International travelers with infectious diseases determined by pathology results, Centers for Disease Control and Prevention — United States, 1995–2015

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Abstract

**Background**—The failure to consider travel-related diagnoses, the lack of diagnostic capacity for specialized laboratory testing, and the declining number of autopsies may affect the diagnosis and management of travel-related infections. Pre- and post-mortem pathology can help determine causes of illness and death in international travelers.

**Methods**—We conducted a retrospective review of biopsy and autopsy specimens sent to the Infectious Diseases Pathology Branch laboratory (IDPBL) at the Centers for Disease Control and Prevention (CDC) for diagnostic testing from 1995 through 2015. Cases were included if the specimen submitted for diagnosis was from a traveler with prior international travel during the disease incubation period and the cause of illness or death was unknown at the time of specimen submission.

**Declarations**

This project was designated nonresearch by a CDC human subjects advisor. None of the authors reported any conflicts of interest.

**Author contributions**

Kristina M. Angelo: Primary writer, primary contributor to data interpretation.
Kira Barbre: Secondary writer, contributor to data interpretation.
Wun-Ju Shieh: Supplied case study information, provided pathologic explanations for the images and manuscript, technical editing, contributor to data interpretation.
Phyllis E. Kozarsky: Critical manuscript revision and writing, technical editing, contributor to data interpretation.
Dianna M. Blau: Critical manuscript revision and writing, technical editing, contributor to data interpretation.
Mark J. Sotir: Conception and design, critical manuscript revision and writing, contributor to data interpretation.
Sherif R. Zaki: Conception and design, technical editing, contributor to data interpretation.

**Disclaimer**

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the United States Centers for Disease Control and Prevention.
Results—Twenty-one travelers, six (29%) with biopsy specimens and 15 (71%) with autopsy specimens, met the inclusion criteria. Among the 15 travelers who underwent autopsies, the most common diagnoses were protozoal infections (7 travelers; 47%), including five malaria cases, followed by viral infections (6 travelers; 40%).

Conclusions—Biopsy or autopsy specimens can assist in diagnosing infectious diseases in travelers, especially from pathogens not endemic in the U.S. CDC’s IDPBL provides a useful resource for clinicians considering infectious diseases in returned travelers.

Keywords
Pathology; Autopsy; International; Travel; Biopsy

1. Introduction

International travel has expanded over the past 50 years. In 2012, annual worldwide international tourist arrivals exceeded one billion, and arrivals will likely reach 1.8 billion by 2030 [1]. Travel destinations continue to diversify, with emerging economies accounting for approximately 533 million tourist arrivals in 2015 [1]. These trends bring more travelers into contact with infectious pathogens, which can have serious individual and public health consequences and can contribute to infectious disease spread [2].

Travelers often acquire infections while abroad, most commonly a gastrointestinal or systemic febrile illness [3]. However, an etiology to explain the travelers’ symptoms may not always be determined in the clinical setting. Ill travelers may require non-routine laboratory or pathology services, including special serologies or biopsies, to confirm a diagnosis and guide effective treatment and public health interventions. In addition, healthcare providers in non-endemic countries may fail to consider travel-related diagnoses such as malaria, leading to delays in treatment, or death. Healthcare providers should take detailed travel histories and have increased suspicion for travel-related infections, using available diagnostic tests as appropriate. Specialized pathological biopsy and autopsy specimen testing provide useful information about causes of undetermined illness and death in travelers [4] and can expedite appropriate treatment. Published data on the total number of deaths due to infectious diseases acquired while traveling abroad is lacking.

We present clinical vignettes and final infectious diseases diagnoses of 21 international travelers with either biopsy or autopsy specimens sent to the Infectious Diseases Pathology Branch Laboratory (IDPBL) at the Centers for Disease Control and Prevention (CDC) for diagnostic assistance of unexplained illnesses and deaths. The IDPBL applies histological, immunohistochemical, molecular, microbiologic, and ultrastructural methodologies to uncover infectious disease diagnoses on tissue specimens or cultures and is available to domestic and international clinicians, hospital systems, and health departments [5].

2. Methods

We conducted a retrospective review of autopsy and biopsy specimens sent to CDC’s IDPBL for diagnostic testing from 1995 through 2015. Cases were included if the specimen was
from an international traveler, the cause of illness or death was unknown at the time of specimen submission, and travel was during the disease incubation period. Clinicians and pathologists submitted assorted information extracted from the travelers’ medical record. We reviewed all available information and recorded traveler demographics, travel destination, travel purpose, reported exposures or behaviors during travel, presumptive clinical diagnoses, and clinical course details, including outcome.

