lb), pregnant people, people breastfeeding infants <5 kg, or patients with severe renal impairment (creatinine clearance <30 mL/min). Proguanil can increase the effect of warfarin, so travelers might need international normalized ratio monitoring or adjustment of warfarin dosage. No data are available, however, regarding the clinical impact of taking atovaquone-proguanil and warfarin at the same time.

CHLOROQUINE & HYDROXYCHLOROQUINE

Chloroquine phosphate or hydroxychloroquine sulfate (Plaquenil) can be used to prevent malaria only in destinations where chloroquine-resistant *Plasmodium* spp. are not active (see Sec. 2, Ch. 5, Yellow Fever Vaccine & Malaria Prevention Information, by Country). Prophylaxis should begin 1–2 weeks before travel to malaria-endemic areas. Travelers should continue taking the drug once a week, on the same day of the week, during travel in malaria-endemic areas, and for 4 weeks after they leave endemic areas (see Table 5-28 for recommended dosages).

Table 5-27 Malaria chemoprophylaxis: prescribing considerations

DRUG	REASONS TO CONSIDER USING THIS DRUG	REASONS TO CONSIDER AVOIDING THIS DRUG
ATOVAQUONE-PROGUANIL	Good for last-minute travelers because the drug is started 1–2 days before travel. Some people prefer to take a daily medicine. Good choice for shorter trips because the traveler takes the medicine for only 7 days after leaving malaria-endemic area, rather than for 4 weeks. Well tolerated and side effects uncommon. Pediatric tablets are available and might be more convenient.	Cannot be used by people who are pregnant or who are breastfeeding a child that weighs <5 kg. Cannot be taken by people with severe renal impairment. Tends to be more expensive than some of the other options, especially for long trips. Some people (including children) would rather not take medicine every day.
CHLOROQUINE	Some people would rather take medicine weekly. Good choice for long trips because it is taken only weekly. Some people are already taking hydroxychloroquine chronically for rheumatologic conditions; in those instances, they might not have to take an additional medicine. Can be used in all trimesters of pregnancy.	Cannot be used in areas with chloroquine or mefloquine resistance. Can exacerbate psoriasis. Some people would rather not take a weekly medication. For short trips, some people would rather not take medication for another 4 weeks after leaving malaria-endemic areas. Not a good choice for last-minute travelers, because drug needs to be started 1–2 weeks before travel.
DOXYCYCLINE	Some people prefer to take a daily medicine. Good for last-minute travelers because the drug is started 1–2 days before travel. Tends to be the least expensive antimalarial drug. People already taking doxycycline chronically to prevent acne do not have to take an additional medicine. Doxycycline also can prevent other infections (e.g., rickettsial infections, leptospirosis); thus, might be preferred by people planning to camp, hike, and swim in fresh water where risk is high	Cannot be used by people who are pregnant or who are breastfeeding a child, or by children aged <8 years. Some people would rather not take medicine every day. For short trips, some people would rather not take medication for another 4 weeks after leaving malaria-endemic areas. People prone to getting vaginal yeast infections when taking antibiotics might prefer taking a different medicine. People might want to avoid the increased risk of sun sensitivity. Some people are concerned about the potential of getting an upset stomach from doxycycline.

(*continued*)

Table 5-27 Malaria chemoprophylaxis: prescribing considerations (continued)

DRUG	REASONS TO CONSIDER USING THIS DRUG	REASONS TO CONSIDER AVOIDING THIS DRUG
MEFLOQUINE	Some people would rather take medicine weekly. Good choice for long trips because it is taken only weekly. Can be used in all trimesters of pregnancy and during breastfeeding.	Cannot be used in areas with mefloquine-resistant *Plasmodium* spp. Cannot be used in patients with certain psychiatric conditions; some travelers without psychiatric conditions would prefer not taking a medication with known neuropsychiatric side effects. Cannot be used in patients with a seizure disorder. Not recommended for people with cardiac conduction abnormalities. Not a good choice for last-minute travelers because drug needs to be started ≥2 weeks before travel. Some people would rather not take a weekly medication. For short trips, some people would rather not take medication for another 4 weeks after leaving malaria-endemic areas.
PRIMAQUINE	One of the most effective drugs for prevention of *P. vivax*; thus, a good choice for travel to places with >90% *P. vivax*. Good choice for shorter trips because the traveler takes the medicine for 7 days after leaving a malaria-endemic area, rather than for 4 weeks. Good for last-minute travelers because the drug is started 1–2 days before travel. Some people prefer to take a daily medicine.	Cannot be used in patients with G6PD deficiency. Cannot be used in patients who have not been tested for G6PD deficiency. Costs and delays associated with getting a quantitative G6PD test might prohibit testing; however, the test only has to be done once. After a normal G6PD level is verified and documented, the test does not have to be repeated the next time primaquine or tafenoquine is considered. Cannot be used by people who are pregnant. Cannot be used by people who are breastfeeding unless the infant has also been tested for G6PD deficiency. Some people (including children) would rather not take medicine every day. Some people are concerned about the potential of getting an upset stomach from primaquine.
TAFENOQUINE	One of the most effective drugs for prevention of *P. vivax* malaria but also prevents *P. falciparum*. Good choice for shorter trips because the traveler takes the medicine once, 1 week after leaving malaria-endemic area, rather than for 4 weeks. Good for last-minute travelers because the drug is started 3 days before travel.	Cannot be used in people with G6PD deficiency. Cannot be used in patients who have not been tested for G6PD deficiency. Costs and delays associated with getting a quantitative G6PD test might prohibit testing; however, the test only has to be done once. After a normal G6PD level is verified and documented, the test does not have to be repeated the next time tafenoquine or primaquine is considered. Cannot be used by children. Cannot be used by people who are pregnant. Cannot be used by people who are breastfeeding unless the infant has also been tested for G6PD deficiency. Not recommended for patients with psychotic disorders.

