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Geography of Infectious Diseases

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KEY CONCEPTS

- The geography of many infections is dynamic.
- Biological characteristics of organisms, human and animal host factors, and bioclimatic factors influence where diseases occur.
- Diseases vary in their potential to be moved from one area to another. Those with a fixed focal distribution often require a specific arthropod vector or intermediate host – or require special geoclimatic conditions.
- The speed, volume and reach of travel and migration and trade have influenced the geography of infectious diseases and facilitate rapid changes in distributions.
- The burden from diseases with a global distribution varies greatly from one population to another and is influenced by socioeconomic, demographic, bioclimatic, environmental, host genetics and other factors.
- The urban population growth in tropical low- and middle-income regions places large, dense human populations with limited resources in geographic sites with high biodiversity and risk for many infections.
- Alternative or unusual routes of transmission (e.g. organ or tissue transplantation) can lead to appearance of diseases outside of usual distributions.

Introduction

Infectious diseases vary by geographic region and population, and they change over time. When moving from one region to another, humans are exposed to a variety of potential pathogens and also serve as part of the global dispersal process.[1] Microbes picked up at one time and in one place may manifest in disease (and potentially be transmitted) far away in time and place. Because many microbes have the capacity to persist in the human host for months, years or even decades, the relevant time frame for study of geographic exposures becomes a lifetime. Furthermore, microbes also move and change and reach humans via multiple channels.

Caring for patients requires an understanding of the basic factors that underlie the geography of human diseases and events that cause shifts in the distribution and burden of specific diseases. Current travel capacity contributes to massive population movements and rapid shifts in diseases and their distributions, but technology also provides communication channels that aid clinicians who care for patients with unfamiliar medical problems. This chapter reviews the factors that shape the global distribution of infectious diseases and the forces that are expected to shift distributions in the future. Examples illustrate the range of factors that affect the distribution and expression of infectious diseases.[2]

Many authors have traced the origins and spread of infectious diseases through history. A century and a half ago, John Snow noted that epidemics of cholera followed major routes of commerce and appeared first at seaports when entering a new region. *Yersinia pestis*, the cause of plague, accompanied trade caravans and moved across oceans with rats on ships. Exploration of the New World by Europeans introduced a range of human pathogens that killed one-third or more of the local populations in some areas of the Americas. The plants and animals introduced as a result of this exploration have also had profound and long-lasting consequences for the ecology and economics of the new environment.[3] The speed, reach and volume of today's travel are unprecedented in human history and offer multiple potential routes to move biologic species around the globe. Pathogens of animals and plants are being transported as well, and this can affect global food security.[4] Establishment of arthropod vectors, such as mosquitoes, that are competent to transmit human pathogens in new geographic areas expands the regions that are vulnerable to outbreaks of some vector-borne infections. This chapter focuses only on pathogens that directly affect human health and on their sources (Table 106-1). When thinking about geography of human infections, it is useful to consider both the origin of the organism and the conveyor or immediate source for the human (Figure 106-1).

This chapter addresses three key issues:

- factors influencing geographic distribution: why are some infectious diseases found only in focal geographic regions or in isolated populations?
- factors influencing the burden of disease: why does the impact from widely distributed infections vary markedly from one region or one population to another? and
- factors influencing emergence of disease: what allows or facilitates the introduction, persistence and spread of an infection in a new region and what makes a region or population resistant to the introduction of an infection?

TABLE 106-1 Origins and Conveyors of Human Pathogens

Origin or Carrier	Conveyor or Immediate Source	Examples of Disease
Humans	Humans	HIV, syphilis, hepatitis B
Humans	Humans (airborne pathogen)	Measles, tuberculosis
Soil	Soil, airborne	Coccidioidomycosis
Soil	Food	Botulism
Animals	Water	Leptospirosis
Humans	Mosquitoes	Malaria, dengue
Humans	Soil	Hookworm, strongyloidiasis
Animals	Ticks	Lyme disease
Animals, humans	Sand flies	Leishmaniasis
Animals	Animals	Rabies
Rodents	Rodent excreta	Hantaviruses
Humans	Water, marine life	Cholera
Humans or animals (with snails as essential intermediate host)	Water	Schistosomiasis
Humans	Food, water	Typhoid fever
Animals	Water	Cryptosporidiosis, giardiasis

*Some pathogens have multiple potential sources.

