Infectious diseases acquired by international travelers visiting the United States

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Abstract

Background: Estimates of travel-related illness have focused predominantly on populations from highly developed countries visiting low- or middle-income countries, yet travel to and within high-income countries is very frequent. Despite being a top international tourist destination, few sources describe the spectrum of infectious diseases acquired among travelers to the United States.

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Methods: We performed a descriptive analysis summarizing demographic and travel characteristics, and clinical diagnoses among non-US-resident international travelers seen during or after travel to the United States at a GeoSentinel clinic from 1 January 1997 through 31 December 2016.

Results: There were 1,222 ill non-US-resident travelers with 1,393 diagnoses recorded during the 20-year analysis period. Median age was 40 years (range 0–86 years); 52% were female. Patients visited from 63 countries and territories, most commonly Canada (31%), Germany (14%), France (9%), and Japan (7%). Travelers presented with a range of illnesses; skin and soft tissue infections of unspecified etiology were the most frequently reported during travel (29 diagnoses, 14% of during-travel diagnoses); arthropod bite/sting was the most frequently reported after travel (173 diagnoses, 15% after-travel diagnoses). Lyme disease was the most frequently reported arthropod-borne disease after travel (42, 4%). Nonspecific respiratory, gastrointestinal and systemic infections were also among the most frequently reported diagnoses overall. Low-frequency illnesses (<2% of cases) made up over half of diagnoses during travel and 41% of diagnoses after travel, including 13 cases of coccidioidomycosis and mosquito-borne infections like West Nile, dengue, and Zika virus diseases.

Conclusions: International travelers to the United States acquired a diverse array of mostly cosmopolitan infectious diseases, including nonspecific respiratory, gastrointestinal, dermatologic, and systemic infections comparable to what has been reported among travelers to low- and middle-income countries. Clinicians should consider the specific health risks when preparing visitors to the United States and when evaluating and treating those who become ill.

INTRODUCTION

The annual number of international tourist arrivals may reach 1.8 billion by 2030.[1] As international travel increases, travelers are increasingly acquiring infectious diseases not endemic in their home countries and may act as sentinels for outbreaks, spreading infectious diseases within a destination country, the next country on a traveler's itinerary or the travelers' own country after returning home.[2] Increased globalization has brought an influx of international travelers to regions of the world with emerging economies, and best estimates of travel-related illness in international travelers have predominantly reflected populations of travelers from highly developed countries visiting low- or middle-income countries.[3] Though more people are traveling to the developing world than ever before, it can be easy for travelers and health care professionals to overlook Western destinations as a perceived low risk for infectious disease, yet international travel to and within the developed world has only increased.

In 2015, 9 of the top 10 international destinations identified by the United Nations World Tourism Organization were in North America or Europe. Combined, these destinations accounted for 454.5 million tourist arrivals.[1] In the United States specifically, 77.5 million international tourists visited in 2015, the most ever recorded. Despite being the second largest international tourist destination overall (only France sees larger volumes), few sources describe travelers to the United States and the spectrum of illnesses they may acquire. This gap in knowledge may impact the health care received by ill travelers who seek care both during travel in the United States and after travel once they return home.

Familiarity with the illnesses seen in international travelers to the United States can inform the development of appropriate pre-travel messages and the medical management of ill international travelers. We describe the demographic and travel characteristics, and the clinical diagnoses, of non-US-resident international travelers who acquired an illness in the United States and presented to clinics in the GeoSentinel Global Surveillance Network.

METHODS

Data source

GeoSentinel is a global clinician-based sentinel surveillance system, established in 1995 as a collaboration between the Centers for Disease Control and Prevention (CDC) and the International Society of Travel Medicine (ISTM). It consists of 70 specialized travel and tropical medicine clinics in 30 countries, mostly affiliated with academic medical centers. All sites have experience diagnosing and treating patients with travel-related infectious diseases and contribute systematic surveillance data on international travelers and migrants seen for a travel-related illness. Analysis of GeoSentinel surveillance data has been approved as non-research by a CDC human subjects advisor.

