Table 11-09 Common causes of fever in the tropics by geographic area

GEOGRAPHIC AREA	COMMON FEVER-CAUSING TROPICAL DISEASES	OTHER INFECTIONS CAUSING OUTBREAKS OR CLUSTERS OF DISEASE AMONG TRAVELERS
CARIBBEAN	Chikungunya Dengue Malaria (on the island of Hispaniola) Zika	Histoplasmosis, acute Leptospirosis
CENTRAL AMERICA	Chikungunya Dengue Malaria (primarily *Plasmodium vivax*) Typhoid or paratyphoid fever Zika	Coccidioidomycosis Histoplasmosis Leishmaniasis Leptospirosis
SOUTH AMERICA	Chikungunya Dengue Malaria (primarily *P. vivax*) Zika	Bartonellosis Histoplasmosis Leptospirosis Yellow fever
SOUTH-CENTRAL ASIA	Dengue Malaria (primarily non–*P. falciparum*) Typhoid or paratyphoid fever	Chikungunya Scrub typhus
SOUTHEAST ASIA	Dengue Malaria (primarily non–*P. falciparum*)	Chikungunya Leptospirosis
SUB-SAHARAN AFRICA	Dengue Malaria (primarily *P. falciparum*) Tickborne rickettsia (main cause of fever in southern Africa) Schistosomiasis, acute (Katayama fever)	Chikungunya Meningococcal meningitis Trypanosomiasis, African Typhoid or paratyphoid fever

travelers. GeoSentinel Surveillance Network data showed that a larger proportion of VFR travelers than tourist travelers presented with serious (requiring hospitalization), potentially preventable travel-related illnesses (see Sec. 9, Ch. 9, Visiting Friends & Relatives: VFR Travel).

CHANGES OVER TIME

Clinicians have access to online resources that provide information about geographic-specific risks, disease activity, and other useful information (e.g., drug-susceptibility patterns for pathogens). Infectious disease outbreaks are dynamic, as demonstrated by the Ebola epidemics in West Africa, spread of chikungunya virus in the Americas beginning in late 2013, nosocomial spread of travel-associated Middle East respiratory syndrome in Korea in 2015, the rapid spread of Zika virus in the Americas in 2015 and 2016, and the global spread of coronavirus disease 2019 (COVID-19). In contrast, because of the wide use of vaccine, hepatitis A infection is now infrequently seen in US travelers.

Infections with typical seasonal transmission in the United States might occur at different times of the year, or throughout the year in the tropics and subtropics. For example, influenza transmission can occur throughout the year in tropical areas, and the peak season in the Southern Hemisphere is late spring/early summer into the fall; clinicians in the Northern Hemisphere should be alert to the possibility of influenza outside the usual wintertime influenza season.

Table 11-10 Clinical findings & fever-associated infectious diseases after tropical travel

CLINICAL FINDING & FEVER	INFECTIOUS DISEASES TO CONSIDER			
	BACTERIAL	VIRAL	PARASITIC	FUNGAL OR OTHER
ABDOMINAL PAIN	Typhoid or paratyphoid fever	None	Liver abscess (amebic or pyogenic)	None
ALTERED MENTAL STATUS OR CENTRAL NERVOUS SYSTEM INVOLVEMENT	Meningococcal meningitis Scrub typhus	Arboviral encephalitides (e.g., JE, WNV) Rabies Tick-borne encephalitis	Angiostrongyliasis Malaria, cerebral Trypanosomiasis, African	None
ARTHRALGIA OR MYALGIA (SOMETIMES PERSISTENT)	None	Chikungunya Dengue Ross River virus Zika	Sarcocystosis, muscular Trichinellosis	None
EOSINOPHILIA	None	None	Angiostrongyliasis Fascioliasis Sarcocystosis Schistosomiasis, acute Trichinellosis Other parasites (rare)	Drug hypersensitivity reaction
FEVER ONSET >6 WEEKS AFTER TRAVEL	Melioidosis Tuberculosis	Acute hepatitis B, hepatitis C, hepatitis E	Liver abscess, amebic Malaria (*Plasmodium ovale*, *P. vivax*) Trypanosomiasis, African	None
FEVER >2 WEEKS (PERSISTENT)	Brucellosis Q fever Tuberculosis Typho id or paratyphoid fever	Cytomegalovirus Epstein-Barr virus HIV, acute	Leishmaniasis, visceral (rare) Malaria Schistosomiasis, acute Toxoplasmosis	None
HEMORRHAGE	Leptospirosis Meningococcemia Rickettsial infections (Spotted fever group)	Viral hemorrhagic fevers (e.g., dengue, Ebola, Lassa, yellow fever)	None	None

JAUNDICE	Leptospirosis	Acute hepatitis A, hepatitis B, hepatitis C, hepatitis E Viral hemorrhagic fevers (including yellow fever)	Malaria, severe	None
MONONUCLEOSIS SYNDROME	None	Cytomegalovirus Epstein-Barr virus HIV, acute	Toxoplasmosis	None
NORMAL OR LOW WHITE BLOOD CELL COUNT	Rickettsial infections Typhoid or paratyphoid fever	Chikungunya Dengue HIV, acute Zika	Malaria	None
RASH	Meningococcemia Rickettsial infections (Spotted fever or Typhus group) Typhoid or paratyphoid fever (rash may be sparse–absent)	Chikungunya Dengue HIV, acute Measles Varicella Zika	None	None
RESPIRATORY SYMPTOMS & PULMONARY INFILTRATES	Legionellosis Leptospirosis Melioidosis Plague, pneumonic Pneumococcus and other common bacterial respiratory pathogens Psittacosis Q fever Tuberculosis	Coronavirus infections (including COVID-19, MERS) Influenza and other common viral respiratory pathogens	Schistosomiasis, acute	Coccidioidomycosis, acute Histoplasmosis, acute

Abbreviations: COVID-19, coronavirus disease 2019; JE, Japanese encephalitis; MERS, Middle East respiratory syndrome; WNV, West Nile virus.

Table 11-11 Febrile syndromes in travelers: potential diseases of public health concern requiring immediate infection containment & control

FEBRILE SYNDROMES (i.e., SYMPTOMS & FEVER)	POTENTIAL DISEASES OF PUBLIC HEALTH SIGNIFICANCE
BRUISING OR UNUSUAL BLEEDING (EASILY, WITHOUT PREVIOUS INJURY)	Viral hemorrhagic fever
COUGH (PERSISTENT)	Pertussis
DECREASED CONSCIOUSNESS	Meningococcal meningitis
DIARRHEA (PERSISTENT, VOLUMINOUS)	Cholera
FLACCID PARALYSIS (RECENT ONSET)	Polio Other enteroviruses
JAUNDICE	Hepatitis A
RAPID RESPIRATORY RATE	Coronavirus disease 2019 (COVID-19) Influenza Middle East respiratory syndrome (MERS) Pneumonic plague
RASH (WITH OR WITHOUT CONJUNCTIVITIS)	Measles Meningococcemia Viral hemorrhagic fevers
VOMITING (PERSISTENT, OTHER THAN AIR OR MOTION SICKNESS)	Norovirus

Travelers can become colonized or infected by bacteria resistant to commonly used antibiotics (see Sec. 11, Ch. 5, Antimicrobial Resistance). Bacteria that produce extended-spectrum β-lactamases and carbapenem-resistant Enterobacterales, including bacteria expressing the metalloprotease NDM-1, have been found in infections acquired during travel, sometimes related to elective or emergency medical care. Travelers to South and Southeast Asia are at high risk of acquiring multidrug-resistant Enterobacterales. Enteric fever (typhoid or paratyphoid fever) has become increasingly resistant to fluoroquinolones, third-generation cephalosporins, and azithromycin, especially in Asia (see Sec. 5, Part 1, Ch. 24, Typhoid & Paratyphoid Fever).

CLINICAL TIPS

For more clinical tips about fever in returning travelers, see Box 11-01.

BOX 11-01 Fever in returning travelers: clinical tips

ANTIMICROBIAL RESISTANT ORGANISMS (see Sec. 11, Ch. 5, Antimicrobial Resistance)

Travelers could be infected or colonized with drug-resistant pathogens, especially travelers who were hospitalized abroad or who took antimicrobial agents to treat travelers' diarrhea.

ARBOVIRAL INFECTIONS (see the chapters in Section 5: Chikungunya, Dengue, Zika)

Dengue is the most common cause of febrile illness among people who seek medical care after travel to Latin America or Asia.

Other arboviral infections are emerging as causes of fever in travelers, including chikungunya and Zika viruses.

COMMON INFECTIONS

Do not overlook common infections (e.g., diarrhea, pneumonia, pyelonephritis) in the search for exotic diagnoses.

FEVER & BLEEDING (see Sec. 5, Part 1, Ch. 10, Leptospirosis; Sec. 5, Part 1, Ch. 13, Meningococcal Disease; Sec. 5, Part 1, Ch. 18, Rickettsial Diseases; and Sec. 5, Part 2, Ch. 25, Viral Hemorrhagic Fevers)

Viral hemorrhagic fevers other than dengue (e.g., Ebola, Lassa fever, Marburg hemorrhagic fever) are important to identify but rare in travelers.

Because of the need to institute prompt, specific treatment, always consider the possibility of bacterial infections (e.g., leptospirosis, meningococcemia, rickettsial infections) that can also cause fever and hemorrhage.

INFECTION CONTROL & PUBLIC HEALTH

Keep in mind infection control, public health implications, and requirements for reportable diseases.

MALARIA (see Sec. 5, Part 3, Ch.16, Malaria)

Malaria is the most common cause of acute undifferentiated fever after travel to sub-Saharan Africa and some other tropical areas.

Malaria can progress rapidly (especially *Plasmodium falciparum*); evaluate promptly and initiate treatment immediately, if diagnosed.

A history of taking malaria chemoprophylaxis does not exclude the possibility of malaria.

Patients with malaria can be afebrile at the time of evaluation, but typically give a history of fever or chills; have prominent respiratory (including acute respiratory distress syndrome), gastrointestinal, or central nervous system findings.

SEXUALLY TRANSMITTED INFECTIONS (see Sec. 11, Ch. 10, Sexually Transmitted Infections)

Sexually transmitted infections, including acute HIV, can cause acute febrile infections.

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ANTIMICROBIAL RESISTANCE

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Antimicrobial resistance enables microbes to avoid or diminish the effects of antimicrobial agents and is acquired through either genetic mutation or the acquisition of resistance genes. Antimicrobial-resistant organisms can cause infections that are difficult to treat, often requiring the use of agents that are more expensive, less effective, or more toxic (see www.cdc.gov/drugresistance/about.html).

Resistance can occur in bacterial, viral, parasitic, and fungal pathogens. The epidemiology of resistant organisms can vary from country to country (and region to region) and might differ from that seen in the United States. International travelers should be aware of their risk of acquiring resistant organisms when abroad, and medical professionals should consider travel history when caring for patients, both to identify effective treatments for infections and to ensure infection-control interventions are in place to prevent the spread of antimicrobial resistance.

This chapter discusses resistant bacteria and an emerging fungal pathogen; these microbes can be acquired from community and health care exposures during international travel and can cause illness or asymptomatic colonization. Additional information about organism-specific resistance is available in the disease-specific chapters of Section 5, Travel-Associated Infections & Diseases. The topic of antimicrobial resistance is also addressed in Sec. 6, Ch. 4, Medical Tourism.

INFECTIOUS AGENTS & EPIDEMIOLOGY

Antimicrobial-Resistant Organisms in the Community

Globally, the emergence and spread of resistance have been linked to widespread use of antimicrobials in agriculture and in animal (veterinary) and human health care. Inadequate sanitation and water purification infrastructure also plays a role. At the community level, antimicrobial resistance can take many forms; two of relevance to travelers are diarrhea-causing bacteria, and bacteria that result in long-term intestinal colonization and (sometimes) extraintestinal infections.

DIARRHEA-CAUSING BACTERIA

Bacteria that cause diarrhea include a variety of enteric pathogens (e.g., *Campylobacter jejuni*, enterotoxigenic *Escherichia coli*, *E. coli* O157, *Salmonella* spp., *Shigella* spp.). Among these enteric pathogens, resistance to recommended treatment agents has risen worldwide in recent years, posing challenges for medical management. Refer to Section 5 for details of antimicrobial resistance in specific bacterial species.

INTESTINAL COLONIZATION & EXTRAINTESTINAL INFECTIONS

Bacterial colonization of the intestine is influenced and facilitated by a person's diet; their use of agents that disrupt normal microbial flora (e.g., antacids, antibiotics); and their interactions with animals, other humans, and the environment. Enteric bacteria that commonly inhabit the human intestine (e.g., *E. coli*, *Klebsiella pneumoniae*) can be transmitted between close contacts (e.g., household members). Similarly, people who become colonized with antimicrobial-resistant bacteria during international travel can pass these to others. If present, intestinal colonization with antibiotic-resistant bacteria can last from a few weeks to >1 year post-travel; rates of colonization typically decline after 2–3 months, however.

Intestinal colonization with bacteria resistant to carbapenems, extended-spectrum cephalosporins, or colistin can also result in a range of difficult-to-treat extraintestinal infections.

SOURCES OF INFECTION

Bacteria resistant to critically important antibiotics (e.g., carbapenems, extended-spectrum cephalosporins, colistin, macrolides, quinolones) have been isolated from a wide range of community

sources, including animals and people, drinking water, meat, and produce. Consuming foods prepared by street vendors, taking antibiotics during travel, and having travelers' diarrhea have all been associated with intestinal colonization with antibiotic-resistant bacteria. People with comorbidities (e.g., chronic bowel disease) also are more likely to become colonized with resistant bacteria during travel.

RISK TO TRAVELERS

The risk for intestinal colonization with antimicrobial-resistant enteric bacteria during travel is related to the prevalence of resistant organisms in the countries visited. Studies have identified that travelers returning from countries in East Africa, northern Africa, South America, South Asia, Southeast Asia, and the Middle East are at risk for colonization with bacteria resistant to extended-spectrum cephalosporins; risk for acquisition was greatest, however, after travel to India, Peru, and Vietnam. Acquisition of carbapenem-resistant Enterobacterales (CRE) has been reported in travelers returning from South Asia and Southeast Asia.

Colonization with *E. coli* carrying a novel gene that confers colistin resistance has been reported in travelers returning from countries in northwest Africa, South America and the Caribbean, East and Southeast Asia, Europe, and the Middle East. Although not used routinely to treat gram-negative infections in the United States, colistin is one of few remaining therapeutic options for extensively resistant infections. Emergence of colistin resistance, then, is of public health concern. In a study of 412 US international travelers, the rate of acquisition of bacteria with the mobile colistin resistance (*mcr*) gene was ≈5%. Bacteria harboring an *mcr* gene (e.g., *mcr*-1) appear to be primarily community-associated; *mcr* genes are often found in extended-spectrum β-lactamase (ESBL)–producing Enterobacterales.