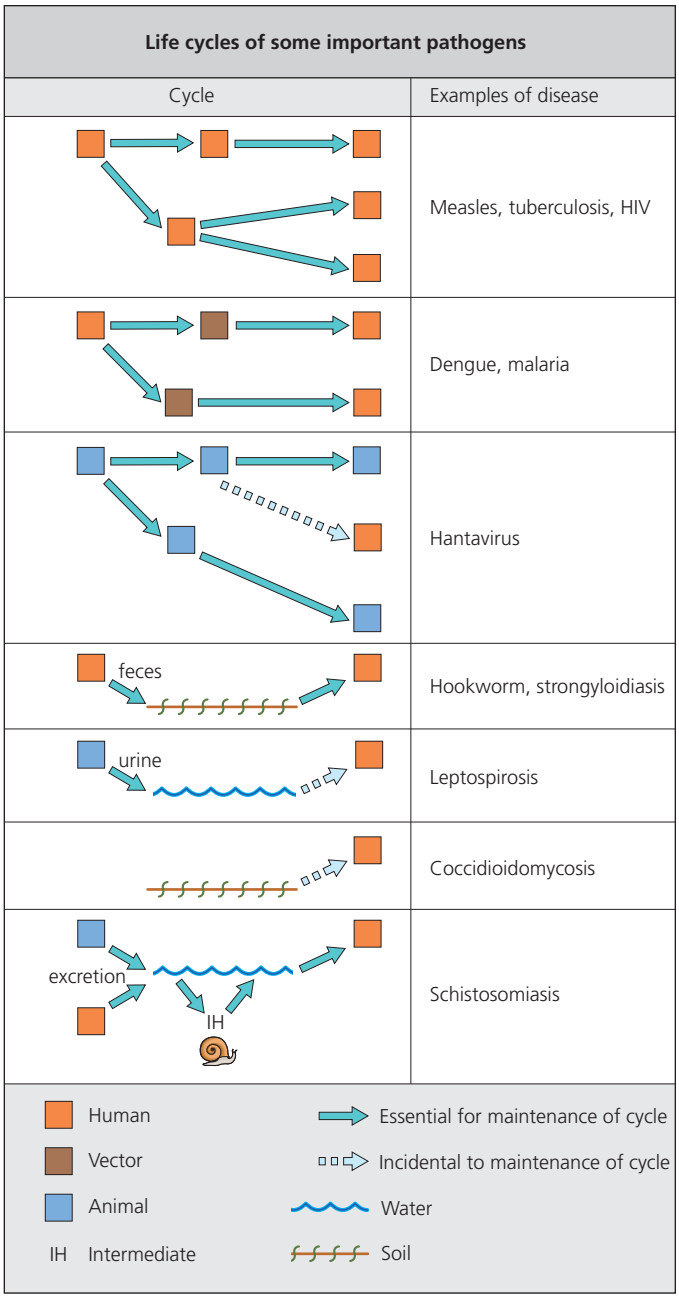

Figure 106-1 Life cycles of some important pathogens.

Factors Influencing Geographic Distribution

In past centuries, lack of contact with other regions could allow an infection to remain geographically isolated. Today, most infections that are found only in focal areas have biologic or geoclimatic constraints that prevent them from being introduced into other geographic regions. For example, the fungus *Coccidioides immitis*, which causes coccidioidomycosis, thrives in surface soil in arid and semiarid areas with alkaline soil, hot summers and short, moist winters; it is endemic in parts of south-western USA, Mexico and Central and South America. People become infected when they inhale arthroconidia from soil. An unusual wind storm in 1977 lifted soil from the endemic region and deposited it in northern California, outside the usual endemic region.[5] In general, infection is associated with residence in or travel through the endemic region. However, because the fungus can persist in the human host for many years following initial infection (which may be mild and unrecognized), disease may be diagnosed far from the endemic regions. Although it is a 'place' disease, coccidioidomycosis has increased in the south-western USA in recent years, in part attributable to a large influx of susceptible humans into the endemic zone and construction and other activities that disturb the soil. Outbreaks are also linked to climatic and environmental changes.[6]

VECTORS

Many microbes require a specific arthropod vector for transmission or an animal reservoir host and hence inhabit circumscribed regions. Malaria is a vector-borne infection that cannot become established in a region unless a competent vector is present. The presence of a competent vector is a necessary but not sufficient condition for human infection. The mosquito must have a source of malarial parasites (gametocytemic human or, rarely, nonhuman primates), appropriate bioclimatic conditions and access to other humans. The ambient temperature influences the human biting rate of the mosquito, the incubation period for the parasite in the mosquito and the daily survival rate of the mosquito. Prevailing temperature and humidity must allow the mosquito to survive long enough for the malarial parasite to undergo maturation to reach an infective state for humans. Competent vectors exist in many areas with no malaria transmission, because the other conditions are not met. These areas are at risk of the introduction of malaria, as illustrated by several recent examples in the USA and elsewhere.[7,8]

