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Recommendations for International Travel

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those who do not. Strong provider recommendations using a presumptive approach (e.g., “You’re due for the flu shot today” vs “What do you want to do about the flu shot?”) have been shown to improve vaccine acceptance (Chap. 3). Providers should be well informed about vaccine risks and benefits so that they can address patients’ common concerns. The CDC and seven provider organizations review and update the schedule for adult immunization on an annual basis and have developed educational materials to facilitate provider-patient discussions about vaccination (www.cdc.gov/vaccines/hcp/).

System Supports Medical offices can incorporate a variety of methods to ensure that providers consistently offer specific immunizations to patients with indications for specific vaccines. Decision-support tools have been incorporated into some electronic health records to alert the provider when specific vaccines are indicated. Manual or automated reminders and standing orders have been discussed (see “Deciding Whom to Vaccinate,” above) and have consistently improved vaccination coverage in both office and hospital settings. Most clinicians’ estimates of their own performance diverge from objective measurements of their patients’ immunization coverage; quantitative assessment and feedback have been shown in pediatric and adolescent practices to increase immunization performance significantly. Some health plans have instituted incentives for providers with high rates of immunization coverage. Specialty providers, including obstetrician-gynecologists, may be the only providers serving some high-risk patients with indications for selected vaccines (e.g., pneumococcal polysaccharide vaccine, zoster vaccine for immunocompromised adults) as well as for other routine vaccinations (e.g., influenza, COVID-19). Immunization Requirements Vaccination against selected communicable diseases is required for attendance at many universities and colleges as well as for service in the U.S. military and in some occupational settings (e.g., child care, laboratory, veterinary, and health care). Immunizations are recommended and sometimes required for travel to certain countries (Chap. 130). PART 5 Infectious Diseases ■ ■ VACCINATION SETTINGS Vaccination of adults occurs in a variety of settings. While the “medical home” remains a critical setting for vaccination of adults, other

settings such as pharmacies have become an increasingly important venue for adult vaccination and help to expand equitable access and convenience to vaccination. Other vaccination settings outside the medical home include health department venues, workplaces, and schools or colleges. Regardless of setting, it remains important for standards of immunization practice to be followed. Consumers should be provided with information on the vaccine and how to report adverse events (e.g., via provision of a VIS), and procedures should ensure that documentation of vaccine administration is forwarded to the primary care provider and the state or city public health immunization registry. Detailed documentation may be required for employment, school attendance, and travel. Personalized health records can help consumers keep track of their immunizations, and some occupational health clinics have incorporated automated immunization reports that help employees stay up to date with recommended vaccinations. Some pharmacy chain establishments are using automated systems to report immunization information to the state or local immunization information system. ■ ■ **PERFORMANCE MONITORING** Tracking of immunization coverage at national, state, institution, and practice levels can yield feedback to practitioners and programs and facilitate quality improvement. Healthcare Effectiveness Data and Information Set (HEDIS) measures related to adult immunization facilitate comparison of health plans. CDC utilizes a number of surveys to monitor vaccination coverage among adults and track progress toward achievement of Healthy People 2030 targets for immunization coverage. These sources include the National Health Interview Survey, the Behavioral Risk Factor Surveillance System, the National Immunization Surveys, Internet panel surveys, and other sources. Vaccination coverage among adults remains suboptimal, and statespecific immunization coverage for certain vaccines reveals substantial

geographic variation in coverage. There are persistent disparities in adult immunization coverage rates by race and ethnicity, as well as other sociodemographic factors. In contrast, racial and economic disparities in immunization of young children have been dramatically reduced during the past 30 years. Much of this progress is attributed to the Vaccines for Children Program, which since 1994 has entitled eligible children, including those who are uninsured or underinsured, to receive free vaccines. ■ ■ **FUTURE TRENDS** Although most vaccines developed in the twentieth century targeted common acute infectious diseases of childhood, more recently developed vaccines prevent chronic conditions prevalent among adults. Hepatitis B vaccine prevents hepatitis B-related cirrhosis and hepatocellular carcinoma, HPV vaccine prevents some types of cervical cancer, genital warts, and anogenital cancers and may also prevent some oropharyngeal cancers, and the herpes zoster subunit vaccine protects against zoster and postherpetic neuralgia. New targets of vaccine development and research may further broaden the definition of vaccine-preventable disease. Research is ongoing on vaccines to prevent insulin-dependent diabetes mellitus, nicotine addiction, and Alzheimer's disease. Expanding strategies for vaccine development are incorporating molecular approaches such as RNA, DNA, vector, and peptide vaccines. New technologies, such as the use of transdermal and other needle-less routes of administration, are being applied to vaccine delivery. **Acknowledgment** The authors thank Anne Schuchat, MD, Lisa A. Jackson, MD, and Nancy Messonnier, MD, for their significant contributions to this chapter in the previous editions. ■ ■ **FURTHER READING** Centers for Disease Control and Prevention: Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th ed, Hamborsky J et al (eds). Washington DC, Public Health Foundation, 2015. Kroger A et al: General best practice guidelines for immunization. Best practices guidance of the Advisory Committee on Immunization Practices (ACIP). Available at [www.cdc.gov/vaccines/hcp/acip-recs/](http://www.cdc.gov/vaccines/hcp/acip-recs/general-) general-

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for International Travel In recent decades, international travel has increased dramatically with globalization and greater access to international flights. According to the United Nations World Tourism Organization, international tourist arrivals increased 50.3% from 2010 to 2019; arrivals exceeded 1.4 billion in 2019, with the highest rate of growth in arrivals to destinations in Asia and the Pacific. In 2018, according to the United Nations Conference on Trade and Development, total global merchandise exports reached

a record 19.5 trillion U.S. dollars, a nearly threefold increase over the previous two decades. Although travel in 2020 dropped drastically during the COVID-19 pandemic, there has been recovery since 2021, resuming prepandemic growth trends. International travel has brought social, economic, and cultural benefits to the world; however, travel also widens the range of infections to which an individual may be exposed. The speed of air travel has been a major factor in the ease with which emerging infectious diseases have quickly spread worldwide in recent years. In the nineteenth century, intercontinental travel took long enough that travelers often recovered or perished from acute infections before arrival at their destinations. However, in the jet age, the time required to circumnavigate the globe has decreased to <24 h. This duration is shorter than the incubation periods for almost all infections, increasing the likelihood that infected travelers can arrive at their destinations prior to symptom onset. Epidemics can result; examples include severe acute respiratory syndrome (SARS) in 2003, Ebola virus disease in 2014, and the COVID-19 pandemic in 2020. Furthermore, introduction of pathogens into vulnerable regions can subsequently lead to infections becoming endemic, as was observed with the reintroduction of dengue throughout much of the Americas beginning in the 1970s and the global spread of HIV infections in the 1980s. Additional challenges include the increasing diversity of travelers. While tourism, business travel, and mission work continue to be popular, recent decades have seen increasing numbers of other types of travelers, including students, migrants, medical tourists, and persons visiting their countries of origin ("visiting friends and relatives" [VFR] travelers). Furthermore, an increasing range of individuals with risk factors for illness or injury are traveling internationally, including elderly persons, infants, pregnant women, and persons with chronic medical conditions (e.g., immunocompromising conditions). Whether practicing travel medicine, primary care, or other specialties, providers will encounter patients who travel internationally. This chapter outlines key considerations and preventive measures for international travelers, particularly those traveling to low- and middle-income countries. **EPIDEMIOLOGY OF TRAVEL-RELATED CONDITIONS** Unanticipated medical problems during travel are common. Although reported rates of travel-related morbidity and mortality vary widely by destination, traveler type, and study methodology, as many as 43–79% of travelers report developing a travel-related illness. Most illnesses are minor, with diarrhea often the most commonly reported and fewer than 1–3% of travelers reporting

hospitalization. Among vaccinepreventable infections in travelers to lower-income countries, influenza historically has been the most commonly reported, although COVID-19 has also become common among travelers since 2020. Typhoid and hepatitis A are reported much less often, but typically are still reported more frequently than other infections commonly discussed in travel medicine but not frequently diagnosed in travelers, including cholera, Japanese encephalitis, meningococcal disease, rabies, poliomyelitis, and yellow fever. However, outbreaks such as the emergence of yellow fever in coastal southeastern Brazil in 2017–2018 or cholera associated with the 2010 earthquake in Haiti can result in an increased incidence of travel-associated cases. Among causes of death in travelers, studies suggest that cardiovascular events (likely associated with preexisting cardiac conditions) and injury are much more common than infections. Among U.S. citizens, the injuries most commonly causing deaths during international travel in 2016–2017 were motor vehicle accidents, homicide, drowning and maritime injuries, and suicide. Stressors encountered during travel can also exacerbate or uncover psychiatric disorders, and psychological conditions such as depression and anxiety are a common reason for medical evacuation.

GENERAL APPROACH TO ADVISING INTERNATIONAL TRAVELERS Whether advising travelers in a travel clinic or in a primary care setting, providers must cover a few key elements in a pretravel consultation (Table 130-1). These include (1) a trip risk assessment based on

detailed review of the itinerary and the traveler's medical profile; (2) immunizations; (3) prevention of arthropod-borne infections, including malaria chemoprophylaxis (when indicated); (4) food and water precautions and travelers' diarrhea management; and (5) prevention of injuries and other conditions associated with travel.

