### **SCABIES**

### Diana Martin

INFECTIOUS ACENT Correctes cookiei una hominia		
INFECTIOUS AGENT: Sarcoptes scabiei var. hominis		
ENDEMICITY	Worldwide	
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Long-term travelers Refugees and asylum seekers Study-abroad students	
PREVENTION METHODS	Avoid contact with infected people	
DIAGNOSTIC SUPPORT	CDC's Parasitic Diseases Branch (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov)	

### **INFECTIOUS AGENT**

Scabies is caused by the human itch mite, *Sarcoptes* scapies var. hominis.

### **TRANSMISSION**

Direct transmission of conventional scabies occurs after prolonged skin-to-skin contact with a person infested with the mite. Indirect transmission of conventional scabies through contact with contaminated objects is rare. Animals are not a source of scabies.

Crusted scabies, by contrast, is more contagious than conventional scabies. Although <20 mites typically are found on a host with conventional scabies, a person with crusted scabies, formerly called Norwegian scabies, can harbor thousands of mites in just a small area of skin. The large number of mites present in crusted scabies greatly increases the chances that a person with crusted scabies will pass mites to others by both direct and indirect routes of transmission.

### **EPIDEMIOLOGY**

Scabies occurs worldwide and is transmitted most easily in settings where skin-to-skin contact is common. Scabies also can be associated with sexual activity due to prolonged skin-to-skin contact. Scabies accounted for 1.5% of dermatologic complaints and <0.5% of all complaints in returning travelers presenting at GeoSentinel clinics. Scabies is more common in travelers with longer

travel (>8 weeks) than in those who travel for shorter periods. Scabies is more common in tourists or volunteers than in business travelers or travelers visiting friends or family. Scabies is common in refugees and asylum seekers.

Crusted scabies most commonly occurs among debilitated, disabled, elderly, or immunosuppressed people, often in institutional settings. No reports of crusted scabies in travelers returning to the United States have been published.

### **CLINICAL PRESENTATION**

The most common signs and symptoms of scabies are intense itching (pruritus), especially at night, and a papular itchy rash. The itching and rash each can affect much of the body or be limited to common sites (e.g., armpits, elbows, wrists, webbing between the fingers, nipples, the beltline or waist, penis, buttocks). The rash also can include small vesicles and scales.

Burrows, caused by the female scabies mite tunneling just beneath the surface of the skin, are sometimes seen. Burrows appear as tiny raised and crooked (serpiginous) grayish-white or skin-colored lines on the skin surface. Because infected people often only have a total of 10–15 mites, these burrows can be difficult to find; they are often in the webbing between the fingers, in the skin folds on the wrist, elbow, or knee, and on the breast, penis, or shoulder blades. In infants and very young children (but not usually in older

children or adults), the head, face, neck, palms, and soles often are involved.

Symptoms occur 2-6 weeks after an initial infestation. For people who previously had scabies, symptoms appear much sooner, typically 1-4 days after exposure. Conventional scabies is characterized by intense itching, particularly at night, and by a papular or papulovesicular erythematous rash. Characteristic features of crusted scabies include widespread crusting and scales containing large numbers of mites; itching might be less prominent than in conventional scabies.

### DIAGNOSIS

Scabies is diagnosed clinically. Telltale signs include burrows, typically found in skin folds and intertriginous areas in a patient with itching, and the characteristic rash. Although finding mites, mite eggs, or scybala (mite feces) under the microscope can confirm the diagnosis of scabies, microscopic identification of mites is far less sensitive than clinical diagnosis. Clinically, crusted scabies often is mistaken for psoriasis, but can be accurately diagnosed by using skin scrapings because of the high number of mites in the sores. The Centers for Disease Control and Prevention (CDC) Parasitic Diseases Branch provides consultations to health care providers at parasites@cdc. gov or 404-718-4745.

### **TREATMENT**

Recommended treatments for conventional scabies include permethrin (5%) cream, which is approved by the US Food and Drug Administration (FDA), and ivermectin, which is not FDA-approved for scabies, but is indicated for scabies in the World Health Organization essential medicines list. Permethrin cream should be applied over the body from the neck down, left on for 8-12 hours or overnight, then washed off; patients will need a second application 1 week later. Treat household members and close contacts along with the index case. Oral ivermectin is reported to be safe and effective to treat conventional scabies at a single dose of 200 µg/kg, repeated after 1-2 weeks. Oral ivermectin should not be used in children weighing <15 kg or in pregnant people.

Treat crusted scabies more aggressively by using a combination of permethrin and ivermectin. Daily full-body application of permethrin for 7 days and ≤7 doses of oral ivermectin might be required. Details of the treatment regimen are found at the CDC's Parasitic Diseases Branch website (www.cdc.gov/parasites/scabies/health professionals/meds.html). No over-the-counter treatments are available for scabies.

### **PREVENTION**

Avoidance is the best way to prevent scabies; no chemoprophylaxis is known. Prolonged skin-toskin contact with people with conventional scabies and even brief skin-to-skin contact with people with crusted scabies are the primary routes of transmission. Travelers should avoid sharing or handling clothing or bed linens used by an infected person, especially if the person has crusted scabies.

**CDC website**: www.cdc.gov/parasites/scabies

### BIBLIOGRAPHY

Bouvresse S, Chosidow O. Scabies in healthcare settings. Curr Opin Infect Dis. 2010;23(2):111-8.

Chen LH, Wilson ME, Davis X, Loutan L, Schwartz E, Keystone J, et al.; GeoSentinel Surveillance Network. Illness in long-term travelers visiting GeoSentinel clinics. Emerg Infect Dis. 2009;15(11):1773-82.

Currie BJ, McCarthy JS. Permethrin and ivermectin for scabies. N Engl J Med. 2010;362(8):717-25.

Davis JS, McGloughlin S, Tong SY, Walton SF, Currie BJ. A novel clinical grading scale to guide the

management of crusted scabies. PLoS Negl Trop Dis. 2013;7(9):e2387.

Lederman ER, Weld LH, Elyazar IR, von Sonnenburg F, Loutan L, Schwartz E, et al. Dermatologic conditions of the ill returned traveler: an analysis from the GeoSentinel Surveillance Network. Int J Infect Dis. 2008;12(6):593.

Warkowski JA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Morb Mortal Wkly Rep. 2015;64(RR-03):1-137.

### **SCHISTOSOMIASIS**

Susan Montgomery, W. Evan Secor

INFECTIOUS AGENT: Schistosoma spp.	
ENDEMICITY	Mostly sub-Saharan Africa, Southeast Asia, China
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventure travelers and ecotourists Immigrants and refugees from endemic areas Travelers who bathe, swim, or wade in contaminated freshwater
PREVENTION METHODS	Avoid bathing, swimming, wading, or other contact with freshwater in disease-endemic countries
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 AGENT**

Schistosomiasis (also known as bilharzia and snail fever) is caused by helminth parasites of the genus *Schistosoma*. Other helminth infections are discussed in Sec. 5, Part 3, Ch. 13, Soil-Transmitted Helminths.

### **TRANSMISSION**

Waterborne transmission occurs when larval cercariae, found in contaminated bodies of freshwater, penetrate the skin. Bathing, swimming, or wading in contaminated freshwater can result in infection; people of all ages are at risk. Human schistosomiasis is not acquired by contact with brackish or saltwater (oceans or seas). Schistosomiasis distribution is very focal and determined by the presence of competent snail intermediate hosts, inadequate sanitation, and infected humans. The specific snail intermediate hosts can be difficult to identify, and laboratory testing is the only way to determine whether snails are infected with human schistosome species.

### **EPIDEMIOLOGY**

An estimated 85% of the world's cases of schistosomiasis are in Africa, where prevalence rates can exceed 50% in local populations. *Schistosoma* 

mansoni and S. haematobium are distributed throughout Africa. Only S. haematobium is found in areas of the Middle East, and only S. mansoni in parts of Brazil, Suriname, and Venezuela. In the Caribbean, risk is very low, but S. mansoni is found Guadeloupe, Martinique, and Saint Lucia, and previously in the Dominican Republic. S. japonicum is found in parts of China, in Indonesia, and in the Philippines. Although schistosomiasis had been eliminated in Europe for decades, transmission of S. haematobium was reported in Corsica in 2014, where cases were identified among travelers who had bathed in the Cavu River. Two other species can infect humans: S. mekongi, found in Cambodia and Laos, and S. intercalatum, found in parts of Central and West Africa. These 2 species are rarely reported causes of human infection.

Many but not all countries endemic for schistosomiasis have established control programs. Countries where development has led to widespread improvements in sanitation and water safety, especially where successful schistosomiasis control programs have been implemented, likely have eliminated this disease. No international guidelines currently exist for verification of elimination, however.

Travelers and expatriates potentially at increased risk for infection include adventure

travelers and ecotourists, missionaries, Peace Corps volunteers, and soldiers. Outbreaks of schistosomiasis have occurred among adventure travelers on river trips in Africa. The geographic distribution of schistosomiasis acquired by travelers reflects travel and immigration patterns.

Most travel-associated cases of schistosomiasis are acquired in sub-Saharan Africa. Some African transmission sites frequently visited by travelers include rivers and water sources in the Banfora region (Burkina Faso) and areas populated by the Dogon people (Mali), Lake Malawi, Lake Tanganyika, Lake Victoria, the Nile River, the Omo River (Ethiopia), and the Zambezi River. As travel to more remote areas increases, travelers should remember that most freshwater surface water sources in Africa are potentially contaminated and can be sources of infection. Travelers should view with skepticism any local claim that a body of freshwater is free from schistosomiasis.

### **CLINICAL PRESENTATION**

The incubation period is typically 14–84 days for acute schistosomiasis, and chronic asymptomatic infection can persist for years. Penetration of cercariae can cause a rash that develops within hours or up to a week after contaminated water exposure. Acute schistosomiasis (Katayama syndrome) is characterized by diarrhea, fever, headache, myalgia, and respiratory symptoms. Eosinophilia often is present; painful hepatomegaly or splenomegaly also can occur.

Clinical manifestations of chronic schistosomiasis are the result of host immune responses to schistosome eggs. Eggs secreted by adult worm pairs living in the bloodstream become lodged in the capillaries of organs and cause granulomatous reactions. *S. japonicum* and *S. mansoni* eggs most commonly lodge in the blood vessels of the liver or intestine and can cause blood in the stool, constipation, and diarrhea. Chronic inflammation can lead to bowel wall ulceration, hyperplasia, polyposis, and, with heavy infections, to periportal liver fibrosis and splenomegaly.

S. haematobium eggs typically lodge in the urinary tract and can cause dysuria and hematuria. Calcifications in the bladder might appear late in the disease. S. haematobium infection can cause genital symptoms and has been associated with

increased risk for bladder cancer. As with acute schistosomiasis, eosinophilia might be present during chronic infection with any species.

Rarely, central nervous system manifestations of schistosomiasis develop; these are thought to result from aberrant migration of adult worms or eggs depositing in the spinal cord or brain. Signs and symptoms are related to ectopic granulomas in the central nervous system and can present as transverse myelitis.

### **DIAGNOSIS**

Diagnosis is made by microscopic identification of parasite eggs in stool (S. japonicum or S. mansoni) or urine (S. haematobium). Serologic tests are useful to diagnose light infections, because egg shedding might not be consistent in travelers and in others who have not had schistosomiasis previously. Antibody tests do not distinguish between past and current infection but are useful for identifying infection in asymptomatic people who might have been exposed during travel and could benefit from treatment. 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 (www.cdc.gov/ DPDx; dpdx@cdc.gov), and from the Parasitic Diseases Hotline for Healthcare Providers (404-718-4745; parasites@cdc.gov).

### TREATMENT

Schistosomiasis is uncommon in the United States; clinicians unfamiliar with management of the condition should consult an infectious disease or tropical medicine specialist for assistance with diagnosis and treatment. Praziquantel is used to treat schistosomiasis. Praziquantel is most effective against adult forms of the parasite and requires a host immune response to the adult worm to be fully effective. Although a single course of treatment is usually curative, in lightly infected patients the immune response can be less robust and repeat treatment might be needed after 2–4 weeks to increase effectiveness.

### **PREVENTION**

No vaccine or drugs are available to prevent infection. Travelers can prevent schistosomiasis

by avoiding bathing, swimming, wading, or other contact with freshwater in disease-endemic countries. Untreated piped water coming directly from freshwater sources could contain cercariae; travelers should use fine-mesh filters, heat bathing water to 122°F (50°C) for 5 minutes, or allow water to stand for ≥24 hours before exposure to help prevent infection (see Sec. 2, Ch. 9, Water Disinfection).

Swimming in adequately chlorinated swimming pools is safe, even in disease-endemic countries, although confirming adequate levels of chlorination is difficult. Vigorous towel-drying after accidental exposure to water has been suggested as a method of removing cercariae before they can penetrate, but this should not generally be recommended as a preventive measure. Topical applications of insect repellents (e.g., DEET) can block penetrating cercariae, but the effect depends on the repellent formulation, could be short-lived, and does not provide adequate coverage to prevent infection reliably.

CDC website: www.cdc.gov/parasites/schistos omiasis

### **BIBLIOGRAPHY**

Berry A, Mone H, Iriart X, Mouahid G, Aboo O, Boissier J, et al. Schistosomiasis haematobium, Corsica, France. Emerg Infect Dis. 2014;20(9):1595-7.

Campa P, Develoux M, Belkadi G, Magne D, Lame C, Carayon MJ, et al. Chronic Schistosoma mekongi in a traveler—case report and review of the literature. J Travel Med. 2014;21(5):361-3.

Clerinx J, van Gompel A. Schistosomiasis in travellers and migrants. Travel Med Infect Dis. 2011;9(1):6-24.

Colley DG, Bustinduy A, Secor WE, King CH. Human schistosomiasis. Lancet. 2014;383(9936):2253-64.

Lingscheid T, Kurth F, Clerinx J, Marocco S, Trevino B, Schunk M, et al. Schistosomiasis in European travelers and migrants: analysis of 14 years TropNet surveillance data. Am J Trop Med Hyg. 2017;97(2):567-74.

Ross AG, Vickers D, Olds GR, Shah SM, McManus DP. Katayama syndrome. Lancet Infect Dis. 2007;7(3):218-24.

World Health Organization Expert Committee. Prevention and control of schistosomiasis and soil-transmitted helminthiasis. World Health Organ Tech Rep Ser. 2002;912:1-57.

### STRONGYLOIDIASIS

Susan Montgomery, Rebecca Chancey, Mary Kamb

INFECTIOUS AGENT: Strongyloides stercoralis	
ENDEMICITY	Worldwide in tropical and subtropical climates
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Immigrants and refugees Immunocompromised travelers Long-term travelers and expatriates Military personnel on long deployments to endemic areas
PREVENTION METHODS	Avoid contact with fecal matter or sewage Wear shoes when walking on soil
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 AGENT**

Strongyloidiasis is caused by an intestinal nematode, *Strongyloides stercoralis*.

### **TRANSMISSION**

Transmission occurs when filariform larva, found in contaminated soil, penetrate human skin. Person-to-person transmission is rare but has been documented. Autoinfection can occur, leading to persistent infection if untreated.

### **EPIDEMIOLOGY**

Strongyloidiasis is endemic to the tropics and subtropics; it has limited foci elsewhere, including Appalachia and the southeastern United States. Estimates of global prevalence range from 30–100 million. Most documented infections in the United States occur in immigrants, refugees, and military veterans living in *Strongyloides*-endemic areas for long periods. Risk for short-term travelers is low, but infections can occur.

