Acute and Potentially Life-Threatening Tropical Diseases in Western Travelers—A GeoSentinel Multicenter Study, 1996–2011

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Abstract. We performed a descriptive analysis of acute and potentially life-threatening tropical diseases among 82,825 ill western travelers reported to GeoSentinel from June of 1996 to August of 2011. We identified 3,655 patients (4.4%) with a total of 3,666 diagnoses representing 13 diseases, including falciparum malaria (76.9%), enteric fever (18.1%), and leptospirosis (2.4%). Ninety-one percent of the patients had fever; the median time from travel to presentation was 16 days. Thirteen (0.4%) patients died: 10 with falciparum malaria, 2 with melioidosis, and 1 with severe dengue. Falciparum malaria was mainly acquired in West Africa, and enteric fever was largely contracted on the Indian subcontinent; leptospirosis, scrub typhus, and murine typhus were principally acquired in Southeast Asia. Western physicians seeing febrile and recently returned travelers from the tropics need to consider a wide profile of potentially life-threatening tropical illnesses, with a specific focus on the most likely diseases described in our large case series.

INTRODUCTION

Each year, an estimated 50 million travelers from Western countries visit tropical regions of the world, and these numbers are rapidly growing.[1] This travel is a modern phenomenon, because only a few generations ago, many parts of the tropics were virtually inaccessible to Western travelers because of the presence of potentially fatal tropical diseases. Vivid historical examples include the ill-fated 1874–1877 Henry Morton Stanley trans-African expedition, during which two-thirds of the participants died of malaria, sleeping sickness, and other conditions, and the French attempt to construct the Panama Canal in the 1880s, an endeavor that was aborted because of heavy human losses from malaria and yellow fever.[2]

Even in the 21st century, western travelers can contract tropical diseases that, if left untreated, can be fatal within the first few weeks of symptom onset. Given the potentially serious consequences for the patients and in some cases, their close contacts and healthcare workers,[3] it is important that life-threatening tropical diseases are swiftly diagnosed. However, a low index of suspicion, especially in the primary care setting, and limited availability of diagnostic tests may preclude optimal management of these diseases, which are unfamiliar to most western physicians.

With the exception of falciparum malaria, enteric fever, and rickettsioses,[4–6] current data on severe tropical diseases in travelers are scarce and usually confined to single case reports and smaller case series.[3,7,8] Here, we describe all cases of acute and potentially life-threatening tropical diseases in western travelers reported to the GeoSentinel Surveillance Network from June of 1996 to August of 2011.

MATERIALS AND METHODS

Data source. GeoSentinel is a global network (www .geosentinel.org) established in 1995 through the International Society of Travel Medicine and the Centers for Disease Control and Prevention with the goal of monitoring travel-related morbidity. Currently, 57 GeoSentinel travel and tropical medicine clinics, located in 26 countries on six continents, contribute clinician-based anonymous information on ill travelers. Most reported cases are seen at the GeoSentinel sites, but sites can also report cases that they have been consulted about at other institutions. Data, entered in a structured query language database at a central data center, include presenting symptoms, demographic information, history of recent travel, reason for travel, outpatient or inpatient status, whether the patient was seen during or after travel, independent versus organized travel, whether the patient had a pre-travel encounter with a healthcare provider, diagnosis, and outcome. To be included in the database, patients must have crossed an international border within 10 years of presentation and must be seeking medical care for a presumed travel-related illness. All GeoSentinel sites use the best available reference diagnostic methods in their own country. The diagnosis of each case may be reported as confirmed, probable, or suspected, and it is selected from a standardized list of > 500 etiologic and syndromic diagnoses. A patient might receive several diagnoses. Non-fatal complications are not systematically reported; the major exception is malaria and dengue, for which complications (e.g., cerebral malaria and dengue hemorrhagic fever/dengue shock syndrome [DHF/DSS]) are routinely reported. Outcomes are categorized as either survival or death.[9]

Inclusion criteria and definitions. We performed a descriptive analysis based on data entered into the GeoSentinel database from June of 1996 to August of 2011. Only ill travelers who lived in North America, Europe, Israel, Japan, Australia, and New Zealand and were seen during or after travel to Central and South America, Africa, Oceania, and tropical and subtropical parts of Asia with a confirmed or probable

