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We live in a world of moving parts, fragmented, altered landscapes, and vast networks of connections. Human travel today is unprecedented in volume, reach, and speed (Wilson, 1995a). Spatial mobility for the average person increased more than 1000-fold between 1800 and 2000 (Cliff and Haggett, 2004; see Figure 1.1). Two million people cross international borders each day (WTO, 2006a). Movement of humans may be the result of planned travel – for business, tourism, education or research, missionary or volunteer work, visiting friends or family, or military purposes – but abrupt displacement of populations can also be a consequence of war, natural disasters, economic, political, or environmental events (Myers, 2001). Human activities have led to unprecedented movement or displacement of other species through intent (e.g. trade) or inadvertence (Smolinski *et al.*, 2003). The conveyances of travel, such as ships and airplanes, can become places for transmission of infectious diseases. The roads and railroad tracks built to carry people and products from one location to another can also fragment habitats and can lead to decreased biodiversity. Table 1.1 provides examples of infectious disease dissemination associated with human travel.

Infectious diseases in people, plants, and animals are dynamic and are influenced by biological, environmental, socioeconomic, political, demographic, and genetic factors (Wilson *et al.*, 1994; Wilson, 1995b). The abundance and variety of microbial life and its ongoing evolution mean that we will continue to encounter new infections or altered expressions of old ones in the foreseeable future. Among the characteristics of the global population today that favor the appearance and spread of infections – size, density, location, vulnerability, inequalities, and mobility – the latter will be the focus of this chapter.

Why does travel matter in the epidemiology of infectious diseases? Although many microbes that cause infectious diseases are found throughout the world, many others have a focal distribution because of the need for specific geoclimatic conditions or a particular intermediate or reservoir host, poor sanitation or control efforts, or other factors. Even for microbes that are globally distributed, risk of

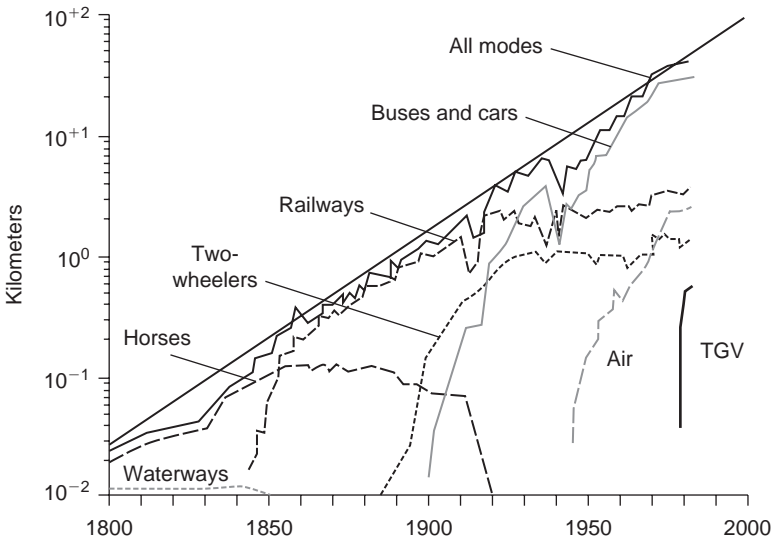


Figure 1.1 Spatial mobility: increased spatial mobility of the population of France, changes over a 200-year period, 1800–2000. The vertical scale is logarithmic, showing that growth in average travel distance has increased exponentially over time. Based on Cliff and Haggett (2004).

exposure may vary greatly from one geographic area to another (Freedman *et al.*, 2006). Humans are interactive biological units; when they travel they can pick up pathogenic microbes that may make them sick (Wilson, 2003a). Whether they get sick or not, they may also carry pathogens or microbial genetic material (including resistance genes and virulence factors) in or on their bodies to a new location. Depending on the type of organism, its transmission mechanisms, and immunity of contacts, travelers may be able to introduce a pathogen into a new population.

Humans are social creatures who carry with them their traditions, customs, practices, dress codes, and values that may be observed and imitated or scorned and rejected by the people they visit. Travel typically is not just an origin and destination, but also includes stops and interactions along the way. Travelers have contact not only with local populations in areas they visit, but also with other travelers – who may reflect a wide range of geographic origins and carry their own microbiological baggage and customs that influence spread.

When people travel, they may engage in activities that they might not undertake at home. The experience in a new environment may lead them to have sexual contacts with new partners, try new foods or types of preparations, engage in risky water and other sports activities, receive injections or tattoos at local facilities, or handle or come into contact with animals. Many of these activities can put them at risk for infections that did not exist in their home environment.

Table 1.1 Examples of infectious disease dissemination associated with human travel

Pathogen	Site of origin	Mode of spread	Consequences	Reference
HIV	Sub-Saharan Africa	Truck routes in Africa; air travel	14.5 million infected outside site of origin; approximately 40 million people lived with HIV worldwide at the end of 2005, 4 million became newly infected, and 2.8 million died.	UNAIDS, 2006
Measles	Asia (China, India), Europe	Air travel	Outbreaks associated with international adoption have occurred. An 11-year-old North Carolina resident traveled home from the United Kingdom via New York and Connecticut and transmitted measles to an infant contact; transmission to multiple states and countries was possible due to infectious period during flights. A 17-year-old adolescent who contracted measles in Bucharest, Romania, initiated an outbreak in Indiana, with 34 confirmed cases. An outbreak occurred in the Greater Boston area since May 2006, following an index case that had arrived recently from India.	CDC, 2004a, 2004b, 2005a, 2005b; Parker <i>et al.</i> , 2006; Massachusetts DPH, 2006
Poliomyelitis	Six endemic countries (Afghanistan, Egypt, India, Niger, Nigeria, Pakistan)	Migration; air travel	Between 2002 and 2005, wild poliovirus spread to 21 previously polio-free countries; introduction led to sustained transmission in 13 countries.	CDC, 2005c, 2006a, 2006b
SARS	China, Hong Kong	Air travel following exposure in infected countries	From 1 November 2002 to 31 July 2003, SARS spread to > 25 countries, causing 8096 reported infections and 774 deaths.	WHO, 2003

(Continued)

Table 1.1 (Continued)

Pathogen	Site of origin	Mode of spread	Consequences	Reference
Dengue	Tahiti	Air travel; association with a returning traveler with dengue-like symptoms	The first autochthonous outbreak in Hawaii since 1944 occurred in 2001–2002 and caused 122 laboratory-confirmed cases.	Effler <i>et al.</i> , 2005
West Nile Virus	Israel	Unknown; possibly air travel via an infected person, bird, or mosquito	Since its initial detection in New York, 16,706 cases were reported to the CDC between 1999 and 2004. WNV has also spread to Canada, the Caribbean, and Latin America.	Hayes <i>et al.</i> , 2005
Influenza	Worldwide	Cruise ships	Outbreaks occurred among cruise-ship passengers between New York and Montreal, Tahiti and Hawaii, and Alaska and the Yukon Territory.	CDC, 1997; Uyeki <i>et al.</i> , 2003
Norovirus	Worldwide	Cruise ships, air travel	The Vessel Sanitation Program at the CDC identified > 12 outbreaks on cruise ships in 2002. An outbreak occurred among the crew of a flight, with limited transmission to passengers.	Widdowson <i>et al.</i> , 2004, 2005
Tuberculosis, including multi-drug resistant tuberculosis	Worldwide, Saudi Arabia	Air travel	The 2005 TB rate in foreign-born persons in the US was 8.7 times that in US-born persons; the incidence of MDR TB is higher in low- and middle-income countries. Comparison of TB tests using a whole-blood assay (Quanti-FERON TB assay) prior to and after return from the Hajj showed 10% conversion consistent with exposure during the pilgrimage.	CDC, 2006c, 2006d; Gushulak and MacPherson, 2004; Wilder-Smith <i>et al</i> 2005

Mumps	UK	Air travel	Summer-camp outbreak in New York involved 31 cases and was associated with a counselor from the UK; attack rate was 5.7%. Outbreak began in Iowa in December 2005, and 2597 cases were reported from 11 states between 1 January and 2 May 2006; some cases were potentially infectious during air travel.	CDC, 2006e, 2006f, 2006g
Meningococcal meningitis	Saudi Arabia	Air travel	Pilgrims to the Hajj became infected and spread strains into other regions.	Moore <i>et al.</i> , 1989; CDC 2000, 2001; Wilder-Smith <i>et al.</i> , 2002; Dull <i>et al.</i> , 2005

The development of the travel industry has also altered the landscape in many countries, where luxury hotels occupy prime real estate and new infrastructure is created to serve travelers. Although much travel tends to follow well-trodden paths to well-known places, increasingly travelers are seeking remote locations – and today’s transportation technology makes it increasingly easier than ever before to reach these areas.