A detailed itinerary, including cities and areas in a country to be visited, activities, and type of accommodations, is critical for assessment of the risks of the trip and determination of the indications for specific vaccinations, malaria prophylaxis, and other preventive measures. Trip duration, sequence of countries visited, and transit stops are important considerations, especially in the assessment of immunization requirements such as those for yellow fever. Numerous online resources offer recommendations for immunizations and malaria prophylaxis, which vary significantly among countries or even within certain countries (Table 130-2). The U.S. Centers for Disease Control and Prevention (CDC) travelers' health website (www.cdc.gov/travel) is a source of comprehensive, up-to-date, country-specific recommendations on numerous topics, including immunizations, malaria chemoprophylaxis, and travel health notices for outbreaks and emerging infections. Because recommendations and requirements can change unexpectedly, providers are advised to routinely review guidance for each country prior to making recommendations. Consideration of the traveler's medical profile is critical to recommendations for appropriate preventive measures. Key considerations include the patient's age, medical and vaccination histories, current medications, allergies (drug, food, and environmental), and pregnancy status. Although any chronic medical problem can be relevant to travel, common issues that can require particular attention include immunocompromising conditions (including HIV infection and treatment with immunosuppressive and immunomodulatory medications), cardiac and pulmonary conditions, pregnancy status, and severe allergies. Significant hepatic and renal impairment due to any etiology can affect the choice of malaria prophylaxis.

CHAPTER 130 Although travel clinics with providers specializing in travel medicine—e.g., those with a Certificate in Travelers' Health issued by the International Society of Travel Medicine—are now common in many cities worldwide, many travelers do not seek pretravel consultations, often because of an underappreciation of

travel risks or a lack of awareness of the resource. Primary care providers are encouraged to routinely ask their patients about upcoming travel. Although some travel-specific vaccinations are often available only at specialized clinics, many recommended vaccines are available from general practitioners or pharmacies. Reasons to refer a patient to a travel specialist include the need for vaccines used exclusively for travel, complex itineraries or traveler medical histories, or unfamiliarity with recommended immunizations or malaria chemoprophylaxis. Because several vaccines are given as a series and all vaccines theoretically take a week or more to induce protective immunity, referral to a travel clinic at least 4–6 weeks before travel is ideal. However, when this time frame is not possible, consultations can still provide much benefit.

Health Recommendations for International Travel While the decision of whether to travel is ultimately that of the traveler, travel medicine providers play a key role in helping travelers identify the risks of a trip so that they can make an informed decision based on their personal risk tolerance. Occasionally, some situations can warrant advice against travel, including trips to areas with dangerous outbreaks or security situations or trips by a traveler who is unable to undertake critical preventive measures (e.g., travel to highly malarious areas without chemoprophylaxis). Unfortunately, travel-related vaccinations and chemoprophylactic medications can be expensive and often are not covered by health insurance. To assist travelers on a limited budget, providers can prioritize preventive measures according to degree of risk so that decisions to decline a recommendation are not based on cost alone.

IMMUNIZATIONS FOR TRAVELERS Historically, the field of travel medicine considered immunizations as routine, recommended, or required. Because infections prevented by routine immunizations for children and adults are encountered worldwide, travelers should be up to date with these immunizations.

TABLE 130-1 Overview of the Pretravel Consultation

CONSULTATION ELEMENT	ITEMS TO BE COVERED
Risk Assessment	Itinerary • Destination countries and regions • Timing • Duration of trip • Mode of travel • Accommodations • Reason for travel and anticipated activities • Altitude
Traveler	• Medical history, medications • Allergies • Pregnancy status and planning • General risk tolerance
Immunizations	Itinerary • Recommended and required vaccinations for itinerary • Administration of vaccines to meet recommendations and Traveler • Immunization history • Precautions and contraindications for specific vaccines
Malaria and Arthropod-borne Infection Prevention	Itinerary • Malaria and other arthropod-borne infection risk at destination • Accommodations and activities • Local malaria resistance to chemoprophylaxis drugs
PART 5 Infectious Diseases	Traveler • Precautions and contraindications to specific malaria chemoprophylaxis agents • Drug–drug interactions of regular medications with malaria chemoprophylaxis
Gastrointestinal Illness	Itinerary • Destination hygienic standards and water quality • Source of meals (e.g., restaurants, street vendors, home-cooking)
Traveler	• Travel style • Adventurous eating habits • Drug–drug interactions of regular medications with self-treatment antibiotics
Other Possible Topics to Address	• Waterborne infection (schistosomiasis, leptospirosis) prevention • Injury and crime avoidance • Animal bite and rabies prevention • Sexually transmitted infections • Altitude illness • Venous thromboembolism • Jet lag • Motion sickness • Severe food, insect sting, and environmental allergies • Travel health and medical evacuation insurance • Traveler health kits and travel with medications • Mental health and cultural adaptation

aICVP, International Certificate of Vaccine Prophylaxis (“yellow card”).

Recommended travel vaccines in adults are those that are not included in routine schedules but that should be considered because of anticipated risks during travel. Required immunizations are those that are mandated by international regulations or specific countries for entry or exit. These

three categories are not mutually exclusive or fixed, as many vaccinations that originally were used exclusively for travel (e.g., hepatitis A vaccine) are now given routinely in the United States. For required travel immunizations, proof of vaccination is provided on the International Certificate of Vaccination Prophylaxis (ICVP, commonly called the “yellow card”) issued by travel medicine

- Risk assessment that considers the itinerary, traveler, and ability to implement recommended preventive measures
- Shared decision-making regarding whether to travel requirements
- Provision of official documentation (ICVPa) for required immunizations
- Prescription of malaria chemoprophylaxis when indicated
- Administration of vaccines for arthropod-borne infections when indicated and available
- Arthropod-bite avoidance advice
- Advice on early recognition of malaria symptoms

See Fig. 130-2 providers. When appropriate, medical waivers for required vaccinations can be granted and documented on the ICVP. While enforcement of vaccine requirements can be unpredictable, travelers without proof or medical waiver for a required immunization can be subject to entry barriers, vaccination upon arrival, quarantine, or other penalties. In some situations, a vaccine may not be routinely recommended for a specific country but is still required for entry. The most common of these situations involves yellow fever vaccination, when a traveler who has recently been in an endemic country enters certain nonendemic countries (see “Yellow Fever,” below).

TABLE 130-2 Online Resources for Travelers and Travel Medicine Providers

SUBJECT RESOURCESa

General and country-specific recommendations, clinic directories CDC Travelers’ Health, www.cdc.gov/travel Country-specific immunization and malaria prevention advice, travel health notices, travel and yellow fever vaccine clinic listings CDC Health Information for International Travel (Yellow Book), available at www.cdc.gov/travel Comprehensive travel medicine reference covering general topics and specific infections, immunizations, special traveler populations, and common itineraries Heading Home Healthy, www.headinghomehealthy.org Traveler and provider tools for trip-specific CDC recommendations U.S. State Department, www.travel.state.gov Country profiles, travel advisories, Smart Traveler Enrollment Program (STEP), traveler advice Government of Canada Travel and Tourism, www.travel.gc.ca Canadian guidelines and advice for international travel National Travel Health Network and Centre (NaTHNaC), www.nathnac.net British resource for international travel and travel medicine providers International Society of Travel Medicine, www.istm.org Global travel clinic directory, resources for travel medicine providers International Association for Medical Assistance to Travellers, www.iamat.org International clinic directory, advice on travel health insurance World Health Organization, www.who.int/travel-advice Travel health updates, traveler advice, technical guidance American Society of Tropical Medicine and Hygiene, www.astmh.org Directory for clinical specialists in tropical medicine, travel medicine, and medical parasitology Jet lag prevention Jet Lag Rooster Jet Lag Calculator, <https://sleepopolis.com/calculators/jet-lag/> Online tool to create jet lag prevention plan for a specific itinerary For travelers with specific conditions American College of Obstetrics and Gynecology, acog.org/search#q=travel&sort=relevancy Advice for pregnant travelers The Global Database on HIV-Specific Travel & Residence Restrictions, www.hivtravel.org General information for HIV-infected travelers and preexposure prophylaxis users and database on HIV-related entry restrictions Asthma and Allergy Foundation of America, www.aafa.org/traveling-with-asthma-allergies Advice for traveling with asthma and allergies FARE, www.foodallergy.org Resources for persons with severe food allergies, including chef card templates in several languages aAll websites last accessed March 21, 2024. Abbreviation: CDC, Centers for Disease Control and

Prevention. All vaccines that are commonly administered for travel can generally be given on the same day; however, oral typhoid vaccine should be administered at least 8 h after oral cholera vaccine. Limited evidence on immunogenicity suggests that the response to live virus vaccines may be impaired if they are given on different days <28 days apart. For this reason, live virus vaccines (i.e., yellow fever, measles-mumps-rubella [MMR], live attenuated influenza, and varicella) should be given on the same day or spaced at least 28 days apart. If neither of these schedules is possible, the recommendation is to repeat the second vaccination after at least 28 days. Table 130-3 outlines common immunizations for travel in adults. ■ ■

IMMUNIZATIONS FOR TRAVELERS TO MOST DESTINATIONS

Hepatitis A Hepatitis A is one of the more commonly reported vaccine-preventable infections in travelers. Transmission occurs primarily through direct person-to-person contact (fecal-oral transmission) or contaminated food and water, and travel is among the most common risk factors for infection among cases reported in the United States. Travelers are at highest risk in countries with inadequate sanitation and hygienic practices; levels of hepatitis A endemicity are highest in South Asia and sub-Saharan Africa. Although hepatitis A immunization is now routinely recommended for persons with certain medical conditions and for all children in the United States, many adults have not been vaccinated. A single dose of monovalent hepatitis A vaccine is considered protective for younger, healthy adults when given prior to travel, and a booster vaccine dose given 6–18 months after the

CHAPTER 130 Health Recommendations for International Travel primary dose confers lifelong immunity. For persons >40 years old, immunocompromised persons, and other individuals with chronic medical conditions that might impair immune response, administration of hepatitis A immune globulin (0.1 mL/kg) at a separate site at the time of primary vaccination can be considered. No efficacy data are available to support single-dose use of hepatitis A/B combined vaccine (Twinrix) before travel.

