Illness in Travelers Returned From Brazil: The GeoSentinel Experience and Implications for the 2014 FIFA World Cup and the 2016 Summer Olympics

Mary E. Wilson,1 Lin H. Chen,2,3 Pauline V. Han,4 Jay S. Keystone,5 Jakob P. Cramer,6 Aluisio Segurado,7 DeVon Hale,8 Mogens Jensenius,9 Eli Schwartz,10,11 Frank von Sonnenburg,12 and Karin Leder13,14; for the GeoSentinel Surveillance Network

1Global Health and Population, Harvard School of Public Health, Boston, 2Mount Auburn Hospital, Cambridge, and 3Harvard Medical School, Boston, Massachusetts; 4Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, Georgia; 5Toronto General Hospital, University of Toronto, Ontario, Canada; 6Division of Tropical Medicine and Infectious Diseases, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; 7Department of Infectious and Parasitic Diseases, School of Medicine, University of Sao Paulo, Brazil; 8Department of Internal Medicine, University of Utah Medical Center, Salt Lake City; 9Oslo University Hospital, Norway; 10Chaim Sheba Medical Center, Tel Hashomer, and 11Tel Aviv University, Israel; 12Department of Infectious Diseases and Tropical Medicine, University of Munich, Germany; and 13Royal Melbourne Hospital, Parkville and 14Monash University, Melbourne, Victoria, Australia

Background. Brazil will host the 2014 FIFA World Cup and the 2016 Olympic and Paralympic Games, events that are expected to attract hundreds of thousands of international travelers. Travelers to Brazil will encounter locally endemic infections as well as mass event-specific risks.

Methods. We describe 1586 ill returned travelers who had visited Brazil and were seen at a GeoSentinel Clinic from July 1997 through May 2013.

Results. The most common travel-related illnesses were dermatologic conditions (40%), diarrheal syndromes (25%), and febrile systemic illness (19%). The most common specific dermatologic diagnoses were cutaneous larva migrans, myiasis, and tungiasis. Dengue and malaria, predominantly Plasmodium vivax, were the most frequently identified specific causes of fever and the most common reasons for hospitalization after travel. Dengue fever diagnoses displayed marked seasonality, although cases were seen throughout the year. Among the 28 ill returned travelers with human immunodeficiency virus (HIV) infection, 11 had newly diagnosed asymptomatic infection and 9 had acute symptomatic HIV.

Conclusions. Our analysis primarily identified infectious diseases among travelers to Brazil. Knowledge of illness in travelers returning from Brazil can assist clinicians to advise prospective travelers and guide pretravel preparation, including itinerary-tailored advice, vaccines, and chemoprophylaxis; it can also help to focus posttravel evaluation of ill returned travelers. Travelers planning to attend mass events will encounter other risks that are not captured in our surveillance network.

Keywords. Brazil; travelers; mass gatherings; dengue; dermatologic.
Olympic Games, which will take place mainly in Rio de Janeiro, will be held 5–21 August 2016, followed by the summer Paralympics, 7–18 September [2]. Based on data from the 2012 Olympics in London, the 2016 Olympic Games and Paralympics are expected to attract 600 000 international visitors, including 15 000–17 000 athletes [3].

Brazil is a large country with abundant natural resources and varied terrain, including the Amazon basin and tropical rain forests. In Rio de Janeiro alone, one can find beaches, mountains, a rain forest, and a lagoon. Although the sports events will be held at specific venues, travelers to these events may also visit other parts of Brazil.
Brazil has made great progress over the last 3 decades in providing safe water, improved sanitary facilities, and access to healthcare, including vaccination and human immunodeficiency virus (HIV) treatment [4]. However, attendees of these sports events will potentially be at risk for health problems, both infectious and noncommunicable, and exacerbation of chronic diseases. Noncommunicable health risks include intentional and unintentional injuries that can be caused by violence and mass gatherings, and environmental stressors. Infectious diseases include locally endemic infections as well as widely distributed infections, such as influenza and sexually transmitted infections (STIs). Risk for the latter may be heightened during mass gatherings [5].

Deaths from infectious diseases in Brazil have dropped dramatically since 1980 [4], yet malaria and yellow fever (YF) remain endemic in parts of the country (Figure 1). Dengue has caused recent massive urban outbreaks; HIV/AIDS is widespread; leishmaniasis and schistosomiasis are present in focal areas [6, 7].

In anticipation of increased travel to Brazil, we have analyzed data collected by the GeoSentinel Surveillance Network about illness in travelers returned from Brazil. Knowledge of these illnesses can inform health providers about specific risks and guide pretravel preparation; it can also help to focus posttravel evaluation of ill returned travelers. Our data describe primarily infectious diseases and underestimate the frequency of injury, which may be a greater risk to those attending mass events [8].

