Travel-Related Infections

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Over 50 million Americans travel internationally every year. Health problems are reported by 22% to 64% of those who travel to the developing world. Of these travelers, up to 8% seek medical care either during their travel or after returning home \cite{1}. The duration of travel has a significant relationship to the risk of illness. Each day abroad adds a 3% to 4% risk of illness. Persons who take trips of longer than 30 days have up to an 80% risk for health complaints during or after their trip \cite{2}. Among North American travelers, young females demonstrate the highest risk for developing an illness abroad.

Ill travelers are likely to present to emergency departments after their return, and their symptoms may be caused by common or exotic diseases. The failure to consider tropical diseases can lead to misdiagnosis and poor outcomes. This article addresses the important factors to discuss when obtaining a travel history and reviews some of the infectious diseases associated with recent travel, organized around the typical presenting symptoms. The most common symptoms for which patients seek medical care following travel include fever, diarrhea, and skin lesions.

History and risk factors

The evaluation of returning travelers should begin the same as the assessment of any other patient. Returning travelers will frequently present with illness unrelated to their recent travel; however, some unique historical
questions for travelers can help elucidate the likelihood of an exotic infection. It is essential to identify risk factors or medical conditions that have an impact on travel-related illnesses. A thorough travel history should be obtained in all patients with travel-related illness. The travel history should include a broad yet detailed description of various aspects of the patient’s trip. Specifically, the following information should be obtained from the patient:

- Prophylactic measures taken before travel, including routine and travel-related vaccines as well as compliance with medications
- Precise dates of travel and return to home
- All destinations and the duration of stay at each destination, including whether the destinations were in industrialized versus developing countries
- Facilities where they stayed and sleeping accommodations (eg, modern hotel versus tent camping)

Discussing the reason for travel can often be helpful in evaluating a patient’s exposures. Business-related travelers most often stay in modern hotels within urban areas. Adventurous travelers and those visiting family often spend significant amounts of time in more rural areas. These factors can drastically impact the exposure risk of the traveler. In addition, travelers returning to their country of origin to visit friends and relatives have an increased risk of travel-related health problems. Some specific exposures that should be questioned include the following:

- Fresh water contact
- Food intake, especially unpasteurized dairy products and potentially raw meat or fish
- Insect or tick bites or stings
- Animal contacts, including any licks, bites, or scratches
- Ill person contacts
- Barefoot exposure
- Sexual contacts
- Needle exposures
- Special activities such as diving, hiking, camping, boating, or rafting

In addition to the travel history, it is critical to obtain a thorough history of present illness and past medical conditions. If a fever has been present, identifying the pattern of the fever, including its onset and severity, can be helpful. Any associated symptoms, including sweats, rigors, chills, headache, or dermatologic symptoms, should be identified. A past medical history is helpful to identify factors that may predispose a patient to travel illness. The elderly often have multiple conditions that predispose them to infectious diseases. A history of splenectomy, immunocompromised status, or possible pregnancy are other important factors to address in the medical history [3,4].
Tropical infections presenting as undifferentiated fever

Fever is present in approximately 3% of patients after international travel [5]. It is the chief complaint in 28% of those who seek medical care after travel. The most common cause of fever in patients presenting after travel is a nonspecific viral illness, the same as in persons who have not left their home country; however, additional diseases must be considered, including malaria, dengue, typhoid, and hepatitis, among others. Certain travel destinations are associated with a higher risk of acquiring specific diseases. For example, malaria is the most likely cause of fever when a traveler returns from Sub-Saharan Africa or Oceania (Fig. 1). A detailed travel history should include the date of return to the home country and the date of the onset of symptoms. If the illness began after the patient’s return and after the termination of exposure to exotic pathogens, an incubation period for the disease can be identified. This information can be useful in developing a differential list of diseases that would be consistent with the time course (Fig. 2) [5,6].

Malaria

After a viral syndrome, malaria is the most common cause of undifferentiated fever in travelers [7]. Malaria exists throughout the tropics and is especially prevalent in South Asia and Sub-Saharan Africa. The most common continent visited by returning travelers with malaria is Africa [8]. Patients who fail to adequately adhere to their chemoprophylaxis regimen are at significantly higher risk for infection [9,10].

