Part I

Key Themes Pertinent to Migration, Health, and Disease

Chapter 2

Population Mobility and the Geography of Microbial Threats

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Introduction

Migration of humans shapes the distribution and patterns of infectious diseases globally (Wilson, 1995a). This has been true throughout recorded history (Berlinguer, 1992; Bruce-Chwatt, 1968; Crosby, 1989; Winkelstein, 1995). Today human travel is unprecedented in volume, reach, and speed. This massive and rapid movement is occurring in the context of global changes that favor the appearance of previously unrecognized microbial threats and a change in the distribution and burden from well known infectious diseases (Smolinski, Hamburg, & Lederberg, 2003; Wilson, Levins, & Spielman, 1994). Humans, in addition to carrying their own assemblage of microbial flora, orchestrate the movement of other species and biological material through extensive global travel and trading networks (Wilson, 2003). Humans also explore and enter new areas and change the environment in ways that place them at risk for new microbial threats (Wilson, 2000). Infectious diseases also threaten plants and animals; infections in other species have economic consequences and have direct and indirect impacts on human health and well being (Wilson, 1995b). Animals increasingly are recognized as a source of many newly recognized infectious diseases in humans. Social, economic, political, climatic, technologic, and environmental patterns influence microbial threats to health as well as their consequences and the responses to them. This chapter will review these themes and the central role of human migration in the dynamic geography of infectious diseases and context in which this is occurring (see Table 2.1).

Migration

Numbers and Reasons

The movement of the human population today is unprecedented in volume, reach, and speed. Data collected by the World Tourism Organization (WTO) (2006) showed that over 800 million people traveled internationally in 2005 and

TABLE 2.1. Key Concepts: Migration and microbial threats

- Human migration shapes the distribution and patterns of infectious diseases.
- Human travel today is unprecedented in volume, reach, and speed.
- The impact of migration is on the individual, on places, and on populations; consequences occur during and may persist long after travel.
- The impact of migration must be considered in the current global context of population size, density, location, vulnerability, and inequalities.
- Infectious diseases in humans, plants, and animals are dynamic; the current global milieu favors the continued changes in microbial threats.
- Animals are a source of many recently identified microbial threats.
- Human activities are potent factors driving changes in microbial threats.
- Social, economic, political, climatic, technologic, and environmental patterns influence disease emergence as well as responses and consequences.
- Addressing changing microbial threats requires a systems approach and participation from a broad range of disciplines.

of these, 45% of inbound tourists arrived by air. Although leisure, recreation, and holidays accounted for more than 50% of global travel in 2005, about 16% of global international travel was for business and professional reasons. In the 1990s, more than 5,000 airports had regularly scheduled international flights, linking urban and periurban areas throughout the world. Destinations are shifting, with increasing numbers of travelers visiting Asia and developing countries in Africa. Through adventure travel organizations using current technology (including small planes, helicopters, boats, etc.), more travelers are reaching remote areas. In the U.S., more than 44 million flights take place annually through 19,500 U.S. airports (Fischetti, 2004). More than 5,000 airplanes are simultaneously airborne at peak times. The projected number of air travelers in the U.S. in 2003 was 641 million with 117 million being international travelers.

Counting tourists captures only a fraction of mobile populations. Troops are regularly mobilized for military, humanitarian, and other support services; populations are displaced because of political, economic, ethnic reasons, or environmental changes, or catastrophic events, such as floods, hurricanes, volcanoes, earthquakes, and tsunamis. Refugees and displaced persons may live in crowded temporary facilities, often with limited access to clean water and food and sanitary facilities (Toole, 1994). Poor housing may allow exposure to mosquitoes and other disease vectors and to rodents and other animals that can be a source of infection (Connolly, Gayer, Ryan, Salama, Spiegel, & Heymann, 2004). Good medical care may be limited or absent, allowing preventable and treatable infectious diseases, such as measles and cholera, to spread in the crowded community with resulting high mortality. As of 2002, an estimated 35 million people worldwide were fleeing war or persecution, the highest number since the 1940s. In the U.S., there are 34.2 million foreign-born residents, more than half from Latin America and about a quarter from Asia (Doyle, 2005). An estimated 10.3 million of them are illegal immigrants, many of whom lack access to preventive services and medical care.