Hepatitis B Hepatitis B is transmitted through contact with contaminated blood, blood products, or other bodily fluids. Travelers are strongly advised against high-risk activities, including tattooing, body piercing, and unprotected sexual intercourse. Even when avoiding activities that pose a high risk of exposure to hepatitis B, travelers seeking health care can be exposed through inadequate infection-control measures or blood-product screening. While all travelers may benefit from hepatitis B vaccination, ensuring immunity to hepatitis B is particularly important for long-term travelers, health care workers, and persons who have sexual encounters. Nonimmune travelers who are departing too soon to complete the standard schedule for recombinant hepatitis B vaccine can consider the rapid hepatitis A/B combined vaccine (Twinrix) series or the recombinant hepatitis B vaccine with novel adjuvant (Heplisav-B).

Influenza and COVID-19 Since respiratory infections such as seasonal influenza and COVID-19 are the most common vaccine-

preventable infections acquired during travel, travelers should be advised to be up to date with routine seasonal influenza and COVID-19 vaccinations. Because of variations in influenza seasons worldwide and

TABLE 130-3 Common Travel Immunizations PRIMARY SERIES IN

UNVACCINATED ADULTS BOOSTER INTERVAL PREGNANCY CONSIDERATIONS VACCINE Consider for Most Destinations Hepatitis A, inactivated (Havrix, Vaqta) 2 doses 6–12 months apart (Havrix); 2 doses 6–18 months apart (Vaqta) Hepatitis A/B combined (Twinrix) 3 doses at 0, 1, and 6 months;

accelerated series: 3 doses on days 0, 7, and 21–30 Hepatitis B, recombinant and recombinant with novel adjuvant (Heplisav-B) Recombinant, 3 doses at 0, 1, and 6 months; recombinant with novel adjuvant, 2 doses at 0 and 1 month Measles, mumps, and rubella (MMR) 2 doses (≥ 28 days apart) None recommended Contraindicated Specific Destinations or Activities Chikungunya vaccine, live 1 dose Undetermined Inadequate data, precaution advised Cholera, live attenuated (Vaxchora), inactivated oral (Dukoral) 1 dose (Vaxchora); 2 doses 1–6 weeks apart (Dukoral) Japanese encephalitis, inactivated Vero cell culture–derived (IXIARO) 2 doses on days 0 and 7–28 ≥ 1 year after primary series Inadequate data, precaution advised against use unless risk of infection outweighs theoretical vaccine risk Meningococcal meningitis, quadrivalent conjugate 1 dose 5 years May be used if indicated Poliomyelitis, inactivated 3 doses if previously unvaccinated Single lifetime adult booster for persons who received primary series as children Rabies, human diploid cell (HDCV), purified chick embryo cell (PCECV) 2 doses on days 0 and 7 A third dose (21 days to 3 years after initial series) or titer check (1–3 years after primary series) recommended for travelers with ongoing (>3 year) exposure risk a PART 5 Infectious Diseases Tick-borne encephalitis vaccine, inactivated 3 doses; second dose 14 days to 3 months after the first, and third dose 5–12 months after the second b Typhoid, Vi capsular polysaccharide and oral live attenuated 1 dose 2 years for Vi capsular polysaccharide; 5 years for oral live attenuated Yellow fever 1 dose None routine; 10-year boosters recommended for certain groups a Readers are advised to refer to the Centers for Disease Control and Prevention Yellow Book or Advisory Committee on Immunization Practices (ACIP) 2022 guidance on rabies vaccination for detailed rabies preexposure prophylaxis recommendations based on exposure risk categories. b Travelers unable to receive the third dose before travel should receive two doses before travel. year-round risk in tropical regions, influenza vaccine should be offered to unvaccinated travelers even when the influenza season has already peaked locally. Travel medicine providers can reinforce the importance of these immunizations for all travelers by emphasizing that even uncomplicated infection can disrupt travel and put their contacts at risk. Preventing infections among those at higher risk for severe illness (e.g., the elderly and persons with immunocompromising conditions) is particularly important, since the availability of appropriate treatments and supportive care can be limited in many destinations. For this reason, other vaccines for respiratory infections not typically associated with travel, including pneumococcus and respiratory syncytial virus, are potentially important for certain travelers at higher risk of severe illness. Other preventative advice for respiratory infections (wearing masks in high-risk situations or avoiding crowded, poorly ventilated areas) can be important for persons at high risk for infection. For travelers at high risk for complicated influenza or COVID-19 infections, providing a course of antivirals for self-treatment might be considered for travel to areas with limited access to treatment. However, travelers must be counseled on the proper use of antivirals, i.e., reserving their use for confirmed or strongly suspected infections. In addition to available SARS-CoV-2 home test kits, rapid multiplex influenza and SARS-CoV-2 tests are now available for home use in the United States. These kits are useful for travelers; however, at-home tests are not sufficiently sensitive to rule out an infection and travelers should seek formal medical evaluation whenever possible. Measles, Mumps, and Rubella According to the World Health Organization (WHO), numbers of measles cases have increased

None recommended Limited data, generally considered safe, use if protection recommended Not recommended except booster at 12 months after accelerated primary series Limited data, generally considered safe, use if protection recommended Not recommended after routine vaccination schedule Recombinant vaccine, 3-dose schedule not contraindicated; Heplisav-B, no

data Undetermined for Vaxchora; 2 years for Dukoral Inadequate data, not recommended May be used if indicated May be used if indicated ≥ 3 years after primary series Inadequate data; consider if risk of infection outweigh potential risks Inadequate data; use Vi polysaccharide if protection needed Precaution globally in recent years, with more cases worldwide in 2019 than in any other year since 1996 (Chap. 211). In the past decade, countries at all income levels have had major outbreaks. Although endemic measles transmission was eliminated in the United States in 2000, cases have increased in recent years because of outbreaks initiated by infected travelers, mostly those who were unvaccinated or undervaccinated. Unfounded vaccine hesitancy (Chap. 3) directed against measles vaccines is not uncommon in the United States and Europe, contributing to a recent worldwide resurgence. Disruption of vaccination programs during the COVID-19 pandemic has also contributed to recent outbreaks. Transmission events in airports and aboard aircraft have been reported, so all nonimmune travelers are potentially at risk. Travelers should have evidence of immunity to measles. For U.S. adults, acceptable criteria include (1) documented vaccination with two doses of live measles virus-containing vaccine given at least 28 days apart; (2) serologic evidence of immunity; (3) laboratory-confirmed illness; or (4) birth before 1957. Although two doses of measles virus-containing vaccine have been recommended for children in the United States since 1989, a significant number of older U.S. travelers born after 1956 may have received only one dose. In this country, the only measles vaccine available for use in adults is the combined MMR vaccine. Travelers should also have evidence of immunity to mumps and rubella; the criteria for immunity to these diseases are similar to those for measles except that a single dose of rubella virus-containing vaccine is considered adequate. Tetanus, Diphtheria, and Pertussis Travelers should be up to date with age-appropriate tetanus, diphtheria, and pertussis

vaccinations (Chap. 129). While the risk of tetanus and pertussis exists worldwide, diphtheria is endemic or epidemic primarily in countries without adequate levels of vaccination. Because a tetanus booster is recommended for tetanus-prone injuries if the preceding booster dose was received >5 years earlier, some experts consider an early booster (before 10 years) for travelers engaging in activities with a high risk of injury in destinations with limited access to health care. A diphtheria booster within 5 years of travel is also recommended for travelers going to countries experiencing a diphtheria outbreak. Typhoid Fever Typhoid fever, caused by *Salmonella enterica* serotype Typhi, is transmitted through ingestion of contaminated food and water. Most cases of typhoid fever reported in the United States are diagnosed in travelers after being acquired in South Asia. Africa and Southeast Asia also are considered high risk. East Asia, South America, and the Caribbean are considered lower risk. As with other food- and waterborne infections, travelers to endemic areas are at increased risk when consuming food or drink under unhygienic conditions. The risk of typhoid fever is usually lower than the risk of travelers' diarrhea and hepatitis A; however, rising levels of antimicrobial resistance in endemic regions (particularly in South Asia) have increased the importance of prevention. Two vaccines are approved for travelers: injectable Vi capsular polysaccharide vaccine and oral live attenuated vaccine. Oral vaccine is contraindicated for immunocompromised persons, and completion of the vaccination course requires 1 week (four doses separated by 48 h). Neither vaccine provides protection against paratyphoid fever (caused by *S. enterica* subtype Paratyphi A, B, or C), which is less commonly reported in U.S. travelers. Varicella Travelers should have evidence of varicella immunity. For most U.S. travelers, this immunity can consist of documented receipt of two doses of varicella vaccine, laboratory evidence of immunity, confirmation of prior varicella or herpes zoster by a health care provider, or birth in the United States before 1980. ■ ■IMMUNIZATIONS FOR CERTAIN