An estimated 77% of the world's population lived in areas with malaria transmission in 1900. By 2002 about 48% lived in at-risk areas, but because of population growth and migration the total global population exposed to malaria had increased by 2 billion since 1900 (see Figure 106-2).[9] For example, in Africa, the population in malaria endemic zones increased by almost 200 million people between 2000 and 2010.[10] This contrasts with the situation in the USA, where malaria was endemic in many areas into the 20th century (Figure 106-3), with estimates of more than 600 000 cases in 1914. Even before extensive mosquito control programs were instituted, transmission declined. Demographic factors (population shifts from rural to urban areas), improved housing with screened doors and windows, and the availability of treatment were among the factors that contributed to this decrease.

The distribution of onchocerciasis in Africa is notable for its association with rivers.[11] The vector of this filarial parasite, the black fly (genus *Simulium*), lays her eggs on vegetation and rocks of rapidly flowing rivers and usually inhabits a region within 5–10 km on either side of a river. Another name for onchocerciasis, river blindness, describes the epidemiology as well as one consequence of infection.

Other pathogens have complex cycles of development that require one or more intermediate hosts. Distribution may remain relatively fixed, even when infected humans travel widely, if other regions do not supply the right combination and geographic proximity of hosts (Figure 106-4). Although persons with schistosomiasis visit many regions of the world, the parasite cannot be introduced into a new region unless an appropriate snail host is present, excreted eggs (in urine or feces) are released into fresh water where they reach the snail hosts, and humans subsequently have contact with the untreated water.[12] However, local ecologic changes and climate change can be associated with expansion of transmission in endemic areas or increased intensity of transmission, and this has been identified as a possible consequence of warming temperatures in China.[13] (For a more detailed consideration of the influence of climate change on the distribution of infectious diseases, see Chapter 4.)

Ebola and Marburg viruses are viruses that have focal distributions but have caused dramatic human outbreaks with high mortality. They also infect nonhuman primates and threaten the survival of great apes.[14] Recent studies suggest that bats may be the reservoir hosts.[15,16] Because these infections can be spread from person to person, secondary household and nosocomial spread in several instances has amplified what began as an isolated event. Lack of adequate resources in