Fig. 1. Regional distribution of travelers returning ill. The percentage of travelers with fever that were diagnosed with various conditions after returning from regions across the globe is shown. Systemic febrile illness and undiagnosed febrile illness have been excluded. (Data from Wilson ME, Weld LH, Boggild A, et al. Fever in returned travelers: results from the GeoSentinel Surveillance Network. Clin Infect Dis 2007;44(12):1560–8.)
Malaria is caused by an intracellular protozoan parasite of the *Plasmodium* genus and is transmitted by the bite of the female *Anopheles* mosquito. The use of DEET-containing repellent, bed nets, and permethrin insecticide has been demonstrated to reduce the rate of *Anopheles* bites and the risk of contracting malaria [11–13]. Four *Plasmodium* species infect humans, but the most significant by far is *Plasmodium falciparum*. Due to its tendency to induce higher parasitemias (the percentage of erythrocytes infected by the parasite) and the adherence of infected cells to the endothelium, *P. falciparum* accounts for the vast majority of malaria deaths.

Patients with malaria will almost always present with a chief complaint of fever, but 20% may not have the sign of fever at the time of their visit to the emergency department, reflecting the intermittent nature of the symptom. The classical cyclical fever is rarely seen. Many other symptoms may accompany malaria, including rigors, night sweats, abdominal pain, diarrhea, and even cough. The complaint of a fever in a returning traveler from a malaria-endemic region should always raise the possibility of malaria, regardless of the associated symptoms. Usual laboratory tests such as a complete blood count, chemistry, and urinalysis are nonspecific in malaria. Elevated billirubin and anemia due the intravascular destruction of erythrocytes are often seen.

Malaria is diagnosed by direct examination of thick and thin blood smears. The thick blood smear is used to identify the presence of any parasites; the thin smear is used to determine the species of the *Plasmodium* infecting the patient. Results of the thin smear are usually described as either “falciparum malaria” or “non-falciparum malaria,” reflecting the importance and severity of *P. falciparum* infection. Because non-falciparum
infections are generally treated the same, there is little need to further speciate the sample. Multiple blood samples drawn throughout a 24-hour period may be needed to adequately rule out malaria. Serology tests for malaria are also available in some centers. These tests are not useful for natives of a malarial region, because they likely were exposed at some point in their life.

The treatment of malaria depends on the type of parasite identified. For non-falciparum species, the treatment of choice remains chloroquine. The initial dose is 600 mg base (1000 mg salt) followed by 300 mg base (500 mg salt) at 6, 24, and 48 hours after the first dose. To eradicate the hypnozoites or liver stage, chloroquine therapy should be followed by primaquine, 30 mg for 2 weeks. Patients with non-falciparum malaria should usually be admitted for treatment, but outpatient therapy can be considered for natives of a malarial region who have some baseline immunity. Because chloroquine has been known to cause a prolonged QT interval, documenting a baseline ECG before beginning therapy would be prudent. Hyperexcitability and tinnitus is expected when taking excessive doses and are an indication to decrease the dose. Is it not an appropriate drug for prolonged (more than 1 to 2 months) malaria prophylaxis because of the risk of retinopathy.

All cases of falciparum malaria must be admitted for therapy owing to the high mortality of the disease. Falciparum malaria is treated with atovaquone-proguanil (Malarone) or quinine sulfate plus doxycycline, tetracycline, or clindamycin. Severe falciparum infection, including cerebral malaria, is treated with intravenous quinidine. Since 1991, quinidine gluconate has been the only parenterally administered antimalarial drug available in the United States. It is recommended to give a loading dose of 6.25 mg base/kg (10 mg salt/kg) of quinidine gluconate infused intravenously over 1 to 2 hours followed by a continuous infusion of 0.0125 mg base/kg/min (0.02 mg salt/kg/min). At least 24 hours of quinidine infusion is recommended. Once the parasite density is less than 1% and the patient can take oral medication, the patient can complete the treatment course with oral quinine at a dosage of 10 mg salt/kg every 8 hours (for a combined treatment course of quinidine/quinine for 7 days if the disease was acquired in Southeast Asia and for 3 days if the patient has returned from Africa and South America) [14,15].