REGIONS OR SITUATIONS Yellow Fever Yellow fever is endemic in much of sub-Saharan Africa and South America (Fig. 130-1). Requirements for yellow fever immunization are among the most common entry rules encountered by travelers. Some endemic countries require proof of immunization for all international arrivals. Other countries, including many nonendemic countries that are prone to epidemics, require proof of immunization for arriving travelers who have recently (i.e., within 10 days prior to arrival) traveled to endemic countries. Transit stops for ≥ 12 h in an endemic country also can result in a requirement for proof of immunization. The United States has no requirement regarding yellow fever immunization for travelers entering the country. Country-specific recommendations and requirements for yellow fever immunization are available from the CDC Travelers' Health website (Table 130-2). Yellow fever vaccine is available only through state-authorized official yellow fever vaccination clinics, and its administration is recorded on the ICPV. Yellow fever immunization is considered valid for entry purposes beginning 10 days after administration and extending for the lifetime of the vaccinee. Evidence indicates that a single dose of yellow fever vaccine provides most recipients with long-term protection; therefore, the previous requirement for boosting every 10 years was removed by the WHO from the International Health Regulations in 2016. Booster doses of yellow fever vaccine are still recommended after 10 years for certain individuals, including women who were pregnant during primary immunization, persons who were infected with HIV at the time of vaccination, and persons who received a hematopoietic stem cell transplant after immunization (provided they are sufficiently immunocompetent). Booster doses are also recommended for travelers who will be at particularly high risk of yellow fever during travel, including travel to areas experiencing epidemics, prolonged stays in highly endemic areas, or travel during peak transmission seasons. All licensed yellow fever vaccines are live attenuated products. Contraindications include severe immunosuppression (e.g., during

immunosuppressive or immunomodulatory therapy, in primary immunodeficiencies, or with symptomatic HIV infection or a CD4⁺ T lymphocyte count of $<200/\mu\text{L}$), malignant neoplasms, thymus gland disorders, and severe egg allergies. Precautions in adults include an age of ≥ 60 years, pregnancy, breastfeeding, and asymptomatic HIV infection with a CD4⁺ T lymphocyte count of 200–499/ μL . Although medical waivers can be issued by yellow fever clinics, travelers must also consider the risks of traveling to endemic areas without vaccination. Common mild adverse reactions to vaccination include fevers, body aches, lymphadenopathy, localized swelling, and rash. Rare severe adverse events include anaphylaxis, neurologic complications (e.g., meningitis, encephalitis, Guillain-Barré syndrome), and yellow fever vaccine-associated viscerotropic disease (YEL-AVD). YEL-AVD is similar to yellow fever and can result in death. The risk of YEL-AVD is estimated to be ~ 0.3 case per 100,000 doses administered, with increased risk among immunosuppressed and elderly persons.

Poliomyelitis Although wild-type poliovirus has been eradicated from most of the world, poliomyelitis caused by circulating vaccine-derived poliovirus has been sporadically reported in numerous countries in Africa, the Middle East, and Asia where immunization rates are inadequate. For adults who have had the primary childhood polio vaccination series and are traveling to countries with reported wild-type or circulating vaccine-derived poliovirus transmission in the previous 12 months, a single booster of inactivated poliovirus vaccine before travel is recommended. This recommendation is sometimes extended to countries bordering those with poliovirus transmission when the risk of imported cases is high, especially for health care or humanitarian aid workers. Travelers who stay >4 weeks in certain countries considered high risk

for exporting polio can also be subject to exit requirements for proof of recent vaccination (4 weeks to 12 months before departure). Because the list of countries with recommendations for polio booster doses is continually updated, providers should routinely review current polio booster guidance in online resources (Table 130-2).

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Cholera Most countries at risk for cholera are in Africa and Asia, with the exception of the island of Hispaniola in the Americas. In 2022, an upsurge in cases was observed worldwide, and this trend continued into 2023. Transmission occurs mostly through consumption of contaminated water, although contaminated food or person-to-person contact also can be responsible. The risk to travelers is extremely low when safe food and water precautions are followed. Cholera vaccination can be considered for travelers to endemic regions, particularly those visiting areas experiencing outbreaks, health care workers, or travelers who cannot adhere to strict hygienic practices. Individuals at higher risk for severe disease (e.g., those with type O blood or comorbid conditions) and those who will be in situations where access to health care will be difficult also might consider vaccination. A single-dose live attenuated oral cholera vaccine (Vaxchora) is approved for travelers in the United States and the European Union. This vaccine had an efficacy of 90% at 10 days and 80% at 3 months after administration; the duration of protection and the need for booster doses remain to be determined. Oral killed cholera vaccines are available outside the United States. Meningococcal Disease Endemic and epidemic meningococcal disease can occur worldwide; however, immunization is primarily recommended for high-risk travelers, including those going to countries in the African “meningitis belt” during the dry season (December to June), when large-scale epidemics can take place. Historically, meningococcal disease in the meningitis belt was caused by serogroup A; however, more recently, serogroups C, W-135, and X have caused outbreaks following the successful serogroup A vaccination program (Meningitis Vaccine Project, <https://www.path.org/our-impact/articles/about-meningitis-vaccine-project/>). Travelers should receive quadrivalent meningococcal vaccine, which protects against serogroups A, C, Y, and W-135. Conjugated meningococcal vaccines are generally preferred over polysaccharide vaccines because of their increased immunogenicity and the reduced carriage of meningococci by vaccinees; in fact, the polysaccharide vaccines are no longer available in the

PART 5 Infectious Diseases A B **FIGURE 130-1** Yellow fever recommendations in (A) Africa and (B) the Americas. Vaccination of travelers to areas with low exposure risk (designated in green) is not routinely recommended but can be considered for travelers at increased risk due to high exposure to mosquitoes or prolonged travel. Recommendations current as of November 2022. See Centers for Disease Control and Prevention Travelers’ Health website for current recommendations. (Reproduced with permission from J Nemhauser et al [eds]: Yellow Book 2024 Health Information for International Travel. New York, Oxford University Press; 2023.)

United States. Pilgrims traveling to the Kingdom of Saudi Arabia for the Hajj and Umrah pilgrimages are required to demonstrate proof of vaccination with quadrivalent meningococcal vaccine within the preceding 3 years. Vaccination against serogroup B meningococcal disease is not recommended for travelers except in specific outbreak situations. Japanese Encephalitis Japanese encephalitis is a potentially severe viral infection passed to humans by evening-biting mosquitoes in much of Asia and parts of the western Pacific (Chap. 215). Although the WHO estimates that as many as 68,000 cases occur each year in Asia, the risk to travelers from nonendemic areas is estimated to be <1 case per 1 million travelers. However, certain travelers are at increased risk, such as long-term expatriates, persons traveling in rural areas during peak transmission seasons,

