Health Care of the International Traveler

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Introduction

The number of travelers crossing borders each year continues to rise. According to the World Tourism Organization, the number of travelers crossing international borders exceeded 1.4 billion in 2020 [1]. Currently, fewer than half of all international travelers seek a travel consultation prior to departure [2]. A basic understanding of traveler's health is necessary to provide travel advice to patients, as family physicians often bridge the gap between knowledge of a patient's health history and travel medicine. In a recent study, primary care providers were second only to the Internet in patient-identified sources of travel health advice [2].

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Pre-Trip Consultation

A pre-trip consultation is recommended at least 4 to 6 weeks prior to departure. The components of the consultation are history intake, review of routine vaccinations, travel-related vaccinations, traveler's diarrhea treatment and prophylaxis, malaria prophylaxis, review of personal protective measures, altitude illness prophylaxis, and safety and accident prevention.

History Intake

This includes the traveler's pertinent medical history, current medications, and allergies, which may affect choices for both travel-related medications and vaccinations. Anticipatory guidance for chronic conditions such as diabetes, heart disease, asplenism, and immune compromise may also need to be addressed. Vaccination history is also relevant, as live vaccines must be given either simultaneously or 28 days apart. Several important travel-related questions are also pertinent, including purpose of travel, specific locations that will be visited in the destination country or countries, accommodations, and traveler habits.

Routine Vaccinations

The travel visit also presents an opportunity to catch up on routine vaccinations. These may include pneumococcal vaccination, Tdap, herpes zoster vaccine, and flu shots. Especially important to verify are MMR and varicella immunity, as immunity is pertinent for travel to parts of the world where disease burden for these illnesses is relatively high. A second MMR is recommended for many endemic countries for adults who can only have a single documented vaccination during childhood or later.

Travel-Related Vaccinations

Hepatitis A

Hepatitis A is transmitted through fecal-oral contamination. Its prevalence in developing countries is often high, and vaccination is recommended for all destinations in these areas. The illness rarely causes death but morbidity is significant. Severity of illness is variable between age groups; the illness tends to be more severe in adults.

Hepatitis A is a 2-dose vaccine series, with each dose separated by at least 6 months. It is licensed for use in patients 1 year and older and is safe for use in pregnant women. The first hepatitis A shot imparts >90% immunity and, in healthy travelers under 40 years old, can be given at any time prior to departure [3]. In older or immunocompromised travelers, it is recommended that at least one hepatitis A dose be given at least 2 weeks prior to departure to generate adequate immunity [3]. Once both doses are given, immunity is considered lifelong for hepatitis A and no further boosters are needed.

Hepatitis A vaccine also exists in a 3-dose series called Twinrix, where it is combined with a hepatitis B vaccine. Only persons aged 18 and older are eligible to receive the Twinrix vaccine. The vaccine is administered at 0, 1, and 6 months. It is important to note that immunity imparted with each Twinrix shot is less than the individual hepatitis vaccines administered separately. For adequate immunity (>95%), two doses of Twinrix are recommended prior to travel [7].

In children less than 1 year old, hepatitis A immunoglobulin (Ig) is available; however, this age group tends to have controlled diets which may reduce hepatitis A risk. There are also conflicting recommendations for hepatitis A Ig use for pretravel prophylaxis [3, 7]. The availability and cost of hepatitis A Ig can also be a challenge; therefore, these considerations should be taken into account.

Hepatitis B

Hepatitis B is transmitted through contact with infected blood or bodily fluid products. Several factors increase the risk of hepatitis B. These include volunteer work in which contact with blood or bodily fluids might be encountered (e.g., medical volunteer projects) as well as the potential for sexual contact. An injury or illness while abroad which leads to local medical care may also increase risk of exposure to hepatitis B. Traveler risk factors should be assessed prior to administration of hepatitis B vaccination.