Travelers often enter environments that are riskier than their home environments. Even today tropical and developing countries are areas where travelers face the risk of diarrhea, malaria, dengue, and other tropical diseases. When a stay in a tropical area is brief and travel rapid, onset of symptoms and period of contagion for those infections that are communicable, may begin after return home, and travelers may spread infection to close contacts (Wilson, 2003). Today much can be done to reduce but not eliminate risk to travelers. In the era before vaccines and antimicrobials were available, visits to most tropical areas were substantially more dangerous. Curtin (1989), in his book, *Death by Migration,* analyzes the excess mortality in European troops stationed in various locations and quantifies what he calls "relocation costs" – comparing mortality of troops in England and France, for example, with those in various locations in Africa and Asia during the same years.

Speed

Travel today is rapid and frequent. In 1850 a person took about a year to circumnavigate the globe. Today it is possible to reach most places on earth within 48 hours and within the incubation period of most infectious diseases. Grubler and Nakicenovic (1991) estimated the spatial mobility of the French population from 1800 to 2000 and concluded that the number of kilometers traveled daily for the average French person had increased more than 1,000-fold over the 200 year period. The rapid dispersal of Severe Acute Respiratory Syndrome (SARS) into Canada and other countries by air travelers is a recent reminder of the global interconnectedness (Peiris, Guan, & Yuen, 2004).

Conveyances and Contact

Travel often involves multiple, sequential shared environments (e.g., bus, train, terminal, airplane, ship, underground railway) and should be seen as a loop and not just an origin and destination (Wilson, 2003). With cruise ships, the time and place of transport become the primary place of activity. Cruise ships are often massive, transporting thousands of passengers and crew in a conveyance with many shared indoor spaces. Passengers from multiple different origins travel together for a few to many days in a common environment and then disperse to multiple destinations, providing an ideal way to disseminate infections that are spread from person to person, such as influenza (Miller, Tam, Maloney, Fukuda, Cox, Hockin, Kertesz, Klimov, & Cetron, 2000) and norovirus infection. Many outbreaks have been documented on cruise ships, including rubella (CDC, 1998), Legionnaires disease (Jernigan, Hofman, Cetron, M, Genese, C, Nuorti, Pekka Fields, Benson, Carter, Edelstein, Guerro, Paul, Lipman, & Breiman, 1996) and gastrointestinal infections (Minooee & Richman, 1999). En route transmission has been documented on airplanes and trains, including potentially fatal infections such as tuberculosis (TB) (and multidrug resistant TB) (Kenyon, Valway, Ihle, Onorato, & Castro, 1996) and SARS. On a 3-hour flight between Hong Kong and Beijing carrying 120 persons, one symptomatic passenger, who later died of SARS, spread infection to 8 of 23 persons seated in the three rows in front of him. Overall, 22 passengers on the plane became ill, 16 with laboratory-confirmed SARS, and others with illness consistent with SARS (Olsen, Chang, Cheung, Tang, Fisk, Ooi, Kuo, Jiang, Chen, Lando, Hsu, Chen, & Dowell, 2003). Transmission of influenza on a commercial aircraft has also been documented (Moser, Bender, Margolis, Noble, Kendal, & Ritter, 1979). During the loop that constitutes travel humans often have contact with a large, diverse sample of people and sometimes animals and arthropod vectors as well.

Human as Interactive Units

Humans can be considered interactive biological units who carry an assemblage of microbial flora along with their immunological profile, shaped by previous exposures, infections, and immunizations (Wilson, 2003). The microbial community in one adult human weighs up to one kg and may include 100 trillion bacteria, the largest numbers residing in the large bowel (Nicholson, Holmes, Lindon, & Wilson, 2004). Humans not only pick up and drop off microbes during travel but interact with them immunologically influencing which strains or variants survive. Humans also carry microbial genetic material, including resistance genes (O'Brien, Pla, Mayer, Kishi, Gilleece, Syvanen, & Hopkins, 1985; Okeke & Edelman, 2001). Humans also have distinctive, individual genetic characteristics, which can make them more or less susceptible to certain infections or likely to suffer severe consequences from them. Humans may provide the vessel where microbes undergo mutation or exchange genetic material. Humans can acquire and transport potential pathogens and resistance genes in the absence of symptoms. For example, strains of *Neisseria meningitidis* W135, a cause of meningitis and sepsis, colonized the nasopharyngeal tissues of pilgrims to the Hajj in Saudi Arabia, often without causing symptoms. In some instances, after the pilgrims returned home, the bacteria spread to family members or other close contacts, leading to serious infection (Dull, Abdelwahab, & Sacchi, 2005; Hahne, Gray, Aguilera, Crowcroft, Nichols, Kaczmarski, & Ramsay, 2002; Wilder-Smith, Barkham, Earnest, & Paton, 2002). Gastrointestinal carriage of the polio virus by visitors to countries with inadequate vaccine coverage, especially if sanitation is poor, can spark new cases (Heymann & Aylward, 2004). Transmission of some human pathogens, such as hepatitis B virus and HIV, can occur in the absence of symptoms and long after the infection was acquired. TB can reactivate years after acquisition in a place far from where it was acquired.