3. Results

Twenty-one travelers met the inclusion criteria (Table 1). Median age was 38 years (range 2–73), 43% were female, and 15 (71%) were U.S. residents. Twelve (57%) contracted their illness in Sub-Saharan Africa; other exposure regions included Central America (two travelers), South America (two travelers), Asia (one traveler), the Caribbean (one traveler), the Middle East (one traveler), North America (one traveler), and Oceania (one traveler). Six (29%) had biopsy specimens and 15 (71%) had autopsy specimens sent to the IDPBL.

3.1. Travelers with biopsies

Among the six travelers with biopsy specimens, five had cutaneous specimens and one had an open lung biopsy specimen; none died (Table 1).

**Traveler 1 (2008)**—A 58-year-old female had a scalp lesion biopsied after returning to the United States from Belize. Gross examination confirmed myiasis with the botfly *Dermatobia hominis* (Fig. 1A).

**Traveler 2 (2011)**—U.S. immigration officials detained a 62-year-old female with extensive face and upper-extremity skin lesions after returning from an 8-week missionary trip to rural Ghana. Tissue Gram stain on skin biopsy specimens sent to the IDPBL yielded Gram-positive cocci, and immunohistochemistry (IHC) demonstrated group A streptococci among diffuse neutrophilic infiltrates with epithelial necrosis, consistent with impetigo (Fig. 1B and C).

**Traveler 3 (2011)**—A 59-year-old male developed fever, myalgia, arthralgia, non-productive cough, hemoptysis, and dyspnea on exertion after returning from a 1-week trip constructing homes in rural Panama. A chest radiograph and computed tomography scan of the chest revealed pulmonary lesions with mediastinal and hilar lymphadenopathy; he underwent an open lung biopsy. Tissue staining revealed multiple small budding yeasts; in conjunction with IHC and polymerase chain reaction (PCR), the IDPBL confirmed acute *Histoplasma capsulatum* pneumonia (Fig. 1D).

**Traveler 4 (2012)**—A 31-year-old male developed a painful, ulcerated leg lesion and fever while traveling in rural Papua New Guinea. An infectious diseases consultant suspected a Buruli ulcer caused by *Mycobacterium ulcerans*. A biopsy sent to IDPBL revealed a tropical phagedenic ulcer with necrotizing dermatitis, hemorrhage, edema and thrombosis, including a polymicrobial infection with *Fusobacterium nucleatum* and *Treponema vincentii*. The traveler underwent debridement and took cephalexin for 1 week, with lesion improvement.
**Traveler 5 (2014)**—A 39-year-old male sustained an insect bite on his leg that ulcerated a few months after returning from Peru. The lesion was biopsied and IHC revealed intra- and extracellular basophilic structures at the IDPBL, consistent with New World cutaneous leishmaniasis (Fig. 1E and F).

**Traveler 6 (2015)**—A 65-year-old female complained of headache, fevers, chills, myalgias, and an eschar on her left calf, where she recalled a tick bite. She recently returned from a 2-week trip to South Africa. Her physician prescribed doxycycline and submitted skin biopsy specimens to the IDPBL. IHC demonstrated epidermal ulceration with lymphohistiocytic inflammation, and PCR yielded *Rickettsia africae*, the causal agent of African tick bite fever (Fig. 1G and H).

### 3.2. Travelers with autopsies

Among the 15 travelers who underwent autopsies, the most common diagnoses were protozoal (7; 47%) and viral (6; 40%) infections. Ten (67%) traveled to Sub-Saharan Africa during their illness incubation periods.

#### 3.2.1. Protozoal infections: malaria—
Upon histological examination of multiple organs and identification of intraerythrocytic *Plasmodium falciparum* trophozoite and schizont staining patterns by IHC, the IDPBL diagnosed travelers 7–11 with fatal *P. falciparum* malaria.

**Travelers 7 and 8 (1996):** Two male (unknown ages) Romanian cargo ship workers in Sub-Saharan Africa died aboard their ship. They had recent port calls in Gabon, Guinea, and South Africa. Authorities suspected Ebola due to a concurrent outbreak in Gabon [6].

**Traveler 9 (2004):** A 36-year-old male cargo ship worker became ill with fever, chills, headache, myalgia, sore throat, nausea, vomiting, jaundice, and bloody urine. Clinicians suspected Lassa fever due to multiple recent port calls in West Africa (Nigeria, Sierra Leone, and Côte d’Ivoire). The traveler died while aboard; authorities detained the ship and crew offshore until autopsy results became available [6].