Hepatitis B vaccine exists in a 3-shot series spaced at least 0, 1, and 6 months apart. It is licensed for use starting at birth and is safe for use in pregnancy. One dose of hepatitis B imparts approximately 30 to 55% immunity, 2 doses 75% immunity, and 3 doses >95% immunity in adults [4]. At least 2 doses of hepatitis B are recommended prior to travel. It is important to note that the immune response to hepatitis B decreases with age; after age 40, protective immunity from full hepatitis B vaccination decreases to below 90% and to 75% by age 60 [4]. Immune suppression can also decrease the response to hepatitis B vaccination. Therefore, for some at-risk travelers, there may be a benefit in checking hepatitis B antibody titers prior to travel.

A new vaccine, based on a novel adjuvant, known as HepB-CpG was licensed in 2018. It could have application in travel in that it is fully immunizing after 2 doses spaced 4 weeks apart.

Typhoid

Typhoid fever indicates an infection by *Salmonella typhi*, which is spread by fecal-oral transmission. *S. paratyphi* can also cause a similar clinical illness.

There are currently two licensed vaccines in the United States. Typhim Vi is a polysaccharide subunit vaccine, given intramuscularly, with an effectiveness of 55–75%. A booster for ongoing exposure is needed after 2 years. Oral typhoid vaccine consists of a live attenuated strain, Ty21a, which confers similar protection. Unlike the polysaccharide vaccine, however, studies have shown that the oral vaccine does confer some protection against paratyphoid [5]. The manufacturer's instructions are for 1 capsule to be taken an hour before eating every 48 h for 4 doses. The capsules require refrigeration, and revaccination is recommended every 5 years. It can be administered concurrently or at any time in relationship with other live viral vaccines (i.e., yellow fever). However, as antibiotics can impact the vaccine's immunogenicity, it is recommended that no antibiotics be given with, or 3 days before or after, the vaccine. In the case of proguanil, which is one of the active components of the antimalarial atovaquone/proguanil (Malarone ®), a 10-day interval should be maintained between completing the oral typhoid vaccine and starting proguanil. Coadministration with mefloquine is not problematic. As no vaccine confers complete protection, attention to hygiene and eating practices should be emphasized in all travelers.

Yellow Fever

Yellow fever has a widespread distribution in Africa, Panama, and parts of South America. Though classified a hemorrhagic fever, liver and kidney injury is responsible for its morbidity and mortality.

There is a safe and effective vaccine based on an attenuated strain, 17D. Many countries mandate vaccination of travelers. Some countries may even require vaccination of travelers who will transit in airports. Vaccination is restricted to certified vaccination centers. Vaccinees should be provided the International Certificate of Vaccination (yellow card) correctly filled out. Travelers should be told to keep this card with their passport as generally it must be displayed before passport control.

The WHO stated in 2013 that a single yellow fever immunization confers lifelong immunity [6]. While yellow fever vaccine is generally safe, as a live vaccine, it is contraindicated for the immunosuppressed and generally is avoided in pregnant and lactating women. In addition, there are visceral and neurological reactions which occur more frequently at the extremes of age. Therefore, yellow fever is relatively contraindicated less than 9 months of age and absolutely contraindicated below 6 months of

age. There is a relative contraindication over age 60 as well, as adverse reactions, though still rare, are increasingly common above this age [7].

Those travelers who have a contraindication to yellow fever vaccination, including age, should be provided an exemption card certifying the medical reason for not receiving the vaccine. The exemption section is included in the International Certificate of Vaccination (yellow card).

Polio

The eradication of polio worldwide has proven to be an elusive goal. At present there are 10 countries in the world that are considered either polio infected or polio exporting. This list evolves rapidly, but those countries affected and recommendations for polio vaccination are listed and maintained on the CDC website (www.cdc.gov). All travelers to countries with polio should have completed the standard series. In addition to this, adults whose polio vaccinations took place in the remote past should have a single, lifetime polio booster. Long-term (more than 4 weeks) travelers to certain high-risk countries may be required to show proof of vaccination within 1 year for entry and exit. Up-to-date information is available from the WHO [8].

