travelers planning to spend ≥1 month in endemic (mainly rural) areas during June–October, when risk for transmission is greatest.

Consider vaccinating shorter-term travelers (<1 month) who plan to visit rural areas, and travelers at increased risk for JE virus exposure based on anticipated activities or itineraries (e.g., those spending substantial time outdoors or staying in accommodations without air conditioning, mosquito nets, or window screens). Sporadic JE cases have occurred on an unpredictable basis in short-term travelers, including in peri-urban Beijing and Shanghai. See Sec. 5, Part 2, Ch. 13, Japanese Encephalitis, for more detailed information.

MALARIA

In the 1940s, China reported >30 million cases of malaria per year. A 70-year eradication campaign progressively reduced numbers, and in 2021, WHO declared China malaria-free. Travelers should still follow insect bite precautions, however, because of the risk for infection with other vectorborne diseases (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

PLAGUE

Plague outbreaks occur sporadically in the northern and southwestern areas of the country (see Sec. 5, Part 1, Ch. 15, Plague). Plague is rarely seen

BOX 10-03 Visiting a giant panda reserve in Sichuan Province: health considerations for travelers

The giant panda (*Ailuropoda melanoleuca*) is China's national emblem and one of its most iconic images. Native to south central China, the giant panda's natural habitat has been greatly encroached upon and only a small number of these animals now exist in the wild, in remote areas where seeing them is almost impossible. In response, the Chinese government established over 60 giant panda reserves across southwestern China. Travel to Sichuan province to visit one or more of these habitats and to see the stunning scenery has become increasingly popular. In some locations, especially during the hot summer months, giant pandas spend much time inside, viewable only through glass. The Sichuan giant panda reserves were designated a UNESCO World Heritage Site in 2006.

CHENGDU RESEARCH BASE OF GIANT PANDA BREEDING

Located just 10 km (≈6 mi) north of the city of Chengdu, the Chengdu Research Base of Giant Panda Breeding is a well-developed park.

In some reserves (including the Chengdu Research Base), visitors can get closer to the animals by joining a Panda Volunteer program. Participation in these programs is generally available only to adults and must be arranged and paid for in advance. Programs can vary from one day to one month in length and some might require participants to provide certification of good health. Opportunities to photograph the wildlife can be limited.

ANIMAL BITES

Sichuan Province has a large population of free-roaming dogs. Consider any dog bite a rabies risk. Because of the distance from definitive medical care, including postexposure prophylaxis, encourage travelers planning to visit Sichuan to consider rabies preexposure prophylaxis.

Despite their cute and cuddly appearance, giant pandas are wild animals with a very powerful bite. They can also be infected with rabies. Travelers should avoid any temptation to get close to giant pandas for a "selfie" or a hug.

ELEVATION & TERRAIN OF GIANT PANDA RESERVES

The terrain harboring the giant panda reserves is often rugged and at elevations ranging from 1,100 m (≈3,600 ft) to 4,400 m (≈14,400 ft). Advise tourists visiting reserves at high elevation to acclimatize slowly, and to consider carrying acetazolamide.

The region has many smaller reserves, some of which are peri-urban, others of which can be quite remote and require considerable travel or trekking, making them inaccessible to physically challenged or less physically fit travelers.

ROAD TRAVEL RISKS APPLY TO THESE MORE REMOTE RESERVES.

Travelers to less urban reserves should be prepared for remoteness and travel with a well-stocked travel health kit.

FOOD & WATER PRECAUTIONS AND SANITATION

Travelers to Sichuan Province should follow safe food and water precautions.

Flush toilets are unlikely to be available.

in tourists but is a risk to campers, hikers, hunters, spelunkers, and others exposed to wild rodents or flea-infested cats and dogs.

TICK-BORNE ENCEPHALITIS

Tick-borne encephalitis (TBE) is present in northeastern parts of China and is a risk during March–November. Consider recommending TBE vaccination for travelers engaging in outdoor activities (e.g., camping, hiking) in endemic areas (see Sec. 5, Part 2, Ch. 23, Tick-Borne Encephalitis). Even among vaccinated travelers, reinforce the importance of taking preventive measures (e.g., wearing long pants tucked into socks, using insect repellent, regularly checking for ticks).

ENVIRONMENTAL HAZARDS & RISKS

Air Pollution

Rapid economic expansion and industrialization since 1978 has resulted in serious air pollution issues, along with water and soil contamination, that peaked in 2013. Regional haze triggered public anxiety and official concern, leading to the Air Pollution and Control Plan, which was implemented in 2013; subsequently a series of other initiatives to control soil, water, and plastic waste pollution began.

To tackle air pollution, China introduced several policies and measures targeted at reducing emissions and promoting alternative energy production. Increased use of natural gas and restrictions against burning coal are key to these plans. Other measures included closing highly polluting factories, moving factories farther away from population centers, afforestation projects (planting trees in areas where there had been no trees before), and promoting the use of electric vehicles. These measures have resulted in a dramatic reduction in air pollution, particularly in fine particulate matter ($PM_{2.5}$).

Once renowned for its toxic haze, Beijing is no longer among the 10 most polluted cities in the world. Nonetheless, pollution remains a problem in many parts of the country; and China still accounts for over half of the world's 200 most polluted cities. In the spring of 2021, several large sandstorms originating in southern Mongolia blanketed eastern China in hazardous dust. These sandstorms are unpredictable and are likely to continue. Travelers can check 5-day air quality forecasts at https://aqicn.org/map/china.

Short-term exposure to the levels of air pollution in China's megacities can irritate the eyes and throat. Travelers with underlying cardiorespiratory diseases, including asthma, chronic obstructive pulmonary disease, or congestive heart failure, might find their condition exacerbated. In addition, exposure to high levels of air pollution significantly increases the risk for upper and lower respiratory tract infections, including otitis, sinusitis, bronchitis, and pneumonia. Children and older people are most vulnerable.

Even before the COVID-19 pandemic, surgical-style facemasks were fashionable in China's large cities, especially Beijing, Hong Kong, and Shanghai; facemasks provide wearers no protection from air pollution, however. Properly fitted N95 masks can filter out particulates and might be advisable for people determined to engage in outdoor exercise at times when air quality is very poor (see Sec. 4, Ch. 3, Air Quality & Ionizing Radiation). Many facilities, particularly schools, have installed sophisticated central air-filtering devices and constructed enclosed sports venues.

Altitude Illness

Western China is home to some of the tallest mountains in the world. Some popular destinations are Xining (2,295 m; ≈7,500 ft), Lijiang (2,418 m; ≈7,900 ft), Shangri-La (3,280 m; ≈11,000 ft), and Lhasa (3,658 m; ≈12,000 ft). Preparation and gradual ascent to acclimatize are the mainstays travelers should follow to prevent the onset of altitude illness (see Sec. 4, Ch. 5, High Elevation Travel & Altitude Illness).

Visitors planning high elevation travel whose itineraries do not permit gradual acclimatization—or people otherwise known to be at risk for developing acute mountain sickness (AMS)—should carry their own supply of acetazolamide, because it is not reliably available in China. Dexamethasone, used to both prevent and treat AMS and high-altitude cerebral edema, and to potentially prevent high-altitude pulmonary

edema (HAPE), reportedly is available in China. Similarly, nifedipine (as a prevention and treatment for HAPE) reportedly is available. The quality and ready availability of either of these drugs is unknown; thus, as with acetazolamide, travelers should carry a personal supply in a travel health kit.

Animal Bites & Rabies

An analysis of data collected by the GeoSentinel Surveillance Network showed that dog bites are surprisingly common among tourists to China. In addition, in China (as in much of Asia) rabies remains a serious problem. Animal rabies is endemic in China and might even be increasing, especially in the dog population. Thus, travelers should consider any dog or other mammal bite received anywhere in China, including urban areas, a high risk for rabies infection (see Sec. 5, Part 2, Ch. 18, Rabies).

Because international-standard rabies immune globulin is often unavailable, animal bites can be trip-enders, requiring evacuation to Bangkok, Hong Kong, or home, to receive appropriate postexposure prophylaxis (PEP). Rabies is a particular risk for younger children, who are more likely to approach animals and less likely to report bites or scratches. Incorporate a discussion of rabies risk and prevention during pretravel consultations, and develop a strategy with travelers for dealing with possible exposures, including purchasing medical evacuation insurance coverage (see Sec. 6, Ch. 1, Travel Insurance, Travel Health Insurance & Medical Evacuation Insurance). Consider providing long-term travelers and expatriates going to live in China with the rabies preexposure vaccination series.

Human rabies deaths in China peaked at 3,300 cases in 2007 and decreased to 290 cases in 2019; the decline in human rabies deaths is mainly attributable to widespread use of PEP and public PEP awareness.

Natural Disasters

Five of the 10 deadliest natural disasters in history have occurred in China. In the last few decades, almost every type of major hazard except volcanic eruption has hit China, including cold waves, droughts, earthquakes, forest and grassland fires, hailstorms, heat waves, red tides, sandstorms, and torrential rains resulting in debris flows and landslides. Typhoons and storm surges occur regularly along the southern and eastern seaboards.

Earthquakes cause significant death and destruction. For instance, devastating earthquakes struck the western provinces of Qinghai in 2010 and Sichuan in 2019. Advise US citizen travelers to enroll with the Department of State's Smart Traveler Enrollment Program (STEP; https://step.state.gov/step); STEP will provide travelers with information and alerts from local US embassies or consulates about disasters, safety, and security issues at their destination.

Vitamin D Deficiency

Vitamin D deficiency is a major issue in the northern provinces of China, where (despite the progress in reducing air pollution noted previously) smog blocks out sunlight, leading to inadequate vitamin D absorption even during the summer months. To decrease the risk of osteomalacia and osteoporosis in travelers spending >6 months in China, prescribe vitamin D supplementation.

Wet Markets

So-called "wet markets" are common throughout China, south Asia, and southeast Asia. The term wet market is a generic one, encompassing many types of marketplaces selling perishable goods; some sell only fruit and vegetables, but others sell live animals that are slaughtered on-site after purchase. Most do not sell wild or exotic animals, and the tendency to lump all wet markets together has fueled Sinophobia related to the origins of the COVID-19 pandemic.

The exotic animal trade has been banned in China, but smuggling of animals (e.g., pangolins) is highly profitable and difficult to control. A coordinated international response will be required to curb the exotic animal trade. Travelers should avoid visiting markets selling live animals because these have been linked with many zoonotic outbreaks, including monkeypox and severe acute respiratory syndrome (SARS). Avian influenza transmission is another reason for travelers to avoid live animal markets.

SAFETY & SECURITY

Crime

Rates of violent crime are low in China, but minor theft, pickpocketing, and various forms of scams and fraud do occur, especially in densely populated and more heavily touristed areas. Scams targeting foreign businesses also have been reported. Travelers should remain vigilant about their personal belongings, and avoid responding to emails from, or giving out sensitive information to, unknown sources.

Political Unrest

Travelers should be aware of and avoid involvement in protests and flare-ups of unrest in places as diverse as Hong Kong, Tibet, and Xinjiang Province. Travelers also should avoid public criticism of the Communist Party or the government. The internet is censored, and many widely used social media sites might be unavailable.

Traffic-Related Injuries

Traffic in China is often chaotic. The rate of traffic crashes, including fatal ones, is among the highest in the world (see Sec. 8, Ch. 5, Road & Traffic Safety). Traffic crashes, even minor ones, can create major traffic jams and sometimes turn into violent altercations, particularly when foreign travelers are involved (see Sec. 4, Ch. 11, Safety & Security Overseas).

China has not signed the convention that created the International Driving Permit and requires travelers to have a Chinese license to drive. Recent regulations have allowed foreign travelers to obtain a temporary (≤3 months) driver's license, if they have a valid overseas driver's license *and* a notarized copy translated into Chinese; in addition, travelers are required to attend lessons on Chinese road safety regulations.

Driving is on the right side of the road in mainland China and Taiwan, but on the left in Hong Kong and Macau. If travelers choose to drive, advise them to avoid driving at night or when weather conditions are bad, and to not assume that traffic rules or rights-of-way will be respected. Despite national seatbelt legislation being in effect since 2004, seatbelt use is inconsistent, and rear seatbelts often are unavailable. Use of child safety seats recently become mandatory. For all these reasons, travelers likely will find it safer and simpler to hire a local driver or to use public transportation than to drive themselves. Travelers should take care when opening the door of a taxi or private vehicle, to avoid hitting cyclists or pedestrians.

ELECTRONIC BICYCLES

Electronic bicycles (E-bikes) are popular in China and do not have to be registered. E-bike riders often travel in pedestrian and bicycle lanes as well as with traffic. Because E-bikes have no engine noise, pedestrians might not readily identify an oncoming E-bike. Motor vehicles and E-bikes often drive without lights, making night travel dangerous. Bicycle helmets are rarely worn in China; a new 2020 law requiring helmet use for riders of motorcycles and E-bikes has resulted in a shortage of available helmets.

AVAILABILITY & QUALITY OF MEDICAL CARE

Strongly encourage travelers to invest in travel health insurance, including medical evacuation insurance coverage (see Sec. 6, Ch. 1, Travel Insurance, Travel Health Insurance & Medical Evacuation Insurance). Many hospitals do not accept foreign medical insurance, and patients are expected to pay a deposit to cover the anticipated cost of treatment before care is delivered. Many major cities, including Beijing, Guangzhou, Hong Kong, Shanghai, and Shenzhen have medical facilities that meet international standards. Hospitals in other cities might have "VIP wards" (*gaogan bingfang*) with English-speaking staff. The standard of care in such facilities is somewhat unpredictable, however, and cultural and regulatory differences can cause difficulties for travelers. In rural areas, rudimentary medical care might be all that is available.

Blood & Blood Product Safety

Hepatitis B and hepatitis C virus transmission from poorly sterilized medical equipment remains a risk in remote areas. The blood supply is heavily regulated and generally deemed safe, but is very limited, especially for rare types, including Rhesus negative blood; hospitals

usually have only a few units of blood on hand. Rhogam legally is available only in Hong Kong, and recently in Shenzhen, under a new program permitting drugs and medical equipment already marketed in Hong Kong to be used in the Guangdong–Hong Kong–Macau "Greater Bay Area" after approval.

Emergency Medical Services

Emergency medical services are scarce in many parts of China, most acutely in rural areas. In major cities, 2 types of ambulance are available: general ambulances and ambulances that carry more advanced medical equipment. No recognized paramedic profession exists in China, and ambulances might be staffed instead with doctors or nurses with variable levels of training. In many rural areas, rather than waiting for an ambulance to arrive, injured travelers might be better off taking a taxi or other immediately available vehicle to the nearest major hospital.

Medical Tourism

Most people who choose to try traditional Chinese remedies do so uneventfully, albeit not without accepting some risk. Remind travelers that acupuncture needles can be a source of bloodborne and skin infections; acupressure might be preferable. Herbal medicine products can be contaminated with heavy metals or pharmaceutical agents.

China is currently witnessing an influx of patients coming from Africa seeking treatment not available in their home countries. Medical tourists from high-income countries looking for as-yet unapproved experimental treatments are also a growing market (see Sec. 6, Ch. 4, Medical Tourism).

Pharmacies

Pharmacies often sell prescription medications over the counter, but these can be counterfeit, substandard, or contaminated (see Sec. 6, Ch. 3, . . . *perspectives*: Avoiding Poorly Regulated Medicines & Medical Products During Travel). Advise travelers to bring all their regular medications in sufficient quantity. If travelers need more or other medications, recommend that they visit a reputable clinic or hospital. China allows travelers to bring controlled medications into the country in quantities "reasonable for personal use." Especially for controlled medications, travelers are expected to carry a copy of the written prescription with them and, whenever possible, a signed note from the prescribing physician written on letterhead stationery.

BIBLIOGRAPHY

Amicizia D, Zangrillo F, Lai PL, Iovine M, Panatto D. Overview of Japanese encephalitis disease and its prevention. Focus on IC51 vaccine (IXIARO®). J Prev Med Hyg. 2018;59(1):E99–107.

Burki T. China's successful control of COVID-19. Lancet Infect Dis. 2020;20(11):1240–1.

Davis XM, MacDonald S, Borwein S, Freedman DO, Kozarsky PE, von Sonnenburg F, et al. Health risks in travelers to China: the GeoSentinel experience and implications for the 2008 Beijing Olympics. Am J Trop Med Hyg. 2008;79(1):4–8.