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diagnosis of an acute and potentially life-threatening tropical disease were included in the analyses. Travelers with immigration as a sole reason for travel were excluded. An acute and potentially life-threatening tropical disease was defined as an infectious disease that, as of this writing, is largely confined to tropical and subtropical areas of the world, with an incubation period of < 4 weeks and an estimated > 5% risk of death within 4 weeks after symptom onset if left untreated. In the GeoSentinel diagnosis list, 21 diseases fulfill these criteria, including 6 viral infections or syndromes, 12 bacterial infections, and 3 protozoan infections (Table 1). Cases of spotted fever group rickettsiosis were included only if they were acquired outside sub-Saharan Africa, where the benign African tick bite fever is the predominant disease.[10] The microbiological diagnostic methods varied according to the infection and included blood smears (for malaria, relapsing fever, and East African sleeping sickness), immunochromatography tests (for falciparum malaria and dengue), bacteriologic cultures (for typhoid and paratyphoid fever and melioidosis), serology (for leptospirosis, rickettsiosis, and viral infections), and polymerase chain reaction (PCR; for knowlesi malaria, relapsing fever, and viral infections). Complicated malaria and DHF/DSS were diagnosed according to World Health Organization (WHO) criteria.[11,12] A confirmed case was defined as illness in a traveler with a pertinent travel history and presentation plus microbiological test results supporting recent infection; a probable case was defined as illness in a traveler with pertinent travel history and presentation but inconclusive or unavailable microbiology test results and no plausible alternate diagnosis. Individual countries were grouped according to the United Nations region and subregion system.[13] Classification of reason for travel related to current disease was grouped into four categories: tourism, business, visiting friends and relatives (VFR), and other reason, including foreign aid and missionary or military deployment.

TABLE 1

Infections and syndromes included in life-threatening tropical diseases in western travelers: data from the GeoSentinel surveillance network, 1996–2011

Viral infections or syndromes	Avian influenza
	DHF/DSS
	Lassa fever and other tropical hemorrhagic fevers
	Japanese encephalitis and other tropical encephalitides
	Rift Valley fever
	Yellow fever
Bacterial infections	Anthrax
	Carrion's disease*
	Epidemic typhus
	Leptospirosis
	Melioidosis
	Murine typhus
	Paratyphoid fever
	Plague
	Relapsing fever
	Scrub typhus
	Spotted fever group rickettsioses†
	Typhoid fever
Protozoan infections	East African sleeping sickness‡
	Falciparum malaria
	Knowlesi malaria

* *Bartonella bacilliformis* infection.
† Only cases acquired outside sub-Saharan Africa.
‡ *Trypanosoma brucei rhodesiense* infection.

Statistical analysis. For each life-threatening diagnosis, a descriptive analysis was performed on demographics and trip characteristics. Time from travel to clinic visit was estimated for post-travel cases only. Simple frequency statistics and percentages were calculated for categorical variables, and median and range statistics were calculated for continuous variables. All data were analyzed by using the SAS software (version 9.2).

RESULTS

We identified 82,825 ill western travelers with exposure in tropical and subtropical regions who had sought medical care or were consulted at a GeoSentinel site from June of 1996 to August of 2011. Of these travelers, 3,655 (4.4%) patients with 3,666 diagnoses had an acute and potentially life-threatening disease, the four most common conditions being falciparum malaria (76.9%), typhoid fever (11.7%), paratyphoid fever (6.4%), and leptospirosis (2.4%). The complete list of diagnoses with accumulated number totals is presented in Figure 1. Demographic, travel characteristics, and hospitalization and death totals are shown in Table 2; 91% of the patients had fever, 60% of patients were hospitalized, and 0.4% of patients died. The geographic distribution of acquisition of the four most common diagnoses is depicted in Figure 2. There were no cases of anthrax, plague, Carrion's disease (*Bartonella bacilliformis* infection), epidemic typhus, diphtheria, avian influenza, Lassa or other African hemorrhagic fevers, yellow fever, Rift Valley fever, or tropical encephalitides, except for a single case of Japanese encephalitis. Cases were reported from all 57 GeoSentinel sites: 62% of the cases were reported from sites in Europe, 20% of the cases were reported from North America, 4% of the cases were reported from New Zealand/Australia, and 14% of the cases were reported from other regions. Data were largely complete for key variables (age = 98.9%, sex = 99.6%, and purpose of travel = 99.9%) but less complete for some supplementary information (pre-travel encounter = 93.6%).

Table 3 presents data for the viral infections examined. DHF/DSS was diagnosed in 18 travelers, which constitutes 0.9% of all dengue cases ($N = 1,910$) among western travelers reported to GeoSentinel network during the study period; one-third of the DHF/DSS cases were contracted in Thailand. A Norwegian female tourist in her fifties who was infected in March of 2008 in Phuket, Thailand, died of PCR-confirmed DHF/DSS. One case of non-fatal serologically confirmed Japanese encephalitis was reported in a female Canadian tourist in her twenties after a 4-week trip to Thailand in September of 2010.