METHODS

The GeoSentinel Surveillance Network (www.istm.org/geosentinel) [9] is an international network of specialized travel and tropical medicine clinics located on 6 continents. All sites collect data by using a standard reporting form on ill travelers seen during or after international travel. Anonymized data on demographics, travel history, reason for travel, pretravel advice, hospitalization, major clinical symptoms, and final diagnoses assigned by the GeoSentinel site clinician are electronically entered into a central database. Diagnoses are selected from a standard list of >500 diagnostic codes, and involve syndromic groupings alone if no etiology is determined or syndromic groupings plus specific etiologies where possible. Individual patients can have >1 final diagnosis. All sites use the best reference diagnostic tests available in their own country. Country of exposure is identified by the clinician based on the travelers’ itinerary, known endemicity patterns of the destinations visited, and incubation period of the illness.

This evaluation includes ill travelers who were seen after travel at a GeoSentinel site from July 1997 through May 2013, with Brazil declared as the single country of exposure; travelers with another country of exposure stated along with Brazil were excluded. Those traveling for immigration were also excluded.

Final diagnoses were included if they had been classified as confirmed or probable. Demographic and travel characteristics of ill travelers returning from Brazil were described by using frequencies and proportions for categorical variables and median and range for continuous variables. Analysis of illness trends over time was based on monthly counts of ill returned travelers aggregated over the entire study period for dengue. Because the World Cup and Olympic Games will take place during the cooler months in Brazil, we specifically examined and aggregated top diagnoses reported during June through September. Numbers of dengue cases per month in Brazil during 2008–2012 are from the Brazilian Ministry of Health (link: http://dtr2004.saude.gov.br/sinanweb/tabnet/dh?sinannet/dengue/bases/denguebrnet.def). All data analysis was performed using SAS software, version 9.2 (Cary, North Carolina).

RESULTS

Table 1 shows the demographic and trip characteristics of 1586 ill returned travelers to Brazil. A majority of these travelers were male (55%), and they were often traveling for tourism (65%). Only 50% sought pretravel advice. Trip duration was <30 days for 59%. Of those who traveled to Brazil, 233 (15%) traveled to other countries within the 6 months before their clinic visit date. Top syndromic diagnoses in ill returned travelers (Table 2) were dermatologic (40%), diarrheal syndromes (25%), and febrile systemic illness (19%). The most frequent specific dermatologic diagnoses were cutaneous parasitic infections including cutaneous larva migrans (CLM), myiasis, and tungiasis; skin and soft tissue infections were also observed (Table 2). CLM was the most common diagnosis during June, July, and September (Table 3).

Among those with both acute and chronic diarrhea syndromes, no specific pathogen was identified for >50%. Campylobacter, the bacterial gastrointestinal pathogen most often identified, was found in 4%; giardiasis was diagnosed in 9%. Intestinal strongyloidiasis was diagnosed in 15 and hyperinfection syndrome in 1; schistosomiasis was diagnosed in 11.

Among 297 diagnoses of systemic febrile illness were 92 (31%) diagnoses of dengue fever and 25 (8%) diagnoses of malaria, 20 of them Plasmodium vivax (2 each Plasmodium falciparum and malaria species unknown, and 1 Plasmodium ovale). There were 17 diagnoses of Epstein-Barr virus/mononucleosis, 7 of cytomegalovirus, and 17 of influenza-like illness (2 confirmed).

Figure 2 shows the number of dengue fever diagnoses according to month for 2008 through 2012. Table 3 shows top diagnoses during the cooler months in Brazil, when fewer dengue infections were seen.

Dengue and malaria were the most common diagnoses leading to hospitalization, recorded for 20% of dengue and 64% of malaria patients. Infrequently diagnosed infections in ill
returned travelers to Brazil included rickettsial infections (n = 3), histoplasmosis (n = 3), visceral leishmaniasis (n = 1), and leptospirosis (n = 1). No deaths were recorded.

Although it was not one of the top diagnoses, HIV infection was found in 28 ill returned travelers, including 3 with AIDS. Eleven had newly diagnosed asymptomatic infection and 9 had acute symptomatic HIV. Among other STIs, syphilis was reported in 3, urethritis 3, lymphogranuloma venereum 1, and STI (undefined) 1.

No cases of measles, mumps, rubella, pertussis, acute hepatitis B, or yellow fever were reported, and most vaccine-preventable infections, except for influenza, were infrequent or not observed. Four cases of enteric fever (2 typhoid, 2 paratyphoid fever) and 4 hepatitis A cases were reported. Seventeen returned travelers were seen for rabies postexposure prophylaxis; specifically reported exposures were dogs (n = 7), monkeys (n = 3), and a cat (n = 1).