Antimicrobial-Resistant Organisms in Health Care Settings

This section describes organisms of concern associated with overseas health care exposures (e.g., hospitalization, surgery). Recent hospitalization in another country can put travelers and medical tourists at risk for colonization or infection with organisms (bacteria, fungi) that possess antimicrobial resistance mechanisms that are rare in the United States. Resistance reports for specific organisms by country are available at https://resistancemap.cddep.org/AntibioticResistance.php.

Gram-negative bacteria resistant to broad-spectrum antibiotics can cause difficult-to-treat infections. Some of the more concerning genetically mediated mechanisms of antibiotic resistance (mechanisms that can confer resistance to carbapenems, extended-spectrum cephalosporins, or colistin) have the potential for rapid spread to other bacteria. ESBL-producing gram-negative bacteria, for example, originally described in health care settings, are now present outside of health care globally, including in the United States.

CARBAPENEMASE-PRODUCING BACTERIA

Carbapenemase-producing bacteria inactivate all or nearly all β-lactam antibiotics and are often highly antibiotic-resistant, making them difficult to treat. In some countries, as compared to the United States, carbapenemase production is the more frequent mechanism of carbapenem resistance, especially for *Pseudomonas aeruginosa*. Around the world, New Delhi Metallo-β-lactamase (NDM) is the most common carbapenemase; in the United States, however, where *K. pneumoniae* carbapenemase (KPC) predominates, NDM is still relatively uncommon.

In the United States, infections with carbapenemase-producing bacteria occur almost exclusively in people who were recently hospitalized or who had other health care exposures, and in residents of long-term care facilities. Among international travelers, infection with carbapenemase-producing bacteria similarly has been linked to hospitalizations and to medical tourism. In 2018, for example, a large outbreak of carbapenem-resistant *P. aeruginosa* occurred among medical tourists from several countries, including the United States, who traveled to Tijuana, Mexico, for elective bariatric surgery. The mechanism of antibiotic resistance was identified as Verona Integron-encoded Metallo-β-lactamase (VIM) carbapenemase. Also in 2018, the European Centre

for Disease Prevention and Control reported an outbreak of carbapenem-resistant *K. pneumoniae* among travelers from 3 countries hospitalized in Gran Canaria, Spain; in this instance, resistance was due to bacterial production of the oxacillinase-48-like (OXA-48-like) carbapenemase.

In some countries, carbapenemase-producing bacteria cause both health care–associated and community-associated infections. In the aforementioned study of 412 US international travelers, the authors identified a low rate (<1%) of carbapenemase-producing CRE acquisition among travelers to South and Southeast Asia who did not have health care exposure.

MOBILE COLISTIN RESISTANCE

While bacteria harboring the *mcr* gene appear to be primarily community-associated, 2 hospital-based outbreaks of *K. pneumoniae* with *mcr* have been reported (one in China, the other in Portugal); the strain in the Portugal outbreak also produced a carbapenemase. Cases of colistin-resistant, carbapenemase-producing Enterobacterales have been associated with health care in other countries as well. Emergence of *mcr* in carbapenemase-producing CRE might result in the rapid spread of strains with extremely limited treatment options in health care settings.

ANTIMICROBIAL-RESISTANT GRAM-POSITIVE BACTERIA

Antimicrobial-resistant gram-positive bacteria are a major cause of health care–associated infections. Methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci (VRE) are endemic to the United States, and travelers hospitalized outside the United States also can become colonized or infected by these organisms. Transmissible linezolid resistance has been identified in gram-positive bacilli, including *S. aureus*, coagulase-negative *Staphylococcus*, and *Enterococcus* spp. from several countries worldwide, particularly in South America. This resistance is of particular concern in VRE, for which treatment options are already limited.

CANDIDA AURIS

The fungal pathogen *Candida auris* has rapidly emerged worldwide; >40 countries have reported cases, but broader spread is suspected. *C. auris* is distinct from other *Candida* species because it tends to cause outbreaks in health care facilities, can result in long-term asymptomatic skin colonization, persists in health care environments, and has high levels of resistance to multiple classes of antifungal agents. Strains of *C. auris* resistant to the 3 main classes of antifungal medications have been identified in several countries, including the United States.

Since *C. auris* was first reported in 2016, the number of cases in the United States has increased greatly. Many of the initial cases reported in the United States occurred in patients who had received health care previously in countries with documented *C. auris* transmission. Currently, however, most cases are the result of local spread in US health care settings, particularly long-term care facilities for high-acuity patients.

C. auris can be misidentified by some laboratory diagnostics, which might contribute to under-detection of cases, both domestically and outside the United States. Improved laboratory detection and targeted colonization screening, especially among health care contacts of known cases, can facilitate earlier identification of *C. auris* and its spread. Notify public health agencies and implement infection-control measures if *C. auris* is identified or suspected.

PREVENTION

In the Community

Contaminated food is the most common source of enteric pathogen exposures among travelers. Foods grown or prepared under unhygienic conditions can be a source of enteric bacteria. Bacteria harboring *mcr* genes have been identified in foods and food animals (e.g., camels, cattle, pigs, poultry) in multiple countries. Contaminated water is another potential source of antibiotic-resistant enteric bacteria (e.g., *Campylobacter* spp., *E. coli*, *Salmonella* spp., *Shigella* spp.). See Sec. 2, Ch. 9, Water Disinfection, for recommendations regarding water treatment. Insects (e.g., flies) also can serve as vectors in the spread of resistant bacteria.

Safe food choices and careful attention to good hand hygiene can reduce the risk for exposure to pathogens, including those that harbor

antimicrobial resistance genes. See Sec. 2, Ch. 8, Food & Water Precautions, for recommendations regarding food consumption and guidance on hand hygiene. In addition, discourage travelers from purchasing or obtaining antibiotics for self-treatment in countries where drugs are available without prescription. Not only can these medications be ineffective for treating the traveler's condition, but their use carries additional risks of unforeseen and untoward side effects. Antibiotics can disrupt the traveler's healthy microbiota and promote acquisition of resistant organisms that can be carried in the traveler's gastrointestinal tract for many months and transfer resistance to other organisms.

Management of mild cough, stomach upset, mild diarrhea, and other minor ailments usually does not require antibiotics. International travelers should include over-the-counter medications in their travel health kit (see Sec. 2, Ch. 10, Travel Health Kits), and clinicians can prescribe antibiotics during a pretravel clinic visit and instruct travelers on self-treatment of moderate diarrheal illness. Educate travelers about health issue warning signs that should prompt them to seek care. More information on management of travelers' diarrhea during travel is available in Sec. 2, Ch. 6, Travelers' Diarrhea.

Travelers and their treating clinicians should be aware that common bacterial infections in destination countries might be resistant to first-line antimicrobial drugs typically used in the United States. For example, fluoroquinolone-resistant enteric pathogens are now found globally. Therefore, if travelers need antibiotics to treat moderate to severe diarrhea, an alternative antibiotic (e.g., azithromycin) might be required. Evidence regarding effective therapies to prevent colonization or infection with resistant enteric organisms in travelers is lacking; investigations into the utility of probiotics and bismuth-containing compounds are under way.

In Health Care Settings

Patients admitted to health care facilities outside the United States, especially in low- and middle-income countries, might be at a greater risk for acquiring antimicrobial-resistant organisms due to a higher prevalence of these organisms and differences in infection-control standards and practices. Exposures can be facilitated by inadequate hand hygiene among staff and personnel, insufficient environmental cleaning, and irregular supply or use of personal protective equipment by health care workers. These gaps are more common in low-resource settings. In addition, access to newer combination therapies (e.g., ceftazidime-avibactam, imipenem-cilastatin-relebactam, meropenem-vaborbactam) used to treat infections caused by highly resistant carbapenemase-producing bacteria can be limited in some low- and middle-income countries.

Information about infection prevention and control services in international health care settings often is limited. When possible (e.g., for non-emergency procedures), people traveling overseas, particularly to low- and middle-income countries, can reduce their risk for health care–associated exposures by choosing facilities with active infection-prevention and control programs (see Sec. 6, Ch. 2, Obtaining Health Care Abroad, and Sec. 6, Ch. 4, Medical Tourism for more details and recommendations). Travelers should opt to receive health care at facilities that have been accredited for their infection-prevention and control programs by national and international authorities. Joint Commission International, an accreditation body used by US facilities, maintains a website of accredited hospitals globally (www.worldhospitalsearch.org/hospital-search). Although accredited health care facilities might have better infection-control practices than non-accredited facilities, accreditation does not necessarily guarantee absence of risk for pathogen transmission.

POSTTRAVEL CONSIDERATIONS

Depending on their travel destination, some patients might be at greater risk for colonization and infection with resistant organisms. Strive to obtain an international travel history going back ≥12 months from patients presenting for care. Travel-related information can play an important role in the clinical care provided and infection control practices employed during clinical encounters.

Health Care Provider Guidance for Returning Travelers

For patients who recently stayed overnight in a health care facility outside the United States, the Centers for Disease Control and Prevention (CDC) has pathogen-specific guidance for CRE and *C. auris*.

CARBAPENEM-RESISTANT ENTEROBACTERALES

When CRE is identified in a patient with a history of an overnight stay in a health care facility outside the United States in the past 6 months, send the CRE isolate for confirmatory susceptibility testing and to determine the carbapenem-resistance mechanism. For patients admitted to health care facilities in the United States after hospitalization in facilities outside the United States within the past 6 months, consider rectal screening to detect CRE colonization; place patients in contact precautions while awaiting the screening cultures. Additional recommendations for patients infected or colonized with CRE can be found in the CRE Toolkit (www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf) and https://stacks.cdc.gov/view/cdc/25250/cdc_25250_DS1.pdf.

CANDIDA AURIS

Consider screening for *C. auris* colonization in patients who have had an overnight stay in a health care facility outside the United States in the previous 12 months, especially if the stay occurred in a country with documented *C. auris* cases (see www.cdc.gov/fungal/candida-auris/tracking-c-auris.html#world). CDC recommendations on how to screen are available from www.cdc.gov/fungal/candida-auris/c-auris-screening.html. All isolates of *Candida* collected from the bloodstream or other normally sterile sites should be identified to the species level. Also consider species identification for *Candida* isolates from nonsterile sites when the patient had an overnight stay in a health care facility outside the United States in the previous 12 months in a country with documented *C. auris* transmission.

Closely monitor patients being treated for *C. auris* for treatment failure. Susceptibility testing can help guide treatment selection. Additional recommendations for providers caring for patients infected or colonized with *C. auris* is available at www.cdc.gov/fungal/candida-auris/health-professionals.html.

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RESPIRATORY INFECTIONS

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Respiratory infections are a major reason for returning travelers seeking medical care. Upper respiratory infection is more common than lower respiratory infection. In general, the respiratory infections that affect travelers are like those in non-travelers, and exotic causes are rare. When evaluating a returning traveler with a respiratory infection, inquire about the details of travel, including type of travel and travel destinations.

INFECTIOUS AGENTS

Bacteria

Bacterial causes of respiratory illnesses include *Bordetella pertussis*, *Burkholderia pseudomallei*, *Chlamydophila pneumoniae*, *Corynebacterium diphtheriae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, and *Streptococcus pneumoniae*. *Coxiella burnetii* and *Legionella pneumophila* can cause outbreaks and sporadic cases of respiratory illness.

Viruses

Viral pathogens are the most common cause of respiratory infection in travelers. Causative agents include adenoviruses, coronaviruses (e.g., severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2], the cause of coronavirus disease 2019 [COVID-19], and the common human coronaviruses, including types 229E, NL63, OC43, and HKU1), human metapneumovirus, influenza virus, measles, mumps, parainfluenza virus, respiratory syncytial virus, and rhinoviruses. Other viruses of special concern to travelers include Middle East respiratory syndrome (MERS) coronavirus and highly pathogenic avian influenza viruses; consider these viruses in travelers with new-onset respiratory illness, including people requiring hospitalization, when no alternative cause has been identified.

CORONAVIRUSES

Include COVID-19 in the differential diagnosis of travelers who develop evidence of upper or lower respiratory tract symptoms, anosmia, diarrhea, fever, myalgia ≤14 days after international travel, and consider referring positive specimens for genomic sequencing. Travelers can be a source of transmission of new SARS-CoV-2 variants from one geographic region to another (see Sec. 5, Part 2, Ch. 3, COVID-19, and www.cdc.gov/coronavirus/2019-ncov/index.html).

Include MERS in the differential diagnosis of travelers who develop fever and pneumonia ≤14 days after traveling from countries in or near the Arabian Peninsula. Contact with a confirmed or suspected case of MERS, or with health care facilities in a MERS transmission area, is of special concern, even in the absence of confirmed pneumonia (see Sec. 5, Part 2, Ch. 14, Middle East Respiratory Syndrome / MERS, and www.cdc.gov/coronavirus/mers/index.html).

AVIAN INFLUENZA VIRUS

Consider a diagnosis of highly pathogenic avian influenza virus (e.g., H5N1, H7N9) in patients with new onset of severe acute respiratory illness requiring hospitalization when no alternative cause has been identified. A history of recent (≤10 days) travel to a country with confirmed human or animal cases—especially if the traveler had contact with poultry or sick or dead birds—increases the likelihood of the diagnosis (see Sec. 5, Part 2, Ch. 12, Influenza, and www.cdc.gov/flu/avianflu/specific-flu-viruses.htm).

Fungi

Fungal pathogens associated with travel include *Blastomyces dermatitidis*, *Coccidioides* spp. (see Sec. 5, Part 4, Ch. 1, Coccidioidomycosis), *Cryptococcus gattii*, *Histoplasma capsulatum* (see Sec. 5, Part 4, Ch. 2, Histoplasmosis), *Paracoccidioides* spp., and *Talaromyces marneffei* (formerly *Penicillium marneffei*).

EPIDEMIOLOGIC CONSIDERATIONS

Outbreaks can occur after common-source exposures on cruise ships, in hotels, among tour

groups, or during international mass gatherings (see Sec. 9, Ch. 10, Mass Gatherings). *Histoplasma capsulatum*, influenza virus, *L. pneumophila*, and SARS-CoV-2 are some of the pathogens associated with outbreaks in travelers. Groups having a greater risk for respiratory tract infection include children, older adults, and people with comorbid pulmonary conditions (e.g., asthma, chronic obstructive pulmonary disease [COPD]).

Air Quality

The air quality at many travel destinations might be poor, and exposure to carbon monoxide, nitrogen dioxide, ozone, sulfur dioxide, and particulate matter is associated with health risks, including respiratory tract inflammation, exacerbations of asthma or COPD, impaired lung function, bronchitis, and pneumonia (see Sec. 4, Ch. 3, Air Quality & Ionizing Radiation).

