CHAPTER 1

Basic epidemiology of infectious diseases

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Infectious conditions comprise a substantial portion of texts and guidelines related to travel medicine [1,2]. To prescribe optimal pre-travel advice, preventive measures, and education to travelers, travel health providers must be familiar with basic epidemiologic concepts, and also the epidemiology and geographic distribution of relevant infections. As past experience may predict future risk, a traveler-specific risk assessment allows possible measures, advice, and behavior modification to be appropriately prioritized for each traveler.

During the past two decades, the most important and relevant data on travel-related disease have come from surveillance of travelers themselves. Although available Ministry of Health data based on people native to an endemic locale may reflect national or state-level trends and identify the most important diseases to monitor within a country, the risk behaviors, eating habits, accommodations, knowledge of preventive measures, and precise itineraries of travelers can differ greatly from those of local populations. The GeoSentinel surveillance system, a collaborative effort between the International Society of Travel Medicine and the US Centers for Disease Control and Prevention, maintains the largest such surveillance database, with more than 200,000 records from patients with a confirmed or probable travel-related diagnosis. GeoSentinel is a global provider-based network of travel and tropical medicine clinics, which, as of August 2013, has 57 participating clinics on six continents. Details of the standard data collection instrument, diagnostic categories, and patient classification methods used in GeoSentinel have recently been published [3]. The network also facilitates rapid communication, obtains data, and reports on unusual or newly emerging health events in travelers [3].

The most recent surveillance results on travelers published from the GeoSentinel network [4] indicate that Asia (32.6%) and sub-Saharan Africa (26.7%) were the most common regions where illnesses were acquired (Figure 1.1). Three-quarters of travel-related illness was due to gastrointestinal (34.0%), febrile (23.3%), and dermatologic (19.5%) diseases. Malaria, dengue, enteric fever, spotted-fever group rickettsioses, chikungunya, and non-specific viral syndromes remained the most important of the acute systemic febrile illnesses. Falciparum malaria was mainly
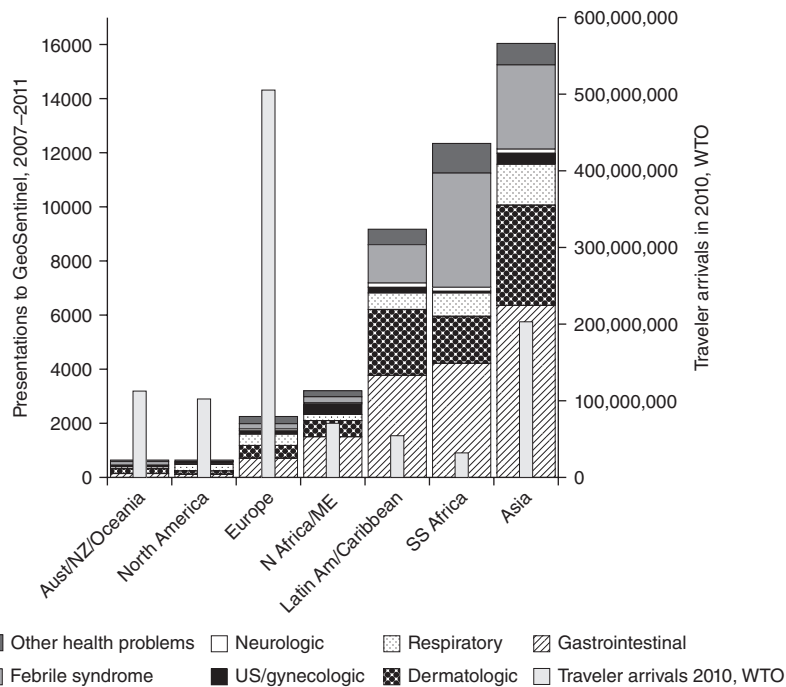
Figure 1.1 Presentations to GeoSentinel by diagnostic category and region (2007–2011), plus 2010 regional WTO traveler arrivals. Left vertical axis shows cumulative number of presentations to GeoSentinel sites by ill returned travelers during 2007–2011 according to syndromic presentation and region of illness acquisition. Right vertical axis (narrow gray bars) shows traveler arrivals in 2010 by region, according to WTO data. WTO, World Tourism Organization; Aust, Australia; NZ, New Zealand, N Africa, North Africa; ME, Middle East; SS Africa, sub-Saharan Africa; GU, genitourinary. Source: Adapted from Leder et al. 2013 [4].

acquired in West Africa, and enteric fever was largely contracted on the Indian subcontinent; leptospirosis, scrub typhus, and murine typhus were principally acquired in South-East Asia. More than two-thirds of dengue infections were acquired in Asia, mostly Thailand, Indonesia, and India; seasonality of dengue varies according to destination. Common skin and soft tissue infections, mosquito bites (often infected), and allergic dermatitis remain the most common dermatologic conditions affecting travelers; of the more exotic infections, hookworm-related cutaneous larva migrans, leishmaniasis, myiasis, and tungiasis are the most important. The relative frequency of many diseases varies with both travel destination and reason for travel, with travelers visiting friends and relatives (VFRs) in their country of origin having both a disproportionately high burden of serious febrile illness (malaria) and very low rates of seeking advice before travel (18.3%). Although the most travel-related illness seen in GeoSentinel clinics comes from Asia, the proportion of travelers who become ill enough to seek specialized care appears to be much higher in travelers returning from Africa or Latin America. Only 40.5% of all ill travelers reported pre-travel medical visits.