**Traveler 10 (2005):** A 43-year-old male complained of fever, cough, myalgia, arthralgia, and “dark urine” after returning from a 2-week missionary trip to the Central African Republic and Côte d’Ivoire. His clinician suspected yellow fever or dengue infection. He did not take malaria chemoprophylaxis. He died upon arrival to the hospital [6].

**Traveler 11 (2011):** A 4-year-old female complained of fever, cough, diarrhea, and vomiting while visiting friends and relatives in Uganda. She did not take malaria chemoprophylaxis. A physician in Uganda treated her for a bacterial infection and tested her for malaria, but she did not receive a confirmed diagnosis or malaria treatment. Her condition worsened and she died shortly after arrival in the United States [7]. (Fig. 2A).
3.2.2. Protozoal infections: other

**Traveler 12 (2009):** A 30-year-old female Sudanese refugee became ill with acute leukemia after arriving in the United States from Kenya. She developed severe cardiac failure 2 months after receiving a bone marrow transplant and died. Cardiac tissue sent to the IDPBL indicated myocarditis with protozoal organisms consistent with *Sarcocystis* spp, confirmed by PCR (Fig. 2B).

**Traveler 13 (2011):** A 2-year-old male became ill with cough, rhinorrhea, and left hemiparesis after returning to the United States from Mexico. Brain imaging suggested neurocysticercosis; he received steroids and albendazole, without improvement. He developed seizures and died. Microscopic examination of brain biopsy specimens sent to the IDPBL revealed granulomatous inflammation with necrosis and amebic organisms highlighted with IHC (Fig. 2C and D). PCR confirmed infection with *Balamuthia mandrillaris*, a free-living ameba causing granulomatous amebic encephalitis.

3.2.3. Viral infections

**Traveler 14 (1999):** A 45-year-old male became ill after returning to the United States from a 10-day trip to Venezuela, where he swam in fresh water and visited the rainforest. He developed fulminant renal and liver failure and disseminated intravascular coagulation, complicated by an intracerebral hemorrhage, and died a few days after admission. Autopsy specimens sent to the IDPBL showed histopathologic changes with massive hepatocellular necrosis, and IHC confirmed the etiologic agent as yellow fever virus.

**Traveler 15 (2004):** A 38-year-old male Liberian-born U.S. resident became ill with fever, chills, sore throat, diarrhea, and back pain while visiting farms in Liberia and Sierra Leone. After returning to the United States, he clinically deteriorated with acute respiratory distress syndrome despite treatment for malaria and typhoid fever. IHC on liver biopsy specimens performed by the IDPBL were positive for Lassa virus. The result was further confirmed by serum antigen detection, virus isolation in cell culture, and virus identification by PCR on blood, liver, and skin specimens [8] (Fig. 2E and F).

**Traveler 16 (2008):** A 33-year-old Zambian male paramedic cared for a 36-year-old woman on a medical evacuation flight from Zambia to South Africa. The woman had a rash, facial swelling, and myalgia and received mechanical ventilation during the flight. The paramedic developed headache, myalgia, and fever six days after the flight and died. Blood, liver, and skin specimens underwent IHC testing, demonstrating scattered hepatocellular necrosis, and PCR revealed a novel Old World arenavirus, Lujo virus. The paramedic’s infection was one of three secondary cases from nosocomial contact with the ill woman [9].

**Traveler 17 (2010):** A 12-year-old female became ill with headache, fever, nausea, vomiting, seizures, and altered mental status after returning to the United States from a 2-week trip to Manila, Philippines. She did not improve with treatment for bacterial meningitis and died. Brain biopsy specimens tested at both the state lab and IDPBL demonstrated meningoencephalitis with neuronal necrosis, neuronophagia, and glial nodules; PCR indicated infection with Japanese encephalitis virus.
Traveler 18 (2011): A 24-year-old male soldier deployed to Afghanistan sustained a dog bite to the right hand. He did not receive rabies post-exposure prophylaxis. He developed severe arm pain and right hand paresthesia while en-route to the United States, followed by progressive meningoencephalitis and death. Nuchal biopsy specimens, saliva, CSF, and autopsy brain samples underwent testing. Microscopic examination of the autopsy brain samples demonstrated Negri bodies, and IHC showed rabies viral antigens (Fig. 2 G–H). PCR confirmed rabies [10].

