Fever in the Returning Traveler

Felicia A. Scaggs Huang, MD*, Elizabeth Schlaudecker, MD, MPH

INTRODUCTION

Millions of children travel annually, whether they are refugees, international adoptees, visitors, or vacationers.1–4 In 2015, the International Tourism Organization reported 1.2 billion overseas trips.5,6 Although most young travelers do well, many develop febrile illnesses during or shortly after their journeys.7 In a study of European children, 53% of all pediatric patients with travel-related infections were visiting friends and relatives (VFRs), 43.4% were tourists, and 2.4% were immigrants.8 Most illnesses are self-limited childhood infections that do not require subspecialist consultation. However, 28% of 24,920 ill American travelers sought care at travel clinics after returning home.9 Additionally, young children with fevers can present a diagnostic dilemma because they may not report symptoms and can be at risk for severe disease, such as malaria. As awareness of tropical illnesses rise in parents, such as the increase in multidrug-resistant bacteria worldwide or the emergence of epidemics with Zika virus in South America, families may be more anxious about serious infections as an etiologic factor of fevers.

Approaching fevers in the returning traveler requires an appropriate index of suspicion to diagnose and treat the child in a timely manner. This article offers a framework

Disclosure Statement: The authors do not have any commercial or financial conflicts of interest.

Division of Infectious Diseases, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, USA

* Corresponding author. 240 Albert Sabin Way, MLC 7017, Cincinnati, OH 45229.

E-mail address: Felicia.ScaggsHuang@cchmc.org

KEYWORDS

• Fever • Child • International travel • Tropical infections • Returning traveler

KEY POINTS

• The initial workup of a febrile child without a clear source will be based on the history, physical examination, and potential risk factors but commonly includes laboratory testing.
• Malaria, enteric fever, and dengue fever are some of the most common and serious tropical infections in pediatric travelers.
• Clinicians need to remain up-to-date on potential etiologic factors for febrile illnesses to develop a focused plan best suited to the patient’s clinical picture.
on how to address these issues by discussing diseases based on geography, incubation period, and affected organ systems, as well as risk factors, diagnostic techniques, and resources.

GENERAL APPROACH

A thorough history is an important initial step when evaluating a pediatric traveler with a fever (Table 1). Discussing a detailed travel itinerary develops a timeline of exposures that can be unique to an urban or rural setting (Table 2).

Many children receive vaccinations and/or antimicrobial prophylaxis, but reported adherence does not preclude an illness with a particular pathogen. Up to 75% of travelers do not adhere to the recommended malaria prophylaxis. Many travel vaccines, including typhoid vaccine, provide only partial protection despite proper administration of these immunizations.

A medically complex individual may have sought care outside of the United States due to necessity or medical tourism, which can increase the risk of infection through body fluid exposures. Multidrug-resistant pathogens can also be associated with health care exposure. Up to half of hospitalized children in Zimbabwe are colonized with extended spectrum beta lactamase producing Enterobacteriaceae on admission to the hospital, a problem that is increasingly seen worldwide. Underlying medical conditions, such as asplenia or immunosuppression from chemotherapy, may predispose children to overwhelming infections and sepsis. Refugee children from countries such as Syria are susceptible to vaccine-preventable diseases such as polio due to infrastructure breakdown.

CLINICAL FINDINGS, DIAGNOSIS, AND MANAGEMENT

Fever is a common and anxiety-provoking sign for parents that can be exacerbated by overseas travel. Up to 34% of patients with recent travel history are diagnosed with routine infections. Of the 82,825 cases of infection in travelers from 1996 to 2011 reported to GeoSentinel, a worldwide data collection network on travel-related diseases, 4% of cases were considered to be life-threatening. A study in Swiss children showed that 0.45% of emergency room visits were due to travel-related morbidities with fever and gastrointestinal symptoms being the most common complaints in 63% and 50% of patients, respectively. The temporality of travel to the onset of fever can offer important clues to the etiologic factors of fevers (Table 3). Because the causes and clinical outcomes associated with fevers in pediatric travelers vary from self-limited to deadly, a systems-based approach can lead to prompt diagnosis and treatment that evaluates for the most likely and serious diseases early in the illness course.

Fever

According to GeoSentinel, 91% of patients with an acute, life-threatening illness will present with fever. There are a broad range of potential tropical infections, including malaria, dengue fever, and enteric fever. The incidence of emerging infections such as Zika virus and chikungunya are not yet known. In both adults and children, pneumonia, sepsis, meningococcemia, and urinary tract infections that were acquired at home or overseas should be on the differential diagnosis.

The initial workup of a febrile child without a clear source will be based on the history, physical examination, and risk factors but commonly includes a complete blood count, liver function tests, creatinine, urinalysis, and blood cultures. Malaria smears are also frequently helpful. Other tests to consider include serologies for dengue fever...
Table 1
Patient history for the returning traveler with fever

| History | Implications |
|---------|--------------|
| Travel itinerary | Offers information on potential diseases based on geography and other exposures |
| Diet history (improperly cooked meats, unpasteurized dairy products, seafood, or contaminated water and produce) | Brucellosis, Campylobacter infection, giardiasis, hepatitis A and E, listeriosis, traveler's diarrhea, enteric fever, trichinosis, viral gastroenteritis (ie, norovirus) |
| Sick contacts (both abroad and since returning to the US) | Routine viral or bacterial illnesses, Ebola infection, influenza, meningococcemia, tuberculosis |
| Fresh water exposure | Bacterial soft tissue infection (Aeromonas spp, atypical Mycobacterium), leptospirosis, schistosomiasis |
| Sexual encounters | Acute human immunodeficiency virus (HIV) infection; gonorrhea; hepatitis A, B, or C infection; primary herpesvirus 1 or 2 infection; syphilis; Zika virus infection |
| Insect bites | Fleas: plague, murine typhus, rickettsioses  
Flies: African sleeping sickness, leishmaniasis, sandfly fever  
Reduviid bugs: Chagas disease  
Mosquitoes: Chikungunya virus infection, dengue fever, filariasis, Japanese encephalitis, West Nile virus infection, Zika virus infection  
Ticks: African tick bite fever, babesiosis, Lyme disease, Q fever rickettsioses, tularemia |
| Animal bites | Cat-scratch disease, rat bite fever, rabies, simian herpesvirus B infection |
| Animal exposure (including exposure to urine, stool, or animal products; eg, infected carcasses or wool) | Anthrax, avian influenza, hantavirus infection, Hendra virus infection, infections from ectoparasites or endoparasites, Nipah virus infection, plague, psittacosis, toxoplasmosis |
| Body fluid exposures (tattoos, piercings, or medical procedures) | Acute HIV infection, babesiosis, cytomegalovirus infection, hepatitis B and C, malaria, multidrug-resistant bacteria, trypanosomiasis |
| Medical history (diseases associated with immunosuppression; eg, malignancy, asplenia, or immunodeficiency) | Cytomegalovirus infection, Epstein-Barr virus infection, fungal infection, mycobacterial infections |
| Vaccinations and prophylaxis (note: these interventions do not preclude infection with the pathogen prophylaxed against) | Malaria prophylaxis, travel-appropriate vaccines |

Adapted from Refs.50–52

or other potential etiologic agents, polymerase chain reaction for Zika virus or other pathogens, chest radiographs, and cultures of the urine and stool. Patients with altered mental status may require head imaging and lumbar puncture. The most common and concerning causes of fever in a returning pediatric traveler are highlighted next.
### Table 2

**Tropical causes of fever based on geography**

| Location                  | Infection                                                                 |
|---------------------------|---------------------------------------------------------------------------|
| Caribbean                 | Acute histoplasmosis, chikungunya, cholera, dengue fever, leptospirosis, malaria (Haiti, primarily *Plasmodium falciparum*) |
| Central America           | Acute histoplasmosis, coccidioidomycosis, dengue fever, hepatitis A and B, malaria (primarily *P. vivax*), tuberculosis |
| South America             | Bartonellosis, dengue fever, malaria (primarily *P. vivax*), enteric fever, leptospirosis, yellow fever |
| South Central Asia        | Dengue fever, enteric fever, hepatitis B, Japanese encephalitis, malaria (primarily non-falciparum *Plasmodium* spp), tuberculosis |
| Southeast Asia            | Chikungunya, cholera, dengue fever, hepatitis A, Japanese encephalitis, malaria (primarily non-falciparum *Plasmodium* spp), yellow fever |
| Sub-Saharan Africa        | Acute schistosomiasis, enteric fever, filariasis, malaria (primarily *P. falciparum*), meningococcus, rickettsioses, yellow fever |

*Adapted from* Centers for Disease Control and Prevention. The yellow book: health information for international travel 2018. Philadelphia: Oxford University Press; 2017. p. 704. Available at: [https://wwwnc.cdc.gov/travel/page/yellowbook-home](https://wwwnc.cdc.gov/travel/page/yellowbook-home). Accessed July 25, 2017; with permission.