The large number of potential contacts of a single traveler is demonstrated by a recent case of measles carried into the U.S. state of Iowa (Dayan, Orftega-Sanchez, LeBaron, Quinlisk, & the Iowa Measles Response Team, 2005). A U.S. student, unvaccinated against measles, became ill on a return trip from India, where he had been exposed to measles. His return itinerary involved connections in two busy airports. Despite a prompt diagnosis of measles and vigorous interventions, two months of containment efforts were required in Iowa at an estimated direct cost of US $142,452 to the public health infrastructure. More than 2,500 hours of personal time were expended to contact exposed passengers, set up vaccination clinics, trace over 1,000 potentially exposed contacts, among other activities.

Other Transport

Humans, in addition to carrying their own microbiological flora, transport or facilitate the transport of other species, including live animals, animal parts, plants, seeds, arthropods (including mosquitoes and other potential vectors of infectious diseases), microbes, and microbial genetic material. The ballast water of ships can contain potential pathogens and invasive species that can contaminate waterways and change local ecology (Carlton & Geller, 1993; McCarthy & Khambaty, 1994; Ruiz, Rawlings, Dobbs, Drake, Mullady, Huq, & Colwell, 2000). Much of the fresh produce eaten in the U.S. is imported from other countries. Contamination has led to outbreaks caused by unusual pathogens, such as *Cyclospora cayetanensis* (Herwaldt, 2000), as well as more common ones. Because of mass processing and wide food distribution networks, outbreaks may involve cases in multiple different countries (Van Beneden, Keene, Strang, Werker, King, Mahonn, Hedberg, Bell, Kelly, Balan, MacKenzie, & Fleming, 1999). Today the food chain is very long and includes multiple points at which contamination or improper handling can occur.

The U.S. also imports live animals, many of them for pets. For example, in 2002, legal imports included 47,000 mammals, 379,000 birds, 2 million reptiles, 49 million amphibians, and 223 million fish (Communication from Paul Arguin, CDC). Many of them are wild caught and not screened for infection prior to shipment to the U.S. A large trade in illegal plants and animals also exists, estimated at US $3 billion per year in the U.S. In 2004 customs inspectors in Brussels seized two eagles carried in hand luggage by a Thai man on a commercial flight from Thailand via Vienna (Van Borm, Thomas, Hanquet, Lambrecht, Boschmans, Dupont, Decaestecker, Snacken, & van den Berg, 2005). Both birds were found to be infected with the influenza H5N1, the strain of avian influenza that causes high mortality in humans.

Animals

One highly visible (and expensive) consequence of animal importations into the U.S. was a 2003 outbreak of monkeypox, an infection caused by a virus previously documented only in Africa (Guarner, Johnson, Paddock, Shieh, Goldsmith, Reynolds, Damon, Regnery, Zaki, & the Veterinary Monkeypox Virus Working Group, 2004; Reed, Melski, Graham, Regnery, Sotir, Wegner, Kazmierczak, Stratman, Li, Fairley, Swain, Olson, Sargent, Kehl, Frace, Kline, Foldy, David, & Damon, 2004). Investigation revealed that prairie dogs (captured in the U.S. to be sold as pets) had been housed with exotic rodents imported from Ghana in Africa. The rodents had unrecognized infection with monkeypox, which spread from them to the prairie dogs, which were sold as pets and infected their human owners. The U.S. also exports animals for pets. In 2002, tularemia, an infection that can be fatal to humans, caused a die-off in wild-caught prairie dogs at a Texas animal facility (Petersen, Schriefer, Carter, Zhou, Sealy, Bawiec, Yockey, Urich, Zeidner, Svashia, Kool, Buck, Lindley, Celeda, Monteneiri, Gage, & Chu, 2004). In June and July of 2002, this facility had distributed more than 1,000 prairie dogs to be sold as pets to 10 states and seven European and Asian countries.