Ideally, travelers will avoid getting malaria by using adequate insect repellents and taking chemoprophylactic medications. There are essentially four choices for anti-malarial prophylaxis: chloroquine, mefloquine (Larium), atovaquone/proguanil, and doxycycline. Chloroquine is taken once per week and may only be used during travel to countries with chloroquine-sensitive areas. These countries include Central America and the Caribbean. Side effects include dizziness, insomnia, pruritis, and an exacerbation of psoriasis. Mefloquine is also taken once per week and is usually effective worldwide (areas of mefloquine-resistant malaria exist, especially in East Africa and South East Asia). Its major limitation is its tendency to cause central nervous system side effects and exacerbate psychiatric illnesses. It is contraindicated in
patients suffering from major depression or a history of psychosis. Doxycycline is taken once per day and may be reliably used throughout the world. It is contraindicated in pregnancy and small children and causes photosensitivity. Atovaquone/proguanil is a relatively new agent for malaria. It is taken once per day, may be used anywhere, and is contraindicated in pregnancy, breastfeeding mothers, infants, and patients with renal impairment (creatinine clearance \(<30\) mL/min) [14].

**Dengue**

Dengue fever, a viral infection from the family Arbovirus, is transmitted by the bite of mosquitoes, most often *Aedes aegypti* and *Aedes albopictus*. The prevalence of this disease is increasing, and it has become one of the world’s most common tropical diseases, especially in South America and Southeast Asia. Many popular tourist destinations, including parts of the developed world such as Hawaii, are endemic. It is now estimated that up to 16% of febrile illness in travelers returning from the tropics may be due to dengue.

The virus features a relatively short incubation period, 2 to 8 days after the initial mosquito bite, which may help distinguish it from other febrile illnesses. Initial symptoms of the disease include fever and headache. In addition, patients complain of chills, photophobia, and severe muscle, joint, and back pain. The musculoskeletal pain that often accompanies the disease has led to its nickname of “breakbone fever.” Other signs of the disease may include a maculopapular or petechial rash, lymph node enlargement, and hemorrhage (usually epistaxis or gastrointestinal bleeding). There are two more serious variants of the disease: dengue hemorrhagic fever and dengue shock syndrome. Although dengue fever is a benign, self-limited disease that calls for supportive care only, fatality rates are much higher for these variants (up to 44% in dengue shock syndrome). Fortunately, these complications are rare in travelers. Diagnosis can be established by viral culture or serologic testing [16,17].

**Rickettsia**

Rickettsia cause several clinical syndromes, including scrub typhus and the various types of spotted fever. They are small obligate intracellular parasites of eukaryote cells that can only be grown in a cell culture. Rickettsial infections are transmitted by the bite of blood sucking arthropods, most often ticks. Activities such as camping, hiking, or traveling through grassy areas increase the risk of exposure. The clinical presentation is variable and depends on the species of organism involved. Typhus, Q fever, trench fever, ehrlichiosis, and at least 14 spotted fever syndromes are all caused by rickettsia organisms. The most common conditions seen in travelers are African tick bite fever and Mediterranean spotted fever [18].
African tick bite fever is usually a mild illness and has not been known to be fatal. Clinical symptoms typically develop 6 to 7 days after the infectious bite. Abrupt onset of fever, myalgia, regional lymphadenitis, and headache in travelers from Africa should prompt suspicion of this disease. Identification of a painless scar, an eschar, at the presumed location of the bite should confirm that suspicion. The lesion is usually black with a red halo and a necrotic center. Due to the aggressive nature of the tick vector, multiple eschars are often documented [18]. Diagnosis is most often made by the clinical history and physical examination. Patients often recover without treatment.

Mediterranean spotted fever is caused by *Rickettsia conorii* and is endemic in urban and suburban areas around the Mediterranean basin, the Middle East, India, and in parts of Sub-Saharan Africa. Because the vector for the disease is the dog tick, there is a close association with domestic dogs. Most patients will demonstrate a single inoculation eschar (in 70% of cases) and a generalized maculopapular rash (in >95% of cases). Complications are relatively common, and if left untreated, the disease carries a 2% mortality rate [18]. Treatment with tetracycline, chloramphenicol, or azithromycin is recommended in all recognized cases [19].

**Leptospirosis**

Leptospirosis is caused by a spirochete and is acquired by humans after contact with contaminated soil or water. Activities associated with infection include swimming or boating in contaminated fresh water as well as gardening or farming. Leptospirosis is most commonly encountered in tropical and subtropical climate regions.