Traveler 19 (2011): A 73-year-old Haitian female developed right shoulder pain, headaches, and difficulty swallowing while visiting friends and relatives in the United States; she developed encephalitis and died. A nuchal skin biopsy sent to the CDC rabies laboratory demonstrated rabies antigens by direct fluorescent antibody testing, and a saliva specimen tested positive by PCR for rabies virus. Autopsy brain samples submitted to IDPBL showed Negri bodies, and IHC was positive for rabies virus. A dog bit the traveler in Haiti and she did not receive post-exposure prophylaxis [11].

3.2.4. Rickettsial infections

Traveler 20 (1995): A 38-year-old Swiss female nurse caring for ill prison inmates in Burundi developed fever, chills, and myalgias associated with severe thrombocytopenia. She received ciprofloxacin for presumed typhoid fever. Despite treatment, she died. Histopathologic examination of autopsy specimens sent to the IDPBL demonstrated vasculitis in multiple organs, and IHC was positive for typhus group rickettsiae. PCR further identified Rickettsia prowazekii, the causative agent of louse-borne epidemic typhus [12].

Traveler 21 (1999): A 39-year-old female developed a furuncle on her left leg associated with fever, chills, myalgias, headache, and a generalized maculopapular rash while on a missionary trip in Kenya. Prior to her illness, her dog had “tick-borne fever” and improved. Despite receiving malaria treatment, her condition worsened. She developed a left leg eschar, in addition to thrombocytopenia (107,000/mm$^3$), and died. Microscopic examination of autopsy tissues showed vasculitis and microthrombi in multiple organs; IHC was positive for rickettsiae, but did not identify a species [13].

4. Discussion

We describe the pathologic diagnoses of travel-related illnesses using specialized diagnostic capacity from CDC’s IDPBL. These findings illustrate the importance of pathology diagnostics in identifying undiagnosed illness or death from infectious diseases. This is particularly important for the rising numbers of international travelers who may become ill with infections rare or non-endemic in the United States. It is also important for travel medicine clinicians who provide care to returned travelers, to utilize these resources for appropriate diagnosis and treatment.

Obtaining an autopsy from undiagnosed deceased individuals can provide useful information not only about causes of death in travelers, but also on illnesses not recognized clinically prior to death [4,14]. For example, an autopsy was recently instrumental in diagnosing the first measles death in the United States in 12 years [15]. Autopsies may decrease gaps in
surveillance, leading to enhanced infectious disease risk estimates, and result in more rapid
diagnosis and treatment of contacts, as well as public health response. Despite the autopsy’s
value for determining cause of death, autopsy rates in the United States have declined
significantly since the 1960s [4]. Prior to 1970, 40–60% of all hospital deaths in the United
States received autopsies, but in recent years, decreased to approximately 5% [16].
Additionally, infectious diseases accounted for 46% of causes of death determined by
autopsy in 2007, down from 79% in 1972 [14]. This may be due to improvement in
infectious disease treatment, but also the relative decrease in medical autopsies and the
relative increase in autopsies due to external causes (e.g., firearms) [14]. This decline may
also be due to cost constraints, clinicians seeking fewer autopsies, and the removal of the
minimum autopsy rate mandate for hospitals by the Joint Commission on Accreditation for
Healthcare Organizations in 1970 [17]. The declining number of medical autopsies has
additional effects, such as a decrease in forensic autopsy experience for training
pathologists, resulting in a lack of experience to recognize subtle findings, or decreased
medical care quality assurance [17].

Among the 15 deaths, more than half were preventable through recommended pre-travel
vaccination or chemoprophylaxis. Almost all deaths were potentially preventable through
eyear diagnosis and treatment, including the five in travelers infected with *P. falciparum*
malaria. The focus on alternative diagnoses, despite travel to a malaria-endemic area,
resulted in diagnostic and treatment delays. Among the more than 1700 reported malaria
infections among U.S. travelers in 2013, Africa was the most common exposure region, *P.
falciparum* comprised the majority of infections, and there were 10 deaths [18]. Malaria
must be on the differential diagnosis for febrile travelers with recent travel to a malaria-
endemic country, and such travelers should visit a healthcare professional immediately if any
malaria symptoms, such as fever, develop during or after travel.

It is imperative to obtain a travel history on all patients, especially those with a fever [3].
Clinicians should also note possible risky exposures (e.g., animal, water, or insect
exposures) in a travelers’ itinerary. Rash was present in only 26%, and an eschar was present
in 55% of U.S. travelers with spotted fever rickettsioses in one report [19], so reliance on the
clinical examination and laboratories alone may not always result in a diagnosis.