and those with increased outdoor exposure (particularly during the evening). Short-term travelers to urban areas appear to be at lowest risk. In addition to mosquito avoidance measures, vaccination can be considered for travelers at risk for infection. Multiple Japanese encephalitis vaccines are available world wide. An inactivated Vero cell culture-derived vaccine (IXIARO) is available in the United States and Europe and can be given to adults as a two-dose primary series, with doses administered 7–28 days apart. Rabies (Chap. 214) is endemic to all continents except Antarctica and to numerous islands worldwide. Although many mammalian species can be infected with rabies virus, terrestrial carnivores and bats are the main reservoirs. In countries without animal control or routine pet vaccination, bites from infected dogs are often the most common source of rabies infection. Management of animal bites carrying a rabies risk is a common reason travelers seek urgent health care during or after travel. Individuals at higher risk for exposure may include children, long-term travelers, travelers whose activities will put them at higher risk of animal contact (e.g., field biologists, cavers), and travelers to remote areas. All travelers should be advised about animal bite avoidance and management of bite and scratch injuries (even minor), including thorough washing of the wound with soap and water (or povidone iodine) and immediate medical evaluation to determine whether rabies postexposure prophylaxis is indicated. The CDC-recommended postexposure prophylaxis regimen requires administration of rabies immune globulin and a rabies vaccination series. Rabies preexposure immunization series can be considered for travelers at higher risk of exposure, particularly those to destinations where access to rabies immune globulin can be difficult. Individuals receiving the rabies preexposure vaccination series should be advised that they will require urgent postexposure booster doses of vaccine following potential exposures. In the United States, the rabies preexposure vaccination series was revised in 2022, and a two-dose series (7 days apart) is now approved for travelers with risk of exposure. A third dose (between 21 days and 3 years after the initial series) or confirmation of protective titer (1–3 years after the initial series) is recommended for travelers who will be at risk for >3 years (see detailed discussion in the CDC Yellow Book, Table 130-2). Tick-Borne Encephalitis Tick-borne encephalitis (Chap. 215) is endemic to parts of Europe and Asia, ranging from France to northern Japan. The infection is transmitted primarily through the bite of an infected Ixodes tick. Transmission is also possible through ingestion of unpasteurized dairy products from infected goats, sheep, or cows. Travelers to endemic regions who engage in outdoor activities in forested areas should consider vaccination prior to travel. An inactivated tick-borne encephalitis vaccine is approved in the United States, given with a three-dose primary series (second dose 14 days to 3 months after the first, and the third dose 5–12 months after the second). For short-term travelers unable to receive the third dose before travel, evidence suggests that vaccine efficacy following the initial two doses is sufficient enough to warrant vaccination with two doses. All travelers should use personal protective measures against tick bites (see “Prevention of Arthropod-Borne Infections,” below). Dengue Dengue (Chap. 215) is the most common arthropod-borne virus (arbovirus) worldwide, transmitted by Aedes mosquitoes. It is the

leading cause of fever in travelers returning from most tropical and subtropical destinations outside of sub-Saharan Africa, where malaria is most common. While most travel-related cases are uncomplicated, severe dengue can occur in travelers, including dengue hemorrhagic fever and dengue shock syndrome. There is currently no U.S. Food and Drug Administration (FDA)-approved dengue vaccine in the United States for travelers, since the only FDA-approved vaccine (Dengvaxia; tetravalent live-attenuated dengue vaccine) has indications limited to individuals residing in regions of endemicity with evidence of a past dengue virus infection. In the European

Union (and some other nonU.S. countries), a newer tetravalent live attenuated dengue vaccine (Qdenga) is approved for persons aged 4 and older. It can be considered for use in travelers, although questions remain regarding its ability to elicit protection against all dengue virus serotypes, specifically in seronegative recipients. All travelers should use personal protective measures against mosquito bites (see “Prevention of Arthropod-Borne Infections,” below).

Chikungunya virus (Chap. 215) is an arbovirus transmitted by *Aedes* mosquitoes that has spread worldwide in recent decades. Approximately 100–200 chikungunya cases are reported annually in U.S. travelers. The highest risk of infection is among travelers to countries experiencing outbreaks. Chikungunya causes an acute febrile illness, and although life-threatening illness is rare, many patients develop severe arthralgias that might become chronic. A live chikungunya vaccine was approved in the United States in 2023 with an indication for individuals 18 years of age and older at increased risk of exposure to chikungunya virus. The vaccine is given as a single dose and is contraindicated in immunocompromised persons. In these trials, ~12% of individuals developed chikungunya-like symptoms. While most reactions were mild or moderate in severity and short-lived, 1.6% of vaccine recipients developed more significant symptoms or fever $\geq 39^{\circ}\text{C}$. New guidance on its use in travelers has been recently released

(<https://www.cdc.gov/chikungunya/hcp/vaccine/index.html>). CHAPTER 130 Health

Recommendations for International Travel PREVENTION OF ARTHROPOD-BORNE INFECTIONS ■

■ **MALARIA PREVENTION** Malaria (Chap. 231) results from infection with one or more of five species of protozoan parasites: *Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi*. The disease remains a significant cause of morbidity and mortality worldwide, and it is the leading cause of life-threatening infections in travelers. The majority of the disease burden, both in endemic populations and in travelers, occurs in regions of sub-Saharan Africa where *P. falciparum* is endemic. In 2018, nearly all of the 1823 malaria cases reported in the United States were acquired during travel to endemic countries. In most cases, the patient had not taken chemoprophylaxis, had adhered to the regimen inconsistently, or had taken an incorrect regimen. Among cases in U.S. residents, visiting friends or relatives was the most common reason for travel. Although there have been significant recent developments in malaria vaccines for use in endemic countries, these vaccines are not approved for travelers. Key elements of malaria prevention in travelers include mosquito avoidance, chemoprophylaxis, and early recognition of infection to prevent the development of severe disease. *Plasmodium* species are transmitted by *Anopheles* mosquitoes, which typically bite from dusk until dawn. Limiting activities to enclosed or well-screened areas during these hours is recommended. Travelers should wear long-sleeved shirts and long pants to limit the amount of exposed skin and should apply a recommended insect repellent to any skin that remains exposed. Both the CDC and the WHO provide lists of reliable insect repellents, with products that contain DEET (20–50%) as the active ingredient being preferred by most experts. Travelers may also wear permethrin-treated clothing to increase protection. If sleeping areas are not well screened, it is recommended that individuals sleep under insecticide-treated bed nets. Indoor insecticide sprays or spatial repellents should be used with caution; the efficacy of these measures in

malaria prevention has not been proven, and there may be risks from direct inhalation.

In addition to mosquito avoidance, chemoprophylaxis to prevent symptomatic disease is recommended for travelers to higher-risk regions. Current drugs used for malaria

chemoprophylaxis include atovaquone-proguanil (Malarone), chloroquine (and hydroxychloroquine), doxycycline, mefloquine, primaquine, and tafenoquine (see Chap. 231 for detailed regimens). Chemoprophylaxis recommendations should be based on careful review of the traveler's itinerary to determine malaria risk, predominant malaria species, and drug resistance patterns. The CDC and other travel medicine resources (Table 130-2) provide current country-specific risk assessments and chemoprophylaxis recommendations. Other important considerations include the traveler's medical history and routine medications; this information is essential in assessing for contraindications to specific drugs or drug-drug interactions. Primaquine and tafenoquine are active against the dormant liver stages of *P. vivax* and *P. ovale*, and both drugs are useful as prophylaxis in persons without glucose-6-phosphate dehydrogenase (G6PD) deficiency traveling to areas where these species are more common. Primaquine can also be used for presumptive antirelapse therapy in returned travelers without G6PD deficiency who had a prolonged risk of exposure to *P. vivax* or *P. ovale* and did not use primaquine or tafenoquine for chemoprophylaxis. Currently approved regimens are well tolerated, and concerns that severe side effects are common are not supported by clinical evidence (e.g., hepatitis with atovaquone-proguanil or psychosis with mefloquine). Providers should emphasize that malaria chemoprophylaxis can be life-saving and that, when prophylaxis is indicated, the benefits outweigh the low risk of serious adverse reactions.

PART 5 Infectious Diseases After the onset of malaria, progression to severe disease can be rapid; therefore, early recognition of symptoms is crucial. Febrile travelers should seek evaluation as soon as possible during or after travel to malarious areas. Although the CDC does not recommend that travelers carry malaria treatment medications for standby emergency therapy as an alternative to chemoprophylaxis, this approach is accepted by some authorities for some travelers to lower-risk areas instead of chemoprophylaxis. However, because chemoprophylaxis failures can occur and locally acquired antimalarial agents can be substandard, prescription of a "reliable-supply" treatment course can be considered (in addition to chemoprophylaxis), to be used as needed under the advice of a medical professional. In the United States, atovaquone-proguanil and artemether-lumefantrine (Coartem) are available oral treatments for malaria, although atovaquone-proguanil should not be prescribed as a reliable-supply treatment course when it is being used for chemoprophylaxis. ■ ■

PREVENTION OF OTHER ARTHROPOD-BORNE INFECTIONS Arthropod-borne infections are present worldwide, and arboviral infections are particularly numerous. Risk of arbovirus acquisition may vary from year to year and by season (rainy vs dry). In addition, risk can increase dramatically during outbreak periods, as witnessed during recent outbreaks of infection with chikungunya virus and Zika virus in the Americas. While dengue, chikungunya, and Zika infections result from the bite of infected *Aedes* mosquitoes, arboviruses may also be transmitted by non-*Aedes* mosquitoes (Japanese encephalitis virus, Mayaro virus, o'nyong-nyong virus), ticks (tick-borne encephalitis virus, Powassan virus), and biting midges (Oropouche virus). In addition to arboviral illness, travelers are at risk for numerous other arthropod-borne infections, including—but not limited to—leishmaniasis (sand flies), filariasis (mosquitoes), African trypanosomiasis (tsetse flies), Chagas disease (triatomine bugs), and many tick-borne infections such as rickettsial diseases (e.g., African tick bite fever, scrub typhus) and Lyme disease. Travel immunizations for arthropod-borne infections are limited to yellow fever, Japanese encephalitis, tick-borne encephalitis, dengue, and chikungunya vaccines, although availability of these vaccines can vary worldwide. Many arboviral infections have no approved vaccines, and furthermore, some travelers might be unable to receive certain

vaccines due to cost or medical barriers (precautions or contraindications). For these reasons, arthropod bite avoidance remains a corner stone of arthropod-borne infection prevention. Recommendations for avoiding arthropod bites in general are similar to those provided for Anopheles mosquito avoidance to prevent malaria. However, in contrast to malaria, many disease-transmitting arthropods bite during the day and may be encountered across a wider range of environments. Travelers at risk for tick bites can tuck pants into socks and perform daily self-inspections for attached ticks. Avoidance of sleeping in mud or thatch housing in areas endemic for Chagas disease is recommended.