Meningococcus

Infections due to *Neisseria meningitidis* occur worldwide. In the United States, quadrivalent meningococcal vaccine (MCV4) is part of the routine vaccination program. There are two destinations for which vaccination is required or recommended: The *Hajj*, the pilgrimage to Mecca in Saudi Arabia, and the meningitis belt of sub-Saharan Africa. In the meningitis belt in Africa, meningitis can occur at any time but is more frequent during the dry season, from December to June. The serotype of greatest concern is group A.

Vaccination should be considered for all travelers to areas within the meningitis belt if their travel will extend within a month of the December to June window. Quadrivalent conjugated vaccine is the only vaccine presently available for all travelers aged 2 month and older, including those over 55. Boosters are required every 5 years should the traveler remain at risk. Adolescents and preadolescents already vaccinated will not need additional boosters for travel.

Vaccination against type B meningococcus is not needed for travel.

Japanese Encephalitis

Japanese encephalitis (JE) is a mosquito-borne illness prevalent in areas of Asia. Its overall prevalence is 1 case per one million travelers [9]. The risk of contracting the illness includes travel lasting 1 month or greater in rural areas or itineraries in at-risk destinations, which include prolonged and extensive outdoor activities. Symptoms of the disease include change in mental status, fever, and seizures. The fatality rate is 20–30% [9]. Long-term neurological and psychiatric sequelae are seen in 30–50% of survivors [9].

Several brands of Japanese encephalitis vaccine exist in different parts of the world. The current vaccination in use in the United States is IXIARO. IXIARO is a 2-dose vaccination, with doses ideally separated by 28 days, although the second dose can be given one after the first, and ideally at least 1 week prior to travel. The first dose imparts approximately 41% immunity, while the second dose leads to 97% immunity [10]. In addition to use in adults, the IXIARO vaccine has now been approved for use in children aged 2 months to 16 years as of May 2013.

Boosters for JE vaccination are recommended in 1 year for adults, if repeat travel to affected areas is planned. Further booster dosing in the pediatric population is still being actively studied.

Rabies

Rabies unfortunately is almost always a fatal illness. The most common transmission occurs through a bite with an infected animal. Worldwide, the most common source of rabies is infected dogs [11]. Children are particularly prone to rabies exposure while traveling, as they are less likely than adults to exercise caution when coming into contact with animals.

Pretravel vaccination against rabies is recommended for travelers who are visiting locations with high animal rates of rabies and inadequate access to rabies treatment [12]. In many

locations in developing countries, access to rabies immunoglobulin (Ig) might not be readily available. Pretravel rabies vaccination would preclude the need for rabies Ig post-exposure in these locales. Vaccination can also be considered for travelers who plan on visiting rabies-endemic locations for extended periods of time (longer than 1 month). Vaccination is often quite expensive and consists of a 3-dose series at days 0, 7, and 21 (or 28). It is licensed for use in persons of all ages and is safe for use in pregnant women.

Post-exposure treatment is 3-pronged [12], consisting of wound care, administration of the rabies immunoglobulin (if no pre-exposure vaccination was given), and postexposure vaccination. See Table 1 for postexposure treatment.

Boosters for rabies are generally not recommended for most travelers on subsequent trips where exposure to rabies may be significant [12]. Exceptions to this are travelers who may be working in a veterinary capacity or research capacity with wildlife, where it is recommended that serum antibody titers for rabies be checked prior to revaccination.