This report provides details on pathology submissions sent the IDPBL for specialized testing
that were shown to be travel-related; however, although only one case each of leishmaniasis
and African tick bite fever are presented, the IDPBL received many traveler’s skin biopsy
specimens from clinicians concerned about these two diseases. The IDPBL identified
*L. major* in 370 of these biopsy specimens (CDC data, unpublished). Due to low
sensitivity and specificity, serologic testing does not play a role in diagnosis; PCR or
specialized tissue diagnostics are necessary. IDPBL also identified *Rickettsia africae* in 16
cutaneous biopsy specimens during the same timeframe; African tick bite fever is the most
common rickettsiosis identified in travelers returning from Africa [19].

One potential limitation is that the clinical data submitted to the IDPBL for each traveler
varied. Although we reviewed all available information and recorded traveler demographics,
travel destination, travel purpose, reported exposures or behaviors during travel, presumptive

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clinical diagnoses, and clinical course details, including outcome, this information may not have been available for all travelers. Efforts are forthcoming to standardize the clinical information sent with submitted specimens. An additional limitation is that clinicians may opt to submit specimens to the IDPBL based upon the lack of availability of diagnostic testing in their institutions or health departments, and the frequency of submission may vary by the type of clinical site (and their specialization) or country.

CDC is committed to promoting pathogen detection through laboratory-based diagnostics, modern point-of-care testing, and facilitation of specimen submission to public health reference laboratories [20]. Access to appropriate diagnostic tests may expedite diagnosis and treatment of travelers with infectious diseases. CDC’s IDPBL has the capability to perform specialized diagnostic testing to help diagnose unexplained deaths among international travelers, and providers are encouraged to use this service (pathology@cdc.gov) when encountering difficult cases.

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References


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Fig. 1. Histopathologic findings of biopsy and autopsy specimens from international travelers submitted to the Centers for Disease Control and Prevention’s Infectious Diseases Pathology Branch laboratory, 1995–2015. A) Traveler 1: Dermatobia hominis myiasis. Microscopic examination demonstrating the cuticle, striated muscles, and spiracles of the larva; H & E staining, original magnification: ×200. B–C) Traveler 2: Group A Streptococcus impetigo. B) Skin biopsy demonstrates epidermal ulceration and neutrophilic infiltrate in dermis; H & E staining, original magnification: ×200. C) Numerous gram-positive cocci in the dermis admixed with neutrophils; Lillie-Twort Gram staining, original magnification: ×400. D) Traveler 3: Acute pulmonary histoplasmosis. Lung biopsy demonstrating necrotizing inflammation with multiple yeast organisms, some with budding feature; Grocott’s
Fig. 2. Histopathologic findings of biopsy and autopsy specimens from international travelers submitted to the Centers for Disease Control and Prevention’s Infectious Diseases Pathology Branch laboratory, 1995–2015. 

A) Traveler 11: *Plasmodium falciparum* malaria. Microscopic examination demonstrates intraerythrocytic parasites with hemozoin in blood vessels of multiple organs; H & E staining, original magnification: ×630.

B) Traveler 12: Sarcocystosis. Autopsy heart tissue demonstrates numerous *Sarcocystis* species with inflammation and myocyte necrosis; H & E staining, original magnification: ×400.

C–D) *Balamuthia mandrillaris* granulomatous amebic encephalitis. C) Autopsy brain tissue demonstrates granulomatous inflammation and vascular necrosis with many amebic organisms around the vessel; H & E staining, original magnification: ×400. D)
Immunostaining of many *Balamuthia mandrillaris* in the brain; immunoalkaline phosphate staining, naphthol fast red substrate with light hematoxylin counterstain, original magnification: ×400. **E-F** Traveler 15: Lassa fever. **E**) Autopsy liver tissue demonstrates multifocal hepatocellular necrosis, H & E staining, original magnification: ×200. **F** Immunostaining of abundant Lassa virus antigens in the liver; immunoalkaline phosphate staining, naphthol fast red substrate with light hematoxylin counterstain, original magnification: ×200. **G–H** Traveler 18: Rabies. **G**) Autopsy brain tissue demonstrates meningoencephalitis with viral inclusions (Negri bodies) in cerebellar Purkinje cells; H & E staining, original magnification: ×400. **H** Immunostaining of rabies virus antigens in the brain; immunoalkaline phosphate staining, naphthol fast red substrate with light hematoxylin counterstain, original magnification: ×200.
Table 1

International travelers with a biopsy or autopsy specimen submitted to the Centers for Disease Control and Prevention’s Infectious Diseases Pathology laboratory, 1995–2015 (n = 21).