Selected data for the 820 cases of bacterial disease are presented in Table 4. Among the patients with the 428 cases of typhoid fever, the two most common reasons for travel were tourism and VFR travel; 67% of cases were acquired in South Central Asia (India, $N = 147$, 34% of total; Nepal, $N = 55$, 13%; Pakistan, $N = 28$, 7%; and Bangladesh, $N = 26$, 6%). Of the 210 travelers with paratyphoid fever, 79% were infected in South Central Asia (India, $N = 79$, 38% of total; Nepal, $N = 63$, 30%; Pakistan, $N = 22$, 10%; and Bangladesh, $N = 11$, 5%). Leptospirosis was diagnosed in 88 travelers, of whom 82% were tourists; most cases were acquired in Southeast Asia (Thailand, $N = 19$, 22% of total; Laos, $N = 11$, 13%; Indonesia, $N = 6$, 7%). Rickettsioses were seen in 58 travelers,
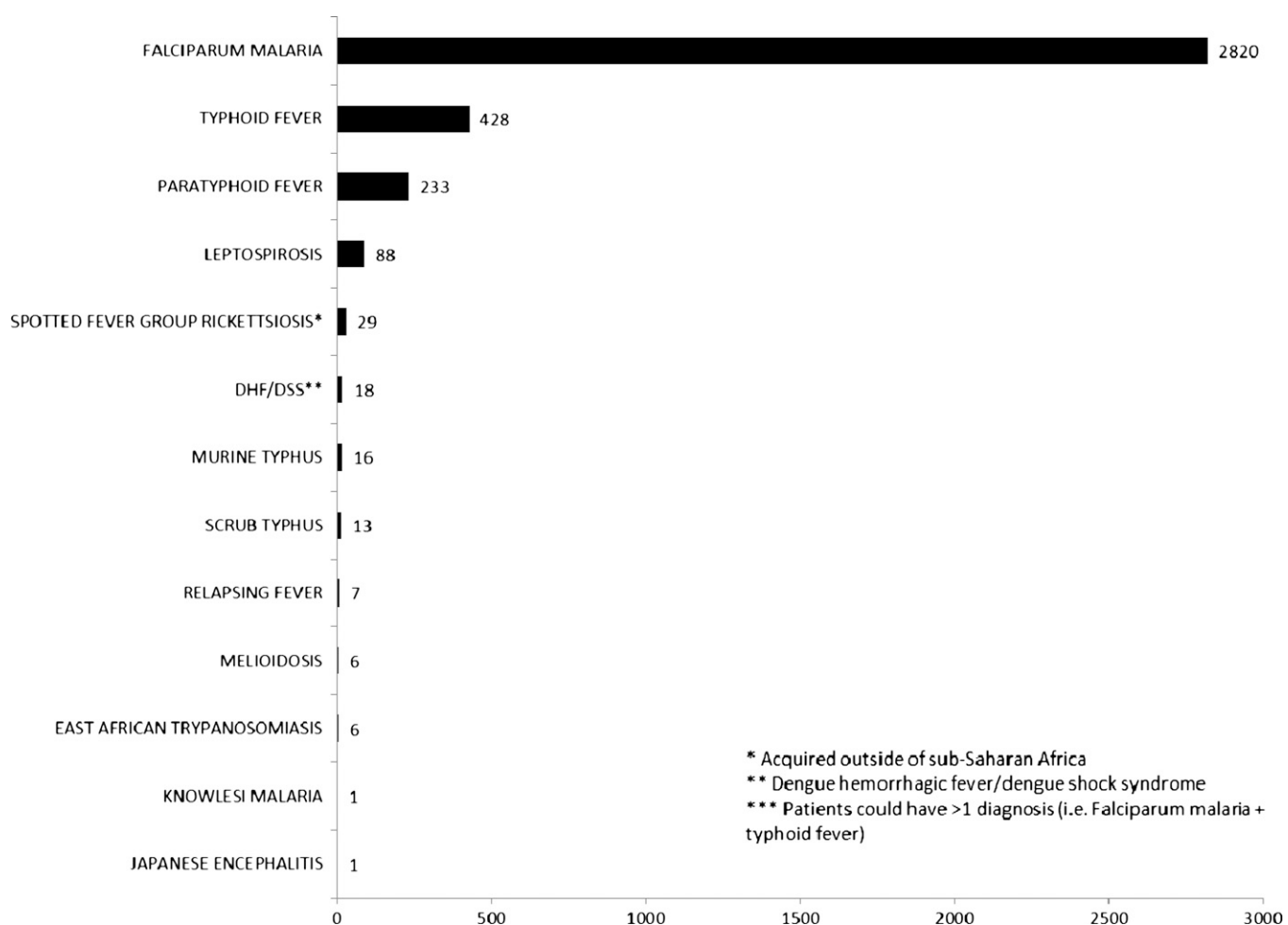
FIGURE 1. Total cases of acute and potentially life-threatening diseases (*N* = 3,666) among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011.

