Infectious Risks of Traveling Abroad
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ABSTRACT A popular leisure activity, international travel can be associated with some infections. The most common travel-related illnesses appear to be gastrointestinal, dermatologic, respiratory, and systemic febrile syndromes. The pretravel medical consultation includes immunizations, malaria chemoprophylaxis, self-treatment for traveler’s diarrhea, and advice on the prevention of a myriad of other infectious causes including dengue, chikungunya, rickettsiosis, leptospirosis, schistosomiasis, and strongyloidiasis. Travel to locations experiencing outbreaks such as Ebola virus disease, Middle East respiratory syndrome, avian influenza, and chikungunya call for specific alerts on preventive strategies. After travel, evaluation of an ill traveler must explore details of exposure, including destinations visited; activities; ingestion of contaminated food or drinks; contact with vectors, animals, fresh water, or blood and body fluids; and other potential exposures. Knowledge of the geographic distribution of infectious diseases is important in generating the differential diagnoses and testing accordingly. Empiric treatment is sometimes necessary when suspicion of a certain diagnosis is strong and confirmatory tests are delayed or lacking, particularly for infections that are rapidly progressive (for example, malaria) or for which timing of testing is prolonged (such as leptospirosis).

INTRODUCTION
International tourist arrivals surpassed 1 billion by 2012 and continue to increase. In 2013, nearly 24 million U.S. residents traveled abroad for leisure or to visit friends and relatives (http://travel.trade.gov/outreachpages/outbound_general_information.outbound_overview.html). Of these travelers, 35% went to Europe, 27% to the Caribbean, 17% to Asia, 7% each to South America and Central America, 6% to the Middle East, and under 3% to Africa.

Past surveys of international travelers have identified patterns of health problems associated with travel. The most commonly reported illnesses included traveler’s diarrhea and other gastrointestinal problems, febrile illnesses, dermatologic problems, and respiratory problems; vaccine-preventable diseases were represented in some of these categories. More recent analyses from collaborations such as the GeoSentinel Surveillance Network have found similar patterns in travel-associated illnesses (Fig. 1). Such data substantiate the recognition that some diseases are preventable or may resolve with self-treatment, and they have led to incorporation into guidelines and recommendations by health authorities (Table 1).

In considering travel for leisure, travel purposes such as business, education, research, volunteer/missionary activities, and humanitarian relief are excluded. This chapter focuses primarily on the tourist traveler. Travel to visit friends and relatives may be considered leisure travel, and the increased risk of these travelers for malaria and typhoid requires special attention for prevention and posttravel evaluation.

PRETRAVEL PREPARATION
The pretravel health consultation is intended to assess the traveler regarding potential health issues that may be encountered during travel; to provide preventive measures including immunizations, chemoprophylaxis,
and medications for self-treatment; and to educate the traveler on preventing health risks and to manage illness that arises. For travelers with complex itineraries, challenging activities, or complicated underlying medical conditions, specialized travel medicine providers are best suited to optimize pretravel health preparation. For healthy travelers with common and popular destinations, many primary care providers are able to provide appropriate preparation.

Some basic information is essential in assessing health risks for the traveler. This includes pre-existing medical conditions, past medical problems, medications, allergies, prior vaccinations, past travel, and risk-taking likelihood. Details regarding the trip that are important in determining potential health risks include destination, reason for travel, planned activities, mode of travel, accommodation, and travel style (e.g., open-ended budget travel versus organized upscale guided group).

**Vaccine-Preventable Diseases: Routine Vaccines**

Immunizations are a key component of pretravel health preparation (see Table 2). The pretravel encounter provides an opportunity to review and update age-appropriate immunizations, in particular measles/mumps/rubella (MMR), influenza, tetanus/diphtheria/pertussis (Tdap), meningococcal, and polio vaccines, and consider some routine vaccines such as hepatitis B for use in travelers.

Additional recommendations are in place for travelers who have immune-compromising conditions or medications including asplenia, hematopoietic stem cell transplant, organ transplant, renal failure, and diabetes. For example, asplenic travelers should receive pneumococcal, meningococcal, and *Haemophilus influenzae* type b vaccines. However, detailed discussion of the proper immunization of these special-risk travelers is beyond the scope of this chapter. Clinicians should consult more specific guidelines from the CDC and IDSA regarding immunization of these individuals.

**MMR**

Among the diseases prevented by routine vaccines, importations of measles and mumps have occurred and have led to outbreaks even in association with travel.
TABLE 1 Resources for the practice of travel medicine, including some international and national authorities, online links, and reference books

<table>
<thead>
<tr>
<th>Resources</th>
<th>URL or authors/editors</th>
</tr>
</thead>
<tbody>
<tr>
<td>National and international recommendations, alerts, and information on travelers’ health</td>
<td><a href="http://www.who.int/ith">www.who.int/ith</a></td>
</tr>
<tr>
<td>WHO International Travel and Health</td>
<td><a href="http://www.cdc.gov/travel">www.cdc.gov/travel</a></td>
</tr>
<tr>
<td>WHO Disease Outbreak News</td>
<td><a href="http://www.cdc.gov/malaria">http://www.cdc.gov/malaria</a></td>
</tr>
<tr>
<td>CDC Travelers’ Health website</td>
<td><a href="http://www.cdc.gov/vaccines">www.cdc.gov/vaccines</a></td>
</tr>
<tr>
<td>CDC Malaria website</td>
<td><a href="http://www.travel.state.gov">www.travel.state.gov</a></td>
</tr>
<tr>
<td>CDC Vaccines website</td>
<td><a href="http://travel.state.gov/content/passports/english/country.html">http://travel.state.gov/content/passports/english/country.html</a></td>
</tr>
<tr>
<td>U.S. Department of State Bureau of Consular Services</td>
<td><a href="http://www.promedmail.org">www.promedmail.org</a></td>
</tr>
</tbody>
</table>

Organizations with focus or resources on traveler’s health

<table>
<thead>
<tr>
<th>Organizations</th>
<th>URL or authors/editors</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Society of Travel Medicine</td>
<td><a href="http://www.istm.org">www.istm.org</a></td>
</tr>
<tr>
<td>American Society of Travel Medicine and Hygiene</td>
<td><a href="http://www.astmh.org">www.astmh.org</a></td>
</tr>
<tr>
<td>Infectious Diseases Society of America</td>
<td><a href="http://www.idsociety.org">www.idsociety.org</a></td>
</tr>
<tr>
<td>International Society for Infectious Diseases</td>
<td><a href="http://www.isid.org">www.isid.org</a></td>
</tr>
<tr>
<td>International Association for Medical Assistance to Travelers</td>
<td><a href="http://www.iamat.org">www.iamat.org</a></td>
</tr>
</tbody>
</table>

Selected major print resources

<table>
<thead>
<tr>
<th>Book Title</th>
<th>URL or authors/editors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Information for International Travel</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CDC Epidemiology and Prevention of Vaccine-Preventable Diseases</td>
<td>Atkinson W, Wolfe S, Hamborsky J, eds.</td>
</tr>
<tr>
<td>Travel Medicine</td>
<td>Keystone JS, Kozarsky PE, Freedman DO, Nothdurft HD, Connor BA, eds.</td>
</tr>
<tr>
<td>Tropical Infectious Diseases</td>
<td>Guerrant RL, Walker DH, Weller PF, eds.</td>
</tr>
<tr>
<td>Infectious Diseases: A Geographic Guide</td>
<td>Petersen E, Chen LH, Schlenkauf P, eds.</td>
</tr>
<tr>
<td>Vaccines</td>
<td>Plotkin SA, Orenstein WA, Offit PA, eds.</td>
</tr>
<tr>
<td>The Practice of Travel Medicine: Guidelines by the Infectious Diseases Society of America</td>
<td>Hill DR, Ericsson CD, Ferson RD, Kozarsky JS, Freedman DO, Kozarsky PE, DuPont HL, Bia FJ, Fischer PR, Ryan ET, Infectious Diseases Society of America</td>
</tr>
</tbody>
</table>

Infectious Risks of Traveling Abroad

Infections occurred widely (for example, measles, mumps, and rubella), immunizations were valued for their ability to reduce morbidity and mortality. Unfortunately, skeptics of immunization programs have increased after such infectious diseases became controlled and their severe consequences ceased to be witnessed. The antivaccine movement and declination of routine immunizations have grown in recent decades. Underimmunized and unimmunized people have acquired infections during travel and have led to outbreaks in their communities at home. In the United States, the Advisory Committee on Immunization Practices recommends that international travelers as well as students and health care workers have two well-documented doses of MMR vaccine, positive serology, or well-documented infection with these diseases.