Abbreviations: G6PD, glucose-6-phosphate-dehydrogenase

Reported side effects of chloroquine and hydroxychloroquine include blurred vision, dizziness, gastrointestinal disturbance, headache, insomnia, and pruritus, but generally, these effects do not require travelers to discontinue the drug. High doses of chloroquine (e.g., those used to treat rheumatoid arthritis) have been associated with retinopathy; this serious side effect appears to be extremely unlikely when chloroquine is used for routine weekly malaria prophylaxis. Chloroquine and related compounds reportedly can exacerbate psoriasis. People who experience uncomfortable side effects after taking chloroquine might tolerate the drug better by taking it with meals. As an alternative, a traveler experiencing side effects might better tolerate the related compound, hydroxychloroquine sulfate.

DOXYCYCLINE

Doxycycline prophylaxis should begin 1–2 days before travel to malaria-endemic areas. Doxycycline should then be taken once a day, at the same time each day, during travel in malaria-endemic areas and daily for 4 weeks after the traveler leaves endemic areas. Insufficient data exist on the antimalarial prophylactic efficacy of related compounds (e.g., minocycline, commonly prescribed for the treatment of acne). People on a long-term regimen of minocycline who need malaria prophylaxis should stop taking minocycline 1–2 days before travel and start doxycycline instead. Minocycline can be restarted after the full course of doxycycline is completed (see Table 5-28 for recommended dosages).

Doxycycline can cause photosensitivity, usually manifested as an exaggerated sunburn reaction. The risk for such a reaction can be minimized by avoiding prolonged, direct exposure to the sun and by using sunscreen (see Sec. 4, Ch. 1, Sun Exposure). In addition, doxycycline use is associated with an increased frequency of vaginal yeast infections.

Gastrointestinal side effects (nausea, vomiting) can be minimized by taking the drug with a meal or by specifically prescribing doxycycline monohydrate or the enteric-coated doxycycline hyclate, rather than the generic doxycycline hyclate, which is often less expensive. To reduce the risk for esophagitis, advise travelers to swallow the medicine with sufficient fluids and to avoid taking doxycycline shortly before going to bed.

Doxycycline is contraindicated in people with an allergy to tetracyclines, in pregnant people, and in infants and children aged <8 years. Vaccination with the oral typhoid vaccine Ty21a should be completed ≥24 hours before taking a dose of doxycycline.

MEFLOQUINE

Mefloquine prophylaxis should begin ≥2 weeks before travel to malaria-endemic areas. Travelers should continue taking the drug weekly, on the same day each week, during travel in malaria-endemic areas and for 4 weeks after leaving endemic areas (see Table 5-28 for recommended dosages).

At prophylactic doses, mefloquine has been associated with rare but serious adverse reactions (e.g., psychosis, seizures); these reactions are more frequent with the higher doses used for treatment. Other side effects reported in prophylaxis studies include abnormal dreams, anxiety disorder, depression, dizziness, gastrointestinal disturbance, headache, insomnia, and visual disturbances. Other neuropsychiatric disorders occasionally reported include aggressive behavior, agitation or restlessness, confusion, encephalopathy, forgetfulness, hallucinations, mood changes, panic attacks, paranoia, and sensory and motor neuropathies (e.g., ataxia, paresthesia, tremors). On occasion, psychiatric symptoms have been reported to continue long after mefloquine has been stopped. FDA also includes a boxed warning about rare reports of persistent dizziness after mefloquine use.

Mefloquine is contraindicated for travelers with a known hypersensitivity to the drug or related compounds (e.g., quinidine, quinine) and in people with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia and other major psychiatric disorders, or seizures. Mefloquine should be avoided in people with psychiatric disturbances or a history of depression.

A review of available data suggests that mefloquine can be used safely in people concurrently taking beta-blockers if they have no underlying arrhythmia. Mefloquine is not recommended for