<table>
<thead>
<tr>
<th>Traveler</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Country of Residence</th>
<th>Exposure Country</th>
<th>Travel Reason</th>
<th>Specific Reported Exposure/Behaviors</th>
<th>Clinical Information</th>
<th>Initial Diagnosis</th>
<th>Histopathologic Findings</th>
<th>Organism(s)</th>
<th>Final Diagnosis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2008</td>
<td>45</td>
<td>F</td>
<td>United States</td>
<td>Belize</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Scalp lesion</td>
<td>None</td>
<td>Myiasis</td>
<td>Dermatobia hominis</td>
<td>Myiasis</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>2011</td>
<td>62</td>
<td>F</td>
<td>United States</td>
<td>Ghana</td>
<td>Missionary</td>
<td>Quotable exposure to animal bites</td>
<td>Extensive fasciitis</td>
<td>None</td>
<td>Cutaneous infarcts</td>
<td>Diffuse myiasis</td>
<td>Imipenem</td>
<td>Death</td>
</tr>
<tr>
<td>3</td>
<td>2011</td>
<td>59</td>
<td>M</td>
<td>United States</td>
<td>Panama</td>
<td>Short-term missionary</td>
<td>Completed a home in a rural area</td>
<td>Multiple, articular, liver, non-purulent subcutaneous abscess, pleural fluid, pericardial effusion</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>Acute pulmonary bacillary anthrax</td>
</tr>
<tr>
<td>4</td>
<td>2012</td>
<td>31</td>
<td>F</td>
<td>United States</td>
<td>Papua New Guinea</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Extensive face and arm lesions with ulcerations</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>Acute pulmonary bacillary anthrax</td>
</tr>
<tr>
<td>5</td>
<td>2014</td>
<td>39</td>
<td>M</td>
<td>United States</td>
<td>Peru</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Ulcerating lesion of lower leg</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>Acute New World Leishmaniasis</td>
</tr>
<tr>
<td>6</td>
<td>2015</td>
<td>65</td>
<td>F</td>
<td>United States</td>
<td>South Africa</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Headache, fever, chills, chills, nightmares</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>African tick bite fever (spotted fever rickettsiosis)</td>
</tr>
</tbody>
</table>