Li Z, Xu Jindong, Xu J, Tan H, Zhang C. Current situation, causes, and countermeasures to NIP vaccine shortages in Guangzhou, China. Hum Vaccin Immunother. 2020;16(1):76–9.

Lu X, Zhang S, Xing J, Wang Y, Chen W, Ding D, et al. Progress of air pollution control in China and its challenges and opportunities in the ecological civilization era. Engineering. 2020;6(12):1423–31.

Miao F, Li N, Yang J, Chen T, Liu Y, Zhang S, et al. Neglected challenges in the control of animal rabies in China. One Health. 2021;12:100212.

Shaw MT, Leggat PA, Borwein S. Travelling to China for the Beijing 2008 Olympic and Paralympic games. Travel Med Infect Dis. 2007;5(6):365–73.

United Nations World Tourism Organization. UNWTO tourism highlights: 2018 Edition. Madrid: The Organization; 2018. Available from: www.e-unwto.org/doi/book/10.18111/9789284419876.

World Health Organization. Global hepatitis report 2017. Geneva: The Organization; 2017. Available from: www.who.int/publications/i/item/global-hepatitis-report-2017.

Xia J, Min L, Shu J. Dengue fever in China: an emerging problem demands attention. Emerg Microbes Infect. 2015;4(1):e3.

Yu X, Li N. Understanding the beginning of a pandemic: China's response to the emergence of COVID-19. J Infect Public Health. 2021;14(3):347–52.

INDIA

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DESTINATION OVERVIEW

India is approximately one-third the size of the United States but has 4 times the population—almost 1.4 billion people—making it the second most populous country in the world, behind China. Rich in history, culture, and diversity, India is the birthplace of 4 of the world's religions: Buddhism, Hinduism, Jainism, and Sikhism. India is experiencing rapid urbanization, as noted in the growth of megacities (e.g., Delhi, Mumbai). India's topography is varied, ranging from tropical beaches to deserts, foothills, and the Himalaya Mountains. Northern India has a more temperate climate; the south is more tropical year-round. Many travelers prefer India during the winter (November–March), when temperatures are more agreeable.

Because of India's size, short-term travelers usually select a region of the country to visit for any given trip. A typical itinerary to the north includes the cities of Agra, Delhi, Varanasi, and cities in Rajasthan State (e.g., Jaipur [the Pink City] and Udaipur). More southern routes might swing through the beaches of Goa and the cities of Bengaluru (Bangalore) and Mumbai. In the east, Kolkata (Calcutta) is considered the cultural capital of the country.

Despite the many and varied itineraries, most health recommendations for travelers to India are similar. The incidence of some illnesses (e.g., those transmitted by mosquitoes) is greater during the monsoon season (June–September), which has high temperatures, heavy rains, and the risk of flooding. Travelers visiting friends and relatives (VFRs) require extra consideration. Because they might stay in rural areas not often visited by tourists or businesspeople, live in homes, and eat and drink with their families, VFR travelers are at greater risk for many travel-related illnesses (see Sec. 9, Ch. 9, Visiting Friends & Relatives: VFR Travel). Some VFR travelers might not seek pretravel health advice since they are returning to their land of origin.

INFECTIOUS DISEASE RISKS

All travelers to India should be up to date with routine immunizations (see www.cdc.gov/vaccines/schedules). Infants 6–11 months old should get 1 dose of measles-mumps-rubella (MMR) vaccine before travel to India; this dose does not count as part of the routine childhood vaccination series. Vaccination against hepatitis A, hepatitis B, and coronavirus disease 2019 (COVID-19) is recommended for travelers to India; specific guidance varies by age of the traveler (see the disease-specific chapters in Section 5). Additionally, India requires travelers coming from countries reporting cases of polio to show proof of oral polio vaccination; travelers should check with the Ministry of Health to learn if there is a requirement for a dose of polio vaccine prior to entry into India.

Enteric Infections & Diseases

CHOLERA

Active cholera transmission has been reported from India in recent years and might be underreported. For current cholera vaccine recommendations for travel to India, refer to the destination page on the Centers for Disease Control and Prevention (CDC) Travelers' Health website (https://wwwnc.cdc.gov/travel/destinations/traveler/none/india). For more information on cholera, see Sec. 5, Part 1, Ch. 5, Cholera.

GIARDIASIS

Giardiasis (see Sec. 5, Part 3, Ch. 12, Giardiasis) is a major cause of diarrheal disease and is associated with morbidity in both children and adults in India. Travelers should maintain good hand hygiene, avoid drinking tap water, and should exclusively consume boiled, bottled, or filtered water (see Sec. 2, Ch. 9, Water Disinfection).

HEPATITIS E

Hepatitis E virus is transmitted through fecally contaminated water and person-to-person

through the fecal–oral route (see Sec. 5, Part 2, Ch. 10, Hepatitis E). Highly endemic to India, hepatitis E is a major cause of acute viral hepatitis and acute liver failure. Infection during pregnancy puts people at greater risk for severe disease as well as adverse pregnancy outcomes (e.g., miscarriage, neonatal demise).

Travelers drinking untreated water or going to areas with poor sanitation are at risk for infection. Travelers should maintain good hand hygiene; avoid tap water; drink only boiled, bottled, or filtered water; and eat thoroughly cooked meats (see Sec. 2, Ch. 8, Food & Water Precautions). Travelers immunized against hepatitis A who develop symptomatic hepatitis likely have hepatitis E.

TRAVELERS' DIARRHEA

Travelers' diarrhea (TD) is acquired through ingestion of contaminated food, water, or beverages, particularly in places where basic hygiene and sanitation infrastructure is poor. Both cooked and uncooked foods are potential vehicles for infection if handled improperly. The risk for TD is high in India; travelers have >60% likelihood of developing TD during a 2-week journey. Discuss self-treatment for diarrheal illness with travelers (see Sec. 2, Ch. 6, Travelers' Diarrhea, and Sec. 2, Ch. 8, Food & Water Precautions).

TYPHOID & PARATYPHOID FEVER

In the United States, ≈85% of cases of typhoid fever are in people who traveled to India or other countries in South Asia (see Sec. 5, Part 1, Ch. 24, Typhoid & Paratyphoid Fever). Thus, even for short-term travel, typhoid vaccine is recommended. Patients hesitant to be vaccinated might be persuaded by learning that typhoid fever acquired in South Asia is typically multidrug-resistant, and in a growing number of instances extensively drug–resistant. Remind all travelers to India to also practice good hand hygiene and follow safe food and water precautions.

Paratyphoid fever, a clinically similar disease caused by *Salmonella enterica* serotypes Paratyphi A, B, and C, has become increasingly prevalent in South Asia, but typhoid vaccines are not protective against this infection.

Respiratory Infections & Diseases

CORONAVIRUS DISEASE 2019

Nationwide, COVID-19 vaccine coverage in India is low. For current information on COVID-19 in India, consult the US Embassy & Consulates in India website (https://in.usembassy.gov/). For the US government's COVID-19 international travel requirements and recommendations, see www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel/index.html. All travelers going to India should be up to date with their COVID-19 vaccines (www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html).

ENDEMIC FUNGI

Four environmentally transmitted fungal pathogens are predominant to India; risk to travelers varies by activity and underlying health conditions.

ASPERGILLOSIS

Aspergillus spp. are airborne fungi that cause a broad array of illnesses ranging from mild to severe. Azole resistance and unavailability of amphotericin B complicate treatment. Most severe aspergillosis illness occurs in patients who are severely immunocompromised or critically ill.

CRYPTOCOCCOSIS

Cryptococcus neoformans exists in the environment worldwide. The fungus is typically found in soil, on decaying wood, in tree hollows, or in bird droppings (see www.cdc.gov/fungal/diseases/cryptococcosis-neoformans/causes.html). When inhaled, *C. neoformans* can cause a pneumonia-like illness. *C. neoformans* also is known to cause meningitis, especially in people who are immunocompromised or living with HIV. Diagnostic testing is limited in India.

HISTOPLASMOSIS

In areas where *Histoplasma* spp. are endemic, occupational and recreational (e.g., bat or bird-watching, cave exploration) activities that disrupt the soil surface can release infectious mold spores into the air. If inhaled, these spores can cause acute pulmonary disease and, more rarely, focal or disseminated extrapulmonary infection (see Sec. 5, Part 4, Ch. 2, Histoplasmosis).

MUCORMYCOSIS

Various modes of transmission (inhalation being most common) for *Mucorales* spp. have been described. Underlying diabetes mellitus and glucocorticoid steroid use are among the major risk factors for mucormycosis in India. Mucormycosis has become a risk among patients recovering from COVID-19 and is associated with poor outcomes in these patients.

INFLUENZA

Influenza virus circulation in India usually peaks during the monsoon season (June–September) with secondary peaks during winter (November–February). Furthermore, the actual timing of the influenza season varies across the country due to differences in regional climates. Influenza vaccine coverage in India is assumed to be very low (no official data are available). Travelers who receive the Northern Hemisphere influenza vaccine might not be fully protected from the viral strain circulating in India and should observe all necessary behavioral precautions to protect themselves from influenza, including frequent handwashing and respiratory etiquette. Travelers to India are strongly encouraged to receive an influenza vaccine directed against the Southern Hemisphere influenza strains from their health care providers, either in the United States (if available) or in India.

TUBERCULOSIS

Approximately 25% of all tuberculosis (TB) cases worldwide are reported from India. Travelers planning to work in high-risk settings or in crowded institutions (e.g., homeless shelters, hospitals, medical clinics, prisons) are at risk for exposure. Travelers visiting ill friends or relatives or engaging in congregate activities (e.g., religious gatherings) also can face TB exposure risk.

Discuss the importance of testing before and after travel, and measures travelers can take to prevent disease. Travelers with anticipated exposure risks should undergo tuberculin skin testing have an interferon-γ release assay (IGRA) before leaving the United States (see Sec. 5, Part 1, Ch. 23, . . . *perspectives*: Testing Travelers for *Mycobacterium tuberculosis* Infection). If a tuberculin skin test is used, CDC recommends the 2-step method for establishing a baseline. If the predeparture test results are negative, repeat the same type of test 8–10 weeks after the traveler returns from India.

Use of bacillus Calmette-Guérin (BCG) vaccine in health care workers who will have increased risk of exposure during travel has been proposed, although this recommendation remains controversial (see Sec. 5, Part 1, Ch. 22, Tuberculosis). US Food and Drug Administration–approved BCG formulations are no longer available in the United States.

Sexually Transmitted Infections & HIV

As of 2019, an estimated 2.3 million people in India were living with HIV infection. Although the reported adult HIV prevalence in India is low, prevalence is much greater in specific locations (e.g., in the states of Manipur, Mizoram, Nagaland) and among high-risk populations (e.g., people who inject drugs, transgender people, men who have sex with men, and female sex workers). Condomless sex increases a traveler's risk for HIV and other sexually transmitted infections, including chlamydia, gonorrhea, and syphilis.

Indian law penalizes acts related to prostitution, including running a brothel, soliciting, and trafficking. High-quality condoms and other barrier methods are available for sale in drugstores in India. Homosexuality is not illegal in India.

Skin Infections

SUPERFICIAL DERMATOPHYTOSIS

In addition to emerging viral and multidrug-resistant bacterial pathogens, superficial dermatophytosis has become a significant problem for travelers to India, largely due to the presence of a widespread fungal strain that is highly resistant to treatment. Indiscriminate use of topical antifungal + highly potent steroid combination preparations is believed to have contributed to the rise of the fungal strain (see www.cdc.gov/fungal/diseases/ringworm/steroids.html). Travelers who develop a rash they think is ringworm should be aware that creams sold widely in drugstores in India can worsen the infection and cause other health problems. Consider prescribing a product that travelers can take in their travel health kit. For severe or recurrent infections, consider

posttravel molecular testing for species identification (see Sec. 11, Ch. 8, Dermatologic Conditions).

Soil- & Waterborne Infections

HELMINTHS

India accounts for 65% of soil-transmitted helminth infections in Southeast Asia, and 27% of all cases globally. Pathogens are found in both urban and rural areas, and include roundworm (*Ascaris lumbricoides*), hookworm (*Ancylostoma duodenale* and *Necatur americanus*), and whipworm (*Trichuris trichiura*). Symptoms might be nonspecific and include abdominal pain, diarrhea (with blood or mucous), fatigue, nausea, vomiting, and weight loss. To reduce the risk for infection, travelers should pay attention to hand hygiene, safe food and water precautions, and always wear shoes (see Sec. 5, Part 3, Ch. 13, Soil-Transmitted Helminths).

Vectorborne Diseases

CHIKUNGUNYA, DENGUE & ZIKA

During the last several years, India has experienced outbreaks of chikungunya, transmitted by infected *Aedes* species (*Ae. aegypti* or *Ae. albopictus*) mosquitoes. Chikungunya symptoms are similar to those of dengue and malaria, but often with severe and persistent arthralgia (see Sec. 5, Part 2, Ch. 2, Chikungunya).

Dengue is transmitted by infected *Aedes* species (*Ae. aegypti* or *Ae. albopictus*) mosquitoes and is endemic to all of India except at high elevation in mountainous regions (see Sec. 5, Part 2, Ch. 4, Dengue). Large outbreaks can occur, including in many urban areas. Incidence is greatest during the wet summer season, which includes the monsoon season (June–September). *Aedes* mosquitoes bite both indoors and outdoors. Travelers to India should take measures to protect themselves from mosquito bites (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

Zika is a risk in India. Because of the possibility for birth defects in infants born to mothers infected with Zika during pregnancy, people who are pregnant or trying to become pregnant should review the most recent recommendations at https://wwwnc.cdc.gov/travel/page/zika-information.

JAPANESE ENCEPHALITIS

Japanese encephalitis (JE) virus is present throughout the country. Transmission occurs mostly from May–October in northern states and year-round in southern states. The JE virus is transmitted to humans who live and work in rural areas (typically around rice paddies and irrigation systems), primarily by *Culex* mosquitoes that feed on infected birds, pigs, and other mammals. Symptoms include diarrhea, fever, severe headache, vomiting, general weakness, and neurological symptoms. Vaccination is recommended for people traveling extensively in rural areas, long-term travelers, and people assigned to work in endemic areas (see Sec. 5, Part 2, Ch. 13, Japanese Encephalitis).

LEISHMANIASIS (KALA AZAR)

Visceral leishmaniasis (VL), transmitted by sandflies (*Phlebotomus argentipes*), presents with acute fever and splenomegaly (see Sec. 5, Part 3, Ch. 15, Visceral Leishmaniasis). Travelers to India should take measures to protect themselves from both day- and night-biting sandflies (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

LYMPHATIC FILARIASIS

Lymphatic filariasis (LF) is transmitted by several mosquito vectors that bite during day, evening, and night, including *Aedes*, *Anopheles*, and *Culex* mosquito spp. (see Sec. 5, Part 3, Ch .9, Lymphatic Filariasis). LF presents with lymphedema and elephantiasis many years after the infection; in men, LF can present with hydrocele (swelling of the scrotum). In most instances, short-term travelers are at low risk because multiple bites over time are necessary for infection. Long-term travelers and expatriates are at greater risk.

MALARIA

Malaria remains a public health problem in India. Both *Plasmodium vivax* and chloroquine-resistant *P. falciparum* are found throughout India, including the cities of Mumbai and New Delhi; most cases occur in 7 states: Chhattisgarh, Gujarat, Jharkhand, Madhya Pradesh, Odisha, Uttar Pradesh, and West Bengal. Malaria-transmitting mosquitoes bite primarily between dusk and dawn. For recommended prophylaxis and mosquito

bite precautions, see Sec. 2, Ch. 5, Yellow Fever Vaccine & Malaria Prevention Information, by Country; Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods; and Sec. 5, Part 3, Ch. 16, Malaria.

RICKETTSIAL DISEASES

Rickettsial infections, including outbreaks, are present across India; scrub typhus is the most common (see Sec. 5, Part 1, Ch. 18, Rickettsial Diseases). Infection is seasonal (after the rainy season), more prevalent in rural areas, and often presents with nonspecific signs and symptoms. Travelers should wear long sleeves and pants and protect exposed skin with insect repellents when visiting potential vector-infested areas, especially areas with forest and vegetation (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods). Counsel travelers to seek prompt medical care for acute fever onset, rash, or eschar (tan, brown, or black tissue) around an insect bite.