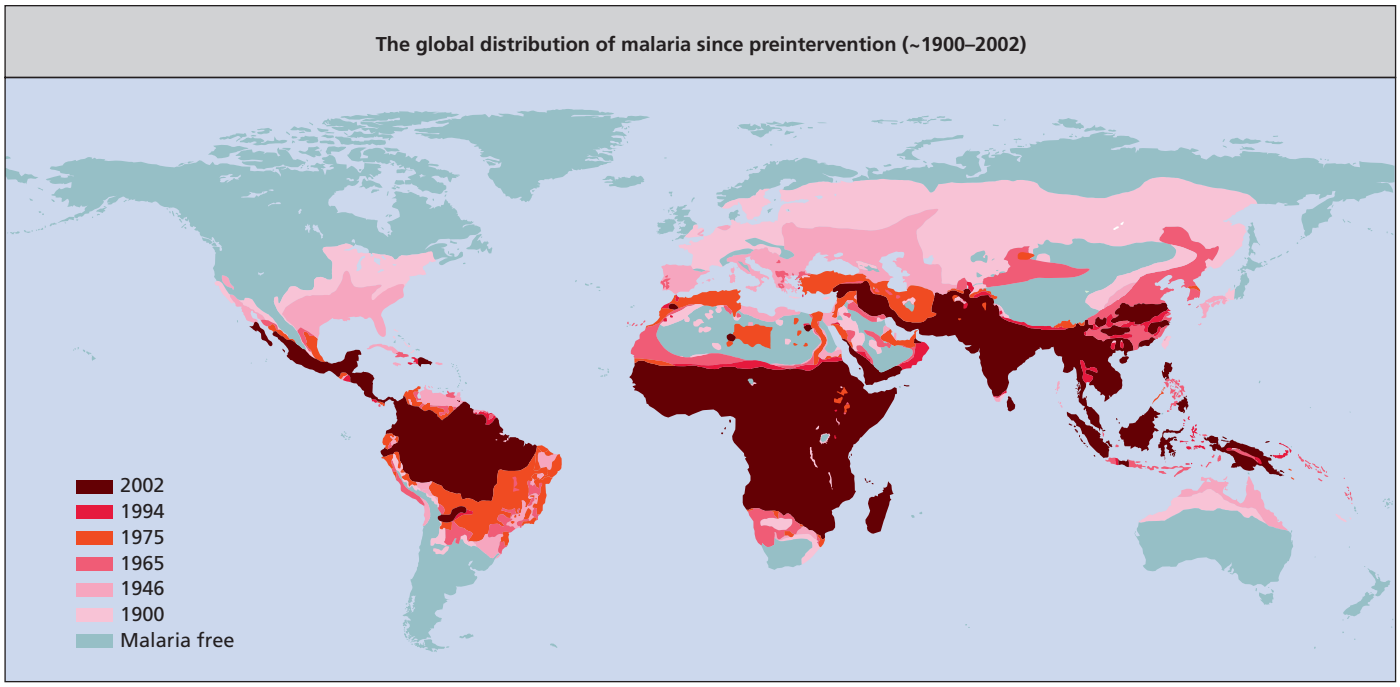

Figure 106-2 The global distribution of malaria since preintervention (~1900–2002). *(From Hay S.I., et al., Lancet Infect Dis 2004; 4(6):327-336.)*

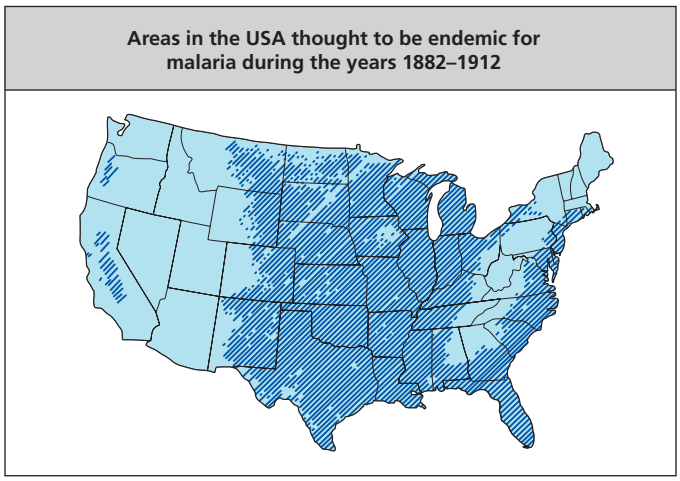

Figure 106-3 Areas of the USA thought to be endemic for malaria during the years 1882–1912. Dark blue indicate areas with malaria.

hospitals in many developing regions contributes to the spread of infections within hospitals and clinics.

Cultural practices can lead to unusual infections in isolated areas. Residents of the highlands of Papua New Guinea developed kuru after ingestion (or percutaneous inoculation) of human tissue during the preparation of the tissues of dead relatives.

The presence of a pathogen in a region may reflect the biologic properties of the organism, its need for a certain physicochemical environment or its dependence on specific arthropods, plants or animals to provide the milieu where it can sustain its life cycle (Box 106-1). The presence of a pathogen in a region does not equate with human disease, because mechanisms must exist for the pathogen to reach a susceptible human host for human disease to occur. Exploration of new regions or changes in land use may place humans in an environment where they come into contact with microbes that were previously unrecognized as human pathogens.

BOX 106-1 BIOLOGIC ATTRIBUTES OF ORGANISMS THAT INFLUENCE THEIR EPIDEMIOLOGY

Host range
Duration of survival in host
Route of exit from host
Route of entry into human
Inoculum needed to establish infection
Virulence
Capacity to survive outside host
Resistance to antimicrobials and chemicals

Factors Influencing the Burden of Disease

Among the infectious diseases that impose the greatest burden of death globally, most are widely distributed: respiratory tract infections (e.g. influenza, *Streptococcus pneumoniae* and others), diarrheal infections, tuberculosis, measles, AIDS and hepatitis B.[16] Most of these infections are spread from person to person. The World Health Organization estimated that about 65% of infectious diseases deaths globally in 1995 were due to infections transmitted from person to person.[17]