Table 5-28 Malaria chemoprophylaxis: dosing information

DRUG	INDICATIONS	ADULT DOSE	PEDIATRIC DOSE	DOSING/CONTRAINDICATIONS/ PRECAUTIONS
ATOVAQUONE-PROGUANIL	Prophylaxis in all malaria-endemic areas	Adult tablets: • Atovaquone 250 mg • Proguanil 100 mg 1 adult tablet taken orally, 1×/day	Pediatric tablets: • Atovaquone 62.5 mg • Proguanil 25 mg Weight-based daily dosing schedule (taken orally, 1×/day) 5 kg to <8 kg: 1/2 pediatric tablet 8 kg to <10 kg: 3/4 pediatric tablet 10 kg to <20 kg: 1 pediatric tablet 20 kg to <30 kg: 2 pediatric tablets 30 kg to <40 kg: 3 pediatric tablets ≥40 kg: 1 adult tablet	Begin taking 1–2 days before travel to malaria-endemic areas. Take 1×/day, at the same time each day, while in malaria-endemic areas. Continue taking 1×/day for an additional 7 days after leaving endemic areas. Contraindicated in people with severe renal impairment (creatinine clearance <30 mL/min). Take with food or a milky drink. Not recommended for children weighing <5 kg, or people who are pregnant or breastfeeding infants weighing <5 kg. A pharmacist might need to prepare and dispense partial tablet doses in individual capsules, as described in the text.
CHLOROQUINE	Prophylaxis only in areas with chloroquine-sensitive malaria	300 mg base (500 mg salt) taken orally, once a week	5 mg/kg base (8.3 mg/kg salt), up to a maximum dose of 300 mg base (500 mg salt), taken orally, 1×/week	Begin taking 1–2 weeks before travel to malaria-endemic areas. Take 1×/week, on the same day each week, while in malaria-endemic areas. Continue taking 1×/week for another 4 weeks after leaving endemic areas. Can exacerbate psoriasis.
DOXYCYCLINE	Prophylaxis in all malaria-endemic areas	100 mg taken orally, 1×/day	≥8 years of age: 2.2 mg/kg, up to a maximum dose of 100 mg, taken orally, 1×/day	Begin taking 1–2 days before travel to malaria-endemic areas. Take 1×/day, at the same time each day, while in malaria-endemic areas. Continue taking 1×/day for another 4 weeks after leaving endemic areas. Contraindicated in children aged <8 years and in people who are pregnant.

Table 5-28 Malaria chemoprophylaxis: dosing information (continued)

DRUG	INDICATIONS	ADULT DOSE	PEDIATRIC DOSE	DOSING/CONTRAINDICATIONS/ PRECAUTIONS
HYDROXY-CHLOROQUINE	An alternative to chloroquine for prophylaxis only in areas with chloroquine-sensitive malaria	310 mg base (400 mg salt) taken orally, 1×/week	5 mg/kg base (6.5 mg/kg salt), up to a maximum dose of 310 mg base (400 mg salt), taken orally, 1×/week	Begin taking 1–2 weeks before travel to malaria-endemic areas. Take 1×/week, on the same day each week, while in malaria-endemic areas. Continue taking 1×/week for another 4 weeks after leaving endemic areas.
MEFLOQUINE	Prophylaxis in areas with mefloquine-sensitive malaria	228 mg base (250 mg salt) taken orally, 1×/week	Weight-based weekly dosing schedule (taken orally, 1×/week) ≤9 kg: 4.6 mg/kg base (5 mg/kg salt) >9–19 kg: 1/4 tablet >19–30 kg: 1/2 tablet >30–45 kg: 3/4 tablet >45 kg: 1 tablet	Begin taking ≥2 weeks before travel to malaria-endemic areas. Take 1×/week, on the same day each week, while in malaria-endemic areas. Continue taking 1×/week for another 4 weeks after leaving endemic areas. Contraindicated in people allergic to mefloquine or related compounds (quinidine, quinine) and in people with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, other major psychiatric disorders, or seizures. Use with caution in people with psychiatric disturbances or a previous history of depression. Not recommended for people with cardiac conduction abnormalities.

(*continued*)

Table 5-28 Malaria chemoprophylaxis: dosing information (continued)

DRUG	INDICATIONS	ADULT DOSE	PEDIATRIC DOSE	DOSING/CONTRAINDICATIONS/ PRECAUTIONS
PRIMAQUINE[1]	Prophylaxis for short-duration travel to areas with principally *P. vivax*. Terminal prophylaxis (presumptive antirelapse therapy) to decrease the risk for relapses of *P. vivax* and *P. ovale*.	30 mg base (52.6 mg salt) taken orally, 1×/day. Same dose used for both primary and terminal prophylaxis; duration of therapy differs.	0.5 mg/kg base (0.8 mg/kg salt), up to maximum dose of 30 mg base (52.6 mg salt), taken orally, 1×/day Same dose for used both primary and terminal prophylaxis; duration of therapy differs.	Begin taking 1–2 days before travel to malaria-endemic areas. Take 1×/day, at the same time each day, while in malaria-endemic areas. Continue taking 1×/day for an additional 7 days after leaving endemic areas. Terminal prophylaxis indicated for people with prolonged exposure to *P. ovale*, *P. vivax*, or both. Take daily for 14 days after departure from the malaria-endemic area. Contraindicated in people with G6PD deficiency. Also contraindicated during pregnancy and breastfeeding unless the breastfed infant has a documented normal G6PD level.
TAFENOQUINE[1]	Prophylaxis in all malaria-endemic areas	200 mg orally	Not indicated for use in children	Begin taking 3 days before travel to malaria-endemic areas. Take 1×/week, on the same day each week, while in malaria-endemic areas. Take 1 additional dose 1 week after leaving endemic areas. Contraindicated in people with G6PD deficiency. Also contraindicated during pregnancy and breastfeeding unless the breastfed infant has a documented normal G6PD level.

Abbreviations: G6PD, glucose-6-phosphate-dehydrogenase

[1]Before prescribing primaquine or tafenoquine to any patient, document a normal G6PD level using a quantitative test.

people with cardiac conduction abnormalities, however. Any traveler receiving a prescription for mefloquine must also receive a copy of the FDA medication guide, which can be found at www.accessdata.fda.gov/drugsatfda_docs/label/2008/019591s023lbl.pdf.