Regional surveillance networks such as TropNet, a consortium of European centers, have contributed additional information on large numbers of travelers with

dengue, schistosomiasis, leishmaniasis, and in particular malaria [5]. Sentinel event detection has led to notifications of outbreaks of travel-related African trypanosomiasis [6], leptospirosis, and malaria that have been indicative of possible changes in destination-specific risk.

Although GeoSentinel and similar traveler surveillance networks offer many advantages over disease-specific studies or data collated at single centers, they have several limitations. The reported cases represent a sentinel convenience sample of ill returned travelers visiting specialist clinics and do not reflect the experience of healthy travelers or those with mild or self-limited illness who visit primary care practices or other healthcare sites. In addition, referral patterns, patient populations, and travel demographic characteristics are not consistent between sites. Although collecting data exclusively from ill patients does not permit absolute or relative risks to be determined, the available data do show the relative frequency and range of illnesses seen in wide samples of travelers.

Estimates of true incidence and true risk in travelers (often expressed as number of events per 100,000 travelers) have been elusive for a number of reasons. Although a number of approaches to measure risk have been discussed in detail [7], such estimates have been limited in terms of obtaining both an accurate numerator (number of cases of disease) and denominator (number of travelers overall or to a specific destination who are susceptible to infection and illness). Many travelers to a specific location who become infected or ill will have returned to their home country by the time they develop signs and symptoms, so will not be captured by surveillance in the country of exposure, even if reporting is good. Similarly, diseases with short incubation periods may have resolved by the return home and not be captured in the country of origin. A denominator for all travelers to a specific location that could be used to calculate incidence is also generally problematic, and those available are typically estimates provided only at the country or region level and not at the actual destination level [8].

Many of the cited data on incidence of infection in travelers, some of which were published more than three decades ago, are based on extrapolations of small single-site studies or limited data collected from small samples of travelers. Authoritative texts such as the 2014 US CDC Yellow Book [1] often contain tables of global risk estimates that may range from 20–40% of all travelers for travelers' diarrhea to 0.0001% for Japanese encephalitis for all travelers to Asia. Although such numbers are useful as a guide to relative disease risks in large populations, the travel advisor should always seek out the most destination-specific information possible. Unfortunately, for many diseases, such information is only available to the national or, at most, the first geographic administrative level and might apply only to native populations and not to travelers.

A number of factors are important in analyzing epidemiologic data on travel-related diseases or in interpreting published reports. First, the characteristics specific to the disease itself, such as mode of transmission (vector-borne, food-borne, water-borne, environmental exposure), incubation period, signs and symptoms, duration of illness, diagnostic testing, and importance of comorbidities in acquiring and presenting with illness, and clinical outcomes must be considered. Second, the presence, frequency, seasonality, and geographic distribution of the disease need to be assessed, and these might change over time due to outbreaks,

emergence or re-emergence in new areas or populations, successful public health interventions, and other factors. Third, as discussed above, travelers represent a unique subset of individuals, hence their exposure might differ compared with that of residents of a destination country.

As a result, along with demographic characteristics, additional travel-specific variables that must be considered would be trip length, destinations (both current and previous), specific travel itineraries (if known), purpose of travel, and type of traveler; preparation before and behaviors during travel also factor into the epidemiology of travel illnesses. Some but not all of these variables are systematically collected by surveillance systems that either focus on travelers, such as GeoSentinel, or collect data on illnesses that affect travelers. In addition, travelers are a heterogeneous group, and because analyses are always composed of samples rather than entire populations, the sample profile must be carefully examined and disclosed. For example, VFRs have consistently represented higher proportions of serious febrile illness, particularly malaria, among travelers [9,10].

Data on the health characteristics and pre-travel healthcare of travelers are important to provide insight into the itinerary, purpose of travel, or existing medical conditions in order to prioritize the most relevant interventions and education. A US-based provider network, Global TravEpiNet (GTEN), systematically collects data from travelers presenting to a consortium of 26 travel and tropical medicine clinics. Of 13,235 travelers seen from 2009 to 2010 in GTEN clinics, India, South Africa, and China were the most common intended destinations for these travelers, with more than one-third of trips occurring in June, July, and August [11]. Travelers seen in sampled GTEN clinics ranged in age from 1 month to 94 years, with a median of 35 years. The median duration of travel was 14 days, although 22% of travelers pursued trips of >28 days, and 3% of travelers pursued trips of >6 months. About 75% were traveling to malaria-endemic countries; of the 72% who were prescribed an antimalarial, 70% of the prescriptions were for atovaquone/proguanil. Of the 87% of travelers who were prescribed an antibiotic for presumptive self-treatment of travelers' diarrhea, a fluoroquinolone or azithromycin was prescribed in almost equal proportions. Vaccines against hepatitis A and typhoid were the most frequently administered. About 38% of travelers were visiting yellow fever-endemic countries, for which they may need a vaccine requiring a higher level of practitioner knowledge. Immunocompromising conditions, such as HIV infection and AIDS, organ transplant, or receipt of immunocompromising medications, were present in 3% of travelers. Although this is a relatively large multicenter sample, GTEN is limited to a subset of specialized travel and tropical medicine clinics in the United States and does not capture travelers who seek pre-travel care from primary care and other providers, and data have only been collected since 2009.

As travel medicine continues to grow with regard to both number of practitioners and subject matter, infectious diseases will remain an important and perhaps an even greater component of the discipline. Likewise, the epidemiology of infectious diseases in travelers will remain important, with surveillance and reporting potentially being enhanced and refined, resulting in more complete and informative data being available to both clinical and public health practitioners and allowing more informed decisions to be made with regard to protecting the health of the traveler.

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