All of this massive movement of the human population and trade is occurring as an overlay on the background of the natural migration of animals. Although birds, land animals, and marine animals can move thousands of kilometers in seasonal migrations, humans today have access to more parts of the Earth than any other species. Humans have also altered the planet (land, sea, and atmosphere) more than any other species.

A brief history of travel and the movement of microbes

Throughout history, travelers have carried microbes to new geographic areas and susceptible populations and provided the spark that could ignite epidemics. Recurrent bubonic plague occurred along the Silk Road as early as the 600s. Plague followed the routes of trade caravans in medieval Europe over the years 1347–52, killing an estimated 20 million people (Cliff *et al.*, 2004). It reached Europe from Central Asia, arriving at Kaffa on the Black Sea in about 1347; from there it was carried by ships to the major ports of Europe and North Africa, and then spread over land routes. Explorers introduced smallpox, measles, and other infectious diseases into the New World, causing an estimated 56 million deaths (Black, 1992) and contributing to the collapse of the Aztec and Inca civilizations (Crosby, 1972).

Although Columbus is described as discovering the New World, the historian Carmichael describes the event as the creation of one new world from two old worlds. Cultural as well as biological transformation of the world followed the expanded movement of European overseas trade and exploration (Carmichael, 2006). Global human disease patterns also changed after 1500.

Aided by the modern steamship, which carried infected rats and fleas, a third bubonic plague pandemic circled the globe between 1884 and the early 1900s (Echenberg, 2002). Carried in grain wagons and other forms of transport, it moved inland from the port cities across southern China, reaching Hong Kong in 1894, Singapore and Bombay in 1896, Alexandria, Oporto, and Honolulu in 1899, Sydney, Buenos Aires, Rio de Janeiro, and San Francisco in 1900, and Cape Town in 1901. Many port cities had overcrowded urban tenements with impoverished populations, often immigrants, who were most often infected and were subjected to isolation, rejection, and stigmatization (Echenberg, 2002).

In 1787, the time to travel from England to Australia by sailing vessel was about a year (Cliff and Haggitt, 2004). Many infections transmitted from person

to person, like measles, were no longer a threat by the time of arrival because passengers were dead or immune. After 1860 the faster steamship quickly replaced the sailing vessel, and with that technological advance came shorter boat trips that increased the risk of transmitting infectious agents across oceans. The time to travel from England to Australia had dropped from 100 days (by clipper in 1840) to 50 days by the early 1900s. The development of relatively inexpensive air travel further increased the risk of spreading infectious agents across vast distances. Now a traveler can reach almost any major city on Earth within 24 hours – less time than the incubation period of most infectious diseases.

Last century, the Spanish flu of 1918–19 spread around the world in three waves, carried by humans, and killed as many as 50 million people (Barry, 2004). In the latter decades of the twentieth century, the virus that causes AIDS was carried throughout the world with human travelers as the primary transporters, who disseminated it to all countries. The best evidence suggests that the virus emerged after multiple introductions of related simian viruses in African monkeys and apes into the human population and the subsequent evolution to the human immunodeficiency virus (HIV) (Hahn *et al.*, 2000). The connectedness and ease of travel in the late twentieth century allowed it to spread widely before the magnitude of the threat was recognized. Infections that can be transmitted from person to person can be carried by travelers to any part of the Earth (Wilson, 2003b).

The number of plant and animal species is higher in tropical areas and decreases as the distance from the equator increases; this is known as the latitudinal species diversity gradient. A recent analysis of species that cause infectious diseases (including parasitic species) shows a link between latitude and the spatial pattern of human pathogens, and suggests that climatic factors play a primary role in this pattern (Guernier *et al.*, 2004).

Even today, the spectrum of disease from infections varies in relation to place. A recent analysis of sentinel surveillance data on >17,000 ill, returned travelers seen at GeoSentinel sites (staffed by clinicians knowledgeable about clinical tropical medicine) found significant regional differences in proportionate morbidity for 16 broad syndromic categories (Freedman *et al.*, 2006). Systemic febrile illness occurred disproportionately among travelers returning from sub-Saharan Africa and Southeast Asia.

Modern global travel

The global population increased from 1.6 billion to 6.1 billion in the twentieth century, and reached 6.5 billion in 2006; everyone born before 1960, when the population was 3 billion, has lived through a doubling of the global population. Global travel has increased even more rapidly. Between 1950 and 2005, international tourist arrivals increased 32-fold, reaching 808 million in 2005 (Table 1.2; WTO, 2006a).

People travel for many reasons – tourism, work, research, study, humanitarian aid, religious purposes or missionary work, visits to friends and relatives, displacement due to catastrophic events, for economic incentives, and due to environmental disasters or sociopolitical upheaval. According to the data from the World Tourism Organization (WTO), international trips to visit friends and relatives and for health or religious purposes rose from 19.7 percent of 441 million in 1990 to 24.2 percent of 763 million in 2004; business and professional travel also increased, from 13.7 percent to 15.7 percent. In contrast, the proportion of visits for leisure and holiday travel declined from 55.4 percent to 51.8 percent in the same period of time (see Table 1.3).

The volume of travel has grown exponentially with an average annual growth of international tourist arrivals of 6.5 percent (WTO, 2006a). In the US, 18 airports receive more than 500,000 international arrivals by air annually (16 have a total of >25 million air travelers per year) and 14 ports each receive more than 150,000 maritime passengers (Sivitz *et al.*, 2006: 127). Figure 1.2 displays the civilian global aviation network and the extensive interconnections. In total, the US has 19,500 airports, and at peak times 5000 airplanes are aloft in US airspace.

Table 1.2 Growth in world population and international tourist arrivals

Year	World population (millions)	International tourist arrivals (millions)
1950	2557	25.3
2005	6451	808
Change	×2.5	×32

Data from the US Census Bureau (<http://www.census.gov/ipc/www/worldpop.html>) and World Tourism Organization (<http://www.world-tourism.org/facts/menu.html>).

Table 1.3 Arrivals by purpose of visit

Reason for travel	1990 (international tourist arrivals = 441 million) % of total international arrivals	2004 (international tourist arrivals = 763 million) % of total international arrivals
Leisure, holiday	55.4	51.8
Business, professional	13.7	15.7
VFR, health, religion	19.7	24.2
Not specified	11.2	8.3

Data from World Tourism Organization: Tourism Indicators (available at <http://www.world-tourism.org/facts/menu.html>).