Traveler's Diarrhea Prophylaxis

Traveler's diarrhea is a common cause of infectious illness while abroad, affecting an estimated 30–70% of travelers [13]. It is defined as three or more episodes of diarrhea in 24 h with at least 1 of the following associated symptoms: fever, nausea, vomiting, abdominal cramps, tenesmus, or bloody stools. Traveler's diarrhea causes significant morbidity, as it leads to significant disruption in traveler activities and itineraries due to symptoms. While adventure travel and avoidance of precautions put a traveler at higher risk, traveler's diarrhea is also reported on luxury travel itineraries as well.

The most common cause of traveler's diarrhea worldwide is enterotoxigenic *Escherichia coli* [13]. On the rise is enteroaggregative *E. coli* as a pathogen. Other pathogens include *Campylobacter*, *Salmonella*, *Shigella*, viral pathogens, and protozoa such as *Giardia*.

Empiric treatment for traveler's diarrhea is guided by balancing likely pathogens, local resistance patterns, and likely side effects. Ciprofloxacin has been the most common antibiotic used to treat traveler's diarrhea in adults, but concerns about resistance patterns and possible side effects have limited its usefulness. Azithromycin is generally considered the preferred agent. It is given as 500 mg daily for 3 days for adults, and 10 mg/kg per day for 3 days for children. Ciprofloxacin may be used in cases of personal preference or in situations where there are drug compatibility problems due to its hepatic metabolism. Azithromycin is the treatment of choice for both pregnant women and children. Many clinicians prescribe treatment doses of antibiotics for traveler's diarrhea for each traveler to fill in advance and take with them on their trips.

Concurrent treatment of traveler's diarrhea with both loperamide and antibiotics has been shown to decrease traveler's diarrhea symptoms more rapidly than either treatment option alone [14]. A recent meta-analysis of traveler's diarrhea in several communities around the world showed increased likelihood of clinical cure at 24 h and 48 h if combination loperamide/antibiotic therapy is given [14].

Prophylaxis for traveler's diarrhea is a controversial topic. The first-line measure of "boil it, cook it, peel it, or forget it" should be reviewed with all travelers. Drinking water that is bottled or boiled at a rolling boil for 1 min to kill potential pathogens is advisable in all at risk locations. The CDC currently does not recommend traveler's diarrhea prophylaxis [13] due to the development of possible antibiotic resistance. It should be noted, however, that prophylaxis is very effective and can be considered for those with risk factors such as inflammatory bowel disease. Options for prophylaxis include quinolones, which can reduce incidence of diarrhea by up to 90% [13]. Rifaximin is limited by expense but is another option for traveler's diarrhea prophylaxis. Daily bismuth subsalicylate (Pepto-Bismol®), an option that is not available to pregnant women or children due to its aspirin component, reduces incidence of diarrhea around 50% [13], though the patient should be warned of black stools.

Table 1 Post-exposure treatment of rabies [12]

Received pre-exposure vaccination?	Wound cleansing needed?	Rabies immunoglobulin administration needed?	Post-exposure immunization schedule
Yes	Yes	No	Days 0 and 3
No	Yes	Yes	Days 0, 3, 7, 14

Lactobacillus is also a popular prophylactic option, though studies regarding its use in traveler's diarrhea prophylaxis are inconclusive [13].

Malaria Prophylaxis

The WHO reported for 2018 an estimated 228 million cases of malaria with 405,000 deaths, most of which are in children in sub-Saharan Africa [15]. Malaria in travelers is potentially lethal, but avoidable. In 2016, there were 2078 cases reported in the United States and 7 deaths, almost all in travelers [16].

Historically, four species, *Plasmodium falciparum*, *P. ovale*, *P. malariae*, and *P. vivax*, caused human disease. A fifth species, *Plasmodium knowlesi*, a primate species, now causes significant human disease in Southeast Asia, with a dozen American cases reported in travelers through 2013 [17] as well as many European cases [18]. While all species contribute to human morbidity, the burden of mortality is due to *P. falciparum.* While resistance patterns vary, in general, prophylaxis and treatment that effectively target *P. falciparum* in a given area will be effective against the other forms of malaria as well.