Inclusion and exclusion criteria

Records with at least one confirmed or probable diagnosis among nonmigrant, non-US-resident international travelers exposed in the United States, as designated by the treating clinician, and seen during or after travel at a GeoSentinel clinic in either the United States or their country of residence from 1 January 1997 through 31 December 2016 were included in this analysis. Data were extracted on traveler demographics (i.e. sex, age, country of residence), trip details (i.e. travel duration, travel reason, destinations), and clinical information (i.e. date of clinic visit, inpatient or outpatient status, if there was a pre-travel consultation with a health care provider, and other diagnoses). The proportion who attended a pre-travel consultation was determined among those who visited the United States as their only destination country to better approximate those who received care specifically for the United States and not another country on the traveler's itinerary. GeoSentinel first started collecting data on pre-existing conditions (e.g. pregnancy, HIV infection, immunosuppressing/immunomodulating agents) in March 2013. Consequently, only a subset of records had this data available for analysis. We performed descriptive analyses of demographic and travel characteristics and diagnoses using SAS Enterprise Guide 7.1 (Cary, NC, USA).

RESULTS

There were 1,222 ill non-US-resident travelers with 1,393 diagnoses reported to GeoSentinel with travel to the United States during the analysis period. The median age of patients was 40 years (range 0–86 years); 52% were female (Table 1). Patients visited from 63 countries and territories, most commonly Canada (31%), Germany (14%), France (9%), Japan (7%), the United Kingdom (4%), Israel (4%), Hong Kong (4%), Switzerland (3%), and Singapore (3%). The majority traveled for the purpose of tourism (82%) or business (14%). The median travel duration was 14 days (range 1–2,584 days). Among 959 who traveled to the

United States and no other destination, 913 had information on pre-travel consultation attendance; 81 (9%) attended a pre-travel health consultation. Of the 1,222 patients with illness acquired in the United States, 177 (14%) were seen during travel and 1,045 (86%) were seen after travel (Table 1).

During travel

Among the 177 patients seen during travel in the United States, 213 diagnoses were reported. Nonspecific skin and soft tissue infections were most frequent (29 diagnoses, 14% of all diagnoses made during travel), followed by acute gastrointestinal illnesses of unspecified etiology (15, 7%), and pneumonia of unspecified etiology (14, 7%) (Table 2A). One hundred thirteen (64%) patients seen during travel were hospitalized, including seven with sepsis. Of 69 patients with an illness acquired in the United States and seen at a US GeoSentinel site since March 2013 when data on pre-existing conditions began being collected, 23 (33%) were reported to have at least one such pre-existing condition; all were hospitalized. Three deaths were reported: one in a person with pneumonia who subsequently died of an unspecified acute cardiac event; one in a person with a pulmonary embolism and one in a cancer patient with pre-existing peritonitis who died in the hospital from sepsis.

After travel

Among the 1,045 patients seen after travel to the United States, 1,393 diagnoses were reported. The most frequent was arthropod bite/sting (173 diagnoses, 15% of all diagnoses made after travel); 81 (47%) of which were tick bites. This was followed by influenza-like illness (ILI, 66, 6%), upper respiratory tract infection (URI, 54, 5%), acute gastrointestinal illnesses of unspecified etiology (53, 4%), and skin and soft tissue infections of unspecified etiology (53, 4%). (Table 2B). Sixteen percent of after-travel patients were hospitalized, primarily with respiratory infections. There were no deaths. Respiratory infections including ILI, URI, influenza, and pneumonia combined accounted for 204 (17%) diagnoses made after travel overall, however 60% of these infections were reported in 1 year, 2009 (Figure 1). Forty-seven (71%) of 66 of the ILI diagnoses, 42/52 (81%) of the influenza diagnoses, 26/54 (48%) of the URI diagnoses, and 7/32 (22%) of the pneumonia diagnoses were recorded after travel in 2009.

Lyme disease was the most frequently reported arthropod-borne disease, diagnosed in 42 travelers; 18 were diagnosed with early or acute Lyme, 24 with late stage Lyme. No other clinical information was available. Of the 42 Lyme cases, 35 (83%) traveled to the United States only; a more specific place of exposure was available for 21 (57%) travelers: New York (6), Massachusetts (4), Wisconsin (3), Maine (2), Maryland (2), New Jersey (2), Minnesota (1), and Vermont (1).