Animals have been the source of many of the recently appearing microbial threats (Smolinski et al., 2003). This underscores a need to have a better understanding of interspecies transmission of viruses and other pathogens (Webby, Hoffmann, & Webster, 2004). Some recently identified agents of zoonoses, in addition to monkeypox virus, include the SARS coronavirus, avian influenza, variant Creutzfeldt-Jakob, HIV, Nipah virus, West Nile virus, several newly identified hantaviruses, and *Escherichia coli* O157:H7. Travel and trade have played a pivotal role in the emergence and spread of most of these, either through movement of infected animals or their tissues or humans. Most, but not all, are viruses. Notably, multiple different modes of transmission are involved. Fortunately for humans, at present only one, HIV, has the characteristics that allow it to undergo sustained transmission from person to person, which it has done inexorably around the globe, largely via sexual transmission. There is good evidence that the AIDS pandemic originated from multiple independent introductions of simian immunodeficiency viruses from African apes and monkeys into humans and their subsequent evolution and spread (Hahn, Shaw, De Cock, & Sharp, 2000; Sharp, Bailles, Chaudhuri, Rodenburg, Santiago, & Hahn, 2001).

The threat of pandemic influenza is ever present, but the concern has been heightened recently because of the appearance of highly pathogenic avian influenza H5N1 that has caused outbreaks in avian species, initially concentrated in Southeast Asia but with recent spread via migratory birds into western China (Chen, Smith, Zhang, Qin, Wang, Li, Webster, Peiris, & Guan, 2005) and Europe. The virus has an expanded mammalian range (including cats and zoo animals, such as tigers and leopards) and has infected humans who have had close contact with avian species. To date, fewer than 200 human cases have been documented, but mortality has been high (about 50%). If the virus evolves, via mutation, recombination or reassortment, to become easily transmissible from person to person, it could cause global devastation. Recently scientists were successful in characterizing the genes of the virus causing the 1918 influenza, which was estimated to cause 40 million or more deaths globally, and found that the virus was likely derived from an avian source (Taubenberger, Reid, Lourens, Wang, Guozhong, & Fanning, 2005).

Recent studies in Africa and Asia have documented ongoing transmission of simian viruses to humans, through contact with primates as pets or with primate tissue through butchering of primates for food (Wolfe, Heneine, Carr, Garcia, Shanmugam, Tamoufe, Prosser, Torimiro, LeBreton, Mpoudi-Ngole, McCutchan, Birx, Folks, Burke, & Switzer, 2005; Wolfe, Switzer, Carr, Bhulla, Shanmugam, Tamoufe, Prosser, Torimiro, Wright, Mpoudi-Ngole, McCutchan, Birx, Folks, Burke, & Heneine, 2004). A survey in rural Cameroon found that more than 60% of local inhabitants reported contact with fresh blood or body fluids from nonhuman primates, most often through hunting and butchering chimpanzees, monkeys, or gorillas (Wolfe, Prosser, Carr, Aamoufe, Mpoudi-Ngole, Torimiro, LeBreton, McCutchan, Birs, & Burke, 2004). In Central Africa alone, the estimate for trade and local and regional consumption of wild animal meat (which includes nonhuman primates) is over 1 billion kg per year (Wilkie & Carpenter, 1999).

In general, the amount of space used by animals is strongly linked to body size; larger animals have a larger home range size (Jetz, Carbone, Fulford, & Brown, 2004). Humans are the only animal that regularly and vastly exceeds the distance that can be traveled by self locomotion. Some birds, land animals and fish migrate long distances, and occasionally animals, plants, and other material can be dispersed over long distances by being carried in water (sometimes on floating logs or debris, especially after major storms), and also via winds and dust storms. Humans stand alone as the species that has been able to inhabit or explore most areas of the earth and to change many of them.