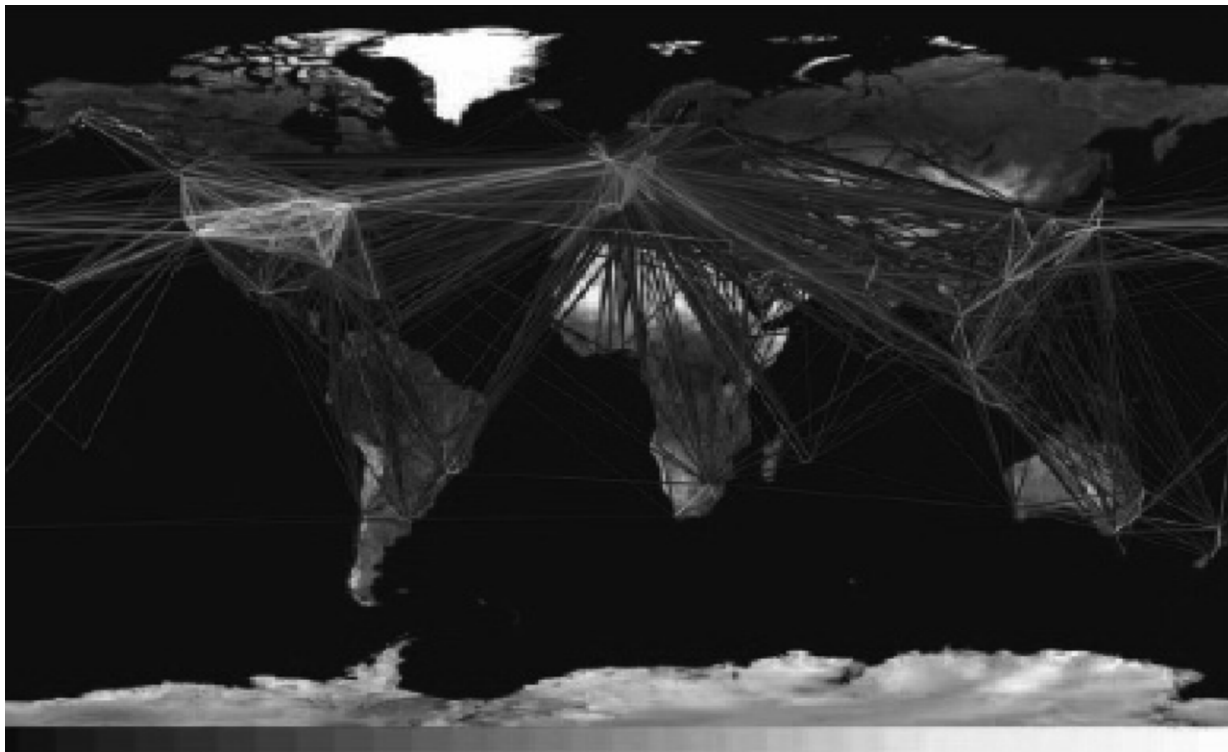


Figure 1.2 The global aviation network: civil aviation traffic among the 500 largest airports in >100 different countries, accounting for >95 percent of international civil aviation traffic. Each line represents a direct connection between airports, and its shade encodes the number of passengers per day (see shaded bar at the bottom) traveling between two airports. From Figure 1 in Hufnagel *et al.* (2004).

Travel by cruise ship is also growing rapidly. In 2003, 184 cruise ships served the US cruise market and 7.4 million cruise passengers went through US ports (Sivitz *et al.*, 2006).

Today, approximately 2 percent of the world's population, or >200 million people, reside outside their country of birth (Gushulak and MacPherson, 2004). These include immigrants, migrant workers, refugees, asylum seekers, and international students. Those who return to their home country to visit friends and relatives (VFR) are more likely to visit rural areas or to stay in accommodations that lack good sanitary facilities and safe water. Because they are "going home," they may be unaware of risks to themselves and their children (who may have been born in a developed country) and thus have inadequate preparation (e.g. vaccines, chemoprophylaxis). VFRs are at higher risk for malaria, typhoid fever, and other infectious diseases than are people traveling for other purposes (Bacaner *et al.*, 2004; Leder *et al.*, 2007) – for example, 43 percent of imported malaria cases in Europe during the period January 1991 to September 2001 occurred in VFRs and other migrant populations (Schlagenhauf *et al.*, 2003). The population of foreign-born in the US is estimated to be 34.2 million, with more than half from Latin America and about a quarter from Asia.

In 2004, international tourist arrivals traveled mainly by air or land, with sea travel contributing only 7.4 percent of the total (WTO, 2006b; Table.1.4). For Africa, America, and the Asia-Pacific regions, air travel surpassed land travel. This indicates a greater proportion of long-haul travel, likely associated with the use of large aircraft, and possibly greater potential for dispersal of organisms into and out of these regions.

Patterns of world travel today

A person with SARS in 2003 illustrates the potential consequences of today's travel patterns (Breugelmans *et al.*, 2004). A 48-year-old businessman flew from

Table 1.4 Arrivals by mode of transport, 2004

	Air (%)	Land (%)	Water (%)	Unspecified route (%)
World	43	49.3	7.4	0.3
Africa	48	43.9	7.8	0.3
America	53.1	41.3	5.5	0.1
Asia and Pacific	46.2	31.9	10.7	1.2
Europe	38.1	54.8	7.0	0.1
Middle East	45.3	49.5	5.3	0.0

Data from World Tourism Organization: Tourism Indicators (at <http://www.world-tourism.org/facts/menu.html>).

Hong Kong to Frankfurt, Germany, on 30 March 2003. He traveled on seven flights throughout Europe during a five-day period from 31 March to 4 April 2003, with stops in Barcelona, London, Munich, and Hong Kong. He was admitted to a hospital in Hong Kong on 8 April with possible SARS, which was confirmed on April 10. His potential contacts spanned many countries.

The “sphere of travel” has enlarged over the years. Bradley described the spatial range of travel in sequential generations of his own family, demonstrating a 10-fold increase with each generation (Bradley, 1989). As travel has become faster, cheaper, and safer, people take more trips and travel longer distances. The average daily distance that an individual in France travels has increased over 1000-fold over the past 200 years, and presumably is similar in other populations in industrialized countries (Cliff and Haggett, 2004). Social and demographic changes have affected travel patterns, and global immigration, migration, and changes in family structure today lead to frequent long-distance travel, often by air, to visit family.

Aircraft and cruise ships are also increasing in size, which expands the population of fellow passengers, often from multiple geographic regions, who come into close contact for a period of hours to days. Assuming homogeneous mixing of passengers, the risk of being exposed to a person with a communicable disease increases four-fold when an aircraft doubles in size – for example, from 200 to 400 passengers (Bradley, 1989). The WTO forecast of growth in long-haul travel between regions over intraregional travel also illustrates the concept of an enlarging sphere of travel (WTO, 2006b). In addition, regional shares for international tourist arrivals are shifting. The WTO predicts an average global growth of 4.1 percent in international tourist arrivals per year, but greater than average growth for Africa, and even greater growth of >6 percent for East Asia and the Pacific, South Asia, and the Middle East (see Figure 1.3). Although Europe is projected to remain the most popular destination, its overall share in the market is predicted to decline.

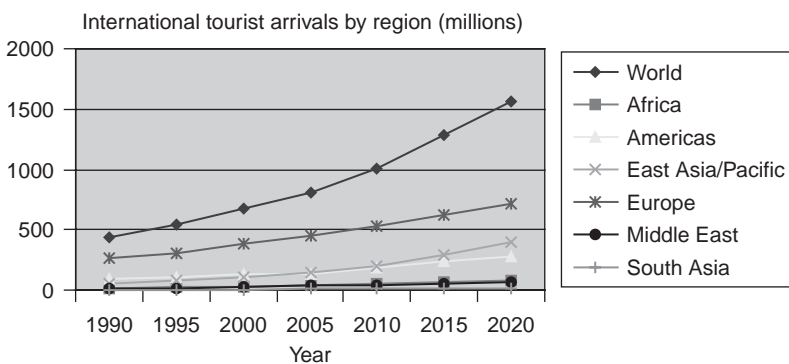


Figure 1.3 International tourist arrivals by region (millions) with forecast. Data from WTO (2006a).