Notable low-frequency diagnoses

Low-frequency illnesses (<2% cases) made up 51% of diagnoses made during travel and 41% of diagnoses made after travel. Non-Lyme tick-borne diseases were observed in three travelers. Two Germans presented with unspecified tick-borne spotted fever rickettsioses, one in 2004 and the other in 2014, and a Canadian with ehrlichiosis was reported in 2014. Mosquito-borne arboviral diseases were also observed, including dengue virus (DENV; three

patients), West Nile virus (WNV; two patients), and Zika virus (ZIKV; one patient) infections. No chikungunya virus (CHIKV) infections were reported. The three patients with DENV infections had exposure times and places consistent with known past focal outbreaks in the United States, including south Florida (one German traveler; 2013) and Hawaii (two Canadian travelers; 2015). Of the two patients with WNV infection, one was hospitalized in the United Kingdom after their return. The ZIKV infection was in a 30-year-old Israeli female who visited Miami, Florida, in August 2016.

Coccidioidomycosis was reported in 13 patients seen post-travel, 4 (31%) of whom were hospitalized. The median age of coccidioidomycosis patients was 61 years (range 0–78 years). Of nine coccidioidomycosis patients with information available, eight travelers were exposed in Arizona and one in California.

Clostridium difficile infection was reported in six travelers: three during travel (all hospitalized) and three after travel (two hospitalized). Of those seen during travel, all had visited Florida and presented 1 week to 5 months after arrival in the United States, two were also diagnosed with lobar pneumonia. Of the two hospitalized after return, one was a 72-year-old Swedish male who visited Orlando, Florida, for 29 days in the summer of 2013 and presented with other comorbidities including a skin and soft tissue infection, vancomycin-resistant enterococci and sepsis, and the other was a 57-year-old Canadian who visited the United States for 12 days in September 2014.[4]

DISCUSSION

We highlight the most frequently reported, and some noteworthy but less frequent diagnoses in GeoSentinel, among non-US residents visiting the United States from 1997 through 2016. Overall, most patients in the study were tourists and acquired a diverse array of mostly cosmopolitan infectious diseases, including nonspecific respiratory, gastrointestinal, dermatologic, and systemic infections comparable to what has been reported among travelers to other international destinations, including the tropics.[5,6] Nonspecific respiratory infections were among the most frequently reported illnesses of ill-returned travelers from the United States, however, 60% of nonspecific respiratory infections were diagnosed in 2009, likely due to increased screening among some GeoSentinel sites for influenza A H1N1. Acute gastrointestinal illnesses and skin and soft tissue infections were also frequently diagnosed, though each accounted for only 5% of diagnoses made after travel overall. Similar to studies of persons traveling to lower-income countries,[6,7,8] it is important for travelers and health care professionals to recognize that travel-related respiratory, gastrointestinal, and dermatologic illnesses also occur among international travelers to developed countries[9] and may vary in relation to specific traveler characteristics, including travel purpose, diet, activities during travel, and the health profile of the individual traveler.[10]

Some notable, less frequently encountered but potentially severe diseases endemic to the United States also occurred. Arthropod exposure, reflecting tick bites and tick-borne disease diagnoses (e.g. Lyme disease), was diagnosed more often than other conditions. Ticks transmit the greatest diversity of arthropod-borne pathogens in the United States and are

responsible for the largest number of vector-borne diseases there.[11,12] In recent decades, the reported number of notifiable tick-borne diseases has steadily increased as the geographic distribution of many ticks and tick-borne diseases has expanded and new tick-borne pathogens have emerged.[11] Human vaccines for tick-borne diseases that occur in the United States are lacking.[11] Therefore, travelers to the United States should avoid tick habitats whenever possible. If that is not possible, travelers should use tick repellents containing DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol or 2-undecanone on exposed skin, use products containing 0.5% permethrin to treat clothing, check for ticks daily and properly remove them, if found.[13]

Lyme disease is the most frequently reported vector-borne disease in the United States and was diagnosed in 42 patients seen after travel.[14] Incidence rates are underreported in the United States, but the true magnitude is estimated at 240,000 to 440,000 cases annually.[11] Approximately 96% of Lyme disease cases have been reported from 14 states in the Northeast, mid-Atlantic, and upper Midwest, though evidence suggests that endemic foci have expanded over time.[14] The expansion of areas with high incidence mirrors the geographic expansion of *Ixodes scapularis* in the eastern United States; infection is less common in the far western United States, where *I. pacificus* is the vector.[11]