### **CLINICAL PRESENTATION**

Most acute and chronic infections are asymptomatic or have minimal symptoms. In acute infections, a localized, pruritic, erythematous papular rash can develop at the site of skin penetration, followed by pulmonary symptoms (a Löffler-like pneumonitis; for more details, see Sec. 5, Part 3, Ch. 13, Soil-Transmitted Helminths), abdominal pain, diarrhea, and eosinophilia. In chronic infections, migrating larvae in the skin can occasionally cause larva currens, a serpiginous urticarial rash on the perineum or upper thighs.

Immunocompromised people, especially those receiving systemic corticosteroids, those infected with human T cell lymphotropic virus type 1, and those with hematologic malignancies or who have had hematopoietic stem cell or organ transplants are at risk for hyperinfection or disseminated disease, characterized by abdominal pain, diffuse pulmonary infiltrates, and septicemia or meningitis from enteric bacteria. Untreated hyperinfection and disseminated strongyloidiasis are associated with high mortality rates.

### **DIAGNOSIS**

Suspect strongyloidiasis in symptomatic patients who have a history of skin contact (i.e., bare feet) with soil in tropical or subtropical regions.

Laboratory diagnosis usually involves blood and stool testing. Although common in intestinal strongyloidiasis, peripheral blood eosinophilia is often absent in hyperinfection and disseminated strongyloidiasis.

Rhabditiform larvae can be visualized on microscopic examination of stool, either directly or by culture on agar plates. Repeated stool examinations or examination of duodenal contents might be necessary. Hyperinfection and disseminated strongyloidiasis are diagnosed by examining cerebrospinal fluid, sputum, stool, and other body fluids and tissues, which typically contain high numbers of filariform larva.

Serologic testing is available through commercial laboratories; diagnostic assistance is available from the Centers for Disease Control and Prevention (CDC)'s Division of Parasitic Diseases and Malaria DPDx laboratory (www.cdc.gov/DPDx; dpdx@cdc.gov), and the Parasitic Diseases Hotline for Healthcare Providers (404-718-4745; parasites@cdc.gov).

### **TREATMENT**

The treatment of choice for acute, chronic, and disseminated disease or hyperinfection is ivermectin. The alternative is albendazole, but it is associated with lower cure rates. Because of the potential for relapse, patients with hyperinfection, disseminated disease, or co-infection with human T cell lymphotropic virus 1 might need prolonged or repeated treatment.

### **PREVENTION**

No vaccines or drugs are available to prevent infection. To protect against *Strongyloides* infection, travelers should wear shoes when walking in areas where humans might have defecated. Perform serologic testing for patients at risk for *Strongyloides* infection who will be placed on corticosteroids or other immunosuppressive drug regimens, or who will undergo procedures that involve immunosuppression (e.g., transplantation). If indicated, treat these patients for strongyloidiasis before initiating immunosuppressive therapy. Consider empiric treatment in people deemed at risk of strongyloidiasis who require immediate immunosuppression.

**CDC website**: www.cdc.gov/parasites/strongyloi des

### **BIBLIOGRAPHY**

- Henriquez-Camacho C, Gotuzzo E, Echevarria J, White Jr AC, Terashima A, Samalvides F, et al. Ivermectin versus albendazole or thiabendazole for *Strongyloides stercoralis* infection. Cochrane Database Sys Rev. 2016(1):CD007745.
- Keiser PB, Nutman TB. Strongyloides stercoralis in the immunocompromised population. Clin Microbiol Rev. 2004;17(1):208–17.
- Krolewiecki A, Nutman TB. Strongyloidiasis: a neglected tropical disease. Infect Dis Clin North Am. 2019;33(1):135–51.
- Nutman TB. Human infection with Strongyloides stercoralis and other related Strongyloides species. Parasitology. 2017;144(3):263–73.
- Puthiyakunnon S, Boddu S, Li Y, Zhou X, Wang C, Li J, et al. Strongyloidiasis—an insight into its global prevalence and management. PLoS Negl Trop Dis. 2014;8(8):e3018.
- Requena-Mendez A, Buonfrate D, Gomez-Junyent J, Zammarchi L, Bisoffi A, Munoz J. Evidence-based guidelines for screening and management of strongyloidiasis in non-endemic countries. Am J Trop Med Hyg. 2017;97(3):645–52.
- Seybolt LM, Christiansen D, Barnett ED. Diagnostic evaluation of newly arrived asymptomatic refugees with eosinophilia. Clin Infect Dis. 2006;42(3):363–7.

## **TAENIASIS**

Susan Montgomery, Sharon Roy

INFECTIOUS AGENTS: Taenia spp.	
ENDEMICITY	Africa Latin America South and Southeast Asia
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventurous eaters Immigrants and refugees from endemic areas
PREVENTION METHODS	Follow safe food precautions Avoid raw or undercooked beef and pork
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**

*Taenia* spp., including *T. asiatica*, *T. saginata* (beef tapeworm), and *T. solium* (pork tapeworm), cause human taeniasis.

### **TRANSMISSION**

Transmission occurs through eating raw or undercooked contaminated beef (*T. saginata*) or pork (*T. asiatica, T. solium*).

### **EPIDEMIOLOGY**

Taeniasis prevalence is greatest in Africa, Latin America, and South and Southeast Asia. Taeniasis has been reported at lower rates in Eastern Europe and the Iberian Peninsula (Portugal and Spain). Tapeworm infections are unusual in travelers.

### **CLINICAL PRESENTATION**

The incubation period is 8–16 weeks for *T. asiatica*, 10–14 weeks for *T. saginata*, and 8–10 weeks for *T. solium*. Symptoms can include abdominal discomfort, anorexia, diarrhea, insomnia, nausea, nervousness, perianal pruritus, weakness, and weight loss. Symptoms are less likely for *T. solium* infection than for *T. saginata* infection.

### **DIAGNOSIS**

Diagnosis is made by detecting eggs, proglottids (segments), or tapeworm antigens in the feces or on anal swabs. Differential diagnosis of *Taenia* spp. is based on morphology of the scolex and gravid proglottids. Clinicians can obtain diagnostic assistance and confirmatory testing from the Centers for Disease Control and Prevention's Division of Parasitic Diseases and Malaria DPDx laboratory (www.cdc.gov/DPDx; dpdx@cdc.gov) and from the Parasitic Diseases Hotline for Healthcare Providers (404-718-4745; parasites@cdc.gov).

## BIBLIOGRAPHY

Cantey PT, Coyle CM, Sorvillo FJ, Wilkins PP, Starr MC, Nash TE. Neglected parasitic infections in the United States: cysticercosis. Am J Trop Med Hyg. 2014;90(5):805–9.

Eom KS, Rim HJ, Jeon HK. *Taenia asiatica*: historical overview of taeniasis and cysticercosis with molecular characterization. Adv Parasitol. 2020;108:133–73.

Wittner M, White ACJ, Tanowitz HB. Taenia and other tapeworm infections. In: Guerrant RL, Walker DH, Weller PF,

### **TREATMENT**

Praziquantel is the drug of choice for taeniasis, except for symptomatic neurocysticercosis (see Sec. 5, Part 3, Ch. 6, Cysticercosis). Niclosamide is an alternative but is not as widely available.

### **PREVENTION**

Travelers should practice safe food precautions and especially avoid eating raw or undercooked meat.

**CDC website**: www.cdc.gov/parasites/taeniasis

editors. Tropical infectious diseases: principles, pathogens and practice, 3rd edition. Philadelphia: Saunders Elsevier; 2011. pp. 839–47.

Zammarchi L, Bonati M, Strohmeyer M, Albonico M, Requena-Mendez A, Bisoffi Z, et al. Screening, diagnosis and management of human cysticercosis and *Taenia solium* taeniasis: technical recommendations by the COHEMI project study group. Trop Med Int Health. 2017;22(7):881–94.

## **TOXOPLASMOSIS**

Anne Straily, Susan Montgomery

INFECTIOUS AGENT: Toxoplasma gondii		
ENDEMICITY	Worldwide	
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	All travelers Risk for congenital transmission when primary infection occurs during pregnancy	
PREVENTION METHODS	Follow safe food and water precautions Pregnant people should avoid contact with cat feces	
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; or contact Sutter Health Palo Alto Medical Foundation Toxoplasma Serology Laboratory (www.pamf.org/serology)	

### **INFECTIOUS AGENT**

*Toxoplasma gondii*, an intracellular coccidian protozoan parasite, causes toxoplasmosis.

### **TRANSMISSION**

*T. gondii* transmission occurs through ingestion of food, soil, or water contaminated with cat feces; ingestion of undercooked meat or shellfish; congenital transmission from a person infected during or shortly before pregnancy; and contaminated blood transfusions or organ transplantation.

### **EPIDEMIOLOGY**

*T. gondii* is endemic throughout most of the world. Risk for infection is greater in developing and tropical countries, especially when people eat undercooked meat or shellfish, drink untreated water, or have extensive soil exposure. Congenital transmission also can occur if a person is infected shortly before becoming pregnant or during pregnancy.

### **CLINICAL PRESENTATION**

Incubation period is 5–23 days. Symptoms can include influenza-like symptoms or a mononucleosis syndrome with prolonged fever, elevated liver enzymes, lymphadenopathy, lymphocytosis, and weakness. Rarely, chorioretinitis or disseminated disease can occur in immunocompetent people. In severely immunocompromised people, severe and even fatal encephalitis, pneumonitis, and other systemic illnesses can occur, most often from reactivation of a previous infection. Infants with congenital toxoplasmosis often are asymptomatic, but eye disease, neurologic disease, or other systemic symptoms can occur, and cognitive deficits, learning disabilities, or visual impairments could develop later in life.

### **DIAGNOSIS**

Serologic tests for *T. gondii* antibodies are available at commercial diagnostic laboratories; because of the inherent difficulty in diagnosing acute

### **BIBLIOGRAPHY**

Anand R, Jones CW, Ricks JH, Sofarelli TA, Hale DC. Acute primary toxoplasmosis in travelers returning from endemic countries. J Travel Med. 2012;19(1):57–60.

toxoplasmosis, however, physicians are advised to seek confirmatory testing through the reference laboratory at Sutter Health Palo Alto Medical Foundation Toxoplasma Serology Laboratory (www.pamf.org/serology). Eye disease is diagnosed by ocular examination. Diagnosis of toxoplasmic encephalitis in immunocompromised people, most often seen in people with AIDS who are not receiving appropriate prophylaxis, can be based on typical clinical course and identification of ≥1 mass lesion by CT or MRI. Biopsy might be needed to make a definitive diagnosis.

### **TREATMENT**

Treatment is reserved for acutely infected immunocompromised or pregnant people and people with severe disease. The recommended treatment regimen includes pyrimethamine, sulfadiazine, and leucovorin (folinic acid). Alternative treatment regimens include pyrimethamine with atovaquone, azithromycin, or clindamycin, but these have not been studied extensively. For the acutely infected pregnant person, recommended treatment depends on the timing of infection during gestation; seek consultation with an infectious disease specialist before initiating therapy in these patients.

### **PREVENTION**

Travelers should adhere to safe food and water precautions (see Sec. 2, Ch. 8, Food & Water Precautions). In addition, travelers should avoid direct contact with sand or soil that could be contaminated with cat feces; if caring for a cat, change the litter box daily. Immunocompromised or pregnant people should avoid changing cat litter, if possible, and should not adopt or handle stray cats. Travelers should wash hands with soap and water after gardening, after contact with sand or soil, and after changing cat litter.

**CDC website**: www.cdc.gov/parasites/toxopl asmosis

Maldonado YA, Read JS; AAP Committee on Infectious Diseases. Diagnosis, treatment, and prevention of congenital toxoplasmosis in the United States. Pediatrics. 2017;139(2):e20163860. Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet. 2004;363(9425):1965–76.

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America; 2021. Available from: https://clinicalinfo.hiv.gov/sites/default/files/gui delines/documents/Adult\_OI.pdf

Sepulveda-Arias JC, Gomez-Marin JE, Bobic B, Naranjo-Galvis CA, Djurkovic-Djakovic O. Toxoplasmosis as a travel risk. Travel Med Infect Dis. 2014;12(6 Pt A):592–601.

## TRYPANOSOMIASIS, AFRICAN

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INFECTIOUS AGENTS: Trypanosoma brucei rhodesiense and T. brucei gambiense		
ENDEMICITY	Sub-Saharan Africa	
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventure tourists Humanitarian aid workers Immigrants and refugees Long-term travelers and expatriates Travelers visiting friends and relatives	
PREVENTION METHODS	Avoid insect bites	
DIAGNOSTIC SUPPORT	Contact CDC's Parasitic Diseases Branch for assistance with serologic testing for <i>T. b. gambiense</i> (www.cdc.gov/parasites; 404-718-4745; parasites@cdc.gov) Parasitological diagnosis: DPDx (www.cdc.gov/DPDx)	

### **INFECTIOUS AGENTS**

Trypanosomiasis is caused by 2 subspecies of the protozoan parasite *Trypanosoma brucei* (*T. brucei rhodesiense* and *T. brucei gambiense*).

### **TRANSMISSION**

Trypanosomiasis is transmitted by the bite of an infected tsetse fly (*Glossina* spp.). Bloodborne, congenital, sexual, and transfusion or transplantation transmission are rare.

### **EPIDEMIOLOGY**

African trypanosomiasis is endemic to rural sub-Saharan Africa. *T. brucei rhodesiense* is reported from eastern and southeastern Africa, mainly Malawi, Tanzania, Uganda, Zambia, and Zimbabwe. *T. brucei gambiense* is reported from central and west Africa, particularly in parts of

the Democratic Republic of the Congo, as well as Angola, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Equatorial Guinea, Gabon, Guinea, South Sudan, (northern) Uganda, and other countries. World Health Organization (WHO) maps and tables of African trypanosomiasis cases, by country, are available at www.who. int/data/gho/data/themes/topics/human-afri can-trypanosomiasis.

In 2018, WHO received 4,977 reports of sleeping sickness cases from African countries; *T. brucei gambiense* accounted for 98% of cases. Many cases, however, are likely not recognized or reported; exported cases also have been reported in expatriates, immigrants, refugees to countries outside of Africa, and tourists. Cases imported into the United States are rare; most cases in international travelers are due to *T. brucei rhodesiense*.

typically acquired during visits to national parks or game reserves.

Tsetse flies inhabit rural areas, including forests and savannah areas, and areas of thick vegetation along rivers and waterholes, depending on the fly species. Travelers to urban areas are at minimal risk, although transmission has been observed in some urban settings in the past. Tsetse flies bite during the day, and <1% are infected. Risk for infection in travelers increases with the number of fly bites, which does not always correlate with duration of travel. People most likely to be exposed to African trypanosomiasis infection are hunters and villagers with infected cattle herds. Tourists and other people working in or visiting game parks are at risk for contracting African trypanosomiasis if they spend long periods in rural areas where the disease is present.

### **CLINICAL PRESENTATION**

### T. brucei rhodesiense

Clinical manifestations generally appear within 1–3 weeks after the infective bite and can include a chancre at the bite site that appears within a few days of the bite; high fever; headache; myalgia; skin rash; thrombocytopenia; and less commonly, cardiac dysfunction, renal failure, or splenomegaly. Central nervous system (CNS) involvement can occur within a few weeks of the exposure and results in sleep cycle disturbance, mental deterioration, and, if left untreated death within months.

### T. brucei gambiense

Clinical manifestations of *T. brucei gambiense* generally appear months to years after exposure, but the incubation period can be <1 month. Signs and symptoms are nonspecific and can include arthralgia, facial edema, intermittent fever, headache, lymphadenopathy, malaise, myalgia, pruritus, and weight loss. CNS involvement occurs after several months to years of infection and is characterized by daytime somnolence and nighttime sleep disturbance, headache, and other neurologic manifestations (e.g., behavioral changes, mood disorders, focal deficits). In residents of endemic areas, the clinical

course of disease caused by *T. brucei gambiense* generally progresses more slowly (estimated average total duration of 3 years) than that caused by *T. brucei rhodesiense*, but if not treated, both forms of African trypanosomiasis typically are fatal.