While Europe's and America's combined share in world tourist arrivals was >95 percent in 1950, it declined to 82 percent in 1990 and 76 percent in 2000. The shift of international travel to developing regions in tropical and subtropical regions also increases potential exposure to microbes and vectors endemic in those regions.

Big international airports are typically situated near large metropolitan areas. In many of the developing, low-latitude regions (most of them tropical or subtropical), large periurban slums surround large cities, often populated by people with families in rural areas. Regularly scheduled international flights and their passengers bring these populations into potential contact, and link urban and rural biota of the world.

Travelers' risk behavior

During travel and exploration of regions far from home, individuals may engage in risky activities that can lead to potential exposure to pathogens in blood and body fluids, including HIV, hepatitis C, hepatitis B, CMV, HTLV-1, and other sexually transmitted infections. Some travelers choose their destinations for sex tourism, and many engage in casual sex with new partners (Marrazzo, 2005). A survey of >9000 European travelers regarding their potential exposure to hepatitis B through sex or other contacts found 6.6–11.2 percent to be at high risk (with 24.4 percent vaccinated), 60.8–75.8 percent had potential risk (with 19.2 percent vaccinated), and only 33.4 percent had no identifiable risk of exposure (Zuckerman and Steffen, 2000).

Among Canadian travelers surveyed, 15 percent had potential exposure to blood and body fluids; 9 percent had sexual intercourse with a new partner, 5 percent shared implements such as a razor or toothbrush, 3.2 percent had an injection for medical treatment, 1 percent had acupuncture or other percutaneous non-traditional treatment, 0.5 percent received tattoos or body piercing, and 0.5 percent experienced abrasive injury (Correia *et al.*, 2001).

In a study of tourists departing from Cuzco, Peru, 5.6 percent indicated that they had engaged in sexual activity with a new partner during their stay there, most commonly with other travelers (54.3 percent). Some reported sex with local partners (40.7 percent) and with commercial sex workers (2.15 percent) (Cabada *et al.*, 2003).

The impact of rumors and fear

Fear of disease can deter travel even if risk is minimal or absent. Individuals, organizations, and countries may not base decisions on sound science. An infectious disease may have a severe economic impact on a region, making governments reluctant to acknowledge its presence. Diseases are not neutral in reputation. Infections such as plague (Wilson, 1995c) and cholera carry stigma,

and may lead to irrational decisions about travel and trade. For example, after reports of a plague outbreak in India in 1994, many countries stopped importing foodstuffs and textiles from India even though the World Health Organization requested that no travel or trade restrictions be imposed on the country. Travel to India dropped, with the loss of at least 2.2 million tourists during one season. The estimated losses secondary to the reported outbreak were more than US\$2 billion (Cash and Narasimhan, 2000).

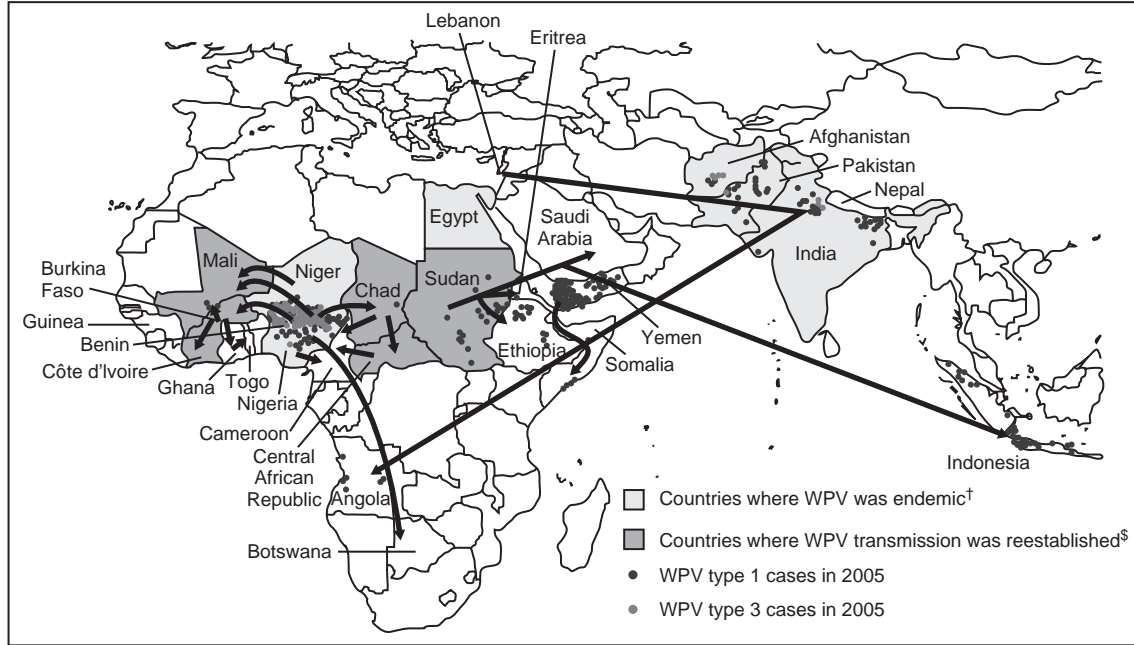
The number of international tourist arrivals declined in 2003 in response to outbreaks of SARS and the associated travel advisories. The WTO reported that arrivals at some affected countries in Asia plunged to below 50 percent of their usual levels in April and May (WTO, 2005). Although the region rebounded quickly, SARS was responsible for a 9 percent overall loss in travel volume for Asia for the year 2003. Estimates of the global cost of SARS associated with lost economic activity have been estimated at about US\$40 billion, and perhaps as high as US\$54 billion (Lee and McKibbin, 2004).

Rumors and fear can also affect the control of infectious diseases. Rumors that polio vaccine contained the AIDS virus and hormones that could sterilize girls in the largely Muslim population led Nigeria's northern states to halt polio vaccination in mid-2003 (Heymann and Aylward, 2004; Samba *et al.*, 2004). Political and religious factors contributed to the decision. By the time additional testing had been completed and the vaccine declared safe, polio outbreaks had spread in Nigeria and fueled outbreaks in other countries (see Figure 1.4).

The human transport of microbes and microbial genetic material

Travelers carry microbes and microbial genetic material, a large portion of it the trillions of bacteria that form the commensal flora (Wilson, 2003a; Sears, 2005). They may carry and transmit pathogenic microbes and microbial genetic material, including resistance and virulence genes, sometimes in the absence of symptoms. Carriage may be transient or long term. Chronic infections, such as HIV, hepatitis C, and hepatitis B, can persist and be transmitted even if the individual is unaware that infection is present. Infections can be latent (e.g. tuberculosis) and can potentially reactivate at a time and place remote from acquisition. Potentially pathogenic microbes can be carried on the skin, in the respiratory tract, in the genital tract, in the gastrointestinal tract, or in blood and body fluids. There are thus multiple potential ways that pathogens can be transmitted.

Even when an infection is already found in a geographic region, travelers may introduce a new serotype or strain that is more virulent or resistant to antimicrobials. Wide use of antimicrobial agents puts pressure on microbial populations and contributes to the emergence of resistant microbes, but travelers may



*Routes (not all importation events) indicated by arrows.

†As of February 1, 2006, Niger and Egypt were considered no longer endemic for WPV because neither country had indigenous transmission during the preceding 12 months.