Arthropod Vectors

Most arthropod vectors, such as mosquitoes and ticks, can travel only limited distances, unless carried by a migrating bird or animal or assisted by humans. Mosquitoes are regularly transported by planes and boats and other conveyances of human transport and trade (Lounibos, 2002). In 1985, the mosquito, *Aedes albopictus* (Asian tiger mosquito) was introduced into North America (Texas) from Asia (Hawley, Reiter, Copeland, Pumpuni, & Craig, 1987). *Aedes* mosquito eggs are desiccation resistant and survived the trip by ship in the protected environment of used tires. The mosquito subsequently spread to at least 25 states over 12 years, its movements following interstate highways, presumably carried by human traffic and trade (Moore & Mitchell, 1997). In recent years it has been introduced into many countries in Latin America. In the past, water containers on ships provided a protected habitat for mosquitoes during travel; modern ships, especially those with container vessels, likewise have been effective in permitting the survival and introduction of mosquitoes into new areas. This is relevant to human health because *Aedes albopictus* is competent to transmit a number of viruses that are human pathogens, and it was the primary vector implicated in the dengue outbreak in Hawaii in 2001-2002 (Effler, Pang, Kitsutani, Ayers, Nakata, Vorndam, Elm, Tom, Reiter, Rigau-Perez, Hayes, Mills, Napier, Clark, & Gubler, 2005).

Mosquitoes can survive long airplane flights. One study reported finding mosquitoes on 12 of 67 airplanes that had arrived in London from Africa. Mosquitoes, house flies, and beetles have also been shown to survive in wheel bays of airplanes on flights of 6 to 9 hours (Russell, 1987). In a quantitative risk assessment of pathways by which West Nile Virus (WNV) could reach Hawaii, investigators estimated that 7 to 70 infected mosquitoes could reach the island each year, based on number of airplane flights arriving from areas with ongoing viral circulation and the expected number of viable mosquitoes per flight. They concluded that human-transported mosquitoes and human-transported birds or other vertebrates posed the greatest risk for introduction of WNV into Hawaii (Kilpatrick, Gluzberg, Burgett, & Daszak, 2004). WNV entered the U.S. (presumably in an infected human, mosquito, or bird) in 1999 (Nash, Mostashari, Fine, Miller, O'Leary, Murray, Huant, Rosenberg, Greenberg, Sherman, Wong, & Layton, 2001) and subsequently has spread throughout the continental U.S., into Canada, Mexico, the Caribbean and Central America. Migrating birds have played an essential role in the movement of WNV in the Americas (Rappole, Derrickson, & Hubalek, 2000), a region already inhabited by several mosquito species competent to transmit it.

Customs and Traditions

Humans also carry with them customs and traditions, including food preferences and methods of preparing foods, sexual mores, ways of dressing, and other behavioral patterns that can influence their risk of exposure to some pathogens. Activities that would not be considered risky in their home environment (e.g., swimming and wading in fresh water; receiving injections at a local clinic; sleeping in a room without screens or bednets) could potentially place them at risk for infections, such as schistosomiasis, blood-borne pathogens (e.g., hepatitis B and C, HIV), or malaria in certain locations. Immigrants and their families may prefer foods from their country of origin. In San Diego, California a review of culture-confirmed TB (1980-1997) in children under 15 years found that 34% were infected with *Mycobacterium bovis*, a type of TB that typically comes from cattle (Dankner, Waecker, Essey, Moser, Thompson, & Davis,1993) and is now rare in the U.S. Approximately 90% were of Hispanic ethnicity (but U.S. born). An important source of infection was thought to be fresh cheese made in Mexico from unpasteurized milk and brought to the U.S.A study published in 2000 found that 17% of cattle sampled at meat-processing plants in Mexico were infected with *M. bovis* (Milian, Sanchez, Toledo, Ramirez, & Santillan, 2000). In the U.S. human infection with *M. bovis* has become rare because of pasteurization of milk and disease control in cattle herds.

