

Expatriates: Special Considerations in Pretravel Preparation

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Abstract Expatriates comprise a diverse set of travelers who face unique medical, psychiatric, and non-health-related risks as a result of increased exposure to host country environment and associated lifestyle. Expatriates have an increased risk of developing malaria, gastrointestinal disorders, latent tuberculosis, vaccine-preventable infections, and psychological disorders, when compared with other travelers, yet the majority of existing pretravel guidelines have been designed to suit the needs of nonexpatriates. Although greater interest in expatriate health issues has led to improved characterization of illness in this population, expatriate-specific risk mitigation strategies—including modifications to chemoprophylaxis recommendations, limiting tuberculosis exposure, and prevention of occupational or sexual blood-borne virus transmission—are poorly described. Occupations and destinations affect travel-related disease risk and should inform the pretravel consultation.

Keywords Expatriates · Rabies vaccine · Japanese encephalitis vaccine · Chemoprophylaxis · Malaria · International travel

Introduction

Despite concerns over the global economy, international travel continues to show resilience, with international arrivals forecast to exceed 1 billion by the end of 2012 [1]. An increasing number of individuals live outside their home country as expatriates (defined as those residing abroad for professional or personal reasons) [2•]. Expatriates include a diverse range of professionals (diplomats, corporate workers, field researchers, humanitarian workers) who may have various comorbidities. Worldwide, the expatriate population has been estimated at up to 50 million [3•, 4]. According to a recent prospective multisite U.S. travel clinic study, 3 % of all international travelers presenting for pretravel consultation planned a trip with a duration of >6 months [5].

Travel to low- and middle-income countries presents health risks that may not exist in developed countries. These risks are magnified for long-term travelers, partly due to cumulative exposures and reduced compliance with preventive measures over time, resulting in increased risk of vector-, food-, and water-borne diseases [6]. This may then lead to an increased need for local medical care, which may have limited resources and inadequate staffing and may result in suboptimal therapy.

Disease risks encountered by expatriates are often specific to the destination and purpose of travel. Expatriate humanitarian workers and adventure travelers are at higher risk of infectious and noninfectious diseases than are other long-term travelers. However, many “low-risk” expatriates also have a nonnegligible risk of health problems; in the U.S., 12 % of corporate travelers sought medical attention for travel-related medical problems [7], and a retrospective evaluation of British diplomats living overseas noted that 3.1 % of diplomatic service staff required medical evacuation in 1995 [8].

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Many summaries of pretravel evaluations focus on the short-term traveler and ignore the health needs of expatriates, who may require long-term malaria prophylaxis, treatment of underlying medical conditions, and more counseling for behaviors, including dietary and sexual indiscretions. It may be impossible to anticipate and educate for all potential scenarios because of deviations from intended itinerary and actual risk-taking behaviors during prolonged travel [9].

There is now a greater focus on how standard pretravel guidelines could be better tailored to the needs of expatriates. In addition to recognizing gastrointestinal infection, vaccine-preventable disease (VPD), and latent tuberculosis as diseases with substantial morbidity among expatriates [3••], psychiatric issues, sexually transmitted infections (STIs), malaria, and emerging infectious diseases are other important potential health issues that should be addressed, particularly for expatriates living in developing regions.

Pretravel Vaccinations

Vaccines for disease prevention are one of the most important aspects of expatriate health promotion. Small studies have shown that incidence rates of VPDs (including hepatitis B, yellow fever, and rabies) are substantially higher among expatriates in the developing world than among short-term travelers [4]. An analysis of 2,883 expatriates and 11,910 nonexpatriates presenting to GeoSentinel network clinics noted that expatriates are more often diagnosed with hepatitis A [3••].

Several recent surveys of travelers departing from international airports to high-risk destinations showed that 35 %–65 % of all individuals did not seek advice or pretravel vaccination from a health-care professional [5, 10, 11]. The proportion of expatriates who do not seek pretravel consultation is unknown because complete denominator data is unavailable. A recent study of returned expatriates who were ill showed that 30 % of the expatriates had not sought pretravel consultation before going abroad [3••], and coverage remains suboptimal [4].