§Countries were considered to have reestablished transmission if WPV was detected for >1 year after importation. The majority of these countries have not experienced WPV type 1 transmission since July 2005.

Figure 1.4 Wild poliovirus (WPV) cases in 2005 and WPV importation routes during the period 2002–2005 worldwide. From CDC (2006b).

be significant in their dissemination. For example, only 10 clones of penicillin-resistant *Streptococcus pneumoniae* were responsible for 85 percent of invasive disease caused by this organism in the US in 1998 (Corso *et al.*, 1998).

Transmission mechanisms

Which means of transmission are most important in serious infectious diseases? A breakdown of the infections causing death globally in 1995 found that infections that are transmitted from person to person (e.g. tuberculosis, measles, HIV) caused 65 percent of deaths; infections acquired from contaminated food, water, or soil (e.g. cholera and many other infections causing diarrhea, hepatitis A) caused 22 percent; vector-borne infections (primarily malaria) caused 13 percent; and infections from animals (e.g. rabies) caused 0.3 percent (WHO, 1996). These numbers are useful as general approximations, but vastly underestimate the role that animals play as a source of human pathogens. Many major human pathogens evolved in the recent or remote past from related pathogens in animals (e.g. HIV, measles, tuberculosis, malaria) (Weiss, 2001), and the majority of recently emerged infectious diseases are zoonoses, many of them viruses (Woolhouse, 2002; Smolinski *et al.*, 2003; see also Chapter 4).

Ease of transmission varies considerably by pathogen and by site of infection. Some microbes are able to spread in multiple ways. For example, the seasonal influenza viruses can be spread by direct contact (e.g. by contaminated objects or from hands of infected person), by large or medium droplets, or by droplet nuclei (tiny-droplet aerosol) (Musher, 2003). Tuberculosis, on the other hand, is spread by droplet nuclei that are small enough to bypass the trapping mechanisms of the upper airway and can reach the lungs. *Neisseria meningitidis* (the cause of meningococcal meningitis and sepsis) is spread by direct contact and large or medium droplets, but not by tiny-droplet aerosol. The mechanisms of transmission and transmissibility are key characteristics of microbes that influence ease of spread and determine what interventions will be effective. Timing of onset of infectiousness relative to onset of symptoms and duration of infectiousness are important factors in transmission dynamics.

Environmental conditions may also influence transmissibility. Influenza virus survives better in cool temperatures and at low humidity, which may partially explain the seasonality of influenza in temperate areas. Several of the summertime outbreaks of influenza have involved transmission in air-conditioned indoor spaces, where air was cool and dried, and people were in close contact (Uyeki *et al.*, 2003).

Basic reproductive rate

Whether infection can be sustained and will spread in a new population depends on the basic reproductive rate (R_0), which is the average number of secondary

infections produced by an infected individual in a susceptible population (Anderson and May, 1991). For an infection to be sustained in a new population, the basic reproductive rate must exceed one (May *et al.*, 2001). The R_0 for a specific infection may vary depending on time, place, and population. For example, in the pre-vaccine era the R_0 for measles was 16–18 in England and Wales in 1950–68, and 5–6 in Kansas, USA, in 1918–21. A plausible explanation for the difference is differences in population density and mixing of populations. In the early 1980s, the R_0 for HIV was 11–12 in Nairobi, Kenya, in a prostitute population and 2–5 in male homosexuals in England and Wales (Anderson and May, 1991). Based on detailed epidemiologic data from Singapore and other locations, Lipsitch and colleagues estimated that the reproductive number for SARS was about 3 (Lipsitch *et al.*, 2003). SARS was barely containable using isolation and quarantine measures. One biological characteristic of SARS that favored its control was that virtually all transmission occurred after patients had developed symptoms. This is not the case for seasonal influenza, HIV, and many other infections that can be transmitted in the absence of symptoms (Fraser *et al.*, 2004).

Multiple factors can influence the R_0 , including population density (noted above), behavior, genetics of the host population, and evolution of the pathogen. If a population includes a large number of hosts who are immunocompromised and remain infected and infectious for a prolonged period, this could also influence R_0 . A pathogen with a high mutation rate that allows it to adapt more readily to new hosts is more likely to be successful in emergence (Antia *et al.*, 2003).

Crossing the species barrier

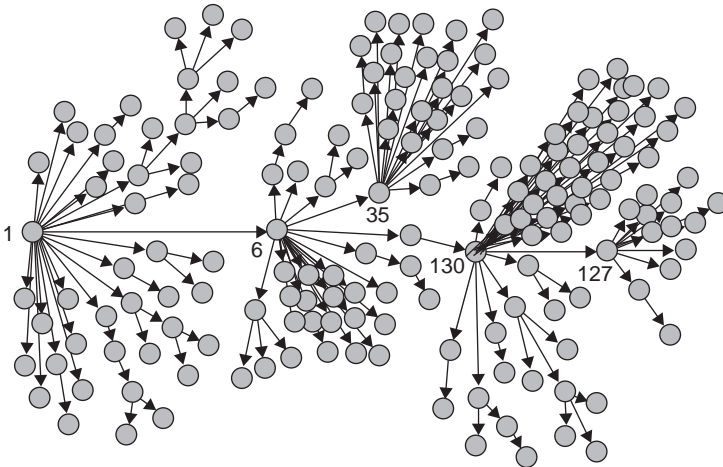
Crossing the species barrier requires several steps, the first being contact with the microbe – and travel today provides more potential exposure events with a wide range of other species or microbes in the environment than ever before. To cross successfully from one species to another, a virus must be able to find a cell type that it can infect (Webby *et al.*, 2004). Even if it can replicate, it must be able to avoid or overcome host immune response, exit from the cell, and infect additional cells. Finally, it must be able to exit the host in such a way that it can be transmitted to other humans. For many animal viruses, humans are always or usually a dead-end host (e.g. hantaviruses causing hantavirus pulmonary syndrome), and are irrelevant in maintenance of the microbe in nature. The avian influenza A virus (H5N1) has not transmitted efficiently from person to person as of mid-2006, and a potential explanation is that the cells in the upper respiratory tract of humans do not have receptors to which the virus can bind. The virus can replicate efficiently only in the lower respiratory tract (alveolar cells) of humans, from which it is not transmitted easily by sneezing and coughing (Shinya *et al.*, 2006).

RNA viruses have been prominent among microbes causing emerging infections. They are extremely mutable; many mutations can occur during replication, and

RNA viruses have few or no proofreading mechanisms (Webby *et al.*, 2004). These characteristics generate viral diversity. Variants with any advantage in a particular host or under specific environmental conditions are selected and can amplify. These viruses can also generate diversity through recombination and reassortment.

Superspreading and heterogeneity of transmission

In SARS and some other infections, a few individuals seem to account for a disproportionate number of the secondary cases. In Singapore, for example, 162 (81 percent) of probable SARS patients showed no evidence of secondary transmission, whereas 5 persons each transmitted infection to 10 or more others (see Figure 1.5; CDC 2003). Lloyd-Smith and colleagues showed that heterogeneity in transmission, instead of being an anomalous event, was a common feature of disease spread (Lloyd-Smith *et al.*, 2005). In several examples, 20 percent of the cases caused 80 percent of the transmission. This is of more than theoretical interest, as it can affect the course of an epidemic and can influence the choice of interventions to try to curb the spread of infection (Galvani and May, 2005). If highly contagious (or highly connected, for sexually transmitted infections) individuals can be identified, it may be possible to contain spread with fewer resources.



* Patient 1 represents Case 1; Patient 6, Case 2; Patient 35, Case 3; Patient 130, Case 4; and Patient 127, Case 5. Excludes 22 cases with either no or poorly defined direct contacts or who were cases translocated to Singapore and the seven contacts of one of these cases. Reference: Bogatti SP. Netdraw 1.0 Network Visualization Software. Harvard, Massachusetts: Analytic Technologies, 2002.