Burden from these diseases is unevenly distributed across populations and among different countries. Poor sanitation, lack of clean water, crowded living conditions and lack of vaccination contribute to the disproportionate burden from many of these infections in low- and middle-income countries (LMIC). In industrialized countries, pockets of high risk persist. Disadvantaged populations have higher rates of tuberculosis, HIV and many other infectious and noninfectious diseases. Rates of reported cases of tuberculosis vary widely by region and within countries (Table 106-2).[18] Figure 106-5 shows the effect of crowded living conditions on rates of tuberculosis in England and Wales in 1992.[19] Among welfare applicants and recipients addicted to drugs or alcohol in New York City, the rate of tuberculosis was 744 per 100 000 person years, or more than 70 times the overall rate for the USA.[20] The impact of an infection also derives from the access to effective therapy. Treatment of a patient with active tuberculosis can cure

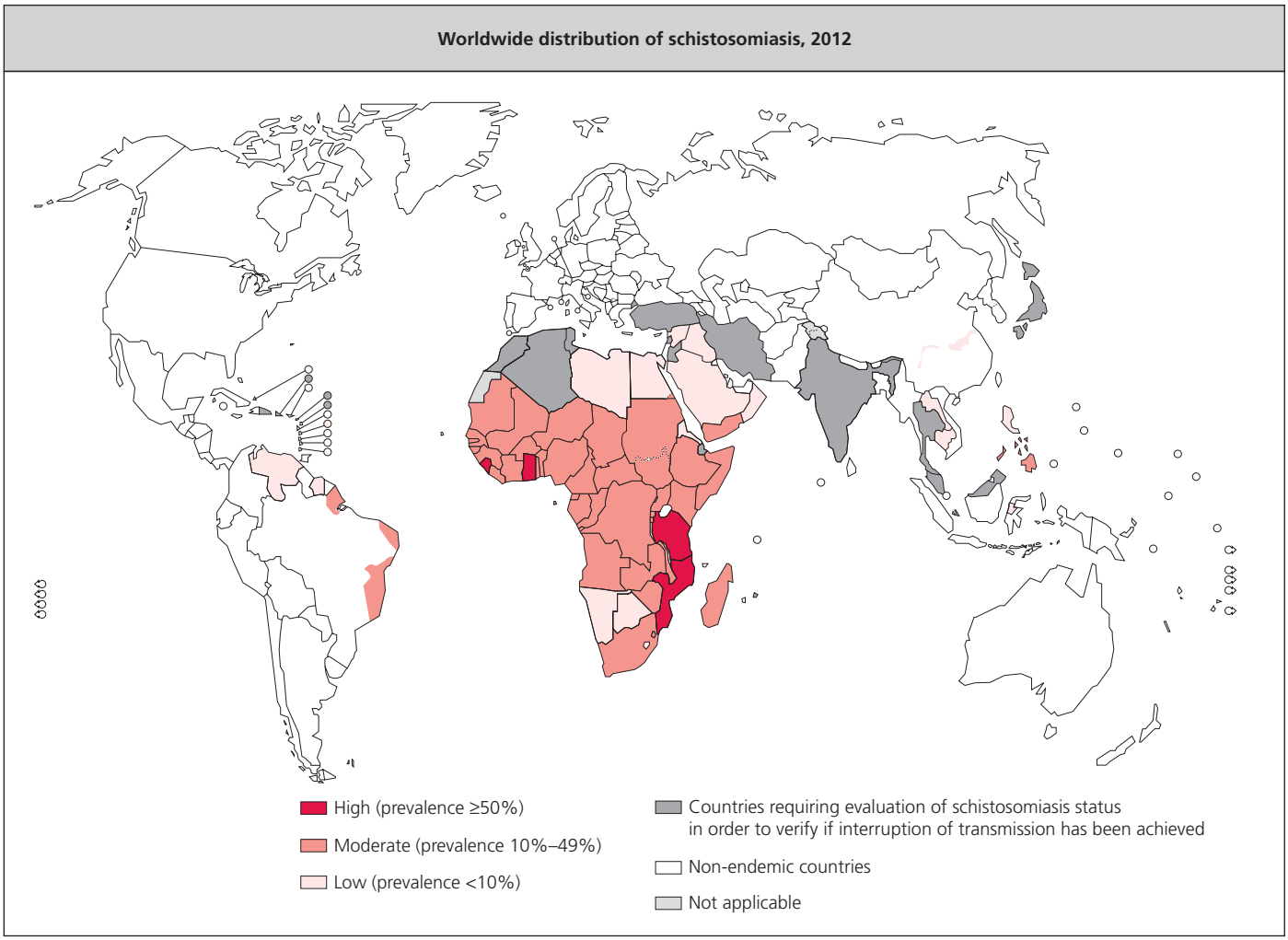

Figure 106-4 Worldwide distribution of schistosomiasis. *(Copyright ©World Health Organization, 2012.)*

TABLE 106-2 Rates of Reported Cases of Tuberculosis Worldwide by Region, 1990 and 2006

	INCIDENCE PER 100 000 POPULATION	
Region	**1990**	**2013**
Africa	162	3255
Americas	65	29
Eastern Mediterranean	111	109
Europe	37	40
South East Asia	200	187
Western Pacific	127	87

Data from World Health Organization: Global tuberculosis report 2013. Geneva: World Health Organization, 2013.