The majority of recent studies have focused on rabies, a potentially fatal infection. Although 48 confirmed cases of rabies among international travelers have been reported since 1990, travel-associated rabies is likely to be underreported among travelers who die abroad [12]. The incidence of injuries caused by potentially rabid animals is 15.4 injuries per 1,000 expatriates per year of stay [13]. Furthermore, two thirds of rabies cases occurred in those traveling for ≥ 3 months [12]. Despite this risk, only 31 % of expatriates report receiving a pretravel rabies vaccination [13]. The often-prohibitive cost of a rabies vaccination—coupled with inadequate traveler knowledge regarding rabies risk and insufficient time to

complete vaccination prior to departure—has been cited as a reason for low preexposure rabies vaccination rates among long-term travelers [12–15]. Analyses of rabies vaccine prices demonstrated an inverse relationship between vaccination uptake and vaccine cost [13]. An intradermal (ID) rabies vaccination costs one third of the price of an intramuscular (IM) rabies vaccine and has been shown to be safe and immunogenic. However, its use in pretravel clinics is limited by off-label restrictions in the U.S., Australia, and several European countries and by the need for follow-up serologic testing to document immunity [12]. A modified schedule consisting of two ID injections (on days 0 and 7, with follow-up serology on days 21–28) was studied as a potential alternative to IM injections in an Australian travel clinic [15]. Travelers who received the modified ID schedule had a similar immunogenicity response, as compared with those receiving the standard ID schedule.

Japanese encephalitis (JE) is the leading cause of vaccine-preventable viral encephalitis in Asia; expatriates (particularly military personnel, aid workers, and missionaries) are at higher risk of JE infection [16]. The risk for rural travelers in JE-endemic areas is estimated at 1 per 5,000–10,000 per month [17]. Previous recommendations for JE vaccination in travelers attempted to balance the risk of the mouse-brain-derived vaccine (JE–MB), which had multiple side effects (including severe immediate and delayed hypersensitivity reactions and neurologic complications) against the low risk of travel-associated infection. With the discontinuation of JE–MB production and the advent of newer and safer JE vaccines—including the IC51 vaccine derived from Vero-cell culture (JE–VC)—current guidelines recommend vaccination of all travelers residing in JE-endemic regions for 1 month or longer during transmission season [16–18]. A JE–VC booster at 12–15 months may be required for expatriates in JE-endemic areas for over a year.

Hepatitis A virus (HAV) infection has historically been one of the most common VPDs among travelers (along with influenza), although the incidence has been decreasing secondary to vaccination; current guidelines recommend the vaccination of all HAV nonimmune individuals traveling to an endemic region [19]. Travel-related HAV infection has been noted to increase with increased duration of stay [20]. Although a GeoSentinel network study notes no difference in the proportionate morbidity for hepatitis A between returning expatriate and nonexpatriate travelers, corporate expatriates were noted to have a higher proportionate morbidity for hepatitis A when compared with corporate nonexpatriate travelers [3••].

An individualized assessment of expatriates traveling to regions endemic to VPDs should include the cost of vaccination and the time available prior to departure in order to guarantee appropriate pretravel recommendations and vaccination. In addition to standard counseling and vaccination

based on duration and destination of travel, occupation-associated risks should be considered in the pretravel visit, as shown in Table 1.

Diarrheal Disease

>Travelers' diarrhea (TD) remains the most common infectious disease among long-term travelers to developing countries [21]. It affects 20 %–50 % of travelers to developing

countries and is frequently associated with inconvenience, incapacitation, and days lost from work [22, 23].

Adherence to standard food and water precautions appears to deteriorate with longer travel duration. A cross-sectional study among long-term travelers in India revealed little adherence to pretravel advice among the 114 participants surveyed [21]. Most travelers (83 %) reported at least one episode of TD, without reduction in episodes as travel durations lengthened. Another cross-sectional study of long-term backpackers in Thailand reported that a longer stay was associated with having