Context

Microbial World

The attributes of the microbial world must be taken into account in trying to understand microbial threats to human health. The microbial world is vast. Only a tiny fraction of microbes have been identified and characterized. Contrary to common belief, most microbes do not harm humans, and many are essential for life as we know it. Human life as it exists today would be impossible without the beneficial services performed by microbes. Microbes are abundant and also resilient, living in a broad range of habitats, and many being able to survive at extremes of heat, cold, pH, and salinity that would kill humans. They also have a short generation time, giving them capacity to undergo rapid evolution. The generation time for a staphylococcus is 20 to 30 minutes, in contrast to 20 to 30 years for humans. Microbes undergo change through mutation and other molecular maneuvers that allow them to exchange or acquire new genetic material (e.g., through recombination, conjugation, reassortment) and respond rapidly to changes in the environment. The exposure of a microbe to an antimicrobial or specific chemical represents just another change in the environment and one that microbes adapt to regularly.

Population Factors

Size

The movement of humans and other species is occurring in the context of other population factors that also influence microbial threats to health. These are population size, density, location, vulnerability, and inequality. The size of the human population is larger than ever in history. The size of the domestic animal population, driven by the need for animal protein and nutrition for the growing human population, is also larger than ever in history. Because of limited habitable space on the earth, more humans are living in close proximity to large animal populations. Figures in China illustrate the changes over a few decades. In 1968, at the time of the last influenza pandemic, the human population of China was 790 million, the pig population was 5.2 million, and the poultry population was 12.3 million. The numbers today are 1.3 billion people, 508 million pigs, and 13 billion poultry (Osterholm, 2005). Many people live in close association with poultry and pigs, a reason for concern given outbreaks of avian influenza H5N1. A larger population provides more hosts in which microbial replication can occur and the potential for the emergence of more transmissible or virulent forms.

As of 2004, there were an estimated 34.2 million foreign born persons in the U.S, accounting for 11.3% of the total population (Doyle, 2005). Half of the growth in the U.S. population is in the foreign born. Many foreign-born residents have close relatives living in other countries, whom they visit regularly. This group of travelers (designated as "visiting friends and relatives" or

VFRs) account for a disproportionate burden of travel-related infections, such as malaria and typhoid fever (Bacaner, Stauffer, Boulware, Walker & Keystone, 2004) in the U.S. and other developed countries (e.g., 45% of imported malaria cases in the U.S. in 2002 and 77% of imported typhoid fever cases. The countries contributing the largest number of foreign born have shifted over the last decades and now include Mexico, China, the Philippines, India, Vietnam, Cuba, and South Korea (Doyle, 2005).

Density

More people are living in urban areas than ever in history (2.9 billion in 2000 and projected to reach 5 billion by 2030), and the mass relocation of rural populations to urban areas that began in the latter half of the twentieth century continues, with cities growing at four times the rate of rural populations (UN Population Division, 2002). Most new megacities (defined as urban areas with a population of 10 million or more) are in developing countries at low latitudes. Many cities are surrounded by vast periurban slums, where access to clean water, sanitation, and health care is limited. Many of those who have migrated to urban areas have families in rural areas, so connections with rural areas persist. Today about half of people globally live in urban areas, but the urban to rural ratio varies greatly by region. In Latin America and the Caribbean about 75% of the population is urban, in contrast to Africa and Asia where only about 37% of the population lived in urban areas in 2000 (UN Population Division, 2002). Many people also live and work in large buildings with shared indoor spaces. The trend in urbanization is expected to continue. The combination of mobility, size, and density of the population means that people are having contact with large numbers of people, including some from distant countries. This is relevant given the importance of person-to-person spread in many infectious diseases. Urban populations also may share water supplies; focal contamination can lead to large outbreaks.

Location

Population growth is most rapid in low latitude areas, many of the countries characterized by tropical and subtropical climates and large low-income populations. At least 40% of urban growth is from migration. Circulation of some viruses is linked to population size, as the virus must continue to find susceptibles to survive. The maintenance of a dengue virus serotype (an infection transmitted by mosquitoes), for example, requires a population of somewhere between 150,000 and one million (Wilson, 2004). More and more urban areas in subtropical regions are reaching a critical population size that will permit sustained circulation of dengue virus and increase the risk of severe and complicated forms of dengue fever (hemorrhagic fever and dengue shock syndrome). Outbreaks of dengue fever have increased in geographic reach and severity. A contributing factor is the global movement of dengue viruses carried by human travelers. Some dengue viruses are more virulent than others as measured by the level of viremia they produce and their potential to cause hemorrhagic infection (which is more likely to be fatal). Recent studies give evidence that more virulent dengue viruses (Southeast Asian genotype) can "out compete" viruses that cause milder infection and can be expected to displace the less virulent viruses. Mosquitoes may also participate in the selection process. In general, mosquitoes are more likely to become infected with a virus that causes higher level and more sustained viremia in humans (Cologna, Armstrong, & Rico-Hesse, 2005).