Influenza

Influenza vaccine merits attention because influenza has been shown to be one of the most common vaccine-preventable disease among travelers. According to European studies, the estimated incidence rate of influenza in travelers visiting tropical and subtropical countries is 1 case per 100 travelers per 1 month of stay. Outbreaks have occurred on cruise ships. Influenza contributes to one of the most common categories of illness that travelers encounter, respiratory tract infections. Because tropical and subtropical regions have influenza circulation year-round, and the Southern Hemisphere’s influenza season occurs during the summer season of the Northern Hemisphere, influenza vaccination should be considered for most if not all travelers.

Polio

Polio, a childhood vaccine that is still routinely administered in most countries including the United States, is specifically indicated as a booster for adults traveling to countries with risk of polio transmission, that is, countries that have active circulation of wild poliovirus and countries with a recent occurrence of wild polio. The number of affected countries has continued to...
decline in the past two decades and currently is limited to Afghanistan, Pakistan, Nigeria, Syria, Israel, the West Bank, Gaza, and some other countries in Africa and the Middle East. The list is updated regularly, and clinicians should refer to the CDC Travelers’ Health website for outbreak reports and recommendations (Table 1).

**Hepatitis A**

Travelers who may have direct contact with blood or body fluids are at risk for hepatitis B. Although most travelers may not anticipate these incidents, longer durations of stay may lead to unplanned exposures due to injury, medical/dental care, sexual contact, and procedures such as tattoos and piercings. Universal infant vaccination was adopted in 1991 in the United States and consists of a three-dose series administered over 6 months. Studies to date suggest protection to last >22 years. The program was expanded to universal adolescent vaccination in 1996; most individuals under the age of 35 years at the time of this writing have been immunized. Unimmunized travelers who plan activities with potential risk should be immunized, as well as those who travel longer or frequently to countries with medium to high endemicity.

**Vaccine-Preventable Diseases: Travel Vaccines**

In the United States, the consideration of travel immunizations includes hepatitis A, Japanese encephalitis, rabies, typhoid, and yellow fever vaccines. Two other vaccines unavailable in the United States, cholera and tick-borne encephalitis vaccines, are available in Europe and in Canada and will be described briefly.

**Hepatitis A**

Acquired usually through the consumption of contaminated food or drinks, hepatitis A is one of the most common vaccine-preventable diseases among travelers. In addition to exposures while traveling to developing areas of the world, some outbreaks have occurred in developed countries such as the United States. In recent years, nontravel hepatitis A outbreaks have been associated with infected food handlers and foods such as frozen berries or raw green onions. The vaccine consists of two doses administered at least 6 months apart and provides long-lasting protection (>17 years) suggested by serologic studies, and likely lifelong based on antibody modeling. Even with imminent departure, a single dose of the vaccine leads to excellent protection for well over a year. Furthermore, a delay in the interval between the two doses appears still to induce excellent response after the second dose.

**Japanese encephalitis**

Japanese encephalitis is transmitted through the bite of Culex mosquitoes that mainly breed in rural Asia, near rice paddies and farms. The mosquitoes are night-biting; thus, risk for the infection is associated with night-time, outdoor, rural activities. Although disease is rare among travelers, infection causes high morbidity and mortality.

Prevention of Japanese encephalitis includes avoidance of mosquito bites with personal protective measures (i.e., apply repellent, sleep in mosquito net, wear long sleeves and pants, use permethrin on clothing). In addition, a two-dose vaccine series can be considered. The series requires a 28-day interval and is considered to protect for 1 to 2 years. Longer travel duration is associated with increased risk based on documented cases in travelers from nonendemic countries. Therefore, the Advisory Committee on Immunization Practices recommends consideration for this vaccine when travel duration is 1 month or longer, but the vaccine should also be considered for shorter trips that include night-time, outdoor, rural exposures.

**Rabies**

Most developing countries do not have rabies vaccination programs for animals. Therefore, a traveler that encounters an animal bite or scratches or contact with saliva on a mucous membrane or nonintact skin should be considered to have rabies exposure. Management after a possible rabies exposure should include appropriate wound care (washing with copious amount of soap and water) and administration of rabies immune globulin and rabies vaccine series (four doses over 2 weeks for healthy people or five doses over 4 weeks for immunocompromised people). However, the supply of human rabies immune globulin and rabies vaccines is
TABLE 2 Immunizations commonly considered in pretravel consultation (for a comprehensive list of routine vaccines, see routine immunization schedules published by the Advisory Committee on Immunization Practices and updated annually)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type of vaccine</th>
<th>Adult dose</th>
<th>Pediatric dose</th>
<th>Route</th>
<th>Standard schedule of immunization</th>
<th>Duration of protection (after primary series)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera (not available in the U.S.)</td>
<td>Killed whole-cell Vibrio cholerae vaccine combined with recombinant B subunit of cholera toxin</td>
<td>1 sachet</td>
<td>Age 2–5 y; ½ sachet; 3 doses 1–6 weeks apart; booster dose after 6 mo</td>
<td>Oral</td>
<td>2 doses 1–6 weeks apart; booster dose after 2 yr</td>
<td>2 yr</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Inactivated virus</td>
<td>1 ml</td>
<td>Age 1–18 y: 0.5 ml</td>
<td>i.m.</td>
<td>2 doses 6–12 mo apart</td>
<td>&gt;17 yr</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Recombinant hepatitis B surface antigen</td>
<td>1 ml</td>
<td>Age &lt;19 y: 0.5 ml</td>
<td>i.m.</td>
<td>3 doses: day 0, 1 mo, and 6 mo</td>
<td>&gt;22 yr</td>
</tr>
<tr>
<td>Combined hepatitis A and B</td>
<td>Inactivated virus and recombinant viral antigen</td>
<td>1 ml</td>
<td>Not FDA approved in the U.S. for children younger than 18 yr</td>
<td>i.m.</td>
<td>3 doses: day 0, 1 mo, and 6 mo</td>
<td>&gt;17 yr</td>
</tr>
<tr>
<td>Influenza</td>
<td>Inactivated virus</td>
<td>0.5 ml</td>
<td>Age 6–35 mo: 0.25 ml</td>
<td>i.m.</td>
<td>1 dose</td>
<td>1 yr</td>
</tr>
<tr>
<td>Japanese encephalitis, tissue culture-derived</td>
<td>Inactivated virus</td>
<td>0.5 ml</td>
<td>Age ≥36 mo: 0.5 ml</td>
<td>i.m.</td>
<td>1 dose</td>
<td>1 yr</td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td>Live-attenuated virus</td>
<td>0.5 ml</td>
<td>Age ≥1 y: 0.5 ml</td>
<td>s.c.</td>
<td>2 doses: day 0, 4 weeks</td>
<td>Lifelong</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>Bacterial polysaccharide</td>
<td>0.5 ml</td>
<td>Age ≥2 y: 0.5 ml</td>
<td>s.c.</td>
<td>1 dose</td>
<td>3–5 yr</td>
</tr>
<tr>
<td>Poliovirus</td>
<td>Inactivated virus</td>
<td>0.5 ml</td>
<td>Age ≥9 mo (Menactra) or &gt;2 yr (Menveo): 0.5 ml</td>
<td>i.m.</td>
<td>1 dose</td>
<td>3–5 yr</td>
</tr>
<tr>
<td>Rabies</td>
<td>Inactivated virus, human diploid cell</td>
<td>1 ml</td>
<td>1 ml</td>
<td>i.m.</td>
<td>3 doses preexposure: days 0, 7, and 21 or 28</td>
<td>Lifelong, after primary childhood series</td>
</tr>
<tr>
<td></td>
<td>Inactivated virus, purified chick embryo</td>
<td>1 ml</td>
<td>1 ml</td>
<td>i.m.</td>
<td>3 doses preexposure: days 0, 7, and 21 or 28</td>
<td>Boostable lifelong; 2 additional doses are required on days 0 and 3 after rabies exposure</td>
</tr>
<tr>
<td>Tetanus diphtheria pertussis (Tdap) or tetanus diphtheria (Td)</td>
<td>Toxoid</td>
<td>0.5 ml</td>
<td>Age ≥7 y: 0.5 ml</td>
<td>i.m.</td>
<td>1 dose booster following primary childhood series</td>
<td>10 yr</td>
</tr>
<tr>
<td>Tick-borne encephalitis (not available in the U.S.)</td>
<td>Inactivated virus</td>
<td>0.5 ml</td>
<td>Age 3–16 y: 0.25 ml initial dose followed by 0.5 ml</td>
<td>i.m.</td>
<td>3 doses: day 0, 1–3 mo, and 5–12 mo</td>
<td>3 yr</td>
</tr>
<tr>
<td>Typhoid</td>
<td>Bacterial polysaccharide</td>
<td>0.5 ml</td>
<td>Age ≥2 y: 0.5 ml</td>
<td>i.m.</td>
<td>1 dose</td>
<td>2 yr</td>
</tr>
<tr>
<td></td>
<td>Live, attenuated bacteria</td>
<td>4 capsules</td>
<td>Age &gt;6 y: 4 capsules</td>
<td>Oral</td>
<td>4-capule series, one every other day</td>
<td>5 yr</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Live, attenuated virus</td>
<td>0.5 ml</td>
<td>Age ≥9 mo: 0.5 ml</td>
<td>s.c.</td>
<td>1 dose</td>
<td>10 yr (possibly lifelong)</td>
</tr>
</tbody>
</table>