TABLE 2

Total cases of acute and potentially life-threatening diseases (*N* = 3,666) among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011

	n (%)
Total number of patients	3,655
Age (median; range in years)	35 (0–80)
Males	2,381 (65)
Reason for travel	
Tourism	1,009 (28)
Business	453 (12)
VFR	1,765 (48)
Other	426 (12)
Pre-travel consultation	1,210 (35)
Exposure region	
Caribbean	69 (2)
Central America	51 (1)
Middle East	8 (< 1)
North Africa	37 (1)
Northeast Asia	8 (< 1)
Oceania	30 (1)
South America	46 (1)
South Central Asia	515 (14)
Southeast Asia	193 (5)
Sub-Saharan Africa	2,700 (74)
Hospitalizations	2,180 (60)
Deaths	13 (< 1)

including 29 cases of spotted fever group rickettsiosis acquired outside sub-Saharan Africa, 16 cases of murine typhus, and 13 cases of scrub typhus. Most cases were seen in tourists. Although spotted fever group rickettsiosis was seen after travel to several regions, murine typhus and scrub typhus were largely confined to travelers to Southeast Asia. Relapsing fever was seen in seven travelers, of whom five were exposed in sub-Saharan Africa. Melioidosis was diagnosed in six patients, of whom a 35-year-old male French tourist to Martinique and a 57-year-old male Australian business traveler to Phuket, Thailand, had septicemia and died.

Table 5 presents selected data for the 2,827 patients with protozoan diseases. Falciparum malaria was mainly seen in males, with the three most common reasons for travel being VFR, tourism, and business. Fifty-four percent of the cases were acquired in West Africa (Ghana, *N* = 380, 13% of total; Nigeria, *N* = 294, 10%; and Côte d'Ivoire, *N* = 195, 7%). Of the 177 (6.3%) patients who developed complicated malaria, 46 (26%) patients were VFR travelers. Ten (0.4%) patients died; among VFR cases, the fatality rate was 1/1,572 (0.06%). The single case of knowlesi malaria was seen in a 40-year-old New Zealand male business traveler to Bintalu, Sabah State, Malaysia, who had complicated disease. The six travelers with East African sleeping sickness (*Trypanosoma brucei rhodesiense* infection) were infected in Tanzania (*N* = 2),
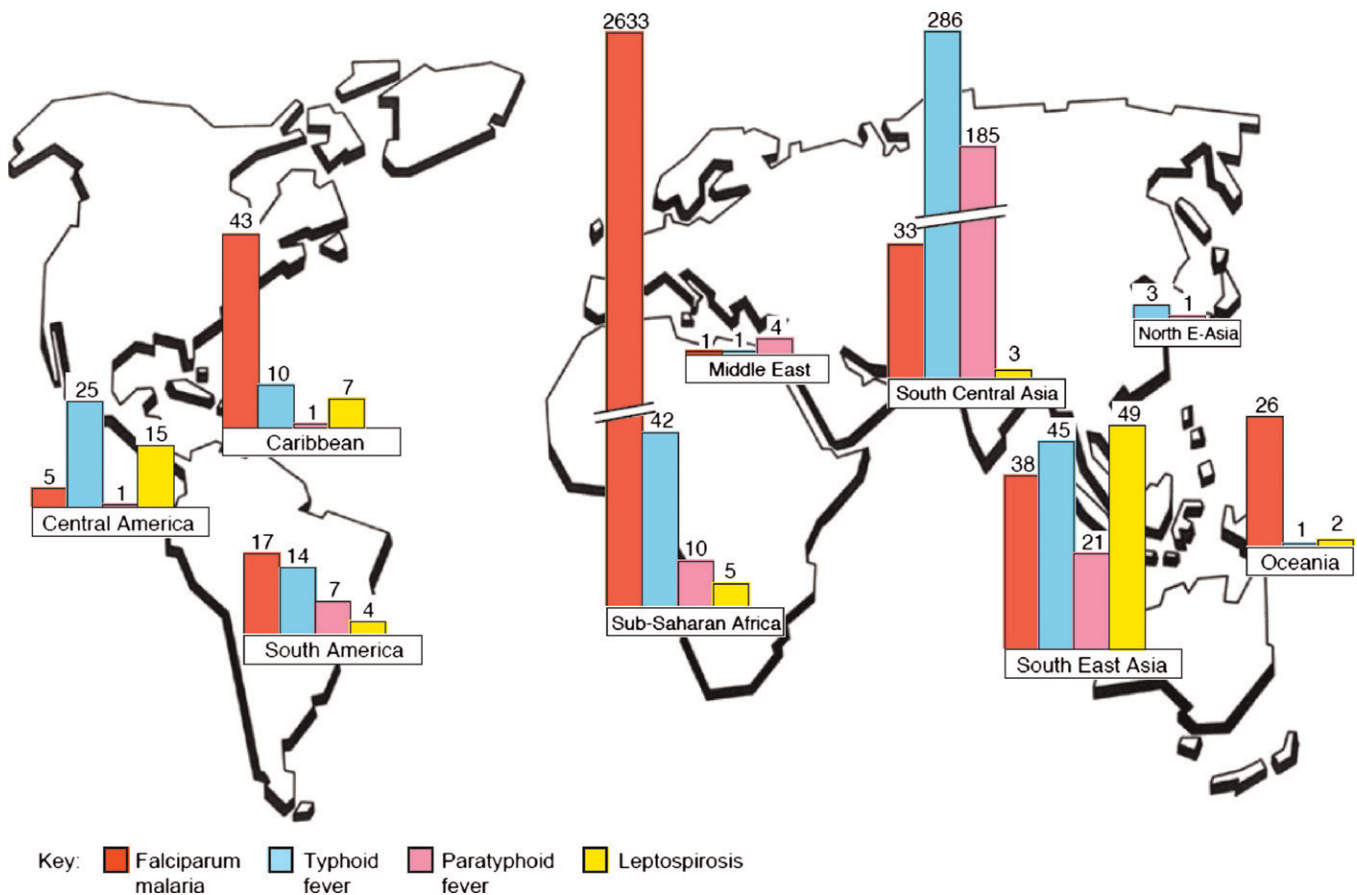
FIGURE 2.   Number of cases of selected acute and potentially life-threatening diseases by exposure region among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011.