Returning travelers with fever, myalgia, headache, rash, and a history of fresh water exposure should prompt suspicion for leptospirosis. The illness can also be associated with uveitis, conjunctivitis, hematuria, and aseptic meningitis. Most commonly, the diagnosis can be established by serology testing. Unfortunately, this method is often not rapid. Dark-field microscopy and subsequent culture can also aid in diagnosis. The ideal specimen to obtain for identification of the spirochete can vary by the timeline. Blood and cerebrospinal fluid are ideal within the first 10 days of disease. After the first week of illness, urine samples have a better yield. Although many cases of leptospirosis are self-limited, treatment with penicillin or tetracycline is effective and is recommended in all cases. No published studies have established the duration of treatment [20,21]. The clinical course may be complicated by renal failure, acute respiratory distress syndrome, or myocarditis. Liver failure, if present, is usually reversible.

**Typhoid fever**

Typhoid fever is caused by the bacterium *Salmonella typhi* and is transmitted by the fecal-oral route, most typically involving contaminated food
or water. Infection after travel to highly endemic regions accounts for the majority of cases; these areas include India, the Philippines, Pakistan, Mexico, El Salvador, and Haiti. The incubation period ranges from 5 to 21 days.

As opposed to some of the other febrile illnesses discussed previously, typhoid may have a more insidious onset of symptoms. After a 5- to 21-day incubation period, typical symptoms of abdominal discomfort, constipation, fever, pulse-fever dissociation, and severe headache develop. Although the disease is caused by a salmonella infection of the Peyer’s patches in the intestine, diarrhea is not a typical presenting symptom. Physical examination is often unremarkable. Typhoid vaccinations are not always effective, and the fact that a patient has been vaccinated should not rule out the diagnosis. The causative organism can be isolated from a blood culture for diagnosis. Other sites that may yield positive cultures include urine, stool, and duodenal contents. The most sensitive culture for typhoid fever is obtained from the bone marrow. The disease usually responds to treatment with fluoroquinolones for 7 to 14 days. Drug-resistant strains to other antibiotics have been reported [6,11]. If left untreated, typhoid fever can last for 3 weeks or longer and carries a mortality rate of 12% to 30%. Complications include perforation of the intestine at the Peyer’s patches.

Hepatitis A

Hepatitis A is one of the most common vaccine-preventable, travel-related infections. It is caused by a virus spread by fecal-oral contact. Approximately 30% of acute hepatitis A can be attributed to travel to endemic areas. Travel to Latin America, Asia, and Africa is associated with a higher risk of infection. Specifically, poor water quality and poor sanitation are factors that contribute to the spread of hepatitis A. Vaccination is most effective when given at least 4 weeks before travel; however, because the vaccine has been shown to be effective when given in post-exposure situations, it may be protective even if given on the day of travel [22]. Over the past 20 years, hepatitis A infections have decreased significantly. Evidence suggests that children may be particularly susceptible [23]. Up to one half of travel-associated hepatitis A cases occur among children, yet the majority of international travelers are adults. North American travelers who were born and raised in developing countries are likely to have acquired immunity to hepatitis A from their childhood [24,25].

Hepatitis A virus is transmitted via a fecal-oral route, most commonly by contaminated food. Its incubation period is typically 28 to 30 days [6]. Patients typically present with fever, right upper quadrant pain, and jaundice. Additionally, they may complain of anorexia, nausea, vomiting, or malaise. Laboratory tests reveal elevations of aminotransferases, possibly into the thousands, and identification of anti–hepatitis A virus IgM antibody is diagnostic. Treatment is supportive. Most cases are self-limited, but fulminant liver failure is a rare complication.
**Meningococcal meningitis**

Meningococcal disease is potentially a morbid and life-threatening illness. Even with appropriate antibiotic regimens, the overall fatality rate is around 10% and is as high as 40% in cases of meningococcal sepsis [26]. In addition, approximately 15% of survivors have significant long-term complications of the illness, including hearing loss, neurologic damage, or loss of an extremity. Vaccination is available to four of the five clinically important serogroups (A, C, Y, and W-135) and should be given at least 7 to 10 days before travel. Documentation of meningococcal vaccination is required for entry into Saudi Arabia during the Haj pilgrimage [27].