Figure 1.5 Superspreaders. Probable SARS cases by reported source of infection, Singapore (25 Feb–30 Apr 2003). From CDC (2003).

A small study that may be relevant to the topic of heterogeneity in transmission of respiratory pathogens assessed exhaled aerosols. Eleven healthy adult volunteers (18–65 years old) were connected to a device that measured the number and size of particles exhaled during quiet breathing. The number of exhaled particles varied dramatically among the subjects, ranging from 1 per liter to >10,000 per liter. Over a 3-month period, the high producers remained high producers on repeat assessment (Edwards *et al.*, 2004).

Receptivity of places and populations

Receptivity of places and populations to the introduction of a microbe by a traveler varies greatly. Many infections require the presence of a specific arthropod vector, such as a mosquito, to support the replication and development of the microbe and to carry it to a susceptible host. Others require a specific animal, such as a rodent, as a reservoir host. Animals such as birds, pigs, and others may serve as an amplifying host – i.e. an animal in which a microbe can replicate to such a level that it can be transmitted, often via an arthropod vector. Environmental conditions (e.g. temperature, humidity, and rainfall, among others) have a profound effect on the survival and abundance of many vectors and reservoir hosts.

West Nile Virus (WNV) became established for the first time in the Western Hemisphere in 1999 in New York, and has since spread across the United States, into Canada, Mexico, Central America, and the Caribbean. Whether the virus initially arrived in an infected person, bird, or mosquito, the virus found a congenial environment in which to persist and expand its geographic reach. Already in place were abundant mosquitoes of multiple species that were competent to support its growth and had frequent contact with humans. Dozens of species of birds were susceptible, and hundreds of thousands of birds died from WNV infection. Crows seemed especially vulnerable. In fact, dead-crow density was used as a marker for the arrival of the virus into new regions, as deaths in birds were often observed before human cases were diagnosed (Eidson *et al.*, 2001).

The physicochemical environment may influence the presence or absence, variety, and abundance of potential vectors and reservoir hosts. Additional factors also affect the receptivity of an area or population to the introduction of pathogens (Wilson, 1995b). These include housing, sanitation, general living conditions, and education. To become infected, a person must be exposed. Crowded living conditions, absence of sanitation, lack of clean water, poor housing (e.g. absence of screens and doors, lack of good ventilation), lack of knowledge regarding preventive measures, and close contact with animals (including rodents, pets, and food animals) all increase the probability of exposures to microbes that are transmitted from person to person, from contaminated food and water, from vectors, and from animals.

In Laredo (Texas) and Nuevo Laredo (Mexico), two urban areas separated only by the Rio Grande River, researchers found that residents of Nuevo Laredo were significantly more likely to have antibodies indicating recent or past infection with dengue virus, a mosquito-borne infection, than were those of Laredo, Texas (Reiter *et al.*, 2003). Environmental sampling showed that the mosquito vector (*Aedes aegypti*) was present in both cities, and infested containers were more common on the Texas side. In a multivariate analysis, residences without air-conditioning were 2.6-fold more likely to have a dengue-positive occupant, suggesting that socioeconomic factors were key determinants in exposure to infection (see also Chapter 4).

When a human pathogen is introduced into a new geographic region, socioeconomic, political, demographic, and other factors potentially influence the geographic extent of spread and the burden of disease in morbidity and mortality. In general, the poorest populations are the most likely to suffer and die from infectious diseases. In the poorest 20 percent of the world population, communicable diseases led to 59 percent of the deaths and 64 percent of the DALYs (disability adjusted life years) lost, whereas in the richest 20 percent communicable diseases accounted for only 8 percent of the deaths and 44 percent of DALYs lost (Gwatkin *et al.*, 1999).

In some instances, however, individuals who are extensively connected because they have resources that allow them to travel may be more likely to come into contact with unusual pathogens. In fact, in some countries, such as Tanzania and Kenya, household wealth is positively associated with HIV prevalence (Shelton *et al.*, 2005). Wealth may be associated with mobility and resources to maintain social interactions and concurrent sexual partnerships. In any country, availability of a strong health-care system and wide access to medical resources make it more likely that a disease will be recognized early and diagnosed. Access to treatment may limit morbidity and mortality, as well as spread of infection. Transparency about reporting infectious diseases and the capacity to organize and support appropriate public health investigation and response may limit the impact of an introduced infection. Social support may also be important in the successful completion of treatment for infections that require prolonged therapy, such as tuberculosis.

Potential receptor populations differ in size, density, location, mobility, vulnerability, and demographics (Wilson, 2003b). The human population today is larger than ever in history, and more urbanized, with about half of the world's population now living in urban areas. The populations that are growing the most rapidly are urban populations in developing countries – typically in low latitude areas. Large periurban slums surround many of these megacities that are linked to the rest of the world by air travel. Two types of vulnerability that characterize populations today (in addition to undernutrition, mentioned below) are AIDS and aging. Both make populations more vulnerable to a variety of infections.

Immunity

In addition to the mechanisms noted above, populations can be completely or relatively resistant to the introduction and establishment of a microbe because of innate or acquired immunity. Levels of immunity may be high because of past infection or immunization. Levels of immunity to hepatitis A are high in many developing countries where most people are infected at a young age because the virus circulates widely. Paradoxically, as socioeconomic status and sanitation in a country improve, outbreaks in older children and young adults begin to occur because exposure has not occurred at a young age (Jacobsen and Koopman, 2004). Hepatitis A as a cause of outbreaks becomes more visible because of the shifting upward of the age at which infection occurs.

High levels of immunity from immunization may protect a population from introduction of infection. In the US today, circulation of endemic measles has been interrupted, yet infections continue to occur sporadically in travelers from endemic regions or their contacts. Measles has a high R_0 , and spread can occur even in populations with high levels of immunity. Figure 1.6 shows measles importations into the Americas in 1997, with source countries in Europe and Asia (de Quadros *et al.*, 2004). Fourteen measles outbreaks were identified in the US during 2001–2004 (CDC, 2005a), seven of which originated with a US



Figure 1.6 Measles importations into the Americas, 1997. From de Quadros *et al.* (2004).

resident traveler. Genetic factors can influence susceptibility to infection or its expression, though for most infections this is not well defined. Nutritional status can influence outcome of infection and may determine the burden from infection in a population. Globally, undernutrition and micronutrient deficiencies are a leading cause of health loss and contribute to deaths from many infections, including malaria, measles, diarrhea, and pneumonia (Ezzati *et al.*, 2002).

The immune deficiency that accompanies HIV infection has led to recognition of infections previously undefined. As a sentinel population, their infections have also helped to chart the presence and geographic distribution of infections that may have previously gone unrecognized. Because of the potential for late reactivation of latent infections, such as visceral leishmaniasis, Chagas disease, and tuberculosis, it is important to review the history of travel and past residence of HIV-infected individuals.

Some types of immune deficiency can predispose to prolonged excretion of live vaccine-associated poliovirus (MacLennan *et al.*, 2004). Virulent vaccine-derived poliovirus has caused cases of paralytic polio in several countries (China, Egypt, Haiti, Madagascar, and the Philippines) (Kew *et al.*, 2002). In March 2005, a 22-year-old woman from Arizona contracted paralytic polio caused by vaccine-derived poliovirus (CDC, 2006a) after travel for a study-abroad program. In Costa Rica, she had had contact with an infant recently vaccinated with live oral poliovirus. She was unvaccinated against polio because of a religious exemption. Cases of vaccine-associated paralytic poliomyelitis (VAPP) had occurred in the past in the US, but no cases had been reported since 1999. The ongoing movement of poliovirus is further highlighted by events in the US. In September 2005, vaccine-derived poliovirus was found in an unvaccinated, immunocompromised infant in Minnesota (CDC, 2005c). Another four other children in the community also had asymptomatic infection. The virus differed about 2.3 percent from the parent Sabin vaccine strain, suggesting that it had been replicating for about two years and most likely originated from a visitor to the US who had received OPV elsewhere. Neither the infant nor the family had traveled internationally.