PRIMAQUINE

Primaquine can cause potentially life-threatening hemolysis in people with glucose-6-phosphate-dehydrogenase (G6PD) deficiency. Rule out G6PD deficiency with a quantitative laboratory test before prescribing primaquine to patients.

Primaquine phosphate has 2 distinct uses for malaria prevention in people with normal G6PD levels: primary prophylaxis in areas with primarily *P. vivax*, and terminal prophylaxis for travelers who have had prolonged exposure in malaria-endemic areas. Among people with normal G6PD levels taking primaquine, the most common adverse event is gastrointestinal upset; this occurs most commonly if the drug is taken on an empty stomach, and can be minimized or eliminated if it is taken with food.

PRIMARY PROPHYLAXIS

When taken for primary prophylaxis, primaquine should be taken 1–2 days before travel to malaria-endemic areas, daily (at the same time each day) while in the malaria-endemic area, and daily for 7 days after leaving the area (see Table 5-28 for recommended dosages).

TERMINAL PROPHYLAXIS

In addition to primary prophylaxis, terminal prophylaxis (also known as presumptive antirelapse therapy) generally is indicated for long-term travelers (e.g., military personnel, missionaries, Peace Corps volunteers) with prolonged exposure to *P. ovale* or *P. vivax* malaria. Terminal prophylaxis involves taking primaquine toward the end of the exposure period (or immediately thereafter) for the presumptive purpose of eliminating hypnozoites (dormant liver stages) of *P. ovale* or *P. vivax*, thereby preventing relapses or delayed-onset clinical presentations of malaria. Because most malaria-endemic areas of the world (except the Caribbean) have ≥1 species of relapsing malaria, travelers to these areas have some risk for acquiring either *P. ovale* or *P. vivax*, although the actual risk for an individual traveler is difficult to define.

When indicated, travelers should take primaquine for 14 days after leaving a malaria-endemic area, concurrently with their primary prophylaxis medication. If chloroquine, doxycycline, or mefloquine are used for primary prophylaxis, prescribe primaquine for travelers to take during the last 2 weeks of postexposure prophylaxis. When atovaquone-proguanil is used for primary prophylaxis, travelers can take primaquine during the final 7 days of atovaquone-proguanil, and then for an additional 7 days. If concurrent administration of primary and terminal prophylaxis is not feasible, instruct travelers to take primaquine after completing their primary prophylaxis medication. Primary prophylaxis with primaquine or with tafenoquine (see the following section) obviates the need for terminal prophylaxis.

TAFENOQUINE

Tafenoquine can cause potentially life-threatening hemolysis in people with G6PD deficiency. Rule out G6PD deficiency with a quantitative laboratory test before prescribing tafenoquine to patients.

PRIMARY PROPHYLAXIS

Tafenoquine (Arakoda 100 mg tablets) can be used to prevent malaria in adults (see Table 5-28 for recommended dosages). Travelers should take a daily loading dose of tafenoquine for 3 days before leaving for a malaria-endemic area; starting 7 days after the loading dose is complete, they should take a weekly maintenance dose while in the malaria-endemic area; then take a final dose in the week after leaving the malaria-endemic area. Doses should be taken on the same day each week.

Tafenoquine is contraindicated in pregnant people and during breastfeeding. Avoid prescribing tafenoquine for people with a history of psychotic disorder; rare psychiatric adverse events have been observed in people with a history of psychotic disorder using higher doses of tafenoquine. The most common adverse events reported with use of tafenoquine are dizziness, gastrointestinal

disturbances, headache, and clinically insignificant decreases in hemoglobin. Tafenoquine should be taken with food.

TERMINAL PROPHYLAXIS

As of 2020, CDC no longer recommends tafenoquine for terminal prophylaxis of *P. ovale* or *P. vivax* malaria.

PROPHYLAXIS FOR INFANTS, CHILDREN & ADOLESCENTS

All children traveling to malaria-endemic areas should use recommended prevention measures, which often include taking an antimalarial drug. In the United States, antimalarial drugs are not available in liquid formulation and can taste bitter. Calculate pediatric doses carefully according to the patient's body weight, but never exceed the adult dose. Pharmacists can pulverize tablets and prepare gelatin capsules for each measured dose. If a child is unable to swallow capsules or tablets, parents should prepare the child's medication dose by breaking open the gelatin capsule or crushing the pill and mixing the drug with a small amount of something sweet (e.g., condensed milk, chocolate syrup, chocolate spread) to ensure the entire dose is delivered to the child. Giving the dose on a full stomach can minimize stomach upset and vomiting.

Atovaquone-proguanil can be used as prophylaxis for infants and children weighing ≥5 kg (11 lb); prophylactic dosing for children weighing <11 kg (24 lb) constitutes off-label use in the United States. Chloroquine and mefloquine are options for infants and children of all ages and weights, depending on drug resistance at the destination. Doxycycline can be used for children aged ≥8 years. Primaquine can be used for children who are not G6PD-deficient and who are traveling to areas with principally *P. vivax*. Pediatric dosing regimens are included in Table 5-28.

PROPHYLAXIS DURING PREGNANCY

Malaria infection can be more severe in pregnant than in nonpregnant people. Malaria increases the risk for adverse pregnancy outcomes, including premature birth, spontaneous abortion, and stillbirth; thus, because no prophylaxis regimen is completely effective, advise people who are pregnant or likely to become pregnant to avoid travel to areas with malaria transmission if possible (see Sec. 7, Ch. 1, Pregnant Travelers). If travel to a malaria-endemic area cannot be deferred, an effective prophylaxis regimen and mosquito avoidance measures are essential.