### Table 3

**Incubation period for common tropical diseases causing**

| Disease                              | Incubation Period          |
|--------------------------------------|---------------------------|
| Incubation of <14 d                  |                           |
| Acute HIV                            | 7–21 d                    |
| Arboviral infections (ie, chikungunya and Zika viruses) | 2–10 d                   |
| Dengue fever                         | 4–8 d                     |
| Enteric fever                        | 7–18 d                    |
| Leptospirosis                        | 7–12 d                    |
| Influenza                            | 1–3 d                     |
| Malaria                              |                           |
| *P. falciparum*                      | 6–30 d                    |
| *P. vivax*                           | 8 d–12 mo                 |
| Rickettsioses                        | 3 d–3 wk                  |
| Incubation of 14 d to 6 wk           |                           |
| Amebic liver abscess                 | Weeks–months              |
| Hepatitis A                          | 28–30 d                   |
| Hepatitis B infection                | 60–150 d                  |
| Rabies                               | Weeks–months              |
| Schistosomiasis                      | 28–60 d                   |
| Tuberculosis                         | Weeks for primary infection |
| Visceral leishmaniasis               | 2–10 mo                   |

*Adapted from* Thwaites GE, Day NP. Approach to fever in the returning traveler. N Engl J Med 2017;376(6):548–60; and Centers for Disease Control and Prevention. The yellow book: health information for international travel 2018. Philadelphia: Oxford University Press; 2017. p. 704. Available at: [https://wwwnc.cdc.gov/travel/page/yellowbook-home](https://wwwnc.cdc.gov/travel/page/yellowbook-home). Accessed July 25, 2017; with permission.
**Malaria**

*Plasmodium falciparum* malaria is one of the most common tropical infections. Approximately 15% to 20% of all imported malaria cases are diagnosed in the pediatric population in industrialized countries each year. Malaria is transmitted via the nocturnal-feeding *Anopheles* genus of mosquito. Children who are VFRs are more likely to become infected with malaria than traditional tourists. Nonimmune children are also susceptible to severe malaria from other malaria strains such as *Plasmodium vivax* and many young patients can present with atypical symptoms such as abdominal pain and vomiting. Older children may present with paroxysmal fever, fatigue, myalgias, headache, abdominal pain, back pain, hepatosplenomegaly, and hemolytic anemia. Additionally, severe malaria is more common in children after the first month of travel due to the incubation period of *P falciparum* (7–90 days), especially in those who visited sub-Saharan Africa. Overall, sub-Saharan Africa is one of the most common geographic regions for acquisition, comprising 71.5% of cases according to a GeoSentinel study of travelers migrating or returning to Canada from 2004 to 2014. Malaria should remain on the differential diagnosis for up to a year in an acutely ill, febrile child after travel to an endemic area where *P vivax* and *P ovale* strains are present. Interestingly, 20% of malaria cases can be acquired during trips as short as 2 weeks with less utilization of pretravel services being a contributing factor.

A minimum of 3 thick and thin blood smears must be performed before malaria can be excluded, preferably collected during febrile episodes. The specificity of blood smears is high but the sensitivity can be low depending on the experience of the individual interpreting the slides. Rapid diagnostic tests that detect specific proteins or lactate dehydrogenase are alternatives for diagnosis at medical centers with limited experience in microbiologic evaluation for malaria. The result should be confirmed, however, through the state public health department. In general, a febrile child without a localizing source or splenomegaly, thrombocytopenia, or indirect hyperbilirubinemia, in addition to exposure to an endemic area, should be presumptively approached as having malaria until an alternative diagnosis can be made.

Treatment of malaria is well-established by the Centers for Disease Control and Prevention (CDC) guidelines. Children with acidosis, hypoglycemia, hyperparasitemia, end-organ dysfunction, and severe anemia meet the criteria for severe malaria and require prompt administration of parenteral medication. There is a growing body of evidence that artesunate may reduce mortality compared with quinidine and is becoming more common as first-line therapy in pediatric patients. Artesunate must be obtained through the CDC Malaria Hotline (1–770–488–7788) because it is not routinely available in the United States. Quinidine may be initiated until the medication arrives. Completion of therapy with an oral regimen for uncomplicated chloroquine-resistant *P falciparum*, such as atovaquone-proguanil, can be offered when the child is able to tolerate the medications and the parasite burden has decreased to less than 1%. Severe disease is less common in *P vivax* and *P ovale* and infection can be treated with chloroquine or hydroxychloroquine in most areas outside of Indonesia and Papua New Guinea.

**Enteric fever (typhoid and paratyphoid)**

Enteric fever accounts for 18% of the 3655 cases with life-threatening tropical diseases reported to GeoSentinel. Most recorded cases were from the Indian subcontinent and in VFRs. Infection with *Salmonella typhi* and *Salmonella paratyphi* are clinically indistinguishable with fever, abdominal pain, nausea, vomiting, myalgias, and arthralgias. Diarrhea is greater than 2.5 times more common in infants than older children or adults, although constipation can also be seen. Patients can exhibit a
typhoid mask with dull features and confusion, as well as a stepladder fever progression with rising temperatures over time in untreated individuals. Relative bradycardia and rose spots are also classic signs. Complications such as gastrointestinal bleeding are more common in young children who have been ill for 2 weeks or more. Transmission is fecal-oral, and humans, especially adults, may be chronic carriers. Diagnosis of enteric fever is confirmed through cultures. The most sensitive sterile site is bone marrow (80%–95%). Blood culture has the highest yield during the first week of illness (70%), and stool cultures are more sensitive as the duration of illness increases. Stool studies should be performed on all fellow travelers, and they must be monitored for signs of illness. Other abnormal laboratory findings include transaminitis and a normal or decreased white blood cell count.

The antimicrobial of choice for treatment varies based on the area in which the infection was acquired because multidrug resistance is increasing. Empiric treatment with ceftriaxone or fluoroquinolones is typically recommended. Strains in Latin America and the Caribbean can be susceptible to ampicillin and trimethoprim-sulfamethoxazole. South and Southeast Asian serovars more frequently require azithromycin or cefixime. Children with multidrug-resistant strains have more complications such as myocarditis and shock than children infected with susceptible strains but case fatality is similar (1.0% vs 1.3%, respectively). Relapse of infection can occur despite appropriate therapy, with the highest mortality in young children (6%).

**Dengue fever**

Dengue remains an important cause of fever in travelers returning from all tropical regions except Africa. The prevalence is rising, even in the United States, with 50 to 100 million global cases reported yearly and 22,000 deaths, primarily in children. Risk factors are dissimilar from those for malaria because transmission occurs in urban areas during the daytime due to the vector *Aedes aegypti*, whereas malaria transmission is more common in rural areas from dusk to dawn with the *Anopheles* species mosquito.