Air Travel

Air pressure changes during ascent and descent of aircraft can result in barotrauma and facilitate the development of sinusitis and otitis media. Direct airborne transmission of pathogens aboard commercial aircraft is unusual because recirculated air passes through a series of filters, and cabin air generally circulates within limited zones or areas of the aircraft. Despite this, COVID-19, influenza, measles, tuberculosis (TB), and other diseases have been transmitted on aircraft.

Transmission could occur via several pathways, including direct droplet spread, direct physical contact, fomites, and suspended small particles (droplet nuclei). Intermingling of large numbers of people in congregate settings (e.g., airports, cruise ships, hotels) also can facilitate transmission of respiratory pathogens.

Seasonality

The peak influenza season in the temperate Northern Hemisphere is during the winter months, typically December–February. In the temperate Southern Hemisphere, peak influenza season runs from late spring or early summer into the fall. Tropical climates have no peak season for influenza, and the risk for infection is year-round. Exposure to an infected person traveling from another hemisphere (e.g., on a cruise ship, as part of a package tour) can lead to an influenza outbreak at any time or place. The potential seasonality of COVID-19 currently is not known; transmission risk might increase during winter months, however.

Tuberculosis

Risk for TB infection among most travelers is low and correlates with the incidence of the disease in the destination country, behavior during travel, and length of stay (see Sec. 5, Part 1, Ch. 22, Tuberculosis).

CLINICAL PRESENTATION

Most respiratory infections, especially those of the upper respiratory tract, are mild. Upper respiratory tract infections often cause pharyngitis or rhinorrhea. Lower respiratory tract infections, particularly pneumonia, can be more severe. Lower respiratory tract infections are more likely than upper respiratory tract infections to cause chest pain, dyspnea, or fever. Cough is often present in either upper or lower respiratory tract infections.

People with influenza commonly have acute onset of cough, fever, headache, and myalgias. People with COVID-19 might have a similar clinical presentation, but mild disease and asymptomatic infection also are common. Consider pulmonary embolism in the differential diagnosis of travelers who present with cough, dyspnea, tachycardia, or fever and pleurisy, especially those who have recently been on long car or plane rides (see Sec. 8, Ch. 3, Deep Vein Thrombosis & Pulmonary Embolism) or who were recently infected with SARS-CoV-2.

DIAGNOSIS

Give special consideration to diagnosing patients with suspected avian influenza (see www.cdc.gov/flu/avianflu/healthprofessionals.htm), or illnesses caused by coronaviruses (e.g., COVID-19 [www.cdc.gov/coronavirus/2019-ncov/index.html], or MERS [www.cdc.gov/coronavirus/mers/interim-guidance.html]). Identifying a specific etiologic agent in immunocompetent hosts, especially in the absence of pneumonia or serious disease, is not always clinically necessary. If indicated, the following diagnostic methods can be used.

Microbiology. Gram stain and culturing of sputum can help identify a causative respiratory pathogen. Microbiologic culturing of blood, while insensitive, is also recommended as part of a diagnostic work-up.

Molecular Methods. Molecular methods are available to detect certain respiratory viruses including adenovirus, human metapneumovirus, influenza virus, parainfluenza virus, respiratory syncytial virus, SARS-CoV-2, and certain nonviral pathogens.

Rapid Diagnostic Tests. Rapid tests are available to detect some bacterial (e.g., *L. pneumophila*, *Streptococcus pneumoniae*, group A *Streptococcus*), viral (e.g., influenza virus, respiratory syncytial virus, SARS-CoV-2), and fungal (e.g., *Histoplasma capsulatum*) pathogens.

TREATMENT

Manage travelers with respiratory infections similarly to non-travelers, but evaluate those who are severely ill for diseases specific to their travel destinations and exposure history. Most viral respiratory infections are mild and do not require specific treatment. Treat travelers with pneumonia of uncertain etiology, as established by the presence of an infiltrate on chest radiography, with antibiotics in accordance with existing guidelines for community-acquired pneumonia. For travelers with influenza who have severe disease or who are at greater risk for complications, treat with antiviral medications. Antiviral treatment for influenza is most effective if begun ≤48 hours of symptom onset. Treat people with COVID-19 per current guidance (www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care.html).

PREVENTION

Vaccines are available to prevent a number of respiratory diseases, including COVID-19 (see www.cdc.gov/coronavirus/2019-ncov/vaccines/index.html), diphtheria, *H. influenzae* type B (in young children), influenza, measles, pertussis, *S. pneumoniae*, and varicella. Unless contraindicated, travelers should be up to date with COVID-19 and influenza vaccines and other routine immunizations, especially against *S. pneumoniae*.

Preventing respiratory illness while traveling might not be possible, but travelers can follow common-sense measures, including adhering to current recommendations regarding advisability of travel and any indicated precautions (e.g., mask wearing, physical distancing); minimizing close contact with people who are coughing and sneezing; avoiding live animal markets; frequently washing hands, either with soap and water or alcohol-based hand sanitizers containing ≥60% alcohol when soap and water are not available; and, if the traveler has a preexisting eustachian tube dysfunction, using a vasoconstricting nasal spray immediately before air travel, which might decrease the likelihood of otitis or barotrauma.

Health care workers should use appropriate infection-control measures while managing any patient with a respiratory infection (www.cdc.gov/flu/professionals/infectioncontrol).

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PERSISTENT DIARRHEA IN RETURNED TRAVELERS

Bradley Connor

Although most cases of travelers' diarrhea (TD) are acute and self-limited, a certain percentage of people afflicted will develop persistent (>14 days) gastrointestinal (GI) symptoms. Details on the management of acute TD are available in Sec. 2, Ch. 6, Travelers' Diarrhea.

PATHOGENESIS

The pathogenesis of persistent diarrhea in returned travelers generally falls into one of the following broad categories: ongoing infection or co-infection with a second organism not targeted by initial therapy; previously undiagnosed GI disease unmasked by the enteric infection; or a post-infectious phenomenon.

Ongoing Infection

Most cases of TD are the result of bacterial infection and are short-lived and self-limited. In addition to immunosuppression and sequential infection with diarrheal pathogens, ongoing infection with protozoan parasites can cause prolonged diarrheal symptoms.

BACTERIAL

Individual bacterial infections rarely cause persistent symptoms, but travelers infected with *Clostridioides difficile* or enteroaggregative or enteropathogenic *Escherichia coli* (see Sec. 5, Part 1, Ch. 7, Diarrheagenic *Escherichia coli*) can experience ongoing diarrhea. *C. difficile*–associated diarrhea can occur after treatment of a bacterial pathogen with a fluoroquinolone or other antibiotic, or after malaria chemoprophylaxis. The association between *C. difficile* and antimicrobial treatment is especially important to consider in patients with persistent TD that seems refractory to multiple courses of empiric antibiotic therapy. The initial work-up of persistent TD should always include a *C. difficile* stool toxin assay. Clinicians can prescribe oral vancomycin, fidaxomicin, or, less optimally, metronidazole to treat *C. difficile*.

PARASITIC

As a group, parasites are the pathogens most likely to be isolated from patients with persistent diarrhea. The probability of a traveler having a protozoal infection, relative to a bacterial one, increases with increasing duration of symptoms. Parasites might also be the cause of persistent diarrhea in patients already treated for a bacterial pathogen.

GIARDIASIS

Giardia (see Sec. 5, Part 3, Ch. 12, Giardiasis) is the most likely parasitic pathogen to cause persistent diarrhea. Suspect giardiasis particularly in patients with upper GI–predominant symptoms. Untreated, symptoms can last for months, even in immunocompetent hosts.

PCR-based diagnostics, particularly the multiplex DNA extraction PCR, are becoming the diagnostic methods of choice to identify *Giardia* and other protozoal pathogens, including *Cryptosporidium*, *Cyclospora*, and *Entamoeba histolytica*. Diagnosis also can be made by stool microscopy, antigen detection, or immunofluorescence. In the absence of diagnostics (given the high prevalence of *Giardia* as a cause for persistent TD), empiric therapy is a reasonable option in the clinical setting. Rare causes of persistent symptoms include

the intestinal parasites *Cystoisospora*, *Dientamoeba fragilis*, and *Microsporidia*.

TROPICAL SPRUE & BRAINERD DIARRHEA

Persistent TD also has been associated with tropical sprue and Brainerd diarrhea. Tropical sprue is associated with deficiencies of vitamins absorbed in the proximal and distal small bowel and most commonly affects long-term travelers to tropical areas, as the name implies. The incidence of tropical sprue appears to have declined dramatically over the past 2 decades. Diagnosed only rarely in travelers, its cause is unknown.

Brainerd diarrhea (www.cdc.gov/ncezid/dfwed/diseases/brainerd-diarrhea/index.html) is a syndrome of acute onset of watery diarrhea lasting ≥4 weeks. Symptoms include 10–20 episodes of explosive, watery diarrhea per day, fecal incontinence, abdominal cramping, gas, and fatigue. Nausea, vomiting, and fever are rare. Although the cause is believed to be infectious, a culprit pathogen has yet to be identified, and antimicrobial therapy is ineffective as treatment. Investigation of an outbreak of Brainerd diarrhea among passengers on a cruise ship to the Galápagos Islands in 1992 identified that individuals with persistent diarrhea (range: 7 to >42 months) were more likely to have consumed contaminated water or eaten raw fruits or vegetables washed with contaminated water.

Underlying Gastrointestinal Disease

CELIAC DISEASE

In some cases, persistent symptoms relate to chronic underlying GI disease or to a susceptibility unmasked by the enteric infection. Most prominent among these is celiac disease, a systemic disease manifesting primarily with small bowel changes. In genetically susceptible people, exposure to antigens found in wheat causes villous atrophy, crypt hyperplasia, and malabsorption. Serologic tests, including tissue transglutaminase antibody testing, support the diagnosis; a small bowel biopsy showing villous atrophy confirms the diagnosis. Patients can be treated with a gluten-free diet.

COLORECTAL CANCER

Depending on the clinical setting and age group, clinicians might need to conduct a comprehensive search for other underlying causes of chronic diarrhea. Consider colorectal cancer in the differential diagnosis of patients passing occult or gross blood rectally or in patients with new-onset iron-deficiency anemia.

INFLAMMATORY BOWEL DISEASE

Idiopathic inflammatory bowel disease, including Crohn's disease, microscopic colitis, and ulcerative colitis, can occur after acute bouts of TD. One prevailing hypothesis is that in genetically susceptible people, an initiating exogenous pathogen changes the microbiota of the gut, thereby triggering inflammatory bowel disease.

Postinfectious Phenomena

In a certain percentage of patients who present with persistent GI symptoms, clinicians will not find a specific cause. After an acute diarrheal infection, patients might experience a temporary enteropathy characterized by villous atrophy, decreased absorptive surface area, and disaccharidase deficiencies, which can lead to osmotic diarrhea, particularly after consuming large amounts of fructose, lactose, sorbitol, or sucrose. Use of antimicrobial medications during the initial days of diarrhea might also lead to alterations in intestinal flora and diarrhea symptoms.

Occasionally, onset of irritable bowel syndrome (IBS) symptoms occurs after a bout of acute gastroenteritis, known as postinfectious IBS (PI-IBS). PI-IBS symptoms can occur after an episode of gastroenteritis or TD. The clinical work-up for microbial pathogens and underlying GI disease in patients with PI-IBS will be negative. Whether using antibiotics to treat acute TD increases or decreases the likelihood of PI-IBS is unknown.

EVALUATION

Traditional methods of microbial diagnosis rely on the use of microscopy. Examine stool specimens collected over 3 or more days for ova and parasites; include acid-fast staining for *Cryptosporidium*, *Cyclospora*, and *Cystoisospora*. *Giardia* antigen testing and a *C. difficile* toxin assay are appropriate elements of a work-up. In addition, a D-xylose absorption test can determine whether patients are properly absorbing nutrients. If underlying gastrointestinal disease is

suspected, include serologic testing for celiac disease and consider inflammatory bowel disease during initial evaluation. Subsequently, studies to visualize both the upper and lower gastrointestinal tracts, with biopsies, might be indicated.

Diagnostic tests to determine specific microbial etiologies in cases of persistent diarrhea have advanced in the past number of years. One of the most useful tools is high-throughput multiplex DNA extraction PCR. This technology uses a single stool specimen to detect multiple bacterial, parasitic, and viral enteropathogens simultaneously. Except for *Cryptosporidium*, these assays have high sensitivity and specificity; the clinical ramifications and the economic impact of using these diagnostic molecular panels have not been determined fully, however. In some cases, molecular testing detects colonization rather than infection, making it difficult for clinicians to interpret and apply the results properly.

MANAGEMENT

Specific treatment of identified enteropathogens is usually indicated, and appropriate management of underlying gastrointestinal disease warranted (e.g., a gluten-free diet for celiac disease, medication for inflammatory bowel disease). Dietary modifications might help patients with malabsorption. Symptomatic treatment or the use of nonabsorbable antibiotics offer potential benefit if small intestinal bacterial overgrowth accompanies the symptom complex. Additionally, chronic diarrhea might cause fluid and electrolyte imbalances requiring medical management involving oral or intravenous replacement based on clinical presentation.

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11

DERMATOLOGIC CONDITIONS

Karolyn Wanat, Scott Norton

Skin and soft tissue problems, including rashes, are among the most frequent medical concerns of returned travelers. Several large reviews of dermatologic conditions in returned travelers have shown that cutaneous larva migrans, insect bite reactions, and bacterial infections (often superimposed on insect bites) represent the most common skin problems identified during posttravel medical visits (Table 11-12).

Clinicians can use several approaches to diagnose and manage skin conditions in returned travelers. One useful approach is to consider

Table 11-12 Most common causes of skin lesions in returned travelers

DIAGNOSIS	PERCENTAGE OF ALL DERMATOLOGIC DIAGNOSES (n = 4,742)
Cutaneous larva migrans	9.8
Insect bite	8.2
Skin abscess	7.7
Superinfected insect bite	6.8
Allergic rash	5.5
Rash, unknown origin	5.5
Dog bite	4.3
Superficial fungal infection	4.0
Dengue	3.4
Leishmaniasis	3.3
Myiasis	2.7
Spotted fever group rickettsiosis	1.5
Scabies	1.5
Cellulitis	1.5
Other	32.5

Source: Modified from Lederman ER, Weld LH, Elyazar IR, von Sonnenburg F, Loutan L, Schwartz E, et al. GeoSentinel Surveillance Network. Dermatologic conditions of the ill returned traveler: an analysis from the GeoSentinel Surveillance Network. Int J Infect Dis. 2008;12(6):593–602.

whether the condition is accompanied by an elevated temperature. Few travelers' dermatoses are accompanied by fever, which could indicate a systemic infection, usually viral or bacterial, that requires prompt attention. A second consideration is the geographic and exposure elements of the travel history. A third consideration is the morphology of the lesions noted on physical examination. The most successful approach combines all 3 considerations supported by laboratory confirmation from cultures, serology, skin biopsy, or microscopy if required or indicated. Box 11-02 includes essential elements of the assessment of returned travelers presenting with skin problems.