*a.i.m., intramuscular; s.c., subcutaneous*
unreliable in developing countries, rendering the post-
exposure management of possible rabies exposure
challenging and anxiety-provoking.

A three-dose rabies vaccine series is available as
pre-exposure prophylaxis (PrEP), administered on days
0-7-28 but could be accelerated to days 0-7-21. Man-
agement after a possible rabies exposure in a person
who has completed the three-dose rabies PrEP only re-
quires two more doses of rabies vaccine—the first doses
as soon as possible and the second dose three days later.
Travelers who have received PrEP do not need rabies
immune globulin after rabies exposure, further simpli-
ifying the management.

A long-standing assumption regarding rabies ex-
posure is that long stays in developing countries are more
likely to be associated with animal contact and rabies
risk. However, recent analyses have found that the du-
ration of travel may have little impact on the likelihood
of having a potential rabies exposure; short-term trav-
elers appear to have a similar likelihood of being bitten
by animals as long-term travelers. It is prudent to con-
sider rabies PrEP for travelers who may have close
contact with animals, especially if they will be in remote
settings without timely care or if they might have diffi-
culty obtaining good-quality postexposure treatment,
for example, if the supply of rabies immune globulin is
uncertain or unavailable.

Typhoid
Enteric fever includes typhoid (caused by Salmonella
enterica serotype Typhi) and paratyphoid (S. enterica
serotype Paratyphi), both resulting from ingestion of
contaminated food or drinks. The highest-risk region is
South Asia, especially in travelers whose purpose for
travel is visiting friends and relatives. In addition to
precaution in food and drinks, two vaccines are avail-
able. The oral typhoid vaccine, a live-attenuated bacte-
rrial vaccine, consists of four capsules and is taken as
one capsule every other day, thus completing the series
in 1 week. The oral typhoid vaccine provides 5 years of
protection. The other vaccine, a polysaccharide vaccine,
is a single injection that provides 2 years of protection.
These vaccines only protect against S. enterica Typhi in
the range of 60 to 70%, and they do not protect against
S. enterica Paratyphi. Travelers may still develop enteric
fever despite vaccination and need to use precaution
even when vaccinated.

Yellow fever
Yellow fever is caused by a flavivirus transmitted
through mosquito bites, particularly the day-biting
Aedes mosquitoes, and has a case fatality rate of up to
50%. The endemic regions include sub-Saharan Africa
and tropical Central and South America, although risk
is generally greater in sub-Saharan Africa. Avoiding
mosquito bites is important in the prevention of yellow
fever, and a live-attenuated virus vaccine may be recom-
ended or required in travelers visiting areas with risk
for yellow fever transmission. A dose of yellow fever
vaccine has been considered by most health authorities
to provide 10 years of protection. The International
Health Regulations apply to yellow fever so that
documentation of yellow fever vaccination within the
previous 10 years may be required for entry into some
countries.

However, the yellow fever vaccine has been associ-
ated with rare but severe adverse events, one called
yellow fever vaccine-associated viscerotropic disease
and another, yellow fever vaccine-associated neurologic
disease. These rare vaccine-adverse events have occurred
at overall rates of 0.4/100,000 doses and 0.8/100,000
doses, respectively, and have led to challenges in yellow
fever vaccine decision and administration.

In 2013, the Strategic Advisory Group of Experts
on Immunization for the World Health Organization
concluded that a single dose of yellow fever vaccine can
provide lifelong protection. The World Health Assembly
subsequently voted to revise the International Health
Regulations to accept yellow fever vaccine as protec-
tive lifelong. Because each country determines its own
requirements, yellow fever vaccine decisions need to
consider the risk-benefit ratio of the individual traveler,
the itinerary, and the specific country requirements. The
U.S. Advisory Committee on Immunization Practices
has finalized its recommendations in 2015 to state
that the yellow fever vaccine may provide long-lasting
protection for most travelers, but some specific pop-
ulations of travelers should be vaccinated if traveling
to risk areas post 10 years of their last yellow fever
vaccination.

Cholera
Caused by the Gram-negative bacteria Vibrio cholerae,
cholera is another disease transmitted via ingestion of
contaminated food or water. Areas with an unreliable
drinking water supply and poor hygiene routinely ex-
perience cholera outbreaks, typically in Africa and Asia.
Since the 2010 earthquake, Haiti has experienced tre-
 mendous outbreaks. Subsequently, the Dominican Re-
public and Cuba have had outbreaks, and Mexico has
also reported cases. Advice to travelers regarding this
disease is to take precautions regarding food and water.
Worldwide, three oral cholera vaccines are currently manufactured, including a killed whole-cell vaccine that is licensed and available in Europe and Canada. There is currently no cholera vaccine in the United States, although a live-attenuated vaccine is under evaluation by the FDA.