TABLE 3

Cases of acute and potentially life-threatening viral diseases ($N = 19$) among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011

	DHF/DSS*	Japanese encephalitis
Total number of cases	18	1
Age (median; range in years)	28.5 (0–60)	26 (NA)
Time to presentation (median; range in days)†	6.5 (0–181)	NA
Males (n, %)	8 (47)	0
Reason for travel (n, %)		
Tourism	9 (50)	1
Business	1 (6)	0
VFR	5 (28)	0
Other	3 (17)	0
Pre-travel consultation (n, %)	5 (33)	0
Exposure region (n, %)		
Caribbean	5 (28)	0
Central America	0 (0)	0
Middle East	0 (0)	0
North Africa	0 (0)	0
Northeast Asia	0 (0)	0
Oceania	0 (0)	0
South America	0 (0)	0
South Central Asia	4 (22)	0
Southeast Asia	9 (50)	1
Sub-Saharan Africa	0 (0)	0
Hospitalizations (n, %)	13 (76)	1
Death (n, %)	1 (6)	0

NA = not applicable.
*WHO criteria.
†For cases seen post-travel only.

Kenya ($N = 1$), Zambia ($N = 2$), and Zimbabwe ($N = 1$). The last three cases were reported from GeoSentinel sites in Canada, the United Kingdom, and the United States from August 24 to November 15, 2010, and they occurred in safari tourists to South Luangwa National Park and South Luangwa Valley in southern Zambia and Mana Pools National Park in northern Zimbabwe. Five of six persons were hospitalized, and all survived.

DISCUSSION

Since colonial times, the risk for western travelers of contracting potentially severe tropical disease has dramatically declined, largely because of containment of these diseases in many endemic areas and better protection of travelers by education, immunization, and use of chemoprophylaxis. The risk, however, is never nil, and the number of travelers to tropical areas is increasing; sub-Saharan Africa and Southeast Asia, in particular, have shown a strong growth in tourist travel.[1] In our study, which is based on the largest cases series available of ill western travelers with exposure in the tropics and subtropics, the proportion of acute and potentially life-threatening tropical disease was as high as 4.6%.