Travelers with an Autopsy Specimen

<table>
<thead>
<tr>
<th>Traveler</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Country of Residence</th>
<th>Exposure Country</th>
<th>Travel Reason</th>
<th>Specific Reported Exposure/Behaviors</th>
<th>Clinical Information</th>
<th>Initial Diagnosis</th>
<th>Histopathologic Findings</th>
<th>Organism(s)</th>
<th>Final Diagnosis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1996</td>
<td>45</td>
<td>M</td>
<td>Romania</td>
<td>South Africa, Gabon, Guine</td>
<td>Business (Congo shipmate)</td>
<td>Stopo, Liberia, Guinea: contact with Ebola virus</td>
<td>Unknown</td>
<td>Ebola</td>
<td>Multiple organisms with intracytoplasmic paramyxovirus-like virus</td>
<td>Plasmodium falciparum</td>
<td>Malaria</td>
<td>Death</td>
</tr>
<tr>
<td>9</td>
<td>2004</td>
<td>36</td>
<td>M</td>
<td>United States</td>
<td>Nigeria, Sierra Leone, Côte d’Ivoire</td>
<td>Business (flight from Gabon)</td>
<td>Port of entry: France, Sierra Leone, Abidjan, Côte d’Ivoire, Lagos, Nigeria: unknown contacts, malnutrition and drug dependence</td>
<td>Fever, chills, headache, myalgias, shortness of breath, coughing, jaundice, bloody urine</td>
<td>Lassa fever</td>
<td>Multiple organisms with intracytoplasmic paramyxovirus-like virus</td>
<td>Plasmodium falciparum</td>
<td>Malaria</td>
<td>Death</td>
</tr>
<tr>
<td>10</td>
<td>2005</td>
<td>43</td>
<td>M</td>
<td>United States</td>
<td>Central African Republic, Côte d’Ivoire</td>
<td>Missionary</td>
<td>Died in jungle, malnutrition and chronic renal failure</td>
<td>Fever, cough, myalgia, arthralgia, “dark” urine</td>
<td>Yellow fever, Dengue</td>
<td>Multiple organisms with intracytoplasmic paramyxovirus-like virus</td>
<td>Plasmodium falciparum</td>
<td>Malaria</td>
<td>Death</td>
</tr>
<tr>
<td>11</td>
<td>2011</td>
<td>4</td>
<td>F</td>
<td>United States</td>
<td>Uganda</td>
<td>Visiting friends and relatives</td>
<td>Died in jungle, malnutrition and chronic renal failure</td>
<td>Fever, cough, diarrhea, vomiting</td>
<td>Bacterial infection</td>
<td>Multiple organisms with intracytoplasmic paramyxovirus-like virus</td>
<td>Plasmodium falciparum</td>
<td>Malaria</td>
<td>Death</td>
</tr>
<tr>
<td>12</td>
<td>2010</td>
<td>30</td>
<td>F</td>
<td>Sudan</td>
<td>Sudan or Kenya</td>
<td>Business</td>
<td>Unknown</td>
<td>Heart failure</td>
<td>None</td>
<td>Mycobacterium tuberculosis</td>
<td>Plasmodium falciparum</td>
<td>Malaria</td>
<td>Death</td>
</tr>
<tr>
<td>13</td>
<td>2011</td>
<td>2</td>
<td>M</td>
<td>United States</td>
<td>Mexico</td>
<td>Unknown</td>
<td>Smoke a wood stove</td>
<td>Cough, rhinorrhea, left tympanitis</td>
<td>Nontyphoidal</td>
<td>None</td>
<td>Plasmodium falciparum</td>
<td>Yellow fever, dengue</td>
<td>Plasmodium falciparum</td>
</tr>
<tr>
<td>14</td>
<td>1999</td>
<td>45</td>
<td>M</td>
<td>United States</td>
<td>Mauritania</td>
<td>Tourism</td>
<td>Tourists in mountain, worn in pink and green</td>
<td>Rapid and low fever, disseminated intravascular coagulation, intracerebral hemorrhage</td>
<td>None</td>
<td>None</td>
<td>Plasmodium falciparum</td>
<td>Yellow fever, dengue</td>
<td>Plasmodium falciparum</td>
</tr>
<tr>
<td>15</td>
<td>2004</td>
<td>38</td>
<td>M</td>
<td>United States</td>
<td>Liberia or Sierra Leone</td>
<td>Business</td>
<td>Travel in Sierra Leone</td>
<td>Fever, chills, shortness of breath, back pain, acute respiratory distress syndrome</td>
<td>Plasmodium falciparum</td>
<td>Malaria, typhoid fever</td>
<td>Plasmodium falciparum</td>
<td>Malaria, typhoid fever</td>
<td>Death</td>
</tr>
</tbody>
</table>