Malaria continues to kill an estimated million people each year, predominantly children in Africa. Projections for the global population at risk for malaria show an increase from about 3 billion exposed in 2002 to 3.4 billion exposed in 2010 based on expected population growth in malarious areas (Hay, Guerra, Tatem, Noor, & Snow, 2004). Despite the reduction by half of the land area supporting malaria during the last century, the total population exposed to malaria risk has increased by 2 billion because of population growth in endemic areas.

Greater biodiversity is found near the equator; the number of marine and terrestrial species declines with distance from the equator, the so-called latitudinal species diversity gradient. Guernier and colleagues looked at the relationship between parasitic and infectious disease species richness and latitude and found that the number of pathogen species also increases near the equator (Guernier, Hockberg, & Guegan, 2004). They reviewed 332 human pathogens across 224 countries and found that, on average, tropical areas had more species diversity than temperate areas. Rainfall was the climatic variable most strongly correlated with species diversity. That the areas of the earth with greatest population growth and with largest poor populations are also those with greatest pathogen diversity suggests that these regions will continue to be those where infectious diseases will thrive and cause a disproportionate burden of disease.

Vulnerability

Three areas of vulnerability that may contribute to the burden from infectious diseases are especially noteworthy and will be mentioned briefly. The continued spread of HIV/AIDS exacts a huge toll on the global population. HIV also kills through other infections, by far the most important one being TB. In some countries in East and southern Africa, rates of reported cases of TB have increased five-fold or more because of the concurrent epidemic of HIV infection (WHO, 2005). Approximately one third of the human population is infected with *Mycobacterium tuberculosis*. The interaction between HIV and TB is bidirectional, with each making the other worse.

The elderly population is growing rapidly. In many countries the most rapidly growing segment of the population is the over 80 year-old group (Kinsella & Velkoff, 2001). In 2000, less than 10% of the global population was older than 60 years (but was almost 20% in Europe). This is expected to exceed 20% by 2050 (and reach 35% in Europe). The elderly are more susceptible to infections because of waning cell-mediated immunity and impaired host defenses but also because of chronic diseases and use of drugs and treatments that may be immunosuppressive. The elderly also respond less well to immunizations.

Poor nutrition and micronutrient deficiencies increase the risk of many infections (including diarrhea, malaria, measles, and pneumonia) and death from them. A study by Ezzati and colleagues identified undernutrition as a leading global cause of loss of health (Ezzati, Lopez, Rodgers, Hoorn, Murray, & the Comparative Risk Assessment Collaborating Group, 2002). They found that globally 9.5% of the disease burden, as measured by disability adjusted life years, could be attributed to childhood and maternal underweight and 6.2% to deficiencies of iron, vitamin A, zinc or iodine.

Technology

Medical

Technologic changes provide many ways to improve lives but also provide the means to amplify the dispersal of microbes that occurs naturally. Injections of medication used to treat schistosomiasis in mass treatment campaigns in Egypt probably contributed to the spread of hepatitis C in the population because the needles were inadequately sterilized between reuse (Frank, Mohamed, Strickland, Lavanchy, Arthur, Magder, Khoby, Abdel-Wahab, Ohn, Anwar, & Saliam, 2000). After WNV entered the U.S., blood transfusions, dialysis, organ and tissue transplantation led to infection in patients who had not been exposed through the usual route, the bite of an infective mosquito (Pealer, Marfin, Petersen, Lanciotti, Page, Stramer, Stobierski, Signs, Newman, Kapoor, Goodman, & Chamberland, for the West Nile Virus Transmission Investigation Team, 2003). Because of good medical diagnostic laboratories, transmission of WNV through breastfeeding, a previously unproven route of transmission, was also identified as a risk. Transmission of Chagas disease (caused by a protozoan parasite that can persist for decades in the human host) in the U.S. was documented after transplantation of organs from a person who had previously lived in endemic areas in Latin America (CDC, 2002).