Individuals exposed to malaria on an ongoing basis often develop a partial immunological protection called premunition. This protection allows a low level of chronic infection but generally does not allow the malaria to develop into clinical illness. Anyone who has been outside a malarious area for over 2 years generally has the same risk as a nonimmune individual, though the precise rate of decay of immunity is unclear.

The best measures against malaria are mosquito avoidance, including application of DEET to the skin, bed nets, and clothing, and taking an approved medication for chemical prophylaxis [19]. There are currently several antimalarials recommended for prophylaxis, discussed below.

Mefloquine

Mefloquine has been widely used for several decades. It is somewhat controversial, with common minor side effects such as vivid dreams and disturbed sleep and rare adverse cardiac and psychiatric effects. Avoidance of this drug in patients with known cardiac problems, especially those who take QT interval prolonging medications, is recommended. Those who have or have had a psychiatric diagnosis, including depression, should use another agent. It is helpful to begin mefloquine prophylaxis 2 weeks prior to travel instead of the traditionally prescribed 1 week prior. This both allows for a period of time to evaluate the development of any side effects and achieves a drug-steady state prior to arrival. Mefloquine should continue to be taken 4 weeks after leaving the malarious area. Areas of increasing resistance have made this drug less useful for much of Southeast Asia [20].

Doxycycline

Doxycycline is useful and effective for malaria prophylaxis. It should be started 2 days prior to travel, taken daily and continued daily for 4 weeks after leaving the malarious area. It is contraindicated in children under 8 years of age and in pregnant and lactating women. Dairy products should be avoided for 2–3-h window before and after ingesting doxycycline. Doxycycline is helpful to take with food to reduce nausea. Photosensitivity has been reported but is not as frequent a problem as with tetracycline. Candida infections can be seen, at times even in men. Interference with oral contraceptives does not seem to be the problem it was once thought to be. However, as with other antibiotics, those

taking warfarin should have their dose monitored while on doxycycline.

Malarone

Atovaquone/proguanil (Malarone®) is generally regarded as the best tolerated and most effective of available antimalarials for prophylaxis. There are very few side effects. It is taken daily, 2 days prior to, during, and only 7 days after travel in a malarious area, making this the shortest "tail." Its main disadvantage is cost.

Primaquine

Primaquine is indicated for presumptive antirelapse treatment (PART), previously known as "terminal prophylaxis." Terminal prophylaxis with primaquine, at a dose of 30 mg [52.6 mg of salt] per day for 14 days [21], is recommended to all who visit areas where *P. vivax* is present. Primaquine is capable of eliminating dormant malarial hypnozoites in the liver, thereby reducing the frequency of relapse. Primaquine triggers a hemolysis in those with G6PD deficiency, so quantitative testing of this enzyme must be performed prior to prescribing this drug. Primaquine should not be prescribed to pregnant women.

Tafenoquine

Tafenoquine, an 8-aminoquinoline like primaquine, was approved in 2018 for prophylaxis of all species of plasmodium, as well for radical cure of vivax [22]. Because of its long half-life, it is possible to give 200 mg daily for 3 days pretravel, then weekly while at risk, and again 1 week after the risk ends. As with primaquine, it is not to be given to those who have not had a quantitative test ruling out G6PD deficiency, or to pregnant women.

Personal Protective Measures

Insect avoidance is an important component of prevention for travelers to the tropics. Medical prophylaxis for malaria works better in combination with avoidance to lessen the parasite exposure. Other protozoal diseases that are transmitted by insects, such as leishmaniasis and trypanosomiasis, have available treatments but are extremely onerous, making prevention strategic. Viral diseases, such as Japanese encephalitis and tick-bourne encephalitis are preventable by vaccination, but the cost and availability of vaccines may discourage their use, especially in short-term travelers. In addition, viral diseases such as dengue, chikungunya, and zika have no treatment or vaccine yet available, so protective measures are the only prevention. Scrub typhus and many other rickettsial diseases may be treated, but are largely preventable.