Travelers with a Biopsy Specimen

<table>
<thead>
<tr>
<th>Traveler</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Country of Residence</th>
<th>Exposure Country</th>
<th>Travel Reason</th>
<th>Specific Reported Exposure/Behaviors</th>
<th>Clinical Information</th>
<th>Initial Diagnosis</th>
<th>Histopathologic Findings</th>
<th>Organism(s)</th>
<th>Final Diagnosis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2008</td>
<td>45</td>
<td>F</td>
<td>United States</td>
<td>Belize</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Scalp lesion</td>
<td>None</td>
<td>Myiasis</td>
<td>Dermatobia hominis</td>
<td>Myiasis</td>
<td>Unknown</td>
</tr>
<tr>
<td>2</td>
<td>2011</td>
<td>62</td>
<td>F</td>
<td>United States</td>
<td>Ghana</td>
<td>Missionary</td>
<td>Quotable exposure to animal bites</td>
<td>Extensive fasciitis</td>
<td>None</td>
<td>Cutaneous infarcts</td>
<td>Diffuse myiasis</td>
<td>Imipenem</td>
<td>Death</td>
</tr>
<tr>
<td>3</td>
<td>2011</td>
<td>59</td>
<td>M</td>
<td>United States</td>
<td>Panama</td>
<td>Short-term missionary</td>
<td>Completed a home in a rural area</td>
<td>Multiple, articular, liver, non-purulent subcutaneous abscess, pleural fluid, pericardial effusion</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>Acute pulmonary bacillary anthrax</td>
</tr>
<tr>
<td>4</td>
<td>2012</td>
<td>31</td>
<td>F</td>
<td>United States</td>
<td>Papua New Guinea</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Extensive face and arm lesions with ulcerations</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>Acute New World Leishmaniasis</td>
</tr>
<tr>
<td>5</td>
<td>2014</td>
<td>39</td>
<td>M</td>
<td>United States</td>
<td>Peru</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Ulcerating lesion of lower leg</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>Acute New World Leishmaniasis</td>
</tr>
<tr>
<td>6</td>
<td>2015</td>
<td>65</td>
<td>F</td>
<td>United States</td>
<td>South Africa</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Headache, fever, chills, chills, nightmares</td>
<td>None</td>
<td>None</td>
<td>Bacillary angioinflammation</td>
<td>Bacillus anthracis</td>
<td>African tick bite fever (spotted fever rickettsiosis)</td>
</tr>
<tr>
<td>Traveler</td>
<td>Year</td>
<td>Age</td>
<td>Sex</td>
<td>Country of Residence</td>
<td>Exposure Country</td>
<td>Travel Reason</td>
<td>Specific Reported Exposures/Behaviors</td>
<td>Clinical Information</td>
<td>Initial Diagnosis</td>
<td>Histopathologic Findings</td>
<td>Organism(s)</td>
<td>Final Diagnosis</td>
<td>Outcome</td>
</tr>
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<tr>
<td>16</td>
<td>2008</td>
<td>33</td>
<td>M</td>
<td>Zambia</td>
<td>Aceh, Indonesia</td>
<td>Business</td>
<td>Mechanically sandwiched by an ill woman on a medical evacuation flight</td>
<td>Headache, myalgia, fever</td>
<td>None</td>
<td>Scattered hepatocellular necrosis</td>
<td>Lujo virus</td>
<td>Old World arenavirus, viral hemorrhagic fever</td>
<td>Death</td>
</tr>
<tr>
<td>17</td>
<td>2010</td>
<td>12</td>
<td>F</td>
<td>Philippines</td>
<td>Philippines</td>
<td>Visiting friends and relatives</td>
<td>Fever, myalgia, nausea, vomiting, headache</td>
<td>Bacterial meningitis</td>
<td>None</td>
<td>Meningoencephalitis with neuronal necrosis, neuronophagia, and glial nodules</td>
<td>Japanese encephalitis virus</td>
<td>Japanese encephalitis</td>
<td>Death</td>
</tr>
<tr>
<td>18</td>
<td>2011</td>
<td>24</td>
<td>M</td>
<td>Afghanistan</td>
<td>Afghanistan</td>
<td>Military</td>
<td>Bitten by a dog on the right hand</td>
<td>Severe pain in right hand, paraesthesia, disorientation, vomiting</td>
<td>None</td>
<td>Meningoencephalitis with viral inclusions in Purkinje cells (Fig. 2G and H)</td>
<td>Japanese encephalitis virus</td>
<td>Japanese encephalitis</td>
<td>Death</td>
</tr>
<tr>
<td>19</td>
<td>2011</td>
<td>75</td>
<td>F</td>
<td>Haiti</td>
<td>Haiti</td>
<td>Visiting friends and relatives</td>
<td>Bitten by a dog</td>
<td>Headache, fever, nausea, vomiting, seizures, altered mental status</td>
<td>None</td>
<td>Meningoencephalitis with viral inclusions in Purkinje cells</td>
<td>Japanese encephalitis virus</td>
<td>Japanese encephalitis</td>
<td>Death</td>
</tr>
<tr>
<td>20</td>
<td>1995</td>
<td>38</td>
<td>F</td>
<td>Switzerland</td>
<td>Burundi</td>
<td>Business</td>
<td>Cared for ill prison inmates with unexplained deaths</td>
<td>High fever, chills, myalgias, severe thrombocytopenia</td>
<td>Viral hemorrhagic fever (fever, petechiae, fever)</td>
<td>Vasculitis in multiple organs</td>
<td>Rickettsia prowazekii</td>
<td>Epidemic (louse-borne) typhus</td>
<td>Death</td>
</tr>
<tr>
<td>21</td>
<td>1999</td>
<td>39</td>
<td>F</td>
<td>United States</td>
<td>Kenya</td>
<td>Missionary</td>
<td>Lived in rural area, bit by an isopod that had &quot;tick-borne fever&quot; prior to her illness</td>
<td>Left leg edema, fever, chills, myalgia, macular rash sparing the palms and soles, abdominal pain, vomiting</td>
<td>Malaria</td>
<td>Vasculitis in multiple organs</td>
<td>Unknown</td>
<td>Spotted Fever Rickettsiosis</td>
<td>Death</td>
</tr>
</tbody>
</table>