Tick-borne encephalitis
Human disease from tick-borne encephalitis, a flavivirus, results mainly from tick bites but can also result from consumption of unpasteurized dairy products. Tick-borne encephalitis distribution and incidence have increased in recent years, and it extends from Europe to far eastern Russia and northern Asia. Although most infections are subclinical, some infected persons may develop aseptic meningitis, encephalitis, and myelitis. Currently, modern cell culture vaccines are available in endemic regions, including a three-dose series in Europe and Canada that protects for 3 years. There is currently no tick-borne encephalitis vaccine in the United States.

Malaria Prevention
Malaria continues to cause significant morbidity and mortality in travelers, and its rapidly progressive course makes it essential to prevent infection. Malaria is caused by the Plasmodium species of parasites and transmitted by the bite of Aedes mosquitoes. The main human species of malaria parasites are Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, and Plasmodium knowlesi, the latter being a monkey species that has been recently identified to cause significant proportions of human infection in Southeast Asia. Emergence of drug-resistant malaria parasites, initially to chloroquine, then mefloquine, and more recently artemisinin derivatives, hampers malaria control. It also introduces challenges in chemoprophylaxis of travelers to malaria-endemic areas. Therefore, it is important to evaluate the risk of malaria for each traveler during the pretravel consultation and recommend appropriate preventive measures. CDC Health Information for International Travel is an accessible and informative reference regarding areas of resistance.

It is pertinent to discuss with the traveler basics in malaria transmission, risk-reduction measures, and chemoprophylaxis. Travelers going to malaria-endemic areas should be advised that the mosquito vectors are night-biters. Thus, the risk-reduction measures include staying in well-screened accommodations, sleeping in nets, wearing long sleeves and long pants, applying repellent, and treating clothing with insecticide.

Several medications are currently available for malaria chemoprophylaxis: chloroquine, hydroxychloroquine, mefloquine, doxycycline, atovaquone-proguanil, and primaquine (Table 3). The choice depends on the presence of resistance, the traveler’s health history and chronic medications with respect to contraindications and drug interactions, and tolerability to the traveler. Chloroquine, one of the oldest chemoprophylaxis drugs, is taken weekly but has limited use given the rise of chloroquine-resistant malaria. It may be used in endemic areas of Central America, the Caribbean, and the Middle East. Hydroxychloroquine is a 4-aminoquinoline chemical similar to chloroquine and is recommended by the CDC for malaria chemoprophylaxis for areas with chloroquine-sensitive parasites. A precaution for these two medications is the possible association with ocular side effects (irreversible macular damage or reversible, asymptomatic keratopathy/retinopathy) in people on long-term therapy. Such associations with chemoprophylaxis occurred in travelers who took hydroxychloroquine for several years, and it is recommended that annual eye exams be performed on people on long-term courses of these drugs.

Mefloquine is a chemoprophylaxis recommended for travelers going to malarious areas that have chloroquine-resistant malaria parasites. It is also taken weekly but needs to be started at least 2 weeks before arriving in the malarious area and continued for 4 weeks after departure from the malarious area. The major advantages of mefloquine include the following: (i) the weekly schedule results in fewer pills (preferred by some long-term travelers), and (ii) it is considered safe during pregnancy and for children. The course requires advance planning, so it is inconvenient for some travelers. More challenging is the association of mefloquine with neuropsychiatric side effects that may be long-lasting or permanent. Although usually these neuropsychiatric side effects are odd or vivid dreams, some people may experience anxiety, depression, and hallucinations. An additional potential disadvantage of chloroquine and mefloquine is the possible prolongation of the QT interval, which complicates the prescribing of antibiotics for traveler’s diarrhea.

Atovaquone-proguanil has become the most popular chemoprophylaxis drug, being effective against chloroquine-resistant and mefloquine-resistant parasites. It is available as a fixed-dose combination in either an adult or pediatric dose and is taken daily starting 1 to 2 days before entering a malarious area and continued for 1 week after departure from a malarious area. It is generally well tolerated with a relatively simple schedule.
TABLE 3  Malaria chemoprophylaxis drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication/instructions</th>
<th>Adult dose</th>
<th>Pediatric dose</th>
<th>Key precautions/contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone-proguanil</td>
<td>May consider for all malarious areas. Take daily starting 1–2 days before arriving in the malarious area and for 7 days after leaving malarious areas. Take with food or a milky drink.</td>
<td>Fixed-dose combination of 250 mg atovaquone–100 mg proguanil</td>
<td>Fixed dose combination of 62.5 mg atovaquone–25 mg proguanil 5–8 kg: 1/2 pediatric tablet daily &gt;8–10 kg: 3/4 pediatric tablet daily &gt;10–20 kg: 1 pediatric tablet daily &gt;20–30 kg: 2 pediatric tablets daily &gt;30–40 kg: 3 pediatric tablets daily &gt;40 kg: 1 adult tablet daily</td>
<td>Not recommended for prophylaxis for children weighing &lt;5 kg, pregnant women, and women breastfeeding infants weighing &lt;5 kg. Contraindicated if creatinine clearance is &lt;30 ml/min. Precaution: reduce dose in patients with renal insufficiency.</td>
</tr>
<tr>
<td>Chloroquine phosphate</td>
<td>Consider only in areas with chloroquine-sensitive malaria. Take weekly starting 12 weeks before arriving in the malarious area and for 4 weeks after leaving malarious areas.</td>
<td>300 mg base (500 mg salt) up to adult dose</td>
<td>5 mg/kg base (8.3 mg/kg salt) up to adult dose</td>
<td>May exacerbate psoriasis. Precaution: long-term use raises concern for retinopathy, and routine ophthalmologic examination is recommended.</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>May consider for all malarious areas. Take daily starting 1–2 days before arriving in the malarious area and for 4 weeks after leaving malarious areas.</td>
<td>100 mg</td>
<td>&gt;8 years of age: 2.2 mg/kg up to adult dose</td>
<td>Contraindicated in children &lt;8 years of age and pregnant women.</td>
</tr>
<tr>
<td>Hydroxychloroquine sulfate</td>
<td>An alternative to chloroquine for prophylaxis only in areas with chloroquine-sensitive malaria. Take weekly starting 1 week before arriving in the malarious area and for 4 weeks after leaving malarious areas.</td>
<td>310 mg base (400 mg salt) up to adult dose</td>
<td>5 mg/kg base (6.5 mg/kg salt) up to adult dose</td>
<td>Precaution: long-term use raises concern for retinopathy, and routine ophthalmologic examination is recommended.</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>May consider in areas with mefloquine-sensitive malaria. Take weekly starting ≥2 weeks before arriving in the malarious area and for 4 weeks after leaving malarious areas.</td>
<td>228 mg base (250 mg salt)</td>
<td>≤9 kg: 4.6 mg/kg base (5 mg/kg salt) &gt;9–19 kg: 1/4 tablet once/week &gt;19–30 kg: 1/2 tablet once/week &gt;30–45 kg: 3/4 tablet once/week &gt;45 kg: 1 tablet once/week</td>
<td>Not recommended for people with cardiac conduction abnormalities. Contraindicated in people with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, other major psychiatric disorders, or seizures. Precaution in people with psychiatric disturbances or a previous history of depression.</td>
</tr>
<tr>
<td>Primaquine</td>
<td>May consider for short-term travel to areas with principally P. vivax. Take daily starting 1–2 days before arriving in the malarious area and for 7 days after leaving malarious areas.</td>
<td>30 mg base (52.6 mg salt)</td>
<td>0.5 mg/kg base (0.8 mg/kg salt) up to adult dose</td>
<td>Contraindicated in people with G6PD deficiency during pregnancy and lactation, unless the infant being breastfed has a documented normal G6PD level.</td>
</tr>
</tbody>
</table>
but should be taken with rich (fatty) foods to be absorbed properly and to minimize possible gastrointestinal upset. Key precautions include possible interaction with warfarin, a fairly common anticoagulant, and the need to reduce the dose in people with severe renal insufficiency.