Arboviral diseases, including WNV, DENV, and ZIKV infections occurred in travelers to the United States. WNV is the leading cause of domestically acquired arboviral disease in the United States, and is primarily spread by mosquito species of the *Culex* genus.[15] During 2015, 2,282 cases of domestic arboviral disease were reported to CDC; 2,175 (95%) were WNV cases. Most human infections are asymptomatic; symptomatic infections commonly manifest as a systemic febrile illness, and, less commonly, as neuroinvasive disease. DENV and ZIKV infections were also reported, but only from known outbreak areas. Unlike WNV, *Aedes aegypti* and *A. albopictus* species are known to variably transmit DENV, ZIKV, and CHIKV. Although *Aedes* species are common in the southern United States, DENV is endemic in northern Mexico, and the US population is largely immune-naïve, the lack of DENV transmission in the continental United States likely reflects more limited contact between people and *Aedes* species mosquitoes than occurs where transmission is more common.[16] Preventing mosquito bites is important when traveling in the United States, especially in Hawaii and the southern states.

Coccidioidomycosis is endemic in the southwestern United States and is underreported.[17] Evidence suggests coccidioidomycosis causes 15–29% of community-acquired pneumonia in certain highly endemic areas.[18] Of states endemic for coccidioidomycosis, the 2016 incidence was highest in Arizona (89.3 per 100,000 population) and California (13.7 per 100,000 population).[19] Some groups may be at higher risk for developing severe forms of coccidioidomycosis, including immunocompromised individuals, pregnant women, individuals with diabetes, persons of African or Filipino descent, and adults in older age groups.[17] Travelers can prevent infection by avoiding areas where *Coccidioides* spores may be present, such as construction or excavation sites, and by avoiding activities that involve close contact with soil or dust, including yard work, gardening, and digging.[17,18,19] Health care providers should be aware of this increasingly common infection when treating persons with ILI or pneumonia who live in or have traveled to endemic areas.[18]

Though the majority of patients were seen after travel with an acute illness, a disproportionate number of patients were hospitalized during travel, many with pre-existing health conditions. In addition, three travelers died during their visit to the United States, while there were no records of deaths among those who visited the United States and were seen at a clinic after travel. Noninfectious conditions are known to cause considerable morbidity and mortality among international travelers,[20] and unspecified chronic health conditions have been associated with health problems experienced during and after travel, including hospitalization.[6] Medical advances are enabling individuals with chronic health conditions opportunities to travel despite their health limitations,[21] but travelers with these problems may have unique health risks making them more susceptible to illness or injury while traveling, leading to exacerbation of their underlying conditions.[22,6]

This analysis has several limitations. First, GeoSentinel surveillance data are not population-based, so disease risks and rates cannot be determined. Further, GeoSentinel sites are travel/tropical medicine focused, therefore our findings may not be representative of all international travelers. Other health problems (e.g. traumatic injuries and chronic disease exacerbations) may be underrepresented. GeoSentinel does not routinely collect detailed information on traveler comorbidities and only began collecting limited information on this parameter in 2013. As such, the number of travelers with underlying chronic health conditions could not be determined. Death is not well captured in the GeoSentinel surveillance network; data are collected from a single time point and may not capture a death that follows the initial clinic visit. Similarly, GeoSentinel has not routinely collected information on antibiotic exposure among travelers, either during travel or since return from travel. Diagnostic codes in GeoSentinel include specific etiologic diagnoses and nonspecific syndromic diagnoses, and nonspecific diagnosis codes are assigned when an etiologic diagnosis cannot be determined or are not pursued. Finally, GeoSentinel relies on the judgement of its clinicians for assignment of diagnoses and place of exposure; diagnostic testing information that could be used to validate assigned diagnoses was not routinely collected during the analysis period.

Travelers to the United States should be aware of the diseases they may acquire, paying particular attention to vector-borne infections. Practicing appropriate arthropod avoidance measures may help prevent these infections. Persons with chronic underlying conditions should take ample supplies of their medications and plan for unanticipated medication shortfalls or possible chronic disease exacerbations. Clinicians, including primary care practitioners, should consider the specific health risks when preparing visitors to the United States and when evaluating and treating those who become ill.