Pregnant people traveling to areas where chloroquine-resistant *P. falciparum* has not been reported can take chloroquine prophylaxis. Chloroquine has not been found to have harmful effects on the fetus when used in the recommended doses for malaria prophylaxis; therefore, pregnancy is not a contraindication for malaria prophylaxis with chloroquine or hydroxychloroquine.

For travel to areas with known chloroquine-resistant *Plasmodium*, mefloquine is the only medication recommended for malaria prophylaxis during pregnancy. Studies of mefloquine use during pregnancy have found no indication of adverse effects on the fetus.

Atovaquone-proguanil is not recommended for use during pregnancy because of limited availability of data on its safety, and because other options are available. If other antimalarial drug options are not feasible, however, clinicians and patients should weigh the options, risks, and benefits of using atovaquone-proguanil to make the best decision for the patient. Doxycycline is contraindicated for malaria prophylaxis during pregnancy because of the risk for adverse effects seen with tetracycline, a related drug, on the fetus. These adverse effects include discoloration and dysplasia of the teeth and inhibition of bone growth. Neither primaquine nor tafenoquine should be used during pregnancy; both drugs can be passed transplacentally to a G6PD-deficient fetus and cause hemolytic anemia in utero.

People planning to become pregnant can use the same medications recommended for use during pregnancy (chloroquine or mefloquine, depending on the area of travel). CDC does not make recommendations about delaying pregnancy after the use of malaria prophylaxis medicines. If the traveler or their health care provider wishes to decrease the amount of antimalarial drug in the body before conception, however, Table 5-29 provides information on the half-lives of the recommended malaria prophylaxis

Table 5-29 Malaria chemoprophylaxis: half-lives

DRUG	HALF-LIFE
Atovaquone	2–3 days
Chloroquine	1–2 months
Doxycycline	15–24 hours
Hydroxychloroquine	1–2 months
Mefloquine	2–4 weeks
Primaquine	4–7 hours
Proguanil	12–25 hours
Tafenoquine	14–28 days

medicines. After 2 half-lives, ≈25% of the drug remains in the body, ≈6% remains after 4 half-lives, and ≈2% remains after 6 half-lives.

PROPHYLAXIS DURING BREASTFEEDING

The quantities of antimalarial drugs excreted in the breast milk of lactating people are insufficient to provide adequate protection to nursing infants. Therefore, infants who require prophylaxis should receive the recommended dosages of antimalarial drugs listed in Table 5-28. Because chloroquine and mefloquine can be prescribed safely to infants, infants also can be safely exposed to the small amounts excreted in breast milk. Data about the use of doxycycline in lactating people are very limited; most experts, however, consider the theoretical possibility of adverse events to the infant to be remote.

Although no information is available on the amount of primaquine or tafenoquine that enters human breast milk, test both the person breastfeeding and the infant for G6PD deficiency before initiating chemoprophylaxis with either one of these drugs. Because data are not yet available on the safety of atovaquone-proguanil prophylaxis in infants weighing <5 kg (11 lb), CDC does not recommend this drug to prevent malaria in people who are breastfeeding infants weighing <5 kg. Atovaquone-proguanil can, however, be used to treat people who are breastfeeding infants of any weight when the potential benefit outweighs the potential risk to the infant (e.g., treating a breastfeeding person who has acquired *P. falciparum* malaria in an area of multidrug-resistant strains and who cannot tolerate other treatment options).

TRAVEL TO AREAS WITH CHLOROQUINE-RESISTANT MALARIA

Chloroquine-resistant *P. falciparum* is found in all parts of the world except the Caribbean and countries west of the Panama Canal. Although chloroquine-resistant *P. falciparum* predominates in Africa, it is found in combination with chloroquine-sensitive *P. vivax* malaria in South America and Asia. Chloroquine-resistant *P. vivax* has been confirmed only in Papua New Guinea and Indonesia. For destinations with known chloroquine-resistant *Plasmodium* spp., in addition to mosquito avoidance measures, prescribe atovaquone-proguanil, doxycycline, mefloquine, or tafenoquine as prophylaxis.

TRAVEL TO AREAS WITH CHLOROQUINE-SENSITIVE MALARIA

Areas with chloroquine-sensitive *Plasmodium* spp. include many Latin American countries where malaria predominantly is caused by *P. vivax*. Chloroquine-sensitive *P. falciparum* is present in the Caribbean and Central American countries west of the Panama Canal. For destinations with known chloroquine-sensitive *Plasmodium* spp., in addition to mosquito avoidance measures, the many effective prophylaxis options include chloroquine, atovaquone-proguanil, doxycycline, mefloquine, and tafenoquine. In countries where *P. vivax* predominates, primaquine is also an option.