Some patients may be asymptomatic, whereas others have hemorrhagic fever and shock. The illness presents as 3 distinct phases: (1) febrile phase over 3 to 7 days characterized by myalgias, headache, retroorbital pain, and rash; (2) critical phase of 24 to 48 days with plasma leakage; and (3) convalescent phase. A rising hemoglobin and gallbladder wall thickening due to increased vascular permeability suggests the development of severe dengue in children. Repeat infections with a different strain may lead to more severe disease.

Serologies are most commonly used for diagnosis, although some rapid diagnostic tests are available. In cases in which infection is unclear, it may be helpful to repeat serologies 2 weeks after initial testing to monitor for an increase in titers. Other common laboratory findings include leukopenia and thrombocytopenia. Treatment consists of hydration and avoidance of salicylate-containing products to decrease the risk for bleeding. Children who develop severe dengue with hemorrhage and shock may require blood products. No antivirals or vaccines are currently available.

**Other causes of fever**

In recent years, arboviral illnesses transmitted via infected *Aedes aegypti* mosquitoes have caused epidemics of Zika virus and chikungunya in South America. A European study of travelers returning from Brazil in 2013 to 2016 reported that of the 29% of patients with travel-related complaints, 6% had dengue fever, 3% had chikungunya, and 3% had Zika virus infection. The prevalence of yellow fever, which is seen
throughout low-resource settings and shares the same vector, has remained stable.\textsuperscript{35} These infections are difficult to distinguish clinically with fever, retroorbital pain, conjunctivitis, and myalgias. Knowledge on perinatal infection with Zika and the neurodevelopmental sequelae of affected infants is rapidly evolving.\textsuperscript{36} A Canadian study found that 5\% of travelers developed neurologic complications such as Guillain-Barre syndrome with Zika, suggesting there is much to learn with this disease in non-perinatally acquired infections.\textsuperscript{37} At this time, treatment is primarily supportive. Additional tropical diseases associated with fevers are outlined in Table 4.

**Gastrointestinal Symptoms**

Vomiting and diarrhea are common complaints in returning travelers. Up to 40\% of children less than 2 years of age may develop diarrhea, with 15\% requiring medical services.\textsuperscript{38} Fevers, nausea, and vomiting can be seen with norovirus that occurs worldwide and is frequently associated with contaminated food and water on cruise ships.\textsuperscript{39} Rotavirus, however, is one of the most frequent causes of diarrheal illnesses worldwide and is a common cause of infant mortality in low-resource settings.\textsuperscript{5} The hepatitides present with a broad range of disease from mild abdominal pain and vomiting to fulminant liver failure, although serious complications are uncommon in pediatric travelers.\textsuperscript{40}

Community-acquired \textit{Clostridium difficile} is uncommon in children but infection should be considered if the patient received recent antimicrobials.\textsuperscript{41} GeoSentinel data reported that 2\% of patients diagnosed with \textit{Clostridium difficile} after travel were 10 to 19 years of age.\textsuperscript{42} There are many other causes of both febrile and nonfebrile gastrointestinal illness in children (Table 5).

**Respiratory Symptoms**

In the pediatric population, common respiratory infections may be seen on return from international trips including pharyngitis, sinusitis, otitis, and pneumonia from pathogens commonly seen in the United States, such as \textit{Streptococcus pneumoniae} and rhinovirus.\textsuperscript{4,43} Local epidemiology of infections can be helpful in diagnosis and management and is available through the CDC. In some tropical regions, influenza may occur throughout the year and should hence remain on the differential for patients who warrant treatment with oseltamivir.\textsuperscript{44}

\textit{Mycobacterium tuberculosis} is an important etiologic factor of lower respiratory tract disease worldwide and should be considered in children with risk factors or who do not recover with antimicrobials for bacterial pneumonia.\textsuperscript{26} Of note, children younger than 3 years of age are more likely to present with miliary tuberculosis or neurologic involvement than adult patients. There are also many other less common causes of febrile respiratory tract infections (Table 6).