Many dermatologic problems in returned travelers represent a flare of an existing condition, perhaps because of interruption in the usual treatment regimen while away from home. Other skin disorders might coincide with travel or appear shortly thereafter but are unrelated to travel itself.

BOX 11-02 Assessing returned travelers presenting with skin problems: essential elements

PERTINENT PAST MEDICAL HISTORY

Systemic diseases and chronic conditions, including preexisting skin conditions

Current medications and allergies

HISTORY OF THE PRESENT ILLNESS

Time of onset of lesions (during or after travel)

Associated symptoms: fever, pain, pruritus

TRAVEL HISTORY

Location and duration of travel

Exposure history: freshwater, marine water, insects, animals, plants, occupational and recreational exposures, sexual and other human contact exposures

Companion travelers with similar findings

Vaccination status

Adherence to standard travel precautions (e.g., safe food and water precautions, insect bite precautions)

Medications taken during travel (could provide adequate prophylaxis for certain conditions or might have cutaneous side effects)

PHYSICAL EXAMINATION

Shape of skin lesions (e.g., macules, nodules, papules, plaques, ulcers)

Number, pattern, and distribution of lesions

Location of lesions: exposed versus unexposed skin surfaces

FEVER & RASH

Many illnesses fall into the category of fever with a rash. Consider the following infections in the differential diagnosis of febrile travelers with rashes: cytomegalovirus, enteroviruses (e.g., coxsackievirus, echovirus), Epstein-Barr virus, hepatitis B virus, histoplasmosis, leptospirosis, measles, syphilis, and typhus. Fever and rash in returned travelers are most often, though not exclusively, due to viral infections.

Systemic Viral Infections & Illnesses

CHIKUNGUNYA

A virus transmitted by *Aedes* spp. mosquitoes, chikungunya has caused major outbreaks of illness in southeast Africa, the Americas and the Caribbean, and South Asia (see Sec. 5, Part 2, Ch. 2, Chikungunya). The rash associated with chikungunya resembles that of dengue (discussed next), but hemorrhage, shock, and death are rare with chikungunya. A major distinguishing feature of chikungunya is its associated arthritis, arthralgia, or tenosynovitis that can persist for months, particularly in older adults. As with dengue, serologic testing is available for diagnosis. After ruling out dengue, treat arthritis with nonsteroidal anti-inflammatory drugs (NSAIDs).

DENGUE

Dengue is caused by 1 of 4 strains of dengue viruses (see Sec. 5, Part 2, Ch. 4, Dengue). The disease is transmitted by *Aedes* spp. mosquitoes often found in urban areas, and its incidence continues to increase. Disease is characterized by abrupt onset of high fever, frontal headache (often accompanied by retro-orbital pain), and myalgia. A widespread but faint macular rash interrupted by islands of uninvolved pallid skin commonly becomes evident 2–4 days after illness onset. A petechial rash might be found in classic and severe dengue.

Diagnostic methods include antigen and antibody detection tests, and PCR assays. A positive IgM serology helps support the diagnosis. Treatment is supportive; avoid NSAIDs, which can increase the risk of bleeding in patients with dengue.

ACUTE HIV

Acute retroviral syndrome can present as a flulike syndrome including fever, generalized lymphadenopathy, malaise, and a generalized skin eruption. Acute HIV infection–associated skin findings are often nonspecific and present as pink to deeply red macules or papules or as a morbilliform eruption, but urticarial and pustular lesions also have been described. Oral ulcers might be present.

ZIKA

Zika is a flavivirus transmitted by *Aedes* mosquitoes. It caused major outbreaks in the Western Hemisphere beginning in 2015 (see Sec. 5, Part 2, Ch. 27, Zika). Sexual transmission has been documented for months after infection. The course of the illness is generally subclinical or mild, characterized by arthralgia, conjunctivitis, fever, lymphadenopathy, and a morbilliform ("maculopapular") rash. In pregnant people, Zika infection can cause fetal loss or fetal microcephaly and neurological damage. Zika-associated Guillain-Barré syndrome also has been reported after infection. Infection is usually diagnosed by using molecular diagnostics and serologic testing. Treatment involves supportive care.

Systemic Bacterial Infections & Illnesses

MENINGOCOCCEMIA

Invasive *Neisseria meningitidis* disease occurs worldwide and often is associated with outbreaks, especially in the meningitis belt of sub-Saharan Africa (see Sec. 5, Part 1, Ch. 13, Meningococcal Disease). Meningococcemia is characterized by acute onset of fever and petechiae that often expand into purpuric macules and patches, commonly accompanied by hypotension and multiorgan failure. Rapid diagnosis and immediate treatment can be lifesaving.

RICKETTSIOSES

AFRICAN TICK-BITE FEVER

Rickettsia africae, the bacteria responsible for African tick-bite fever (South African tick typhus), is transmitted by the bite of a hard tick (*Hyalomma* spp.). Travelers who hike and camp outdoors or who are on safari are particularly at risk for this disease, a frequent cause of fever and rash in southern Africa (see Sec. 5, Part 1, Ch. 18, Rickettsial Diseases).

Disease is characterized by fever and an eschar at the site of the tick bite. The eschar, or *tache noire*, is a mildly painful black necrotic lesion with a red rim. Several lesions might be present because people often suffer multiple tick bites. Within a few days, patients develop a fine petechial or papular rash, associated with localized lymphadenopathy. Diagnosis is usually made through clinical recognition and is confirmed by serologic testing. Treatment is doxycycline.

Other rickettsial infections (e.g., Mediterranean spotted fever, rickettsialpox, scrub typhus) might present with eschars or maculopapular, vesicular, or petechial rashes. Each has distinctive geographic or epidemiologic exposure risks.

ROCKY MOUNTAIN SPOTTED FEVER

Rocky Mountain spotted fever (RMSF) is a tick-borne rickettsial disease that is more severe than the other spotted fevers. RMSF occurs in North America (the United States and Mexico) and parts of Central and South America, but it is uncommon in travelers. Nevertheless, because of its potential severity and the need for early treatment, consider RMSF when evaluating patients with fever and rash.

Most patients with RMSF develop a rash 3–5 days after illness onset. The typical rash of RMSF begins on the ankles and wrists and spreads centrally and to the palms and soles. The rash commonly starts as a blanching maculopapular eruption that becomes petechial, although in some patients it begins with petechiae. Doxycycline is the treatment of choice.

BACTERIAL SKIN INFECTIONS

Bacterial skin infections occur most frequently when the skin's surface has been interrupted, often by abrasions, bites, or minor scratches, particularly when maintaining good hygiene is difficult. Common organisms responsible are *Staphylococcus aureus* and *Streptococcus pyogenes*. Resulting infections are collectively called pyodermas (Greek for "pus skin") and can present as cellulitis and erysipelas, ecthyma (ulcers or open sores), folliculitis, furuncles (also called abscesses or boils), impetigo, and lymphangitis.

Cellulitis & Erysipelas

Cellulitis and erysipelas manifest as red, warm, edematous areas that might start at the site of a minor injury or opening in the skin, or without an obvious underlying suppurative focus. Unlike cellulitis, erysipelas tends to be raised, with a clear line of demarcation at the edge of the lesion due to involvement of superficial lymphatics, and is more likely to be associated with fever. Cellulitis, erysipelas, and lymphangitis are usually caused

by β-hemolytic streptococci. *S. aureus* (including methicillin-resistant strains), and gram-negative aerobic bacteria also can cause cellulitis.

Furunculosis

People whose skin or nasal mucosa is colonized with *S. aureus* are at risk for recurrent folliculitis or furunculosis. Boils can continue to occur weeks or months after a traveler returns; if associated with *S. aureus*, treatment usually involves a decolonization regimen with nasal mupirocin and a skin wash with an antimicrobial skin cleanser. Some decolonization protocols advise similar treatment for household members and close contacts.

Many travelers who develop boils when abroad mistakenly attribute the tender lesions to spider bites. Outside a few endemic areas, however, necrotizing spider bites are extremely rare. The lesions in these cases are far more likely to be abscesses caused by methicillin-resistant *S. aureus* and should be treated accordingly.

Impetigo

Impetigo is another common bacterial skin infection, especially in children in the tropics, and is caused by *S. aureus* or *S. pyogenes*. Impetigo is a highly contagious superficial skin infection that generally appears on the arms, legs, or face as golden or "honey-colored" crusting formed from dried serum. Streptococcal impetigo is usually what causes the classic crust seen in the midface of children. Staphylococcal impetigo often appears in body folds, especially the axillae, and might present as delicate pustules.

Treatment

Use soap and water for local cleansing of bacterial skin infections. A topical antibiotic, preferably mupirocin, also can be used; bacitracin zinc and polymyxin sulfate (often in combination) are an alternative. Topical antibiotic ointments widely available in other countries contain neomycin (a known, common cause of acute allergic contact dermatitis) or gentamicin. Other "triple cream" type products available for purchase in low- and middle-income countries often contain ultrapotent steroids that can interfere with the healing of common infections and have their own side effects. In many low- and middle-income countries, an application of gentian violet or potassium permanganate is the treatment of choice for impetigo.

Minor skin abscesses often respond to incision and drainage without the need for antibiotics. Oral or parenteral antibiotics might be required if the skin infection is deep, expanding, extensive, painful, or associated with systemic symptoms (e.g., fever). Consider antibiotic resistance if the condition does not respond to empiric therapy. Bites and scratches from animals (both domestic and wild) can be the source of unusual gram-negative organisms and anaerobic bacteria; appropriate treatment might require care from specialists who can obtain bacterial cultures, prescribe focused antibiotic therapy, and perform surgical debridement, as needed (see Sec. 4, Ch. 7, Zoonotic Exposures: Bites, Stings, Scratches & Other Hazards).

SKIN LESION MORPHOLOGY

Linear Lesions

CUTANEOUS LARVA MIGRANS

Cutaneous larva migrans, a condition in which the skin is infested with the larval stage of cat or dog hookworm (*Ancylostoma* spp.), manifests as an extremely pruritic, serpiginous, linear lesion (see Sec. 5, Part 3, Ch. 4, Cutaneous Larva Migrans). The migrating larvae advance relatively slowly in the skin's uppermost layers. A deeper lesion that resembles urticarial patches and that progresses rapidly might be due to larva currens (running larva), caused by cutaneous migration of filariform larva of *Strongyloides stercoralis* (see Sec. 5, Part 3, Ch. 21, Strongyloidiasis).

LYMPHOCUTANEOUS OR SPOROTRICHOID SPREAD OF INFECTION

Lymphocutaneous or sporotrichoid spread of infection occurs when organisms ascend proximally along superficial cutaneous lymphatics, producing raised, cordlike, linear lesions. Alternatively, this condition can present as an ascending chain of discontinuous, sometimes ulcerated nodules (termed nodular lymphangitis) that occur after primary percutaneous inoculation of certain pathogens. Causative pathogens can be bacterial

(e.g., *Francisella tularensis*; atypical *Mycobacterium* spp. [such as *M. marinum* after exposure to brackish water or rapidly growing *Mycobacteria* after pedicure footbaths]; *Nocardia* spp.), parasitic (e.g., *Leishmania* spp., particularly those responsible for causing Western Hemisphere leishmaniasis), or fungal (e.g., *Coccidioides* spp., *Sporothrix*).

PHYTOPHOTODERMATITIS & OTHER NONINFECTIOUS EXPOSURES

Phytophotodermatitis is a noninfectious condition resulting from the interaction of natural psoralens, most common in the juice of limes, and ultraviolet A radiation from the sun. The result is the equivalent of an exaggerated sunburn that creates a painful line of blisters, after which asymptomatic hyperpigmented lines appear that can take weeks or months to resolve.

Long linear lesions caused by cnidarian envenomation (e.g., stings from the tentacles of jellyfish and the Portuguese man o' war [*Physalia physalis*]), often resemble phytophotodermatitis. Another common, but self-evident, cause of an itchy, often blistering eruption, is acute contact dermatitis due to black henna. In places where temporary tattooing is practiced, paraphenylenediamine is added to red or brown henna to make a longer-lasting pigment, black henna. Travelers who receive temporary tattoos using black henna (rather than the red or brown), are at risk for developing a cutaneous reaction to paraphenylenediamine.

Macular Lesions

Macules and patches (flat lesions) are common, often nonspecific, and frequently due to drug reactions or viral exanthems. Purpura are typically macular, and any purpuric lesion associated with fever could indicate a life-threatening emergency (e.g., meningococcemia).

CORONAVIRUS DISEASE 2019

Some patients with coronavirus disease 2019 (COVID-19), particularly young children and young adults, develop a condition known as COVID toes. The condition is characterized by the sudden onset of painful, dusky red macules and patches, typically on the plantar aspect of the distal phalanges of ≥1 toes. Clinically and histologically, COVID toes resembles conditions known as chilblains (a cold weather injury) or lupus pernio (a skin finding in some patients with systemic lupus erythematosus). Although an epidemiologic link with the COVID-19 pandemic seems apparent, viral, molecular, and serologic studies have not confirmed a causal relationship. Nevertheless, young travelers who develop this medical condition warrant further evaluation for COVID-19.

LEPROSY / HANSEN'S DISEASE

Leprosy frequently presents with hypopigmented or erythematous patches that are hypoesthetic to pin prick and associated with peripheral nerve enlargement. Newly diagnosed leprosy cases occur almost exclusively in immigrants arriving from low- or middle-income countries where the disease is endemic. Diagnosis is made by skin lesion biopsies. The National Hansen's Disease Clinical Center in Baton Rouge, Louisiana, provides consultations (nhdped@hrsa.gov; 800-642-2477; www.hrsa.gov/hansens-disease/index.html).

LYME DISEASE

Lyme disease is caused by the spirochete *Borrelia burgdorferi* sensu lato (see Sec. 5, Part 1, Ch. 11, Lyme Disease). Endemic to temperate latitudes in North America, Asia, and Europe, the bacteria that causes Lyme disease is transmitted through the bite of infected hard ticks, genus *Ixodes*.

Infected travelers present with ≥1 large erythematous patch (erythema migrans). If ≥1 lesion is present, the first lesion to appear is where the tick bite occurred; subsequent lesions are due to secondary, probably hematogenous, spread of *Borrelia*, not multiple tick bites. Erythema migrans often is described as targetoid, but central clearing or red-and-white bands do not occur with every case. The lesions generally are asymptomatic. Pruritus, if present, is usually intermittent and very mild. Lesions that are severely or persistently pruritic are unlikely to be erythema migrans.

TINEA

Tinea (ringworm) is caused by a variety of superficial fungi (e.g., *Microsporum*, *Trichophyton*).

Typical lesions appear as expanding, red, raised rings, with an area of central clearing. Diagnostic methods include fungal culture, microscopy (prepare skin scraping samples using a 10% solution of potassium hydroxide [KOH]), and PCR. Treatment usually involves several weeks' application of a topical antifungal (e.g., clotrimazole, ketoconazole, miconazole, terbinafine) or a course of an oral antifungal (e.g., fluconazole, griseofulvin, terbinafine). Nystatin-based topical agents are ineffective.