TRAVEL TO AREAS WITH MEFLOQUINE-RESISTANT MALARIA

Mefloquine-resistant *P. falciparum* has been confirmed in Southeast Asia on the borders of Thailand with Burma (Myanmar) and Cambodia, in the western provinces of Cambodia, in the eastern states of Burma on the border between Burma

Table 5-30 Malaria chemoprophylaxis: changing medications due to side effects

DRUG BEING STOPPED	DRUG BEING STARTED	DIRECTIONS FOR USE & COMMENTS
ATOVAQUONE-PROGUANIL	CHLOROQUINE	Not recommended
	DOXYCYCLINE	Begin taking doxycycline; continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for another 4 weeks after leaving the endemic area.
	MEFLOQUINE	Not recommended
	PRIMAQUINE	This switch would be unlikely because primaquine is recommended as primary prophylaxis for people with normal G6PD activity traveling to areas with mainly *Plasmodium vivax*. Should that be the case, begin taking primaquine. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for an additional 7 days after leaving the endemic area.
	TAFENOQUINE	Not recommended
CHLOROQUINE	ATOVAQUONE-PROGUANIL	If the switch occurs ≥3 weeks before departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day. Continue taking 1×/day for an additional 7 days after leaving the area. If the switch occurs <3 weeks before departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day, for 4 weeks after the switch. If the switch occurs after departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day, for 4 weeks after leaving the area.
	DOXYCYCLINE	Begin taking doxycycline. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for another 4 weeks after leaving the area.
	MEFLOQUINE	Not recommended
	PRIMAQUINE	Primaquine is recommended as primary prophylaxis for people with normal G6PD activity traveling to areas with mainly *P. vivax*. Should that be the case, begin taking primaquine. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for an additional 7 days after leaving the area.
	TAFENOQUINE	For people with normal G6PD activity, begin taking tafenoquine as soon as possible after taking the last dose of chloroquine in a malaria-endemic area. Start by taking tafenoquine 1×/day for 3 days, then 1×/week while still in the area. Take 1 final dose during the week after leaving the endemic area.

Table 5-30 Malaria chemoprophylaxis: changing medications due to side effects (continued)

DRUG BEING STOPPED	DRUG BEING STARTED	DIRECTIONS FOR USE & COMMENTS
DOXYCYCLINE	ATOVAQUONE-PROGUANIL	If the switch occurs ≥3 weeks before departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day. Continue taking 1×/day for an additional 7 days after leaving the endemic area. If the switch occurs <3 weeks before departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day, for 4 weeks after the switch. If the switch occurs following departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day, for 4 weeks after leaving the endemic area.
	CHLOROQUINE	Not recommended
	MEFLOQUINE	Not recommended
	PRIMAQUINE	This switch would be unlikely because primaquine is recommended as primary prophylaxis for people with normal G6PD activity traveling to areas with mainly *P. vivax*. Should that be the case, begin taking primaquine. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for an additional 7 days after leaving the endemic area.
	TAFENOQUINE	Not recommended
MEFLOQUINE	ATOVAQUONE-PROGUANIL	If the switch occurs ≥3 weeks before departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day. Continue taking 1×/day for an additional 7 days after leaving the endemic area. If the switch occurs <3 weeks before departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day, for 4 weeks after the switch. If the switch occurs after departure from a malaria-endemic area, take atovaquone-proguanil 1×/day, at the same time each day, for 4 weeks after leaving the endemic area.
	CHLOROQUINE	Not recommended
	DOXYCYCLINE	Begin taking doxycycline. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for another 4 weeks after leaving the endemic area.
	PRIMAQUINE	This switch would be unlikely because primaquine is recommended as primary prophylaxis for people with normal G6PD activity traveling to areas with mainly *P. vivax*. Should that be the case, begin taking primaquine. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for an additional 7 days after leaving the endemic area.

(*continued*)

Table 5-30 Malaria chemoprophylaxis: changing medications due to side effects (continued)

DRUG BEING STOPPED	DRUG BEING STARTED	DIRECTIONS FOR USE & COMMENTS
	TAFENOQUINE	For people with normal G6PD activity, begin taking tafenoquine as soon as possible after taking the last dose of mefloquine in a malaria-endemic area. Start by taking tafenoquine 1×/day for 3 days, then 1×/week while still in the endemic area. Take 1 final dose during the week after leaving the endemic area.
PRIMAQUINE	ATOVAQUONE-PROGUANIL	Begin taking atovaquone-proguanil. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for an additional 7 days after leaving the endemic area.
	CHLOROQUINE	Not recommended
	DOXYCYCLINE	Begin taking doxycycline. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for another 4 weeks after leaving the endemic area.
	MEFLOQUINE	Not recommended
	TAFENOQUINE	Not recommended
TAFENOQUINE	ATOVAQUONE-PROGUANIL	Begin taking atovaquone-proguanil. Continue taking 1x/day, at the same time each day, while in malaria-endemic areas. Take 1x/day for an additional 7 days after leaving the endemic area.
	CHLOROQUINE	Not recommended
	DOXYCYCLINE	Begin taking doxycycline. Continue taking 1×/day, at the same time each day, while in malaria-endemic areas. Take 1×/day for another 4 weeks after leaving the endemic area.
	MEFLOQUINE	Not recommended
	PRIMAQUINE	Not recommended

Abbreviations: G6PD, glucose-6-phosphate-dehydrogenase

and China, along the borders of Burma and Laos, and in southern Vietnam. For destinations with known mefloquine-resistant *Plasmodium* spp., in addition to mosquito avoidance measures, prophylaxis options are atovaquone-proguanil, doxycycline, and tafenoquine.