Acknowledgments

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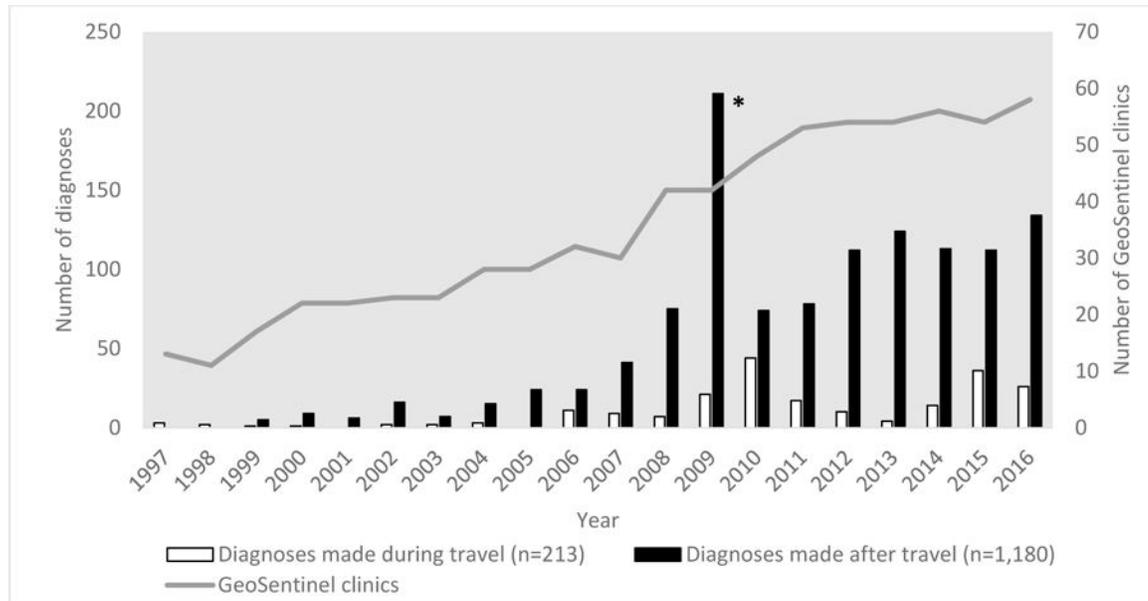
Figure 1.
During- and after-travel diagnoses among non-US-resident travelers visiting the United States, GeoSentinel, 1997–2016.

*In 2009, 211 diagnoses were reported after travel, the most of any single year in the analysis period. Screening practices for influenza A (H1N1) increased in 2009 compared to all other years in the analysis period, and may have contributed to the increase. The most frequently reported diagnoses that year were influenza-like illness (ILI n=47; 22% of 2009 diagnoses and 71% of all ILI diagnoses for the study period), influenza (n=42; 20% of 2009 diagnoses and 81% of all influenza diagnoses), upper respiratory infection (URI) of unspecified etiology (n=26; 12% of 2009 diagnoses and 48% of all unspecified URI diagnoses), and pneumonia of unspecified etiology (n=32, 3% of 2009 diagnoses and 22% of all unspecified pneumonia diagnoses).

Table 1.

Demographic and travel characteristics of ill non-US-resident travelers visiting the United States and presenting to Geosentinel clinics, 1997–2016.

	All travelers (n=1,222)[a]	Presented to clinic during visit in United States (n=177)[a]	Presented to clinic after visit to United States (n=1,045)[a]
Gender			
Male	591 (48%)	100 (57)	491 (47)
Female	628 (52%)	75 (43)	553 (53)
Age (years)			
Median	40	42	40
Range	(0–86)	0–86	0–86
Age groups			
17 years	107 (9)	18 (10)	89 (9)
18–34	373 (31)	46 (27)	327 (31)
35–49	332 (27)	45 (25)	287 (27)
50–64	266 (22)	39 (22)	227 (22)
65 years	140 (11)	29 (16)	111 (11)
Travel reason			
Tourism	999 (82)	147 (83)	852 (82)
Business	171 (14)	22 (13)	149 (14)
Student	29 (2)	4 (2)	25 (2)
Missionary/volunteer/researcher/aid work	14 (1)	2 (1)	12 (1)
Military	2 (<1)	0 (0)	2 (<1)
Medical tourism	3 (<1)	1 (1)	2 (<1)
Travel duration (days)[b]			
Median	14	10	15
Range	(1–2,584)	(1–339)	(1–2,584)
Pre-travel care received[b]			
Yes	81 (9)	12 (8)	69 (9)
No	559 (61)	99 (62)	460 (61)
Do not know	273 (30)	48 (30)	225 (30)