Travel risk is relatively low, except for a few specific destinations. The highest documented risk for travelers is in pilgrims to Mecca and Medina in Saudi Arabia during the Haj. Annual epidemic meningococcal infections occur in the countries of the “meningitis belt,” a swath of Sub-Saharan Africa stretching from Senegal to Ethiopia. Outbreaks typically occur during the dry season, which is December through June.

The incubation period typically ranges between 2 and 10 days. Viral upper respiratory symptoms are accompanied by fever and malaise. Soon after, severe headache, nausea, vomiting, and stiff neck may follow [26,28]. Petechiae or ecchymotic lesions are the most common skin findings in this disease and may occur early in the course before systemic complications develop. Suspected cases should be treated with high-dose parenteral antibiotics such as ceftriaxone and vancomycin. Because steroids are likely to be helpful in pneumococcal meningitis, an initial dose of dexamethasone, 10 mg intravenously, should be given at the initiation of antibiotics. The steroid can be discontinued once meningococcal infection is confirmed, because it is probably not beneficial in meningococcal disease [29]. Once the gram-negative cocci has been identified in the cerebrospinal fluid, alternate therapies such as penicillin or chloramphenicol may be considered. Close contacts of patients should be offered antibiotic prophylaxis with rifampin or ciprofloxacin.

**Tropical diseases presenting as diarrhea**

**Traveler’s diarrhea**

Traveler’s diarrhea is the most common travel-related infection. It can be caused by a number of pathogens but most frequently is associated with enterotoxigenic *Escherichia coli* (ETEC) or *Campylobacter*. Travelers to Central America, Africa, and the Middle East are most frequently infected with ETEC, whereas travelers to Asia most often encounter *Campylobacter*. The risk of infection varies significantly based on destination but increases directly with increased exposure to local food and water [30]. Traveler’s diarrhea is defined as an illness after travel featuring three or more unformed stools in 24 hours and is associated with at least one symptom of enteric
disease, such as cramping, abdominal pain, nausea, vomiting, and fever. Traveler’s diarrhea needs to be distinguished from dysentery, which is defined as the presence of visible blood in the stool. Dysentery may be caused by *Salmonella*, *Shigella*, and many of the same organisms that cause uncomplicated traveler’s diarrhea, such as *Campylobacter*.

Patients who present with acute non-bloody diarrhea may be treated empirically with fluids, antibiotics, and antimotility agents. A single dose of ciprofloxacin, 750 mg, or azithromycin, 1 g by mouth, is effective for curing most cases. Additionally, antimotility agents such as loperamide are safe and effective at reducing the duration of symptoms [31,32]. Stool cultures for identifying causative organisms are not usually indicated because treatment with antibiotics and antimotility agents is so effective.

Although multiple prophylactic regimens are available for the prevention of traveler’s diarrhea, they are not generally recommended for several reasons. First, prompt self-treatment with quinolones and antimotility agents can reduce the duration of illness to 1 day or less. Second, patients taking antibiotics for a long period of time will sustain more morbidity from side effects of the medication than from the traveler’s diarrhea itself. Third, widespread antibiotic use promotes the development of resistant organisms.

Prophylactic therapy can be justified in certain situations, especially in immunocompromised patients who would face significant morbidity from bacterial enteritis. Bismuth subsalicylate (30 mL or two tablets four times a day) has been recommended in the past, but it is a difficult regimen to follow and can lead to salicylate toxicity in young patients. A newer agent, rifaximin, has been demonstrated to be effective in a placebo-controlled trial and caused only minimal change in gut flora [33]. It is probably less likely to promote resistant organisms.

For dysentery, a 3-day course of ciprofloxacin or azithromycin is recommended rather than a single dose. Randomized trials suggest that antimotility agents are safe to use even in the case of dysentery [34]. *Shigella* infections treated with antimotility agents alone are prone to develop complications such as toxic mega colon and prolonged infection; therefore, symptomatic therapy should always be combined with antibiotics when treating cases of dysentery.