Table 1 Occupation-related health risks in expatriates

Occupation	Risk Category	Pretravel Recommendations
Peace Corps volunteers and humanitarian relief	Malaria [39, 49, 60]	<ul style="list-style-type: none"> • Educate on malaria symptoms and antimalarial adverse effects • Discuss access to qualified medical assistance at destination • Select a chemoprophylaxis strategy (continuous, seasonal, stand-by)
	Tuberculosis [53]	<ul style="list-style-type: none"> • Assess risk of TB at destination • Pre- and posttravel screen for LTBI (TST or IGRA) • Advice about respirator masks and minimizing risk
	Psychiatric disorders [51, 61]	<ul style="list-style-type: none"> • Pretravel mental health screening • Pretravel advice about stress and acculturation issues for expatriates • Psychological support and debriefing, especially with conflict or trauma
	Sexually transmitted disease [49, 60]	<ul style="list-style-type: none"> • Recommend consistent condom use, discuss contraception • Regular STD and HIV screening for sexually active patients • <i>Vaccines</i>: Hepatitis B vaccine, HPV vaccine in women 9–26 years of age
Corporate	Trauma [8]	<ul style="list-style-type: none"> • Educate regarding road safety, seatbelts • Advice about recreational activities
	Malaria [6, 32]	<ul style="list-style-type: none"> • Educate on malaria symptoms and antimalarial adverse effects • Discuss access to qualified medical assistance at destination • Select a chemoprophylaxis strategy (continuous, seasonal, stand-by)
	Dental emergencies [66–68]	<ul style="list-style-type: none"> • Pretravel dental examination • For those with preexisting dental conditions, ensure access to on-base or local dental services
Military	Malaria [62]	<ul style="list-style-type: none"> • Educate regarding personal protective equipment • Educate on malaria symptoms and antimalarial adverse effects • Select a chemoprophylaxis strategy (continuous, seasonal, stand-by)
	Diarrheal disease [63, 64]	<ul style="list-style-type: none"> • Advice on cooked food, bottled or boiled water • Minimize food from off-base vendors • Ciprofloxacin or azithromycin for stand-by treatment • <i>Vaccines</i>: Hepatitis A vaccine, typhoid vaccine, adult polio booster
Health care workers	Needlestick exposure [58, 65, 69]	<ul style="list-style-type: none"> • Needlestick management • Educate regarding postexposure prophylaxis (PEP) • Ensure PEP availability, provide PEP kit (2- or 3-drug ARV regimen) • <i>Vaccines</i>: Hepatitis B and tetanus vaccines
	Tuberculosis [53, 57, 59]	<ul style="list-style-type: none"> • Assess risk of TB at destination • Pre- and posttravel screen for LTBI (TST or IGRA) • Advice about respirators and fit test prior to departure • Recommend minimizing time in high-risk areas with poor ventilation

diarrhea [24]. Persistent TD risk was also seen in expatriates residing in Nepal for up to 2 years [25].

Although theoretically shielded by eating prepackaged meals at bases, recent studies evaluating TD in the military demonstrated elevated rates of diarrhea among service members (69 % of French forces stationed in Chad during a 5-month period and 27 % of U.S. military training in El Salvador for a week) [26, 27]. Both studies cite living in close quarters (facilitating person-to-person transmission of enteric pathogens) and the consumption of food purveyed by off-base local vendors as risk factors.

To avoid TD morbidity and postinfectious sequelae, recent studies have examined the efficacy of antibiotics for TD prophylaxis. A meta-analysis of four randomized control trials with 502 participants indicated that rifaximin prophylaxis significantly reduced the risk of TD (OR 0.41, 95 % CI 0.3–0.56, $p < .00001$) [28], with comparable side effects to placebo. Another meta-analysis of nine TD antibiotic prophylaxis studies showed a similar protective effect for fluoroquinolones and rifaximin (pooled relative risk estimate of 0.33, 95 % CI 0.24–0.45 for rifaximin and 0.12, 95 % CI 0.07–0.20 for fluoroquinolones) [29]. However, long-term antimicrobial use may lead to the development of antimicrobial resistance, which would limit the usefulness of prophylactic antibiotics in developing countries. Poor adherence to antimalarials among long-term expatriates suggests that adherence to antimicrobial prophylaxis might be similarly suboptimal, but with greater potential for widespread resistance. Until further data are available to support the use of long-term antibiotic prophylaxis for diarrhea, such a practice is not recommended.

Malaria

Expatriates in malaria-endemic regions are generally nonimmune and at varying risk for malaria depending on location and season. A GeoSentinel clinic study noted that expatriates had a greater proportionate morbidity for malaria than did nonexpatriates [30•]. Recommendations regarding malaria prophylaxis must be tailored to the destination, symptom knowledge, and access to health care. Several alternatives to continuous chemoprophylaxis for long-term travelers have been suggested, and the societal risk–benefit ratio of long-term malaria prophylaxis has been evaluated in recent studies.

Malaria prevention for expatriates is complicated by the prolonged duration of travel, with long-term toxicity and compliance fatigue. Adherence to chemoprophylaxis is poor across geographic locations, job descriptions, and medical literacy levels [30•, 31–33]. Longer duration of residence in malaria-endemic regions is associated with increased termination of chemoprophylaxis [6, 31, 32]. Retrospective evaluation of pediatric travelers returning from sub-Saharan Africa

from 2000 to 2008 showed only 20 % adherence, and among patients who did take prophylaxis, 50 % were taking an ineffective prophylactic agent [33]. Only a minority of expatriate medical professionals in Equatorial Guinea remained on chemoprophylaxis within 3 months of arrival; treatment side effects and concern regarding the safety of long-term use were cited as reasons for discontinuing chemoprophylaxis [31].