GASTROINTESTINAL ILLNESS

Depending on the itinerary and season, as many as 30–70% of travelers report travelers' diarrhea (TD). Symptoms can include urgently passed loose stools, abdominal pain, fever, and vomiting, and more severe cases can result in volume depletion or bloody diarrhea (dysentery). The majority (~80%) of TD cases result from bacterial infections, with the most common pathogens being *Escherichia coli* and *Campylobacter*, *Shigella*, and *Salmonella* species. A minority of cases are caused by viruses, preformed bacterial toxins, and protozoa (most commonly *Giardia*). Although travelers may develop gastrointestinal illness during travel to any destination, TD is most likely to occur in low- and middle-income countries, where unhygienic food preparation practices constitute the greatest risk for development of disease.

Precautions

Recommendations for the prevention of TD center on appropriate food and beverage selection as well as hand hygiene. Food is safest when cooked and served hot. Uncooked fruits and vegetables, unless they can be washed and peeled by the traveler, are considered risky. Dairy products should be pasteurized. Travelers are advised to drink bottled or purified water during travel and to avoid drinking beverages with ice, which may be made with water from unsafe sources. Before drinking any bottled or canned beverage, travelers should confirm that the factory seal is intact, as refilling of bottles with untreated water or questionable beverages is common. Street-side vendors can be particularly risky. Individuals traveling to more remote areas without access to bottled water can use one of a number of methods to purify water, including boiling, chemical treatments, filtration, or ultraviolet irradiation devices.

Prophylaxis

For prophylaxis of TD, bismuth subsalicylate can be considered for short-term use. This medication, taken as two tablets (or 2 oz of liquid) four times daily, has been shown to decrease TD incidence by 50% in Mexico. The safety of bismuth subsalicylate prophylaxis when used for >21 days has not been established. Furthermore, the high dosing frequency of this regimen, common side effects (constipation, black tongue), and potential drug interactions (e.g., with acetazolamide or warfarin) limit its utility. No recommendation can be made for probiotics for TD prevention given the limited number of studies and varied results, which may vary by specific strain of probiotic used. Likewise, data supporting prebiotics for TD prevention are limited and inconclusive. Prophylactic antibiotics generally are not recommended for TD prevention given increasing concerns about adverse reactions, colonization or infection with multidrug-resistant pathogens, and development of *Clostridioides difficile* infection. However, short-term antibiotic prophylaxis (with rifaximin favored over fluoroquinolones) can be considered in rare situations for travelers at high risk for complications from TD. Oral killed cholera vaccine (Dukoral, available in Europe and Canada) shows some cross-protection against enterotoxigenic *E. coli*; however, given the wide range of TD pathogens, the protection conferred by this vaccine against TD is likely to be minimal.

Self-Treatment

In general, TD is a self-limited illness, with symptoms resolving in 3–7 days for bacterial infections. Recovery times are typically shorter for infections with viral pathogens and may be prolonged for parasitic infections. For travelers who develop TD, initiation of self-treatment should be based on the patient-assessed functional impact of illness (Fig. 130-2). TD can be considered mild (not distressing and has no impact on activities), moderate (distressing and may

interfere with planned activities), or severe (incapacitating

• Food and water precautions • Definition of travelers' diarrhea and severity classification • Importance of oral rehydration and salt intake for all types of travelers' diarrhea • Different travelers' diarrhea treatments and possible provision of antibiotics for self-treatment • Antibiotic prophylaxis (considered only for travelers at high risk for complications from travelers' diarrhea)

Pre-travel During travel Self-determination of travelers' diarrhea severity Moderate Distressing or interferes with activities Mild Tolerable, not distressing, and does not interfere with planned activities May use: Loperamide or antibiotics* or loperamide and antibiotics* May use: Loperamide or bismuth subsalicylates *Azithromycin is preferred as first line for severe diarrhea or diarrhea acquired in areas with widespread quinolone resistance including Southeast and South Asia. Quinolones and rifaximin may be considered second-line treatment in moderate diarrhea or severe diarrhea without dysentery or high fever. FIGURE 130-2 Management of travelers' diarrhea. (Adapted from MS Riddle et al: Guidelines for the prevention and treatment of travelers' diarrhea: A graded expert panel report. J Travel Med 24:S63, 2017.) or prevents participation in planned activities). All dysenteric TD is considered severe. For all levels of severity, replacement of fluid and electrolyte losses resulting from diarrhea and/or vomiting is a mainstay of treatment. In severe cases, replacement with oral rehydration solution (available over the counter) is ideal; however, milder cases can be managed with any potable liquid. In addition, for patients with mild or moderate TD, self-treatment with antimotility agents alone (e.g., loperamide) can be considered. Antibiotic treatment can decrease the duration of TD to 1–2 days, with potential further benefits from adjunctive loperamide. However, the risks of adverse effects, drug–drug interactions, and alterations in the traveler's microbiota are increasingly recognized in patients treated with antibiotics. Consequences of an altered microbiota can include *C. difficile* colitis and acquisition of multidrug-resistant organisms. Studies have shown that international travelers, particularly those who take antibiotics during travel, are at risk for becoming colonized with multidrug-resistant organisms, including extended-spectrum β -lactamase-producing Enterobacteriaceae. Travelers colonized with multidrug-resistant organisms may be at elevated risk for drug-resistant infections (e.g., urinary tract infection). The role of travelers in the global spread of multidrug-resistant organisms is uncertain. Given these concerns, routine self-treatment with antibiotics is recommended only in severe TD. Self-treatment with antibiotics, with or without antimotility agents, can be considered for moderate TD cases. Increasing quinolone resistance, most clearly documented in *Campylobacter* in Southeast and South Asia, has limited the utility of this antibiotic class for TD. The authors' preferred antibiotic regimen for TD self-treatment is azithromycin at a dose of 500 mg daily for 3 days, although a single 1000-mg dose also is effective. Rifaximin or rifamycin SV can also be considered, especially for persons unable to take other antibiotics because of drug–drug interactions. However, *Campylobacter* species are resistant to rifamycins, and their efficacy against dysentery has not been established. Treatment regimens for TD are covered in detail in Chap. 138. Empirical treatment of acute TD with antiprotozoal agents such as metronidazole is not recommended. A small proportion of individuals develop prolonged symptoms (≥ 14 days), which may result from persistent infection (most often secondary to protozoa), secondary infection (*C. difficile*), or postinfectious irritable bowel syndrome. Antibiotic treatment for acute TD has not been proven to reduce the incidence of postinfectious

Counsel travelers on Severe Incapacitating or prevents planned activities Non-dysentery Dysentery Should use: Antibiotics* Should use: Antibiotics* with or without loperamide CHAPTER 130 irritable

bowel syndrome, and patients with protracted symptoms should undergo a thorough evaluation.

PREVENTION OF OTHER TRAVEL-RELATED PROBLEMS Health Recommendations for International Travel

■ **ACTIVITY-SPECIFIC INFECTION RISKS** Travelers should avoid direct contact with freshwater bodies (lakes, ponds, rivers) because of possible risks of leptospirosis and schistosomiasis. Schistosomiasis is endemic in Africa, Asia, and South America. Diving in African Rift Valley lakes (especially Lake Malawi) and rafting on the Nile River are popular activities that put travelers at risk for schistosomiasis. Appropriate footwear is important in tropical countries to prevent infection with *Strongyloides stercoralis* and hookworm as well as snakebites. Animals of all types (wild, stray, or even pets) are best avoided to minimize bite risk. Travelers who engage in casual sex, including that with commercial sex workers, should be aware that the risk of sexually transmitted infections (Chap. 141) can be high, especially when barrier protections are not used. The multinational outbreak of mpox in 2022 was spread through close (skin-to-skin) contact, largely among networks of men who have sex with men (MSM). Given the continued transmission of mpox worldwide, vaccination against mpox should be considered for travelers who may engage in high-risk activity. Injection drug use, tattooing, and even acupuncture in unhygienic settings can pose a high risk for blood-borne infections such as HIV infection and hepatitis B and C.

■ **VENOUS THROMBOEMBOLISM** Travelers are at risk for venous thromboembolism (Chap. 122), particularly after long-haul flights or other extended periods of limited mobility. General precautions for prevention include ambulation during travel, calf exercises, and aisle seating. Travelers at increased risk for venous thromboembolism may benefit from graduated compression stockings. Anticoagulation may be considered for high-risk individuals.

■ **ALTITUDE ILLNESS** Travelers to high-altitude destinations (>2500 m) should be counseled on altitude illness, and the prescription of medications for prophylaxis, such as acetazolamide, may be indicated (Chap. 475). Popular high-altitude destinations include Cusco, Peru (the usual gateway to Machu

Picchu), mountains that attract climbers (e.g., Mt. Kilimanjaro), and Nepal (trekking).