Doxycycline is an effective antimalarial, taken daily starting 1 to 2 days before arriving in malarious areas and continued for 4 weeks after departure from those areas. The adherence is suboptimal, and doxycycline can lead to sun sensitivity and Candida vaginitis, common discomforts in the tropics. Moreover, it is contraindicated during pregnancy and in young children. However, its role as an antibiotic may serve to prevent leptospirosis and rickettsioses, helpful properties for travelers who may have exposure to fresh water or ticks.

Primaquine can be prescribed for malaria chemoprophylaxis for travelers going to areas with P. vivax predominance because it appears to be the only licensed medication that prevents hypnozoite formation. Although not FDA-approved for primary chemoprophylaxis, a number of series have demonstrated its efficacy. Primaquine can lead to life-threatening hemolysis in people with G6PD deficiency; therefore, G6PD must be confirmed to be normal before this medication is prescribed. It is contraindicated during pregnancy.

Traveler’s Diarrhea
Traveler’s diarrhea is the most common health problem encountered by travelers, reported by 30 to 70% of travelers in various studies. When specifically sought and identified, the predominant causative agents were found to be bacterial, particularly Escherichia coli, Campylobacter jejuni, Shigella spp., and Salmonella spp. Viruses such as norovirus, rotavirus, and astrovirus may cause traveler’s diarrhea but are not frequently identified. Giardia is the most common protozoan etiology identified, and less common are Entamoeba histolytica, Dientamoeba fragilis, Cryptosporidium, and Cyclospora.

To minimize the risk of traveler’s diarrhea as well as other foodborne illnesses, routine advice for travelers to developing regions of the world (with substandard hygiene practices) is to exercise caution regarding consumption of food and beverages. The basic concept is “boil it, cook it, peel it, or forget it,” although studies have not shown a positive impact of such precautions. Probiotics also have not demonstrated definitive benefit in preventing traveler’s diarrhea. On the other hand, evidence does support the use of bismuth subsalysalate in traveler’s diarrhea prevention, taking two chewable tablets four times daily. Prophylactic antibiotics are also effective, but because of the added expense, potential side effects, and possible selection for drug resistance, prophylactic antibiotics for traveler’s diarrhea are not recommended for most travelers.

Self-management of traveler’s diarrhea is important to discuss with travelers because of the frequency of occurrence. Travelers may approach it in a stepwise manner. Mild cases may improve and resolve simply with fluid rehydration. Moderate cases may benefit from the addition of an antimotility drug, loperamide, for symptomatic relief. More severe cases may need empiric antibiotics for faster resolution. The currently preferred antibiotic choices for self-treatment of traveler’s diarrhea include ciprofloxacin 500 mg twice a day (or another fluoroquinolone) and azithromycin 500 mg daily, up to 3 days. Ciprofloxacin is generally well tolerated, but fluoroquinolone resistance in parts of the world, particularly Southeast and South Asia, has led to the need for an alternative class—thus azithromycin.

Road Traffic Injuries
It would be remiss to omit road traffic crashes in discussing travel-related health problems, since they cause more deaths of healthy U.S. citizens in foreign countries than all other causes (excluding wars), including infectious diseases, crime, and terrorism. Motor vehicle crashes led to at least one-quarter of deaths abroad from 2009 to 2011, a statistic that merits a reminder to travelers that developing regions of the world have relatively poor road conditions, inexperienced drivers, poor traffic regulations and maintenance of vehicles, and lack adequate services such as emergency transport and trauma centers. Key messages are: wear seat belts, use appropriate child restraint systems, choose safe vehicles and drivers, and travel during the day (rather than night).

Adventure Travel: High Altitude, Fresh Water Exposure
Water sports have gained popularity among travelers going to foreign destinations. An associated potential danger is drowning, which could be associated with unfamiliarity with the waters (for example, rip tide and undertow). Even in calm fresh water, travelers can be exposed to leptospirosis and schistosomiasis. Travelers with itineraries that suggest such activities should be advised to avoid the risk.

A brief mention of acute mountain sickness is worthwhile, although it is not an infectious consequence, since
a sizable number of travelers visit high-altitude destinations, typically 8,000 feet or higher. Such travel is associated with possible development of acute mountain sickness. In more severe situations, high-altitude pulmonary edema and high-altitude cerebral edema can occur and result in fatality. Assessing the planned ascent for travelers for a change of >1,600 feet in sleeping altitude in one day may show potential problems associated with high altitude. Key messages for travelers are to ascend gradually, to climb high/sleep low, to have an emergency evacuation arrangement, and to carry with them some basic medications for prevention and treatment, including acetazolamide, nifedipine, dexamethasone, salmeterol, sildenafil, and ibuprofen (see Infectious Diseases at High Altitude).

Travel Health Kit
Carrying a travel medical kit allows travelers to respond to health problems should they arise, which is another goal of the pretravel health evaluation. CDC Health Information for International Travel has informative sections on self-treatable problems and travel health kits (see resources in Table 1). In addition to the traveler’s routine medications, malaria chemoprophylaxis, and antibiotics for traveler’s diarrhea treatment, basic items to include are those for first aid, anti-inflammatories and analgesics, antihistamines, and medications for other gastrointestinal disorders, respiratory infections, altitude illness, and motion sickness.

Assistance During Travel and Medical Evacuation
When travelers fall ill abroad, they face challenges to locate high-quality medical facilities. The U.S. State Department website has some information, and travelers can link to U.S. embassies and consulates in the country they are visiting for hospital information. The International Society of Travel Medicine has a travel clinic directory, searchable by country/state/city. The International Association for Medical Assistance to Travelers also has a network of medical providers with particular interest in providing care to travelers. Medical facilities in developing countries that have received accreditation from the Joint Commission International are expected to have a reasonable standard of quality. Travelers with complicated chronic conditions should try to identify in advance possible medical providers at their destination.

Most travelers are not aware that medical care in a foreign country usually requires cash or credit card payment and that their health insurance coverage from home may not cover medical care while traveling. Travelers need to be advised to find out what their health insurance covers and consider travel health insurance and/or medical evacuation insurance.

POSTTRAVEL MANAGEMENT
The most common illnesses encountered in returning travelers are diarrhea, respiratory tract infections, skin rashes, and fever. To evaluate ill returned travelers, details of travel must be sought, including destinations visited, activities, food and drink safety, and other potential contacts listed in Table 4.

Diarrhea and Other Gastrointestinal Illness
Gastrointestinal complaints, especially diarrhea, are common issues both during and after travel. In approximately 800 returned travelers surveyed in the United States, diarrhea was the most common diagnosis. Frequently, episodes of travel-related diarrhea resolve spontaneously or in response to self-treatment with antibiotics or antimotility agents. For diarrhea lasting ≥2 weeks a diagnosis can be made in up to 75% of cases, and it is usually due to bacteria or viruses. Diagnoses of Giardia, Cryptosporidiosis, Entameoba histolytica, and Cyclospora increase with the duration of diarrhea. Etiologies such as malabsorption and tropical sprue are of concern when there are prolonged complaints of diarrhea.