A common perception is that VFRs and long-stay travelers, such as missionaries, aid workers, and volunteers, would be most susceptible to serious exotic infections. Indeed, in this study, less than 30% of travelers overall were standard tourists. However, this percentage is mostly because of the large

TABLE 4

Cases of acute and potentially life-threatening bacterial diseases (N = 820) among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011

	Typhoid fever	Paratyphoid fever	Leptospirosis	Spotted fever group rickettsiosis*	Murine typhus	Scrub typhus	Relapsing fever	Melioidosis
Total number of cases	428	233	88	29	16	13	7	6
Age (median; range in years)	28 (1–77)	27 (6–75)	34.5 (19–66)	36.5 (15–73)	29.5 (19–69)	30 (19–67)	39 (21–62)	38 (27–58)
Time to presentation (median; range in days)†	12 (1–179)	15 (1–150)	9 (1–140)	9.5 (1–115)	14 (1–43)	6 (1–102)	16 (1–144)	14 (1–28)
Males (n, %)	232 (54)	137 (59)	72 (82)	16 (55)	8 (50)	9 (69)	5 (71)	5 (83)
Reason for travel (n, %)								
Tourism	210 (49)	131 (56)	71 (82)	20 (69)	9 (56)	11 (85)	2 (43)	3 (50)
Business	36 (8)	17 (7)	8 (9)	4 (14)	0 (0)	2 (15)	1 (14)	3 (50)
VFR	123 (28)	54 (23)	3 (4)	4 (14)	3 (19)	0 (0)	1 (14)	0 (0)
Other	59 (14)	31 (13)	5 (6)	1 (4)	4 (25)	0 (0)	3 (43)	0 (0)
Pre-travel consultation (n, %)	160 (40)	113 (53)	32 (40)	12 (43)	5 (33)	6 (50)	3 (43)	1 (20)
Exposure region (n, %)								
Caribbean	10 (2)	1 (< 1)	7 (8)	2 (7)	0 (0)	0 (0)	0 (0)	1 (17)
Central America	25 (6)	1 (< 1)	15 (17)	4 (14)	1 (6)	0 (0)	0 (0)	0 (0)
Middle East	1 (< 1)	4 (2)	0 (0)	1 (4)	0 (0)	0 (0)	1 (14)	0 (0)
North Africa	1 (< 1)	3 (1)	3 (3)	5 (17)	1 (6)	0 (0)	1 (14)	0 (0)
Northeast Asia	3 (1)	1 (< 1)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)	0 (0)
Oceania	1 (0.3)	0 (0)	2 (2)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)
South America	14 (3)	7 (3)	4 (5)	2 (7)	1 (6)	0 (0)	0 (0)	1 (17)
South Central Asia	286 (67)	185 (79)	3 (3)	6 (21)	1 (6)	2 (15)	0 (0)	0 (0)
Southeast Asia	45 (11)	21 (9)	49 (56)	5 (17)	10 (63)	10 (77)	0 (0)	4 (67)
Sub-Saharan Africa	42 (10)	10 (4)	5 (7)	0 (0)	2 (13)	0 (0)	5 (71)	0 (0)
Hospitalization (n, %)	191 (45)	133 (57)	44 (50)	13 (45)	8 (50)	2 (15)	6 (86)	4 (67)
Death (n, %)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (33)

NA = not applicable.
*For cases exposed outside of sub-Saharan Africa.
†For cases seen post-travel only.

TABLE 5

Cases of acute and potentially life-threatening protozoan diseases (N = 2,827) among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011

	Falciparum malaria	Knowlesi malaria	East African trypanosomiasis
Total number of cases	2,820	1	6
Age (median; range in years)	37 (0–80)	40 (NA)	45.5 (31–71)
Time to presentation (median; range in days)*	10 (1–341)	22 (NA)	6 (1–38)
Males (n, %)	1,890 (67)	1	3 (50)
Reason for travel (n, %)			
Tourism	541 (19)	0	5 (83)
Business	381 (14)	1	1 (17)
VFR	1572 (56)	0	0 (0)
Other	323 (11)	0	0 (0)
Pre-travel consultation (n, %)	879 (33)	0	2 (33)
Exposure region (n, %)			
Caribbean	43 (2)	0	0 (0)
Central America	5 (< 1)	0	0 (0)
Middle East	1 (< 1)	0	0 (0)
North Africa	23 (1)	0	0 (0)
Northeast Asia	1 (< 1)	0	0 (0)
Oceania	26 (1)	0	0 (0)
South America	17 (1)	0	0 (0)
South Central Asia	33 (1)	0	0 (0)
Southeast Asia	38 (1)	1	0 (0)
Sub-Saharan Africa†	2,633 (93)	0	6 (100)
Western Africa	1,527		
Central Africa	349		
Eastern Africa	286		
Northern Africa	23		
Southern Africa	11		
Hospitalizations (n, %)	1,765 (63)	0	5 (83)
Complicated malaria‡ (n, %)	177 (6)	1	NA
Deaths (n, %)	10 (< 1)	0	0 (0)