### **DIAGNOSIS**

Tsetse fly bites are characteristically painful, and a chancre can develop at the bite location. No serologic tests for *Trypanosoma brucei* are available in the United States. Diagnosis of T. brucei rhodesiense is made by microscopic identification of parasites in specimens of blood, chancre fluid, or tissue; cerebrospinal fluid (CSF); bone marrow aspirates; or lymph node aspirates. The level of parasitemia is lower in T. brucei gambiense than T. brucei rhodesiense infections. Microscopic identification generally requires serial examinations of samples concentrated by techniques such as centrifugation followed by buffy coat examination, microhematocrit centrifugation, or mini-anion exchange centrifugation.

Serologic testing for *T. brucei gambiense*, available outside of the United States, can assist in diagnosis; the Centers for Disease Control and Prevention (CDC) can provide contact information. All patients diagnosed with African trypanosomiasis must have their CSF examined on a wet preparation to look for motile trypomastigotes and white blood cells (WBC) to determine whether the CNS is involved; the choice of treatment drugs depends on the disease stage. Patients with ≤5 WBC/mL and no trypomastigotes in CSF are in the first stage, and those with >5 WBC/mL or trypomastigotes in CSF are in the second stage.

Diagnostic assistance is available from CDC's Division of Parasitic Diseases and Malaria DPDx laboratory (www.cdc.gov/DPDx; dpdx@cdc.gov), and from the Parasitic Diseases Hotline for Healthcare Providers (404-718-4745; parasites@cdc.gov).

### **TREATMENT**

Treat people diagnosed with African trypanosomiasis with a drug course specific to the type of infection (T. brucei rhodesiense or T. brucei gambiense) and disease stage (i.e., presence or absence of CNS involvement). Pentamidine, the recommended treatment for first-stage T. brucei gambiense infection, is available in the United States. Nifurtimox was approved by the US Food and Drug Administration in August 2020 and is commercially available. Other drugs used to treat African trypanosomiasis (e.g., eflornithine [used in combination with nifurtimox], melarsoprol, suramin) are not commercially available in the United States but can be obtained from CDC. Physicians can consult with CDC staff to obtain otherwise unavailable treatment drugs (parasites@cdc.gov, 404-718-4745, or www.cdc. gov/parasites/sleepingsickness/health\_profes sionals/index.html).

No test of cure is available for African trypanosomiasis. After treatment, closely follow patients for 24 months and monitor for relapse. Recurrence of symptoms will require examination of body fluids, including CSF, to detect the presence of trypanosomes.

### **BIBLIOGRAPHY**

Büscher P, Cecchi G, Jamonneau V, Priotto G. Human African trypanosomiasis. Lancet. 2017;390(10110):2397-409.

Franco JR, Simarro PP, Diarra A, Jannin JG. Epidemiology of human African trypanosomiasis. Clin Epidemiol. 2014;6:257-75.

Kennedy PGE. Clinical features, diagnosis, and treatment of human African trypanosomiasis (sleeping sickness). Lancet Neurol. 2013;12(2):186-94.

Neuberger A, Meltzer E, Leshem E, Dickstein Y, Stienlauf S, Schwartz E. The changing epidemiology of human African trypanosomiasis among patients from nonendemic countries-1902-2012. PLoS One. 2014;9:e88647.

### **PREVENTION**

No vaccines or prophylactic drugs against African trypanosomiasis are available. To reduce the risk for infection, travelers should minimize contact with tsetse flies by wearing long-sleeved shirts and long pants made of medium-weight fabric in neutral colors. Tsetse flies are attracted to bright or dark colors, especially blue and black, and can bite through lightweight clothing. Travelers should inspect vehicles before entering, because the flies are attracted to the motion and dust from moving vehicles. Travelers should avoid bushes, because tsetse flies are less active during the hottest part of the day but will bite if disturbed. Although permethrin-impregnated clothing and insect repellent have not proven to be particularly effective against tsetse flies, travelers should use DEET repellent to prevent other insect bites that can cause illness (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

**CDC website**: www.cdc.gov/parasites/sleepings ickness

Simarro PP, Diarra A, Ruiz Postigo JA, Franco JR, Jannin JG. The human African trypanosomiasis control and surveillance programme of the World Health Organization 2000-2009: the way forward. PLoS Negl Trop Dis. 2011;5(2):e1007.

Simarro PP, Franco JR, Cecchi G, Paone M, Diarra A, Ruiz Postigo JA, Jannin JG. Human African trypanosomiasis in non-endemic countries (2000-2010). J Travel Med. 2012;19:44-53.

World Health Organization. Control and surveillance of human African trypanosomiasis. World Health Organ Tech Rep Ser. 2013;984:1-237.

# TRYPANOSOMIASIS, AMERICAN / CHAGAS DISEASE

Susan Montgomery, Sharon Roy, Christine Dubray

INFECTIOUS AGENT: Trypanosoma cruzi	
ENDEMICITY	Parts of Mexico, and Central and South America
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Immigrants and refugees from endemic areas Long-term travelers to endemic areas
PREVENTION METHODS	Avoid contact with triatomines (reduviid bugs) Avoid sleeping in thatch, mud, or adobe housing in endemic areas
DIAGNOSTIC SUPPORT	A clinical laboratory certified in high 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 AGENT**

Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi*.

### **TRANSMISSION**

Human infection occurs when *T. cruzi* in the feces of an infected triatomine insect (reduviid bug) enters the body. Entry portals include breaks in the skin (e.g., at the site of a reduviid bug bite), through the eyes by touching or rubbing with contaminated fingers, and through the gastrointestinal tract by consuming contaminated food or beverages. *T. cruzi* also can be transmitted through blood transfusions, organ transplantation, and vertically, from mother to infant.

### **EPIDEMIOLOGY**

*T. cruzi* is endemic to many parts of Mexico and Central and South America; rare locally acquired Chagas disease cases have been reported in the southern United States. No vectorborne transmission has been documented in the Caribbean islands. In the United States, Chagas disease is primarily a disease of immigrants from endemic areas of Latin America. The risk to travelers is extremely low, but travelers could be at risk if they

stay in poor-quality housing or consume contaminated food or beverages in endemic areas.

### **CLINICAL PRESENTATION**

Acute illness typically develops ≥1 week and ≤60 days after exposure. A chagoma (indurated local swelling) might develop at the site of parasite entry (e.g., Romaña's sign, edema of the eyelid and ocular tissues). Most infected people never develop symptoms, but remain infected throughout their lives. Approximately 20%-30% of infected people develop chronic manifestations after a prolonged asymptomatic period. Chronic Chagas disease usually affects the heart; clinical signs include conduction system abnormalities, ventricular arrhythmias, and, in late-stage disease, congestive cardiomyopathy. Chronic gastrointestinal problems (e.g., megaesophagus, megacolon) are less common, and can develop with or without cardiac manifestations. Reactivation disease can occur in immunocompromised patients.

### **DIAGNOSIS**

During the acute phase, parasites can be detected in fresh preparations of buffy coat or stained peripheral blood specimens; PCR testing also can help detect acute infection. After the acute phase, diagnosis requires ≥2 serologic tests to detect *T. cruzi*–specific antibodies, most commonly ELISA, immunoblot, and immunofluorescent antibody test.

PCR is not a useful diagnostic test for chronic-phase infections because parasites cannot be detected in the peripheral blood during this phase. 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 (www.cdc.gov/DPDx; dpdx@cdc.gov), and from the Parasitic Diseases Hotline for Healthcare Providers (404-718-4745; parasites@cdc.gov).

### **TREATMENT**

Antitrypanosomal drug treatment is always recommended for acute, early congenital, and reactivated *T. cruzi* infection, and for chronic *T. cruzi* infection in children <18 years old. In adults with chronic infection, treatment is usually recommended.

The 2 drugs used to treat Chagas disease are benznidazole and nifurtimox. Benznidazole is approved by the US Food and Drug Administration (FDA) for use in children 2–12 years old and is commercially available. Nifurtimox is approved

by the FDA for treatment of children from birth to <18 years old who weigh at least 2.5 kg. The drug was approved in August 2020 and became commercially available later that year. Side effects are common with both drugs, and tend to be more frequent and more severe with increasing age. Contact CDC (parasites@cdc.gov; 404-718-4745) for assistance with clinical management (see www.cdc.gov/parasites/chagas/health\_profes sionals/tx.html for more information).

### **PREVENTION**

To avoid Chagas disease, travelers should follow insect bite precautions (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods) and food and water precautions (see Sec. 2, Ch. 8, Food & Water Precautions). Travelers also should avoid sleeping in adobe, mud, or thatch housing in endemic areas, and use insecticides in and around such homes. Insecticide-treated bed nets are helpful. Screening blood and organs for Chagas disease prevents transmission via transfusion or transplantation. Screening of pregnant people coming from endemic areas and early detection and treatment of mother-to-baby (congenital) cases also will help reduce disease burden.

**CDC website**: www.cdc.gov/parasites/chagas

### **BIBLIOGRAPHY**

Bern C. Antitrypanosomal therapy for chronic Chagas' disease. N Engl J Med. 2011;364(26):2527–34.

Bern C, Messenger LA, Whitman JD, Maguire JH. Chagas disease in the United States: a public health approach. Clin Microbiol Rev. 2019;33(1):e00023-19.

Bern C, Montgomery SP, Herwaldt BL, Rassi A Jr, Marin-Neto JA, Dantas RO, et al. Evaluation and treatment of Chagas disease in the United States: a systematic review. JAMA. 2007;298(18):2171–81. Carter YL, Juliano JJ, Montgomery SP, Qvarnstrom Y. Acute Chagas disease in a returning traveler. Am J Trop Med Hyg. 2012;87(6):1038–40.

Edwards MS, Stimpert KK, Montgomery SP. Addressing the challenges of Chagas disease: an emerging health concern in the United States. Infect Dis Clin Pract. 2017;25(3):118–25.

Rassi A Jr, Rassi A, Marin-Neto JA. Chagas disease. Lancet. 2010;375(9723):1388–402.

## **PART 4: FUNGAL**

# COCCIDIOIDOMYCOSIS / VALLEY FEVER

Mitsuru Toda, Kaitlin Benedict, Tom Chiller

INFECTIOUS AGENTS: Coccidioides immitis and C. posadasii		
ENDEMICITY	The Americas (Central and South America, northern Mexico, and the United States, specifically Arizona and Southern California)	
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventure tourists Humanitarian aid workers Long-term travelers and expatriates Study abroad students Travelers visiting friends and relatives	
PREVENTION METHODS	Limit exposure to outdoor dust in endemic areas Use personal protective equipment (e.g., N95 respirator) when working outdoors in endemic areas Preventive antifungal medication	
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; or contact CDC's Mycotic Diseases Branch Reference Laboratory Team (404-639-2569)	

### **INFECTIOUS AGENTS**

Valley fever (coccidioidomycosis) is caused by the fungi *Coccidioides immitis* and *C. posadasii*.

### **TRANSMISSION**

Transmission occurs through inhalation of fungal conidia from the environment. Transmission from person to person does not occur.

### **EPIDEMIOLOGY**

Coccidioides is endemic to the western United States, particularly Arizona and Southern

California, and parts of Mexico and Central and South America. Travelers, including adventure tourists, expatriates, humanitarian aid workers, long-term travelers, and travelers visiting friends and relatives (VFRs) are at increased risk if they participate in activities that expose them to soil disruption and outdoor dust. Participating in activities like community house-building projects, gardening, four-wheeling, and horseback riding can put people at risk. Coccidioidomycosis outbreaks have been associated with activities such as archaeological



excavation, construction, and military training exercises.

### **CLINICAL PRESENTATION**

The incubation period is 7-21 days. About 40% of infected people develop symptomatic infections, ranging from primary pulmonary illness to severe disseminated disease. The most common symptoms of primary pulmonary coccidioidomycosis are cough and persistent fatigue, with only about half of patients reporting fever. Other symptoms include shortness of breath, headache, joint pain, muscle aches, night sweats, and rash. Symptoms can be indistinguishable from bacterial pneumonia. Coccidioidomycosis infections are often self-limited, typically resolving in a few weeks to months, but also can be severe, requiring hospitalization. An estimated 5%-10% of people develop serious or chronic lung disease (e.g., bronchiectasis, cavitary pneumonia, pulmonary fibrosis). About 1% of illnesses result in meningitis, which can require lifelong antifungal therapy; dissemination to bones, joints, and skin also can occur.

People ≥65 years of age, people with diabetes, people who smoke, and people with high inoculum exposure are at increased risk of developing severe pulmonary complications. Those with depressed cellular immune function (e.g., people with HIV, organ transplant recipients) and people who are pregnant are at increased risk for developing disseminated disease. Epidemiological data suggest that the risk for severe illness is increased among people of African American, Filipino, and Pacific Island descent, but further study is needed to understand the reasons for this association.

### **DIAGNOSIS**

Coccidioidomycosis is a nationally notifiable disease in the United States. The most common methods to diagnose coccidioidomycosis are culture, histopathology, molecular techniques, and serology. Isolation of *Coccidioides* from fungal culture of respiratory specimens or tissue provides a definitive diagnosis. Microscopy of sputum or tissue can identify *Coccidioides* spherules but has low sensitivity. Molecular techniques include DNA probe

for confirmation of cultures, as well as PCR for direct detection from clinical specimens, which became commercially available in early 2018. EIA is a sensitive serologic method to detect IgM and IgG antibodies. Immunodiffusion and complement fixation can also detect antibodies and are often used to confirm diagnosis. Lateral flow assays to detect any antibodies in serum became commercially available in 2018.

### **TREATMENT**

Expert opinions differ on the proper management of patients with uncomplicated primary pulmonary disease in the absence of risk factors for severe or disseminated disease. Some experts recommend no therapy, since most illnesses are self-limited, whereas others advise treatment to reduce the intensity or duration of symptoms. Treatment with antifungal agents has not been proven to prevent dissemination. People at high risk for dissemination should receive antifungal therapy, as should people with clinical manifestations of severe acute pulmonary disease, chronic pulmonary disease, or disseminated disease. Depending on the clinical situation, a variety of antifungal agents can be used, including amphotericin B and fluconazole (or itraconazole).

### **PREVENTION**

To reduce risk for coccidioidomycosis, travelers should limit exposure to outdoor dust in endemic areas, or wear an N95 respirator if they cannot avoid dusty areas while in this environment. During dust storms, travelers should stay inside and close windows. Travelers to known endemic areas also should avoid activities that require close contact with dirt or dust, including digging, gardening, and yard work. Air filtration measures can be used indoors. Preventive antifungal medication (fluconazole or itraconazole) can be taken in certain circumstances if recommended by a health care provider.

**CDC websites**: www.cdc.gov/fungal/diseases/coccidioidomycosis; www.cdc.gov/niosh/topics/valleyfever/; www.cdc.gov/fungal/diseases/coccidioidomycosis/factsheets/be-aware-of-valleyfever.html

#### **BIBLIOGRAPHY**

Diaz, JH. Travel-related risk factors for coccidioidomycosis. J Travel Med. 2018;25(1):tay027.

Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Geertsma F, Hoover SE, et al. 2016 Infectious Diseases Society of America (IDSA) clinical practice guideline for the treatment of coccidioidomycosis. Clin Infect Dis. 2016;63(6):e112–46.

Freedman M, Jackson BR, McCotter O, Benedict K. Coccidioidomycosis outbreaks, United States and worldwide, 1940–2015. Emerg Infect Dis. 2018;24(3):417–23.