Dengue fever is an example that illustrates the interplay of multiple factors in the emergence and spread of an infection (see also Chapter 4). Dengue, a flavivirus transmitted by *Aedes* mosquitoes in tropical and subtropical regions, is increasing in incidence and in geographic range. An estimated 100 million cases of dengue fever and 25,000 cases of dengue hemorrhagic fever (DHF), and 25,000 deaths, occur annually (Gubler, 2002). Four serologically distinct serotypes exist. Because infection confers immunity only to the infecting serotype, a person can be infected up to four times. Having had prior infection with a dengue virus increases the likelihood of severe dengue fever (hemorrhagic fever or shock syndrome) if there is then infection with a different serotype. Viremic travelers are essential for the movement of the virus from place to place. The incubation period (usually 2–7 days) allows a person to move to another location before infection manifests. If mosquitoes competent to transmit dengue are present and

one or more bite the infected person at the time the virus is in the bloodstream (median of 5 days but range of 1–12 days) (Gubler *et al.*, 1981) and survive to transmit the virus to another human, infection can be established in a new area. The main mosquito vector, *Aedes aegypti*, is well adapted to the contemporary urban landscape. It breeds well in discarded plastic cups, flower pots, used tires, and other urban litter, it prefers human blood, and it enters homes. Among the multiple reasons for the increase in dengue globally are: increased regional and global travel (including especially travel to tropical and subtropical areas) and trade; poor vector control and pesticide resistance, which has allowed expansion of the areas infested with *Aedes aegypti*; poor housing (absence of screens, doors) and water supply (water stored in containers that are good breeding sites for mosquitoes); growth of urban populations in tropical areas globally; and increase in number of urban areas that have reached a population size sufficient to sustain the ongoing circulation of dengue viruses. Over the past two centuries, the number of dengue lineages has been increasing roughly in parallel with the size of the human population.

In addition, another competent vector, *Aedes albopictus*, the Asian tiger mosquito, has also been introduced into a number of countries. In the US it was introduced in 1985, probably via used tires shipped from Asia, and has subsequently spread (Moore and Mitchell, 1997). Its dispersal followed interstate highways. It was the mosquito vector responsible for an outbreak in Hawaii in 2001 (Effler *et al.*, 2005). Phylogenetic analysis found that the Hawaiian virus was similar to contemporaneous dengue isolates from Tahiti, suggesting that viremic travelers introduced the virus from the South Pacific.

In some dengue-endemic countries, such as Thailand and Vietnam, epidemics tend to occur in cycles of every three to five years, postulated to be because of the introduction of new genetic variants with greater epidemic potential and virulence. In an analysis that modeled data from 850,000 dengue infections from 72 provinces in Thailand during the period 1983–97, Cummings and colleagues found a spatial–temporal traveling wave in the incidence of DHF (Cummings *et al.*, 2004; Gubler, 2004). Furthermore, they found that the wave started in Bangkok, the largest city, and moved radially at about 148 km per month. Although all four serotypes are continuously present in Bangkok, smaller communities may experience periods without infection from specific serotypes. In epidemic years, a lag of 10 months may occur before outbreaks develop in some areas. It suggests that dense urban centers are the genesis of viruses that cause epidemics that then migrate (in humans) to surrounding regions.

Movement of animals (vectors and intermediate hosts)

Migrating birds can move potential human pathogens into new regions, as has been shown with West Nile virus and H5N1 influenza A (avian) virus (Rappole

et al., 2000; Chen *et al.*, 2005; Liu *et al.*, 2005). Much movement of animals (live, dead, parts) is orchestrated by humans, sometimes with disastrous consequences. The importation of wild animals from Ghana that were then housed with wild-caught prairie dogs from the United States led to an outbreak of monkeypox (a disease previously known to exist only in Africa) in the Midwest (Reed *et al.*, 2004). Hunting of bushmeat, as local populations seek a source of protein and as logging roads make trade easier, threatens some wild animal species. Killing and butchering wild animals also puts people at risk for becoming infected with pathogens in animals (Wolfe *et al.*, 2005). The global market in bushmeat has grown. A report from the UK Department of Environment, Food and Rural Affairs estimated that 11,600 tons of illegal bushmeat were smuggled into the UK in 2003 (*Daily Telegraph*, 5 September 2004; <http://www.telegraph.co.uk/news/main.jhtml>). Shipments included monkey, rat, bat, gorilla, camel, and elephant. Consumption is on the increase outside of Asia, Africa, and South America as immigrant populations expand in Europe, North America, and other areas.

Illegal trade may also be a source of imported pathogens. Two Crested Hawk-Eagles were confiscated in Brussels after being carried from Thailand via Vienna in hand luggage placed in an overhead storage bin on airplanes. Although the birds did not appear ill, both were found to be infected with highly pathogenic H5N1 virus (van Borm *et al.*, 2005).

Mosquitoes are regularly carried on commercial flights and ships, and can be introduced into new regions where they may be able to survive and become established locally (Sutherst, 2004). Depending on the local environment and opportunities, they may be able to transmit tropical infections to humans. During the period 1969 through August 1999, 12 countries reported 89 cases of confirmed or probable cases of “airport malaria” – instances when an infected mosquito was transported by plane from a malaria-endemic region to an area without malaria and survived long enough to transmit malaria to a local resident. Most countries were in Europe, but the US, Australia, and Israel also reported cases (Muentener *et al.*, 1999; Gratz *et al.*, 2000).

Vehicles of travel

Outbreaks in travelers can be traced to infection acquired in the vehicle of travel – *en route* transmission. Food-borne outbreaks (e.g. salmonellosis, shigellosis, cholera, staphylococcal food poisoning, and others) have been linked to food or beverages served on flights (Mangili and Gendreau, 2005). Infections transmitted directly from person to person, and those that are airborne, also pose a risk to airplane travelers. Published reports describe transmission of tuberculosis, SARS, measles, and influenza on aircraft. In one outbreak, 72 percent of 54 passengers on a plane that had been grounded for Three hours because of a failed air-circulation system developed influenza-like illness; influenza A was documented (Moser *et al.*, 1979). Norovirus,

a cause of acute gastroenteritis, has probably also been transmitted on an airplane (Widdowson *et al.*, 2005). Following a single 3-hour flight between Hong Kong and Beijing that included an ill passenger who later died of SARS, confirmed or probable SARS developed in 18 of 120 passengers. Those seated within three rows in front of the index case were most likely to become infected (Olsen *et al.*, 2003).

People tend to think of cruises as an outdoor activity, but on large cruise ships passengers spend much time in indoor shared spaces. Gastrointestinal infections have long been associated with cruise ships, but more recently outbreaks of other infections have been reported (Minooee and Rickman, 1999). These include legionellosis (CDC, 2005d; Kura *et al.*, 2006) and infections, like influenza (Brotherton *et al.*, 2003) and rubella, with person-to-person spread. Noroviruses have emerged as a major problem for cruise ships. Not only can these viruses be spread from person to person by fecal–oral transmission and airborne transmission, they can also be spread via contaminated food and water and by contact with contaminated surfaces in the environment (Bull *et al.*, 2006). They can persist in the environment despite disinfection efforts (Widdowson *et al.*, 2005). New virus variants have emerged and have been associated with an increase in outbreaks on cruise ships (Lopman *et al.*, 2004; Widdowson *et al.*, 2004). The dispersal of passengers after cruise-ship travel may allow seeding of multiple communities with infections.