For recalcitrant tinea infections associated with international travel, consider obtaining culture for species identification. Prolonged courses of higher dose oral antifungals might be needed to treat severe or recurrent infections caused by emerging resistant *Trichophyton* species.

Topical medications that combine an antifungal agent with a potent corticosteroid (e.g., betamethasone, clobetasol) are available in many countries; caution travelers against their use. Adverse events associated with steroid-containing antifungal preparations include longer-lasting infections; more extensive spread of the infection over large areas of the body; invasion of the fungal pathogen into the deeper skin layers; unusual presentation of infection (making diagnosis more challenging); and severe redness and burning.

TINEA VERSICOLOR

Caused by several species of the fungus *Malassezia* (e.g., *M. furfur* [previously *Pityrosporum ovale*], *M. globosa*), tinea versicolor is characterized by abundant, asymptomatic, round to oval skin patches. Lesions are often 1–3 cm in diameter, but dozens of lesions can coalesce to form a "map-like" appearance on the upper chest and back. Affected skin typically has a dry or dusty surface. Lesions can be skin-colored, slightly hypopigmented, or slightly hyperpigmented (*versicolor* means "changed color"), but all lesions on a person have a uniform color.

Tinea versicolor can be diagnosed in various ways. A clinical diagnosis often is based on the appearance of the lesions. Under the light of a Wood ultraviolet lamp, the lesion produces a subtle yellowish-green hue, corroborating the diagnosis. Microscopic examination using a KOH preparation can be confirmatory.

Topical azoles (e.g., clotrimazole cream, ketoconazole shampoo used as a body wash), selenium sulfide shampoo, or topical zinc pyrithione are recommended treatments. Systemic azoles (e.g., fluconazole) can be used for infections that are severe, relapsing, or recalcitrant to first-line therapies. In many countries, the most common treatment is Whitfield ointment (salicylic acid 3% and benzoic acid 6%, mixed in a vehicle such as petrolatum). Oral griseofulvin and oral terbinafine are ineffective against *Malassezia*.

Nodular & Subcutaneous Lesions

GNATHOSTOMIASIS

Gnathostomiasis is a nematode infection primarily occurring in equatorial Africa, along the Pacific coast of Ecuador and Peru, in parts of Mexico, and in Southeast Asia. Infection results from eating raw or undercooked freshwater fish, amphibians, or reptiles. Infected travelers experience transient, migratory, subcutaneous, pruritic, and painful nodules that can occur weeks or even years after exposure. Symptoms are due to migration of the nematode through the body; central nervous system involvement is possible. Eosinophilia is common, and serologic tests are available for diagnosis. Treat cutaneous gnathostomiasis with albendazole or ivermectin.

LOIASIS

Caused by *Loa loa*, a deerfly-transmitted nematode, loiasis occasionally occurs in long-term travelers living in rural equatorial Africa. Infected travelers present with transient, migratory, subcutaneous, painful, or pruritic nodules (called Calabar swellings) produced by adult nematode migration through the skin. Rarely, the worm can be observed crossing the conjunctiva or eyelid. Peripheral eosinophilia is common.

Loiasis can be diagnosed by finding microfilariae in blood collected during daytime; because microfilaremia might be indetectable, however, serologic testing is useful. Treatment is complicated, and consultation with an expert is required for nearly all cases. Two medications are required to control both the larval microfilariae and the adult filariae; the most common regimen includes use of both albendazole and diethylcarbamazine (DEC).

Due to relative contraindications for DEC use in patients with onchocerciasis, special management considerations are warranted for travelers who visited areas endemic for both loiasis and onchocerciasis. Treating loiasis with ivermectin can cause adverse neurological side effects. For additional details regarding contraindications to use of DEC and ivermectin (and a recommendation to consult a specialist in tropical diseases for management advice and support), see Sec. 5, Part 3, Ch. 9, Lymphatic Filariasis, and Sec. 5, Part 3, Ch. 17, Onchocerciasis / River Blindness).

MYIASIS

In sub-Saharan Africa, myiasis is caused by a skin infestation with the larva of the tumbu fly, also known as the mputsi fly (*Cordylobia anthropophaga* and related species). In the Western Hemisphere, larva of the botfly (*Dermatobia hominis*) cause furuncular myiasis; the botfly's range extends from central Mexico to the northern half of South America. Solitary or multiple painful nodules resembling a furuncle might be present; each lesion holds only a single larva. The center of the lesion has a small punctum through which the larva both breathes and expels waste.

More mature larvae sometimes exit on their own to pupate, or can be gently squeezed out of nodules. Extracting larva can be difficult; obstructing the breathing punctum as a first step can be helpful and is easily achieved by applying an occlusive dressing or covering (e.g., a bottle cap filled with petroleum jelly), for several hours. Removal might require minor incision, carefully performed to avoid puncturing the larval body, after which newly vacant cavity should be flushed with sterile water. Treatment for secondary infection and appropriate prophylaxis for tetanus also could be required.

TUNGIASIS

Tungiasis is a skin infestation caused by adult female sand fleas (*Tunga penetrans*). Gestating females burrow into the usually thick skin on the sole of the foot or around the toes. Most people with tungiasis have multiple lesions. Individual lesions have a strikingly uniform appearance with a round, 5 mm diameter, white, slightly elevated surface. In the center of the lesion, a minute, frequently black, opening is present, through which the embedded flea breathes, eliminates waste, and eventually extrudes eggs. Clustered lesions can appear as crusty, dirty, or draining plaques, which are typically itchy, painful, and continue to expand as the uterus of the sand flea fills with eggs.

Treatment includes extracting the burrowed fleas, empirical antibiotics for secondary bacterial infection, and appropriate prophylaxis for tetanus, if required. In many countries, extraction is performed at home using a heat-sterilized needle to pluck out the mature flea with eggs.

Papular Lesions

ARTHROPOD BITES

Arthropod bites are probably the most common cause of papular lesions. Biting arthropods include bed bugs, fleas, headlice, midges, mosquitoes, and sandflies. Itching associated with arthropod bites is due to hypersensitivity reactions to proteins and other components in arthropod saliva.

Individual bites usually appear as small (4–10 mm diameter) edematous, pink to red papules with a gentle "watch-glass" profile. The center of many bites will have a small, subtle break in the epidermis where the arthropod's mouth parts entered the surface of the skin. The pink to red color generally does not extend beyond the elevated part of the lesion, and often a subtle pale hypovascular surrounding halo is apparent.

Lesions are almost invariably quite pruritic; scratching will often excoriate or erode the skin's surface. Such bites are vulnerable to secondary bacterial infections, usually with *Staphylococcus* spp. or *Streptococcus* spp. Many types of arthropods produce bite reactions with characteristic shapes, patterns, and distributions. For example, bites from bed bugs and fleas often appear as scattered clusters of discrete red papules on unclothed surfaces of the body.

SCABIES

Scabies infestation usually manifests as a generalized or regional pruritic papular rash with erythema, abundant excoriations, and secondarily infected pustules (see Sec. 5, Part 3, Ch. 19, Scabies). Scabies generally has regional symmetry and most commonly involves the volar wrists and finger web spaces. Most boys and men with scabies will have nodular lesions on the scrotum and

penis. Scabies burrows are short, delicate, linear lesions involving just the most superficial part of the epidermis; they are pathognomonic but can be difficult to detect.

OTHER PAPULAR LESIONS

Many other conditions present as widespread, extremely pruritic eruptions, often with numerous fine, slightly elevated, somewhat indistinct papules. Examples include acute allergic contact dermatitis (perhaps due to plants) and photosensitive dermatitis (often associated with photosensitizing medications, e.g., doxycycline). Onchocerciasis (specifically onchocercal dermatitis due to microfilaria migrating through the skin) can occur in expatriates living in endemic areas in sub-Saharan Africa and manifests as a generalized pruritic, papular dermatitis (see Sec. 5, Part 3, Ch. 17, Onchocerciasis / River Blindness). Swimmer's itch (cercarial dermatitis) and hookworm folliculitis are extremely itchy eruptions composed of papules on skin surfaces exposed to fresh water and fecally contaminated soils, respectively.

Ulcerative Lesions

Skin ulcers form when a destructive process damages or erodes the epidermis, the skin's superficial layer, and then enters the dermis, the skin's deeper, more leathery layer. The most frequent causes of acute (duration <1 month) cutaneous ulcers are the common pyogenic bacteria, staphylococci and streptococci. These create well-demarcated, shallow ulcers with sharp borders and are known as bacterial or common ecthyma; treatment is described earlier in this chapter.

ANTHRAX

Cutaneous anthrax produces a large, surprisingly painless edematous swelling. The surface develops a shallow ulcer that progresses into a necrotic black eschar. Nearly all cases of travel-associated anthrax are cutaneous and result from exposure to live cattle, goats, or sheep, or from handling unprocessed products made from animal hides or wool (see Sec. 5, Part 1, Ch. 1, Anthrax).

BURULI ULCER

Buruli ulcer is a rare infection in travelers caused by *Mycobacterium ulcerans*, a freshwater bacterium found most commonly in equatorial Africa (especially Ghana and Nigeria) and in the Australian state of Victoria. Buruli ulcers typically start as edematous nodules that arise at sites of minor skin injury. The nodules ultimately break down into expanding invasive wounds. Tropical ulcer has a similar clinical presentation but is exceptionally painful. Unlike Buruli ulcer, tropical ulcer likely represents a polymicrobial bacterial infection, including some mycobacteria.

CUTANEOUS LEISHMANIASIS

The main areas of risk for cutaneous leishmaniasis (CL) are Africa's northeastern quadrant, Latin America, south and central Asia, the Mediterranean coastal areas, and the Middle East (see Sec. 5, Part 3, Ch. 14, Cutaneous Leishmaniasis). The *Leishmania* parasite is transmitted by the bite of an infected sandfly, and CL lesions start as localized, typical insect bite reactions. Lesions then evolve slowly over several weeks into shallow ulcers with raised margins, resembling a broad, shallow, volcanic caldera; the ulcer's surface can be covered by a dried crust or a raw, fibrinous coat. In the absence of secondary bacterial infection, ulcers are generally painless.

Special techniques are necessary to confirm CL diagnosis. In travelers, pathogen speciation often is necessary to determine whether the lesion is strictly cutaneous and self-healing or will require treatment with medication (oral, topical, or intravenous) or possibly cryotherapy or heat therapy. Refer to the Centers for Disease Control and Prevention (CDC) webpage, www.cdc.gov/parasites/leishmaniasis/index.html, or call or email the CDC for recommendations on diagnosis and treatment (404-718-4745; parasites@cdc.gov).

SPIDER BITES

Necrotizing spider bites are usually caused by recluse spiders, the most common culprit being *Loxosceles reclusa*, the brown recluse, found in the south-central United States. The Mediterranean recluse spider (*Loxosceles rufescens*), native to regions around the Mediterranean Sea and the Near East, resembles the brown recluse. *L. rufescens* has become a widespread "tramp" species giving it a large, nearly worldwide distribution;

it bites only rarely and has venom of low toxicity. Many studies have shown that outside a few endemic areas, most alleged spider bites are, in fact, methicillin-resistant *S. aureus* infections and should be treated accordingly.

UNCOMMON CAUSES

A less common cause of skin ulcers is cutaneous diphtheria (*Corynebacterium diphtheriae*). On several island groups in the southwestern Pacific, *Haemophilus ducreyi* causes nonvenereal cutaneous ulcers. *Trypanosoma brucei rhodesiense*, the causative agent of African trypanosomiasis, can produce a chancre at the bite site of the transmitting tsetse fly (*Glossina* spp.). Several sexually transmitted infections (e.g., syphilis [*Treponema pallidum*], chancroid [*H. ducreyi*]), also can ulcerate the skin.

MISCELLANEOUS SKIN INFECTIONS

Bite-Associated

Wound infections after cat and dog bites are caused by a variety of microorganisms including *S. aureus*, α-, β-, and γ-hemolytic streptococci, several genera of gram-negative organisms, and several anaerobes. *Pasteurella multocida* infection classically occurs after cat bites but also can occur after dog bites. Patients lacking spleens are at particular risk for severe cellulitis and sepsis due to *Capnocytophaga canimorsus* after dog bites. Management of cat and dog bites includes consideration of rabies postexposure prophylaxis (see Sec. 5, Part 2, Ch. 18, Rabies), as well as tetanus immunization and antibiotic prophylaxis. Avoid primary closure of puncture wounds and dog bites to the hand.

Antibiotic prophylaxis after dog bites is controversial, although most experts treat patients lacking spleens prophylactically with amoxicillin-clavulanate. Consider antibiotic prophylaxis of cat bites (*P. multocida*) with amoxicillin-clavulanate or a fluoroquinolone for 3–5 days.

Monkey bite management includes wound care, tetanus immunization, rabies postexposure prophylaxis, and consideration of antimicrobial prophylaxis. Bites and scratches from Old World macaque monkeys showing no signs of illness have been associated with fatal encephalomyelitis due to B virus infection in humans (see Sec. 5, Part 2, Ch. 1, B Virus); valacyclovir is the recommended postexposure prophylaxis for high-risk macaque exposure.

Water-Associated

Skin and soft tissue infections (SSTI) can occur after exposure to fresh, brackish, or salt water, particularly if the skin's surface is compromised. Skin trauma (e.g., abrasions or lacerations sustained during swimming or wading, bites or stings from marine or aquatic creatures, puncture wounds from fishhooks) can result in waterborne infections.

The most virulent SSTIs associated with marine and estuarine exposures are due to *Vibrio vulnificus* and related non-cholera *Vibrio*. For freshwater exposures, *Aeromonas hydrophila* is the most dangerous pathogen. A variety of skin and soft tissue manifestations can occur in association with these infections, including abscess formation, cellulitis, ecthyma gangrenosum, and necrotizing fasciitis.

Pending identification of a specific organism, treat acute infections related to aquatic injury with an antibiotic that provides both gram-positive and gram-negative coverage (e.g., fluoroquinolone or third-generation cephalosporin).

MYCOBACTERIUM MARINUM

M. marinum lives in brackish water. Infection can occur on skin surfaces injured by minor abrasions or shallow puncture wounds; typical locations include knees, shins, and the dorsal surfaces of hands and feet where water-associated minor trauma occurs most commonly.

Patients often describe divergent healing patterns after minor water-associated injury—areas that were injured but not infected heal quickly, whereas areas that were injured and infected with *M. marinum* go on to develop the irregularly bordered, expanding, multinodular violaceous plaques characteristic of this infection. Treatment with antimycobacterial agents for weeks to months is required because lesions do not resolve spontaneously. Occasionally, lymphocutaneous or sporotrichoid spread of infection (see the discussion earlier in this chapter) can occur, resulting in

proximal movement of lesions along superficial lymphatics.