Rosenstein NE, Emery KW, Werner SB, Kao A, Johnson R, Rogers D, et al. Risk factors for severe pulmonary and disseminated coccidioidomycosis: Kern County, California, 1995–1996. Clin Infect Dis. 2001;32(5):708–15.

Toda M, Gonzalez FJ, Fonseca-Ford M, Franklin F,
Huntington-Frazier M, Gutelius B, et al. Notes from
the field: multistate coccidioidomycosis outbreak in
U.S. residents returning from community service trips
to Baja California, Mexico—July–August 2018. MMWR
Morb Mortal Wkly Rep 2019;68(14):332–3.

### **HISTOPLASMOSIS**

Jeremy Gold, Diego Caceres, Brendan Jackson, Kaitlin Benedict

INFECTIOUS AGENT: Histoplasma capsulatum		
ENDEMICITY	Worldwide	
TRAVELER CATEGORIES AT GREATEST RISK FOR EXPOSURE & INFECTION	Adventure tourists Humanitarian aid workers Immigrants and refugees Long-term travelers and expatriates Study-abroad students Travelers visiting friends and relatives	
PREVENTION METHODS	Avoid exposure to soil contaminated with bird droppings or bat guano Chemoprophylaxis might be appropriate in rare circumstances for immunocompromised people	
DIAGNOSTIC SUPPORT	A clinical laboratory certified in moderate complexity testing; or contact CDC's Mycotic Diseases Branch Reference Laboratory Team (404-639-2569)	

### **INFECTIOUS AGENT**

Histoplasmosis is caused by *Histoplasma capsulatum*, a thermal-dimorphic fungus that grows as a mold in the environment and as a yeast in animal and human hosts.

### **TRANSMISSION**

Histoplasmosis is transmitted through inhalation of spores (conidia) from the environment, often soil contaminated with bat guano or bird droppings, but is not transmitted from person to person.

### **EPIDEMIOLOGY**

Knowledge of global histoplasmosis epidemiology is incomplete, and cases in travelers are likely underreported to public health authorities. Travelers, including adventure tourists, humanitarian aid workers, long-term travelers and expatriates, study-abroad students, and people visiting

friends and relatives could be at increased risk for histoplasmosis if they engage in activities involving soil disruption (e.g., caving, construction, demolition, excavation, farming, gardening), particularly in areas where bats and birds roost. Histoplasmosis also occurs in immigrants from endemic regions who become immunocompromised.

### **CLINICAL PRESENTATION**

Incubation period is typically 3–17 days for acute disease. About 90% of infections are asymptomatic or result in a mild influenza-like illness. Acute pulmonary histoplasmosis often involves body aches, chest pain, chills, cough, fatigue, fever, and headache. Most people spontaneously recover several weeks after symptom onset, but fatigue might persist longer. High-dose exposure can lead to severe disease. Dissemination, especially to the central nervous system and gastrointestinal tract, can occur in immunocompromised people. Histoplasmosis might be misdiagnosed as other illnesses, particularly as tuberculosis in people who travel from regions where both pathogens are endemic.

### **DIAGNOSIS**

Several methods to diagnose histoplasmosis are available. Although culture and histopathologic identification remain the gold standards, a combination of antigen and antibody testing could be more useful in diagnosing travel-associated histoplasmosis. Rapid *Histoplasma* antigen testing by enzyme immunoassays, reagents for immunodiffusion, and complement fixation are commercially available as in vitro diagnostic kits. In immunocompetent patients, antigen testing is most useful when performed within 2

weeks of a high-dose exposure. Antibody testing of specimens collected during the acute and convalescent phases of illness can improve diagnostic yield; obtaining serial antigen and antibody titers can aid in monitoring response to treatment.

The Centers for Disease Control and Prevention (CDC)'s Mycotic Diseases Branch reference laboratory supports histoplasmosis diagnosis and outbreak investigations. Laboratory support includes immunodiagnostics by antibody and antigen testing, and molecular testing. To obtain diagnostic support from CDC, contact the Mycotic Diseases Branch reference laboratory team (404-639-2569).

### **TREATMENT**

Treatment is not usually indicated for immunocompetent people with acute, localized pulmonary infection. People with more extensive disease or persistent symptoms lasting >1 month generally can be treated with an azole drug (e.g., itraconazole) for mild to moderate illness, or amphotericin B for severe infection. Patients with acute respiratory distress might benefit from steroids as well as antifungal treatment.

### **PREVENTION**

People at increased risk for severe disease should avoid high-risk areas (e.g., bat-inhabited caves, hollow trees). No vaccine for histoplasmosis is available. Chemoprophylaxis with itraconazole is recommended for certain people living with HIV, and might be appropriate in specific circumstances for other immunosuppressed people.

**CDC website**: www.cdc.gov/fungal/diseases/his toplasmosis

### **BIBLIOGRAPHY**

Adenis AA, Valdes A, Cropet C, McCotter OZ, Derado G, Couppie P, et al. (2018). Burden of HIV-associated histoplasmosis compared with tuberculosis in Latin America: a modelling study. Lancet Infect Dis. 2018;18(10):1150–9.

Armstrong PA, Beard JD, Bonilla L, Arboleda N, Lindsley MD, Chae S-R, et al. Outbreak of severe histoplasmosis among tunnel workers—Dominican Republic, 2015. Clin Infect Dis. 2018;66(10):1550–7.

Azar MM, Hage CA. Laboratory diagnostics for histoplasmosis. J Clin Microbiol. 2017;55(6):1612–20.

Bahr NC, Antinori S, Wheat LJ, Sarosi GA. Histoplasmosis infections worldwide: thinking outside of the Ohio River valley. Curr Trop Med Rep. 2015;2(2):70–80.

Centers for Disease Control and Prevention. Outbreak of histoplasmosis among travelers returning from El Salvador—Pennsylvania and Virginia, 2008. MMWR Morb Mortal Wkly Rep. 2018;57(50):1349–53.

- Cottle LE, Gkrania-Klotsas E, Williams HJ, Brindle HE, Carmichael AJ, et al. A multinational outbreak of histoplasmosis following a biology field trip in the Ugandan rainforest. J Travel Med. 2013;20(2):83–7.
- Kauffman CA. Histoplasmosis: a clinical and laboratory update. Clin Microbiol Rev. 2007;20(1):115–32.
- Staffolani S, Buonfrate D, Angheben A, Gobbi F, Giorli G, Guerriero M, et al. Acute histoplasmosis in
- immunocompetent travelers: a systematic review of literature. BMC Infect Dis. 2018;18(1):673.
- Wheat LJ, Freifeld AG, Kleiman MB, Baddley JW, McKinsey DS, Loyd JE, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. Clin Infect Dis. 2007;45(7):807–25.



## **Health Care Abroad**

# TRAVEL INSURANCE, TRAVEL HEALTH INSURANCE & MEDICAL EVACUATION INSURANCE

Rhett Stoney

Severe illness or injury abroad could cause a financial burden to travelers. Regardless of whether they have a domestic health insurance plan, travelers can substantially reduce their out-of-pocket costs for medical care received abroad by purchasing specialized insurance policies in advance of their trip. Three types of policies—travel insurance, travel health insurance, and medical evacuation insurance—each provide different types of coverage in the event of an illness or injury. Such policies might be particularly beneficial to travelers with preexisting medical conditions. Besides protection against costs, the insurance might also help travelers obtain medical care abroad.

Basic accident or travel health insurance might be necessary for travelers with certain

itineraries. For example, although cruise lines employ health care staff, the cost for medical treatment delivered onboard a ship might not be included in the price of a passenger's ticket; thus, travelers on cruise ships might want to consider investing in specialized insurance policies.

## DOMESTIC HEALTH INSURANCE & OVERSEAS TRAVEL

Some US health insurance carriers cover medical emergencies that occur when policyholders travel internationally. Encourage travelers to contact their insurer before traveling to learn what medical services, if any, their policies cover. Box 6-01 includes suggested questions travelers should ask their insurance company.

## BOX 6-01 Supplemental travel health insurance: suggested questions to ask before purchasing a policy

### **COVERAGE REQUIREMENTS**

Do I need preauthorization before receiving treatment, hospital admission, or other medical services? Do I need a second opinion before I can receive

What are company policies regarding coverage of care received "out of network"?

Does the company provide policyholders access to a 24/7/365 physician-backed support center?

### **POTENTIAL EXCLUSIONS**

emergency treatment?

Does this policy include or exclude coverage for treatment of injuries sustained while participating in high-risk activities (e.g., skydiving, scuba diving, mountain climbing)?

Does this policy include or exclude coverage for mental health (psychiatric) emergencies?

### PREEXISTING MEDICAL CONDITIONS

Does this policy cover exacerbations of preexisting medical conditions?

Does this policy cover complications of pregnancy or neonatal intensive care?

## PAYING FOR HEALTH SERVICES RECEIVED ABROAD

During the pretravel consultation, discuss insurance options and suggest that all travelers consider purchasing supplemental medical insurance coverage (see Box 6-02 for a discussion checklist), particularly if they are going to remote destinations or places lacking high-quality medical facilities. Strongly encourage supplemental medical insurance coverage for travelers planning extended international travel, those with underlying health conditions, and those participating in high-risk activities (e.g., scuba diving, mountain climbing) abroad. In addition to covering costs of treatment or medical evacuation, travel health insurers can assist the international traveler by organizing and coordinating care and by keeping relatives informed in the event of a medical emergency, which is especially important when the traveler is severely ill or injured and requires medical evacuation.

Nationalized health care services at a given destination do not necessarily cover health care costs of nonresidents. Even with a supplemental travel health insurance policy in force, receiving medical care abroad usually requires a cash or credit card payment at the point of service, which can result in expenditures of thousands of dollars. US citizens paying for health care abroad should obtain copies of all charges and receipts and, if necessary, contact a US consular officer, who can assist the traveler with transferring funds from the United States.

The US Department of State might be able to offer limited emergency medical assistance loans to US citizens who experience a medical emergency abroad but have no means to pay at point of service and cannot arrange for a transfer of funds from the United States. Travelers must repay these loans, but the funds might be available for temporarily destitute US citizens and their qualified dependents. Once a loan is issued, the Department of State will limit the traveler's US passport and, in most cases, will not issue a new passport until the loan is paid in full. US citizens should contact the nearest US embassy or consulate, or the US Department of State, Office of Overseas Citizens Services, at 888-407-4747 (or from abroad, +1-202-501-4444), for information about assistance options and eligibility requirements.

### TRAVEL INSURANCE

Travel insurance protects the traveler's financial investment in a trip, including lost baggage and trip cancellation. Travelers who become ill before departing are more likely to avoid or postpone travel if they know their financial investment in the trip is protected. Depending on the policy, travel insurance might not cover medical expenses abroad, so travelers need to carefully research the coverage offered to determine their need for additional travel health and medical evacuation insurance.

### BOX 6-02 Supplemental travel health insurance: discussion checklist

### TRAVEL MEDICINE PROFESSIONAL RESPONSIBILITIES

- ☐ Determine travelers' health profile, including underlying medical conditions.
- ☐ Identify potential medical needs abroad, including health risks based on itinerary and destination, duration of travel, method of transportation (air-, land-, or water-based), lodgings or accommodations, and planned activities.
- ☐ Instruct travelers to review domestic health policies to identify gaps in coverage for identified potential medical needs.
- □ Discuss the differences between the 3 types of supplemental insurance (travel, travel health, and medical evacuation), and explain how to choose supplemental policies that cover potential medical needs abroad.
- ☐ Remind travelers of the steps to take should they require medical care abroad:
  - O Travelers should be prepared to pay out of pocket at the time services are rendered, in some instances even before care is received, and then provide insurers with copies of bills and invoices to initiate reimbursement afterward.
  - Travelers should plan for potential emergencies in advance by identifying health care providers at the destination who see international travelers.

### TRAVELER RESPONSIBILITIES

### Before travel

 Review domestic health insurance policies to determine what medical services are or are not covered overseas.

- Purchase supplemental travel health insurance coverage based on potential medical needs and health risks.
- ☐ Identify medical service providers at destination (for a directory of English-speaking health care providers, see International Association for Medical Assistance to Travelers [www.iamat.org]].
- ☐ Check with the insurance company to confirm they reimburse for out-of-pocket payments made to healthcare providers abroad. In most cases, health care providers abroad do not accept payment from insurance carriers, and travelers must pay up front (with cash or credit card) for all services received.

### During travel

- Carry insurance policy identity cards (including supplemental travel health insurance) and insurance claim forms while traveling.
- Have contact information of medical providers at destination(s).
- □ Keep copies of all charges and receipts for medical care received.

### After travel

- Promptly seek medical attention upon return to the United States and at the first sign of any unexpected complications from care received internationally.
- ☐ Bring copies of all summary records, charges, and receipts for medical care received abroad.
- ☐ Give the US health care provider the following details: dates of travel, dates medical care received, contact information for the facility and all international health care providers seen.

## SUPPLEMENTAL TRAVEL HEALTH & MEDICAL EVACUATION INSURANCE

Travel health insurance and medical evacuation insurance are 2 types of short-term supplemental policies that cover health care costs incurred while abroad. Each is relatively inexpensive. Many commercial companies offer travel health insurance; travelers can purchase such policies separately or together with medical evacuation insurance. Some recommended features to consider when purchasing supplemental travel health and medical evacuation insurance include whether the insurer arranges with hospitals to guarantee direct payment; provides assistance via

a 24-hour physician-backed support center, which is critical for medical evacuation insurance; offers emergency medical transport to facilities in the home country (repatriation) or to facilities equivalent to those in the home country; and covers high-risk activities (e.g., scuba diving).

Although travel health insurance covers some international health care costs, the quality of care might be inadequate and medical evacuation (sometimes referred to as "medevac") from a resource-poor area to a hospital delivering definitive care might be necessary. The total cost of medevac varies by location, ranging from \$25,000 for transport within North America to ≥\$250,000 for more distant, and remote locations. Costs



increase when the patient being evacuated is critically ill or needs complex infection control measures. In such cases, medevac insurance covers the cost of transportation, including transportation to another country if necessary.

Some medical evacuation companies have more extensive experience working in some parts of the world than others; travelers should ask about a company's resources in each region of travel, especially if planning trips to hard-to-reach locations in a region. Even if travelers select their insurance provider carefully, unexpected delays in care can still arise, especially in remote destinations. Thus, if the health risks are too high, a traveler might want to postpone or cancel their international trip.

### FINDING AN INSURANCE **PROVIDER**

Several organizations provide information about purchasing travel health and medical evacuation insurance, including the US Department of State (https://travel.state.gov/content/travel/ en/international-travel/before-you-go/yourhealth-abroad/insurance-providers-overseas. html); International Association for Medical Assistance to Travelers (www.iamat.org); US Travel Insurance Association (www.ustia.org); and the American Association of Retired Persons (www.aarp.org), among others. The Centers for Disease Control and Prevention does not endorse any provider or medical insurance company.

### TRAVELERS WITH UNDERLYING MEDICAL CONDITIONS

Travelers with underlying medical conditions should discuss any concerns with the insurer before departure. In a study of international travelers with travel health insurance claims, insurance companies fully paid only 2/3 of claims, and the main reasons for coverage refusal were preexisting illness and poor documentation of expenses incurred.

### **BIBLIOGRAPHY**

American Association of Retired Persons. Overview of Medicare supplemental insurance 2010. Available from: www.aarp.org/health/medicare-insurance/info-10-2008/ overview\_medicare\_supplemental\_insurance.html.

Beyond purchasing supplemental travel health insurance coverage, encourage travelers with medical conditions to take additional steps before departure. To facilitate ease of access to health records when overseas, travelers should store copies of their health records with a medical assistance company. Instruct travelers to obtain letters from their health care providers listing all medical conditions and current medications, including generic drug names, written in the local language if possible. Travelers should pack medications in the original packaging in carry-on luggage during transport. To facilitate ease of entry through customs, travelers should check with the destination country's embassy before departure to ensure that none of the medications they are bringing are considered illegal in that region. Anyone with a known heart condition should carry a copy (paper or electronic) of their most recent electrocardiogram.