**Urinary Symptoms**

Children who present with dysuria, hematuria, and fevers may require urinalysis and culture to evaluate for urinary tract infection and/or pyelonephritis. Gross hematuria with the passage of clots in an afebrile child with exposure to freshwater in Africa, the Middle East, China, and Southeast Asia should be tested for the helminth parasite from the genus \textit{Schistosoma} via serologies or microscopic identification of eggs in stool.\textsuperscript{45} Praziquantel is the treatment of choice and may improve anemia and nutrition in some children.\textsuperscript{46} Patients who may have early disease or a high parasite burden may require a repeat treatment.\textsuperscript{45} Children who are at risk for sexual abuse and adolescents should undergo testing for sexually transmitted infections such as \textit{Chlamydia trachomatis} and \textit{Neisseria gonorrhoea}.
| Disease                        | Etiologic Pathogen | Geographic Regions                                                                 | Vector or Exposure | Incubation Period | Presentation                                                                 | Diagnosis                                | Management                                                                 |
|-------------------------------|--------------------|-------------------------------------------------------------------------------------|--------------------|-------------------|------------------------------------------------------------------------------|------------------------------------------|----------------------------------------------------------------------------|
| Acute retroviral syndrome      | HIV worldwide, highly prevalent in sub-Saharan Africa | Anal or vaginal sex, perinatal, needle stick, blood transfusion                      | 1–3 wk             | Arthralgia, fever, rash, lymphadenopathy, pharyngitis                         | HIV-1 RNA, p24 antigen, immunoassay for HIV-1 and HIV-2 antibodies (preferred) | Antiretroviral therapy, consider trimethoprim-sulfamethoxazole prophylaxis |
| Anthrax                       | Bacillus anthracis  | Central and South America, sub-Saharan Africa, Central and Southwestern Asia, Eastern Europe | Ingestion or handling of contaminated meat, playing drums from contaminated hides, contaminated heroin in drug users | 1–17 d, Gastrointestinal: 1–7 d, Injection: 1–4 d, Inhalation: 7–60 d | Varies with infection type: black eschar, cough, fever, nausea, meningitis, severe soft tissue infection, shock | Bacterial culture, RT-PCR | Combination antimicrobial therapy |
| Brucellosis                    | Brucella species   | Central and South America, Unpasteurized dairy products, undercooked meat, contaminated meat | 2–4 wk             | Fever, headache, myalgias, abdominal pain, malaise, night sweats, myalgias, night sweats, bone marrow, PCR | Culture of sterile site (blood or bone marrow), PCR | Culture of sterile site (blood or bone marrow), PCR | Combination antimicrobial therapy |
| Carrión’s disease (Oroya fever) | Bartonella bacilliformis, Bartonella rochalimae, and Bartonella bacilliformis | South America, especially Peru | Malaise, abdominal pain, fever headache, malaise, Culture of sterile site (blood or bone marrow, PCR) | 10–210 d | Fever, headache, myalgias, abdominal pain, anemia followed by nodular skin lesions | Bacterial culture, Combination antimicrobial therapy | Antimicrobial therapy (aminoglycosides, tetracyclines, fluoroquinolones) |
| Scraggs Huang & Schlaudecker  |                    |                                      |                    |                   |                                                                              |                                         |                                                                            |
| Condition                        | Pathogen                        | Affected Areas                          | Inciting Agent      | Incubation Period | Symptoms                                      | Diagnostic Tests | Treatment                                      |
|---------------------------------|---------------------------------|----------------------------------------|---------------------|------------------|-----------------------------------------------|------------------|-----------------------------------------------|
| Cat-scratch disease             | *B. henselae*                    | Worldwide                               | Scratches from infected cats or kittens | 1–3 wk           | Fever, lymphadenitis, follicular conjunctivitis, encephalitis | Culture, serologies, PCR | Usually self-limited, antimicrobials (macrolides) |
| Chikungunya                     | Chikungunya virus               | Africa, Asia, Central and South America, Pacific Islands | *Aedes aegypti* and *Aedes albopictus* mosquito | 3–7 d            | Fever, arthritis, headache, conjunctivitis, maculopapular rash, myalgias | Virus-specific IgM, PCR | Supportive care, nonsteroidal antiinflammatory drugs for joint pain |
| Ebola & Marburg virus diseases  | Ebola virus & Marburg virus     | Africa                                  | Body fluids *Rousettus aegyptiacus* (fruit bat), nonhuman primate contact, sex | 2–21 d           | Prodrome of fever, arthralgias, headache, myalgias followed by conjunctivitis, coagulopathy, profuse diarrhea, shock | Antigen detection, RT-PCR, serologies | Experimental immune therapies & antivirals, supportive care |
| Endemic typhus                  | *Rickettsia typhi*               | Worldwide, especially Southeast Asia     | Rodent fleas (eg, *Xenopsylla cheopis*) | 7–14 d           | Fever, headache, malaise, nausea and vomiting, rash | IgM and IgG ELISA, PCR | Antimicrobial therapy (chloramphenicol, doxycycline) |
| Epidemic typhus                 | *R. prowazekii*                  | Central Africa, Asia, Central and South America | *Pediculus humanus* (human body louse) | 7–14 d           | Fever, headache, malaise, nausea and vomiting, rash | IgM and IgG ELISA, PCR | Antimicrobial therapy (doxycycline) |
| Japanese encephalitis           | Japanese encephalitis virus     | Asia, Western Pacific                    | *Culex* species mosquito | 5–15 d           | Febrile illness, aseptic meningitis, acute encephalitis | IgM ELISA | Supportive care |
| Disease | Etiologic Pathogen | Geographic Regions | Vector or Exposure | Incubation Period | Presentation | Diagnosis | Management |
|---------|-------------------|--------------------|-------------------|------------------|-------------|-----------|------------|
| Lassa fever and other arenaviral infections | Argentine hemorrhagic fever, Lassa virus, Lujo virus, LCMV | Africa, Asia, Europe, North America, and South America | Rodent urine and feces | 2–21 d | Fever, myalgia, arthralgia, headache, meningeal signs, retrosternal pain, coagulopathy, birth defects (Lassa and LCMV) | Cell culture, IgM ELISA, RT-PCR | Antimicrobial therapy (ribavirin for Lassa fever), supportive care |
| Leptospirosis | *Leptospira* species | Caribbean, sub-Saharan Africa, South America, Southeast Asia | Infected animal body fluid or urine, contaminated water, food, or soil | 2–30 d | Fever, conjunctival suffusion, back pain, rash, diarrhea, vomiting, renal and liver failure | IgM and IgG ELISA, PCR | Antimicrobial therapy (penicillins, doxycycline) |
| Lyme disease | *Borrelia burgdorferi* | Europe, Northern to Central Asia | *Ixodes* ticks | 3–30 d | Fever, cranial nerve palsy, erythema migrans, headache, malaise, myalgia, myocarditis, meningitis | 2-tiered serologic testing (ELISA or IFA & Western blot) | Antimicrobial therapy (beta-lactams, doxycycline) |
| Murray Valley encephalitis | Murray Valley encephalitis virus | New Guinea, Northwestern or southeastern Australia | *Culex* mosquito | 7–28 d | Fever, meningeal signs, seizures | IgM ELISA, neutralizing antibodies, RT-PCR | Supportive care |
| Plague | *Yersinia pestis* | Central and Southern Africa, Central Asia, Northeastern South America | *X cheopis* flea | 1–6 d | Varies with infection type; fever, lymphadenitis, overwhelming pneumonia, sepsis with gangrene | Culture, serologies | Antimicrobial therapy (aminoglycoside, fluoroquinolone, tetracyclines) |
| Disease                  | Pathogen                             | Region(s)                          | Mode of infection                                      | Incubation period | Clinical presentation                                                                 | Diagnostic methods | Treatment                                                                                     |
|-------------------------|--------------------------------------|------------------------------------|---------------------------------------------------------|-------------------|----------------------------------------------------------------------------------------|-------------------|-----------------------------------------------------------------------------------------------|
| Poliomyelitis            | Enterovirus types 1, 2, 3            | Sub-Saharan Africa, Middle East, South and Southeast Asia | Fecal-oral                                              | 7–21 d            | Flaccid paralysis, respiratory failure                                                  | Cell culture, NAAT, PCR | Supportive care                                                                               |
| Q fever                 | *Coxiella burnetii*                   | Africa, Middle East, Europe        | Aerosolized birth fluids or feces from infected livestock | 2–3 wk           | Self-limiting respiratory illness, pneumonia, hepatitis, cardiac disease                | Serial IgG IFA, PCR | Antimicrobial therapy (doxycycline, trimethoprim-sulfamethoxazole, fluoroquinolones)         |
| Rabies                  | Rabies virus                         | Africa, Asia, Central and South America | Saliva from infected animal bite (especially bats)       | Weeks–months      | Prodrome of fever, pain, paresthesias followed by hydrophobia, delirium, seizures, death | Neutralizing antibodies, RT-PCR, IFA | Supportive care, experimental Milwaukee protocol                                             |
| Rat lungworm            | *Angiostrongylus cantonensis*        | Caribbean, Asia, Pacific islands   | Ingestion of infected snails & slugs or contaminated produce | 1–3 wk           | Fever, meningeal signs, paresthesias                                                   | Serum antibodies, PCR | Supportive care                                                                               |
| Relapsing fever         | *Borrelia recurrentis*               | Sub-Saharan Africa                 | *Pediculus humanus* (human body louse)                  | 4–14 d           | Fever, headache, myalgia, arthralgia, rash                                             | Microscopic evaluation of blood smear, IgM and IgG ELISA, PCR | Antimicrobial therapy (doxycycline)                                                           |
| Rickettsioses           | Genera *Rickettsia*, *Orientia*, *Ehrlichia*, *Neorickettsia*, *Neoehrlichia*, *Anaplasma* | Africa, Europe, India, and Middle East | Ectoparasites (fleas, lice, mites and ticks)             | 7–14 d           | Fever, headache, eschar (*R conorii*) at bite site, malaise, nausea and vomiting, rash maculopapular or petechial | Clinical diagnosis, PCR, serologies, biopsy of eschar | Antimicrobial therapy (doxycycline)                                                           |