NA = not applicable.
*For cases seen post-travel only.
†Sub-Saharan Africa categories based on United Nations region.
‡WHO criteria.[9]

number of falciparum malaria cases in the study cohort, where VFR travelers have a large predominance. For many other acute and potentially life-threatening diseases, standard tourists (i.e., the traveler type most commonly seen in the pre-travel consultation context) predominate: typhoid fever (49%), paratyphoid fever (56%), leptospirosis (82%), rickettsioses (69%), melioidosis (50%), and severe dengue (50%).

Among the > 82,000 ill western travelers evaluated in our study, no cases were reported of much-feared tropical viral infections such as yellow fever, Lassa fever, and Ebola virus infection. Actually, the prevalence among ill travelers reported to GeoSentinel of potentially severe viral disease was very low, and we detected only 1 case of Japanese encephalitis and 18 cases of DHF/DSS. The rarity of viral hemorrhagic fevers as a cause of imported fever has been emphasized by others and should be borne in mind when making a risk assessment about investigation, management and possible isolation of a febrile returned traveler. National guidelines for dealing with febrile travelers usually focus on the potential severity of a viral hemorrhagic fever and reduction of the risk of potential nosocomial transmission rather than its extreme rarity.[14]

We identified 867 cases of potentially life-threatening bacterial diseases. The most commonly seen entity, enteric fever caused by *Salmonella enterica serotype* Typhi and *S. enterica serotype* Paratyphi, has an untreated mortality rate in the range of 10–20%, which is indicated by studies from the pre-antibiotic era.[15] However, consistent with recent studies from developed countries,[16,17] no fatalities were identified among the 661 patients in this analysis, a finding that may reflect the efficacy of modern treatment of enteric fever. Most of our cases were acquired by males and travelers to the Indian subcontinent, but in contrast to other studies,[16–18] we identified most cases in tourists and relatively fewer among VFR

travelers. The proportion of *S. enteric serotype* Paratyphi infection in this case series highlights this pathogen as an emerging infection throughout the Indian subcontinent for which vaccine is not available.[5,19]

Our 88 cases of leptospirosis, a zoonosis caused by various members of the *Leptospira* species and typically acquired during freshwater activities such as rafting and swimming, were largely seen in males, tourists, and persons traveling to Southeast Asia. This finding is consistent with the findings of a recent Israeli study, where most of the patients were male tourists infected in the Mekong River in Laos.[20] None of our patients reportedly died, but untreated cases infected with certain serogroups (e.g., *L. icterohaemorrhagiae*) may carry a substantial mortality.

Rickettsioses are vector-borne bacterial diseases that typically present as an acute febrile illness with constitutional symptoms and skin eruptions. Most travel-associated cases represent the benign African tick bite fever caused by *Rickettsia africae* and are acquired in rural sub-Saharan Africa,[10] but occasionally, travelers to other destinations may contract potentially life-threatening rickettsioses, such as scrub typhus, Mediterranean spotted fever, Indian tick typhus, and murine typhus.[6] Most of our 58 cases of rickettsioses were acquired by tourists. Whereas spotted fever group rickettsiosis was acquired in diverse regions, scrub typhus and murine typhus were largely confined to visitors to Southeast Asia. Forty percent of our cases with rickettsioses were hospitalized, but no fatalities were identified, a finding that, in part, may be explained by the frequent empiric use of doxycycline in cases of suspected rickettsial infection at GeoSentinel sites.[6]

Melioidosis caused by *Burkholderia pseudomallei*, a motile gram-negative rod found in soil and surface water in tropical Asia, northern Australia, and Latin America, is rarely seen in western travelers.[7] Melioidosis may have a dramatic course, with rapid clinical deterioration and fatal outcome. Two of our six cases died with septicemia, underscoring that clinicians seeing returnees from endemic areas with fulminant bacterial infections should consider the possibility of acute melioidosis and institute an antipseudomonal antibiotic (e.g., ceftazidime or a carbapenem).[21]