YELLOW FEVER

India has no risk for yellow fever (YF), and CDC has no recommendations for travelers to receive YF vaccine before going to India. The Government of India, however, has strict and carefully defined country entry requirements for proof of vaccination against yellow fever from travelers ≥9 months old (infants <9 months old exempted) arriving from areas with risk of yellow fever virus transmission (for details, see Sec. 2, Ch. 5, Yellow Fever Vaccine and Malaria Prevention Information, by Country).

ENVIRONMENTAL HAZARDS & RISKS

Air Quality

Air pollution is a major public health problem across India, and travelers might encounter high-level exposures to various pollutants in urban, peri-urban, and rural settings. All travelers to India should be aware of local air pollution concerns and any advisories in effect on a day-to-day basis (see Sec. 4, Ch. 3, Air Quality & Ionizing Radiation). Vulnerable groups (e.g., children, older people) and people with preexisting health conditions (e.g., asthma, chronic lung disease, coronary artery disease) are particularly at risk for adverse outcomes. When air quality is poor or expected to deteriorate, travelers should avoid outdoor activities and follow local health guidance from the Government of India, Ministry of Environment and Forests (MOEF), Central Pollution Control Board (www.moef.gov.in), and the US Embassy and US Consulates in India (https://in.usembassy.gov/).

Altitude Illness & Acute Mountain Sickness

Popular tourist destinations in India include the high-elevation Himalayas. Inform travelers visiting these areas about the early symptoms of altitude illness and acute mountain sickness, to not ascend to higher elevations when experiencing symptoms, and to descend if symptoms become worse while resting at the same elevation (see Sec. 4, Ch. 5, High Elevation Travel & Altitude Illness). Travelers with certain underlying medical problems can be at increased risk for adverse events associated with travel to high elevations and should consult a physician familiar with this topic prior to departure.

Animal Bites & Rabies

India has the highest burden of rabies in the world; rabid dogs are common (see Sec. 5, Part 2, Ch. 18, Rabies). Travelers bitten or scratched by a dog or other mammal in India might have limited or no access to postexposure rabies treatment; rabies immune globulin is generally not available in India. Encourage travelers to consider purchasing a medical evacuation insurance policy that will cover travel to receive recommended rabies postexposure prophylaxis. Discuss preexposure rabies vaccination with travelers who have high exposure risk, including adventure travelers, campers, cave explorers, children, people for whom there is an occupational exposure risk (e.g., veterinarians, wildlife biologists), and people visiting rural areas.

Animal bites and wounds can transmit diseases other than rabies. Cellulitis, fasciitis, and wound infections can result from the scratch or bite of any animal. Potentially fatal to humans, B virus is carried by macaques (see Sec. 5, Part 2, Ch. 1, B Virus). These Old World monkeys inhabit many of the temples in India, scatter themselves in many tourist gathering places, and are kept as pets. Macaques can be aggressive and often seek

food from people. When visiting temples, travelers should not carry any food in their bags, hands, or pockets. Stress to travelers that they should not approach or attempt to handle monkeys or other animals. If bitten, travelers should seek immediate medical care.

Travelers, particularly those going to rural areas, should be aware of the risk for snake bites, and should take precautions to wear solid shoes or boots and use a flashlight when walking outside at night.

Climate & Sun Exposure

Sun exposure and heat-related illnesses are concerns for travelers in India, particularly during summer months and at high elevations (see Sec. 4, Ch. 1, Sun Exposure, and Sec. 4, Ch. 2, Extremes of Temperature). Travelers should eat and drink regularly, wear loose and lightweight clothing, and limit physical activity at times when temperatures are high.

Natural Disasters

Natural disasters, including cyclones, droughts, earthquakes, floods, and landslides, are not uncommon in India. Travelers should become aware of the natural disaster risks at their destination. Encourage US citizens and nationals traveling and living in India to enroll in the US Department of State's Smart Traveler Enrollment Program (https://step.state.gov/step) to receive information from the US embassy on safety conditions, and to help the US embassy in India contact them in an emergency, including during natural disasters.

SAFETY & SECURITY

Crime

Crime does occur in India, but rarely is it directed toward foreign travelers; verbal and sometimes physical harassment of female foreign travelers is a concerning exception. Although most victims of harassment are locals, attacks in tourist areas highlight the fact that visitors to India are also at risk and should exercise vigilance and situational awareness. Petty crimes (e.g., pickpocketing, purse snatching) are very common when using public transportation, while out walking, and in heavily populated tourist areas.

Mass Gatherings

Drawing tens of millions of people, Kumbh Mela is the largest mass gathering event / religious pilgrimage in the world. Celebrated according to the Hindu calendar, Kumbh Mela occurs 4 times over an approximately 12-year cycle. During each observance of this normally 4-month long festival, pilgrims ritually bathe in one of 4 sacred rivers in India; in 2021, Kumbh Mela was limited to 30 days due to the COVID-19 pandemic. Mass casualty trauma (e.g., crush injuries, stampedes) and transmission of antimicrobial-resistant organisms and enteric and respiratory pathogens are among the more serious risks to health and safety associated with attendance (see Sec. 9, Ch. 10, Mass Gatherings).

Political & Religious Unrest

Demonstrations and general strikes (*bandh*) often cause inconvenience. Religious violence occurs occasionally. Travelers should obey curfews and travel restrictions, and avoid demonstrations and rallies because of the potential for violence.

Terrorism

India continues to experience terrorist and insurgent activities that can affect US citizens directly or indirectly. Terror attacks have targeted public places (e.g., cinemas, hotels, markets, mosques, restaurants in large urban areas, trains and train stations), including some places frequented by tourists. Although an attack can occur at any time, they generally take place during the busy evening hours in markets and other crowded places. Travelers should pay attention to US Department of State advisories regarding issues that arise at some borders, religious tensions, or terrorist activities. In times of instability, travelers should seek guidance from the US Embassy or Consulates in India website (https://in.usembassy.gov/) for appropriate action (see Sec. 4, Ch. 11, Safety & Security Overseas).

Traffic-Related Injuries

India's roadways are some of the most hazardous in the world, and have large numbers of traffic-related deaths, including among pedestrians (see Sec. 8, Ch. 5, Road & Traffic Safety). Animals,

bicycles, overcrowded buses, motor scooters, people, rickshaws, and trucks all compete for space on streets and roads, increasing the risk for crashes. Travelers should fasten seat belts when riding in cars, and wear a helmet when riding bicycles or motorbikes. Advise travelers to avoid boarding overcrowded buses and not to travel by bus into the interior of the country or on curving, mountainous roads. Discourage nighttime driving (long-distance travel in particular), even with a hired, paid driver.

AVAILABILITY & QUALITY OF MEDICAL CARE

While India ranks highly in the international quality standards maintained at its major private hospitals that employ the bulk of the country's doctors, it lags in postoperative care (e.g., environment, hygiene, infection control) and regulations (e.g., facilitators, hospitals, insurance, medicolegal issues) as compared to regional competitors.

Travelers needing medical care while traveling can contact the US embassy in India (https://in.usembassy.gov/) for referrals, speak to a hotel concierge, or check www.indiahealthcare.org, which includes links to find medical treatment by category, and a list of hospitals accredited by the National Accreditation Board for Hospitals & Healthcare Providers (Constituent Board of the Quality Council of India). Most major hospitals in big cities accept payment by major credit cards; hospitals and doctors in smaller cities might only accept cash.

Medical Tourism

Well-trained English-speaking health care practitioners and low cost for high-quality treatment make India a health care destination for a mix of alternative (ayurveda, homeopathy, yoga), curative (cosmetic, surgical), and wellness medicine.

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BIBLIOGRAPHY

Banerjee S, Denning DW, Chakrabarti A. One Health aspects & priority roadmap for fungal diseases: a mini-review. Indian J Med Res. 2021;153(3):311–9.

Children's Investment Fund Foundation. Worms in India: the scale up and success of a world-leading deworming program. 2019. Available from: https://ciff.org/news/worms-india-scale-and-success-world-leading-deworming-programme.

Date KA, Newton AE, Medalla F, Blackstock A, Richardson L, McCollough A, et al. Changing patterns in enteric fever incidence and increasing antibiotic resistance of enteric fever isolates in the United States, 2008–2012. Clin Infect Dis. 2016;63(3):322–9.

de Saussure PPH. Management of the returning traveler with diarrhea. Ther Adv Gastroenterol. 2009;2(6):367–75.

Federation of Indian Chambers of Commerce and Industry. FICCI knowledge paper: building best practices in healthcare services globally. New Delhi: The Federation; 2019.

National AIDS Control Organization. Sankalak: status of national AIDS response, second edition. New Delhi: NACO, Ministry of Health and Family Welfare, Government of India; 2020. Available from: http://naco.gov.in/sites/default/files/Sankalak%20Status%20of%20National%20AIDS%20Response,%20Second%20Edition%20(2020).pdf.

Sharma A, Mishra B. Rickettsial disease existence in India: resurgence in outbreaks with the advent of 20th Century. Indian J Health Sci Biomed Res. 2020;13:5–10.

Sudarshan M, Narayana DA. Providing evidence for effective prevention and control of rabies in India. Indian J Public Health. 2019 Sep;63(Suppl 1):S1.

Verma R, Khanna P, Chawla S. Recommended vaccines for international travelers to India. Hum Vaccin Immunother. 2015;11(10):2455–7.

World Health Organization. World malaria report 2019. Geneva: The Organization; 2019. Available from: www.who.int/publications/i/item/9789241565721.

NEPAL

David Shlim

DESTINATION OVERVIEW

Home to >29 million people, Nepal stretches for 805 km (500 mi) along the Himalayan mountains that form its natural border with China (see Map 10-13). The topography rises from low plains at 70 m (≈230 ft) elevation to the highest point in the world at 8,848 m (≈29,029 ft), the summit of Mount Everest. Kathmandu, the capital city with a population of >2 million people, sits in a lush valley at 1,324 m (≈4,344 ft) elevation.

Nepal's latitude of 28°N (the same as Florida) means that its non-mountainous areas are temperate year-round. Most annual rainfall comes during the monsoon season (June–September). The main tourist seasons are the spring (March–May) and fall (October–November). The winter months, December–February, are pleasant in the lowlands but can be too cold to make trekking enjoyable in the high mountains.

Approximately 30% of travelers to Nepal go to trek into the mountains; others go to experience the country's culture and stunning natural beauty. Lumbini, in the Terai region, is the birthplace of the Buddha and has become an increasingly popular and beautifully developed pilgrimage destination for Buddhists from around the world. In recent years, trekkers have begun traveling to the Manaslu area, which offers a hiking experience featuring less-developed lodges and extended time away from roads. Notable in this area is the Nubri Valley, which also has many sacred Buddhist sites.

In addition to trekking, Nepal has some of the best rafting and kayaking rivers in the world. Jungle lodges in Chitwan National Park allow visitors to see a wide range of wildlife, including crocodiles, rhinoceros, tigers, and a huge variety of exotic birds. Less adventurous travelers can drive to comfortable hotels offering commanding views of the Himalayas, both near Kathmandu and near Pokhara. The airport near Lumbini is being upgraded to an international airport. Pokhara airport also is scheduled to become an international airport in the future, giving visitors more options for traveling in and out of Nepal.

INFECTIOUS DISEASE RISKS

Enteric Infections & Diseases

Travelers to Nepal are at high risk for enteric diseases. Hepatitis A vaccine and typhoid vaccine are the 2 most important pretravel immunizations. The risk for typhoid fever and paratyphoid fever among visitors to Nepal is among the highest in the world, and the prevalence of fluoroquinolone resistance also is high (see Sec. 5, Part 1, Ch. 24, Typhoid & Paratyphoid Fever). Tap water in Nepal is not considered safe for drinking, and travelers should only drink boiled or bottled water (see Sec. 2, Ch. 8, Food & Water Precautions, and Sec. 2, Ch. 9, Water Disinfection).

CYCLOSPORIASIS

Cyclospora cayetanensis, an intestinal protozoal pathogen, is highly endemic to Nepal (see Sec. 5, Part 3, Ch. 5, Cyclosporiasis). Risk for infection is distinctly seasonal; transmission occurs almost exclusively during May–October, with a peak in June and July. Because transmission occurs outside the main tourist seasons, cyclosporiasis primarily effects expatriates who stay through the monsoon. In addition to watery diarrhea, profound anorexia and fatigue are the hallmark symptoms of *Cyclospora* infection. The treatment of choice is trimethoprim-sulfamethoxazole; no highly effective alternatives have been identified.

HEPATITIS E

Hepatitis E virus is endemic in Nepal, and several cases each year are diagnosed in visitors or expatriates. No vaccine against hepatitis E is commercially available; travelers should follow safe food and water precautions (see Sec. 5, Part 2, Ch. 10, Hepatitis E).

TRAVELERS' DIARRHEA

Travelers' diarrhea is a risk, and the risk during the spring trekking season (March–May) is double that of the fall trekking season (October–November). Because many visitors head to remote areas that do not have available medical care, provide

MAP 10-13 Nepal

travelers with medications for self-treatment (see Sec. 2, Ch. 6, Travelers' Diarrhea). Extensive resistance to fluoroquinolones has been documented among bacterial diarrheal pathogens in Nepal.

Respiratory Infections & Diseases

Respiratory illnesses among travelers are common, both in Kathmandu and on trekking routes. The advent of coronavirus disease 2019 (COVID-19) makes it more difficult to assume the etiology of a respiratory infection. Prolonged symptoms beyond 7–10 days often requires a medical assessment.

CORONAVIRUS DISEASE 2019

For current information on COVID-19 in Nepal, consult the US Embassy in Nepal website (https://np.usembassy.gov/). For the US government's COVID-19 international travel requirements and recommendations, see www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel/index.html. All travelers going to Nepal should be up to date with their COVID-19 vaccines (www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html).

INFLUENZA

Influenza is a risk in Nepal, particularly in crowded teahouses at higher elevations. Trekkers should receive a current influenza immunization before travel.

TUBERCULOSIS

Tuberculosis (TB) disease that exists among local people can be due to drug-resistant strains of *Mycobacterium tuberculosis*. Both multidrug-resistant and extensively–drug resistant TB have been reported in Nepal. Overall, however, risk to travelers is low.

Vectorborne Diseases

DENGUE

In 2019, the Ministry of Health in Nepal reported ≈18,000 cases of dengue, and in 2022, >46,000 cases. Counsel all travelers going to Nepal during the warmer, wetter months to pack an Environmental Protection Agency–registered insect repellent in their travel health kit and to practice insect bite precautions (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

JAPANESE ENCEPHALITIS

Japanese encephalitis (JE) is endemic to Nepal; the greatest disease risk is in the Terai region during and immediately after monsoon season (June–October). JE has been identified in local residents of the Kathmandu Valley, but only 1 case of JE acquired in Nepal has been reported in a foreign traveler, a tourist who spent time in the Terai region in August. JE vaccine is not routinely recommended for people trekking to higher elevation areas or spending short periods in Kathmandu or Pokhara en route to such treks. JE vaccine is recommended for expatriates living in Nepal (see Sec. 5, Part 2, Ch. 13, Japanese Encephalitis).

MALARIA

Although targeted for complete elimination of malaria by 2020, Nepal continues to report low (and decreasing) numbers of indigenous cases, primarily *Plasmodium vivax*. No malaria transmission occurs in Kathmandu or Pokhara, and all the main Himalayan trekking routes are free of malaria, but documented transmission persists in some areas of the country. For this reason (and until malaria is eliminated from Nepal), the Centers for Disease Control and Prevention continues to recommend chemoprophylaxis for travelers visiting destinations below 2,000 m (≈6,500 ft) elevation.

ENVIRONMENTAL HAZARDS & RISKS

Air Quality

Air pollution problems in the Kathmandu valley are frequent. People with underlying cardiorespiratory illness, including asthma, chronic obstructive pulmonary disease, or congestive heart failure can suffer exacerbations in Kathmandu, particularly after a viral upper respiratory infection. Short-term exposure to these levels of air pollution can irritate the eyes and throat. In addition, exposure to high levels of air pollution greatly increases the risk for both upper and lower respiratory tract infections, including otitis, sinusitis, bronchitis, and pneumonia (see Sec. 4, Ch. 3, Air Quality & Ionizing Radiation). Children and older people are the most vulnerable.