In areas of risk, permethrin-impregnated bed nets are a major element in malaria prevention. Travelers should take advantage of these when available. Permethrin is also available as a spray-on product for the treatment of clothes [19], which is strategic for many arthropod-borne illnesses, in particular scrub typhus in Asia and tick-bourne typhus in Europe.

DEET (*N*, *N*-diethyl-meta-toluamide) is a repellent with a long history of safe use. Adverse effects are rare. However, it is best to use clothing that covers much of the body so that DEET can be applied sparingly. The American Academy of Pediatrics recommends 10–30% strength for children older than 2 months of age. Picaridin is a product that can be used as well.

Trypanosomiasis is a rare disease in travelers, but there have been reported cases from those going on game drives. Long sleeves and pants and permethrin treatment are helpful strategies for avoidance. In addition, given that tsetse fly traps are purposefully made in royal blue and black colors to attract the flies, these are good clothing colors to avoid during such activities.

Schistosomiasis is one of the most common diseases of returned travelers. There are several species of this fluke, which in its larval stage is an infection of freshwater snails. Travelers to the tropics should be counseled against swimming in freshwater. Wading and even dangling a body part in the water can also transmit the fluke, as well as bathing with untreated lake or river water.

Certain preventive strategies are difficult to apply to those at highest risk: children under the age of 1, pregnant women, and the

immunocompromised. For such travelers, it is helpful to encourage thoughtful reflection as to the risks and benefits of travel. In some cases, travel plans can be modified in such a way that the risk can be mitigated.

Altitude Illness Prophylaxis

In several destinations in the world, altitude illness and prevention become a concern. Symptoms of altitude illness include headache, insomnia, nausea, fatigue, and dizziness. Severity of altitude illness can range from acute mountain sickness which is mild to more serious complications such as high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE).

A discussion of altitude prophylaxis is recommended for destinations that involve overnighting above 2,500 m [23]. The most widely accepted preventive measure is slow ascent [23]. Several medications are available for altitude prophylaxis, including acetazolamide and dexamethasone. Recommended dosing for acetazolamide is 125 mg by mouth twice per day, to start 2 days prior to ascent and to continue until the traveler has acclimatized at their maximum altitude (generally 48–72 h) [23]. Acetazolamide can cause side effects such as diuresis and paresthesia and cannot be used in patients with sulfa allergies. Dexamethasone is a second-line prophylactic option, but as it does not aid in acclimation, it can cause rebound symptoms of acute mountain sickness once stopped. Local herbal remedies are also popular and available in high-altitude destinations worldwide, but efficacy in preventing altitude illness is unproven in studies [23]. The most effective treatment for altitude illness is descent.

Safety and Accident Prevention

A significant proportion of the pretravel visit is dedicated toward the discussion of pre-trip immunizations, malaria, and traveler's diarrhea. However, the primary cause of death among travelers is accidents, such as motor vehicle accidents and falls [24]. For this reason, the topic of safety and accident prevention deserves specific mention during the pre-trip consultation. Depending on the destination, standards and safety for driving can vary significantly. There may be political or civil unrest occurring in various destinations that a traveler should be aware of. Registering an international trip with the US State Department and consulting their website may be helpful in trip preparation.

Sexually transmitted diseases are a risk for travelers who might consider having sex while abroad. Assessing for the likelihood of this during the pre-trip consultation is important, and these travelers should be reminded of both the incidence of STDs in their destinations and the use of barrier protection. There can be variability in the quality of condoms purchased abroad.

Finally, trip and evacuation insurance should be considered prior to departure. This might be most useful for those travelers abroad for an extended period of time, especially in remote locations or for travelers who have one or more chronic illnesses.