Acute diarrhea
When assessment for microbiologic causes is performed, an etiologic agent can be identified in 50 to 94% of traveler’s diarrhea. Enterotoxogenic E. coli and entero-aggregative E. coli are the most often isolated in many parts of the world and are most often caused by ingestion of fecally contaminated food or beverages. In Southeast Asia, however, Campylobacter and Salmonella are more common. While most cases of acute traveler’s diarrhea are caused by bacterial pathogens, viruses such as norovirus and rotavirus account for 5 to 25% of the reported pathogens, depending on the region traveled, and are generally self-limited even when accompanied by fever. While most travelers returning home with diarrhea do not seek treatment, diarrhea in adults who seek treatment and in whom a bacterial pathogen is suspected (but without fever or dysentery) can be treated with ciprofloxacin, azithromycin, or rifaximin. More severe diarrhea associated with fever, bloody stool, and mucous are usually attributable to Salmonella spp., Shigella, and Campylobacter. Stool culture and blood cultures should be obtained to exclude
typhoid fever. *V. cholerae* O1 should be considered if severe dehydrating watery diarrhea is present. *Clostridium difficile* should be considered in the returned traveler with diarrhea who has used antimicrobials during the trip, because treatment with oral metronidazole is necessary.

### Chronic diarrhea

Diarrhea lasting >14 days occurs in approximately 2% of returning travelers. Pathogens responsible for chronic diarrhea in the returning traveler can be bacteria, protozoa, or helminths. *Giardia* is a protozoa usually ingested in contaminated food or beverage but can also be spread person to person fecal-orally. Symptoms can last up to weeks and involve abdominal pain, nausea, and persistent watery diarrhea. Diagnosis is through stool ova and parasite examination or stool antigen assay, and treatment is with tinidazole, metronidazole, or nitazoxanide.

*E. histolytica* is the cause of amoebiasis and is acquired via ingestion. Ninety percent of cases are self-limited and asymptomatic. Symptomatic disease occurs with mucosa and submucosa invasion. About 1% of these cases cause liver involvement as the organism makes its way into the portal circulation causing liver abscess(es). Diagnosis of *E. histolytica* as the etiology for diarrheal illness is through stool antigen assay, whereas positive serology is supportive of abscess. Treatment includes metronidazole with paromomycin.

Less common causes of chronic diarrhea include *Strongyloides* and *Schistosoma* spp., and these diagnoses should be considered particularly in travelers with eosinophilia (see eosinophilia section below). Diagnosis for both *Strongyloides* and *Schistosoma* spp. can be made through stool microscopy for ova and parasites, but serology is more sensitive. Treatment for strongyloidiasis is ivermectin and for schistosomiasis is praziquantel.

In returning travelers with chronic diarrhea, protozoal causes such as *Giardia*, *Cyclospora*, and *Cryptosporidium* should be evaluated for via stool microscopy. Less common organisms such as *Aeromonas*, *Plesiomonas*, *Vibrio*, and *Yersinia*, should be specifically sought. Treatment is thereby directed at the pathogen found. Rarely, a comprehensive gastrointestinal evaluation is needed to exclude inflammatory bowel disease. Other possible causes of chronic diarrhea include lactose intolerance, postinfectious irritable bowel syndrome, tropical sprue, and celiac sprue.

### Fever in the Returned Traveler

Because fever can herald serious infections in returned travelers, expedited evaluation is paramount to rapidly exclude diagnoses that are life threatening or transmissible. An astute clinician evaluating the returning traveler needs to be aware of any outbreaks pertinent to the areas visited in addition to obtaining details of potential exposure (Table 4). As the Ebola virus disease of 2014–2015 illustrated, knowing a patient traveled to an affected country has significant repercussions and management implications when dealing with the febrile returned traveler. While most of those affected by Ebola...
virus disease were natives to those countries or visiting health care workers, it is still an important part of a patient’s overall assessment to be aware of potential outbreak exposure (see resources in Table 1).

Malaria

Fever in a traveler returning from a malaria-endemic area should prompt an immediate evaluation for malaria even in the setting of purported chemoprophylaxis. Among American travelers surveyed, only 80% of those prescribed malaria chemoprophylaxis adhered to their regimen as prescribed. *P. falciparum* can present as early as 6 days and as many as 30 days (or longer) posttravel to an endemic area. Malaria is rapidly progressive, and delays in diagnosis or treatment can result in severe malaria, cerebral malaria, and fatal outcome. Despite global eradication measures, malaria is still endemic in many parts of the world, and transmission patterns can change frequently (see resources in Table 1).

When malaria is suspected, rapid diagnostic testing can quickly guide treatment, and microscopy is the “gold standard.” Various immunoassays have been developed which can detect malarial antigens in blood samples within minutes. The downside to using these rapid diagnostic tests is that microscopy must still be performed to assess parasitemia and assist with species determination. PCR of specimens is ultimately most reliable for species confirmation (see resources in Table 1).

Dengue

Dengue is a flavivirus infection transmitted through the bite of day-biting *Aedes* mosquitoes. Many popular tropical and subtropical destinations are dengue endemic—hence the rising incidence of dengue infections over the last 50 years and the overall spread of dengue. Dengue is among the most common differential diagnoses in febrile returning travelers, along with treatable severe illnesses such as malaria or typhoid fever. Although a significant number of dengue infections are asymptomatic or only mildly symptomatic, dengue can also present with severe symptoms including hemorrhage and shock. Certain clinical and laboratory findings can predict dengue fever if present simultaneously: fever, rash, and leukopenia. PCR during acute infection, or paired acute and convalescent serology, can confirm the diagnosis. Severe dengue or dengue hemorrhagic fever accounts for about 6% of symptomatic dengue infections in endemic areas. Travelers only rarely present with dengue hemorrhagic fever. Treatment for dengue is largely supportive, so avoidance of mosquitoes during travel is paramount.

Chikungunya

Since 2004 many local epidemics of chikungunya have emerged in areas of Africa and Asia, spreading periodically to more temperate areas such as Italy in 2007. In December 2013, chikungunya was confirmed in St. Martin (French side) and subsequently led to a large outbreak throughout the Americas, especially the Caribbean. Transmission is through the bite of *Aedes* mosquitoes, and up to about 30% of those exposed develop symptomatic illness with an incubation period ranging from 2 to 12 days. Typically, illness onset is characterized by acute fever and arthralgias of hands, feet, and proximal joints with or without rash, leukopenia, thrombocytopenia, and elevated liver function tests. Case series have shown that 20 to 50% of symptomatic chikungunya patients may develop persistent or relapsing arthritis/arthralgias. Unfortunately, chikungunya can coexist with other illnesses such as malaria, dengue, and leptospirosis, so careful history and exposure history can assist with the differential. Diagnosis can be confirmed by PCR during the acute infection or by serology. As in dengue infection, treatment is supportive, but those infected should be protected from further mosquito exposure to prevent further transmission.

Tick-borne infections

Travelers presenting with fever, headache, and body aches with or without rash who have participated in outdoor activities in the spring and summer months should be evaluated for rickettsial infections. Travelers are at risk for a broad range of rickettsial infections depending on the area visited and the activities performed, including African tick bite fever, Mediterranean tick typhus, scrub typhus, *Anaplasma*, *Ehrlichia*, *Rocky Mountain spotted fever*, etc. The diagnosis of rickettsial infections is usually presumptive with the initiation of treatment, typically with doxycycline while serologic or PCR confirmation is made.