Altitude Illness & Acute Mountain Sickness

The destinations for most trekkers are the Annapurna region west of Kathmandu, the Langtang trekking area north of Kathmandu, and the Mount Everest region east of Kathmandu. In the Annapurna region, short-term trekkers can choose to hike to viewpoints in the foothills without reaching any high elevations. Others can undertake a longer trek around the Annapurna massif, going over a 5,416 m (≈17,769 ft) pass, the Thorung La.

The highest point in the Langtang region (the summit of Langtang Lirung) is 7,245 m (23,770 ft); overall, however, high-elevation exposure in Langtang National Park is generally less than in the Everest region. By contrast, trekkers in the Mount Everest region routinely sleep at elevations of 4,267–4,876 m (≈14,000–16,000 ft) and hike to elevations >5,486 m (≈18,000 ft). This prolonged exposure to very high elevations means that travelers must be knowledgeable about the risk for altitude illness and might need to carry specific medications to prevent and treat the problem (see Sec. 4, Ch. 5, High Elevation Travel & Altitude Illness).

Most trekkers in the Mount Everest region arrive by flying to a tiny airstrip at Lukla at 2,860 m (≈9,383 ft) elevation; they then reach Namche Bazaar at 3,440 m (≈11,286 ft) elevation the next day. Acetazolamide prophylaxis can substantially decrease the chances of developing acute mountain sickness in Namche.

Animal Bites & Rabies

Rabies is highly endemic among the dogs in Nepal, but in recent years Kathmandu has had fewer stray dogs. Half of all traveler exposures to a possibly rabid animal occur near Swayambunath, a beautiful hilltop shrine also known as the monkey temple. Advise travelers to be extra cautious with dogs and monkeys in this area. Monkeys can be aggressive if approached, and will jump on a person's back if they smell food in a backpack. Clinics in Kathmandu that specialize in the care of foreign travelers almost always have complete postexposure rabies prophylaxis, including human rabies immune globulin. Private helicopter companies in Nepal

provide rescue; thus, most people can return to Kathmandu from a trek within 1–2 days. Even in the absence of helicopter rescue, trekkers bitten in the mountains have been able to return to Kathmandu in an average of 5 days.

Natural Disasters

In April 2015, a major earthquake in Nepal caused extensive damage and killed >9,000 people. Most of the damage occurred in non-tourist areas and the infrastructure for tourism has largely been repaired. The Langtang trekking area, north of Kathmandu, was virtually destroyed by a landslide triggered by the earthquake; since then, many services have been rebuilt, and tourism is returning to the area.

Large glacial lakes formed by melting glaciers can fail massively and cause intense downstream destructive flooding. Sudden snowstorms have occasionally occurred during trekking seasons, resulting in some deaths and numerous stranded trekkers. Ordinarily, though, the weather during the trekking seasons is mild.

SAFETY & SECURITY

Road Construction Issues

In recent years, Nepal has seen a frenzy of motorable road construction. Once the most roadless country in the world, much of Nepal is now connected by roads that vary in quality from well-constructed and maintained to terrifying. Hasty planning and construction have resulted in many road washouts and landslides, especially during the heavy rains of the monsoon, and road travel in general is an uncomfortable experience.

Motor roads have been constructed up the 2 major valleys of the Around-Annapurna Trek, shortening the trip from 21 to 5 days for people traveling by vehicle. In many cases, traditional trekking trails are no longer being maintained or have been subsumed by the road, substantially changing the nature of the experience and leading trekkers to seek out the few remaining roadless areas for a more traditional hiking experience. Encourage trekkers to inquire about road construction in areas where they intend to hike, because many have found that hiking on dusty or muddy roads, alongside buses, jeeps, and motorcycles, is not the experience they were anticipating.

AVAILABILITY & QUALITY OF MEDICAL CARE

Contact information for 2 clinics in Kathmandu specializing in the care of foreign travelers in Nepal is available on the International Society of Travel Medicine website (www.istm.org). Hospital facilities have improved steadily over the years, and general and orthopedic emergency surgery are available and reliable in Kathmandu. Acute cardiac care also is available, including the placement of coronary artery stents. Modern hospitals tend to compete for foreign patients, and travelers should carry the names of reliable clinics and hospitals so they can request the hospital of their choice. Occasionally, patients are taken to an alternative hospital without their consent; when reaching a hospital, patients or their companions should ascertain whether they are indeed in the hospital they requested. Medical evacuation points providing definitive care outside of Nepal include locations in India and in Thailand.

Medical Evacuation

Helicopter evacuation from most areas is readily available. Communication has improved from remote areas because of satellite and cellular telephones, and private helicopter companies accept credit cards and are eager to perform evacuations for profit. Evacuation can often take place on the same day as the request, weather permitting. Helicopter rescue is usually limited to morning hours because of afternoon winds in the mountains. Helicopter rescue is billed at ≈$4,000 per hour, with an average total cost of $8,000–$10,000 US. Evacuation insurance policies generally require that rescues be arranged through the insurance provider; if not, the cost of the rescue will be borne by the traveler. Because of ready access to helicopter evacuation, trekkers have sometimes requested rescues for trivial conditions. Due to the potential for abuse of unnecessary helicopter rescue, some international evacuation insurance companies no longer provide coverage for Nepal or impose an additional surcharge for coverage there.

BIBLIOGRAPHY

Cave W, Pandey P, Osrin D, Shlim DR. Chemoprophylaxis use and the risk of malaria in travelers to Nepal. J Travel Med. 2003;10(2):100–5.

Government of Nepal, Ministry of Health and Population, Department of Health Services, Epidemiology and Disease Control Division. Situation update of dengue 2022. Available from: http://edcd.gov.np/news/download/situation-update-of-dengue-2022.

Hoge CW, Shlim DR, Echeverria P, Rajah R, Herrmann JE, Cross JH. Epidemiology of diarrhea among expatriate residents living in a highly endemic environment. JAMA. 1996;275(7):533–8.

Murphy H, Bodhidatta L, Sornsakrin S, Khadka B, Pokhrel A, Shakya S, et al. Traveler's diarrhea in Nepal—changes in etiology and antimicrobial resistance. J Travel Med. 2019;26(8):taz054.

Pandey P, Lee K, Amatya B, Angelo KM, Shlim DR, Murphy H. Health problems in travellers to Nepal visiting CIWEC clinic in Kathmandu—a GeoSentinel analysis. Travel Med Infect Dis. 2021;40:101999.

Schwartz E, Shlim DR, Eaton M, Jenks N, Houston R. The effect of oral and parenteral typhoid vaccination on the rate of infection with *Salmonella typhi* and *Salmonella paratyphi* A among foreigners in Nepal. Arch Intern Med. 1990;150(2):349–51.

THAILAND

James Heffelfinger, Joshua Mott, Sopon Iamsirithaworn

DESTINATION OVERVIEW

Thailand, a geographically diverse country a little smaller than the state of Texas (see Map 10-14), is a popular destination for tourists, offering beaches, a wide range of cultures and cuisine, eco-adventure opportunities, nightlife, and shopping. Thailand is also a regional business hub. In 2019, ≈40 million visitors spent >1 night in Thailand—the number of visitors to Thailand increased annually during each of the 5 years before the onset of the coronavirus disease 2019 (COVID-19) pandemic. During 2020, Thailand had <7 million visitors, an 80% reduction compared with 2019, mainly due to COVID-19 travel restrictions.

Of a total population of 70 million people, >10 million live in the capital city of Bangkok, a major commercial center. Tourists to Bangkok visit historic and cultural sites including Buddhist temples, the Grand Palace, and the Emerald Buddha. The main arteries of Bangkok are the Chao Phraya River and its canals, which provide access to tourist sites, the floating market, and restaurants. Bangkok includes many culinary options, from sidewalk noodle stands to 4- and 5-star restaurants representing a variety of global cuisines. Although Thai is a tonal language that can be difficult for Americans to learn, English is commonly spoken at most popular destinations. Maps, road signs, and tourist guides frequently provide information in both English and Thai.

Many visitors to Thailand also visit Chiang Mai in the north. The old city is surrounded by a moat and defensive wall; beyond the wall are >300 temples, a popular night bazaar for shopping, and easy access to handicraft villages, elephant nature parks, and other popular outdoor adventures.

Thailand's central location and major international airport in Bangkok make it an easy access point for other destinations in Asia. In addition, the country has become a popular retirement destination for people from around the world, including many US citizens. The warm climate and low cost of living make Thailand an attractive place to live.

INFECTIOUS DISEASE RISKS

All travelers should be up to date on their routine vaccinations, including seasonal influenza. In addition, vaccination against hepatitis A and hepatitis B is strongly recommended. Consider Japanese encephalitis (JE) and typhoid fever vaccines based on the traveler's potential risk during a visit to, or residence in, Thailand.

Enteric Infections & Diseases

CHOLERA

Active cholera transmission has been infrequently reported from Thailand in recent years.

MAP 10-14 Thailand

For current recommendations for travelers to Thailand, see the Centers for Disease Control and Prevention (CDC) Travelers' Health website (https://wwwnc.cdc.gov/travel/destinations/traveler/none/thailand).

TRAVELERS' DIARRHEA

Thailand's street food is convenient, delicious, and inexpensive. Unfortunately, it also can be a source of travelers' diarrhea (TD) because lack of clean running water in outdoor eateries precludes good hand and food preparation hygiene. For travelers determined to experience Thai street food, the risk for foodborne illness might be mitigated to some degree by following some basic food and water safety precautions. For instance, visit only restaurants or food stalls that cook food to order, avoid raw or undercooked food, eat only steaming hot food served on new disposable dishes, avoid raw garnishes, eat fruit that you peel yourself, and only drink beverages from sealed containers (see Sec. 2, Ch. 8, Food & Water Precautions). For further information about travelers' diarrhea, see Sec. 2, Ch. 6, Travelers' Diarrhea. Fluoroquinolone-resistant enteric pathogens are widespread in Thailand and other areas of Southeast Asia.

TYPHOID FEVER

Typhoid fever is endemic to Thailand. Incidence has been declining, however, and was estimated to be 3 cases per 100,000 population in 2014. People planning extended stays or travel to remote parts of the country should be vaccinated against typhoid (see Sec. 5, Part 1, Ch. 24, Typhoid & Paratyphoid Fever).

Respiratory Infections & Diseases

CORONAVIRUS DISEASE 2019

For current information on COVID-19 in Thailand, consult the US Embassy & Consulate in Thailand website (https://th.usembassy.gov/). For the US government's COVID-19 international travel requirements and recommendations, see www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel/index.html. All travelers going to Thailand should be up to date with their COVID-19 vaccines (www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html).

TUBERCULOSIS

Thailand has a high burden of tuberculosis (TB). Immunocompromised travelers who visit Thailand for extended visits could be at increased risk for TB. Travelers should avoid people known to have active TB, and refrain from consuming unpasteurized dairy products (see Sec. 5, Part 1, Ch. 22, Tuberculosis).

Sexually Transmitted Infections & HIV

Thailand is a destination for tourists seeking sex (see Sec. 9, Ch. 12, Sex & Travel). Although commercial sex work is illegal, it is practiced in many places in Thailand. Visitors to Thailand's red-light districts should be aware that these areas have been associated with human trafficking.

In 2019, ≈470,000 people were living with HIV/AIDS in Thailand. The number of new HIV infections reported nationwide each year decreased during 2010–2019. A 100% condom program, which encourages sex workers and their customers to always use condoms, has helped slow the spread of HIV and other sexually transmitted infections (STIs). Nonetheless, HIV infection remains concentrated in many populations. In 2020, an estimated 12% of men who have sex with men, and 3% of sex workers (≈4% of male sex workers and 1.7% of female sex workers) in Thailand were living with HIV.

Travelers should be aware of the risks of acquiring HIV and other STIs in Thailand, always use condoms during sex, and avoid injecting drugs or sharing needles. Travelers whose practices put them at high risk for HIV infection should discuss preexposure prophylaxis with their primary care and travel medicine providers (see Sec. 5, Part 2, Ch. 11, Human Immunodeficiency Virus / HIV).

Soil- & Waterborne Infections

LEPTOSPIROSIS & MELIOIDOSIS

Leptospirosis (see Sec. 5, Part 1, Ch. 10, Leptospirosis) cases occur mainly in the southern and northeastern regions of the country; melioidosis (see Sec. 5, Part 1, Ch. 12, Melioidosis) is highly endemic to northeast Thailand. For both diseases, most cases occur during the rainy

season, July–October. Adventure travelers can be at increased risk for these diseases because their activities expose them to soil and surface water. Advise travelers visiting endemic areas to avoid contact with soil and water and to ensure that any open wounds are covered to prevent exposure. When contact cannot be avoided, travelers should wear protective clothing and footwear to reduce their exposure risk. Counsel travelers to immediately and thoroughly clean abrasions, burns, or lacerations contaminated with soil or surface water.

Vectorborne Diseases

DENGUE & ZIKA

Dengue (see Sec. 5, Part 2, Ch. 4, Dengue) is endemic throughout Thailand. Large epidemics occur every several years. Peak transmission is during the rainy season, although cases are reported year-round even in non-epidemic years. Travelers to Thailand should take measures to protect themselves from mosquito bites to prevent dengue (see Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods).

Transmission of Zika virus (see Sec. 5, Part 2, Ch. 27, Zika) has occurred in Thailand, but no evidence suggests recent outbreaks. Because of the risk for birth defects in infants born to people infected with Zika during pregnancy, however, travelers who are pregnant or trying to become pregnant should review the most recent CDC recommendations at https://wwwnc.cdc.gov/travel/page/zika-information.

JAPANESE ENCEPHALITIS

JE is endemic to many parts of Thailand outside the capital. Transmission occurs year-round, with seasonal epidemics occurring in the northern provinces during May–October. Although most outbreaks occur in the Chiang Mai valley, cases have occurred in travelers who visited resorts or coastal areas in southern Thailand. JE vaccine is recommended for travelers who plan to visit Thailand for ≥1 month and should be considered for people visiting for a shorter period who have an increased risk for JE virus exposure due to their itineraries or activities (see Sec. 5, Part 2, Ch. 13, Japanese Encephalitis).

MALARIA

Malaria is endemic to specific areas in Thailand, particularly the rural, forested areas bordering Burma (Myanmar), Cambodia, and Laos, and the provinces of the far south along the border with Malaysia. Transmission is year-round, peaking during the rainy season, with a second, smaller peak in December. Approximately 80% of cases are due to *Plasmodium vivax*; <20% are due to *P. falciparum*. CDC recommends protection against mosquito bites and antimalarial prophylaxis for travelers visiting any of the endemic areas (see Sec. 2, Ch. 5, Yellow Fever Vaccine and Malaria Prevention Information, by Country; Sec. 4, Ch. 6, Mosquitoes, Ticks & Other Arthropods; and Sec. 5, Part 3, Ch. 16, Malaria). Atovaquone-proguanil, doxycycline, or tafenoquine are the recommended prophylactic antimalarial drugs for travelers going to malaria-endemic areas in Thailand; mosquito avoidance only (no chemoprophylaxis) is recommended for people traveling to areas where cases of malaria transmission are rare to few (e.g., Bangkok, Chiang Mai, Phuket).

ENVIRONMENTAL HAZARDS & RISKS

Air Quality

Air quality in Thailand varies by province and fluctuates throughout the year, with seasonal smog becoming an increasing health concern in some areas of the country (see Sec. 4, Ch. 3, Air Quality & Ionizing Radiation). The air quality in several provinces (Bangkok, Chiang Mai, Chiang Rai, Khon Kaen, Lampang, Lamphun, Mae Hong Son, Nan, and Samut Sakhon) has exceeded Thai and US government daily standards for fine particulate matter ($PM_{2.5}$) during parts of the year. In Chiang Mai and other northern provinces, air quality is frequently poor during February–April because of agricultural burning and forest fires.

Animal Bites & Rabies

Government-sponsored mass vaccination campaigns for cats and dogs have reduced the prevalence of rabies in Thailand, but a small risk persists. Preexposure vaccination is recommended only for

travelers whose occupation puts them at risk for exposure (e.g., veterinarians) or people who will be traveling to areas where immediate access to care and rabies biologics will be difficult (see Sec. 5, Part 2, Ch. 18, Rabies). Rabies vaccine for preexposure and postexposure prophylaxis and human rabies immune globulin are readily available in all provincial and most district hospitals throughout Thailand.