**DISCUSSION**

Mass gatherings entail a series of event-specific, individual health risks. In the past, many injuries and casualties have been attributable to stampedes and crush injuries, violence, crime, and even terrorist attacks, traffic accidents, and trauma associated with drug and alcohol intoxication [8]. Emotional stress, aggression, and cardiovascular events may be heightened risk, in particular during sports events, in addition to outdoor activity–specific health risks such as sunburn, heatstroke, or dehydration [8]. Although weather and environmental factors cannot be altered and many preventive and preemptive measures have to be organized by local authorities,
many of the above-listed health risks can be, at least partly, controlled by the individual (eg, using sun protection, continuous rehydration, and avoiding dangerous areas and excess alcohol consumption). Pretravel preparation should include education about these risks.

Travelers to Brazil may encounter Brazil-endemic infections as well as mass event–related problems. Based on GeoSentinel data, we have identified dermatologic problems, diarrhea, and febrile systemic infections (especially dengue) as the most common diagnoses in returned travelers from Brazil. Dengue fever and malaria were the most common reasons for hospitalization. Skin problems accounted for 40% of diagnoses in ill returned travelers. The most common diagnosis, CLM, was found in 11%. The etiologic agents of CLM are common in Brazil [10].

<table>
<thead>
<tr>
<th>Month and No. of Diagnoses</th>
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<td><strong>Table 3. Frequency of Top 5 Specific Diagnoses of Ill Returned Travelers Exposed in Brazil Seen at GeoSentinel Clinics, by Month, June–September</strong></td>
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<tr>
<td>CLM</td>
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<td>Acute diarrhea, etiology unknowna</td>
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Abbreviations: CLM, cutaneous larva migrans, hookworm-related; PI-IBS, irritable bowel syndrome, postinfectious; URTI, upper respiratory tract infection.

a Acute diarrhea, etiology unknown: diarrhea, acute bacterial; diarrhea, acute unspecified; gastroenteritis.
b There were 5 cases for each diagnosis.

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**Figure 2.** Dengue fever diagnoses of ill returned travelers exposed in Brazil seen at GeoSentinel clinics, by month, 2008–2012 (n = 48). Source: Ministry of Health (MOH), Brazil (http://dtr2004.saude.gov.br/sinanweb/tabnet/dh/sinannet/dengue/bases/denguebnet.def).
Almost 90% of dogs and 94.2% of cats in Adrandina Municipality, Sao Paulo, were infected with *Ancylostoma caninum* and *Ancylostoma brasiliense* [11]. Thirty percent of beach sand samples from Alto Beach, Pernambuco (near Recife) contained larvae of these organisms [12]. Most travelers acquire infection during beach exposures. Many popular tourist destinations and sites for the sports events, such as Rio de Janeiro, Salvador, Recife, and Fortaleza have coastal locations. Hookworm larvae in sand and soil penetrate the dermis and migrate superficially, causing migrating linear, serpiginous tracks accompanied by severe pruritus [13] (Figure 3). The feet are most often affected (39%), followed by the buttocks and abdomen. Infection may persist weeks to months, rarely up to a year. Oral albendazole or ivermectin provides safe, effective treatment [14, 15]. Prevention is by avoidance of skin contact with soil/sand.

Myiasis and tungiasis each accounted for >2% of diagnoses in ill returned travelers. Furuncular myiasis is a skin infection with the larva of a Diptera fly, most frequently *Dermatobia hominis* [16]. The adult fly lays its eggs on the underbelly of a mosquito that subsequently feeds on humans. The eggs lodge in the dermis and develop to third-stage larvae over 1–5 months, each manifesting as a small papule that enlarges to a tender nodule with a central punctum through which serosanguinous fluid drains (Figure 4). Treatment is by suffocation and removal of the larva [17]; prevention is by use of insect repellents and/or wearing long sleeves and trousers during the day.

Tungiasis, caused by penetration of the epidermis by the female sand fly *Tunga penetrans* and related species, can occur virtually anywhere on the skin, although >97% are found on the feet [18, 19]. Black papules at the site of penetration develop into nodules with a pale halo. Treatment is removal of the flea [20] (Figure 5); prevention is by the use of closed-toed footwear and avoidance of skin contact with soil.

Cutaneous leishmaniasis was seen infrequently in travelers returned from Brazil, although it remains a public health problem in focal areas (>20 000 new cases reported annually in Brazil) [21]; visceral leishmaniasis is a growing problem [4]. Travelers should be advised to reduce bites from sandflies, whose bite transmits infection, by using insect repellent and/or wearing long-sleeved shirts and trousers during evening hours in endemic regions.