**Cholera**

Cholera is a watery diarrheal disease that can be associated with acute dehydration. It is caused by *Vibrio cholerae*, a gram-negative rod. *V cholerae* is most frequently acquired via contaminated water or food. Although cholera can be contracted locally, foreign travel accounts for the majority of cases diagnosed in North America. Although travelers to developing countries are at risk of contracting cholera, it is estimated to occur at a rate of only 0.2 cases per 100,000 North American or European travelers. This risk is likely underestimated because, in the vast majority of instances, cholera is
actually mild and may remain clinically undetected or mistaken for a more routine traveler's diarrhea.

Primary treatment for cholera is oral rehydration. In patients with severe illness, intravenous fluids and electrolyte replacement should be administered. Antibiotics usually shorten the duration of symptoms and decrease *V. cholerae* excretion by half, reducing potential spread of the disease [35]. Antibiotics used in traveler's diarrhea, such as ciprofloxacin, doxycycline, and azithromycin are also effective against *V. cholerae*. Localized areas of antibiotic resistance, especially to doxycycline and ciprofloxacin, are becoming more common. Cholera toxin, not the bacteria itself, mediates the disease process. Antimotility medications are not recommended and should be avoided because they carry a risk of prolonging the disease [36,37].

**Tropical infections with a primarily dermatologic presentation**

*Cutaneous larva migrans*

Cutaneous larva migrans is an epidermal eruption caused by infiltration of hookworm larvae through intact skin, usually in the feet. Infections occur most often in Africa, the Caribbean, and South-East Asia. Detailed questioning reveals a history of exposure of walking barefoot at a beach in over 95% of cases.

The incubation period for cutaneous larva migrans can vary widely, ranging from minutes to weeks. The lesions are typically described as being intensely itchy and growing a few centimeters each day. Cutaneous larva migrans appears as an erythematous tract that is typically described as serpiginous, although it may be linear. Bacterial infection of the initial lesions can subsequently occur. The most commonly affected anatomic sites include the foot, buttock, and abdomen or trunk [38].

Cutaneous larva migrans can be treated effectively with topical thiabendazole 15% for 1 to 2 weeks. Oral thiabendazole twice a day for 2 days can be used but is frequently associated with side effects such as altered mental status, gastrointestinal upset, or rash [39]. Another more recent treatment approach is a single dose of ivermectin. Cryotherapy can be attempted in pregnant patients but is often ineffective [40].

*Cutaneous myiasis*

Cutaneous myiasis, also called furuncular myiasis, is caused by the human botfly or the tumbu fly. It is the implantation and development of fly larvae in human skin. The larvae are transmitted to humans via a mosquito bite or by eggs hatching on the skin with subsequent penetration. The incubation period varies with the type of fly. Incubation with the botfly is usually 5 to 12 weeks and that with the tumbu fly usually 7 to 10 days. Cutaneous myiasis is typically acquired in tropical areas. The botfly is most commonly
encountered in Central and South America, whereas the tumbu fly is more commonly found in Africa.

The lesions are often described as furuncle-like with discharge. The discharge can be crusting, odoriferous, purulent, or serosanguinous. Movements of the larva or bubbles can be visualized within a central punctum. The size of the lesion typically ranges from 1 to 2 cm. Patients often complain of crawling sensations within the lesion and itching. Lesions from tumbu flies are often painful. Anatomic regions typically involved with botfly bites include the head, forearms, and legs. The tumbu fly most often produces lesions on the trunk, buttocks, and thighs.

The diagnosis is clinical, and treatment consists of removal of the larva by several approaches. Manual pressure along the outside of tumbu fly lesions can express the larva. Occlusive substances applied to the lesion can cause the larva to migrate to the skin surface. Surgical excision can be employed but is often not necessary. It is important to not rupture the larva to avoid hypersensitivity or foreign body reactions to the larval antigens [19].

**Leishmaniasis**

Leishmania is transmitted by the bite of the sandfly. Symptoms frequently occur between 1 week and 3 months after the bite. It is caused by a tiny intracellular protozoan parasite of the genus *Leishmania*. Twenty species of organisms have been identified throughout the world, each causing a variety of clinical syndromes. Two major forms are recognized—visceral and cutaneous. Visceral leishmaniasis is rare in travelers, but cutaneous cases are occasionally seen. Over 90% of cutaneous cases occur in one of seven countries: Algeria, Iran, Iraq, Afghanistan, Saudi Arabia, Brazil, and Peru. Military personnel represent a particularly at-risk population. Several hundred cases of cutaneous leishmaniasis have been diagnosed in US soldiers returning from Iraq.