■ **MOTION SICKNESS** Motion sickness triggered by various modes of transportation can be significant for many travelers. Nonpharmacologic interventions can be helpful, such as avoiding known triggers, staying hydrated, getting adequate rest, and optimizing positions in vehicles near windows. For travelers with significant motion sickness history, over-the-counter and prescription antihistamines (e.g., dimenhydrinate, cyclizine, promethazine) can be effective in preventing and treating motion sickness; however, sedation and anticholinergic effects can limit their use. Non-sedating antihistamines appear to be less effective. A prescription for transdermal scopolamine patches can be helpful for susceptible travelers who anticipate prolonged risk periods (e.g., on cruises or extended bus trips), although like the antihistamines, anticholinergic and central nervous system effects are a concern with scopolamine, particularly in elderly travelers. While the evidence supporting complementary and integrative health approaches to prevent and treat motion sickness is limited or anecdotal, approaches such as acupressure bands or ginger are relatively simple to use and might have some benefit for individual travelers. Travelers should be counseled about potential drug-drug interactions between supplements and their routine medications.

■ **JET LAG** Jet lag (Chap. 33) occurs when travel across time zones causes the traveler's circadian rhythm to become asynchronous with the local time zone. Symptoms are most significant with travel across more than three time zones and can result in poor sleep, daytime sleepiness (with poor physical and mental performance), gastrointestinal symptoms, and altered mood. Strategies to help circadian rhythms adjust to new time zones include shifting of sleep schedules prior to travel,

timed light exposures after arrival, and melatonin use. Online resources to assist travelers in timing interventions to minimize jet lag are available (Table 130-2), although none has been validated in clinical trials. While caffeine use can reduce daytime drowsiness, it can also disrupt sleep.

Prescription of hypnotics (e.g., zolpidem) for travel-related insomnia should generally be avoided, since adverse effects, including excessive fatigue and impaired cognition upon awakening, can be problematic during travel. When used, the lowest effective dose of a hypnotic medication should be used, and travelers should be cautioned about use during flights (when extended immobilization is problematic) or any situation when a full course of sleep is not possible. Sedativehypnotic and anxiolytic medications are among the classes of drugs that are potentially restricted by certain countries (see "Traveling with Prescription Medications," below). PART 5 Infectious Diseases ■

■INJURIES International travel presents numerous factors that contribute a higher risk of injuries and death. Travelers may face unfamiliar environments and language barriers and rely heavily on other people (e.g., drivers and tour operators) for protection. Furthermore, in low- and middleincome countries, safety protections that are typical in high-income countries are often less stringent, unenforced, or nonexistent. Travelers often exhibit increased risk-taking behaviors during travel, frequently in association with the use of alcohol. When injuries do occur, access to adequate trauma care can be limited. Motor vehicle accidents are a common cause of injury deaths in travelers. In addition to poor road conditions, traffic rules are often less strictly enforced overseas. Riding on motorbikes (especially without a helmet), on overcrowded public transit, in improperly maintained vehicles, and in vehicles without seatbelts should be avoided. Drowning prevention and crime avoidance are important safety topics. The U.S. State Department provides country-specific safety and security advice for U.S. travelers (Table 130-2). TRAVELERS WITH PREEXISTING

MEDICAL CONDITIONS Travel is increasingly common for persons with chronic medical conditions. Risks vary depending on the condition, destination, and activities. Travelers with chronic medical conditions are encouraged to

plan their trips carefully and to consult with their physicians to assess fitness for travel. Notably, cardiovascular events are a frequent cause of in-flight emergencies and death during travel. Travel across time zones and changes in diet can create challenges in conditions—e.g., diabetes mellitus—that require regulation of diet and consistent medication timing. Providers can assist travelers by providing copies of prescriptions (or medication lists), a medical problems list, and a baseline electrocardiogram. Adverse events caused by drug-drug interactions can be difficult to manage during travel, especially in destinations with limited emergency care. Therefore, providers should review the traveler's medication list for potential drug interactions when prescribing prophylactic or self-treatment medications. Azithromycin and quinolones prescribed for travelers' diarrhea self-treatment can cause additive QT interval prolongation when used with some antidepressant and antiarrhythmic medications. Malaria prophylaxis medications can affect the international normalized ratio in patients who are taking warfarin. ■ ■IMMUNOCOMPROMISED

TRAVELERS An increasing number of immunocompromised persons are traveling, including organ transplant recipients, HIV-infected persons, cancer patients, persons with asplenia, and persons receiving immunosuppressive therapies (e.g., biologic agents, antimetabolites, or chronic high-dose glucocorticoids). Although each of these conditions has unique risks, general concerns include increased susceptibility to infection, decreased vaccine efficacy, and—for patients with severe immunosuppression—contraindications to live virus vaccines. Routinely recommended precautions

(e.g., food and water hygiene, insect bite avoidance) are particularly important for travelers with immunocompromising conditions. Conditions associated with severe immunocompromise that preclude use of live virus vaccines include active leukemia or lymphoma, generalized malignancy, graft-versus-host disease, HIV/AIDS (with a CD4+ count of <200 cells/μL), and congenital immunodeficiencies. Immunosuppressive therapies that preclude live virus vaccines include high-dose glucocorticoid treatment (defined as ≥ 20 mg of prednisone or the equivalent daily for ≥ 2 weeks), alkylating agent administration, antimetabolite therapy (e.g., azathioprine, methotrexate), transplant-related immunosuppression, cancer chemotherapy, radiation therapy, and treatment with biologic agents, including tumor necrosis factor blockers, checkpoint inhibitors, and lymphocyte-depleting agents. If possible, travel immunizations should be administered prior to iatrogenic immunosuppression (≥ 2 weeks for inactivated vaccines and ≥ 4 weeks for live vaccines). The duration of immunosuppression after discontinuation of immunosuppressive therapies can be prolonged, particularly for biologic agents. Travelers unable to receive a required yellow fever vaccine because of immunosuppression should be given a medical waiver if travel cannot be avoided. Providers are advised to review the detailed guidance for immunizing immunocompromised travelers provided in the CDC Yellow Book (Table 130-2) and other resources.

■ ■ **HIV-INFECTED TRAVELERS** Infection risk in HIV-infected individuals generally correlates with the level of immunosuppression (i.e., the CD4+ T-cell count). Adults with HIV infection and CD4+ counts of >500 cells/μL are generally considered to have levels of risk similar to those faced by travelers without immunocompromising conditions. Live MMR and varicella vaccines can generally be administered to HIV-infected travelers with a CD4+ count of >200 cells/μL for ≥ 6 months. Guidance for yellow fever immunization of HIV-infected persons is reviewed above. Oral live attenuated typhoid and live attenuated influenza vaccines should not be administered to HIV-infected persons, given the availability of polysaccharide and inactivated versions of these vaccines, respectively. The number of countries that restrict the entry of HIV-infected persons has decreased in recent years, particularly for short-term travelers and tourists. However, HIV-infected travelers should review the policies of their destination, especially when they plan to work abroad or stay for longer terms. Unnecessary disclosures of HIV status to customs

or immigration officials should be avoided. Resources include embassies in destination countries, the U.S. State Department, and online resources for travelers with HIV infection (Table 130-2). ■

■ **PREGNANT TRAVELERS** Travel medicine providers should assess pregnancy status and the possibility of conception during travel. The pregnant traveler faces numerous unique risks. These include limited availability of emergency care for pregnancy complications, increased risk of certain infections, and exposure to specific infections that can result in pregnancy complications. Although most airlines will allow pregnant women to travel up to 36 weeks of pregnancy, the American College of Obstetrics and Gynecology recommends travel during the middle period of pregnancy (weeks 14–28), when morning sickness has improved, before mobility becomes impaired, and when the risk of spontaneous abortion or premature labor is minimal. Pregnancy-related contraindications and relative contraindications to travel are numerous and are reviewed in the CDC Yellow Book (Table 130-2). Pregnant travelers are at increased risk of various infections (e.g., malaria, influenza, hepatitis E, listeriosis) and/or severity of illness when traveling. Some infections, notably Zika virus disease, toxoplasmosis, and rubella, can result in birth defects or fetal death. Pregnant travelers should contemplate the infectious risks of their destination and consider delaying travel to areas where particularly dangerous infections, such as malaria or Zika, are present. Currently, only mefloquine and chloroquine are approved for malaria chemoprophylaxis in