Given the frequency of both acute and chronic diarrheal syndromes among ill travelers returning from Brazil, food and water precautions are recommended. Clinicians may provide symptomatic anti-diarrheal agents and antibiotics for presumptive self-treatment should diarrhea develop (eg, loperamide plus quinolone or azithromycin for bacterial pathogens).
Dengue, the most frequent specified cause of systemic febrile illness, was reported in almost 6% of ill returned travelers; 20% were hospitalized. Cases occurred throughout the year (Figure 2). Since 1986, dengue in Brazil has increased in incidence and severity [22]. Massive epidemics have affected urban centers, including Rio de Janeiro and Sao Paulo [22, 23]; 3.5 million cases were reported during 2000–2009. Three dengue serotypes, DENV-1, DENV-2, and DENV-3, circulate widely in Brazil; DENV-4 has caused recent outbreaks [24]. Transmission is most intense during February through June. The day-biting main mosquito vector, Aedes aegypti, is widespread in urban areas. The primary way to avoid infection is to prevent mosquito bites with repellent on exposed skin. Only travelers to certain areas of Brazil will be at risk for malaria, but travelers to all areas will be at risk for dengue.

Malaria transmission persists in the Brazilian Amazon region (Figure 1); about 300,000 cases are reported annually, with P. vivax accounting for >80% and P. falciparum <20% of cases. GeoSentinel cases reflect these proportions. Travelers who visit malaria-endemic areas can be protected with chemophylaxis [25]. Some non-US guidelines recommend standby emergency treatment as an alternative.

No cases of yellow fever were recorded among 1586 ill returned travelers to Brazil; however, cases still occur in Brazil despite vaccination programs. From 1973 through 2008, among the 831 notified cases of YF in Brazil, mortality was 51%. Groups most affected were migrant laborers, farm workers, and tourists [26]. In recent years, the Brazil Ministry of Health has expanded the areas for which YF vaccination is recommended. Vaccination is not recommended for travel to the large eastern cities of Rio de Janeiro, Sao Paulo, Salvador, Recife, and Fortaleza, but is recommended for several cities hosting World Cup events, including Belo Horizonte, Brasilia, and Manaus (Figure 1). Urban areas in Brazil are infested with mosquitoes competent to transmit YF virus [27]. Brazil has reported to the World Health Organization that no YF vaccine is required—except for the Southern Hemisphere, but if that is not available, then pretravel vaccination with the Northern Hemisphere strains should be considered. Influenza outbreaks can spread rapidly during mass events, and returning travelers aid global virus dispersal [40].

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Traveler Dengue prevention and other vector avoidance measures
Measles-mumps-rubella
Hepatitis A
Malaria chemoprophylaxis
Yellow fever vaccine
Skin disorder precautions

Review needs based on specific travel destination:
• Yellow fever vaccine
• Malaria chemoprophylaxis

All travelers should be up-to-date on their routine vaccines. In particular, document receipt of vaccination for (or immunity to):
• Hepatitis A
• Influenza
• Measles-mumps-rubella

Advise travelers on specific risks:
• Dengue prevention and other vector avoidance measures
• Traveler’s diarrhea prevention and self-management
• Skin disorder precautions

Review needs based on specific travel destination:
• Yellow fever vaccine
• Malaria chemoprophylaxis

Limitations
These results reflect sentinel surveillance data among ill returned travelers visiting specialist (GeoSentinel) clinics and are not representative of all ill returned travelers. Individuals traveling to the World Cup or Olympic events may have a different spectrum of illnesses. Those with mild or self-limited illnesses may not seek care or may see their primary care provider. People do not seek care for injuries or STIs at a GeoSentinel clinic. Hospitalized patients may not be captured in the database. Denominators including travelers who remained healthy are lacking, so the incidence of illness in travelers cannot be calculated. Additionally, immunization status and use of malaria chemoprophylaxis are unknown. In only 10% of diagnoses was the probable location of illness acquisition within Brazil recorded, too small to derive meaningful conclusions about regional differences. Finally, this analysis is based on past events. Future risks could be different, including potential disrupters, such as chikungunya virus, a novel coronavirus, and new influenza viruses. Although local transmission of chikungunya virus has not yet been reported in Brazil, competent vectors are present [40]. Since December 2013, local transmission has been reported in the Americas [42]. Introduction into Brazil is a serious threat, given large numbers of visitors from areas with ongoing chikungunya virus transmission [43].

Although this paper highlights risks for travelers to mass sports events, the findings are also relevant to those traveling to Brazil for other reasons and at other times. Preparation for Brazil travel (Table 4) involves reviewing the itinerary for potential need for YF vaccination and malaria chemoprophylaxis. Influenza vaccination, if available, would be prudent for those visiting during May–August, especially for those attending mass events. Travelers should be reminded about avoiding blood-borne infections and STIs, including HIV. Education about avoiding food and water-borne infections, vector-borne infections, and CLM and other common skin infections should be part of the preparation for all travelers (Table 4). The findings in this analysis also will be helpful to clinicians caring for ill returned travelers from Brazil by providing data about more and less common diagnoses and directing them to useful resources.

Notes
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