Cutaneous leishmaniasis should be suspected in a patient with a nonpainful, slowly growing ulcer over a period of weeks to months. Patients suffer a mean of 4 to 9 months from symptom onset to diagnosis. The ulcer usually ranges between 3 and 12 cm in diameter. Up to half of patients can present with multiple lesions. The border of the ulcer is violaceous and the base granular. The lesion can progress from an initial papule to a nodule and subsequently ulcerate. The lower legs and face are the typical sites affected. Diagnosis is made by skin scraping. Although some lesions may heal spontaneously, treatment consists of prolonged intravenous therapy with sodium stibogluconate, a pentavalent antimony compound [41,42].

**Lyme disease**

Lyme disease is caused by *Borrelia burgdorferi*, a bacterial spirochete. It is transmitted to humans through a prolonged bite of the *Ixodes* tick.
Lyme disease is prevalent in Europe, Asia, and North America. Skin lesions generally appear 3 to 30 days after the bite. An initial erythema migrans rash is present in 60% to 80% of patients. This lesion appears as an erythematous papule at the site of the bite. It typically expands over the next days to weeks with central clearing to result in the classic annular lesion. Other early manifestations of Lyme disease include malaise, myalgia, arthralgia, and generalized lymphadenopathy. In 60% of untreated patients, the disease progresses to monoarticular or oligoarticular arthritis. A smaller percentage may experience neurologic complaints, such as facial nerve palsy, or cardiac complications, most commonly atrial-ventricular block [43].

Diagnosis can be made clinically if the characteristic rash is identified; otherwise, serology is used. Treatment for early disease consists of 21 days of cefuroxime, doxycycline, or amoxicillin [44]. The key to prevention is preventing the infected tick’s bite by wearing long sleeves and long pants, avoiding walks in heavily forested areas, and wearing insect repellent (preferably containing DEET). For patients who discover an attached tick in an area endemic for Lyme disease, a single 200-mg dose of doxycycline has been shown to be effective at preventing the disease [45].

**Important tropical diseases rarely occurring in travelers**

**Yellow fever**

Yellow fever is a rare disease that can occur in unvaccinated travelers. Transmitted by *Aedes* sp mosquitoes, the virus causing this hemorrhagic fever is a small (40 to 60 nm), single-stranded RNA virus of the family Flaviviridae. The disease is endemic in jungle areas in South America and Africa. From 1970 to 2002, there were nine reported cases from the United States and Europe. Immunization is the most important method of prevention, followed by prevention of mosquito bites. Immunization should ideally occur 4 weeks before travel, but the vaccine may be protective in as few as 10 days. The vaccine, a live attenuated virus, is usually well tolerated. A yellow fever–like systemic disease within 3 to 5 days (yellow fever vaccine-associated viscerotropic disease) and a post-vaccination encephalitis within 8 days (yellow fever vaccine-associated neurotropic disease) have been reported following vaccination. Patients aged more than 60 years are at higher risk for these rare complications.

Clinical presentation of yellow fever can include fever, jaundice, hemorrhage, and renal failure. Viral load is at its peak within 2 to 3 days after infection. The illness typically occurs in three phases:

1. Initial symptoms are fever, malaise, myalgia, nausea, vomiting, irritability, and dizziness. Leukopenia and elevated transaminase levels are seen for 36 to 48 hours.
2. In the latent phase, improvement of symptoms is seen for up to 48 hours with reduced fever. Some patients recover without development of jaundice.

3. In 15% of cases there is a clinical recurrence of initial symptoms with the addition of jaundice and bleeding diathesis followed by multiorgan system failure. If present, this recurrence develops 3 to 6 days after the initial symptoms begin.

Diagnosis can be confirmed by ELISA. Treatment is supportive and should involve intensive care for severe cases [46,47].