Enteric fever

In contrast to other etiologies of fever in a returning traveler, enteric fever due to *S. enterica* serotypes Typhi and Paratyphi may have a more insidious onset. In addition to fever, those infected with enteric fever may present with headache, abdominal pain, and constipation or diarrhea. The risk for enteric fever acquisition is up to 30 times higher in those traveling to Southeast Asia than to other destinations. Vaccines may offer only partial protection. There is no serologic test for enteric fever, and blood cultures may be positive in only 50% of
Infectious Risks of Traveling Abroad

Influenza
Influenza is common throughout the world. Flu season is October through May in the Northern Hemisphere and April through September in the Southern Hemisphere. Travel in and of itself does not increase one’s risk for influenza acquisition. Travel to an area during flu season may result in a traveler presenting febrile with influenza outside of the typical season. While not everyone with influenza will have fever, they may feel feverish and present also with chills, body aches, sore throat, nasal congestion, and gastrointestinal symptoms. Testing can be performed via rapid testing, but the sensitivity of such tests is substantially lower than for reverse transcription-PCR or viral culture. Therefore, a negative rapid test result does not exclude influenza infection. Antiviral treatment is recommended for any patient with confirmed or suspected influenza who is hospitalized, has severe or progressive illness, or has risks for complications.

Hepatitis
Hepatitis A is common in the developing world, and risk for acquisition during travel increases with exposure to contaminated food or beverages or travel in rural areas with poor sanitation. The incubation period can range from 15 to 50 days, and symptoms are fever, anorexia, and malaise followed by jaundice. Diagnosis is suspected based on symptoms and abnormal liver function tests (LFTs) and is confirmed with a positive IgM antibody. Treatment is supportive. For hepatitis B infection, the risks for travelers are for those who come in contact with infected blood or body fluids, usually through unprotected sexual contact, tattooing, acupuncture, or possibly through medical devices if traveling for medical tourism. The incubation period is 60 to 150 days, usually 90 days. Signs and symptoms are nonspecific but can include anorexia, malaise, nausea, abdominal pain, skin rash, and arthritis. Serologic testing is necessary to diagnose hepatitis B at any stage of infection. Approximately 2 to 3% of the world’s population is infected with hepatitis C, and risk for acquisition for travelers is generally low. It is transmitted by exposure to blood or blood-contaminated materials. Most cases of hepatitis C infection are initially asymptomatic, but nonspecific symptoms of anorexia, malaise, nausea, and jaundice may occur. Diagnosis is through serology. Hepatitis E is primarily transmitted via the fecal-oral route, and epidemics have largely been waterborne in developing countries. Travelers to such countries are at risk for infection especially with ingestion of contaminated meat and seafood products. The incubation period for hepatitis E is 2 to 9 weeks, and symptoms include fever, jaundice, anorexia, and lethargy. Usually infection is self-limited, although pregnant women and those with chronic liver disease can progress to fulminant liver failure. Diagnosis is through serology.

Leptospirosis
Travelers presenting with fever, headache, myalgia, and rash with exposure to urine or reproductive fluids from animals or water or soil contaminated with such fluids should be evaluated for leptospirosis. Conjunctival suffusion with the above symptoms is considered pathognomonic for leptospirosis but is present in only up to 44% of cases. The growth of ecotourism and adventure sports has increased the number of travelers at risk and periodic outbreaks in travelers of leptospirosis. The incubation period is usually 2 days to 3 weeks. About 5 to 10% of cases present as the severe form, Weil’s disease, with jaundice, renal failure, hemorrhage, pneumonitis, and hemodynamic collapse. Diagnosis is presumptive and confirmed via serology. Doxycycline and penicillin are effective therapies.

HIV
The risk for HIV infection in travelers is generally low and more often determined by risk behavior such as unprotected sexual contact, needle sharing, and either planned or unplanned medical or dental interventions. Any returning traveler who suspects they may have been exposed to HIV warrants testing. Symptoms of acute HIV in either a suspecting or unsuspecting returned traveler may include fever, pharyngitis, rash, and lymphadenopathy. Testing for acute HIV should be performed with RNA PCR testing because antibodies to HIV may not be present in some cases until 8 weeks after infection. Treatment for HIV is complex, and referral should be made to an experienced provider.

Schistosomiasis: Katayama syndrome
Acute schistosomiasis, otherwise named Katayama syndrome, usually presents 14 to 84 days after freshwater exposure via swimming or wading in an endemic area, most often sub-Saharan Africa. Cercariae penetration may occur. Diagnosis is through serology. Hepatitis E is primarily transmitted via the fecal-oral route, and epidemics have largely been waterborne in developing countries. Travelers to such countries are at risk for infection especially with ingestion of contaminated meat and seafood products. The incubation period for hepatitis E is 2 to 9 weeks, and symptoms include fever, jaundice, anorexia, and lethargy. Usually infection is self-limited, although pregnant women and those with chronic liver disease can progress to fulminant liver failure. Diagnosis is through serology.

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subsequently. Acute infection presents with fever, headache, diarrhea, myalgia, eosinophilia, and hepatosplenomegaly. Diagnosis is through stool microscopy or eventually through serology. Treatment is with praziquantel that is best at least 6 weeks after infection because it is most active against adult worms; a repeat course of praziquantel may be needed.

**Amoebic abscess**

*E. histolytica*, the cause of amoebiasis, is acquired via ingestion. Ninety percent of cases are self-limited and asymptomatic. Symptomatic disease occurs with mucosa and submucosa invasion. About 1% of these cases cause liver involvement as the organism makes its way into the portal circulation causing liver abscess(es). Amoebic liver abscesses can be asymptomatic, but most present with fever with or without abdominal pain. Diagnosis of the diarrheal form is through stool antigen assay, whereas positive serology supports liver abscess. Treatment involves metronidazole or tinidazole followed by a luminal agent such as paromomycin.

**Less Common Infections**

**Brucellosis**

Usually *Brucella* is ingested via contaminated dairy products, but it can also be transmitted via inhalation and contact with nonintact skin and mucous membranes. Typically symptoms begin 2 to 4 weeks after exposure and are fever, sweats, and body aches and can be associated with lymphadenopathy and splenomegaly. Diagnosis is usually via serology, although blood or bone marrow culture is the gold standard. Treatment consists of combination therapy with doxycycline, rifampin, gentamicin, or ciprofloxacin.

**Coxiella burnetii (Q fever)**

*C. burnetii* is distributed worldwide, and those infected during travel have usually had direct contact with livestock via farms or visiting rural areas. Over half of cases are asymptomatic or characterized by a mild flu-like illness. More severe cases can present with pneumonia or hepatitis. In people with underlying cardiac abnormalities, infection can progress to chronic disease such as endocarditis. Diagnosis is via serology, and doxycycline is the treatment of choice.

**Visceral Leishmaniasis**

Visceral leishmaniasis is a parasitic infection of the tropics/subtropics and is caused by the species *Leishmania donovani* and *Leishmania chagasi* and transmitted by a sand fly. The incubation period is weeks to months, and symptoms can either have an acute or gradual onset and are typically fever, weight loss, hepatosplenomegaly, and pancytopenia. Serology can be helpful, but diagnosis is usually through detecting parasites or DNA in tissue biopsies.

**Histoplasmosis**

*Histoplasma capsulatum* is transmitted via inhalation of spores in contaminated soil throughout the world. Travelers are rarely infected but are at risk if spelunking, especially in bat infested caves. Usually immunocompetent individuals present with isolated pulmonary disease, but dissemination is possible.

**Anthrax**

Anthrax is most prevalent in agricultural regions in Central and South America, sub-Saharan Africa, Central and Southwestern Asia, and Southern and Eastern Europe because it infects herbivores in these areas. Humans become infected by direct or indirect contact with infected hides or animals. There have been several outbreaks of inhalational, gastrointestinal and cutaneous disease through drum playing either directly or indirectly. Treatment is usually ciprofloxacin, doxycycline, penicillin, and gentamicin.

**Dermatologic Problems**

Skin disorders are fairly common in returned travelers. A GeoSentinal Surveillance Network analysis from 1997 to 2006 found that 18% of patients seen were given a skin-related diagnosis. Most commonly diagnosed were cutaneous larva migrans, insect bites, skin abscesses, and allergic reactions. Notably, for the purposes of evaluating returned travelers, there are significant relationships between dermatologic findings and the demographic and clinical characteristics of the traveler.