PSEUDOMONAS AERUGINOSA

So-called "hot tub folliculitis" can occur after using inadequately disinfected swimming pools or hot tubs. Folliculitis (tender or pruritic follicular centric red papules, papulopustules, or nodules) typically develops 8–48 hours after exposure to water contaminated with *Pseudomonas aeruginosa*. Usually, several dozen discrete lesions occur on skin surfaces submerged in the infectious water. Most patients have malaise, some have low-grade fever. The condition is self-limited to 2–12 days; typically, no antibiotic therapy is required.

SHEWANELLA

Shewanella, a genus of motile gram-negative bacilli found in warm marine waters worldwide, causes SSTIs that clinically and epidemiologically resemble *V. vulnificus* infections. Patients, often those with chronic liver disease, can develop sepsis and multiple organ failure. Migrants crossing the Mediterranean with prolonged exposure of their feet and legs to contaminated seawater have developed *Shewanella* infection.

VIBRIO

Necrotizing *Vibrio vulnificus* skin infections can occur when contaminated brackish or saltwater, or the juices or drippings from contaminated raw or undercooked seafood, contact open wounds. Infections also happen from consuming *Vibrio*-contaminated shellfish. The illness is especially severe in people with underlying liver disease and can manifest as a dramatic cellulitis with hemorrhagic bullae and severe sepsis. In general, infections caused by these organisms can be more severe in immunosuppressed people.

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DELUSIONAL PARASITOSIS

Susan McLellan

Delusional parasitosis (DP) is the term most often applied to a condition in which a patient presents to a health care provider with an established conviction that they are infected with an arthropod or parasite. Although not unique to travelers, many of those who present with DP have a history of travel, and travel and tropical medicine specialists often assist in evaluating these patients at the request of colleagues.

CLINICAL PRESENTATION

Primary DP is diagnosed when no underlying medical conditions typically associated with disordered thinking are present. Affected people frequently were previously successful in their professions, relationships, and other activities. In the absence of a prior history of a mental health disorder, DP is considered only after multiple visits for care. Symptoms (e.g., itching, skin sensations) are most common and lead to a preponderance of literature from the dermatologic field. Clinical manifestations also can be neurologic (e.g., "brain fog," fatigue, pain, weakness); gastrointestinal (e.g., constipation, diarrhea, sensation of movement in the gut); and auditory or visual. Morgellons syndrome is a specific variant in which sufferers see fibers emerging from the skin.

Secondary DP occurs in association with identifiable health conditions (e.g., alcoholism, bipolar disease, severe depression, drug abuse, schizophrenia, syphilis, thyroid disorders, vitamin deficiencies). In such cases, treatment of the underlying condition might resolve the fixation on parasite infestation.

Unique to DP is the conviction that the illness is due to a parasite, and the frequent auditory or visual identification of it; patients often can describe or draw the organism ("a blue and black body with 8 legs") or define activity and intent ("they buzz when they get angry"). Submitting multiple specimens collected from clothing, orifices, skin, stool, toilets, and around the house is common (the "specimen sign"). With the advent of mobile phones, we now also have the "digital specimen sign," photographs of skin lesions and purported parasites. In many cases, family members or friends are drawn into the delusion in a "folie a deux"; in a more disturbing scenario, a parent might project the delusion onto a child, resulting in potentially harmful attempts to cure the illness.

People suffering from DP can present without objective physical manifestations, or, in the classic dermatologic case, with few to extensive skin lesions attributed to the parasite. Patients might have tried multiple home therapies, including potentially toxic applications or injections (e.g., pouring permethrin in the ears to quell the buzzing of the insects, as reported by one of my patients). Patients often are prescribed empiric treatments for parasitic or arthropod infections by well-meaning practitioners. These treatments are rarely successful, but they are often reported to have provided temporary symptomatic relief—a placebo effect reinforcing the patient's erroneous belief that they are infected with a parasite.

Often, the next step is referral to a specialist, with the hope on the part of the referring provider that "they will know something I don't," "the patient will believe Dr X," or "Dr X will assume care of the patient." Eventually, depending on their presentation, description of symptoms, and the number of practitioners seen, a patient with DP will have undergone multiple examinations of specimens, biopsies of skin or other body parts, colonoscopies, imaging, and

laboratory evaluations, none of which reveals a reasonable parasitic cause for their symptoms, and which are usually all "normal."

Suggestions to consider alternative diagnoses are rarely accepted; in particular, recommendations that the patient try psychiatric medications, even just for symptom relief, are frequently met with anger and rejected out of hand. Both patient and practitioner become frustrated; the patient feels they are being told "it's all in your head," and the practitioner is exhausted from the attempt to be compassionate and medically appropriate while faced with an often angry and occasionally insulting patient.

APPROACH & MANAGEMENT

Therapy for DP has relied on the use of antipsychotics. Pimozide, which selectively blocks dopamine type-2 receptors, was the drug first reported to be useful in the condition, and several series indicated a good response in most patients who accepted it. Currently, second-generation antipsychotics (SGAs) are preferred because of a lower side effect profile; no randomized clinical trials are available, however, and reported cases suggest similar efficacy.

Hence, our paradoxical "state of the art" is to treat a patient who is convinced that they do not have a mental health issue with a recognizable antipsychotic. Getting to a point where the patient will consider such medication takes nuanced communication, sympathy, and a great deal of time over multiple appointments. Referral for psychiatry consultation is notoriously unsuccessful. How best to approach the patient who presents with a fixed conviction that they have a parasite, then? Two concrete characteristics are necessary for a successful therapeutic relationship to develop: (1) the provider must be willing to take on a patient who will be complicated, emotionally challenging, needy, and time consuming; and (2) the patient must be willing and able to maintain a relationship and follow up with the provider, meaning the provider must be both geographically and financially accessible.

Ideally, the patient has a primary care provider (PCP) who can act as the long-term caregiver and assure that any other medical needs are being addressed in an integrated manner. Unfortunately, in many cases, the DP sufferer has rejected early providers and is at the stage of traveling long distances to seek out "experts" with whom they cannot feasibly establish an ongoing relationship. In such cases, one approach is for the "expert" to require that the patient identify a PCP, and to discuss the case with them with the goal of education and support, to assure a reasonable work-up for true parasites or any other underlying reversible causes, and to assist and guide them in working with the patient. Such long-distance consultation might enable rebuilding of the PCP–patient relationship with assurance that the "experts" are guiding the diagnostic and therapeutic approach.

Whichever provider accepts a patient with potential DP, a long-term relationship should be expected. Moriarty et al. have suggested a thoughtful, phased, multi-visit approach in which the health care provider takes the patient through the stages of considerate but strategic history-taking, managed expectations, appropriate diagnostic approach, and eventual introduction and maintenance of antipsychotic therapy. Low doses of medication are usually effective in improving or resolving symptoms, but maintenance should continue for months, and relapse is common. See Box 11-03 for a list of additional considerations.

Treating patients with DP can be exhausting and frustrating, and it is easy for practitioners to dismiss these patients as out of their scope of expertise and disruptive to their usual practice. If a relationship of trust can be maintained, however, pharmacologic therapy combined with ongoing behavioral support can be successful in reversing a debilitating condition. Primary care providers should be encouraged and enabled to provide these interventions; specialists with experience in DP can be invaluable as mentors, even from a distance.

BOX 11-03 Delusional parasitosis: management suggestions for health care providers

CREATE A WORKING RAPPORT

Allow the patient to tell their story but set limits on expectations for each visit.

Assure patients they are not alone in having these kinds of problems (e.g., "We have seen this before and have been able to help.").

Neither agree nor argue with patients about the delusion itself, but affirm the severity and significance of the symptoms they describe.

CONDUCT AN APPROPRIATE WORK-UP

Do not be distracted by the patient's interpretation of cause; pay attention to the history and consider alternative conditions that can cause similar symptoms.

Review records, including all medications, both prescribed and over the counter; obtain basic laboratory studies and thyroid function and sedimentation rate; consider hepatitis and HIV testing, syphilis serology, toxicology, vitamin deficiencies.

Send specimens brought in for formal analysis; allow the patient to choose the best examples.

MANAGEMENT

Reassure patients about the results of basic laboratory tests (e.g., "The labs we have done indicate that your bone marrow, kidneys, liver, thyroid, etc., are all healthy and working properly.").

As clinical reports return indicating no parasites found in specimens and no other underlying pathologies, introduce the idea of symptom control as a strategy (e.g., "We know it is safe to focus on symptoms even if we haven't found the cause.").

Don't make a distinction between mental and physical health; instead, discuss the growing understanding of the mind–body connection and how we are just learning about how neurologic signaling affects our bodily well-being.

Explain the use of an antipsychotic drug in terms of addressing the mind–body connection (e.g., "You don't have schizophrenia, but this medication has helped people who have the same kind of problem; we don't yet fully understand how or why it works.").

As much as possible, recruit the patient's family and friends to help the patient normalize what might have been a severely disrupted life.

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. . . *perspectives* chapters supplement the clinical guidance in this book with additional content, context, and expert opinion. The views expressed do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

SEXUALLY TRANSMITTED INFECTIONS

Hilary Reno, Laura Quilter

More than 2 dozen bacterial, viral, and parasitic pathogens can cause sexually transmitted infections (STIs). STIs are among the most common infectious diseases reported worldwide. In 2018, ≈26 million new STI cases were reported in the United States; and in 2016, ≈376 million cases of chlamydia, gonorrhea, syphilis, and trichomonas were reported globally. STIs can be transmitted from person to person during sexual activity involving anal, genital, or oral mucosal contact.

EPIDEMIOLOGY

Casual sex during travel is common; a systematic review showed a 35% prevalence. In addition, some people travel for sex tourism (see Sec. 9, Ch. 12, Sex & Travel). Sex partners abroad might include commercial sex workers among whom STI prevalence is elevated. International travel was an independent risk factor for chlamydia infection in a study conducted at one sexual health clinic. Among travelers, documented risk factors for acquiring STIs or HIV include alcohol and other drug use, longer duration of travel, male gender, and increased number of new partners.

Before travel, counsel travelers at risk of engaging in condomless sex to have condoms available, and provide guidance regarding other risk-modifying behaviors. Providers caring for returning travelers should know where to find current information about global epidemiology and antimicrobial resistance patterns of STIs from national and international public health authorities, such as the Centers for Disease Control and Prevention (CDC) Antibiotic-Resistant Gonorrhea website (www.cdc.gov/std/gonorrhea/arg/default.htm) and World Health Organization (WHO), Gonococcal Antimicrobial Resistance (AMR) Surveillance Programme (www.who.int/data/gho/data/themes/topics/who-gonococcal-amr-surveillance-programme-who-gasp).

The epidemiology and clinical presentations of common bacterial, viral, and parasitic STIs are shown in Table 11-13, Table 11-14, and Table 11-15, respectively. Ask returning travelers about sexual activity during their trip, and include specific questions about region of travel, sexual partners, types of sexual exposure, and condom use. Assessing risk in men who have sex with men (MSM) is important because they have elevated rates of certain infections, including chlamydia, gonorrhea, lymphogranuloma venereum, and syphilis. Screen travelers seeking an evaluation for STI or with evidence of STI for other common STIs as well as HIV. For patients with HIV infection, provide information on HIV care and treatment services if they are not already receiving care.

CLINICAL PRESENTATION

Because many infections are asymptomatic, assess for chlamydia, gonorrhea, HIV, and syphilis in returning travelers who had sex outside of a monogamous relationship while traveling. Advise any traveler who develops STI symptoms (e.g., rectal, urethral, or vaginal discharge; unexplained rash or genital lesion; genital or pelvic pain) following a sexual exposure to abstain from sex and seek prompt medical evaluation.

Human papillomavirus (HPV) infection is commonly acquired ≤2 years of sexual debut and usually clears spontaneously. Although most STIs involve the genital tract, some (e.g., gonorrhea, herpes, syphilis) also cause disseminated disease. Consider STIs in returning travelers, because infection can result in serious and long-term complications including adverse birth outcomes, cancer (anal and cervical), infertility, pelvic inflammatory disease, and an increased risk for HIV acquisition and transmission.

Table 11-13 Epidemiology, clinical manifestations, diagnosis, & treatment of select bacterial STIs

STI *CAUSATIVE ORGANISM*	GEOGRAPHIC DISTRIBUTION	TYPICAL CLINICAL PRESENTATION (OFTEN ASYMPTOMATIC)	INCUBATION PERIOD	DIAGNOSIS	FIRST-LINE THERAPY
CHANCROID *Haemophilus ducreyi*	Regional (Africa, Asia, Caribbean)	Irregular, painful genital ulcer Tender, suppurative inguinal lymphadenopathy	4–7 days	Culture with specialized media	Azithromycin 1 g PO ×1 OR Ceftriaxone 250 mg IM ×1 OR Ciprofloxacin 500 mg PO BID ×3 d OR Erythromycin base 500 mg PO TID ×7 d
CHLAMYDIA *Chlamydia trachomatis*	Worldwide	Cervicitis Urethritis	7–21 days	NAAT	Doxycycline 100 mg PO BID ×7 d OR Azithromycin 1 g PO ×1
GONORRHEA *Neisseria gonorrhoeae*	Worldwide	Cervicitis Urethritis	1–14 days	NAAT	Ceftriaxone 500 mg IM ×1
GRANULOMA INGUINALE (DONOVANOSIS) *Klebsiella granulomatis*	Southern Africa Australia India Papua New Guinea	Extensive genital ulcerations with granulation and easy bleeding Tender lymphadenopathy	4–28 days	Microscopy shows Donovan bodies in macrophages	Azithromycin 1 g PO weekly ×3 weeks or until resolution OR Azithromycin 500 mg PO daily ×3 weeks or until resolution

(*continued*)

Table 11-13 Epidemiology, clinical manifestations, diagnosis, & treatment of select bacterial STIs (continued)

STI *CAUSATIVE ORGANISM*	GEOGRAPHIC DISTRIBUTION	TYPICAL CLINICAL PRESENTATION (OFTEN ASYMPTOMATIC)	INCUBATION PERIOD	DIAGNOSIS	FIRST-LINE THERAPY
LYMPHOGRANULOMA VENEREUM *Chlamydia trachomatis* serovar L1-3	Worldwide	Self-limited ulcer Tender inguinal lymphadenopathy Proctocolitis	3–30 days	NAAT, serology	Doxycycline 100 mg PO BID ×21 d
SYPHILIS *Treponema pallidum*	Worldwide	Primary syphilis Typically painless (can be painful) genital ulcer Regional lymphadenopathy Secondary syphilis Maculopapular skin rash	10–90 days	Darkfield microscopy (primary infection) Serology	Benzathine penicillin G 1°, 2°, and early latent infection: 2.4 MU IM ×1 Late latent infection or latent syphilis of unknown duration: 2.4 MU IM weekly ×3 weeks

Abbreviations: BID, twice daily; IM, intramuscularly; MU, million units; NAAT, nucleic acid amplification testing; PO, orally; STI, sexually transmitted infection; TID, 3 times daily.