Antimicrobials are lifesaving for a number of infections, yet their wide use and misuse has contributed to the emergence of resistant microbes, not just for a few minor pathogens, but for major killers including parasites (e.g., malaria), viruses (e.g., HIV, influenza), bacteria (e.g., *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*), and even some fungi. Sometimes alternative forms of treatment exist, but they may be more toxic or more expensive or in short supply, making them operationally unavailable for many, particularly poor populations. Travel of humans has contributed to the movement of resistance genes and pathogens (Aires de Sousa, Santos Sanches, Ferro, Vaz, Saraiva, Tendeiro, Serra & de Lencastre, 1998). Resistance that develops in an individual patient can potentially affect a larger population if the infection is transmissible, such as is the case with TB, HIV, and many other infections.

Habitats and Land Use

Humans have made profound changes in the biophysical environment by clearing lands, building dams, creating large urban areas, and building roads. Clearing lands may change the ecology for arthropod vectors (that can transmit human infections) and for reservoir and intermediate hosts, such as rodents. Humans may intrude on environments inhabited by potentially pathogenic microbes that were previously unrecognized. Roads provide paths for travel but also breach biophysical barriers and fragment habitats. They provide a path for the movement of other species, in addition to humans. Two examples show how roads may have contributed to the spread of HIV. In Africa logging roads have facilitated the trade in bushmen (Laurent, Bourgeois, Mpoudi, Butei, Peeters, Mpoudi-Ngole, & Delaporte, 2004; Nisbett & Monath, 2001). In Asia and elsewhere HIV spread along trucking routes, traveled by men away from home for long periods.

Geographic areas and populations vary in their receptivity to the introduction and establishment of new pathogens (Wilson, 2004). Infections that can be spread from person-to-person, such as TB, HIV, and influenza, can be carried by travelers to any part of the earth. Some infections require a specific arthropod vector or intermediate host, so may not be easily transplanted into a new geographic area. Many other factors may influence receptivity and spread. These include housing, sanitation, and living conditions. Good nutrition and immunity through vaccination or past infection may blunt the impact of an infection. Education and change in behavior may be able to stop the spread. Good surveillance, solid public health infrastructure, and access to care can also stem the spread and burden from infection. Stigma and concern about economic consequences have sometimes inhibited free sharing information about outbreaks (Cash & Narasimhan, 2000), a problem that persists today.

Although the continental southern U.S. had massive outbreaks of dengue fever in the past and is inhabited by competent vectors (*Ae. aegypti* and *Ae. albopictus*), few locally acquired infections have been documented in recent years. In a seroepidemiological study, investigators surveyed 622 randomly selected households in Laredo (Texas, U.S.A.) and Nuevo Laredo (Mexico), cities separated by the Rio Grande River but with similar climate and extensive cross-border traffic. They collected blood samples and assessed housing conditions. Residents of Nuevo Laredo were more likely to test positive for dengue IgM and IgG (16% and 48%, respectively) than residents of Laredo (1.3%; 23%) were. In a multivariate analysis, air conditioning was significantly associated with positive dengue serology. Dwellings without air conditioning were 2.6-fold more likely to have dengue positive occupant (Reiter, Lathrop, Bunning, Biggerstaff, Singer, Tiwari, Baber, Amador, Thirion, Hayes, Seca, Mendez, Ramirez, Robinson, Fawlings, Vorndam, Waterman, Gubler, Clark, & Hayes, 2003). This is one of multiple ways that economic factors can influence risk of exposure to infection.

Conclusions

The changes in infectious diseases that are occurring today are global in distribution. The impact has been broad, involving many species, populations, and disciplines. Many of the events have played out rapidly (e.g., SARS); the consequences are potentially long-lasting and may be irreversible. West Nile Virus, for example, is now clearly established in North America. Given its ecology, the virus cannot be eliminated with currently available approaches. Perhaps the best option is to protect humans through vaccination, though bird and other animal populations also are affected. The changes in infectious diseases are ongoing and can be expected to continue. The unprecedented rate of change in infectious diseases does not reflect a temporary period of instability. Given the global circumstances today, the global community should work to identify high risk populations and situations and improve surveillance, laboratory support, and communication networks. Many basic interventions, such as clean water, sanitary control of waste, good housing, good nutrition (and provision of micronutrients), handwashing, vaccinations, and education (including safe sex practices) could reduce the burden from infectious diseases and reduce the vulnerability to the spread of new microbial threats.

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