(continued on next page)
| Disease                                      | Etiologic Pathogen          | Geographic Regions                  | Vector or Exposure                                                                 | Incubation Period | Presentation                                                                 | Diagnosis                       | Management                                      |
|---------------------------------------------|-----------------------------|-------------------------------------|-------------------------------------------------------------------------------------|-------------------|-------------------------------------------------------------------------------|----------------------------------|------------------------------------------------|
| RVF and other bunyaviral infections         | RVF virus, CCHF, hantavirus | Africa, Eurasia, Middle East, North and South America | *Aedes* species mosquito, *Hyalomma* ticks, infected animal carcasses, rodent urine and feces | 2–21 d            | Fever, myalgia, arthralgia, headache, meningeal signs, vision loss (RVF), coagulopathy, renal failure (hantavirus), ecchymoses (CCHF) | Cell culture, IgM ELISA, RT-PCR | Antimicrobial therapy (ribavirin for CCHF), supportive care |
| Rubella                                     | Rubella virus               | Africa, Middle East, South and Southeast Asia | Person-to-person and droplet                                                      | 14 d              | Fever, conjunctivitis, lymphadenopathy, rash; congenital defects               | Serologies, RT-PCR               | Supportive care                                  |
| Scrub typhus                                | *Orientia tsutsugamushi*    | Asia, Pacific regions               | Larval mite (chigger)                                                             | 6–20 d            | Fever, headache, malaise, nausea and vomiting, rash                           | IgM and IgG ELISA, PCR           | Antimicrobial therapy (chloramphenicol, doxycycline) |
| Sleeping sickness                           | *Trypanosoma brucei*       | Sub-Saharan, Central, and Western Africa | *Glossina* species (tsetse) fly                                                    | 7–21 d            | Fever, chancre at bite site, splenomegaly, renal failure, sleep cycle disruption | Microscopic examination of sterile sites or chancre-tissue biopsy | Antimicrobial therapy (suramin for early stage, eflorenlithine & nifurtimox for late stage) |
| Tetanus                                     | *Clostridium tetani*       | Worldwide, most common rurally      | Contaminated wounds with dirt, excrement; punctures                              | 10 d              | Cranial nerve palsies, muscle spasms and rigidity, respiratory failure         | Clinical diagnosis               | Human tetanus immune globulin, tetanus toxoid, supportive care |
| Illness                  | Pathogen          | Geographical Distribution          | Mode of Transmission                                                                 | Prodrome Duration | Symptoms                                                                 | Diagnostic Tests | Management                     |
|-------------------------|-------------------|-----------------------------------|---------------------------------------------------------------------------------------|-------------------|---------------------------------------------------------------------------|------------------|---------------------------------|
| Tick-borne encephalitis | Tick-borne encephalitis virus | Central and Eastern Europe and Northern Asia | *Ixodes* species ticks, ingestion of unpasteurized dairy products                      | 4–28 d            | Prodrome of febrile illness followed by aseptic meningitis, encephalitis, myelitis | IgM ELISA, RT-PCR | Supportive care                  |
| Toxoplasmosis           | *Toxoplasma gondii* | Worldwide                         | Ingestion of undercooked meat or contaminated water, cat feces                         | 5–23 d            | Fever, lymphadenopathy, chorioretinitis, encephalitis or pneumonitis if immunocompromised; congenital syndrome | Serologies, oculorexamination, CT or MRI for intracranial lesions | Supportive care or antimicrobial therapy (pyrimethamine, sulfadiazine, leucovorin) |
| Yellow fever            | Yellow fever virus | Sub-Saharan Africa, South America  | *Aedes* species mosquito                                                                 | 3–6 d             | Fever, headache, back pain, nausea, vomiting, coagulopathy, shock         | RT-PCR, IgM ELISA | Supportive care                  |
| Zika                    | Zika virus        | Africa, Asia, South and Central America | *Aedes* species mosquito, body fluids, sex                                           | 3–12 d            | Fever, arthralgia, conjunctivitis, headache, rash; congenital syndrome    | RT-PCR, serologies | Supportive care                  |

Abbreviations: CCHF, Crimean-Congo hemorrhagic fever; ELISA, enzyme-linked immunoassay; Ig, immunoglobulin; IFA, immunofluorescence assay; LCMV, lymphocytic choriomeningitis; NAAT, nucleic acid amplification test; PCR, polymerase chain reaction; RT-PCR, real-time polymerase chain reaction; RVF, Rift Valley fever.

*Adapted from* Centers for Disease Control and Prevention. *The yellow book: health information for international travel 2018*. Philadelphia: Oxford University Press; 2017. p. 704. Available at: [https://wwwnc.cdc.gov/travel/page/yellowbook-home](https://wwwnc.cdc.gov/travel/page/yellowbook-home). Accessed July 25, 2017; with permission.
| Disease       | Etiologic Pathogen | Geographic Regions          | Vector or Exposure                  | Incubation Period | Presentation                                                                 | Diagnosis                                      | Management                                                                 |
|--------------|--------------------|-----------------------------|------------------------------------|-------------------|-------------------------------------------------------------------------------|-----------------------------------------------|----------------------------------------------------------------------------|
| amebiasis    | *Entamoeba histolytica* | Worldwide                  | Fecal-oral, contaminated food or water | Days–weeks        | Abdominal cramps, watery or bloody diarrhea, weight loss, liver abscess with abdominal pain | Microscopic evaluation of stool, serologies   | Antimicrobial therapy (metronidazole + iodoquinol or puromycin)             |
| Campylobacteriosis | *Campylobacter jejuni, Campylobacter coli* | Worldwide                  | Contaminated foods (raw poultry) and water, unpasteurized milk, fecal-oral | 2–4 d             | Abdominal pain, fever, bloody diarrhea, nausea and vomiting, pseudoappendicitis, reactive arthritis, Guillain-Barre syndrome | Stool culture, darkfield microscopy, NAAT   | Supportive care, antimicrobial therapies (fluoroquinolone, macrolide)       |
| Chagas disease | *T cruzi*            | Central and South America   | Reduviid bug, contaminated food or water, blood transfusion | 7 d               | Chagoma (eg, Romaña sign), ventricular arrhythmias, megacolon, megaesophagus | Microscopic evaluation of blood smear, IgM ELISA, PCR (acute disease only) | Antimicrobial therapy (benznidazole, nifurtimox)                             |
| Cholera      | *Vibrio cholerae*   | Africa, Caribbean, Southeast Asia | Aquatic plants, brackish water, shellfish | 5 d               | Profuse, watery diarrhea, nausea and vomiting, muscle cramps, hypovolemic shock | Stool culture                                  | Supportive care, antimicrobial therapy (azithromycin, doxycycline)           |
| Cyclosporiasis | *Cyclospora cayetenenisis* | Worldwide                  | Contaminated produce and water      | 2–14 d            | Watery diarrhea, anorexia, weight loss, abdominal cramps, myalgias, vomiting | Microscopic evaluation of stool for oocysts    | Antimicrobial therapy (trimethoprim-sulfamethoxazole)                        |
| Disease                  | Cause                          | Region                          | Transmission                              | Incubation Period | Symptoms                                      | Diagnosis                  | Treatment                                |
|-------------------------|-------------------------------|---------------------------------|-------------------------------------------|------------------|------------------------------------------------|---------------------------|------------------------------------------|
| Echinococcosis          | *Echinococcus* species        | Eurasia, Central and South America, Africa | Contaminated dog feces, contaminated food or water | 5–15 y           | Hydatid cysts in liver and lungs, abdominal pain, liver failure | Imaging (ultrasound, computed tomography scan), serologies | Supportive care, surgical excision if cyst >10 cm, antimicrobial therapy (albendazole, praziquantel) |
| Traveler’s diarrhea     | Enterotoxigenic *Escherichia coli* (ETEC) | Worldwide                       | Fecal-oral, contaminated food or water | 9 h–3 d          | Abdominal pain, watery diarrhea                  | Clinical diagnosis, NAAT | Supportive care, antimicrobial therapy (ciprofloxacin, azithromycin) |
| Fascioliasis            | *Fasciola hepatica* and *F. gigantica* | South America, Middle East, Southeast Asia | Watercress or other aquatic plants, freshwater | 6–12 wk         | Intermittent, fever eosinophilia, abdominal pain, weight loss, urticaria, biliary colic, liver failure | Microscopic evaluation of stool, serologies, liver imaging | Antimicrobial therapy (triclabendazole)  |
| Giardiasis              | *Giardia intestinalis*        | Worldwide                       | Fecal-oral, sexual contact, contaminated water | 1–2 wk          | Abdominal pain, anorexia, foul-smelling diarrhea, flatulence, nausea, reactive arthritis | Microscopic evaluation of stool, DFA | Antimicrobial therapy (metronidazole, tinidazole, nitazoxanide) |
| Peptic ulcer disease    | *Helicobacter pylori*         | Worldwide                       | Fecal-oral, oral-oral                     | Unknown         | Epigastric pain, nausea and vomiting, anorexia, gastric cancer | Fecal antigen assay, urea breath test | Antimicrobial therapy (proton pump inhibitor + clarithromycin + amoxicillin) |
| Pinworm                 | *Enterobius vermicularis*    | Worldwide                       | Fecal-oral, contaminated objects         | 1–2 mo           | Perianal pruritus                                | Scotch tape test, microscopic evaluation of fingernails | Antimicrobial therapy (albendazole, pyrantel pamoate) |