Climate & Sun Exposure

Because Thailand is close to the equator, the climate is often hot and humid (see Sec. 4, Ch. 1, Sun Exposure, and Sec. 4, Ch. 2, Extremes of Temperature). Flooding is always a possibility, and various regions are prone to flash floods. Monsoon rains typically fall during July–October and can last until relatively cooler, drier weather begins in November, making November–February a popular time of year to visit.

Natural Disasters

Tsunamis are a risk in Thailand; the 2004 tsunami was the deadliest on record. Two other tsunamis have hit Thailand since 2004, resulting in ≈8,000 deaths.

SAFETY & SECURITY

Crime

The crime rate in Thailand exceeds that of some other countries in Asia. Although most crime involves petty theft, crime related to drug use and the illegal drug trade, gambling, and human trafficking and prostitution also occur. And while more violent crime (e.g., homicide, rape) involving visitors is uncommon in Thailand, it has happened.

Political Unrest

Thailand has experienced political unrest throughout the country and ethnonationalist violence in the southern provinces. In 2014, a caretaker military government was established to maintain peace, develop a constitution, and facilitate democratic elections. The country remains politically divided, however, and demonstrations and government protests continue. Prudent travelers should avoid these gatherings because no one can predict whether they will stay peaceful or turn violent (see Sec. 4, Ch. 11, Safety & Security Overseas).

To find out if, when, and where political protests might occur, travelers should monitor the local news, social media outlets, and the US Embassy & Consulate in Thailand website (https://th.usembassy.gov/). In addition, by enrolling with the US Department of State's Smart Traveler Enrollment Program (https://step.state.gov/step), US citizens and nationals traveling and living in Thailand receive safety alerts from the US embassy; it also enables the US embassy to contact them in the event of an emergency.

Terrorism

Recent terrorism-related incidents in Thailand have been related to the South Thailand insurgency, a separatist group with roots in ethnic and religious tensions. The insurgency has been ongoing for several decades and is concentrated in 4 provinces (Narathiwat, Pattani, Songkhla, Yala) in the far south of the country, near the Malaysian border. Martial law is enforced in these provinces. Due to safety concerns, US government employees need official authorization to travel to these areas, and the US embassy in Thailand strongly discourages all other Americans from going. The Royal Thai Government has taken active measures to counter terrorism through legislation, capacity-building, and communication and collaboration with other countries in the region.

Traffic-Related Injuries

Traffic accidents are common in Thailand. According to the World Health Organization, in 2018, Thailand had one of the world's highest traffic-related fatality rates, due in large part to reckless driving (see https://travel.state.gov/content/travel/en/international-travel/International-Travel-Country-Information-Pages/Thailand.html#ExternalPopup). Approximately 20,000 motor vehicle deaths occur in Thailand each year. Motorcycles, a cheap and popular mode of travel, are among the most vulnerable vehicles on the road. During 2019–2021, 85% of road accidents involved motorcycles or scooters, and a substantial proportion (73% in 2012) of motor vehicle deaths are due to motorcycle and scooter crashes. Travelers should avoid riding

motorbikes, including motorbike taxis, but if they must ride, they should wear a helmet. Travelers also should fasten seat belts when riding in cars (see Sec. 8, Ch. 5, Road & Traffic Safety).

AVAILABILITY & QUALITY OF MEDICAL CARE

Health care in Thailand is generally considered to be of good quality and less costly than in many high-income countries. Approximately 20% of hospitals are private, and many accept online registration and have English-speaking staff. Most major medical centers are in larger metropolitan areas. In rural areas, availability and quality of medical care is more limited.

Medical Tourism

Medical tourism to Thailand increased during 2010–2019. The cost of medical or surgical treatment is lower, and the level of care is considered comparable to that of many places in the United States. Thailand is among the top medical tourism destinations worldwide. Travelers intending to obtain medical care abroad should research the facilities at their destination; learn about health insurance coverage, travel regulations, and requirements for visitors seeking medical care in Thailand; and consult with their primary care physician and a travel medicine specialist in advance of their trip (see Sec. 6, Ch. 4, Medical Tourism).

BIBLIOGRAPHY

AIDSinfo. Global dataset on HIV epidemiology and response. Available from: https://aidsinfo.unaids.org.

Hinjoy S, Hantrakun V, Kongyu S, Kaewrakmuk J, Wangrangsimakul T, Jitsuronk S, et al. Melioidosis in Thailand: present and future. Trop Med Infect Dis. 2018;32(2):38.

US Central Intelligence Agency. The world fact book 2021; East and Southeast Asia: Thailand. Washington, DC: The Agency; 2021. Available from: www.cia.gov/the-world-factbook/countries/thailand.

US Department of State, Bureau of Consular Affairs. Travel and transportation: Thailand. Available from: https://travel.state.gov/content/travel/en/international-travel/International-Travel-Country-Information-Pages/Thailand.html.

World Health Organization. Global status report on road safety 2018. Geneva: The Organization; 2018. Available from: www.who.int/publications/i/item/9789241565684.

World Health Organization. Towards a rabies-free Thailand by 2020. Available from: www.who.int/news-room/feature-stories/detail/towards-a-rabies-free-thailand-by-2020.

11 Posttravel Evaluation

GENERAL APPROACH TO THE RETURNED TRAVELER

Jessica Fairley

As many as 43%–79% of travelers to low- and middle-income countries become ill with a travel-associated health problem. Although most of these illnesses are mild, some travelers become sick enough to seek care from a health care provider. Most posttravel infections become apparent soon after returning from abroad, but incubation periods vary, and some syndromes can present months to years after initial infection or after travel.

When evaluating a patient with a probable travel-associated illness, approach the differential diagnosis by incorporating both the patient presentation and risk factors related to travel (e.g., destination, duration of travel, and exposures; see Table 11-01). Salient points of the history of present illness and the travel and medical history, descriptions of common nonfebrile syndromes, and initial management steps are outlined below. The differential diagnosis and management for a traveler with fever (or febrile syndrome) is discussed in detail in Sec. 11, Ch. 4, Fever in the Returned Traveler.

THE POSTTRAVEL EVALUATION

History of the Present Illness

As with any medical evaluation, the history of the present illness and associated clinical factors are the first considerations when approaching an ill returned traveler. Information about the timing of illness, immunization and prophylaxis history, itinerary, exposures, and comorbidities can help refine the diagnosis.

TIMING OF ILLNESS IN RELATION TO TRAVEL

Because most common travel-associated infections have short incubation periods, most ill travelers will seek medical attention ≤1 month

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Table 11-01 Elements of a complete travel history in an ill returned traveler

ELEMENT	DETAILS
HISTORY OF THE PRESENT ILLNESS	Symptoms: primary & associated Date of symptom or illness onset Geographic location at time of symptom onset (e.g., while away, in transit, after return) Healthcare received while abroad and after return (e.g., medications, hospitalizations)
TRAVEL DETAILS	Destinations visited and itineraries Duration of travel (date of departure and date of return) Reason for travel • Business (include details about possible exposures and type of work done) • Immigration • Leisure • Missionary, volunteer, humanitarian aid work • Providing or receiving medical care • Research or education • Visiting friends & relatives Accommodations and sleeping arrangements • Camping • Hostel • Hotel with or without air conditioning, window screens, or mosquito nets • Safari, including camping outdoors, in a lodge, in a luxury tent • Someone's home Transportation used
RECREATIONAL ACTIVITIES	Camping and hiking Safari Sightseeing Water exposures • Boating or rafting • Fresh water (lake, river, stream) bathing, boating, swimming, wading • Hot springs • Hot tubs, swimming pools • Ocean (diving, snorkeling, surfing; consider marine life exposure) Other activities
EXPOSURES	Animal or arthropod bites, stings, scratches Drinking water (bottled, purified, tap, use of ice) Foods • Raw fruits, vegetables • Undercooked meat • Unpasteurized dairy products • Seafood Insect bites (mosquito, tick, sand fly, tsetse fly) Medical or dental care (planned or unplanned) Disease outbreaks in visited destinations Sexual activity during travel (document condom use, new partner[s]) Tattoos or piercings while traveling
VECTORBORNE DISEASE PRECAUTIONS	Adherence to malaria prophylaxis Insect repellent use (25%–40% DEET or other Environmental Protection Agency–registered product) Mosquito nets

Table 11-01 Elements of a complete travel history in an ill returned traveler (continued)

ELEMENT	DETAILS
VACCINES RECEIVED	Coronavirus disease 2019 (COVID-19) Hepatitis A Hepatitis B Influenza Japanese encephalitis Measles-mumps-rubella (MMR) Meningococcal disease Polio Rabies Tetanus-diphtheria-acellular pertussis (Tdap) Typhoid Varicella Yellow fever
MEDICATIONS TAKEN	Malaria prophylaxis All medicines taken (whether routinely or for symptomatic treatment), including antibiotics • Herbal, complementary, alternative • Over the counter • Prescription
PAST MEDICAL HISTORY	Chronic medical conditions • Autoimmune disease • Cancer • Diabetes • Heart disease • Immunosuppressive conditions Recent illnesses or surgeries
ADDITIONAL INFORMATION	Alcohol, tobacco, illicit drug use Family history Recent travel, domestic or international, especially ≤6 months

of returning from their destinations. Dengue and other arboviral infections, influenza, and travelers' diarrhea are examples of infections with shorter incubation periods (<2 weeks). Diseases with slightly longer incubation periods, ≤4–6 weeks, include viral hepatitis, acute HIV, leishmaniasis, malaria, and typhoid fever, among others. Occasionally, some infections (e.g., leishmaniasis, malaria, schistosomiasis, tuberculosis) might become manifest months or even years after a traveler returns. Consider malaria in the differential diagnosis of any traveler who traveled to a malaria-endemic area ≤1 year of presentation. A detailed travel history that extends beyond a few months before presentation is important. The most common travel-associated infections by incubation period are listed in Table 11-02, Table 11-03, and Table 11-04.

IMMUNIZATION & PROPHYLAXIS HISTORY

When evaluating an ill returned traveler, review the traveler's vaccination history and malaria prophylaxis used. Fewer than half of US travelers who visit low- and middle-income countries seek pretravel medical advice, increasing the likelihood that they did not receive pretravel vaccines and did not receive or take antimalarial drugs. Although adherence to malaria prophylaxis does not rule out the possibility of malaria,

Table 11-02 Common travel-associated infections by incubation period: <14 days

DISEASE	USUAL INCUBATION PERIOD	INCUBATION PERIOD (RANGE)	DISTRIBUTION
Chikungunya	2–4 days	1–14 days	Tropics, subtropics
Coronavirus disease 2019 (COVID-19)	3–7 days, or less, depending on the predominate, circulating variant		Worldwide
Dengue	4–8 days	3–14 days	Tropics, subtropics
Encephalitis, arboviral (e.g., Japanese encephalitis, tick-borne encephalitis, West Nile)	3–14 days	1–20 days	Agents vary by region
Enteric (typhoid or paratyphoid) fever	7–18 days	3–60 days	Especially in South Asia
HIV infection, acute	10–28 days	10 days–6 weeks	Worldwide
Influenza	1–3 days		Worldwide, can be acquired during travel
Legionellosis	5–6 days	2–10 days	Worldwide
Leptospirosis	7–12 days	2–26 days	Worldwide, most common in tropical areas
Malaria, *Plasmodium falciparum*	6–30 days	98% have onset within 3 months of travel	Tropics, subtropics
Malaria, *Plasmodium vivax*	8 days–12 months	≈50% have onset >30 days after completion of travel	Widespread in tropics and subtropics
Spotted fever rickettsiosis	Few days to 2–3 weeks		Causative species vary by region
Zika	3–14 days		Widespread in Latin America; endemic through much of Africa, Southeast Asia, and Pacific Islands

it substantially reduces the risk and increases the possibility of an alternative diagnosis.

Likewise, history of vaccination against hepatitis A and yellow fever would make these diseases unlikely causes of hepatitis or jaundice in a returning traveler. Remember to ask about routine vaccinations like measles-mumps-rubella (MMR) and tetanus-diphtheria-pertussis (Tdap). The most common vaccine-preventable diseases among returned travelers seeking care at GeoSentinel clinics during 1997–2010 included hepatitis A, hepatitis B, influenza, and typhoid

Table 11-03 Common travel-associated infections by incubation period: 14 days–6 weeks

DISEASE	USUAL INCUBATION PERIOD	INCUBATION PERIOD (RANGE)	DISTRIBUTION
Encephalitis, arboviral Enteric (typhoid or paratyphoid) fever HIV infection, acute Leptospirosis Malaria	See Table 11-02 for usual incubation periods		See Table 11-02 for global distribution
Amebic liver abscess	Weeks–months		Most common in low- and middle-income countries
Hepatitis A	28–30 days	15–50 days	Most common in low- and middle-income countries
Hepatitis E	26–42 days	2–9 weeks	Worldwide
Schistosomiasis, acute (Katayama syndrome)	4–8 weeks		Most common in sub-Saharan Africa

fever. More than half of these patients with vaccine-preventable diseases were hospitalized.

ITINERARY & TRAVEL DURATION

A traveler's itinerary is crucial to formulating a differential diagnosis because exposures differ depending on the region of travel and the specific areas (e.g., rural vs. urban). A febrile illness with nonspecific symptoms could be dengue, malaria, rickettsial disease, or typhoid fever, among others, depending on the itinerary and endemicity of these infections. Being able to exclude certain infections based on the travel itinerary can help avoid unnecessary testing.

A 2013 study from the GeoSentinel Surveillance Network found that the frequency of certain

Table 11-04 Common travel-associated infections by incubation period: >6 weeks

DISEASE	USUAL INCUBATION PERIOD	INCUBATION PERIOD (RANGE)	DISTRIBUTION
Amebic liver abscess Hepatitis E Malaria Schistosomiasis, acute	See Table 11-03 for usual incubation periods		See Table 11-03 for global distribution
Hepatitis B	90 days	60–150 days	Worldwide
Leishmaniasis, visceral	2–10 months	10 days–years	Africa, Latin America, Asia, southern Europe, and the Middle East
Tuberculosis	Primary, weeks Reactivation, years		Worldwide, rates and resistance levels vary widely

diseases varied depending on the region of the world visited; among travelers with fevers, for example, dengue was diagnosed most frequently among travelers coming from Asia, while malaria was diagnosed most frequently among travelers returning from Africa.

Travel duration is also a factor because the risk for a travel-associated illness increases with the length of the trip. A tropical medicine specialist can assist with the differential diagnosis and might be aware of outbreaks or the current prevalence of an infectious disease in an area. The 2014–2015 Ebola virus epidemic in West Africa highlighted the importance of epidemiologic factors and travel itineraries in managing patients and protecting staff and the community.

EXPOSURES

Knowing a patient's exposures during travel (e.g., consumption of contaminated food or water, insect bites, freshwater swimming) also can assist with the differential diagnosis. In addition to malarial parasites, mosquitoes transmit viruses (e.g., chikungunya, dengue, yellow fever, Zika) and filarial parasites (e.g., *Wuchereria bancrofti*). Depending on the clinical syndrome, a history of a tick bite could suggest a diagnosis of tick-borne encephalitis, African tick-bite fever, or other rickettsial infections. Tsetse flies are the vector for transmission of *Trypanosoma brucei*, a protozoan that causes African sleeping sickness. Tsetse flies are large, and their bites are painful; patients often recall being bitten. Freshwater bathing, swimming, wading, or other contact can put travelers at risk for leptospirosis, schistosomiasis, and other diseases.

Accommodations and activities also can influence the risk of acquiring certain diseases while abroad. Travelers who visit friends and relatives are at greater risk for malaria, typhoid fever, and other diseases, often because they stay longer, travel to more remote destinations, have more contact with local water sources, and typically do not seek pretravel advice (see Sec. 9, Ch. 9, Visiting Friends & Relatives: VFR Travel). Travelers backpacking and camping in rural areas have a greater risk for certain diseases than those staying in luxury, air-conditioned hotels.

COMORBIDITIES

Underlying illnesses can affect a traveler's susceptibility to infection as well as the clinical manifestations and severity of disease. An increasing number of international travelers are immunosuppressed, whether due to HIV infection, treatment with immune-modulating medications, being an organ transplant recipient, or other primary or acquired immunodeficiencies (see Sec. 3, Ch. 1, Immunocompromised Travelers). In addition, several factors associated with travel can exacerbate underlying conditions (e.g., chronic lung disease, inflammatory bowel disease, ischemic heart disease).