[a] All data are reported as number (%) of travelers.

[b] Among those who traveled to the United States only.

Table 2.

Most frequent diagnoses among non-US residents with illness acquired while traveling in the United States[a]

2A. Diagnosed during travel (n=213 diagnoses)		2B. Diagnosed after travel (n=1,180 diagnoses)	
Diagnosis	n (%)	Diagnosis	n (%)
Skin and soft tissue infections, unspecified etiology[b]	29 (14)	Arthropod bite/sting	173 (15)
Acute gastrointestinal illnesses, unspecified etiology[c]	15 (7)	Influenza-like illness[e]	66 (6)
Pneumonia, unspecified etiology[d]	14 (7)	Upper respiratory tract infection, unspecified etiology[e]	54 (5)
Injury/trauma	10 (5)	Acute gastrointestinal illnesses, unspecified etiology[f]	53 (4)
Thrombophlebitis	9 (4)	Skin and soft tissue infections, unspecified etiology[g]	53 (4)
Sepsis, unspecified etiology	5 (2)	Viral syndrome	52 (4)
Pyelonephritis	5 (2)	Influenza[e]	52 (4)
Heart disease/coronary artery disease/angina/arrhythmia	5 (2)	Lyme disease[h]	42 (4)
Upper respiratory tract infection, unspecified etiology	4 (2)	Pneumonia, unspecified etiology[e,i]	32 (3)
Viral syndrome	4 (2)	Marine envenomation/fish sting	27 (2)
Influenza	4 (2)	Chronic diarrhea, unspecified etiology	26 (2)
		Acute bronchitis	22 (2)
		Rash, unknown etiology (nonfebrile)	21 (2)
		Dog/Cat/Bat bite	18 (2)

[a] Diagnoses shown represent ≥2% of diagnoses.

[b] Includes the following individual GeoSentinel diagnosis codes: erysipelas/cellulitis/gangrene (23); skin abscess/secondary bacterial infection of existing lesion (5); superficial impetigo/folliculitis/furuncle/carbuncle/paronychia/ecthyma (1).

[c] Includes the following individual GeoSentinel diagnosis codes: acute gastroenteritis (8), acute diarrhea (5), nausea/vomiting (2).

[d] Includes the following individual GeoSentinel diagnosis codes: lobar pneumonia (12), atypical pneumonia (2).

[e] Screening practices for influenza A (H1N1) increased in 2009 compared to all other years in the analysis period. Respiratory infections including influenza-like illness (ILI), upper respiratory tract infection of unspecified etiology (URI), influenza, and pneumonias combined accounted for 204 (17%) diagnoses made after travel overall, 60% of these infections were reported in 2009. Forty-seven (71%) of 66 ILI diagnoses, 42/52 (81%) of the influenza diagnoses, 26/54 (48%) of the URI diagnoses, and 7/32 (22%) of the pneumonia diagnoses were recorded after travel in 2009.

[f] Includes the following individual GeoSentinel diagnosis codes: acute diarrhea (34), acute gastroenteritis (19).

[g] Includes the following individual GeoSentinel diagnosis codes: skin abscess/secondary bacterial infection of existing lesion (24); superficial impetigo/folliculitis/furuncle/carbuncle/paronychia/ecthyma (15); erysipelas/cellulitis/gangrene (14).

[h] Includes the following individual GeoSentinel diagnosis codes: late Lyme disease (24); early Lyme disease (18).

[i] Includes following individual GeoSentinel diagnosis codes: lobar pneumonia (15); atypical pneumonia (10); fungal pneumonia (7).