### MEDICARE BENEFICIARIES

Medicare beneficiaries are no different from other travelers; they need to examine their coverage carefully and supplement it with additional travel health insurance, as required. Except in limited circumstances, the Social Security Medicare program does not provide coverage for medical costs incurred outside the United States, nor does it cover medical evacuation. Medicare beneficiaries can purchase supplemental Medigap plans to fill gaps, including for travel coverage. Medigap plans C, D, F, G, M, and N cover some emergency care received outside the United States. After meeting the yearly \$250 deductible, this benefit pays 80% of the cost of emergency care during the first 60 days of international travel. The coverage has a \$50,000 lifetime maximum. International travelers can find more information on Medicare and Medigap options at www.medicare.gov/supplements-otherinsurance/medigap-travel.

Centers for Medicare and Medicaid Services. Medigap & travel. Available from: www.medicare.gov/supplementsother-insurance/medigap-travel.

- Flaherty G, De Freitas S. A heart for travel: travel health considerations for patients with heart disease and cardiac devices. Ir Med J. 2016;109(10):486.
- Leggat PA, Carne J, Kedjarune U. Travel insurance and health. J Travel Med. 1999;6(4):243–8.
- Leggat PA, Leggat FW. Travel insurance claims made by travelers from Australia. J Travel Med. 2002;9(2):59–65.
- Teichman PG, Donchin Y, Kot RJ. International aeromedical evacuation. N Engl J Med. 2007;356(3):262–70.
- US Department of State. Emergency financial assistance for U.S. citizens abroad. Available from: https://travel.state.gov/content/travel/en/international-travel/emergencies/emergency-financial-assistance.html.
- US Department of State. Insurance providers for overseas coverage. Available from: https://travel.state. gov/content/travel/en/international-travel/bef ore-you-go/your-health-abroad/insurance-providersoverseas.html.

## **OBTAINING HEALTH CARE ABROAD**

Stefan Hagmann

While abroad, travelers might seek medical care ranging from treatment for self-limited minor ailments, to care for chronic conditions, to sophisticated medical management of major illnesses or injuries. Insurance plans might not cover emergency health care, and travelers should check with their insurance carriers before departure to confirm the limits of their coverage and to identify any additional coverage requirements. For example, travel health insurance alone does not usually pay for the cost of an emergency medical evacuation or itinerary alterations needed to receive medical care during travel. Travelers can buy specific policies to cover these expenses, but should understand that such policies often do not cover expenses related to preexisting conditions.

Supplemental medical insurance plans purchased prior to traveling often furnish access to preselected local providers in many countries through a 24-hour emergency hotline; some even provide medical assistance via a nurse- or physician-backed support center (see Sec. 6, Ch. 1, Travel Insurance, Travel Health Insurance & Medical Evacuation Insurance, for more details). Travelers should be prepared to pay out of pocket when services are rendered and, in some instances, even before care is received, then provide insurers with copies of bills and invoices to initiate reimbursement afterward.

Travelers also should be aware (in advance) of destinations on their itinerary where coronavirus disease 2019 (COVID-19) vaccine coverage of the local population is low (https://ourworldind

ata.org/covid-vaccinations), or where case rates and hospitalizations are high (https://ourworl dindata.org/covid-hospitalizations). Availability of health care resources in such places could be strained, and treatment options (for severe COVID-19 and other conditions) could be limited. Destination-specific COVID-19 travel recommendations are available at https://travel.state.gov/content/travel/en/traveladvisories/COVID-19-Country-Specific-Information.html.

## LOCATING HEALTH CARE FACILITIES & PROVIDERS ABROAD

The level and availability of medical care around the world varies by country and even within countries. During pretravel preparation, travelers should consider how they will access health care during their trip should a medical problem or emergency arise (Box 6-03). Encourage travelers likely to need health care to research thoroughly and identify potential health care providers and facilities at their destination. For example, people who require regular dialysis treatments need to arrange appointments in advance at a site with appropriate equipment. Pregnant travelers should know the names and locations of reliable obstetric medical centers. Travelers should be aware that more choices are generally available in urban areas than in rural or remote locations.

Travelers, particularly those with preexisting or complicated medical issues, should know and ideally have documented in a doctor's letter the names

### BOX 6-03 Obtaining health care abroad: a checklist for travelers

- ☐ Identify quality health care providers and facilities at destination, prior to traveling.
- ☐ Carry a provider letter that lists all active medical problems, current medications, and allergies. If possible, download travel health mobile applications to input medical records, medications, and other health information (e.g., electrocardiogram) so these are accessible if needed.
- □ Pack an adequate supply of medication in original, labeled containers, and know how to

- get additional safe and effective medications while abroad.
- ☐ Request documentation of any medical care received abroad, including medications, and share with health care providers delivering subsequent care while traveling and at home.
- ☐ If a blood transfusion is required while traveling, make every effort to ensure that the blood has been screened for transmissible diseases, including HIV.

of their conditions, any allergies, their blood type, and current medications, including generic names. If possible, this list should be in the local language of the travel destination. Travelers also should carry copies of prescriptions, including for glasses and contact lenses, and wear medical identification jewelry (e.g., a MedicAlert bracelet), as appropriate. Travelers should check with the foreign embassy of the countries they plan to visit to ensure current medications are permitted. Many mobile phone applications enable travelers to download their medical records, medications, electrocardiogram, and other information so that they can access

these when needed. Remind travelers to request documentation of any medical care received during travel, including a list of medications received. Travelers can then share this information with any health care providers seen subsequently in the event they require ongoing care.

Box 6-04 includes a list of suggested resources international travelers can use to help identify health care providers and facilities around the world. The Centers for Disease Control and Prevention does not endorse any provider or medical insurance company, and accreditation does not necessarily ensure a good outcome.

### **BOX 6-04** Finding a health care provider overseas

The nearest US embassy or consulate (www.usemba ssy.gov) can help travelers locate medical services and notify friends, family, or employer of an emergency. Emergency consular services are available 24 hours a day, 7 days a week, overseas and in Washington, DC (888-407-4747 or 202-501-4444).

The US Department of State maintains a list of travel medical and evacuation insurance providers on their website, https://travel.state.gov/content/travel/ en/international-travel/before-you-go/your-healthabroad/insurance-providers-overseas.html.

The International Society of Travel Medicine (www.istm.org) maintains a directory of health care professionals with expertise in travel medicine in more than 80 countries.

The International Association for Medical Assistance to Travelers (www.iamat.org/doctors\_ clinics.cfm) maintains a list of physicians, hospitals, and clinics that have agreed to provide care to members. Membership is free, although donations are suggested.

Travel agencies, hotels, and credit card companies (especially those with special benefits) also might provide information.

The following travel medicine websites, organized by country, provide access to clinicians:

AUSTRALIA: Travel Medicine Alliance (www.travelm edicine.com.au)

CANADA: Health Canada (www.phac-aspc.gc.ca and https://travel.gc.ca)

CHINA: International Travel Healthcare Association (www.itha.org.cn/)

GREAT BRITAIN: National Travel Health Network & Centre (www.nathnac.org) and British Global & Travel Health Association (www.bgtha.org)

SOUTH AFRICA: South African Society of Travel Medicine (www.sastm.org.za)

### AVOIDING TRAVEL WHEN ILL

Advise travelers to self-evaluate before leaving home and to avoid or postpone travel if acutely ill with fever or other signs or symptoms of a communicable disease. Traveling while ill increases the chances that a person will have to interact with an unfamiliar and potentially inadequately equipped health care system and that they could transmit their illness to travel partners and/or other passengers. Moreover, travelers should be aware that airlines can request that they complete a brief health questionnaire and that local health authorities might conduct body temperature checks anywhere in the airport, including the waiting area and during boarding; passengers who fail such screenings might be prohibited from boarding their flight. Because people often are reluctant to postpone or cancel travel, trip cancellation insurance can protect some (or all) of their investment and increase compliance with the recommendation not to travel when ill.

### **DRUGS & OTHER PHARMACEUTICALS**

The quality of drugs and medical products acquired abroad might not meet the same regulated standards established by the US Food and Drug Administration. Worse yet, drugs or medical products could be counterfeit and contain no active ingredients or could contain harmful ingredients (for more information, see the following chapter in this section, ... perspectives: Avoiding Poorly Regulated Medicines & Medical Products During Travel). Travelers whose original supply of medication is used up, lost, stolen, or damaged should take steps to ensure that the replacement medicines they buy are safe and effective.

To minimize risks associated with substandard drugs and pharmaceuticals, travelers should bring enough medicine for the entire time they are away, and include an additional supply in case of trip delays. Travelers should carry all medications in the original labeled containers in their carry-on luggage, not in checked baggage; this also applies to travelers who might require an epinephrine autoinjector (Epi-Pen) to treat known severe, potentially life-threatening allergies. For Epi-Pens, travelers should carry a letter from the prescribing physician explaining their allergies and a copy of the written prescription.

Travelers who need injections while abroad should insist that health care providers use new needles and syringes. Travelers who know they require injections can bring their own supplies, but also should bring a letter from their provider attesting to the need for this equipment.

### **BLOOD SAFETY**

A medical emergency abroad (e.g., a motor vehicle accident, other trauma) could require a lifesaving transfusion of whole blood or blood components (e.g., platelets, fresh frozen plasma). Not all countries accurately, reliably, and systematically screen blood donations for infectious agents, putting recipients at risk for transfusion-related diseases. Consequently, all travelers should consider receiving hepatitis B virus immunization before travel (see Sec. 2, Ch. 3, Vaccination & Immunoprophylaxis-General Principles, and Sec. 5, Part 2, Ch. 8, Hepatitis B). Hepatitis B vaccination is especially important for travelers who frequently visit or have long-term stays in lowand middle-income countries, travelers who have underlying medical conditions that increase their risk of requiring blood products while traveling, and travelers whose activities (e.g., adventure travel) put them at increased risk for serious injury.

Ensuring the safety of the blood supply can be difficult, but travelers can take a few measures to increase their chances of a safe blood transfusion. For instance, the traveler or a companion, if the traveler is incapacitated, can ask about blood supply screening practices for transfusiontransmissible infections, including HIV. Because obtaining information on the safety of the blood supply can be difficult at the point of service, travelers with known medical conditions that might require transfusions can identify medical services at their destination before travel to increase their chances of obtaining higher-quality care. Travelers also can register with agencies (e.g., the Blood Care Foundation [www.bloodcare.org.uk/ blood-transfusionsabroad.html]) that attempt to deliver reliable blood products rapidly to members at international locations.

### **BIBLIOGRAPHY**

- Kolars JC. Rules of the road: a consumer's guide for travelers seeking health care in foreign lands. J Travel Med. 2002;9(4):198-201.
- US Department of State, Bureau of Consular Affairs. Your health abroad. Available from: www.travel.state.gov/ content/travel/en/international-travel/before-you-go/ your-health-abroad.
- World Health Organization. Blood safety and availability. Available from: www.who.int/news-room/fact-sheets/ detail/blood-safety-and-availability.
- World Health Organization. Substandard and falsified medical products. Available from: www.who.int/newsroom/fact-sheets/detail/substandard-and-falsifiedmedical-products.
- World Health Organization. Technical considerations for implementing a risk-based approach to international travel in the context of COVID-19: Interim guidance, 2 July 2021. Available from: www.who.int/publications/ i/item/WHO-2019-nCoV-Risk-based-international-tra vel-2021.1.

## ... perspectives

# AVOIDING POORLY REGULATED MEDICINES & MEDICAL PRODUCTS DURING TRAVEL

Michael Green

In many low- and middle-income countries, national drug regulatory authorities lack the capacity to monitor and enforce drug quality standards effectively and to keep poor-quality products, including drugs, vaccines, and medical devices, off the market. Consequently, substandard and fake medicines are a public health concern in these locations. Many poor-quality products also are trafficked by pharmacy websites that misrepresent themselves as reputable or located in countries with mature regulatory systems. Even highincome countries are not immune to the problem, because counterfeiters become adept at thwarting the efforts of more advanced regulatory systems.

Poor regulatory oversight breeds poor-quality medicines, whether they are counterfeit, falsified, substandard, or degraded (Box 6-05). A report from the World Health Organization identified that 10% of medical products circulating in low- and middle-income countries are either substandard or falsified. Another study found that 9%–41% of tested drugs failed quality specifications. In specific regions in Africa, Latin America, and Asia, the chance of purchasing a counterfeit drug can be >30%.

Because counterfeit drugs are not made by legitimate manufacturers and are produced under unlawful circumstances, improper or toxic ingredients in these products can cause serious harm. For example, the active pharmaceutical ingredient could be absent, present in small quantities, or replaced with a less effective compound. In addition, the wrong inactive ingredients (excipients) can contribute to poor drug dissolution, bioavailability, and toxicity. As a result, a patient might not respond to treatment or could have adverse reactions to unknown substituted or toxic ingredients.

Vaccines and other products (e.g., condoms, disinfectants, insecticide-treated mosquito nets, masks, water purification devices) also could have quality problems or be counterfeit. Vaccine integrity typically depends on a temperature-controlled supply chain, and, unlike medicines with stated amounts of active ingredients, the potency of vaccines is difficult to monitor and therefore easy to counterfeit. As expected, criminal networks have exploited the coronavirus disease 2019 (COVID-19) pandemic by producing fake vaccines. An international alert issued by INTERPOL resulted in confiscation of thousands of fake

### **BOX 6-05** Definitions of poorly regulated medical products

### **IMITATIONS**

Counterfeit: A counterfeit product bears the unauthorized representation of a registered trademark on a product identical or similar to one for which the trademark is registered.

Falsified: A falsified product falsely represents the product's identity, source, or both.

### **AUTHENTICS**

Substandard: A substandard product fails to meet national specifications cited in an accepted pharmacopeia or in the manufacturer's approved dossier.

Degraded: A degraded product has undergone chemical or physical changes due to incorrect storage conditions.

(continued)



### AVOIDING POORLY REGULATED MEDICINES & MEDICAL PRODUCTS **DURING TRAVEL (CONTINUED)**

vaccines in China and in South Africa, INTERPOL's Secretary General described the number of seized vaccines as being "the tip of the iceberg."

### AVOIDING COUNTERFEIT DRUGS WHEN TRAVELING

The best way to avoid counterfeit drugs is to reduce the need to purchase medications abroad. Instruct travelers to purchase anticipated amounts of medications for chronic conditions (e.g., arthritis, diabetes, hypertension), medications for travelers' diarrhea, and prophylactic medications for infectious diseases (e.g., malaria) before traveling. Advise travelers to avoid buying drugs online, because the source of the medication often cannot be verified. Travelers should also be aware that other health-related items obtained abroad (e.g., medical devices, insect repellents, mosquito nets) also could be counterfeit, falsified, or substandard.

In preparation for international travel, travelers should obtain all medicines and other health-related items needed for the trip. Prescriptions written in the United States usually cannot be filled overseas, and although many US prescription medications are available for over-the-counter purchase in foreign countries, some might not be available at all. Because checked baggage can get lost, travelers should pack medications and first aid items in a carryon bag, and bring extra medicine in case of travel delays. Travelers should carry medicines in their original containers; for prescription drugs, the patient's name and dose regimen should appear on the container. Travelers also should bring the "patient prescription information" sheet, which provides information on common generic and brand names, use, side effects, precautions, and drug interactions. Travelers should check with the embassies of their destination countries for prohibited drugs; many countries have restrictions on medicines, including over-the-counter medications, entering their borders.