Symptoms & Illness Severity

Although the symptoms of many infectious and travel-associated syndromes overlap, the initial symptoms and presentation should ultimately guide the differential diagnosis: gastrointestinal symptoms and febrile illnesses are the most common syndromes in returning travelers. Remember that conditions such as appendicitis, urinary tract infections, and domestically acquired viral infections also can present in returning travelers.

Severity of illness is not only important for patient triage but also can help clinicians distinguish certain infections. Is the traveler hemodynamically stable? Is the infection potentially life-threatening (e.g., malaria)? Does the traveler have a severe respiratory syndrome or signs of hemorrhagic fever? Some suspected illnesses might necessitate prompt involvement of public health authorities. For more details, see General Management, later in this chapter.

COMMON SYNDROMES

The 3 most common clinical syndromes after travel to low- and middle-income countries are dermatologic conditions, diarrheal diseases, and systemic febrile illnesses, each of which is described in more detail elsewhere in this section (see Dermatologic Conditions, Persistent Diarrhea in Returned Travelers, and Fever in the Returned Traveler). Evaluate febrile travelers returning from malaria-endemic destinations immediately. Other common clinical presentations and findings include animal bites and scratches, asymptomatic eosinophilia, and respiratory illnesses.

Animal Bites & Scratches

Promptly evaluate any traveler who reports animal exposures during travel (see Sec. 4, Ch. 7, Zoonotic Exposures: Bites, Stings, Scratches & Other Hazards). Consider travelers with animal bites and scratches as high-risk for rabies exposure, and provide rabies postexposure prophylaxis, as indicated (see Sec. 5, Part 2, Ch. 18, Rabies). If the traveler was exposed to a macaque, herpes B postexposure prophylaxis might be indicated (see Sec. 5, Part 2, Ch. 1, B Virus).

Asymptomatic Eosinophilia

Eosinophilia in a returning traveler suggests possible helminth infection. Allergic diseases, hematologic disorders, and a few other viral, fungal, and protozoan infections also can cause eosinophilia. Eosinophilia can be present during pulmonary migration of parasites (e.g., *Ascaris*, hookworm, schistosomiasis, *Strongyloides*).

Other parasitic infections associated with eosinophilia include lymphatic filariasis, chronic strongyloidiasis, acute trichinellosis, and visceral larva migrans. These infections might be asymptomatic, but also could have associated symptoms (e.g., rash, swelling). In an outbreak of sarcocystosis among travelers returning from Tioman Island, Malaysia, those affected presented with eosinophilia and myalgias and had eosinophilic myositis on muscle biopsy (see Sec. 5, Part 3, Ch. 18, Sarcocystosis).

Parasitic infections are rare in most travelers, so consider other etiologies for eosinophilia; for instance, eosinophilia can be a sign of a hematologic malignancy. See Section 5 for more information on specific diseases.

Respiratory Illnesses

Respiratory illnesses are frequent among returned travelers and are typically associated with common respiratory viruses, including influenza and now, severe acute respiratory syndrome coronavirus 2, the cause of coronavirus disease 2019 (COVID-19). Since the pandemic began in early 2020, coronavirus disease (COVID-19) has overtaken influenza in overall global incidence. And although historically influenza has been the most common vaccine-preventable disease associated with international travel, COVID-19 could surpass it in that regard. To make that determination, however, a better understanding of the epidemiology of travel-associated COVID-19 transmission is needed (see Sec. 5, Part 2, Ch. 3, COVID-19).

If the travel history is appropriate and respiratory symptoms do not have a clear alternative diagnosis, include other emerging respiratory infections (e.g., avian influenza, Middle East respiratory syndrome [MERS]) in the differential diagnosis. In suspected cases of an emerging respiratory infection, alert local public health authorities and the Centers for Disease Control and Prevention (CDC) immediately. See relevant chapters in Section 5 for more information on these emerging infections; for a list of febrile respiratory illnesses that can occur after exposures in tropical destinations, see Table 11-10 in the chapter, Fever in the Returned Traveler.

Delayed illness onset and chronic cough after travel could be tuberculosis, especially in a long-term traveler or health care worker. Helminths and helminth infections associated with pulmonary symptoms include *Ascaris*, hookworms (*Ancylostoma* or *Necator*), paragonimiasis, schistosomiasis, and strongyloidiasis.

GENERAL MANAGEMENT

Triage

Most posttravel illnesses can be managed on an outpatient basis, but some patients, especially those with systemic febrile illnesses, might need to be hospitalized. Furthermore, potentially severe, transmissible infections (e.g., COVID-19, Ebola, MERS) require enhanced infection control measures and often, higher levels of care. Severe clinical presentations (e.g., acute respiratory distress, hemodynamic instability, mental status changes) require inpatient care. Have a low threshold for admitting a febrile patient if malaria is suspected; complications can occur rapidly. Management in an inpatient setting is especially vital for patients unlikely to follow up reliably or who have no one at home to assist if symptoms quickly worsen.

Initial Evaluation

After conducting a thorough physical exam, paying particular attention to skin manifestations or evidence of prior insect bites, order

tests based on chief complaint and exposure history. Frequently useful tests include complete blood count with differential (to look for anemia, eosinophilia, leukocytosis, leukopenia, thrombocytopenia); blood cultures and malaria rapid diagnostic tests (depending on the presence of fever and travel itinerary); a complete metabolic profile (to identify electrolyte, renal, or liver dysfunction); serologic or PCR tests for arboviral infections (as needed); and stool cultures and ova and parasite exams. These tests often can help narrow the differential diagnosis and determine disease severity.

Antimicrobial Resistance

Be aware of the risk to international travelers for acquiring antimicrobial resistant organisms. Carefully consider travel history when caring for patients, both to identify effective treatments for infections and to ensure infection control interventions are in place to prevent spread of antimicrobial resistance (see Sec. 11, Ch. 5, Antimicrobial Resistance).

Consultation

Consult an infectious disease specialist when managing complicated or severe travel-associated infections, or when the diagnosis remains unclear. A tropical medicine or infectious disease specialist should be involved in cases that require specialized treatment (e.g., leishmaniasis, severe malaria, and neurocysticercosis).

Involve local, state, and federal public health authorities whenever managing transmissible, high-consequence infections. CDC provides on-call assistance with the diagnosis and management of parasitic infections at 404-718-4745 (for parasitic infections other than malaria) or 770-488-7788 (toll-free at 855-856-4713) for malaria, during business hours. After business hours or for other conditions, call the CDC Emergency Operations Center at 770-488-7100.

BIBLIOGRAPHY

Angelo KM, Kozarsky PE, Ryan ET, Chen LH, Sotir MJ. What proportion of international travellers acquire a travel-related illness? A review of the literature. J Travel Med. 2017;24(5):tax046.

Boggild AK, Castelli F, Gautret P, Torresi J, von Sonnenburg F, Barnett ED, et al. Vaccine preventable diseases in returned international travelers: results from the GeoSentinel Surveillance Network. Vaccine. 2010;28(46):7389–95.

Centers for Disease Control and Prevention. Notes from the field: acute muscular sarcocystosis among returning travelers—Tioman Island, Malaysia, 2011. MMWR Morb Mortal Wkly Rep. 2012;61(2):37–8.

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

Fairley JK, Kozarsky PE, Kraft CS, Guarner J, Steinberg JP, Anderson E, et al. Ebola or not? Evaluating the ill traveler from Ebola-affected countries in West Africa. Open Forum Infect Dis. 2016;3(1):ofw005.

Hamer DH, Connor BA. Travel health knowledge, attitudes and practices among United States travelers. J Travel Med. 2004;11(1):23–6.

Hendel-Paterson B, Swanson SJ. Pediatric travelers visiting friends and relatives (VFR) abroad: illnesses, barriers and pre-travel recommendations. Travel Med Infect Dis. 2011;9(4):192–203.

Leder K, Torresi J, Libman MD, Cramer JP, Castelli F, Schlagenhauf P, et al. GeoSentinel surveillance of illness in returned travelers, 2007–2011. Ann Intern Med. 2013;158(6):456–68.

Ryan ET, Wilson ME, Kain KC. Illness after international travel. N Engl J Med. 2002;347(7):505–16.

Schulte C, Krebs B, Jelinek T, Nothdurft HD, von Sonnenburg F, Loscher T. Diagnostic significance of blood eosinophilia in returning travelers. Clin Infect Dis. 2002;34(3):407–11.

RAPID DIAGNOSTIC TESTS FOR INFECTIOUS DISEASES

Elizabeth Rabold, Jesse Waggoner

Rapid diagnostic tests (RDTs) refer to a group of diagnostics categorized by performance characteristics rather than the specific analyte or test platform. Such assays have relatively short performance times, provide results to inform clinical decision making, and enable management at the point-of-care (POC). RDTs are available in a variety of test formats and platforms and for various detection targets. RDTs are designed for detecting pathogen-specific antigens or nucleic acid sequences, as well as host antibody responses against certain pathogens (Table 11-05).

To select an appropriate RDT, factor in the pros and cons of the different analytes, timing of patient presentation, and specifics of the disease or syndrome under investigation (e.g., acute versus chronic infection). RDTs described here include any pathogen-specific or syndrome-based test that can be incorporated into a POC testing protocol for a given infection or clinical syndrome.

Tests that meet the definition of an RDT may be performed under a certificate of waiver (so-called "waived" tests) indicating they are simple to perform with a low risk for yielding an incorrect result. The certificate of waiver is specific to the United States. Nevertheless, some of its requirements are useful when considering using RDTs in international settings. For example, although

Table 11-05 Common rapid diagnostic test analytes & testing formats: advantages & disadvantages

RDT ANALYTE	ADVANTAGES	DISADVANTAGES	FORMAT	EXAMPLES
Antibody	IgM+ in late-acute/early convalescent phase IgG+ in chronic infections or after previous exposure Rapid and inexpensive	Antibodies from prior exposure and cross-reactivity limit specificity Insensitive in acute disease	Lateral flow Latex agglutination	Dengue Hepatitis B Hepatitis C HIV Syphilis
Antigen	Direct detection of pathogen antigens Detected in acute/active infection Rapid and inexpensive	Less sensitive than nucleic acid testing Does not provide type/strain information	Lateral flow Latex agglutination Solid phase "dipstick"	Dengue Ebola HIV Influenza Malaria SARS-CoV-2
Nucleic acid (RNA or DNA)	Sensitive and specific in acute phase Can provide quantitative information	Expensive Requires specific instrumentation Longer performance time	PCR/RT-PCR LAMP/RT-LAMP RPA/RT-RPA	Chlamydia Multiplex respiratory and gastrointestinal panels *Neisseria* SARS-CoV-2

Abbreviations: LAMP, loop-mediated amplification; PCR, polymerase chain reaction; RPA, recombinase polymerase amplification; RT, reverse transcription; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

mandated personnel requirements for such tests are minimal, testers must be trained and document proficiency on use of the assay. Waived tests can only be performed on unmodified specimens (whole blood, saliva, urine) according to the most recent manufacturer recommendations. Deviations from the specimen type or manufacturer protocol make the test high-complexity and require that it be performed in a dedicated laboratory setting. Finally, RDT reagents might have specific storage requirements and a limited shelf life. These factors impact accuracy of the test and necessitate oversight and quality assessments to ensure proper performance.

Some tests with performance characteristics of an RDT might not be readily compatible with POC testing. For instance, an increasing number of waived, sample-to-answer molecular diagnostics (nucleic acid amplification tests) are becoming available. At a given institution, these assays might only be performed in a central laboratory at specific times, thereby limiting their applicability at the POC. These assays typically must be performed with dedicated bench-top equipment; adding this capacity at clinical sites, therefore, might not be feasible.

RAPID DIAGNOSTIC TESTS FOR CLINICAL SYNDROMES

RDTs, including multiplex molecular panels (Table 11-06 and Table 11-07), are available for many common clinical syndromes among travelers, the etiologies of which can overlap substantially with those of non-travel–associated syndromes. Thus, clinics might augment RDT diagnosis of common pathogens with specialized or follow-up testing for rare pathogens or positive results.

In general, RDTs for antigen and antibody detection are less sensitive than standard laboratory assays. Rapid HIV tests that use blood and cheek swab samples are widely available and perform well in identifying individuals with chronic infections. Even later-generation antigen/antibody tests remain less sensitive than molecular testing for acute HIV infection, however, and in high-risk patients, molecular testing or repeat testing is warranted. The sensitivity of rapid antigen tests for influenza and certain gastrointestinal pathogens (e.g., norovirus, rotavirus) are notably poor. Negative results should not dictate therapy decisions, and positive results should be confirmed with molecular testing.

Multiplex molecular panels are becoming more common for central nervous system (CNS), gastrointestinal, and respiratory infections, and new panels are under evaluation for febrile returning travelers. These panels often are very sensitive and can test for many pathogens in a single sample. These tests are expensive, however, and results must be interpreted in the clinical context; certain pathogens might require additional testing when there is high clinical suspicion. Notably, available multiplex assays do not test for common bacterial causes of pneumonia. Also, detection of emerging or novel pathogens is not feasible with large, preconstructed testing panels. When interpreting results provided by multiplex molecular panels, consider the prolonged shedding periods of certain pathogens, the possibility of multiple positive results or co-infections, the detection of asymptomatic carriage, and the variable accuracy for different agents on the panel (e.g., cryptococcus in CNS panels, adenovirus in respiratory panels).

Undifferentiated acute febrile illness is a common and potentially life-threating clinical presentation among returning travelers that poses a diagnostic challenge and requires prompt evaluation, diagnosis, and management. RDTs might be unavailable or insufficient to diagnose the many possible causes of febrile illness. For example, a commercial RDT for malaria has been cleared for use in hospitals and laboratories but not for individual clinics; microscopy is still the diagnostic tool of choice in malaria cases to identify the species and calculate the level of parasitemia (see Sec. 5, Part 3, Ch. 16, Malaria). Furthermore, patients with malaria can be co-infected with other pathogens that can contribute to and complicate diagnosis and management. RDTs are not available in the United States for other common causes of undifferentiated acute febrile illness in travelers (e.g., dengue, leptospirosis).

Coronavirus Disease 2019

High demand for diagnostics for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease

Table 11-06 Lateral-flow immunochromatographic tests & small panels for pathogens in returning international travelers: selected features

SYNDROME	PATHOGENS	SPECIMEN TYPES	ADDITIONAL INFORMATION
SYSTEMIC FEBRILE ILLNESS	Dengue virus	Serum	Not FDA-cleared; highly variable performance; antibodies may cross-react between flaviviruses
	Ebola virus	Whole blood	Received Emergency Use Authorization from FDA and Emergency Use Listing from WHO
	Plasmodium spp.	Whole blood	Best performance characteristics for *Plasmodium falciparum* infections
GASTROINTESTINAL INFECTIONS	*Vibrio cholerae*	Stool sample	Not FDA-cleared; may be accurate for O1- and/or O139-positive strains
	Norovirus, rotavirus	Stool sample	Available in the United States separately or in combination
RESPIRATORY INFECTIONS	Influenza virus	Nasopharyngeal or throat swab	Rapid test sensitivity 50%–70%; negative testing should not direct treatment
	SARS-CoV-2	Nasal or nasopharyngeal swabs	RDT and "at home" test availability increasing; performance with variants under investigation
SEXUALLY TRANSMITTED INFECTIONS	*Chlamydia trachomatis* and *Neisseria gonorrhea*	Urine, vaginal swab	Molecular tests remain gold standard; a sample-to-answer molecular assay is available
	HIV	Whole blood, oral fluids	Antibody and antibody/antigen kits available; molecular testing preferred for acute infection
	Treponema pallidum	Whole blood	Antibody detection; may not be appropriate for acute infection

Abbreviations: FDA, US Food and Drug Administration; IDSA, Infectious Disease Society of America; RDT, rapid diagnostic test; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization

2019 (COVID-19), combined with an emphasis on decreasing exposures to people infected with the virus, led the US Food and Drug Administration (FDA) to issue an Emergency Use Authorization for several RDTs and multiplex panels that include SARS-CoV-2. RDTs include rapid antigen diagnostics and the first molecular diagnostic for home use. These can be performed with self- or caregiver-collected samples. Some home test kits require that users download a smartphone application that provides test interpretation for the user and reports de-identified data for public health surveillance. These diagnostic kits perform best in symptomatic people; results in asymptomatic people should be interpreted with caution.