Persons who are older and have chronic medical problems make up a high percentage of travelers on some cruises. On one cruise ship with an outbreak of influenza, 77.4 percent of 1448 passengers were 65 years of age or older, and 26.2 percent had chronic medical problems (CDC, 1997).

The arrival of travelers changes places and affects the host population. This can occur through building hotels, providing food and other services for travelers, building new roads, and changing the habitat or landscape to make it more desirable to visitors. These activities can bring economic benefits to a region and provide new jobs for local residents. There are also negative consequences – destruction of pristine habitats, alteration of ecosystems and fragmentation of habitats; increased traffic and pollution; increased inequalities; disruption or corruption of local activities and customs; sexual tourism; and increased crime as wealthy tourists have close contact with impoverished local residents. Much of the wealth from tourism to a region may flow out of the country in cases where hotels and other concessions are owned by foreign investors.

Tools

Powerful tools now aid in answering epidemiologic questions. Advances in laboratory methods enable surveillance at the microbial level. Computer technology can estimate disease transmission and control. Clinicians also participate in the surveillance of diseases, especially specialists in travel and tropical medicine.

Laboratory techniques

Molecular markers can determine the similarity or divergence between two isolates of an organism, and assess whether a patient has a new infection or a relapse of an old one. When multiple infections occur in a population, it can be determined whether infections were related to the same source. It is possible to pinpoint an animal, arthropod, food or environmental source. It is also often possible to characterize the patterns of spread and the mode of transmission. Other questions that can be addressed are whether some strains are more transmissible, more virulent, or associated with different clinical characteristics (e.g. longer carriage). Devising sensible and effective interventions is more likely if the routes of transmission and epidemiological patterns are known.

Use of predictive models

Models have been developed to simulate the estimated impact of infectious diseases, and some have focused on air travel or have integrated data about air travel into the models (Brockmann *et al.*, 2005, 2006; Colizza *et al.*, 2006). The rapid spread of SARS showed that estimates on the spread of modern epidemics need to consider the pattern of travel, the global aviation network, the number of flights departing from and arriving at airports, the number of passengers carried, and the size of aircraft (Hufnagel *et al.*, 2004). Simulations can be used to model the potential impact of different interventions on the control of epidemics – for example through vaccination (where reducing the susceptible population leads to fewer “reproducers”) as well as travel restrictions, and especially by isolation of largest cities.

The present pattern of air travel is expected to alter the dynamics of an influenza pandemic compared to past pandemics. The pandemic influenza of 1918–19 spread by ships, over land, and reached some remote areas by dog sled. In 1968–69, the time of the Hong Kong pandemic, 160 million persons traveled internationally on commercial flights. The Hong Kong influenza strain diffused through the network of cities globally by air travel, first to northern and then to southern latitudes (Rvachev and Longini, 1985). Simulation of the epidemic using 2000 air-transportation data for 52 global cities showed the virus spread concurrently to cities in both northern and southern hemispheres, resulting in little seasonal swing and a very short time for public health intervention (Grais *et al.*, 2003). The simulation showed that disease would spread first to nearby cities, but also to distant cities with high air-travel volumes, such as Sydney, Singapore, Johannesburg, Melbourne, Perth, and Wellington. The estimated time for the pandemic to reach northern-hemisphere cities, using the 2000 travel data, was 111 days shorter than in 1968 (Grais *et al.*, 2003).

Travel medicine: origin and evolution of travel medicine as a specialty

Over the past 25 years a new specialty has evolved to address the needs of travelers, especially those who visit resource-poor regions (Hill, 2006). Travel medicine has been defined as the “discipline devoted to the maintenance of the health of international travelers through health promotion and disease prevention” (Kozarsky and Keystone, 2004). It is an interdisciplinary specialty with a global focus, by integrating an understanding of global health issues into the care of travelers. Pioneers in the field advocated analyzing epidemiological data to define risks associated with travel, and ways to reduce them (Steffen, 1991).

Travel medicine focuses on prevention involving such specialties as clinical tropical medicine, infectious diseases, public health, occupational health, high-altitude and diving medicine, wilderness medicine, travel-related women’s health and pediatric medicine, psychiatry, migration medicine, environmental health, and military medicine. The International Society of Travel Medicine (ISTM) was established in 1991 from this multi-disciplinary interest. In the globalized economy, the business community is also drawing upon the expertise of travel-medicine specialists as companies send workers and their families to other countries for extended periods.

GeoSentinel and other networks

Travel and tropical medicine clinics are in a position to detect disease outbreaks that may be heralded by returning travelers. Surveillance networks of travel and tropical medicine clinics have been established to systematically collect data on travel-associated diseases and be on the alert for disease outbreaks or changes in patterns of infections. GeoSentinel is such a network, established in 1995 through collaborative agreement between the International Society of Travel Medicine and the Centers for Disease Control and Prevention (Freedman *et al.*, 1999). TropNetEurop is another network that primarily has sites in Europe. The GeoSentinel network now has 31 sites located in six continents. Studies published by members of the GeoSentinel network are also contributing to the database that will allow clinicians to make recommendations based on evidence.

GeoSentinel analysis of morbidity in travelers can provide guidance on identifying common illnesses in travelers and risk of travel to health (Freedman *et al.*, 2006). Moreover, GeoSentinel has disseminated alerts regarding a number of diagnoses in returning travelers – leptospirosis in participants returning from Eco-Challenge in Borneo, Malaysia; SARS in travelers returning to Canada from Asia; and malaria in travelers to resorts in Punta Cana, Dominican Republic. Subsequent to these notifications, clinicians identified additional cases in travelers, and public health responses were initiated.

ProMED, a program of the International Society of Infectious Diseases, has also accelerated the dissemination of outbreak reports through the use of the Internet. Networks such as GeoSentinel and ProMED have enabled rapid information-sharing between public health authorities and clinicians.

Conclusions

Travel changes people and places. The traveler can be the target and sufferer from microbial threats; the traveler can also provide the microbial transport system. Traveling humans alter infectious diseases patterns by introducing pathogenic microbes or resistance or virulence factors into new populations. The movement of pathogenic microbes through history has been intimately linked to the capacity of humans to travel and to migrate to new locations. Today, humans have the capacity to reach virtually any city in the world within a day or two. Travel to tropical and developing countries is increasing more rapidly than travel to developed countries, and all projections suggest that human travel will continue to increase in the foreseeable future. Infectious diseases influence decisions about travel and trade; and travelers change the epidemiology of infectious diseases.

Travel has played an essential role in the movement of HIV/AIDS throughout the world. Rapid international air travel moved the virus that causes SARS to multiple countries within weeks. Travel has been and will continue to be important in the movement of human influenza.

Recent experiences with SARS and avian influenza underscore several observations:

- travel and trade are major forces in the global economy
- movement of humans and animals influences the biogeography of infectious diseases
- many important human pathogens originate from related microbes in animals
- interactions between humans and animals are common and widespread
- animal populations (for food) are growing even faster than human populations
- animals and birds can migrate
- humans have some control over animal trade (though illegal movement and marketing is huge)
- humans cannot control movement of microbes through bird migration
- surveillance is critical and must be global and linked to response capability
- communication among scientists must be frequent and open
- isolates of microbes must be made available to scientists
- international collaboration is essential and must be multidisciplinary
- communication about risks must be timely and accurate
- poverty and ignorance are risk factors for infectious diseases
- poverty limits choices.

Travel consists of sequential shared environments, often with people from diverse regions of the world. It should be considered a loop, and not just an origin and destination. Travel has created one, extensively interconnected world in terms of microbial threats. Approaches must consider the global community.

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