If travelers run out of and require additional medications, they should take steps to ensure the medicines they buy are safe (see Box 6-06

### **BOX 6-06** Purchasing medicines overseas: a good practices checklist for international travelers

- ☐ Obtain medicines from a legitimate pharmacy; the local US embassy or consulate might be able to help locate legitimate local pharmacies. Do not buy from open markets, street vendors, or suspicious-looking pharmacies; request a receipt when making the purchase.
- ☐ Do not buy medicines priced substantially lower than the typical price. Although generic medications are usually less expensive, many counterfeit brand names are sold at prices substantially lower than normal.
- ☐ Make sure the medicines are in their original packages or containers. If you receive medicines as loose tablets or capsules supplied in a plastic bag or envelope, ask the pharmacist to show you the container from which the medicine was dispensed. Record the brand, batch number, and expiration date.

- Sometimes a wary consumer will prompt the seller into supplying quality medicine rather than a counterfeit or substandard medicine.
- ☐ Be familiar with your medications. The size, shape, color, and taste of counterfeit medicines might be different from the authentic product. Discoloration, splits, cracks, spots, and stickiness of tablets or capsules are indications of possible counterfeit. These defects also could indicate improper storage. Keep examples of authentic medications to compare if you purchase the same brand.
- ☐ Be familiar with the packaging. Different color inks, poor-quality printing or packaging materials, and misspelled words are clues to counterfeit drugs. Keep an example of packaging for comparison and observe the expiration date.

Table 6-01 Online resources for travelers purchasing medicines & medical products overseas

ORGANIZATION / SOURCE	RESOURCE	AVAILABLE FROM
Drugs.com	Pill Identifier	www.drugs.com/pill_identification.html
International Society of Travel Medicine	Database on International Regulations on Importation of Medicines for Personal Use	www.istm.org/files/Documents/Groups/ PPG/2nd%20Edition%20Carrying%20 Medicines%20Database.pdf
Transportation Security Administration	Disabilities and Medical Conditions	www.tsa.gov/travel/special-procedures
US Centers for Disease Control and Prevention	Counterfeit Medicines	https://wwwnc.cdc.gov/travel/page/ counterfeit-medicine
US Customs and Border Protection	Prohibited and Restricted Items (see Medication)	www.cbp.gov/travel/us-citizens/ know-before-you-go/ prohibited-and-restricted-items
US Food and Drug Administration	Drug Safety and Availability	www.fda.gov/drugs/ drug-safety-and-availability
US Pharmacopeia	Medicines Quality Database (MQDB)	www.usp.org/global-public-health/ medicines-quality-database
World Health Organization	Substandard and falsified medical products	www.who.int/news-room/fact-sheets/detail/ substandard-and-falsified-medical-products

for a traveler checklist of good practices, and Table 6-01 for a list of online resources). One way to ensure medication safety is by comparing distinguishing features of the packaging, especially when authentic packaging is

unavailable or if the traveler is not familiar with the brand. For example, the batch and lot numbers, manufacturing date, and expiration date printed on the outside of the box should match what is on the insert or blister pack.

### **BIBLIOGRAPHY**

INTERPOL. Fake COVID vaccine distribution network dismantled after INTERPOL alert, 3 March 2021. Available from: www.interpol.int/ News-and-Events/News/2021/Fake-COVID-vacc ine-distribution-network-dismantled-after-INTER POL-alert.

Institute of Medicine. Countering the problem of falsified and substandard drugs. Washington, DC: The National Academics Press; 2013.

Nayyar GML, Bremen JG, Herrington JE. The global pandemic of falsified medicines: laboratory and field innovations and policy perspectives. Am J Trop Med Hyg. 2015;92(6 suppl):2-7.

World Health Organization. Full list of WHO Medical Products Alerts. Available from: www.who.int/ teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts.

World Health Organization. Medicines: counterfeit medicines [fact sheet no. 275]. Geneva: World Health Organization; 2018. Available from: www. who.int/news-room/fact-sheets/detail/substand ard-and-falsified-medical-products.

... perspectives chapters supplement the clinical guidance in this book with additional content, context, and expert opinion. The views expressed do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).



### MEDICAL TOURISM

Matthew Crist, Grace Appiah, Laura Leidel, Rhett Stoney

Medical tourism is the term commonly used to describe international travel for the purpose of receiving medical care. Medical tourists pursue medical care abroad for a variety of reasons, including decreased cost, recommendations from friends or family, the opportunity to combine medical care with a vacation destination, a preference to receive care from a culturally similar provider, or a desire to receive a procedure or therapy not available in their country of residence.

Medical tourism is a worldwide, multibillion-dollar market that continues to grow with the rising globalization of health care. Surveillance data indicate that millions of US residents travel internationally for medical care each year. Medical tourism destinations for US residents include Argentina, Brazil, Canada, Colombia, Costa Rica, Cuba, the Dominican Republic, Ecuador, Germany, India, Malaysia, Mexico, Nicaragua, Peru, Singapore, and Thailand. Categories of procedures that US medical tourists pursue include cancer treatment, dental care, fertility treatments, organ and tissue transplantation, and various forms of surgery, including bariatric, cosmetic, and non-cosmetic (e.g., orthopedic).

Most medical tourists pay for their care at time of service and often rely on private companies or medical concierge services to identify foreign health care facilities. Some US health insurance companies and large employers have alliances with health care facilities outside the United States to control costs.

## CATEGORIES OF MEDICAL TOURISM

### Cosmetic Tourism

Cosmetic tourism, or travel abroad for aesthetic surgery, has become increasingly popular. The American Society of Plastic Surgeons (ASPS) reports that most cosmetic surgery patients are women 40–54 years old. The most common procedures sought by cosmetic tourists include abdominoplasty, breast augmentation, eyelid surgery,

liposuction, and rhinoplasty. Popular destinations often are marketed to prospective medical tourists as low cost, all-inclusive cosmetic surgery vacations for elective procedures not typically covered by insurance. Complications, including infections and surgical revisions for unsatisfactory results, can compound initial costs.

## Non-Cosmetic Medical Tourism CANCER TREATMENT

Oncology, or cancer treatment, tourism often is pursued by people looking for alternative treatment options, better access to care, second opinions, or a combination of these. Oncology tourists are a vulnerable patient population because the fear caused by a cancer diagnosis can lead them to try potentially risky treatments or procedures. Often, the treatments or procedures used abroad have no established benefit, placing the oncology tourist at risk for harm due to complications (e.g., bleeding, infection) or by forgoing or delaying approved therapies in the United States.

### **DENTAL CARE**

Dental care is the most common form of medical tourism among US residents, in part due to the rising cost of dental care in the United States; a substantial proportion of people in the United States do not have dental insurance or are underinsured. Dentists in destination countries might not be subject to the same licensure oversight as their US counterparts, however. In addition, practitioners abroad might not adhere to standard infection-control practices used in the United States, placing dental tourists at a potential risk for infection due to bloodborne or waterborne pathogens.

### **FERTILITY TREATMENTS**

Fertility tourists are people who seek reproductive treatments in another country. Some do so to avoid associated barriers in their home country, including high costs, long waiting lists, and restrictive policies. Others believe they will receive higher quality care abroad. People traveling to other countries for fertility treatments often are in search of assisted reproductive technologies (e.g., artificial insemination by a donor, in vitro fertilization). Fertility tourists should be aware, however, that practices can vary in their level of clinical expertise, hygiene, and technique.

### PHYSICIAN-ASSISTED SUICIDE

The practice of a physician facilitating a patient's desire to end their own life by providing either the information or the means (e.g., medications) for suicide is illegal in most countries. Some people consider physician-assisted suicide (PAS) tourism, also known as suicide travel or suicide tourism, as a possible option. Most PAS tourists have been diagnosed with a terminal illness or suffer from painful or debilitating medical conditions. PAS is legal in Belgium, Canada, Luxembourg, the Netherlands, Switzerland, and New Zealand, making these the destinations selected by PAS travelers.

## REHAB TOURISM FOR SUBSTANCE USE DISORDERS

Rehab tourism involves travel to another country for substance use disorder treatment and rehabilitation care. Travelers exploring this option might be seeking a greater range of treatment options at less expense than what is available domestically (see Sec. 3, Ch. 5, Substance Use & Substance Use Disorders, and Box 3-10 for pros and cons of rehab tourism).

### TRANSPLANT PROCEDURES

Transplant tourism refers to travel for receiving an organ, tissue, or stem cell transplant from an unrelated human donor. The practice can be motivated by reduced cost abroad or an effort to reduce the waiting time for organs. Xenotransplantation refers to receiving other biomaterial (e.g., cells, tissues) from nonhuman species, and xenotransplantation regulations vary from country to country. Many procedures involving injection of human or nonhuman cells have no scientific evidence to support a therapeutic benefit, and adverse events have been reported.

Depending on the location, organ or tissue donors might not be screened as thoroughly as they are in the United States; furthermore, organs and other tissues might be obtained using unethical means. In 2009, the World Health Organization released the revised Guiding Principles on Human Cell, Tissue, and Organ Transplantation, emphasizing that cells, tissues, and organs should be donated freely, in the absence of any form of financial incentive.

Studies have shown that transplant tourists can be at risk of receiving care that varies from practice standards in the United States. For instance, patients might receive fewer immunosuppressive drugs, increasing their risk for rejection, or they might not receive antimicrobial prophylaxis, increasing their risk for infection. Traveling after a procedure poses an additional risk for infection in someone who is immunocompromised.

## THE PRETRAVEL CONSULTATION

Ideally, medical tourists will consult a travel medicine specialist for travel advice tailored to their specific health needs 4-6 weeks before travel. During the pretravel consultation, make certain travelers are up to date on all routine vaccinations, that they receive additional vaccines based on destination, and especially encourage hepatitis B virus immunization for unvaccinated travelers (see Sec. 2, Ch. 3, Vaccination & Immunoprophylaxis-General Principles, and Sec. 5, Part 2, Ch. 8, Hepatitis B). Counsel medical tourists that participating in typical vacation activities (e.g., consuming alcohol, participating in strenuous activity or exercise, sunbathing, swimming, taking long tours) during the postoperative period can delay or impede healing.

Advise medical tourists to also meet with their primary care provider to discuss their plan to seek medical care outside the United States, to address any concerns they or their provider might have, to ensure current medical conditions are well controlled, and to ensure they have a sufficient supply of all regular medications to last the duration of their trip. In addition, medical tourists should be aware of instances in which US medical professionals have elected not to treat medical tourists presenting with complications resulting from

recent surgery, treatment, or procedures received abroad. Thus, encourage medical tourists to work with their primary care provider to identify physicians in their home communities who are willing and available to provide follow-up or emergency care upon their return.

Remind medical tourists to request copies of their overseas medical records in English and to provide this information to any health care providers they see subsequently for followup. Encourage medical tourists to disclose their entire travel history, medical history, and information about all surgeries or medical treatments received during their trip.

### RISKS & COMPLICATIONS

All medical and surgical procedures carry some risk, and complications can occur regardless of where treatment is received. Advise medical tourists not to delay seeking medical care if they suspect any complication during travel or after returning home. Obtaining immediate care can lead to earlier diagnosis and treatment and a better outcome.

### Infection

Among medical tourists, the most common complications are infection related. Inadequate infection-control practices place people at increased risk for bloodborne infections, including hepatitis B, hepatitis C, and HIV; bloodstream infections; donor-derived infections; and wound infections. Moreover, the risk of acquiring antibioticresistant infections might be greater in certain countries or regions; some highly resistant bacterial (e.g., carbapenem-resistant Enterobacterales [CRE]) and fungal (e.g., Candida auris) pathogens appear to be more common in some countries where US residents travel for medical tourism (see Sec. 11. Ch. 5. Antimicrobial Resistance).

Several infectious disease outbreaks have been documented among medical tourists, including CRE infections in patients undergoing invasive medical procedures in Mexico, surgical site infections caused by nontuberculous mycobacteria in patients who underwent cosmetic surgery in the Dominican Republic, and Q fever in patients who received fetal sheep cell injections in Germany.

### **Noninfectious Complications**

Medical tourists have the same risks for noninfectious complications as patients receiving medical care in the United States. Noninfectious complications include blood clots, contour abnormalities after cosmetic surgery, and surgical wound dehiscence.

### Travel-Associated Risks

Traveling during the post-operative or postprocedure recovery period or when being treated for a medical condition could pose additional risks for patients. Air travel and surgery independently increase the risk for blood clots, including deep vein thrombosis and pulmonary emboli (see Sec. 8, Ch. 3, Deep Vein Thrombosis & Pulmonary Embolism). Travel after surgery further increases the risk of developing blood clots because travel can require medical tourists to remain seated for long periods while in a hypercoagulable state.

Commercial aircraft cabin pressures are roughly equivalent to the outside air pressure at 6,000-8,000 feet above sea level. Medical tourists should not fly for 10 days after chest or abdominal surgery to avoid risks associated with changes in atmospheric pressure. ASPS recommends that patients undergoing laser treatments or cosmetic procedures to the face, eyelids, or nose, wait 7-10 days after the procedure before flying. The Aerospace Medical Association published medical guidelines for air travel that provide useful information on the risks for travel with certain medical conditions (see www.asma.org/asma/media/asma/Travel-Publi cations/paxguidelines.pdf).

### **RISK MITIGATION**

Professional organizations have developed guidance, including template questions, that medical tourists can use when discussing what to expect with the facility providing the care, with the group facilitating the trip, and with their own domestic health care provider. For instance, the American Medical Association developed guiding principles on medical tourism for employers, insurance companies, and other entities that facilitate or incentivize medical care outside the United States (Box 6-07). The American College of Surgeons (ACS) issued a similar statement on medical and surgical tourism, with the additional recommendation.

## **BOX 6-07** American Medical Association's guiding principles on medical tourism<sup>1</sup>

Employers, insurance companies, and other entities that facilitate or incentivize medical care outside the United States should adhere to the following principles:

- Receiving medical care outside the United States must be voluntary.
- Financial incentives to travel outside the
  United States for medical care should not
  inappropriately limit the diagnostic and
  therapeutic alternatives that are offered to
  patients or restrict treatment or referral options.
  Patients should only be referred for medical care
  to institutions that have been accredited by
- to institutions that have been accredited by recognized international accrediting bodies (e.g., the Joint Commission International or the International Society for Quality in Health Care).
- Prior to travel, local follow-up care should be coordinated, and financing should be arranged to ensure continuity of care when patients return from medical care outside the United States.
- Coverage for travel outside the United States for medical care should include the costs of

- necessary follow-up care upon return to the United States.
- Patients should be informed of their rights and legal recourse before agreeing to travel outside the United States for medical care.
- Access to physician licensing and outcome data, as well as facility accreditation and outcomes data, should be arranged for patients seeking medical care outside the United States.
- The transfer of patient medical records to and from facilities outside the United States should be consistent with Health Insurance Portability and Accountability Action (HIPAA) guidelines.
- Patients choosing to travel outside the United States for medical care should be provided with information about the potential risks of combining surgical procedures with long flights and vacation activities.

<sup>1</sup>American Medical Association (AMA). New AMA Guidelines on Medical Tourism. Chicago: AMA; 2008. Available from: www.medretreat.com/templates/UserFi les/Documents/Whitepapers/AMAGuidelines.pdf.

that travelers obtain a complete set of medical records before returning home to ensure that details of their care are available to providers in the United States, which can facilitate continuity of care and proper follow-up, if needed.

### Reviewing the Risks

Multiple resources are available for providers and medical tourists assessing medical tourism–related risks (see Table 6-02). When reviewing the risks associated with seeking health care abroad, encourage medical tourists to consider several factors besides the procedure; these include the destination, the facility or facilities where the procedure and recovery will take place, and the treating provider.