TRAVEL TO AREAS WITH LIMITED MALARIA TRANSMISSION

For destinations where malaria cases occur sporadically and risk for infection to travelers is considered low, CDC recommends that travelers use mosquito avoidance measures only, and no chemoprophylaxis (see Sec. 2, Ch. 5, Yellow Fever Vaccine & Malaria Prevention Information, by Country).

CHANGING MEDICATIONS AS A RESULT OF SIDE EFFECTS DURING PROPHYLAXIS

Medications recommended for malaria prophylaxis have different modes of action that affect the parasites at different stages of the life cycle. Thus, if the medication needs to be changed because of side effects before a full course has been completed, some special considerations exist (see Table 5-30).

Table 5-31 US Food and Drug Administration recommendations for deferring blood donation in people returning from malaria-endemic areas

GROUP	BLOOD DONATION DEFERRAL
Travelers to malaria-endemic areas	Not permitted to donate blood for 1 year after travel.
Former residents of malaria-endemic areas	Not permitted to donate blood for 3 years after departing. If they return to a malaria-endemic area within that 3-year period, they are deferred for an additional 3 years.
People diagnosed with malaria	Not permitted to donate blood for 3 years after treatment.

OBTAINING MEDICATIONS OVERSEAS

Medications recommended for malaria prophylaxis might be available at overseas destinations. Combinations of these medications and additional drugs that are not recommended might be commonly prescribed and used in other countries, however. Strongly discourage travelers from obtaining prophylaxis medications while abroad. The quality of these products is not known; products might be produced under substandard manufacturing practices, be counterfeit, contain contaminants, not be protective, or be dangerous. Additional information on medications obtained while traveling can be found in Sec. 6, Ch. 3, . . . *perspectives*: Avoiding Poorly Regulated Medicines & Medical Products During Travel, and on the FDA website, www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/BuyingMedicinefromOutsidetheUnitedStates/default.htm.

BLOOD DONATION AFTER TRAVEL TO MALARIA-ENDEMIC AREAS

People who have been in an area where malaria transmission occurs should defer donating blood after returning from the malaria-endemic area to prevent transmission of malaria through blood transfusion (see Table 5-31).

Risk assessments can differ between travel health providers and blood banks. A travel health provider advising a traveler going to a country with relatively low malaria transmission for a short period of time and engaging in low-risk behaviors might suggest the traveler use only mosquito bite precautions and no prophylaxis. Upon the traveler's return, however, a blood bank might still choose to defer blood donations from that traveler for 1 year because of travel to an area where transmission occurs.

CDC website: www.cdc.gov/malaria

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ONCHOCERCIASIS / RIVER BLINDNESS

Paul Cantey, Sharon Roy

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INFECTIOUS AGENT: *Onchocerca volvulus*	
ENDEMICITY	Sub-Saharan Africa Foci in South America and Yemen
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Immigrants and refugees Long-term travelers and expatriates Travelers visiting friends and relatives
PREVENTION METHODS	Avoid blackfly habitats Avoid insect bites
DIAGNOSTIC SUPPORT	Serologic testing: National Institutes of Health Laboratory of Parasitic Diseases (301-496-5398) or CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENT

Onchocerca volvulus, a filarial nematode, causes onchocerciasis, also known as river blindness.

TRANSMISSION

Transmission occurs through female blackfly (genus *Simulium*) bites. *Simulium* vectors typically bite during the day and breed near rapidly flowing rivers and streams.

EPIDEMIOLOGY

Onchocerciasis is endemic to much of sub-Saharan Africa. Small endemic foci also are present in the Arabian Peninsula (Yemen) and in the Americas (Brazil and Venezuela). Foci center around blackfly breeding sites, located near rapidly flowing water. Most transmission occurs in rural areas, but some transmission occurs in semi-urban and urban areas. Infections diagnosed in the United States are most commonly in immigrants, people visiting friends and relatives in endemic areas, long-term travelers to endemic areas, and expatriates. Although rare, infection can occur in short-term (< 1 month) travelers, particularly to areas with intense exposure. The incidence of infections identified outside endemic areas might be declining due to successful implementation of ivermectin mass drug administration in many endemic areas.

CLINICAL PRESENTATION

Clinical signs and symptoms include highly pruritic, papular dermatitis; subcutaneous nodules; lymphadenitis; and ocular lesions, which can progress to vision loss and blindness. Symptoms begin after patent infections are established, which can take 18 months. Symptoms in travelers are primarily dermatologic, typically acute erythematous papular rash and pruritus, sometimes just edema, occurring years after departure from endemic areas. Signs of chronic skin changes are rare in travelers. Subcutaneous nodules and chronic skin changes (e.g., depigmentation, lichenification, hyperpigmented flat-topped papules), are more common in endemic populations. Peripheral eosinophilia is often present in symptomatic travelers and migrants.

DIAGNOSIS

The standard method of diagnosis is examination of a skin snip biopsy to determine the presence of microfilariae. The diagnosis also can be made by identifying adult worms in histologic sections of excised nodules or characteristic eye lesions. Serologic testing is most useful for detecting infection when microfilariae are not identifiable. Determination of serum filarial antibody is available through the National Institutes of Health (301-496-5398) or the Centers for Disease Control and Prevention (CDC). Instructions on how to submit a serum specimen to CDC for testing can be found at www.cdc.gov/laboratory/specimen-submission/index.html. Assistance with parasitological diagnosis can be obtained through DPDx (www.cdc.gov/DPDx). General assistance with the diagnosis or treatment of onchocerciasis can be obtained by contacting CDC's Parasitic Diseases Branch (parasites@cdc.gov; 404-718-4745).