**Leishmaniasis**

Cutaneous leishmaniasis is transmitted via the bite of the female phlebotomine sand fly. Most cases of cutaneous leishmaniasis occur in Afghanistan, Algeria, Iran, Iraq, Saudi Arabia, and Syria in the Old World, and Belize, Bolivia, Brazil, Colombia, Costa Rica, Nicaragua, and Peru in the New World. Sand flies bite most often from dusk to dawn and because of their diminutive size may go unnoticed. Typically travelers develop open or closed lesions on their skin weeks to months after travel, usually progressing from papules to
nodules to open “crater-like” lesions. Most lesions heal on their own over time, but concern lies with New World cutaneous leishmaniasis that can progress to mucosal lesions many years after primary infection if untreated and cause significant facial deformity. Diagnosis is via detection of the parasites in histopathology or via DNA of nonhealing ulcers. Several treatment options are available, some under IND through the CDC, so individual treatment is best determined by an infectious disease clinician.

Cutaneous larva migrans

For travelers presenting with a creeping skin eruption who have had skin contact with soil or sand and have traveled to the Caribbean, Africa, Asia, or Central or South America, one should suspect cutaneous larva migrans. The usual sites are the buttocks or feet, but any skin surface can be affected. Treatment is with albendazole.

Myiasis

Myiasis is caused by the invasion into the skin of a larval fly. Those at risk have traveled to tropical or subtropical areas and present with one or more painful subcutaneous nodules. These lesions may house larvae from Cordylobia anthropophaghi (tumbu fly) from Africa or Dermatobia hominis (bot fly) from Latin America. Those afflicted describe a boil-like lesion that has a central draining opening, often with a sensation of movement within the nodule. Treatment is via extraction, achieved by occluding the air hole, thus prompting the larva to come to surface so it can be grasped with forceps.

Tungiasis

Tungiasis can be seen in travelers returning from Latin America, Africa, and India and is an infestation of the female sand flea, Tunga penetrans. Infestation usually occurs around the toenails but can also be seen on the hands and face. The initial area of infestation becomes erythematous, and then a white papule with a central area of darkening develops corresponding to the genital opening. Diagnosis is usually made by examination of the lesion and then microscopic evidence of the flea and eggs. Treatment involves removal of the flea. If extraction does not occur, a secondary bacterial infection can develop.

Respiratory Tract Infections

Several travelers’ surveys and surveillance networks have found respiratory tract infections to be frequently encountered illnesses. Among these are the common cold, influenza (see previous section), and streptococcal pharyngitis. Because of their cosmopolitan presence, they must be considered as well as the geographically related diagnoses.

Legionella

Legionella pneumophila is ubiquitous throughout the world. Travelers older than 50 who are smokers or are immunocompromised are at increased risk for infection. Disease can occur after exposure to aquatic settings that promote the growth of bacteria. Outbreaks in travelers have been associated with cruise ships, whirlpool spas, or touring areas of buildings with cooling towers. Legionellosis usually presents 2 to 14 days after exposure and is most often a severe pneumonia, although some of those affected present with a flu-like illness without pulmonary infiltrates, known as Pontiac fever. Treatment is with a fluoroquinolone or macrolide antibiotic.

Tuberculosis

Tuberculosis also is ubiquitous throughout the world, but there is a wide range in annual incidence, with sub-Saharan Africa and parts of Asia being the highest. Those who plan to visit or work for a prolonged period in areas with increased risk such as homeless shelters, prisons, or hospitals should be tested prior to travel and again 8 to 10 weeks after their return, as should those spending a prolonged time in a highly endemic country without the high-risk exposures listed above. Most cases of tuberculosis affect the lungs, and symptoms include prolonged cough with or without hemoptysis, weight loss, night sweats, and fever. The diagnosis should be suspected in a traveler with appropriate exposure/travel history, abnormal imaging, and symptoms with or without a conversion in their tuberculin skin test or interferon-γ release assay. Diagnosis should be confirmed with isolation of the bacteria from sputum or other affected body tissues. Any traveler with a conversion in their tuberculin skin test or interferon-γ release assay should be evaluated by an infectious disease physician.

Eosinophilia

Eosinophilia in a returned traveler is usually associated with helminthic infections where worms dwell in or have migrated through tissues. In association with fever, one should consider Katayama fever, toxocariasis, and acute trichinosis. Evaluation of the returned traveler with eosinophilia should include stool microscopy, serologic testing for helminthic infections, and potentially, evaluation for filariasis.
**Strongyloides**

*Strongyloides stercoralis* is the most common *Strongyloides* spp. in humans, and filariform larvae penetrate skin when it is exposed to contaminated soil and then migrate to the lungs via the bloodstream, making their way to the trachea and being swallowed to the small intestine. Symptoms can include pruritic skin rashes, abdominal pain, diarrhea, and eosinophilia. Diagnosis is through stool microscopy for ova and parasites. Treatment is with ivermectin.

**Schistosomiasis**

*Schistosoma* are found in contaminated bodies of freshwater, and transmission occurs when cercariae penetrate the skin. Swimming, wading, and bathing in contaminated water may result in infection, which usually presents 14 to 84 days after freshwater contact. Cercariae penetration can be associated with a rash within hours up to a week subsequently. Acute infection may be asymptomatic but may present with fever, headache, diarrhea, myalgia, eosinophilia, and hepatosplenomegaly. Chronic schistosomiasis is the result of immune responses to schistosome eggs secreted by adult worms in organs (usually liver or bladder depending on species) and causing granulomatous, fibrotic reactions. Diagnosis is through stool microscopy or serology; the latter may only become positive several weeks after infection. Treatment is with praziquantel, which works best at least 6 weeks after infection because it is most active against adult worms; a repeat course of praziquantel may be needed.

**Filarial Lymphatic Nematodes**

The filarial nematodes *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* are transmitted via the bite of a mosquito and cause lymphatic filariasis. Most infections are asymptomatic, but symptomatic infection can cause lymphedema and painful swellings. In the United States, *Loa loa* and *Onchocerca volvulus* are more frequently encountered, transmitted via the bites of flies. *Loa loa* may be associated with soft tissue swelling or a worm crawling across the eye (hence the name eye worm). Onchocerciasis may be associated with nodular dermatitis and pruritus and may lead to blindness in endemic populations, but this rarely occurs in travelers. Travelers are at low risk overall. In addition, tropical pulmonary eosinophilia results from the immune response to microfilaria within the pulmonary capillaries. Diagnosis can be made via detection on blood smears or antibodies. Treatment is most often with diethylcarbamazine (DEC), which must be obtained from the CDC under an investigational new drug (IND).

**PRACTICAL TIPS**

- Pretravel health consultation provides advice for prevention of common travel-associated illnesses and self-management of some health problems, including immunizations, malaria chemoprophylaxis, and self-treatment of traveler’s diarrhea.
- Malaria chemoprophylaxis should be optimized based on traveler characteristics, risk at destination, potential drug toxicity, and drug interactions.
- Traveler’s diarrhea occurs frequently, and advice for self-treatment is beneficial; the choice of therapy depends on the severity of symptoms, antimicrobial resistance patterns at the destination, and drug interactions.
- In febrile travelers returning from malaria-endemic areas (or with a past history of travel to malaria-endemic areas), malaria must be considered and treated promptly or ruled out.
- Assessment of a detailed exposure history, incubation period, and geographic distribution of pathogens is essential for the assessment of a travel-related illness.

**RECOMMENDED READINGS**