*(continued on next page)*
### Table 5 (continued)

| Disease            | Etiologic Pathogen                | Geographic Regions          | Vector or Exposure          | Incubation Period | Presentation                                                                 | Diagnosis                                                                                                      | Management                                                                                               |
|--------------------|----------------------------------|-----------------------------|-----------------------------|-------------------|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Sarcocystosis      | *Sarcocystis* species             | Worldwide, especially Southeast Asia | Undercooked beef or pork    | 2 wk              | Fever, malaise, myalgia, headache, cough, arthralgia, nausea and vomiting, diarrhea, palpitations | Microscopic evaluation of stool, PCR, muscle biopsy                                                             | Antimicrobial therapy (trimethoprim-sulfamethoxazole)                                                  |
| Soil-transmitted helminths | *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (hookworm), *Necator americanus* (hookworm), *Trichuris trichiura* (whipworm) | Worldwide                   | Fecal-oral, skin penetration with contaminated soil (hookworms) | Variable           | Abdominal pain, malnutrition, bowel obstruction, anemia, cough, chest pain | Microscopic evaluation of stool                                                                        | Antimicrobial therapy (albendazole, mebendazole)                                                     |
| Strongyloidiasis   | *Strongyloides stercoralis*       | Worldwide                   | Auto-inoculation, skin penetration | Variable  | Pruritic rash at penetration site, serpiginous rashes (larva currens), respiratory symptoms (Löffler-like pneumonitis), abdominal pain, diarrhea, severe disease if immuno-compromised | Microscopic evaluation of stool other body fluids if disseminated (e.g., sputum, CSF)                        | Antimicrobial therapy (ivermectin, albendazole)                                                                |
| Disease | Pathogen | Geographic Distribution | Symptoms | Diagnostic Methods | Treatment |
|---------|----------|-------------------------|----------|--------------------|-----------|
| Taeniasis | *Taenia solium* (pork) and *T. saginata* or *T. asiatica* (beef) | Central and South America, Africa, South and Southeast Asia | Abdominal discomfort, weight loss, anorexia, perianal pruritus, insomnia, weakness | Microscopic evaluation of stool for eggs | Antimicrobial therapy (praziquantel, niclosamide unless symptomatic neurocysticercosis) |
| Visceral leishmaniasis | *Leishmania donovani* and *L. infantum-chagasi* | South America, Central and Southwest Asia, East Africa | Fever, weight loss, hepatosplenomegaly, pancytopenia | Light-microscopic evaluation of specimens, culture, molecular methods | Antimicrobial therapy (amphotericin B, miltefosine) |
| Yersiniosis | *Yersinia enterocolitica* | Japan, Northern Europe | Fever, abdominal pain (pseudoappendicitis), bloody diarrhea, necrotizing enterocolitis in infants, reactive arthritis, erythema nodosum | Stool culture (or other body sites; eg, CSF, blood) | Supportive care, antimicrobial therapy if severe (trimethoprim-sulfamethoxazole, fluoroquinolones, aminoglycosides) |

**Abbreviations:** CSF, cerebrospinal fluid; DFA, direct fluorescent antibody.

Adapted from Centers for Disease Control and Prevention. The yellow book: health information for international travel 2018. Philadelphia: Oxford University Press; 2017. p. 704. Available at: https://wwwnc.cdc.gov/travel/page/yellowbook-home. Accessed July 25, 2017; with permission.
| Disease                  | Etiologic Pathogen          | Geographic Regions                      | Vector or Exposure                | Incubation Period | Presentation                                                                 | Diagnosis                      | Management                                      |
|--------------------------|-----------------------------|-----------------------------------------|-----------------------------------|-------------------|-------------------------------------------------------------------------------|---------------------------------|-------------------------------------------------|
| Avian bird flu           | H5N1 and H7N9 influenza A virus | East and Southeast Asia                 | Poultry                           | 2–8 d             | Fever, malaise, myalgia, headache, nasal congestion, cough, acute respiratory distress syndrome (ARDS) | RT-PCR                          | Supportive care                                 |
| Diphtheria               | *Corynebacterium diphtheriae* | Asia, South Pacific, Middle East, Eastern Europe, Caribbean | Person-to-person (oral or respiratory droplets), fomites | 2–5 d             | Fever, dysphagia, malaise, anorexia, pseudomembranes                           | Bacterial culture               | Supportive care, equine diphtheria antitoxin (DAT), antimicrobial therapy (erythromycin, penicillin) |
| Coccidioidomycosis       | *Coccidioides immitis* and *Coccidioides posadasii* | Central and South America               | Inhalation of spores from soil    | 7–21 d            | Fever, malaise, cough, headache, night sweats, myalgias, arthritis, rash       | Culture, IgM and IgG ELISA, immunodiffusion and complement fixation | Supportive care, antimicrobial therapy if ill or at high risk of dissemination (amphotericin B, azoles) |
| Histoplasmosis           | *Histoplasma capsulatum*     | Worldwide, especially river valleys     | Inhalation of spores from soil, bird droppings, bat guano | 3–17 d            | Fever, headache, cough, pleuritic chest pain, malaise                         | Culture, microscopic examination, PCR, EIA on serum or other samples, immunodiffusion complement fixation | Supportive care, antimicrobial therapy (azole for mild to moderate disease, amphotericin B for severe) |
| Condition                        | Organism | Region                                    | Mode of transmission                      | Incubation period (days) | Symptoms                                      | Diagnostic testing                             | Antimicrobial therapy |
|--------------------------------|----------|-------------------------------------------|-------------------------------------------|--------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------|
| Legionellosis (Legionnaire’s disease and Pontiac fever) | *Legionella* species | Worldwide | Inhalation of freshwater aerosol | 2–10 | Fever, headache, myalgias, pneumonia, respiratory distress | Urine antigen assay, paired serologies, PCR | Antimicrobial therapy (fluoroquinolones, macrolides) |
| Melioidosis | *Burkholderia pseudomallei* | Central and Southeast Asia, northern Australia, South America | Subcutaneous inoculation, inhalation, ingestion; body fluids | 1–21 | Fever, cough, weight loss, pneumonia | Culture, indirect hemagglutination assay | Antimicrobial therapy (ceftazidime, meropenem) |
| Middle Eastern Respiratory Syndrome (MERS) | MERS coronavirus | North Africa, Middle East | Dromedary camel, person-to-person | 2–14 | Fever, cough, arthralgia, diarrhea, myalgia, acute respiratory failure, multiple organ dysfunction | RT-PCR | Supportive care |
| Pertussis (whooping cough) | *Bordetella pertussis* | Worldwide | Person-to-person (aerosolized respiratory droplets, respiratory secretions) | 7–10 | Paroxysmal cough, post-tussive vomiting, apnea in infants | Culture, serologies, PCR | Antimicrobial therapy (macrolides) |