Table 11-07 Multiplex molecular panels for pathogens in returning international travelers: selected features

SYNDROME	PATHOGENS	SPECIMEN TYPES	ADDITIONAL INFORMATION
ACUTE FEBRILE ILLNESS	Bacteria, viruses, and parasites from different regions	Whole blood	Research use only; clinical performance for many targets has not been determined.
GASTROINTESTINAL PATHOGENS	Includes common bacteria, viruses, and parasites	Stool sample	Sensitive; certain positive results might be unrelated to active infection.
MENINGITIS & ENCEPHALITIS	Includes common bacteria, viruses, and fungi	CSF	Not a replacement for CSF bacterial culture; negative results do not exclude an infectious etiology of meningitis or encephalitis.
RESPIRATORY PATHOGENS	Includes atypical bacteria, common viruses, and SARS-CoV-2	Nasopharyngeal swab	Pathogens can have prolonged shedding time; positive results might not rule out infection from other pathogens.

Abbreviations: CSF, cerebrospinal fluid; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

DIAGNOSTIC TESTING PERFORMED DURING TRAVEL

People who become ill while traveling might seek medical care abroad; development and availability of RDTs for diagnosis of tropical infectious diseases has expanded greatly in recent years, and travelers might return home having been diagnosed based on results from these tests. RDTs for tropical infections typically are lateral-flow immunochromatographic tests that detect antigens from or antibodies to certain pathogens. Because only 1 such test (for malaria) is cleared for use in the United States, the diagnostic characteristics of RDTs used overseas are unfamiliar to most providers. Additionally, a variety of RDTs might be available for certain pathogens (e.g., dengue) in other countries, with widely varying or poorly studied performance characteristics. Institutions that do not have continuous access to a single brand of test further complicates interpretation of results provided by the laboratory.

The following is an illustrative, though by no means exhaustive, list of several common infections for which RDTs are available.

Dengue. Rapid, lateral-flow assays are available to detect the dengue nonstructural protein 1 (NS1) antigen, and IgM and IgG. Dengue tests have widely variable performance characteristics depending on the manufacturer, circulating dengue types, a patient's past medical history, and symptom duration.

Emerging Infections. Emerging pathogens represent a diagnostic challenge. Rapid assays became available after outbreaks of chikungunya, Ebola, and Zika. Such assays might not be available or well-studied at the peak of an outbreak, however.

Leishmaniasis. Assays to detect antibodies against the rK39 antigen (visceral leishmaniasis) have demonstrated good specificity in endemic regions, and highest sensitivity for detecting disease in South Asia.

Leptospirosis. Because of the many pathogenic and intermediate *Leptospira* serotypes that result in human disease worldwide, the usefulness of serologic assays for diagnosing leptospirosis is limited.

Malaria. An FDA-cleared RDT for malaria is available, and malaria RDTs are widely used throughout the world. In general, these tests perform best for *Plasmodium falciparum*, with variable or poor performance for other *Plasmodium* species.

Typhoid. Rapid serologic tests have demonstrated only moderate accuracy to diagnose typhoid. Additionally, these tests are designed to detect *Salmonella enterica* serotype Typhi only.

FUTURE DIRECTIONS

The number of assays compatible with POC testing will undoubtedly continue to increase. Building upon testing milestones achieved during the COVID-19 pandemic, "at home" testing, including molecular testing, is expected to increase in the coming years for both respiratory viruses and other pathogens. Because of the wide breadth and diversity of infecting pathogens in returned travelers, use of POC testing for nondomestic infectious diseases might not be practical for most centers once test volume, personnel training, and cost are taken into consideration. POC testing for common syndromes that affect travelers and nontravelers alike (e.g., respiratory tract and gastrointestinal infections) could provide rapid diagnosis, inform triage decisions, and limit unnecessary laboratory testing.

BIBLIOGRAPHY

Babady NE. The FilmArray respiratory panel: an automated, broadly multiplexed molecular test for the rapid and accurate detection of respiratory pathogens. Expert Rev Mol Diagn. 2013;13(8):779–88.

Centers for Disease Control and Prevention. Ready? Set? Test! Patient testing is important. Get the results right. Atlanta: The Centers; 2019. Available from: www.cdc.gov/labquality/images/waived-tests/RST-Booklet_Dec-2019.pdf.

Gonzalez MD, McElvania E. New developments in rapid diagnostic testing for children. Infect Dis Clin North Am. 2018;32(1):19–34.

Hunsperger EA, Yoksan S, Buchy P, Nguyen VC, Sekaran SD, Enria DA, et al. Evaluation of commercially available diagnostic tests for the detection of dengue virus NS1 antigen and anti-dengue virus IgM antibody. PLoS Negl Trop Dis. 2014;8(10):e3171.

Infectious Disease Society of America. IDSA practice guidelines. Available from: www.idsociety.org/practice-guideline/practice-guidelines.

Pai NP, Vadnais C, Denkinger C, Engel N, Pai M. Point-of-care testing for infectious diseases: diversity, complexity, and barriers in low- and middle-income countries. PLoS Med. 2012;9(9):e1001306.

US Food and Drug Administration. CLIA—Clinical Laboratory Improvement Amendments—currently waived analytes. Available from: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm.

US Food and Drug Administration. In vitro diagnostics EUAs. Available from: www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas.

SCREENING ASYMPTOMATIC RETURNED TRAVELERS

Michael Libman, Sapha Barkati

Except for coronavirus disease 2019 (COVID-19), CDC has no official guidance or recommendations for screening asymptomatic international travelers in the absence of specific risk factors for infectious diseases. Nevertheless, screening travelers returning from developing countries represents a substantial portion of the activity of many travel health and tropical medicine clinics.

The scientific literature on the clinical utility and cost effectiveness of screening asymptomatic travelers is sparse. Asymptomatic travelers can harbor many infections acquired during travel, some of which have the potential to cause serious sequelae or have public health implications. In some cases, these will include pathogens rarely found in the traveler's country of origin. US medical practitioners might have little familiarity with these travel-associated diseases, and specific diagnostic tests might not be readily available or will require expertise in their proper interpretation.

DECIDING TO SCREEN

The decision to screen an asymptomatic person for travel-acquired pathogens depends on their exposure history, itinerary, type of travel, and the public health implications of identifying infection. Screening healthy short-term travelers for infectious diseases other than COVID-19, especially people who do not report a particular exposure, is usually not necessary. On the other hand, consider obtaining specific tests for long-term travelers (e.g., adventure travelers, expatriates, humanitarian aid workers, missionaries, travelers visiting friends and relatives) who might have prolonged or heavy exposure to epidemiologically relevant pathogens with potential for long-term consequences. A traveler's exposure history might be unreliable or not predictive of infection, however, and the value of a detailed itinerary can be limited by incomplete information. Finally, the type of travel might not provide a practical assessment of risk.

For the long-term traveler on hiatus from a continuing assignment abroad, the periodic travel health consultation offers the clinician a chance to screen for infectious diseases, conduct a general health evaluation, and to review health behaviors, malaria prophylaxis, and vaccination status. Promote and reinforce primary prevention by discussing behavioral or other risk factors that could predispose the traveler to ill health (e.g., exposures to contaminated food and drink, arthropods, and freshwater sources; drug use; high-risk sex). The usual recommendations for a periodic health exam, which might include screening for cardiovascular disorders, diabetes, hypertension, and malignancy, also apply.

Benefit & Risk of Screening Asymptomatic Travelers

Before scheduling screening tests for asymptomatic returned travelers, evaluate the sensitivity and specificity of the test, and the risk and cost to the patient. The low prevalence of tropical infections in asymptomatic travelers will heavily influence the positive predictive value of the screening tests, leading to an increased likelihood of false-positive results. As a result, the asymptomatic traveler could be subjected to further investigations, generating greater costs, anxiety, and other possible harms related to diagnostic follow-up, creating complex considerations of benefit versus risk.

Screening traditionally has been viewed as a secondary prevention intervention, that is, an attempt to identify occult illnesses or health risks. Cost effectiveness of screening depends

on the disease of interest, potential outcomes associated with the disease both for the individual traveler and the public's health, and whether an early intervention could reduce morbidity or mortality. One exception regarding asymptomatic screening is newly arrived immigrants and refugees; for recommendations regarding these individuals see Sec. 11, Ch. 11, Newly Arrived Immigrants, Refugees & Other Migrants.

SCREENING FOR NONPARASITIC INFECTIONS

Arboviruses

CHIKUNGUNYA & DENGUE

Screening for chikungunya and dengue in asymptomatic travelers typically is not recommended because there are no specific treatments for infection once identified. Travelers concerned about the risk for complications after a secondary dengue infection sometimes request screening. The absolute risk elevation is minimal, however, and generally there is no specific intervention. The exception are children 9–16 years old living in dengue-endemic areas; Dengvaxia vaccine is a prevention option for those presenting with laboratory-confirmed previous dengue infection (see Sec. 5, Part 2, Ch. 4, Dengue).

ZIKA

The prevalence of Zika virus infection in many countries has decreased dramatically since 2017; as a result, the likelihood of a false-positive test result has increased. Moreover, Zika virus IgM antibody persists months after infection, making it difficult to determine the date of infection, which is crucial information for judging the risk in a pregnant person. Nonetheless, remain vigilant for the potential reemergence of Zika, and review screening guidelines for travelers, including pregnant people and their partners (see Sec. 5, Part 2, Ch. 27, Zika, and www.cdc.gov/zika/hc-providers/index.html).

Coronavirus Disease 2019

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has had vast health, social, and economic effects. The emergence of variants makes the evolution of this pandemic unpredictable. As the pandemic progresses, guidance for populations and travelers evolve, as do requirements and recommendations for crossing international borders (see www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel/index.html). For patients who test positive for SARS-CoV-2 after international travel, consider prioritizing specimens for whole genome sequencing, as applicable.

Sexually Transmitted Infections & Bloodborne Pathogens

High rates of sexual activity with new partners, including sex workers, have been documented in overseas backpackers, military personnel, expatriate workers, and people doing volunteer work. Of concern are the low rates of reported condom use. Moreover, travelers might engage in other high-risk activities (e.g., getting a tattoo or piercing, using injection or intranasal drugs, receiving medical or dental care). Returning travelers with acute hepatitis B, hepatitis C, HIV, monkeypox, or syphilis infection pose public health risks and might be hesitant to volunteer a relevant exposure history.

A detailed questionnaire on risk factors for sexually transmitted infections and bloodborne pathogens is recommended for all travelers; always consider screening according to published guidelines. Screening people with relevant exposures should include HIV and syphilis serologic tests, and nucleic acid amplification testing for chlamydia and gonorrhea in urine and at sites of contact (e.g., pharynx, rectum). For travelers with an identified specific risk factor (e.g., blood exposure, condomless sex) who have not been previously vaccinated against

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hepatitis B virus (HBV), perform HBV testing; hepatitis C virus (HCV) testing also is indicated. Test all travelers born between 1945 and 1965 for HCV if not previously tested.

Tuberculosis

The incidence of tuberculosis (TB) infection related to travel is difficult to estimate. Those with a history of work in high-prevalence settings (e.g., health care institutions, refugee camps) merit screening. Pretravel and posttravel tuberculin skin testing (TST) can require as many as 4 visits to a health care provider—2 pretravel visits for a 2-step test, and 2 posttravel visits after potential exposure. The TB screening process can be simplified by using the interferon-γ release assay (IGRA), which is more expensive but less likely to yield false-positive results in people who received a previous bacillus Calmette-Guérin (BCG) vaccination.

Studies assessing IGRA use for serial testing demonstrated large variations in the rate of conversion and reversion. Fully investigate any positive TST or IGRA result, assess symptoms suggestive of active TB disease, and obtain a chest x-ray. For more information, see Sec. 5, Part 1, Ch. 23, . . . *perspectives*: Testing Travelers for *Mycobacterium tuberculosis* Infection.

SCREENING FOR PARASITIC INFECTIONS

Travelers often are most concerned about the possibility of an occult parasitic infection (see also Sec. 11, Ch. 9,. . . *perspectives*: Delusional Parasitosis). Unfortunately, the literature shows that patient questionnaires and common laboratory testing used to screen for parasitic diseases have poor sensitivity and specificity. Studies have shown that even an exhaustive risk-factor history in asymptomatic patients is unable to reliably detect those who would or would not have evidence of parasitic infection. Physical examination is equally unrevealing.

Most commonly, a stool examination is performed, typically microscopy. Several molecular assays are commercially available to detect a panel of bacterial, viral, and parasitic pathogens. In some cases, these panels are more sensitive than traditional testing methods, and even asymptomatic people often are found to harbor pathogens. The clinical implications of asymptomatic carriage, sometimes at a low level, are unknown for most of these agents, and the risks and benefits of treatment are not well studied. Serologic tests typically are more sensitive for parasitic infections; some have performance limitations related to specificity, but are often preferred for screening asymptomatic travelers.

For questions about parasites and screening for parasitic infections, see www.cdc.gov/parasites/, or contact the CDC at www.cdc.gov/parasites/contact.html.

Helminths

Travelers often are concerned about "worms," by which they usually mean intestinal helminths (see Sec. 5, Part 3, Ch. 13, Soil-Transmitted Helminths). Infections of travelers with large burdens of the common nematodes (e.g., *Ascaris*, hookworm, *Trichuris*) are rare, however. Questioning returning expatriates infected with intestinal helminths has disclosed no attributable symptoms compared with uninfected controls. The life cycles of almost all helminths preclude any real risk of ongoing person-to-person transmission from asymptomatic hosts in high-income countries; helminths generally have a natural lifespan of months to a few years, which ensures eventual spontaneous clearance. In addition, low-intensity infections are of limited clinical importance, though in rare cases aberrant migration of *Ascaris* spp. can result in clinical disease. The exception to this is *Strongyloides stercoralis*.

STRONGYLOIDIASIS

For *Strongyloides* infections, serious complications are well known, nonspecific symptoms can easily be overlooked, duration of carriage after infection is unlimited due to its autoinfection

cycle, and the original burden of infection is irrelevant (see Sec. 5, Part 3, Ch. 21, Strongyloidiasis). Specific types of immune suppression (e.g., corticosteroid therapy, hematologic malignancy, hematopoietic stem cell transplant, human T-lymphotropic virus type 1 [HTLV-1] infection, solid organ transplant) are risk factors for developing a potentially lethal hyperinfection syndrome or disseminated strongyloidiasis. The COVID-19 pandemic has prompted widespread, urgent dexamethasone use, which could lead to an increased risk for severe strongyloidiasis in exposed travelers and migrants.

Consider screening for strongyloidiasis in select high-risk travelers with potential skin exposure to human feces, usually a result of walking barefoot in areas without proper sanitation facilities. Unfortunately, the sensitivity of stool-based biomolecular and parasitological methods is low. Molecular detection of helminths is more sensitive and specific compared to microscopy, but sensitivity is still insufficient for screening purposes. Moreover, molecular techniques are not widely available outside the reference laboratory and research setting. Serologic methods are often required, as discussed elsewhere in this chapter.

SCHISTOSOMIASIS

There is no evidence to demonstrate that the low-burden *Schistosoma* infections typically found in travelers lead to the types of complications found in endemic areas (e.g., liver fibrosis, malignancy). Nevertheless, the possibility of complications cannot be entirely ruled out, particularly in people who have more intense exposures (see Sec. 5, Part 3, Ch. 20, Schistosomiasis). Even brief exposures to freshwater lakes and rivers in known endemic areas in Africa are associated with substantial seroconversion rates. In addition, complications due to ectopic egg migration occasionally can occur in light infections and without warning.

Consider serologic screening in asymptomatic travelers who bathed or swam in freshwater canals, lakes, or rivers in areas endemic for schistosomiasis. Other types of fresh water (e.g., adequately chlorinated swimming pools) carry minimal exposure risk because they do not support the larval parasitic forms. Screening becomes most sensitive only 8–10 weeks after potential exposure and is useful only in those who have not been infected with a schistosome previously. *Schistosoma* antigens (e.g., circulating anodic antigen [CAA]) can be detected in blood and urine in active infection and can be used to monitor cure after treatment, but sensitivity in asymptomatic travelers is not well studied, and these tests are not widely available.