TREATMENT

Ivermectin is the drug of choice to relieve symptoms. Patients might require repeated annual or semiannual doses to control symptoms, because the drug kills the microfilariae but not the adult worms. Some experts recommend treating patients with 1 dose of ivermectin, then 6 weeks of doxycycline to kill *Wolbachia*, an endosymbiotic rickettsia-like bacterium that appears to be required for the survival of the *O. volvulus* adult worm and for embryogenesis. Individuals at risk for co-infection with *Loa loa* should have blood evaluated to assess for the presence of *Loa loa* microfilariae. If co-infected, enlist the aid of a tropical medicine expert for management due to the risk of *Loa loa*–related fatal post-treatment reactions associated with ivermectin.

Diethylcarbamazine is contraindicated as a treatment for onchocerciasis because it leads to microfilarial death and, in some cases, systemic reactions associated with an increased risk for causing blindness in some patients with eye disease.

PREVENTION

Travelers should avoid blackfly habitats (e.g., fast-flowing rivers and streams) and use protective measures against biting insects (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

CDC website: www.cdc.gov/parasites/onchocerciasis

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SARCOCYSTOSIS

Douglas Esposito

INFECTIOUS AGENT: *Sarcocystis* spp.	
ENDEMICITY	Intestinal disease endemic worldwide Muscular disease endemic in tropical and subtropical Southeast Asia; especially, Malaysia
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventurous eaters
PREVENTION METHODS	Follow safe food and water precautions Avoid undercooked or raw beef and pork
DIAGNOSTIC SUPPORT	CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)

INFECTIOUS AGENT

Intracellular coccidian protozoan parasites in the genus *Sarcocystis* cause sarcosystosis.

TRANSMISSION

Intestinal Sarcocystosis

Humans are the natural definitive host for *Sarcocystis heydorni*, *S. hominis*, and *S. suihominis*, acquired by eating undercooked sarcocyst-containing beef or pork.

Muscular Sarcocystosis

Dead-end intermediate host infection with *S. nesbitti* and possibly other species can occur in humans who ingest food, water, or soil contaminated with the feces from a reptilian sporocyst-shedding definitive host, likely snakes.

EPIDEMIOLOGY

Human intestinal sarcocystosis occurs worldwide, but the prevalence is poorly defined and can vary regionally. Recent outbreaks of symptomatic muscular sarcocystosis among tourists in Malaysia suggest that intermediate-host infection could be a public health concern. Most reported cases have been acquired in the tropics and subtropics, particularly in Southeast Asia; only a few cases have been reported among US travelers and military personnel.

CLINICAL PRESENTATION

Most people with intestinal sarcocystosis are asymptomatic or experience mild gastroenteritis, but severe illness has been described. Differences in symptoms and illness severity and duration might reflect the number and species of the sarcocysts ingested. The disease is thought to be self-limited in immunocompetent hosts.

Intermediate-host infection can range from asymptomatic to severe and debilitating disease. In people who develop symptoms, onset occurs in the first 2 weeks after infection, and symptoms typically resolve in weeks to months.

Some patients can remain symptomatic for years, however. The most common symptoms are arthralgia, cough, fatigue, fever, headache, and myalgias. Less frequent symptoms include diarrhea, nausea, vomiting; lymphadenopathy; rash; wheezing; and symptoms reflecting cardiac involvement (e.g., palpitations). Fever and muscle pain can be relapsing and occur in 2 distinct phases: early (beginning during the second week after infection) and late (beginning during the sixth week after infection). Early-phase disease might reflect a generalized vasculitis, and late-phase disease can coincide with the onset of a diffuse focal myositis.

DIAGNOSIS

Consider intestinal sarcocystosis in patients with gastroenteritis and a history of eating raw or undercooked meat. Oocysts or sporocysts in stool can be confirmed by light or fluorescence microscopy; PCR testing is not widely available, and no serologic assays have been validated for use in humans.

Include muscular sarcocystosis in the differential diagnosis of people presenting with myalgia, with or without fever, and a history of travel to a tropical or subtropical region, especially Malaysia. Diagnosis during the early phase of infection is difficult, however, because of the lack of specificity of symptoms and clinical and laboratory findings. In the absence of an alternative diagnosis, consider serial investigations for evidence of myositis and eosinophilia. In people with myositis, exclude trichinellosis as a possible cause. Confirmation of muscular sarcocystosis requires biopsy and histologic observation of sarcocysts in muscle. Diagnostic assistance is available through the Centers for Disease Control and Prevention (www.cdc.gov/dpdx; dpdx@cdc.gov).

TREATMENT

No proven treatments are available for sarcocystosis. Trimethoprim-sulfamethoxazole might act against schizonts in the early phase of muscular sarcocystosis, but data are scant. Glucocorticoids and nonsteroidal anti-inflammatory medications can improve the symptoms associated with myositis.

PREVENTION

Intestinal sarcocystosis can be prevented by thoroughly cooking or freezing meat, which kills the infective bradyzoites. Travelers can reduce the risk for muscular sarcocystosis by following standard food and water precautions (see Sec. 2, Ch. 8, Food & Water Precautions).

CDC website: www.cdc.gov/parasites/sarcocystosis/index.html

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