pregnancy, and plasmodial resistance to these drugs can further limit options. Travel immunizations considered safe during pregnancy also are limited (Table 130-3). When used as directed, insect repellents registered by the Environmental Protection Agency, such as DEET, are considered safe during pregnancy. ■ ■TRAVELERS WITH SEVERE ALLERGIES Travelers with severe allergies to food, insect stings, and environmental allergens can be at increased risk during travel, particularly in destinations without adequate emergency care. Avoidance of food allergens can be challenging, particularly when eating in restaurants or catered settings. Language barriers can present difficulties in avoiding exposures to allergens in food or medications. Regional variations in culinary practices and ingredients can lead to unexpected food allergen exposure. Outdoor activities can increase the risk of stings by hymenopterous insects (bees, wasps, ants). Solo travelers can face particular challenges when experiencing severe allergies. Providers should ensure that travelers have an emergency care plan for severe allergies and an adequate supply of emergency self-treatment, including epinephrine auto-injectors and antihistamines. For travelers who will have no immediate access to health care, it can be prudent to bring other medications that might be indicated, including rescue bronchodilator inhalers (for individuals with asthma) and short courses of glucocorticoids. Written documentation of the allergic disorder and self-treatment medications should be carried, especially when injectable medications are involved. Travelers with severe food allergies should alert restaurants and hosts. Printable food allergy alert cards in various languages are available online (Table 130-2). OTHER PRETRAVEL PREPARATIONS ■ ■TRAVEL HEALTH KITS A carefully planned travel health kit can minimize the need to seek care for self-treatable conditions. The ideal contents depend on the destination, duration, and activities during travel as well as on individual health issues. Routine and trip-specific prescription medications (e.g., malaria prophylaxis, travelers' diarrhea self-treatment antibiotics) should be carried in original labeled prescription bottles to aid in identification. A digital thermometer and typically used over-the-counter medications, such as analgesics and antipyretics, antidiarrheal medications, medications for motion sickness, antacids, laxatives, oral rehydration salts, antihistamines, and topical steroid creams, can be important. Basic first-aid items, such as gloves, bandages, tape,

antibiotic ointment, and tweezers, are helpful. Critical medications should always be carried and not packed in checked luggage; however, travelers must consider any restrictions about flying with sharp objects or liquids, particularly in their carry-on baggage.

■ ■TRAVELING WITH PRESCRIPTION MEDICATIONS Carrying copies of prescriptions (or a signed medication list from a physician's office) is recommended. Many countries, particularly in Asia, the Middle East, and Africa, have stringent restrictions on certain drugs that are less restricted in the United States. These regulations can include controlled substances such as opioid analgesics, anxiolytics and sedatives, and medications for attention deficit hyperactivity disorder. Even some over-the-counter medications such as pseudoephedrine and diphenhydramine are restricted in certain countries. Requirements for traveling with restricted medications can include carrying copies of prescriptions or even obtaining advance approval from the destination country's health ministry. Levels of enforcement and penalties for violations vary widely. Travelers who plan to carry potentially restricted medications should contact the embassy of their destination to review policies. The International Narcotics Control Board also maintains a listing of regulations for travelers carrying controlled medications to specific countries (Table 130-2). Travelers taking antiviral medications for HIV preexposure prophylaxis going to countries that restrict entry to

persons living with HIV/AIDS might take specific precautions to avoid challenges when entering (see online resource for HIV-infected travelers, Table 130-2). Travelers should carry amounts appropriate for the duration of their itinerary, including a limited number of extra doses for use in cases of a delay in return. CHAPTER 130 Although many medications that require prescription in the United States are available over the counter overseas, the quality of locally acquired pharmaceuticals can vary. Counterfeit medications, particularly antimalarials, are common in much of the world. Whenever possible, travelers are cautioned to avoid obtaining critical medications such as malaria chemoprophylaxis during travel. Health Recommendations for International Travel ■ ■ HEALTH CARE OVERSEAS AND TRAVEL

HEALTH INSURANCE Travelers should consider where they would seek urgent or emergency health care, particularly if they have chronic health conditions, are pregnant, or will participate in activities with a high risk of injury or illness (e.g., altitude sickness). International travelers should be aware that most countries do not accept routine health insurance from other countries and that such insurance is unlikely to cover out-of-pocket health care costs or to provide assistance in identifying providers overseas. Travelers are advised to review their health insurance policies before travel to assess the scope of international coverage (including emergency care, hospitalization, psychiatric care, and obstetric care, if applicable) and the availability of 24-h physician-backed support. For many travelers, supplemental insurance coverage of some type is prudent. Travel insurance usually consists of coverage for financial losses due to trip cancellation (e.g., due to unexpected illness) or lost baggage. Supplemental travel health insurance policies cover health care costs overseas and typically provide 24-h support centers. Medical evacuation (medevac) insurance can be a part of a travel health insurance policy or a stand-alone policy and covers medical evacuation when it is determined that the local level of care is inadequate. Further information on travel health insurance is available from online resources listed in Table 130-2.

SPECIAL TRAVEL POPULATIONS Travelers are increasingly diverse in their reasons for and types of travel, each of which poses unique risks and challenges (Table 130-4). A major challenge in travel medicine is presented by VFR travelers who are visiting their countries of origin. VFR travelers face increased risks for travel-related infections, as they often travel to areas not frequented by tourists, stay in local homes, and adopt local food and transportation habits. Immunity resulting from malaria infection is not long-term, but immigrants from malaria-endemic countries often incorrectly assume that they are immune. Barriers to appropriate

TABLE 130-4 Risks and Prevention Strategies in Special Travel Populations

GROUP	RISKS AND CHALLENGES	PREVENTION STRATEGIES
Travelers visiting friends and relatives (VFR)	• Greater likelihood of visiting areas outside usual travel destinations • Frequent adoption of food, accommodation, and transportation habits similar to those of locals • May underestimate importance of travel immunizations or malaria prophylaxis • Financial or cultural barriers to seeking pretravel advice or immunization	• Budget travelers • Financial barriers to seeking pretravel advice or immunization • Lower quality of accommodations, transportation, and food establishments • Last-minute travelers • Minimal advance notice for pretravel consultations or immunizations • Long-term travelers • Increased risk of infection and injury due to longer duration • Increased likelihood of adopting local food, accommodation, and transportation standards • Potential need for extended supply of malaria chemoprophylaxis • Health care workers on medical missions • Risk of infections acquired through patient care because of inadequate infection-control standards • Potentially high prevalence of untreated transmissible infections in patients • Limited

or no access to urgent postexposure PART 5 Infectious Diseases prophylaxis for HIV infection and hepatitis B • Exposure to emerging infections and outbreaks Medical tourists • Nosocomial infections and other complications of medical procedures overseas • Substandard accreditation, infection control, safety guidelines, drugs, and blood-product screening • Increased risk of thromboembolism following surgery Abbreviation: CDC, Centers for Disease Control and Prevention. pretravel advice can include financial and language issues or a lack of trust in the medical system. POSTTRAVEL MEDICAL CARE Acute febrile illness in returning travelers can represent a potentially life-threatening illness, such as malaria, typhoid fever, or leptospirosis. Early diagnosis and treatment can be critical and potentially lifesaving for many travel-related infections. Although most acute febrile illnesses have incubation periods of <14 days, infections including typhoid, malaria, leptospirosis, and acute schistosomiasis can have prolonged incubation periods. Travelers should be advised to always inform their health care providers of their travel history, even when their travel does not immediately precede illness onset. Exposure risk occurring as much as a year prior to illness onset should be considered for malaria. Providers unfamiliar with infections common to a region recently visited by an acutely ill traveler should consult with infectious disease or travel medicine specialists and/or their local public health departments.

OUTBREAKS AND EMERGING

INFECTIOUS DISEASES Emerging and reemerging infectious diseases create challenges for international travel. During outbreaks of novel or emerging infections (e.g., the 2020 COVID-19 pandemic, recent Ebola virus disease epidemics in western and central Africa, or the emergence of Zika in the Americas in 2015–2016), information can be limited or can rapidly change. Significant travel disruption can also occur when outbreaks of

- Questions about planned travel during routine care visits
- Prioritization of vaccines and prophylaxis for highest-risk infections when resources are limited
- Prioritization of vaccines and prophylaxis for highest-risk infections when resources are limited
- Education about high-risk activities (e.g., motorbike taxis)
- Several vaccines are effective with a single dose.
- Some vaccination series can be accelerated.
- Some malaria chemoprophylaxis can be started 1 day prior to entering risk areas.
- Consider broad immunization coverage and standing malaria chemoprophylaxis supply for aircrews or other travelers with unpredictable, last-minute trips.
- Increased emphasis on importance of certain vaccines, such as hepatitis B, rabies, typhoid, or Japanese encephalitis (in endemic areas)
- Long-term malaria chemoprophylaxis
- Ensure that traveler has received recommended immunizations for health care workers.
- Advise traveler to assess availability of adequate personal protective equipment and medications for HIV postexposure prophylaxis and to consider potential need to bring own supplies.
- Advise traveler against working with organizations inexperienced in delivering care in the destination area.
- Advise traveler on potential risks.
- Direct tourist to internationally accredited facilities and providers.
- Tourist should acquire a copy of medical records for providers who will provide follow-up care.
- See CDC Yellow Book (Table 130-2) for specific resources.

well-known infections take place in previously unaffected areas, such as the 2017–2018 yellow fever outbreak in southeastern Brazil, which included the metropolitan areas of Rio de Janeiro and São Paulo, two major travel destinations for which vaccination had not previously been recommended. Providers counseling travelers can help them make informed decisions by carefully reviewing available travel health notices, surveillance reports, and potential risks to travelers. Individuals may be advised against travel to certain areas when risks are significant. ■ ■

FURTHER READING Angelo KM et al: What proportion of international travellers acquire a travel-related illness? A review of the literature. J

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