Adapted from Centers for Disease Control and Prevention. The yellow book: health information for international travel 2018. Philadelphia: Oxford University Press; 2017. p. 704. Available at: [https://wwwnc.cdc.gov/travel/page/yellowbook-home](https://wwwnc.cdc.gov/travel/page/yellowbook-home). Accessed July 25, 2017; with permission
| Disease                          | Etiologic Pathogen | Geographic Regions                                      | Vector or Exposure                                      | Incubation Period | Presentation | Diagnosis                  | Management                                                                 |
|---------------------------------|--------------------|--------------------------------------------------------|----------------------------------------------------------|-------------------|---------------|---------------------------|----------------------------------------------------------------------------|
| B virus                         | Macacine herpesvirus I or B virus | Worldwide                                                | Bites, scratches, body fluids of infected macaque       | 3–30 d            | Fever, headache, myalgias, vesicular lesions near exposure site with neuropathic pain, ascending encephalomyelitis | PCR, virus-specific antibodies | Supportive care, postexposure prophylaxis (valacyclovir), antimicrobial therapy (acyclovir, ganciclovir) |
| Cutaneous leishmaniasis         | Leishmania species | Middle East, Southwest and Central Asia, North Africa, Southern Europe, Central and South America | Phlebotomine sand fly                                     | Weeks–months      | Papules that progress to ulcerated plaques, regional lymphadenopathy, and nodular lymphangitis | Light-microscopy evaluation of specimens, cultures, molecular methods | Antimicrobial therapy (miltefosine, amphotericin B)                          |
| Cutaneous larva migrans         | Ancylostoma species (hookworms) | Caribbean, Africa, Asia, South America                    | Skin contact with contaminated sand                       | 1–5 d             | Serpiginous track on skin with pruritus and edema        | Clinical                     | Supportive care, antimicrobial therapy if desired (albendazole, ivermectin) |
| Loiasis (African eye worm)      | Loa loa            | Central and West Africa                                 | Genus Chrysops (deerflies)                               | 7–12 d            | Localized edema of extremities and joints (Calabar swelling), diffuse pruritus, eye pruritus and pain, and photophobia | Microscopic evaluation of adult worm from eye, microscopic evaluation of microfilariae on blood smear, serologies | Surgical excision of adult worms, antimicrobial therapy (diethylcarbamazine, albendazole) |
| Disease | Organism | Region | Initial Symptoms | Duration | Laboratory Tests | Treatment |
|---------|----------|--------|-----------------|----------|------------------|----------|
| Lymphatic filariasis | *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* | Sub-Saharan Africa, Southern Asia, Pacific Islands, South America, Caribbean | Years | Lymphatic dysfunction with affected limb edema and pain | Microscopic evaluation of peripheral blood smear, serologies | Antimicrobial therapy (diethylcarbamazine, doxycycline) |
| Myiasis | Maggots of *Dermatobia hominis* (human bot fly), *Cochliomyia hominivorax* (screw worm), and others | Central and South America, Africa, Caribbean | Localized skin nodule, pruritus, discharge from punctum | Clinical, serologies | Surgical excision of larvae |
| Rat-bite fever | *Streptobacillus moniliformis* and *Streptobacillus minus* | Worldwide | Relapsing fever, maculopapular or purpuric rash, migratory polyarthritis, lymphadenopathy | Culture, darkfield microscopy, stained peripheral blood smear | Antimicrobial therapy (penicillin G) |
| River blindness (onchocerciasis) | *Onchocerca volvulus* | Sub-Saharan Africa, Middle East, South America | Pruritic, popular rash with subcutaneous nodules, lymphadenitis, ocular lesions, vision loss | Microscopic evaluation of skin shavings with microfilariae, histologic evaluation, serologies | Antimicrobial therapy (ivermectin + doxycycline) |

(continued on next page)
| Disease      | Etiologic Pathogen                  | Geographic Regions | Vector or Exposure                                      | Incubation Period | Presentation                                                                 | Diagnosis                                      | Management                                                        |
|--------------|------------------------------------|--------------------|--------------------------------------------------------|-------------------|------------------------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------------------------|
| Scabies      | *Sarcoptes scabiei* var. *Hominis* | Worldwide          | Prolonged skin-to-skin contact, fomites if crusted scabies | 2–6 wk            | Nocturnal pruritus, papulovesicular rash, crusts and scales if crusted scabies | Microscopic evaluation of skin scraping          | Antimicrobial therapy (permethrin, ivermectin creams)             |
| Strongyloidiasis | *Strongyloides stercoralis* (roundworm) | Worldwide          | Skin penetration with contaminated soil                | Unknown           | Localized, pruritic, erythematous popular rash, pulmonary symptoms (Löffler-like pneumonitis), diarrhea, abdominal pain, eosinophilia, serpiginous urticarial rash (larva currens) | Microscopic evaluation of stool, peripheral blood eosinophilia if disseminated, serologies | Antimicrobial therapy (ivermectin, albendazole)                    |
| Tungiasis    | *Tunga penetrans* (chigoe flea, jigger, sand flea) | Africa, South America | Skin penetration (especially walking barefoot)         | 1–2 d             | Localized pruritus and pain with lesions and ulcerations with central black dot | Clinical                                        | Extraction of flea using sterile needle                         |

*Adapted from Beeching N, Beadsworth M. Fever on return from abroad. In: Acute medicine-A practical guide to the management of medical emergencies. 5th edition. 2017. p. 207–14; and Centers for Disease Control and Prevention. The yellow book: health information for international travel 2018. Philadelphia: Oxford University Press; 2017. p. 704. Available at: https://wwwnc.cdc.gov/travel/page/yellowbook-home. Accessed July 25, 2017; with permission.*
**Dermatologic Symptoms**

Rashes are a source of concern for parents without the context of travel and may be even more worrisome after going abroad. The differential diagnosis includes typical childhood illnesses, such as roseola or staphylococcal cellulitis, in addition to tropical infections. A study of Canadian travelers from 2009 to 2012 found that cutaneous larva migrans (13%) and skin and soft tissue infections (12.2%) were some of the most common infectious dermatologic complaints among tourists.47

In countries where vaccination rates are low, varicella zoster virus or rubella may cause disease, especially in young children who have not completed their immunization series. Measles remains an important risk, with tourists comprising 44% of the 94 cases reported to GeoSentinel from 2000 to 2014, and 13% of patients being younger than 18 years of age, although this may represent underreporting due to the surveillance system’s primarily adult focus.48 Petechiae on the extremities in an ill-appearing child may indicate a serious systemic process such as meningococcal or rickettsial infection. There are many other infections with primarily dermatologic manifestations that may not cause fevers (Table 7).49

**SUMMARY**

As the numbers of children who travel abroad continues to increase, clinicians need to remain up-to-date on potential etiologic factors for febrile illnesses on families’ return home. After ruling out life-threatening disorders that can be acquired locally or internationally, physicians are able to develop a focused diagnosis and management plan best suited to the patient’s clinical picture. There is a growing body of resources to assist clinicians, such as the CDC (www.cdc.gov/travel/) and GeoSentinel (www.istm.org/geosentinel) for data on epidemiology, geography, and other risk factors.

In the future, physicians will need to be prepared to deal with the global epidemic of antimicrobial drug resistance, evolving epidemics and pandemics caused by emerging pathogens, reemerging infections due to vaccine hesitancy or international conflicts, and medical tourism in both healthy and medically complex children.