Interpreting traditional tests for the parasites that cause schistosomiasis and strongyloidiasis can be challenging. Urine and stool examination for *Schistosoma* spp. and stool examination for *Strongyloides* lack sensitivity, particularly in low-burden infection; thus, serologic testing has been advocated as the best screening tool. Problems inherent to serologic screening include expense, lack of easy availability, and lack of standardization. Serologic tests often are designed to maximize sensitivity, typically at the expense of specificity. Unfortunately, specificity is almost impossible to define. Seropositivity in the absence of direct pathogen detection is common, and its clinical significance can be difficult to determine.

Fortunately for patients with schistosomiasis (or strongyloidiasis), treatment is easy and effective; for people deemed at risk of strongyloidiasis who require immediate immunosuppression, consider empiric treatment. The common antihelminthic agents used for short-course therapy (e.g., albendazole, ivermectin, praziquantel) have excellent safety profiles. Be aware, however, that rare but severe adverse events can occur when using certain antihelminthics in patients who have occult, unsuspected co-infection with other parasites. Of note, albendazole can cause increased intracranial pressure with focal signs, seizures, and retinal damage in people infected with *Taenia solium*; diethylcarbamazine can provoke ocular damage in people infected with *Onchocerca*; and

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SCREENING ASYMPTOMATIC RETURNED TRAVELERS (CONTINUED)

ivermectin can cause encephalopathy in people infected with *Loa loa*.

FILARIASIS

Reports of travelers with late complications from asymptomatic filarial infections are virtually nonexistent, and filarial screening (blood or skin snips for microfilaria) is generally not recommended for asymptomatic travelers.

OTHER HELMINTHIC INFECTIONS

Helminth parasitic infections rarely seen in returning travelers include fascioliasis, neurocysticercosis, and paragonimiasis, among others. Screening asymptomatic travelers for these infections is generally not appropriate. Primary care providers should refer patients to an infectious disease specialist when biological, clinical, or radiologic abnormalities increase suspicion for these infections. Intestinal helminths (e.g., *Ascaris*, *Enterobius*, hookworms, *Strongyloides*, *Trichuris*) rarely cause severe illness in travelers. Other than for *Strongyloides* in select high-risk travelers, screening is not recommended for intestinal helminth infections.

Protozoa

BLOOD- & TISSUE-DWELLING

MALARIA

No justification can be made for screening most asymptomatic travelers for malaria, whether by blood film, molecular methods, or serologic tests. No available tests can detect the latent hepatic forms (hypnozoites) of *Plasmodium vivax* or *P. ovale*. Remind travelers to seek evaluation for unexplained fever and to notify practitioners of international travel within the past 12 months.

Immigrants with frequent and regular exposure to malaria might gradually develop partial immunity, which can result in low-level parasitemia with minimal symptoms. Immigrants from malaria-endemic areas might later recrudesce with more severe illness, but this phenomenon is rare in non-immigrant travelers. Of note, in rare cases, travelers compliant with prophylaxis might still acquire malaria; often they will present with low parasitemia infections, and their symptoms can manifest after ending prophylaxis. In these cases, testing asymptomatic travelers is generally inadequately sensitive and not recommended. Rather, advise travelers to remain vigilant for symptoms, particularly unexplained fever.

TRYPANOSOMIASIS

Occult trypanosomiasis in asymptomatic travelers (as opposed to immigrants) appears to be extremely rare. Screening tests (e.g., molecular diagnostics, serology) are of unknown value. Consider *Trypanosoma cruzi* testing for travelers who lived for >6 months in rustic housing (e.g., shelters with mud walls and thatched roofs) in endemic areas of Latin America, especially if they report having seen triatomine bugs inside their dwelling. Also consider testing in people who received blood products in an endemic area, or in travelers with clinical manifestations compatible with acute Chagas disease (see Sec. 5, Part 3, Ch. 25, American Trypanosomiasis / Chagas Disease).

East African trypanosomiasis has affected travelers but typically causes acute symptoms. West African trypanosomiasis generally is not reported in travelers. Refer patients to an infectious disease specialist when these infections are suspected based on biological, clinical, or radiologic abnormalities.

INTESTINAL

Treat symptomatic intestinal protozoa infections, particularly *Entamoeba histolytica* which can cause severe disease and ectopic infections (e.g., liver abscess). Except for *E. histolytica* infection (which is only rarely asymptomatic), the finding of pathogenic protozoa in asymptomatic patients is of questionable significance.

The most common protozoa found in asymptomatic travelers are *Blastocystis* and *Giardia* species. History of exposure to contaminated food or water has poor predictive value. No

evidence suggests that asymptomatic carriers are likely to develop symptoms later, and the medications used to treat these protozoa can have adverse effects. In theory, asymptomatic carriers pose a public health risk, but transmission by asymptomatic travelers appears to be rare. In addition, stool microscopy for protozoa is expensive, not very sensitive, not highly reproducible, and many laboratories have limited expertise; thus, screening is not recommended unless evidence of onward transmission is present.

Microscopy cannot distinguish *Entamoeba histolytica* from *E. dispar*. Differentiation requires further specimen collection and testing. Studies reveal that most travelers with *Entamoeba* on microscopy are carrying *E. dispar*. Antigen testing for *E. histolytica* and *Giardia* (among others) is fairly reliable but lacks the potential to screen for all intestinal parasites with a single test, and only some antigen tests are able to differentiate *E. histolytica* from *E. dispar*.

Commercial molecular methods to screen stool specimens for multiple pathogens simultaneously typically include several protozoa, generally with better sensitivity than microscopy. These assays also can specifically distinguish potentially pathogenic *E. histolytica* from nonpathogenic amoebae. They offer rapid turnaround times and, although costs remain high, these assays are increasingly being used in returned travelers with suspected protozoal infections. Some of these panels detect organisms for which pathogenicity remains controversial, (e.g., *Blastocystis* and *Dientamoeba*). Identifying these pathogens can lead to patient anxiety and unnecessary treatment; thus, screening asymptomatic travelers for intestinal protozoa is not routinely recommended.

GENERAL GUIDELINES

Eosinophilia

Screening for eosinophilia is a common test because it is quick, universally available, and theoretically of value in detecting invasive helminths, if not protozoa. Multiple studies have shown, however, that testing for eosinophilia has poor sensitivity for identifying parasitic infections; the low prevalence of infection in asymptomatic travelers means that the positive predictive value is poor, and the finding of eosinophilia can lead to an extensive and often fruitless search for a cause, generating patient anxiety and high costs. Many cases of eosinophilia resolve spontaneously, possibly because of infection with nonpathogenic organisms or a noninfectious cause (e.g., allergy, drug reaction). Repeat eosinophil counts after several weeks or months before embarking on an extensive investigation.

A recent study in travelers and migrants showed that those with helminthic infection (as compared to other diagnoses) had much higher eosinophil counts. Counts can be highly variable, though, even within a single day, and are suppressed by endogenous or exogenous steroids. Using absolute eosinophil counts, rather than eosinophils as a percentage of leukocytes, is more reproducible and predictive.

Duration of Travel & Other Risk Factors

Table 11-08 and the following traveler classification scheme provide general guidelines for screening asymptomatic returned travelers for imported infections.

ALL TRAVELERS

For guidance regarding international travel and posttravel COVID-19 testing, refer to www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel/index.html.

SHORT-TERM TRAVELERS

Screening asymptomatic short-term (<3–6 months) travelers is usually low-yield and should be directed by specific risk factors revealed in the history. A history of prolonged (>2 weeks) digestive symptoms during travel can suggest protozoal infection. Consider serologic testing of travelers who bathed or swam in unchlorinated freshwater sources in regions

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Table 11-08 Considerations for screening asymptomatic travelers

RISK FACTOR OR EXPOSURE	SUGGESTED SCREENING TESTS
All travelers Short stay (<3–6 months) No identified risk factor/exposure	COVID-19[1] No additional screening
Long-stay (>3–6 months) Poor sanitation or hygiene	CBC with eosinophil count Creatinine CRP Liver transaminases Consider stool ova and parasites
Sexual contact	Chlamydia Gonorrhea HBV, if not previously vaccinated (for men who have sex with men, people who have sex with unknown partners) HCV (if risk factors present or if born between 1945–1965) HIV Syphilis
Injection or intranasal drug use Medical or dental care Piercing Tattoo	HBV, if not previously vaccinated (for injection drug use) HCV (for injection or intranasal drug use, unregulated tattoos) HIV
Pregnant people who traveled in known current Zika virus–endemic or epidemic area or sexual contact with a partner who traveled in these areas	Screening asymptomatic pregnant travelers who have potential exposure (but without ongoing risk) is not routinely recommended outside an outbreak situation NAAT ≤12 weeks after potential exposure in endemic or epidemic regions can be considered in pregnant people
Health care worker	TB screening (TST or IGRA)
Prolonged residence (>6 months) with population in a highly TB-endemic area	TB screening (TST or IGRA)
Walking barefoot on soil potentially contaminated with human feces or sewage	*Strongyloides* serology
Exposure to freshwater rivers, lakes, or irrigation canals	*Schistosoma* serology

Abbreviations: CBC, complete blood count; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; HBV, hepatitis B virus; HCV, hepatitis C virus; NAAT, nucleic acid amplification test; TB, tuberculosis; TST, tuberculin skin test; IGRA, interferon-γ release assay

[1]Recommendation might change with the evolution of the pandemic. Refer to the updated recommendations available from: www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel/index.html.

with known schistosomiasis risk, especially sub-Saharan Africa.

In addition, consider serology testing for *Strongyloides* in select high-risk travelers who have skin exposure to soil likely to be contaminated with human feces, usually individuals with a history of frequently walking barefoot outdoors. Obtain a sexual history; screen for

sexually transmitted and bloodborne infections, if warranted. Zika virus testing for asymptomatic travelers (including pregnant people) with potential exposure is generally not recommended (see Sec. 5, Part 2, Ch 27, Zika). Consider TB screening for those returning from work in health care or other high-risk settings.

LONG-TERM TRAVELERS & EXPATRIATES

The overall yield of screening increases for longer-stay (>3–6 months) travelers. The emphasis should be on those with the longest stays and the most problematic sanitary conditions or other exposures. In some cases, employers require certain tests, partly for liability reasons. Performing stool examinations mostly provides psychological reassurance. Consider obtaining serologic testing for schistosomiasis and strongyloidiasis in people with recent or remote travel histories to endemic areas and who report some level of risk.

A complete blood count with white blood cell differential and eosinophil counts, liver transaminases, creatinine, and C-reactive protein are usually the basic set of tests performed. Interpret results cautiously; abnormalities might trigger further testing. Zika virus testing for asymptomatic travelers with potential exposure, including pregnant people, is generally not recommended outside of a recognized outbreak. Limit TST or IGRA testing to travelers who worked in a health care or similar setting or who had intimate and prolonged contact with residents of a highly TB-endemic area for ≥6 months. Only perform other screening based on exceptional exposures or knowledge about local outbreaks.

BIBLIOGRAPHY

Baaten GG, Sonder GJ, van Gool T, Kint JA, van den Hoek A. Travel-related schistosomiasis, strongyloidiasis, filariasis, and toxocariasis: the risk of infection and the diagnostic relevance of blood eosinophilia. BMC Infect Dis. 2011;11:84.

Casacuberta-Partal M, Janse JJ, van Schuijlenburg R, de Vries JJC, Erkens MAA, Suijk K, et al. Antigen-based diagnosis of *Schistosoma* infection in travellers: a prospective study. J Travel Med. 2020;27(4):1–9.

Centers for Disease Control and Prevention. International travel during COVID-19; 2020. Available from: www.cdc.gov/coronavirus/2019-ncov/travelers/international-travel-during-covid19.html.

Centers for Disease Control and Prevention. Zika virus for health care providers; 2022. Available from: www.cdc.gov/zika/hc-providers.

MacLean JD, Libman M. Screening returning travelers. Infect Dis Clin North Am. 1998;12(2):431–43.

Overbosch FW, van Gool T, Matser A, Sonder GJB. Low incidence of helminth infections (schistosomiasis, strongyloidiasis, filariasis, toxocariasis) among Dutch long-term travelers: A prospective study, 2008–2011. PLoS ONE. 2018;13(5):e0197770.

Salzer HJF, Rolling T, Vinnemeir CD, Tannich E, Schmiedel S, Addo MM, et al. Helminthic infections in returning travelers and migrants with eosinophilia: diagnostic value of medical history, eosinophil count and IgE. Travel Med Infect Dis. 2017;20:49–55.

Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, et al. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. MMWR Recomm Rep. 2012;61(RR-4);1–18.

Soonawala D, van Lieshout L, den Boer MA, Claas EC, Verweij JJ, Godkewitsch A, et al. Post-travel screening of asymptomatic long-term travelers to the tropics for intestinal parasites using molecular diagnostics. Am J Trop Med Hyg. 2014;90(5):835–9.

US Preventive Services Task Force. Final recommendation statement. Hepatitis C: screening; 2022. Available from: www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/hepatitis-c-screening.

Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. MMWR Recomm Rep. 2008;57(RR-8):1–20.

Yansouni CP, Merckx J, Libman MD, Ndao M. Recent advances in clinical parasitology diagnostics. Curr Infect Dis Rep. 2014;16(11):434.

. . . *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).

FEVER IN THE RETURNED TRAVELER

Mary Elizabeth Wilson

Fever often accompanies serious illness in returned travelers. The most common life-threatening tropical disease associated with fever in returned travelers is malaria. Because an increased temperature can signal a rapidly progressive infection, initiate early evaluation, especially in people who have visited areas with malaria in recent months (see Sec. 5, Part 3, Ch. 16, Malaria).

The initial focus in evaluating a febrile returned traveler should be on identifying infections that are potentially life-threatening, treatable, or transmissible. In some instances, public health officials must be alerted if the traveler was possibly contagious while traveling or infected with a pathogen of public health concern (e.g., Ebola virus, yellow fever virus) at the origin or destination. During an outbreak (e.g., the Ebola epidemic in West Africa), special screening protocols could be needed. A specific cause for fever might not be identified in ≥25% of returned travelers.

NARROWING THE DIFFERENTIAL DIAGNOSIS

Most illnesses in returned travelers (e.g., diarrhea, pneumonia, or pyelonephritis) are caused by common and cosmopolitan infections that must be considered along with the more unusual ones. Because the geographic area of travel determines the relative likelihood of major causes of fever, identifying where the febrile patient traveled and/or lived is essential (see Table 11-09). Ask about travel-related activities (e.g., cave exploration, dental or medical care, sexual activity, newly acquired tattoos); exposures (e.g., animal bites, freshwater exposure in schistosomiasis-endemic areas); and living arrangements (e.g., dwelling type, use of mosquito nets, air conditioning, window screens), any of which might elicit useful clues. Pretravel preparation (e.g., vaccinations, malaria prophylaxis) will markedly reduce (although not eliminate) the likelihood of some infections, so this is also a relevant part of the history.

Because each infection has a characteristic incubation period (the range is extremely wide for some), define timing of exposure for different geographic areas; this can help exclude some infections from the differential diagnosis. Most serious febrile infections manifest within the first month after return from tropical travel, yet infections related to travel exposures occasionally occur months or even >1 year after return. In the United States, >90% of reported cases of *Plasmodium falciparum* malaria manifest ≤30 days of return, but almost half of cases of *P. vivax* malaria manifest >30 days after return.

FINDINGS REQUIRING URGENT ATTENTION

Presence of fever plus certain associated signs, symptoms, or laboratory findings can suggest specific infections (see Table 11-10). Findings that should prompt urgent attention include hemorrhage, low blood pressure, altered consciousness, and high respiratory rate. Even if an initial physical examination is unremarkable, repeat the exam if the diagnosis is not clear, because new findings might appear that will help in the diagnostic process (e.g., skin lesions, a tender liver). Although most febrile illnesses in returned travelers are related to infections, bear in mind that other conditions, including pulmonary emboli and drug hypersensitivity reactions, also can be associated with fever.

Fever accompanied by a syndrome (see Table 11-11) deserves further scrutiny, because it could indicate a disease of public health concern, for which immediate infection containment and control measures are indicated.

Travelers visiting friends and relatives (VFR) often do not seek pretravel medical advice and are at greater risk for some diseases than other