Falciparum malaria was overwhelmingly the most commonly imported potentially severe tropical disease in our study. Cases were primarily seen among males, VFR travelers, and visitors to West Africa, a finding that suggests that health education is particularly inadequate for some ethnic minorities visiting their countries of origin and that stronger efforts to reach these risk groups are needed. As in a United Kingdom study of > 24,000 cases seen from 1987 to 2006, we found that a significant proportion of cases were acquired in Nigeria, Ghana, and Côte d'Ivoire, none of which are typical tourist destinations.[4] Similarly, in a large analysis of > 12,000 cases of imported pediatric malaria, the main risk areas were VFR destinations rather than tourist targets.[22] Immigrants from endemic areas may consider malaria a benign condition, but it should be noted that 26% of our cases with complicated falciparum malaria did occur in this particular subgroup of travelers. Still, only 0.06% of our VFR patients with falciparum malaria are known to have died. This percentage is even lower than in a recent large United Kingdom survey on imported malaria, where the fatality rate was 0.32% among VFR travelers.[23] We assume that such findings might be explained by a high proportion of some degree of immunity combined with

rapid and proper medical management at many western hospitals.[24,25] In our study, males represented 67% of the falciparum malaria cases. This finding is consistent with an Israeli study on post-travel–related hospitalization, where 75% of malaria cases were seen in males,[26] and it probably reflects different risk-taking behaviors between the sexes.

We detected six cases of East African sleeping sickness, a disease that, in contrast to its West African counterpart (*T. brucei gambiense* infection), may be fatal within a few weeks if not properly managed. Interestingly, three of our cases were reported within less than 3 months in 2010 and occurred in safari tourists to nearby areas in northern Zimbabwe and southern Zambia. Two additional cases infected in the same region were reported by others,[27] but whether these five cases in close temporal proximity represent sentinel events for increased focal activity in the South Luangwa Valley or reflect increased incursions by travelers into this sparsely populated area is unknown. Only four other travel-related cases infected in this region were reported to the WHO during the past decade (Simarro P, personal communication).

To swiftly diagnose and properly manage acute and potentially fatal tropical diseases in returning travelers is one of the most important tasks in post-travel medicine. Given the huge numbers of ill returnees presenting with various symptoms, this endeavor may seem impossible. However, the present study may provide some useful hints. First, our cases had a median time lag from travel to clinic visit of less than 17 days, and 91% of the patients had fever. Thus, when evaluating ill travelers from the tropics, the attending physician should always initially focus on recent returnees who present with a febrile illness not obviously explained by other causes. Second, consistent with a previous GeoSentinel paper,[9] our study suggests that the spectrum of acute and potentially life-threatening tropical diseases illness varies with the type of traveler and the geographic destination. Whereas falciparum malaria was mainly acquired by males, VFR travelers, and visitors to West Africa, enteric fever was largely seen in VFR travelers, tourists, and visitors to the Indian subcontinent. Likewise, leptospirosis, scrub typhus, and murine typhus were typically contracted by males, tourists, and travelers to Southeast Asia.

That said, infections with a global distribution (such as meninogococcemia and other forms of septicemia and severe bacterial pneumonia, including legionnaires) can also be life-threatening and must be considered by clinicians evaluating febrile returnees. These cosmopolitan infections can account for one-third or more of patients hospitalized with fever post-travel.[28] Clinicians must focus on all types of potentially life-threatening infections and not just the less familiar tropical ones.

The limitations of this study are shared by other reports published by the GeoSentinel network.[6,9,25,28] Because most GeoSentinel sites are located within academic medical institutions, our data may be biased to unusual or complicated cases and may not reflect the typical pattern of disease seen by general practitioners. The seemingly high proportion of benign clinical courses could be explained by the protocols at some high-volume GeoSentinel sites that see mainly outpatients, and where subsequent hospitalizations might not be captured and reported to GeoSentinel. Therefore, the low rate of hospitalization and death should not necessarily be interpreted as most cases were of mild severity. The seemingly long time from symptom onset to clinic visit for some cases can be explained by the fact that most GeoSentinel sites

also act as referral centers, to which patients are referred for a second opinion sometimes weeks or months after the acute illness. A major strength of our study is the detail in core epidemiologic factors, such as sex, age, reason for travel, and travel destination, for these life-threatening diseases.

In summary, our study suggests that clinicians need to consider a wide range of potentially life-threatening tropical infections in recently returned febrile travelers from the tropics and subtropics based on sex, reason for travel, and destination. Despite marked improvements in diagnostic and therapeutic options, deaths do still occur and can be prevented only if astute clinicians consider, diagnose, and treat these conditions rapidly.

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