Despite decreasing malaria prophylaxis over time among expatriates, a recent study showed that chemoprophylaxis for travelers to malaria-endemic countries is cost effective for visits of >25 days to West Africa and >45 days to India and Indonesia [34].

In sub-Saharan Africa, the risk of malaria transmission is lower in urban areas and higher in periurban and rural areas [30•]. Knowledge of geographic and seasonal malaria trends may facilitate periodic dosage of chemoprophylaxis limited to the wet and early dry seasons. Although not intended as pretravel recommendations for expatriates, a recent evaluation of rainfall patterns and seasonal malaria incidence in endemic regions identified Sahelian and sub-Saharan Africa as suitable locations for seasonal malaria chemoprevention [35]. Seasonal prophylaxis prevented 75 % of clinical malaria episodes among preschool children in West Africa [36], suggesting that expatriates in regions with clearly defined wet and dry seasons may benefit from the use of intermittent season-based chemoprophylaxis.

Expatriates who reside strictly within the city confines may not require chemoprophylaxis [30•, 37]. Seeking treatment promptly when symptomatic is another approach for expatriates who choose not to take continuous chemoprophylaxis. Expatriates must be educated on malaria symptoms and the importance of early presentation during the pretravel visit. If access to health-care facilities cannot be ensured, the expatriate should be strongly encouraged to take chemoprophylaxis [30•].

Standby emergency treatment (SBET) may be a reasonable option for travel to low-risk areas and is recommended when prompt medical attention is unavailable within 24 h of the onset of symptoms [38]. SBET should not replace chemoprophylaxis in regions of high malaria endemicity (such as sub-Saharan Africa) but can be offered to long-term travelers with gaps in chemoprophylaxis adherence [38]. Malaria rapid diagnostic tests (RDTs) are an option that may allow expatriates to confirm a diagnosis of malaria and decrease the incidence of inappropriate treatment. However, RDTs cannot determine parasite density, may be difficult to interpret, and are degraded by exposure to tropical temperatures [38, 39]. An evaluation of international oilfield service employees in sub-Saharan Africa and India found that 15 % of participants had difficulty with the self-test and most of those who took SBET did not have a positive self-test result [32]. False-negative and false-positive test results do occur; expatriates should be aware that treatment may be required despite negative tests.

In a survey of 2,701 Peace Corps volunteers (PCVs) in malaria-endemic regions, 62 % of respondents experienced at least one antimalarial-related adverse event; 23 % of participants changed their regimen [40]. Another trial of malaria-prophylactic regimens showed that 30 %–45 % of participants had mild to moderate adverse events and 6 %–12 % experienced severe adverse events [41]. Having multiple drug regimens available to the expatriate may help to maintain adherence. Local in-country drug supply may be compromised by counterfeit medications, particularly in Africa and Southeast Asia [42].

The continuous use of personal protection measures (ITNs and insect repellents) and vector control (drainage of stagnant water, residential screening, indoor air conditioning, and residual insecticides) become more important if chemoprophylaxis is stopped. A study of expatriate health-care workers in Equatorial Guinea found that residing on the top floors was protective, as compared with living on the ground floors of apartment buildings (HR=0.24) [31].

An individual risk assessment based on location, seasonality, and duration of travel should determine whether the risk of serious adverse events from chemoprophylaxis exceeds the risk of infection.

Psychosocial Disorders

Displacement from familiar environments can lead to disorientation. This may be exacerbated by social isolation, stressful work conditions, language barriers, and culture shock. A GeoSentinel analysis found psychological diagnoses (including depression and anxiety) reported more often in expatriates [3••]. Other studies of corporate travelers show higher levels of anxiety, depression, and excessive alcohol consumption, as compared with nontravelers [43, 44]. Stress levels and psychiatric morbidity are affected by reason for long-term travel. Recurrent occupational exposure to trauma experienced by several expatriate groups (military, humanitarian, and disaster relief personnel and health-care workers) carries a greater risk of posttraumatic stress disorder, depression, and anxiety [45, 46], possibly due to *vicarious trauma*, a strong identification with the population served [46]. Among British missionaries serving in developing countries, 60 % of premature repatriations occurred due to psychiatric illness [47].