**Avian flu**

Millions of cases of influenza A occur every year. Since its emergence in 1997, H5N1 highly virulent avian influenza or “avian flu” has infected less than 500 people, most with an identified close contact with chickens, waterfowl, or other birds. Cases have been identified mostly in poultry farm workers or persons living with birds. Human-to-human contact, thus far, seems rare or impossible. Avian influenza typically presents with a febrile respiratory illness 2 to 5 days after exposure. The temperature of the patient is usually greater than 100.4°F and is often accompanied by leukopenia or lymphopenia. The typical initial influenza symptoms are followed by a subsequent pneumonia and worsening respiratory distress. H5-specific RNA is diagnostic when detected by polymerase chain reaction from pharyngeal or nasal swabs. Pharyngeal swabs are preferred because the virus is present in higher concentrations in the throat and lower respiratory tract [48]. Neuraminidase inhibitors such as zanamivir and oseltamivir should be started in any suspected cases. Ninety-five percent of viral isolates from South East Asia demonstrate an in vitro resistance to amantadine and rimantadine [49]. The mainstay of prevention of annual influenza in the United States, the influenza vaccine, is a subject of extensive investigation for avian flu. Although many vaccines are in clinical trials, thus far only one has been approved by the US Federal Drug Administration for use in humans [50]. It is not currently available for commercial production but will be included in the national stockpile of medications for distribution in a health care emergency.

**African sleeping sickness**

Sleeping sickness, also known as African trypanosomiasis, is caused by Trypanosoma parasites and transmitted by Glossina tsetse flies. This disease is fatal if untreated; death may occur from weeks to years from the time of infection depending on the type of parasite infection. The risk to travelers is low, but there are approximately one or two imported cases each year [51]. The disease is endemic in 36 countries in Sub-Saharan Africa. Prevention of the bite of the tsetse fly is key to avoiding the disease in prevalent areas.
Travelers should wear long sleeves, long pants, and DEET-containing repellent.

Recent travelers to East Africa who present with fever and cutaneous chancres should prompt suspicion of trypanosomiasis. The symptoms of this illness may mimic several other travel-related infections, including malaria and rickettsia infection. Additional symptoms may include lethargy, headache, gastrointestinal symptoms, myalgia, and delirium. The parasites can be identified in the blood or other aspirates to confirm the diagnosis. Lumbar puncture is essential to rule out central nervous system involvement, because it dictates the choice of antiparasitic therapy. In patients without central nervous system involvement, treatment with suramin is indicated. Suramin is a polysulfonated naphthylamine derivative of urea administered as a sodium salt. Due to a risk of anaphylaxis, a 200-mg test dose should be tried before administering the drug by slow infusion. The complete drug protocol, as well as the only US source of the drug, can be obtained through the Centers for Disease Control.

Patients who have positive lumbar punctures should be treated with melarsoprol, a trivalent arsenic compound [52,53]. It is commonly associated with significant toxicity. It causes vomiting, abdominal pain, hepatotoxicity, peripheral neuropathy, paraplegia, cardiac arrhythmias, and albuminuria. Arsenic encephalopathy occurs in as many as 10% of treated patients and is frequently fatal [54]. The 5% to 10% risk of mortality from the therapy is outweighed by the risk of the disease, because the mortality of central nervous system infection with African trypanosomiasis is 100%. As is true for suramin, melarsoprol is only available in the United States through the Centers for Disease Control.

Summary

Infections in travelers are a common problem presenting to the emergency department. A detailed travel history including the places visited, the activities enjoyed, and the living conditions will provide clues for the clinician regarding the risk of unusual tropical infections. Any patient returning from a malaria-endemic region with an undifferentiated fever must be ruled out for *Plasmodium* infection by the use of blood smears. The most common condition in returning travelers by far is traveler’s diarrhea, which can be effectively managed with antibiotics and antimotility agents. A linear pruritic rash in a patient returning from a beach vacation to the Caribbean is most likely a sign of cutaneous larval migrans. Avian flu, yellow fever, and African sleeping sickness are dramatic but fortunately rare diseases in the returning traveler. Many of the infections acquired overseas can be prevented by vaccines, food and water precautions, and insect bite avoidance. The yellow fever vaccine is required for travel to certain regions. The risk of enteric diseases can be lessened by avoiding uncooked foods, thoroughly washing foods in clean water, and eating only peeled fruit.
(“boil it, cook it, peel it, or forget it”). The most severe imported diseases, including malaria, can be prevented by avoiding insect bites by wearing long sleeves and long pants, using permethrin-coated bed nets, and applying DEET-containing repellent.

References