Emerging Diseases

In the years prior to this edition, the world has dealt with multiple global infections including Zika, MERS-CoV, and COVID-19. Each of these has had impact on travel, whether regional or global, and temporary or long-term. It is not known now what the impact of these viruses or other as yet unidentified viruses will be on travel planning at a future time when the reader reads these words. The best advice is to survey excellent electronic resources such as the CDC's yellow book, the National Health Service UK's "Travel Health Pro" website, and www.promedmail.org, which relies on observers on the ground to give real-time updates of local epidemiological conditions.

Post-Trip Consultation

The goal of the pretravel consultation is the avoidance of illness during and after travel. There will be times when such measures fail. The likelihood of illness is negatively correlated with preventive measures taken. Pathologies frequently encountered in returned travelers include fever, gastrointestinal disease, skin disease, eosinophilia, and latent tuberculosis.

Fever in Returned Traveler

For purposes of this discussion, fever will be defined as an oral temperature $>$ 100.0 °F, although given the cyclical nature of many fevers, subjective reports of fever should be taken seriously. Even remotely completed travel can cause illness, but the large proportion of fever cases present within weeks to months of return from travel. One exception is non-*falciparum* malaria, which can incubate for up to a year, and delayed relapse can occur many years later [25].

The most critical subgroups of febrile returned travelers are those with hemorrhagic symptoms. All patients with fever and hemorrhage who have returned within 21 days from travel should be considered to have a viral hemorrhagic fever and placed in isolation (contact, droplet, and aerosol) until proven otherwise. Not all of these diseases are contagious, but until a specific identification has been made, high transmissibility should be assumed.

The next most important task in the care of returned travelers is to identify potential cases of malaria. In many cases, malaria is the most important cause of fever in a returned traveler [26], and the risk of mortality from this pathogen in non-immune patients makes its rapid identification and treatment critical. Malaria can be contracted in any tropical continent and is the most frequent cause of fever in those traveling from Africa. Dengue is the most frequently encountered pathogen from Southeast Asia, and enteric fever (typhoid) is the most frequently encountered fever from the Indian subcontinent [27]. Other important causes of fever include schistosomiasis, leptospirosis, amebic abscess, tuberculosis, and sexually transmissible diseases, including HIV.

Workup for fever should include a careful history, including the itinerary, associated symptoms, and a physical exam emphasizing ENT, pulmonary, GI, neurological, and integumentary systems. A lab workup including a CBC with differential, thin, and thick smears for malaria and blood cultures can also be helpful. For clinical situations such as dengue or chikungunya, specific viral serologies can also be considered.

In practice settings where results are likely to be delayed, empiric treatment with an antimalarial should be strongly considered. Atovaquone/proguanil is widely available as a prophylactic and is effective as a treatment as well. The same can be said for mefloquine. A more ideal medication artemether-lumefantrine (Coartem) is preferred as a treatment and avoids the theoretical problem of using a medication as treatment that may have failed as a prophylactic agent. For severe malaria, of which there are around 300 cases annually in the US, the drug of choice is parenteral artesunate, which had only been available directly from the CDC but has now received FDA authorization and will soon be available for hospital pharmacies to stock [28]. Quinine has a long-track record, but its potential for arrhythmias limits its utility and it is no longer available in parenteral form in the USA.

GI Illness in Returned Traveler

GI illness is one of the most common illnesses in the returned traveler [13]. A history of destination, activities during travel, and onset of symptoms can help distinguish whether or not the illness is travel related. A more in-depth discussion of traveler's diarrhea is reviewed in the pre-trip consultation section of this chapter.

Diarrheal symptoms lasting more than 2 weeks should prompt screening for *Giardia,* amebiasis, and other parasites. Multiple stool samples for O and P testing may need to be submitted to accurately diagnose parasitic infection. Three stool O and P samples on 3 different days is preferred, as 1 sample can miss potential infection dependent

on time of collection. In cases where clinical suspicion persists despite negative microscopic results, stool testing for *Giardia* and *Cryptosporidium* antigen is available and is sensitive.