Make patients aware that medical tourism websites marketing directly to travelers might not include (or make available) comprehensive details on the accreditations, certifications, or qualifications of advertised facilities or providers. Local standards for facility accreditation and provider certification vary, and might not be the same as

those in the United States; some facilities and providers abroad might lack accreditation or certification. In some locations, tracking patient outcome data or maintaining formal medical record privacy or security policies are not standard practices.

Medical tourists also should be aware that the drugs and medical products and devices used in other countries might not be subject to the same regulatory scrutiny and oversight as in the United States. In addition, some drugs could be counterfeit or otherwise ineffective because the medication expired, is contaminated, or was improperly stored (for more details, see the previous chapter in this section, . . . perspectives: Avoiding Poorly Regulated Medicines & Medical Products During Travel).

### **Checking Credentials**

ACS recommends that medical tourists use internationally accredited facilities and seek care from providers certified in their specialties through a process equivalent to that established by the

### Table 6-02 Online medical tourism resources

ORGANIZATION / SOURCE	RESOURCE	AVAILABLE FROM
Accreditation Association for Ambulatory Health Care	Accredited health care organization search tool	https://eweb.aaahc.org/eweb/dynamicpage. aspx?site=aaahc_site&webcode=find_orgs
Aerospace Medical Association	Medical Guidelines for Airline Passengers (2002)	www.asma.org/asma/media/asma/Travel- Publications/paxguidelines.pdf
The Aesthetic Society	Find a Plastic Surgeon search tool	www.surgery.org/consumers/find-a-plastic- surgeon
	Guidelines for patients seeking cosmetic procedures abroad	www.surgery.org/consumers/consumer- resources/consumer-tips/guidelines-for- patients-seeking-cosmetic-procedures-abroad
American Academy of Orthopaedic Surgeons	Bulletin (July 2007)	https://aaos.org/aaosnow/2007/jul/cover/cover1/
	Bulletin (February 2008)	https://aaos.org/aaosnow/2008/feb/managing/ managing7/
American College of Surgeons	Statement on Medical and Surgical Tourism	www.facs.org/about-acs/statements/ 65-surgical-tourism
	Find a Surgeon search tool	www.facs.org/search/find-a-surgeon
American Medical Association	Ethics: Medical Tourism	www.ama-assn.org/delivering-care/ethics/ medical-tourism
	Guidelines on Medical Tourism	www.medretreat.com/templates/UserFiles/ Documents/Whitepapers/AMAGuidelines.pdf
American Society of Plastic Surgeons	ASPS Cautions Plastic Surgery Patients to Approach Holiday Medical Tourism with Vigilance (November 2012)	www.plasticsurgery.org/news/press-releases/ asps-cautions-plastic-surgery-patients-to- approach-holiday-medical-tourism-with- vigilance
	Medical Tourism for Cosmetic Surgery High Risk of Complications, High Costs for Treatment (June 2017)	www.plasticsurgery.org/news/press-releases/ medical-tourism-for-cosmetic-surgery-high- risk-of-complications-high-costs-for-treatment
	Plastic Surgery Abroad Can Lead to Severe Complications after Returning to the US (March 2018)	www.plasticsurgery.org/news/press-releases/ plastic-surgery-abroad-can-lead-to-severe- complications-after-returning-to-the-us
	Medical Tourism Can Put Patients in Legal Limbo (September 2018)	www.plasticsurgery.org/news/press-releases/ medical-tourism-can-put-patients-in-legal-limbo

Table 6-02 Online medical tourism resources (continued)

ORGANIZATION / SOURCE	RESOURCE	AVAILABLE FROM
	Briefing Paper: Cosmetic Surgery Tourism	www.plasticsurgery.org/news/briefing-papers/ briefing-paper-cosmetic-surgery-tourism
	Plastic Surgeon match tool	https://find.plasticsurgery.org
International Society for Aesthetic Plastic Surgery	Find-a-surgeon search tool	www.isaps.org/member-directory/
Joint Commission International	Accredited facilities outside of the United States	www.jointcommissioninternational.org/ JCI-Accredited-Organizations/
US Department of State	Your Health Abroad	https://travel.state.gov/content/travel/en/ international-travel/before-you-go/your-health- abroad.html
World Health Organization	Guiding principles on human cell, tissue and organ transplantation	www.who.int/transplantation/Guiding_ PrinciplesTransplantation_WHA63.22en.pdf

member boards of the American Board of Medical Specialties. Advise medical tourists to do as much advance research as possible on the facility and health care provider they are considering using. Also, inform medical tourists that accreditation does not guarantee a good outcome.

### **FACILITIES**

Accrediting organizations (e.g., The Joint Commission International, Accreditation Association for Ambulatory Health Care) maintain listings of accredited facilities outside of the United States. Encourage prospective medical tourists to review these sources before committing to having a procedure or receiving medical care abroad.

#### **PROVIDERS**

ACS, ASPS, the American Society for Aesthetic Plastic Surgery, and the International Society of Aesthetic Plastic Surgery all accredit physicians abroad. Medical tourists should check the credentials of health care providers with search tools provided by relevant professional organizations.

### Travel Health Insurance

Before travel, medical tourists should check their domestic health insurance plan carefully to understand what services, if any, are covered outside the United States. Additionally, travelers might need to purchase supplemental medical insurance coverage, including medical evacuation insurance; this is particularly important for travelers going to remote destinations or places lacking medical facilities that meet the standards found in high-income countries (see Sec. 6, Ch. 1, Travel Insurance, Travel Health Insurance & Medical Evacuation Insurance). Medical tourists also should be aware that if complications develop, they might not have the same legal recourse as they would if they received their care in the United States.

### Planning for Follow-Up Care

Medical tourists and their domestic physicians should plan for follow-up care. Patients and clinicians should establish what care will be provided abroad, and what the patient will need upon return. Medical tourists should make sure they understand what services are included as

part of the cost for their procedures; some overseas facilities and providers charge substantial fees for follow-up care in addition to the base cost. Travelers also should know whether followup care is scheduled to occur at the same facility as the procedure.

### **ADDITIONAL GUIDANCE FOR US HEALTH CARE PROVIDERS**

Health care facilities in the United States should have systems in place to assess patients at admission to determine whether they have received medical care in other countries. Clinicians should obtain an explicit travel history from patients, including any medical care received abroad. Patients who have had an overnight stay in a health care facility outside the United States within 6 months of presentation should be screened for CRE. Admission screening is available free of charge through the Antibiotic Resistance Laboratory Network (www.cdc.gov/ drugresistance/solutions-initiative/ar-lab-netw ork.html).

Notify state and local public health as soon as medical tourism-associated infections are identified. Returning patients often present to hospitals close to their home, and communication with public health authorities can help facilitate outbreak recognition. Health care facilities should follow all disease reporting requirements for their jurisdiction. Health care facilities also should report suspected or confirmed cases of unusual antibiotic resistance (e.g., carbapenem-resistant organisms, C. auris) to public health authorities to facilitate testing and infection-control measures to prevent further transmission. In addition to notifying the state or local health department, contact the Centers for Disease Control and Prevention at medicaltourism@cdc.gov to report complications related to medical tourism.

### **BIBLIOGRAPHY**

- Adabi K, Stern C, Weichman K, Garfein ES, Pothula A, Draper L, et al. Population health implications of medical tourism. Plast Reconstr Surg. 2017;140(1):66-74.
- Al-Shamsi, H, Al-Hajelli, M, Alrawi, S. Chasing the cure around the globe: medical tourism for cancer care from developing countries. J Glob Onc. 2018;4:1-3.
- Kracalik I, Ham C, Smith AR, Vowles M, Kauber K, Zambrano M, et al. (2019). Notes from the field: Verona integron-encoded metallo-β-lactamase-producing carbapenem-resistant Pseudomonas aeruginosa infections in U.S. residents associated with invasive medical procedures in Mexico, 2015-2018. MMWR Morb Mortal Wkly Rep. 2019;68(20):463-4.
- Pavli A, Maltezou HC. Infectious complications related to medical tourism. J Travel Med. 2021;28(1):taaa210.
- Pereira RT, Malone CM, Flaherty GT. Aesthetic journeys: a review of cosmetic surgery tourism. J Travel Med. 2018;25(1):tay042.

- Robyn MP, Newman AP, Amato M, Walawander M, Kothe C, Nerone JD, et al. Q fever outbreak among travelers to Germany who received live cell therapy—United States and Canada, 2014. MMWR Morb Mortal Wkly Rep. 2015;64(38):1071-3.
- Salama M, Isachenko V, Isachenko E, Rahimi G, Mallmann P, Westphal LM, et al. Cross border reproductive care (CBRC): a growing global phenomenon with multidimensional implications (a systematic and critical review). J Assist Reprod Genet. 2018;35(7):1277-88.
- Schnabel D, Esposito DH, Gaines J, Ridpath A, Barry MA, Feldman KA, et al. Multistate US outbreak of rapidly growing mycobacterial infections associated with medical tourism to the Dominican Republic, 2013-2014. Emerg Infect Dis. 2016;22(8):1340-7.
- Stoney RJ, Kozarsky PE, Walker AT, Gaines JL. Populationbased surveillance of medical tourism among US residents from 11 states and territories: findings from the Behavioral Risk Factor Surveillance System. Infect Control Hosp Epidemiol. 2022;43(7):870-5.



# **Family Travel**

### PREGNANT TRAVELERS

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Pregnancy can cause physiologic changes that require special consideration during travel. With careful preparation, however, most pregnant people can travel safely.

### PRETRAVEL CONSULTATION

The pretravel consultation and evaluation of pregnant travelers (Box 7-01) should begin with a careful medical and obstetric history, specifically assessing gestational age and the presence of factors and conditions that increase risk for adverse pregnancy outcomes. A visit with an obstetric health care provider also should be a part of the pretravel assessment to ensure routine prenatal care and identify any potential problems. Instruct pregnant travelers to carry with them a copy of their prenatal records and physician's contact information.

Review the pregnant person's travel itinerary, including accommodations, activities, and destinations, to guide pretravel health advice. Discourage pregnant travelers from undertaking

unaccustomed vigorous activity. Swimming and snorkeling during pregnancy generally are safe, but falls during waterskiing have been reported to inject water into the birth canal. Most experts advise against scuba diving for pregnant people because of risk for fetal gas embolism during decompression (see Sec. 4, Ch. 4, Scuba Diving: Decompression Illness & Other Dive-Related Injuries). Riding animals, bicycles, or motorcycles presents risks for abdominal trauma.

Educate pregnant people on how to avoid travel-associated risks, manage minor pregnancy discomforts, and recognize more serious complications. Advise pregnant people to seek urgent medical attention if they experience contractions or premature labor; symptoms of deep vein thrombosis (e.g., unusual leg swelling and pain in the calf or thigh) or pulmonary embolism (e.g., unusual shortness of breath); dehydration, diarrhea, or vomiting; severe pelvic or abdominal pain; symptoms of preeclampsia (e.g., severe headaches, nausea and vomiting, unusual

### **BOX 7-01** Pretravel consultation for pregnant travelers: a checklist for health care providers

- ☐ Review vaccination history (e.g., COVID-19, hepatitis A, hepatitis B, measles, pertussis, rubella, varicella, tetanus) and update vaccinations as needed (see text for contraindications during pregnancy)
- □ Policies and paperwork
  - O Discuss supplemental travel insurance, travel health insurance, and medical evacuation insurance; research specific coverage information and limitations for pregnancy-related health issues
  - O Advise travelers to check airline and cruise line policies for pregnant travelers
  - O Provide letter confirming due date and fitness to travel
  - O Provide copy of medical records
- ☐ Prepare for obstetric care at destination
  - O Advise traveler to check medical insurance coverage

- O Advise traveler to arrange for obstetric care at destination, as needed
- ☐ Review signs and symptoms requiring immediate care, including
  - Bleeding
  - O Contractions or preterm labor
  - O Deep vein thrombosis or pulmonary embolism symptoms, which include unusual swelling of leg with pain in calf or thigh, unusual shortness of breath
  - O Pelvic or abdominal pain
  - O Preeclampsia symptoms (e.g., unusual swelling, severe headaches, nausea and vomiting, vision changes)
  - O Rupture of membranes
  - O Vomiting, diarrhea, dehydration

swelling, vision changes); prelabor rupture of the membranes; or vaginal bleeding.

### Contraindications to Travel During Pregnancy

Absolute contraindications are conditions for which the potential harm of travel during pregnancy always outweighs the benefits of travel to the pregnant person or fetus. Relative contraindications are conditions for which travel should be avoided if the potential harm from travel outweighs its benefits (Box 7-02).

Although travel is rarely contraindicated during a normal pregnancy, pregnancies that require frequent antenatal monitoring or close medical supervision might warrant a recommendation that travel be delayed. Educate pregnant travelers that the risk of obstetric complications is greatest in the first and third trimesters of pregnancy.

### Planning for Emergency Care

Obstetric emergencies are often sudden and lifethreatening. Advise all pregnant travelers (but especially those in their third trimester or otherwise at high risk) to identify, in advance, international medical facilities at their destination(s) capable of managing complications of pregnancy, delivery (including by caesarean section), and neonatal problems. Counsel against travel to

### **BOX 7-02** Contraindications to travel during pregnancy

### **ABSOLUTE CONTRAINDICATIONS**

Abruptio placentae Active labor Incompetent cervix Premature labor Premature rupture of membranes Suspected ectopic pregnancy Threatened abortion / vaginal bleeding Toxemia, past or present

### **RELATIVE CONTRAINDICATIONS**

Abnormal presentation Fetal growth restriction History of infertility History of miscarriage or ectopic pregnancy Maternal age <15 or >35 years Multiple gestation Placenta previa or other placental abnormality areas where obstetric care might be less than the standard at home.

Many health insurance policies do not cover the cost of medical treatment for pregnancy or neonatal complications that occur overseas. Pregnant people should strongly consider purchasing supplemental travel health insurance to cover pregnancy-related problems and care of the neonate, as needed. In addition, pregnant travelers should consider medical evacuation insurance coverage in case of pregnancy-related complications (see Sec. 6, Ch. 1, Travel Insurance, Travel Health Insurance & Medical Evacuation Insurance).

### Medications

Over-the-counter drugs and nondrug remedies can help a pregnant person travel more comfortably. For instance, pregnant people can safely use a mild bulk laxative for constipation. In addition, several simple available remedies are effective in relieving the symptoms of morning sickness. Nonprescription remedies include ginger, available as a powder that can be mixed with food or drinks (e.g., tea), and as candy (e.g., lollipops). Similarly, pyridoxine (vitamin B6) is effective in reducing symptoms of morning sickness and is available in tablet form, as well as lozenges and lollipops. Antihistamines (e.g., dimenhydrinate, meclizine) often are used in pregnancy for morning sickness and motion sickness and appear to have a good safety record.

Carefully consider appropriate pain management and use of analgesics during pregnancy. Acetaminophen remains the nonopioid analgesic of choice during pregnancy. Although low-dose aspirin has been demonstrated to be relatively safe during pregnancy for certain clinical indications, it should be used cautiously. Aspirin can increase the incidence of abruption, and other anti-inflammatory agents can cause premature closure of the ductus arteriosus.

Various systems are used to classify drugs with respect to their safety in pregnancy (see www.fda.gov/consumers/free-publications-women/medicine-and-pregnancy). Refer to specific data about the effects of a given drug during pregnancy rather than depending on a classification. Counsel patients to help them make a

balanced decision on the use of medications during pregnancy.

### **Vaccinations**

In the best possible scenario, people should be up to date on routine vaccinations before becoming pregnant. The most effective way of protecting the infant against many diseases is to vaccinate the pregnant person. A summary of current Advisory Committee on Immunization Practices (ACIP) guidelines for vaccinating pregnant people is available at www.cdc.gov/vaccines/pregnancy/hcp/guidelines.html.