Table 11-14 Epidemiology, clinical manifestations, diagnosis & treatment of select viral STIs

STI *CAUSATIVE ORGANISM*	GEOGRAPHIC DISTRIBUTION	TYPICAL CLINICAL PRESENTATION (OFTEN ASYMPTOMATIC)	INCUBATION PERIOD	DIAGNOSIS	FIRST-LINE THERAPY
HEPATITIS A Hepatitis A virus	Worldwide	Anorexia Fatigue Jaundice Malaise	28 days	Serology	Supportive care (see Sec. 5, Part 2, Ch. 7, Hepatitis A)
HEPATITIS B Hepatitis B virus	Worldwide	Anorexia Fatigue Jaundice Malaise	60–150 days	Serology	Several options available (see Sec. 5, Part 2, Ch. 8, Hepatitis B) Consult with an expert
HEPATITIS C Hepatitis C virus	Worldwide	Anorexia Fatigue Jaundice Malaise	15–50 days	Serology	Several options available (see Sec. 5, Part 2, Ch. 9, Hepatitis C) Consult with an expert
HERPES SIMPLEX Herpes simplex virus (HSV)	Worldwide	≥1 typically painful (can be painless) genital ulcers	2–7 days	Culture or PCR	Acyclovir 400 mg PO TID ×7–10 d OR Valacyclovir 1 g PO BID ×7–10 d OR Famciclovir 250 mg PO TID ×7–10 d
GENITAL WARTS Human papillomavirus (HPV)	Worldwide	Warts	14–240 days	Clinical or pathologic	Topical therapy or removal of lesions

Abbreviations: BID, twice daily; IM, intramuscularly; PCR, polymerase chain reaction; PO, orally; STI, sexually transmitted infection; TID, 3 times daily.

Monkeypox

Although not considered an STI, transmission of monkeypox virus during the 2022 multinational outbreak has been associated with close skin-to-skin contact, including that which occurs during sex. Moreover, some patients have presented with physical findings and/or symptoms that could be consistent with an STI (e.g., anogenital lesions, proctitis, dysuria). In some instances, this has resulted in misdiagnosis and delays in initiating proper medical management. In other cases, patients have been co-infected with monkeypox virus and an STI. For details on the transmission, epidemiology, and management of monkeypox during the 2022 monkeypox outbreak, see Sec. 5, Part 2, Ch. 22, Smallpox & Other

Table 11-15 Epidemiology, clinical manifestations, diagnosis & treatment of select parasitic STIs

STI *CAUSATIVE ORGANISM*	GEOGRAPHIC DISTRIBUTION	TYPICAL CLINICAL PRESENTATION (OFTEN ASYMPTOMATIC)	INCUBATION PERIOD	DIAGNOSIS	FIRST-LINE THERAPY
TRICHOMONIASIS *Trichomonas vaginalis*	Worldwide	Vaginal discharge, itching	5–28 days	NAAT	Metronidazole Females: 500 mg PO BID ×7 d Males: 2 g PO ×1 OR Tinidazole 2 g PO ×1 (both females & males)

Abbreviations: BID, twice daily; NAAT, nucleic acid amplification testing; PO, orally; STI, sexually transmitted infection

Orthopoxvirus-Associated Infections; Sec. 9, Ch. 12, Sex & Travel; and www.cdc.gov/poxvirus/monkeypox/index.html.

TREATMENT

Base STI evaluation, management, and follow-up on the most recent national and international guidelines from CDC and WHO. Because of limited availability of diagnostic testing in many countries, WHO follows a syndromic approach to STI management; in the United States, therefore, following CDC treatment guidelines is preferred. Consider drug resistance if an infection does not respond to first-line therapy. This is particularly relevant in travelers who have a persistent gonococcal infection, given the global spread of multidrug-resistant *Neisseria gonorrhoeae*.

PREVENTION

Prevention and control of STIs is based on accurate risk assessment, counseling and education, early identification of asymptomatic infection, and effective treatment of travelers; prompt evaluation and treatment of sex partners also is necessary to prevent reinfection and to disrupt STI transmission. As part of pretravel advice, include specific messages and strategies on how to avoid acquiring or transmitting STIs. Abstinence or mutual monogamy between uninfected partners is the most reliable way to avoid acquiring and transmitting STIs.

For people whose sexual behaviors place them at risk for STIs, correct and consistent use of external or internal latex condoms can reduce the risk for HIV infection and other STIs, including chlamydia, gonorrhea, and trichomoniasis. Preventing lower genital tract infections might reduce the risk for pelvic inflammatory disease in female patients. Correct and consistent use of latex condoms also reduces the risk of chancroid, genital herpes, HPV infection, and syphilis. Advise travelers to use only water-based lubricants with latex condoms, because oil-based lubricants (e.g., massage oil, mineral oil, petroleum jelly, shortening) can weaken latex. Also remind travelers that contraceptive methods that are not mechanical barriers (e.g., oral contraceptives) do not protect against HIV or other STIs, and that spermicides containing nonoxynol-9 do not prevent HIV or STIs.

Preexposure vaccination is among the most effective methods for preventing certain STIs. HPV vaccines, for example, are available and licensed for people ≤45 years of age. Both hepatitis A and hepatitis B can be transmitted sexually (see Sec. 5, Part 2, Ch. 7, Hepatitis A, and Sec. 5, Part 2, Ch. 8, Hepatitis B). The Advisory Committee on Immunization Practices (ACIP) recommends hepatitis B vaccination for all adults aged 19–59 years, and hepatitis A vaccine for MSM. Travelers at risk of acquiring HIV infection might benefit from preexposure prophylaxis (see Sec. 5, Part 2, Ch. 11, Human Immunodeficiency Virus / HIV, and www.cdc.gov/hiv/prep).

CDC website: www.cdc.gov/std

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NEWLY ARRIVED IMMIGRANTS, REFUGEES & OTHER MIGRANTS

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Millions of travelers enter the United States every year. The majority are non-immigrants (e.g., short-term visitors, students, and temporary workers), but others are immigrants, refugees, or other migrants. Table 11-16 outlines the various immigrant and non-immigrant arrivals into the United States during fiscal year 2019. Many arriving travelers and migrants will encounter the US health care system during their stay; therefore, at some time during their careers, US health professionals likely will provide care to newly arrived foreign-born patients.

Most newly arrived travelers and migrants do not undergo an official medical examination prior to their travel to the United States, but for others, a medical examination is required by the Immigration and Nationality Act (INA). The INA mandates that all immigrants and refugees undergo a medical screening examination before travel to the United States to identify inadmissible health conditions.

The Centers for Disease Control and Prevention (CDC) develops the guidance for and monitors the quality of the screening medical examinations for people who fall under relevant categories listed in Table 11-16. CDC also provides guidance for additional pretravel public health interventions and post-arrival medical screening for US-bound refugees (described later in this chapter). In contrast, no specific guidelines cover the examination of people who do not hold an immigrant or refugee visa, or people categorized as temporary visitors or undocumented migrants.

Table 11-17 summarizes requirements and recommendations for overseas and post-arrival

Table 11-16 Immigrant & non-immigrant arrivals to the United States, fiscal year (FY) 2019

ENTRANT CATEGORY	DESCRIPTION	NUMBER OF ARRIVALS, FY 2019
IMMIGRANTS	Immigrant arrivals from foreign countries	460,000
	Lawful permanent residents[1] status–adjusters	570,000
	International adoptees	4,000
REFUGEES	For definition, see Box 11-04	30,000
NONREFUGEE MIGRANTS & OTHER TRAVELERS	Long-term visitors[2]	6 million
	Other non-immigrant entrants	180 million

[1]Also known as "Green Card holders."

[2]Includes people staying >6 months (e.g., exchange visitors, students, temporary workers).

health examinations and public health interventions for immigrants, refugees, and other migrants. For definitions of immigrants, refugees, and other migrants, and the special categories of medical professionals (i.e., panel physicians, civil surgeons) who see them before and after arrival to the United States, see Box 11-04.

THE PRETRAVEL HEALTH ASSESSMENT

Immigrants

OVERSEAS MEDICAL SCREENING EXAMINATION

A medical screening examination is mandatory for all immigrant visa applicants. CDC guidelines

Table 11-17 Health examination & intervention requirements for immigrants, refugees & other migrants

ENTRANT CATEGORY	OVERSEAS (PREDEPARTURE)			AFTER ARRIVAL
	HEALTH ASSESSMENT	VACCINATIONS	OTHER INTERVENTIONS	MEDICAL EXAMINATION
IMMIGRANTS	Required[1]	Required[2]	None[3]	None[3]
REFUGEES	Required[4]	Recommended[5]	Various (see text)[6]	Recommended (usually done)[7]
OTHER MIGRANTS	None[3]	None[3]	None[3]	None[3]

[1]See www.cdc.gov/immigrantrefugeehealth/panel-physicians.html.

[2]See www.cdc.gov/immigrantrefugeehealth/panel-physicians/vaccinations.html.

[3]No requirements or recommendations.

[4]See www.cdc.gov/immigrantrefugeehealth/guidelines/overseas-guidelines.html.

[5]See www.cdc.gov/immigrantrefugeehealth/guidelines/overseas-guidelines.html#vaccination-program.

[6]See www.cdc.gov/immigrantrefugeehealth/guidelines/refugee-guidelines.html.

[7]See www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/domestic-guidelines.html.

BOX 11-04 Definitions: immigrants, refugees, other migrants & the medical professionals who see them

IMMIGRANT

A foreign-born person traveling to the United States on an official immigrant visa.

MIGRANT

Any person who moves away from their home, either temporarily or permanently, for any reason. This term is not defined under international law and can apply to a wide range of people. In this chapter, we use the term broadly to describe both immigrants and refugees, as well as other people settling in the United States, whether temporarily or permanently (e.g., undocumented immigrants and others).

REFUGEE

A refugee, according to Article 1 of the 1951 Refugee Convention, is a person who is outside their country of nationality or habitual residence; has a well-founded fear of persecution because of their race, religion, nationality, membership in a particular social group or political opinion; and is unable or unwilling to avail themselves of the protection of that country, or to return there, for fear of persecution.[1]

STATUS ADJUSTER

A person who does not arrive on an immigrant visa, but who adjusts their status to lawful permanent resident while in the United States.

TEMPORARY VISITORS

Non-immigrants in the United States for a length of time, as defined by their visa class. Temporary workers and their families, students and exchange visitors, diplomats and other foreign government officials, and people traveling for business or pleasure are all examples of temporary visitors.

CIVIL SURGEONS

US medical doctors authorized by US Citizenship and Immigration Services (USCIS) to perform official immigration medical examinations required for the adjustment of status to lawful permanent resident after arrival in the United States. Approximately 5,000 physicians have been designated as civil surgeons.

PANEL PHYSICIANS

Medical doctors practicing outside the United States, selected by the US Department of State to conduct overseas medical screening examinations for immigrants and refugees bound for the United States. More than 600 panel physicians perform these examinations worldwide.

[1]See www.unhcr.org/en-us/news/stories/2001/6/3b4c06578/frequently-asked-questions-1951-refugee-convention.html#_Toc519482140.

for this examination, referred to as Technical Instructions, are available at www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/technical-instructions-panel-physicians.html. The purpose of the screening examination is to detect inadmissible health conditions, including communicable diseases of public health significance, mental health disorders associated with harmful behaviors, and substance-use or substance-induced disorders. The medical screening process includes a brief physical examination, a mental health evaluation, a review of vaccination records, testing for gonorrhea (by nucleic acid amplification), testing for syphilis (by serology), and tuberculosis (TB) screening.

Chest radiographs are required for all applicants ≥15 years of age. Applicants 2–14 years old from high TB-burden countries (i.e., countries with incidence rates ≥20 cases per 100,000 population as estimated by the World Health Organization) must have an interferon-γ release assay (IGRA); those with a positive IGRA are required to have chest radiographs. Additional acid-fast bacillus smears and sputum cultures are required for anyone whose x-ray is suspicious for TB, has signs or symptoms compatible with TB disease, or has known HIV infection. For anyone diagnosed with TB disease, CDC's Technical Instructions require *Mycobacterium tuberculosis* culture, drug-susceptibility testing, and directly observed TB therapy through the end of treatment before immigration is permitted. Pre-immigration treatment also is required for certain other inadmissible conditions, including gonorrhea, syphilis, and leprosy (Hansen's disease).

CLASSIFICATION OF MEDICAL CONDITIONS

Medical conditions of public health significance are categorized as either Class A or Class B. Class

A, or inadmissible, conditions preclude entry into the United States. An immigrant with a Class A condition might be issued a visa after the condition has been treated or after the Department of Homeland Security US Citizenship and Immigration Services (USCIS) approves a waiver of visa ineligibility. Class B conditions indicate a departure from normal well-being, and post-arrival follow-up with a health care provider is recommended.

PRE-ARRIVAL VACCINATIONS

Before immigration to the United States, immigrant visa applicants are required to receive any age-appropriate, Advisory Committee on Immunization Practices (ACIP)–recommended vaccines that are available in their country of residence. Panel physicians administer vaccines according to CDC's Vaccination Technical Instructions for Panel Physicians and Civil Surgeons (www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/vaccination-panel-technical-instructions.html). These instructions are based on ACIP recommendations, with some modifications for immigrants.

HEALTH NOTIFICATIONS AT THE TIME OF ARRIVAL

CDC informs state or local health departments of all arriving immigrants who have received USCIS waivers for Class A (notifiable) conditions, as well as those who have Class B conditions for which follow-up is recommended. Panel physicians document this information in eMedical, an electronic health processing system used to record and transmit most immigrants' medical examination information. State and local health departments performing medical follow-up are asked to report their findings back to CDC, along with information about any other serious conditions of public health concern identified. This reporting helps CDC track epidemiologic patterns of disease among these populations and enables monitoring of the quality of overseas medical examinations.

Internationally Adopted Children

OVERSEAS MEDICAL SCREENING EXAMINATION

Children adopted internationally by parents residing in the United States (see Sec. 7, Ch. 5, International Adoption) are considered a subcategory of immigrants. As such, an overseas medical screening examination is mandatory, as described in the Technical Instructions.

VACCINATIONS

Parents adopting children internationally can request an immunization waiver for children <10 years of age by agreeing to begin immunizations ≤30 days of arrival in the United States; they should, however, be made aware of the potential health risks associated with delaying the immunization process, even by a month. Vaccinating children before their arrival to the United States reduces the child's risk of contracting and importing diseases of public health concern, such as measles, which was reported in unvaccinated children adopted from China in 2004, 2006, and 2013. Of note, as of October 2021, some internationally adopted children (depending on age and country of departure) are required to receive an approved coronavirus disease 2019 (COVID-19) vaccine prior to leaving for the United States.