Extended symptoms of diarrhea can also be seen with postinfectious irritable bowel syndrome (IBS), a diagnosis of exclusion in travelers with prolonged diarrheal symptoms more than 30 days after travel [29]. The incidence of postinfectious IBS is variable and ranges from 4% to 31% across all studies [29]. In one study of North American travelers to Mexico, the incidence was 11% of all travelers with diarrhea, with 10% of this number being newly diagnosed cases of IBS [30]. There is no widely accepted strategy for treatment, but options are similar to those recommended for noninfectious IBS including probiotics, antispasmodics, and low doses of tricyclic antidepressants [30].

A subset of patients who return from travel present with symptoms that they attribute to parasites, with no objective findings to support this belief. In many such patients this belief can become fixed and life-altering. Many will travel from specialist to specialist seeking help. While this phenomenon can be a manifestation of preexisting psychiatric disorders, it can present in those who are otherwise normal. An approach to delusional parasitosis is to perform limited reasonable rule-out procedures, offer a rational inexpensive empiric treatment, seek to establish a therapeutic relationship, and encourage the patient to accept that like phantom pain, the body sometimes tells the patient that there is a parasite when the parasite never was there, or was successfully treated, and these feelings can be helped by atypical antipsychotics.

Skin Lesions in the Returned Traveler

Skin lesions and rashes are common after return from travel. They may reflect a discrete condition (i.e., cutaneous larva migrans, swimmers itch, or tungiasis) or a systemic illness (i.e., dengue, chikungunya). History of activities during travel and specific locations visited during travel are important in the diagnoses of these conditions.

Eosinophilia

Perhaps the most common laboratory abnormality in a returned traveler is eosinophilia. Rather than focusing on the percentage, and absolute eosinophilia of 500×10^6 or higher should prompt further evaluation. The most common causes of eosinophilia in travelers are schistosomiasis, filariasis, and nematode infections [31], but *Strongyloides stercoralis* is an important consideration and may present decades after a stay in the tropics. Stool for ova and parasites may shed light on certain species of schistosomes and nematodes. Urinalysis should be performed for hematuria and schistosomal ova. Skin exam and a snip test can be helpful with filariasis.

Tuberculosis Screening in the Returned Traveler

In travelers to some destinations, especially developing countries, screening for tuberculosis on return is advised. If the trip itinerary includes a work in healthcare settings or frequent face-to-face contact with persons residing in a TB-endemic location, a PPD screen is recommended 8 weeks after return [32]. In some populations, a PPD may not be appropriate. These would include travelers with a history of BCG vaccine, as immunity is variable and a PPD test in these populations may be positive for decades. For these special populations, an interferon gamma release assay (IGRA)-based test such as QuantiFERON®-TB Gold is preferable for screening [33]. In populations in which there are no special indications for IGRA-based testing, there is no superiority of the IGRA-based test over the PPD test for screening [33]. For travelers who convert either their PPD- or IGRA-based screening to positive, a chest x-ray is recommended to assess for active tuberculosis. Persons with active disease are reportable to the local health department. Persons with latent disease should receive a discussion on the risks and benefits of treatment for latent tuberculosis. The McGill University decision tool is a very useful guide for such discussions [34].

Reentry for Long-Term Travelers: Psychological Concerns

For many return travelers who have been abroad long-term, reentry into life in the United States can be difficult. A variety of emotions can arise on the return, from happiness to anger and sadness. Long-term expatriates can feel isolated and unable to connect with loved ones from home after their experiences abroad. Reverse culture shock can occur as well. Screening for depression, anxiety, and PTSD should be considered for all long-term returned travelers when seen by their primary care providers, especially for those who may have suffered adverse events, or who were required to return involuntarily. Counseling is highly recommended for travelers with psychological concerns on reentry.

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