### **CORONAVIRUS DISEASE 2019**

Pregnant people are more likely to become more severely ill from coronavirus disease 2019 (COVID-19) than people who are not pregnant. Having COVID-19 during pregnancy increases a person's risk of complications that can affect their pregnancy. For these reasons, the Centers for Disease Control and Prevention (CDC) recommends that people who are pregnant, trying to get pregnant, or who might become pregnant in the future get vaccinated against COVID-19 (www.cdc.gov/coro navirus/2019-ncov/vaccines/recommendations/ pregnancy.html). As of August 2022, the COVID-19 vaccines authorized or approved for use in the United States are nonreplicating vaccines that do not cause infection in the pregnant person or the fetus. Pregnant people may choose to receive any of the COVID-19 vaccines authorized or approved for use in the United States; the ACIP does not state a preference.

COVID-19 vaccination can be safely provided before pregnancy or during any trimester of pregnancy. Available vaccines are highly effective in preventing severe COVID-19, hospitalizations, and deaths; data have shown that the benefits of vaccination during pregnancy, to both the pregnant person and their fetus, outweigh any potential risks. Pregnant people might want to speak with their health care provider before making a decision about receiving COVID-19 vaccine (www.acog.org/covid-19/covid-19-vaccines-and-pregnancy-conversation-guide-for-clinicians), but a consultation is not required before vaccination. Side effects from COVID-19 vaccination in pregnant people are like those expected among

nonpregnant people. Pregnant people can take acetaminophen if they experience fever or other post-vaccination symptoms.

### **INFLUENZA**

The ACIP recommends that all people who are or who will become pregnant during the influenza season have an annual influenza vaccine using inactivated virus. Influenza vaccines can be administered during any trimester.

### **HEPATITIS**

The safety of hepatitis A vaccination during pregnancy has not been determined; because hepatitis A vaccine is produced from inactivated virus, though, the risk to the developing fetus is expected to be low. Weigh the risk associated with vaccination against the risk for infection in pregnant people who could be at increased risk for exposure to hepatitis A virus. According to the ACIP, pregnant people traveling internationally are at risk of hepatitis A virus infection; ACIP recommends vaccination during pregnancy for nonimmune international travelers (www.cdc.gov/ mmwr/volumes/69/rr/rr6905a1.htm).

Limited data suggest that developing fetuses are not at risk for adverse events resulting from vaccination of pregnant people with hepatitis B vaccine (for details, see Sec. 5, Part 2, Ch. 8, Hepatitis B). ACIP recommends vaccinating pregnant people identified as being at risk for hepatitis B virus infection during pregnancy; risk factors include >1 sex partner during the previous 6 months, being evaluated or treated for a sexually transmitted infection, recent or current injection drug use, or having a HBsAg-positive sex partner. In November 2021, ACIP recommended vaccination of all adults 19-59 years old.

### **JAPANESE ENCEPHALITIS**

Data are insufficient to make specific recommendations for use of Japanese encephalitis vaccine in pregnant people (see Sec. 5, Part 2, Ch. 13, Japanese Encephalitis).

### LIVE-VIRUS VACCINES

Most live-virus vaccines, including live attenuated influenza, measles-mumps-rubella, live typhoid (Ty21a), and varicella, are contraindicated during pregnancy. Postexposure prophylaxis of a nonimmune pregnant person exposed to measles can be provided by administering measles immune globulin (IG) within 6 days of exposure; for varicella exposures, varicella-zoster IG can be given within 10 days. Advise people planning to become pregnant to wait ≥4 weeks after receiving a live-virus vaccine before conceiving.

### YELLOW FEVER

Yellow fever vaccine is the exception to the rule about live-virus vaccines being contraindicated during pregnancy. ACIP considers pregnancy a precaution (i.e., a relative contraindication) for yellow fever vaccine. If travel is unavoidable, and the risk for yellow fever virus exposure outweighs the vaccination risk, it is appropriate to recommend vaccination. If the risks for vaccination outweigh the risks for yellow fever virus exposure, consider providing a medical waiver to the pregnant traveler to fulfill health regulations. Because pregnancy might affect immune responses to vaccination, consider performing serologic testing to document an immune response to yellow fever vaccine. Furthermore, if a person was pregnant (regardless of trimester) when they received their initial dose of yellow fever vaccine, they should receive 1 additional dose before they are next at risk for yellow fever virus exposure (see Sec. 5, Part 2, Ch. 26, Yellow Fever).

#### **MENINGOCOCCAL**

According to the ACIP, pregnant (and lactating) people should receive quadrivalent meningococcal vaccine, if indicated (www.cdc.gov/mmwr/ volumes/69/rr/rr6909a1.htm). Meningococcal vaccine might be indicated for international travelers, depending on risk for infection at the destination (see Sec. 5, Part 1, Ch. 13, Meningococcal Disease).

### **POLIO**

No adverse events linked to inactivated polio vaccine (IPV) have been documented among pregnant people or their fetuses. Vaccination of pregnant people should be avoided, however, because of theoretical concerns, IPV can be administered in accordance with the recommended immunization schedule for adults if a

pregnant person is at increased risk for infection and requires immediate protection against polio (see Sec. 5, Part 2, Ch. 17, Poliomyelitis).

### **RABIES**

Administer rabies postexposure prophylaxis with rabies immune globulin and vaccine after any moderate- or high-risk exposure to rabies; consider preexposure vaccine for travelers who have a substantial risk for exposure (see Sec. 5, Part 2, Ch. 18, Rabies).

### **TETANUS-DIPHTHERIA-PERTUSSIS**

Tetanus, diphtheria, and acellular pertussis vaccine (Tdap) should be given during each pregnancy irrespective of a person's history of receiving the vaccine previously. To maximize maternal antibody response and passive antibody transfer to the infant, optimal timing for Tdap administration is between 27 and 36 weeks' gestation (earlier during this time frame is preferred), but it may be given at any time during pregnancy.

### Malaria Prophylaxis

Malaria, caused by Plasmodium spp. parasites transmitted by mosquitoes, can be much more serious in pregnant than in nonpregnant people and is associated with high risks of illness and death for both mother and fetus. Malaria in pregnancy can be characterized by heavy parasitemia, severe anemia, and profound hypoglycemia, and can be complicated by cerebral malaria and acute respiratory distress syndrome. Placental sequestration of parasites might result in fetal loss due to abruption, premature labor, or miscarriage. An infant born to an infected mother is apt to be of low birth weight, and, although rare, congenital malaria is possible.

Because no prophylactic regimen provides complete protection, pregnant people should avoid or delay travel to malaria-endemic areas. If travel is unavoidable, the pregnant person should take precautions to avoid mosquito bites and use an effective prophylactic regimen.

Chloroquine is the drug of choice for pregnant travelers going to destinations with chloroquinesensitive Plasmodium spp., and mefloquine is the drug of choice for pregnant travelers going to destinations with chloroquine-resistant *Plasmodium* 

spp. Doxycycline is contraindicated because of teratogenic effects on the fetus after the fourth month of pregnancy. Primaquine is contraindicated in pregnancy because the infant cannot be tested for glucose-6-phosphate dehydrogenase deficiency, putting the infant at risk for hemolytic anemia. Atovaquone-proguanil is not recommended because of lack of available safety data. A list of the available antimalarial drugs and their uses and contraindications during pregnancy can be found in Sec. 5, Part 3, Ch. 16, Malaria.

### Travel Health Kits

In addition to the recommended travel health kit items for all travelers (see Sec. 2, Ch. 10, Travel Health Kits), pregnant travelers should pack antacids, antiemetic drugs, graduated compression stockings, hemorrhoid cream, medication for vaginitis or yeast infection, prenatal vitamins, and prescription medications. Encourage pregnant travelers to consider packing a blood pressure monitor if travel will limit access to a health center where blood pressure monitoring is available.

### **INFECTIOUS DISEASE** CONCERNS

Respiratory and urinary infections and vaginitis are more likely to occur and to be more severe during pregnancy. Pregnant people who develop travelers' diarrhea or other gastrointestinal infections might be more vulnerable to dehydration than nonpregnant travelers. Stress the need for strict hand hygiene and food and water precautions (see Sec. 2, Ch. 8, Food & Water Precautions). Drinking bottled or boiled water is preferable to chemically treated or filtered water. Pregnant people should not consume water purified by iodine-containing compounds because of potential effects on the fetal thyroid (see Sec. 2, Ch. 9, Water Disinfection).

### Coronavirus Disease 2019

As mentioned previously, pregnant people are at increased risk for severe COVID-19-associated illness (e.g., requiring invasive ventilation or extracorporeal membrane oxygenation) and death compared with people who are not pregnant (see www.cdc.gov/coronavirus/2019-ncov/ need-extra-precautions/pregnant-people.html).

Underlying medical conditions (e.g., chronic kidney disease, diabetes, obesity) and other factors (e.g., age, occupation) can further increase a pregnant person's risk for developing severe illness. Additionally, pregnant people with COVID-19 are at greater risk for preterm birth and other adverse outcomes.

Pregnant people, recently pregnant people, and those who live with or visit them should take steps to protect themselves from getting COVID-19. CDC recommends that people (including those who are pregnant) not travel internationally until they are up to date with their COVID-19 vaccines (www.cdc.gov/coro navirus/2019-ncov/vaccines/stay-up-to-date. html). Additional information for international travelers is available at www.cdc.gov/coronavi rus/2019-ncov/travelers/international-travel/ index.html.

### Hepatitis

Hepatitis A and hepatitis E are both spread by the fecal-oral route (see Sec. 5, Part 2, Ch. 7, Hepatitis A, and Sec. 5, Part 2, Ch. 10, Hepatitis E). Hepatitis A has been reported to increase the risk for placental abruption and premature delivery. Hepatitis E is more likely to cause severe disease during pregnancy and could result in a case-fatality rate of 15%-30%; when acquired during the third trimester, hepatitis E is also associated with fetal complications and fetal death.

### Listeriosis & Toxoplasmosis

Listeriosis and toxoplasmosis (see Sec. 5, Part 3, Ch. 23, Toxoplasmosis) are foodborne illnesses of particular concern during pregnancy because the infection can cross the placenta and cause spontaneous abortion, stillbirth, or congenital or neonatal infection. Warn pregnant travelers to avoid unpasteurized cheeses and uncooked or undercooked meat products. Risk for fetal infection increases with gestational age, but severity of infection is decreased.

### Other Parasitic Infections & Diseases

Parasitic infections and diseases can be a concern, particularly for pregnant people visiting friends and relatives in low- and middle-income

countries. In general, intestinal helminths rarely cause enough illness to warrant treatment during pregnancy. Most, in fact, can be addressed safely with symptomatic treatment until the pregnancy is over. On the other hand, protozoan intestinal infections (e.g., Cryptosporidium, Entamoeba histolytica, Giardia) often do require treatment. These parasites can cause acute gastroenteritis, severe dehydration, and chronic malabsorption resulting in fetal growth restriction. *E. histolytica* can cause invasive disease, including amebic liver abscess and colitis. Pregnant people also should avoid bathing, swimming, or wading in freshwater lakes, rivers, and streams that can harbor the parasitic worms (schistosomes) that cause schistosomiasis (see Sec. 5, Part 3, Ch. 20, Schistosomiasis).

### Travelers' Diarrhea

The treatment of choice for travelers' diarrhea is prompt and vigorous oral hydration; azithromycin or a third-generation cephalosporin may, however, be given to pregnant people if clinically indicated. Avoid use of bismuth subsalicylate because of the potential impact of salicylates on the fetus. In addition, fluoroguinolones are contraindicated in pregnancy due to toxicity to developing cartilage, as noted in experimental animal studies.

### Vectorborne Infections

Pregnant people should avoid mosquito bites when traveling in areas where vectorborne diseases are endemic. Preventive measures include use of Environmental Protection Agencyregistered insect repellants (see www.epa.gov/ins ect-repellents), protective clothing, and mosquito nets (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods). For details on yellow fever vaccine and malaria prophylaxis during pregnancy, see above.

### ZIKA

Zika virus is spread primarily through the bite of an infected Aedes mosquito (Ae. aegypti and Ae. albopictus) but can also be sexually transmitted. The illness associated with Zika can be asymptomatic or mild; some patients report acute onset of conjunctivitis, fever, joint pain, and rash that last for several days to a week after infection.

Birth defects caused by Zika virus infection during pregnancy include brain, eye, and neuro-developmental abnormalities. Because of the risk for birth defects, CDC recommends pregnant people avoid travel to areas with a Zika outbreak, and, for the duration of the pregnancy, to avoid sex or use condoms with anyone who has traveled to a risk area.

Advise pregnant people considering travel to areas with Zika to carefully assess the risks of Zika infection during pregnancy; provide information about prevention strategies, signs and symptoms, and the limitations of Zika testing. Pregnant people should strictly follow steps to prevent mosquito bites and sexual transmission. Additional information, including the most current list of countries and territories where Zika is active, is available at https://wwwnc.cdc.gov/travel/page/zika-information. Guidance for pregnant people can be found on the CDC Zika website, www.cdc. gov/pregnancy/zika/index.html.

## ENVIRONMENTAL HEALTH CONCERNS

Pregnant people should be aware of specific current environmental issues in their international destinations (e.g., natural disasters, special events or gatherings, travel warnings). More information can be found at the CDC Travelers' Health website (https://wwwnc.cdc.gov/travel/notices) and on the destination pages of the US Department of State website (https://travel.state.gov/content/travel/en/international-travel/International-Tra vel-Country-Information-Pages.html).

### Air Quality

Air pollution causes more health problems during pregnancy because ciliary clearance of the bronchial tree is slowed, and mucus is more abundant. For more details on traveling to destinations where air quality is poor, see Sec. 4, Ch. 3, Air Quality & Ionizing Radiation.

### **Extremes of Temperature**

Body temperature regulation is not as efficient during pregnancy, and temperature extremes can create more physiological stress on the pregnant person (see Sec. 4, Ch. 2, Extremes of Temperature). In addition, increases in core temperature (e.g., heat exhaustion, heat stroke), might harm the fetus. The vasodilatory effect of a hot environment and dehydration might cause fainting. For these reasons, then, encourage pregnant travelers to seek air-conditioned accommodations and restrict their level of activity in hot environments. If heat exposure is unavoidable, the duration should be as short as possible to prevent an increase in core body temperature. Pregnant travelers should take measures to avoid dehydration and hyperthermia.

### **High Elevation Travel**

Pregnant people should avoid activities at high elevation unless they have trained for and are accustomed to such activities; those not acclimated to high elevation might experience breathlessness and palpitations. The common symptoms of acute mountain sickness (insomnia, headache, and nausea) frequently are associated with pregnancy, and it might be difficult to distinguish the cause of the symptoms. Most experts recommend a slower ascent with adequate time for acclimatization. No studies or case reports show harm to a fetus if the mother travels briefly to high elevations during pregnancy; recommend that pregnant people not sleep at elevations >12,000 ft (≈3,600 m) above sea level, if possible. Probably the greatest concern is that high-elevation destinations often are inaccessible and far from medical care (see Sec. 4, Ch. 5, High Elevation Travel & Altitude Illness).

## TRANSPORTATION CONSIDERATIONS

Advise pregnant people to follow safety instructions for all forms of transport and to wear seat belts, when available, on all forms of transportation, including airplanes, buses, and cars (see Sec. 8, Ch. 5, Road & Traffic Safety). A diagonal shoulder strap with a lap belt provides the best protection. The shoulder belt should be worn between the breasts with the lap belt low across the upper thighs. When only a lap belt is available, pregnant people should wear it low, between the abdomen and across the upper thighs, not above or across the abdomen.