HEALTH NOTIFICATIONS AT THE TIME OF ARRIVAL

The guidance applying to immigrants regarding health notifications at the time of arrival also applies to internationally adopted children.

US-Bound Refugees

Refugees come to the United States through the US Refugee Admissions Program (USRAP). Whereas immigrants travel to the United States individually or with their families, refugees resettle in groups, on a predetermined schedule, with a 3- to 6-month window between the required medical screening examination and departure.

OVERSEAS MEDICAL SCREENING EXAMINATION

Like immigrants, refugees resettling to the United States are required to undergo an overseas medical screening examination with a panel physician. The content and Technical Instructions for this examination are identical to those for immigrants.

PRE-ARRIVAL VACCINATIONS

Unlike immigrants, refugees bound for the United States are not statutorily required to

be vaccinated, leaving them vulnerable to vaccine-preventable diseases during the migration process. In response, a voluntary global immunization program for US-bound refugees was implemented in 2012 as a public health intervention to protect the health of refugees and US health security.

Through this program, overseas panel sites offer refugees bound for the United States most ACIP-recommended vaccines (≤2 doses per vaccine) depending on age, documented immunization history or records, and vaccine availability. Pre-vaccination testing for Hepatitis B virus infection using hepatitis B surface antigen (HBsAg) is also offered where available. The vaccine schedule for US-bound refugees is based on CDC guidance and can be found at www.cdc.gov/immigrantrefugeehealth/guidelines/overseas/interventions/immunizations-schedules.html.

Resettled refugees applying for permanent residence in the United States ≥1 year after their arrival are not required to undergo a repeat medical examination; instead, they must demonstrate proof of receipt of age-appropriate, ACIP-recommended vaccinations to a US civil surgeon during the adjustment-of-status process. In some states, refugees' overseas vaccination records are transferred electronically to state immunization information systems.

OTHER OVERSEAS PUBLIC HEALTH INTERVENTIONS

The 3- to 6-month window between the predeparture medical screening examination and departure affords an opportunity to implement additional public health interventions aimed at improving the health of US-bound refugees and ensuring US health security.

PARASITIC INFECTIONS: PRESUMPTIVE TREATMENT

Many refugees resettle to the United States from places with high prevalence of region-specific parasites and other neglected tropical diseases. Depending on regional epidemiology, panel physicians offer refugees presumptive oral therapy to treat malaria (artemether/lumefantrine), intestinal roundworms (albendazole), schistosomiasis (praziquantel), and *Strongyloides stercoralis* (ivermectin) days before the refugee departs for the United States. Details on each of these diseases and their treatment can be found in Section 5, Travel-Associated Infections & Diseases.

Data from 2 large evaluations indicate that this strategy dramatically decreases the prevalence of soil-transmitted helminth infections among US-bound refugees. For further details and regional treatment recommendations, see www.cdc.gov/immigrantrefugeehealth/guidelines/overseas-guidelines.html#ipg.

FITNESS TO FLY

During the predeparture screening examination, panel physicians might identify refugees who have chronic medical conditions (e.g., cardiac disease, moderate or severe malnutrition, sickle cell disease). While these conditions do not pose a public health risk—and therefore do not make the refugee inadmissible—they can result in decompensation during air travel. CDC, in close collaboration with partners (e.g., the International Organization for Migration), has developed specific protocols to identify, manage, and stabilize refugees with various chronic medical conditions before their departure, with the goal of improving travel fitness (www.cdc.gov/immigrantrefugeehealth/panel-physicians/supplemental-guidance.html).

HEALTH NOTIFICATIONS AT THE TIME OF ARRIVAL

The guidance that applies to immigrants regarding health notifications at the time of arrival also applies to refugees bound for the United States.

NEW-ARRIVAL HEALTH ASSESSMENT

In addition to screening for diseases, consider the new-arrival health assessment as an opportunity to deliver needed health care, preventive health services (e.g., vaccines), and individual counseling. Taken together, these activities serve to establish a medical "home" where people newly arrived in the United States can receive ongoing primary care and an orientation to the US health care system.

Challenges to providing comprehensive health services to people newly arrived in the United States include a general lack of health care provider

familiarity with diseases endemic to the migrant's country of origin; lack of access to trained interpreters and translators; insufficient knowledge of social and cultural beliefs and practices of immigrants and migrants; and uncertainty about which elements of the overseas pretravel assessments (screening tests, vaccinations) were completed or when. In addition, immigrants and refugees often have other resettlement priorities (e.g., attending English classes or school, locating permanent housing and work) that can take precedence over accessing health care services.

Medical Screening

Ideally, all immigrants, refugees, and other migrants should receive screening for migration-associated illnesses, communicable and noncommunicable diseases, and any age-appropriate screening. Screening for infectious diseases of long latency, especially hepatitis B, HIV, and TB, is crucial for almost all groups; at each subsequent medical encounter, ensure completeness of screening.

Screening each person for diseases specific to their country of origin, migration route, and individual epidemiologic risk also is important. The Minnesota Center for Excellence in Refugee Health has developed an interactive clinical assessment tool, Clinical Assessment for Refugees (CareRef; https://careref.web.health.state.mn.us), based on CDC's Domestic Screening Guidance for Newly Arrived Refugees (www.cdc.gov/immigrantrefugeehealth/guidelines/domestic-guidelines.html). CareRef customizes screening guidance for refugees based on their age, sex, and country of origin. No standard guidelines cover other migrant groups, but the following sections provide an approach, with modified guidance based on experience with refugees and internationally adopted children.

Immigrants & Other Nonrefugee Migrants

Immigrants and other nonrefugee migrants enter the country in different ways, and access health care at different points and with providers who have varying levels of expertise in migrant medicine. Nonetheless, they can derive important benefits from their introduction to the US health care system and participation in a comprehensive new-arrival health assessment. Unlike refugees, who are eligible to receive Medicaid funding or Refugee Medical Assistance (described later in this chapter), immigrants and other nonrefugee migrants do not have access to funding sources to cover the costs of a standard comprehensive health assessment.

INITIAL ASSESSMENT

Initial assessment should include taking a medical and family history and reviewing all medications and treatments a person received before and during migration. Most experts agree that testing for hepatitis B, HIV, and TB should be performed for all new immigrants and other nonrefugee migrants who do not have documentation of post-arrival screening. Repeat screening for these infections if risk is ongoing.

For most people, a complete blood count with differential facilitates finding evidence of a hemoglobinopathy or diagnosing anemia or eosinophilia. Urinalysis, although no longer routinely recommended for screening of asymptomatic people, might be appropriate if the person has symptoms of renal disease or signs or symptoms of a urinary tract infection. A basic metabolic panel might be indicated, especially for people of appropriate age or with evidence of conditions such as diabetes or renal disease.

Follow age- and risk-based guidelines provided by the United States Preventive Services Task Force (USPSTF) for the general US population. Consider diagnostic testing of people who present with symptoms consistent with a particular parasite endemic to their country of origin (e.g., malaria, intestinal parasites). Consider screening for sexually transmitted or congenital infections (e.g., chlamydia, gonorrhea, hepatitis C, HIV, syphilis) beyond what is recommended for the US general population if the person's migration history places them at substantial risk. See Table 11-18 and Table 11-19 for a summary of screening tests to consider for new-arrival health assessments.

VACCINATIONS

Many people arrive to the United States without having received predeparture vaccinations. Review all immunization records, laboratory evidence of

Table 11-18 Immigrants & nonrefugee migrants to the United States: recommended new arrival infectious disease screening[1]

SCREENING TEST	AGE	POPULATION	COMMENTS
CBC with differential	All	All	Absolute eosinophilia can be evidence of parasitic infection
Hepatitis B surface antigen[2] (HBsAg)	All	Home country hepatitis B infection prevalence ≥2% People with risk factors	Consider surface antibody testing if unimmunized Consider core antibody testing If surface antibody testing is obtained before a vaccine series is complete, finish the vaccine series even if the antibody result is positive (assuming surface antigen is negative)
Hepatitis C	18–79 years	All Include people outside this age range if risk factors present	For most recent USPSTF guidelines, see Hepatitis C Virus Infection in Adolescents and Adults: Screening (www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/hepatitis-c-screening1)
HIV	>13 years[3]	All May include others outside this age range	Test and evaluate based on standard guidelines
Malaria	All	Clinical signs or symptoms and migration route includes malaria-endemic areas	Consider malaria if symptomatic or from highly endemic area within 3 months of arrival and did not receive predeparture treatment
Parasite serology Schistosomiasis Strongyloidiasis Soil-transmitted helminths	All	Where endemic if high risk for exposure or clinical indication	Consider screening with exposure history, unexplained eosinophilia Some experts treat empirically Empiric treatment for *Strongyloides* is recommended When immigrant is about to receive steroids or become immunocompromised; If testing is unavailable; or When there is insufficient time to obtain results. CAUTION: Individuals from or who have lived in places endemic for *Loa loa*: do not treat presumptively for *Strongyloides* with ivermectin until high microfilarial load from *Loa loa* has been ruled out

(*continued*)

Table 11-18 Immigrants & nonrefugee migrants to the United States: recommended new arrival infectious disease screening (continued)

SCREENING TEST	AGE	POPULATION	COMMENTS
STI Chlamydia Gonorrhea Syphilis Others (as indicated)	15–65 years (<15 if sexually active, if concerns about congenital infection, or if concerns about sexual trauma in any age group)	All	Test choice based on standard guidelines Consider whether migration history adds increased risk
Tuberculosis screen: IGRA	≥2 years	Anyone without a prior documented positive test	Test and evaluate based on standard guidelines Rule out tuberculosis disease and offer treatment for latent tuberculosis infection to people with positive test result
Tuberculosis screen: TST	<2 years		
Urinalysis	All, if clinically indicated	Those with clinical indications	Consider if symptoms of a urinary tract infection are present

Abbreviations: CBC, complete blood count; IGRA, interferon-γ release assay; MCV, mean corpuscular volume; STI, sexually transmitted infection; TST, tuberculin skin test; USPSTF, United States Preventive Services Task Force.

[1]Recommendations outlined in this table are intended for nonrefugee migrants. For comprehensive medical screening recommendations for newly arriving refugees, consult CDC's Domestic Screening Guidance for Newly Arrived Refugees (www.cdc.gov/immigrantrefugeehealth/guidelines/domestic-guidelines.html) and CareRef (https://careref.web.health.state.mn.us/).
[2]Take into account that the prevalence of HBsAg in a country might change over time, hence older birth cohorts could have been at greater risk than younger cohorts.
[3]Consider in younger children who have signs or symptoms of disease, risk factors for transmission, or mother is missing or deceased or has illness compatible with HIV.

immunity, and history of vaccine-preventable diseases. Immunization records provided by patients can be considered valid if, at a minimum, the month and year of the vaccine are documented, and the vaccine was given at an appropriate age according to the US vaccination schedule.

Provide age-appropriate immunizations during an initial encounter with a newly arrived immigrant or migrant, and complete immunization series according to ACIP schedules during subsequent encounters (www.cdc.gov/vaccines/schedules/hcp/index.html). A vaccine series does not need to be restarted if documentation of prior doses is available.

MENTAL HEALTH SCREENING

Mental health screening includes gathering information about coping strategies and support systems, and permits appropriate and timely referral to resources if necessary.

FUTURE TRAVEL

Immigrants and other migrants are likely to travel back to their country of origin and might be at risk for travel-associated infectious diseases (see Sec. 9, Ch. 9, Visiting Friends & Relatives: VFR Travel). Ask these patients about future travel plans to allow time to plan appropriate travel vaccines, medications, and advice.

Table 11-19 Immigrants & nonrefugee migrants to the United States: recommended new arrival toxic & metabolic screening[1]

SCREENING TEST	AGE	POPULATION	COMMENTS
Blood lead level[2]	<16 years People who are pregnant or lactating Clinical indication	All	Consider if no previous lead test and additional risk factors, e.g., • Lived in highly industrialized city with potential exposure to industrial waste; • Developmental delay; or • Medical conditions consistent with lead exposure.
CBC with differential + MCV	All	All	Screen for chronic anemias
Urinalysis (basic metabolic panel)	All, if clinically indicated	Those with clinical indications	Consider if symptoms of renal disease are present

Abbreviations: CBC, complete blood count; MCV, mean corpuscular volume.

[1]Recommendations outlined in this table are intended for newly arrived nonrefugee migrants. For comprehensive medical screening recommendations for newly arriving refugees, consult CDC's Domestic Screening Guidance for Newly Arrived Refugees (www.cdc.gov/immigrantrefugeehealth/guidelines/domestic-guidelines.html) and CareRef (https://careref.web.health.state.mn.us).

[2]Lead screening recommendations are specific to immigrants and nonrefugee migrants and differ slightly from recommendations for newly arrived refugees.

Internationally Adopted Children

See Sec. 7, Ch. 5, International Adoption, for detailed guidance regarding the post-arrival health assessment of international adoptees, and preparation for the family, other household members, and close contacts. In addition, the *Red Book: Report of the Committee on Infectious Diseases*, published by the American Academy of Pediatrics (AAP), offers guidance to pediatricians and other clinicians who will serve this population after their arrival to the United States. *Red Book* is free for AAP members (http://aapredbook.aappublications.org).

Refugees

CDC, in collaboration with the US Department of Health and Human Services Administration for Children and Families' Office of Refugee Resettlement (ORR), clinical and subject matter experts outside CDC, and representatives of the Association of Refugee Health Coordinators (ARHC), has developed evidence-based guidance for domestic refugee medical screening. Comprehensive guidance outlining the screening components and recommended testing is available at www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/domestic-guidelines.html. Population-specific health profiles are available for some refugee populations (Bhutanese, Burmese, Central American minors, Congolese, Iraqi, Somali, and Syrian) at www.cdc.gov/immigrantrefugeehealth/profiles/index.html.

A goal of the domestic refugee health assessment is to arrange and coordinate ongoing primary care. Many refugees have not received age-appropriate screening for chronic conditions (e.g., cancer, diabetes, heart disease; dental, hearing, or vision problems; mental health problems). These screening tests are best introduced in a culturally sensitive way and tailored to the health literacy of the individual patient. Integrating behavioral health screening and services into the domestic health assessment and subsequent primary care visits provides opportunities to screen for acute risk factors and to triage refugees in need of urgent mental health treatment.

Refugees might qualify for state Medicaid programs that cover medical screening and any needed ongoing medical care. Refugees determined ineligible for Medicaid are eligible for Refugee Medical

Assistance in many states, which provides for their medical needs for ≤8 months from their date of arrival. For more information, clinicians and refugees can contact their state health department and can access more information through ORR (www.acf.hhs.gov/programs/orr/programs/cma).

Other published resources available to clinicians include consensus documents on evidence-based screening for newly arriving refugees to Canada, provided by the Canadian Collaboration for Immigrant and Refugee Health (https://ccirhken.ca/ccirh_main).

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