**REFERENCES**

1. Cavagnaro CS, Brady K, Siegel C. Fever after international travel. Clin Pediatr Emerg Med 2008;9(4):250–7.
2. Bottieau E, Clerinx J, Schrooten W, et al. Etiology and outcome of fever after a stay in the tropics. Arch Intern Med 2006;166(15):1642–8.
3. Ladhani S, Aibara RJ, Riordan FA, et al. Imported malaria in children: a review of clinical studies. Lancet Infect Dis 2007;7(5):349–57.
4. Summer A, Stauffer WM. Evaluation of the sick child following travel to the tropics. Pediatr Ann 2008;37(12):821–6.
5. Tate JE, Burton AH, Boschi-Pinto C, et al. 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. Lancet Infect Dis 2012;12(2):136–41.
6. World Tourism Organization. International tourist arrivals up 4% reach a record 1.2 billion in 2015. 2016. Available at: http://media.unwto.org/press-release/2016-01-18/international-tourist-arrivals-4-reach-record-1-2-billion-2015. Accessed July 25, 2017.
7. Freedman DO, Weld LH, Kozarsky PE, et al. Spectrum of disease and relation to place of exposure among ill returned travelers. N Engl J Med 2006;354(2):119–30.
8. Leuthard D, Berger C, Staubli G, et al. Management of children with travel-related illness evaluated in a pediatric emergency room. Pediatr Infect Dis J 2015;34(12):1279–82.
9. 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.
10. Hill DR, Ericsson CD, Pearson RD, et al. The practice of travel medicine: guidelines by the infectious diseases society of america. Clin Infect Dis 2006;43(12):1499–539.
11. Anwar E, Goldberg E, Fraser A, et al. Vaccines for preventing typhoid fever. Cochrane Database Syst Rev 2014;(1):CD001261.
12. Magwenzi MT, Gudza-Mugabe M, Mujuru HA, et al. Carriage of antibiotic-resistant Enterobacteriaceae in hospitalised children in tertiary hospitals in Harare, Zimbabwe. Antimicrob Resist Infect Control 2017;6:10, eCollection 2017.
13. Cousins S. Syrian crisis: health experts say more can be done. Lancet 2015;385(9972):931–4.
14. Jensenius M, Davis X, von Sonnenburg F, et al. Multicenter GeoSentinel analysis of rickettsial diseases in international travelers, 1996-2008. Emerg Infect Dis 2009;15(11):1791–8.
15. Genton B, D’Acremont V, Rare L, et al. Plasmodium vivax and mixed infections are associated with severe malaria in children: a prospective cohort study from Papua New Guinea. PLoS Med 2008;5(6):e127.
16. Stauffer W, Fischer PR. Diagnosis and treatment of malaria in children. Clin Infect Dis 2003;37(10):1340–8.
17. Griffith KS, Lewis LS, Mali S, et al. Treatment of malaria in the United States: a systematic review. JAMA 2007;297(20):2264–77.
18. Boggild AK, Geduld J, Libman M, et al. Malaria in travellers returning or migrating to canada: surveillance report from CanTravNet surveillance data, 2004-2014. CMAJ Open 2016;4(3):E352–358.
19. Moody A. Rapid diagnostic tests for malaria parasites. Clin Microbiol Rev 2002;15(1):66–78.
20. Taylor SM, Molyneux ME, Simel DL, et al. Does this patient have malaria? JAMA 2010;304(18):2048–56.
21. Dondorp A, Nosten F, Stepniewska K, et al. South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. Lancet 2005;366(9487):717–25.
22. Dondorp AM, Fanello CI, Hendriksen IC, et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. Lancet 2010;376(9753):1647–57.
23. Centers for Disease Control and Prevention. Artesunate is available to treat severe malaria in the United States. 2012. Available at: https://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html. Accessed July 25, 2017.
24. Britto C, Pollard AJ, Voysey M, et al. An appraisal of the clinical features of pediatric enteric fever: Systematic review and meta-analysis of the age-stratified disease occurrence. Clin Infect Dis 2017;64(11):1604–11.
25. Nield LS, Stauffer W, Kamat D. Evaluation and management of illness in a child after international travel. Pediatr Emerg Care 2005;21(3):184–95 [quiz:196–8].
26. Basnyat B, Maskey AP, Zimmerman MD, et al. Enteric (typhoid) fever in travelers. Clin Infect Dis 2005;41(10):1467–72.
27. Frenck RW Jr, Nakhla I, Sultan Y, et al. Azithromycin versus ceftriaxone for the treatment of uncomplicated typhoid fever in children. Clin Infect Dis 2000;31(5):1134–8.

28. Azmatullah A, Qamar FN, Thaver D, et al. Systematic review of the global epidemiology, clinical and laboratory profile of enteric fever. J Glob Health 2015;5(2):020407.

29. Schwartz E, Weld LH, Wilder-Smith A, et al. Seasonality, annual trends, and characteristics of dengue among ill returned travelers, 1997-2006. Emerg Infect Dis 2008;14(7):1081–8.

30. Centers for Disease Control and Prevention. Dengue 2014. Available at: https://www.cdc.gov/dengue/epidemiology/index.html. Accessed July 25, 2017.

31. Wilder-Smith A, Schwartz E. Dengue in travelers. N Engl J Med 2005;353(9):924–32.

32. Gould EA, Solomon T. Pathogenic flaviviruses. Lancet 2008;371(9611):500–9.

33. Gautret P, Mockenhaupt F, Grobusch MP, et al. Arboviral and other illnesses in travellers returning from Brazil, June 2013 to May 2016: implications for the 2016 Olympic and Paralympic Games. Euro Surveill 2016;21(27). https://doi.org/10.2807/1560-7917.ES.2016.21.27.30278.

34. Barnett ED, Wilder-Smith A, Wilson ME. Yellow fever vaccines and international travelers. Expert Rev Vaccines 2008;7(5):579–87.

35. Hagmann SHF. Clinical impact of non-congenital Zika virus infection in infants and children. Curr Infect Dis Rep 2017;19(8):29.

36. Boggild AK, Geduld J, Libman M, et al. Surveillance report of Zika virus among Canadian travellers returning from the Americas. CMAJ 2017;189(9):E334–40.

37. Pitzinger B, Steffen R, Tschopp A. Incidence and clinical features of traveler’s diarrhea in infants and children. Pediatr Infect Dis J 1991;10(10):719–23.

38. Ang JY, Mathur A. Traveler’s diarrhea: updates for pediatricians. Pediatr Ann 2008;37(12):814–20.

39. Rendi-Wagner P, Korinek M, Mikolasek A, et al. Epidemiology of travel-associated and autochthonous hepatitis A in Austrian children, 1998 to 2005. J Trav Med 2007;14(4):248–53.

40. Cheng G, Li Z, Dai X, et al. Analysis of Clostridium difficile associated diarrhea in pediatric patients with antibiotic-associated diarrhea. Zhonghua Er Ke Za Zhi 2015;53(3):220–4.

41. Michal Stevens A, Esposito DH, Stoney RJ, et al. Clostridium difficile infection in returning travellers. J Trav Med 2017;24(3). https://doi.org/10.1093/jtm/taw099.

42. Barbosa F, Barnett ED, Gautret P, et al. Bordetella pertussis infections in travelers: data from the GeoSentinel global network. J Trav Med 2017;24(3). https://doi.org/10.1093/jtm/taw094.

43. Blanton L, Kniss K, Smith S, et al. Update: Influenza activity–united states and worldwide, may 24-september 5, 2015. MMWR Morb Mortal Wkly Rep 2015;64(36):1011–6.

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

45. Stephenson LS, Latham MC, Kurz KM, et al. Single dose metrifonate or praziquantel treatment in Kenyan children. II. Effects on growth in relation to Schistosoma haematobium and hookworm egg counts. Am J Trop Med Hyg 1989;41(4):445–53.

46. Stevens MS, Geduld J, Libman M, et al. Dermatoses among returned Canadian travellers and immigrants: Surveillance report based on CanTravNet data, 2009-2012. CMAJ Open 2015;3(1):E119–26.
47. Sotir MJ, Esposito DH, Barnett ED, et al. Measles in the 21st century, a continuing preventable risk to travelers: data from the GeoSentinel global network. Clin Infect Dis 2016;62(2):210–2.

48. Lederman ER, Weld LH, Elyazar IR, et al. Dermatologic conditions of the ill returned traveler: an analysis from the GeoSentinel surveillance network. Int J Infect Dis 2008;12(6):593–602.

49. Jensen K, Alvarado-Ramy F, Gonzalez-Martinez J, et al. B-virus and free-ranging macaques, Puerto Rico. Emerg Infect Dis 2004;10(3):494–6.

50. Beeching N, Beadsworth M. Fever on return from abroad. In: Acute medicine - A practical guide to the management of medical emergencies. 5th edition. Wiley; 2017. p. 207–14.

51. Thwaites GE, Day NP. Approach to fever in the returning traveler. N Engl J Med 2017;376(6):548–60.

52. Centers for Disease Control and Prevention. The yellow book: health information for international travel 2018. Philadelphia: Oxford University Press; 2017. p. 704. Available at: https://wwwnc.cdc.gov/travel/page/yellowbook-home. Accessed July 25, 2017.