The literature suggests unmet psychosocial needs among expatriates, and more research is needed on stress prevention and treatment. Companies that employ expatriates should facilitate cultural adjustment, language training, and social networks. Medical and psychosocial support for humanitarian and disaster relief workers should be integrated into debriefing efforts. Predeparture medical and psychological assessment—particularly for those entering regions of

conflict or working in low-resource settings—may identify latent psychiatric disorders and provide counseling regarding acculturation and coping mechanisms.

Sexually Transmitted Infections (STIs)

Risk-taking behaviors during travel include excessive alcohol consumption and unprotected sexual encounters. Among corporate expatriates in western Ghana, a quarter of expatriates reported sexual encounters with local partners, and of these, 50 % used condoms inconsistently [6]. A review of travel-associated casual sex noted that 20.4 % of travelers had casual sexual intercourse, and of these, 49.4 % reported having unprotected sex [48]. The number of casual sexual encounters is thought to be higher among expatriates, who are more likely to have casual sex abroad than are other types of travelers [49]. Among returning International Committee of the Red Cross workers, 30 % reported engagement in casual sex [50], and, of 1,080 PCVs studied, 60 % had at least one casual sexual encounter [49].

Longer duration of travel has been associated with higher risk of new sexual partnerships and unprotected sex. Expatriates are also more likely to seek commercial sex [48], exposing expatriates to a range of STIs, including HIV, hepatitis B, and hepatitis C. The emergence of drug-resistant gonorrhea in Africa, the Caribbean, and Asia places sexually active expatriates at risk for STI treatment failure and chronic complications [49].

Counseling on sexual health is therefore an important component of the pre-travel visit; discussion of abstinence, contraception, partner testing, and HBV and HPV vaccination should be covered on the basis of risk assessment. “Stand-by” antibiotic therapy for self-treatment of STIs is not recommended due to the risk of inappropriate use, potential behavior disinhibition, and drug resistance [49].

Respiratory Illness

Travel is a well-publicized mode for the global spread of respiratory viral infections, from SARS and influenza to tuberculosis [50]. Respiratory infections account for 14 %–25 % of febrile illnesses in returning travelers [51, 52]. However, a GeoSentinel study found that returned expatriates experience a lower proportionate morbidity for respiratory infections (including influenza), possibly because these are usually short-incubation diseases seen during travel instead [3••].

Long-term travel to endemic regions has a well-defined association with risk for the acquisition of *Mycobacterium*

tuberculosis. Expatriates have higher proportionate morbidity for latent tuberculosis infection (LTBI) than do nonexpatriate travelers [3••]. Studies of expatriates in regions with high tuberculosis endemicity have measured an LTBI risk of 1.3–4 per 1,000 person-months—a rate similar to that in the local population [4, 53, 54]. High-risk occupational groups, such as expatriate health-care workers, are noted to be at even higher risk, with a tuberculin purified protein derivative (PPD) conversion rate of 7.9 per 1,000 person-months [54]. With rising incidence of multidrug-resistant tuberculosis (MDR-TB) in many endemic regions, reducing tuberculosis exposure becomes even more important for expatriates.

Pre- and posttravel tuberculosis testing allows prompt treatment of LTBI when infection is detected, but only 30 %–66 % of expatriates receive appropriate screening and counseling [4, 55]. Screening options include two-step tuberculin skin test and interferon gamma release (IGRA). There are currently few evidence-based guidelines to recommend one screening method over the other for expatriates, although IGRA may be preferred in individuals with previous Bacille Calmette-Guérin (BCG) vaccine [56, 57]. Expatriates should be rescreened 2 months after returning from travel [56, 58•]. Expatriates anticipating close contact with tuberculosis patients should also be counseled about the use of respirators; expatriates should bring supplies when traveling to resource-limited settings [58•]. Although BCG vaccination 2–6 months predeparture has been suggested for adults without LTBI at high risk of contracting MDR-TB, there are insufficient data to support this [4, 52].

Conclusions

Pretravel assessment should recognize health concerns and risks specific to expatriates and tailor guidelines to the reality of expatriate experience. The previously referenced studies highlight the increased risks of gastrointestinal disorders, malaria, LTBI, rabies, STIs, and psychiatric illness among expatriates. A thorough, individualized assessment based on destination, occupation, planned risk-taking behavior, and preexisting health conditions will inform pretravel vaccination and advice. Gaps in our knowledge of expatriate health should be addressed, and further research will serve to enhance the effectiveness of pretravel visits for expatriate travelers.

Compliance with Ethics Guidelines

Conflict of Interest Cassandra M. Pierre, Poh-Lian Lim, and Davidson H. Hamer declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of major importance

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