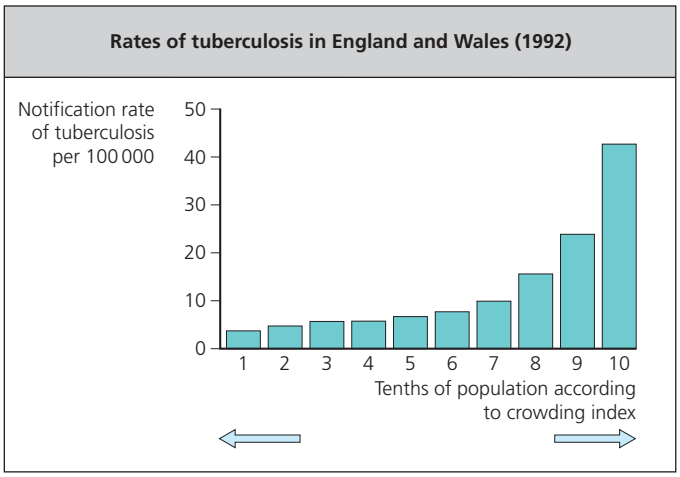

Figure 106-5 Rates of tuberculosis in England and Wales by crowding index (1992). *(Adapted from Bhatti* et al. *World Health Organization: Global tuberculosis report 2013. Geneva: World Health Organization, 2013.)*

the individual and eliminate a source of infection for others in the community.

Diphtheria, controlled in many parts of the world through the use of immunization, resurged in new independent states of the former Soviet Union in the 1990s, a reminder of the tenuous control over many infectious diseases.[21] Populations in other countries also felt the impact as cases related to exposures in the Russian Federation were reported in Poland, Finland, Germany and the USA. Serologic studies in America and Europe suggest that up to 60% of adults may be susceptible to diphtheria.

Travelers to tropical and LMIC can pick up geographically focal, often vector-borne or animal-associated infections,[22] but travelers most often acquire infections with a worldwide distribution that are

BOX 106-2 FACTORS THAT INFLUENCE THE TYPES AND ABUNDANCE OF MICROBES IN A COMMUNITY

- Biogeoclimatic conditions.
- Socioeconomic conditions.
- Public health infrastructure.
- Urban versus rural environment.
- Density and mobility of population.
- Season of the year.
- Animal populations.

BOX 106-3 FACTORS THAT INFLUENCE THE PROBABILITY OF EXPOSURE TO PATHOGENS

- Living accommodation.
- Level of sanitation.
- Occupational and recreational activities.
- Food preparation and preferences.
- Sexual activities and other behavior.
- Contact with pets, other animals, vectors.
- Time spent in the area.

common in areas lacking good sanitation.[23] Food- and water-borne infections lead to travelers' diarrhea, which is caused by multiple agents, typhoid fever and hepatitis A. Respiratory tract infections may be acquired from other travelers as well as from local residents. Boxes 106-2 and 106-3 note factors that influence the types and abundance of microbes in a community and the probability of exposure to pathogens.

Hepatitis A virus remains a common cause of infection in LMIC where most persons are infected at a young age and become immune for life. Infection in young children is typically mild or inapparent. Persons living in areas of high transmission may be unaware of the presence of high levels of transmission, although nonimmune; older people (such as travelers) who enter the environment may develop severe, and occasionally fatal, infection. Countries with an improving standard of living may observe a paradoxical increase in the incidence of hepatitis A disease as the age of exposure increases, shifting the age of infection to a time when jaundice and other symptoms are more likely to occur.

Travelers also contribute to the global spread of infectious diseases.[24,25] *Neisseria meningitidis*, a global pathogen, occurs in seasonal epidemics in parts of Africa (Figure 106-6).[26] Irritation of the throat by the dry, dusty air probably contributes to invasion by colonizing bacteria.[27] Pilgrims carried an epidemic strain of *N. meningitidis* type A from southern Asia to Mecca in 1987. Other pilgrims who became colonized with the epidemic strain introduced it into sub-Saharan

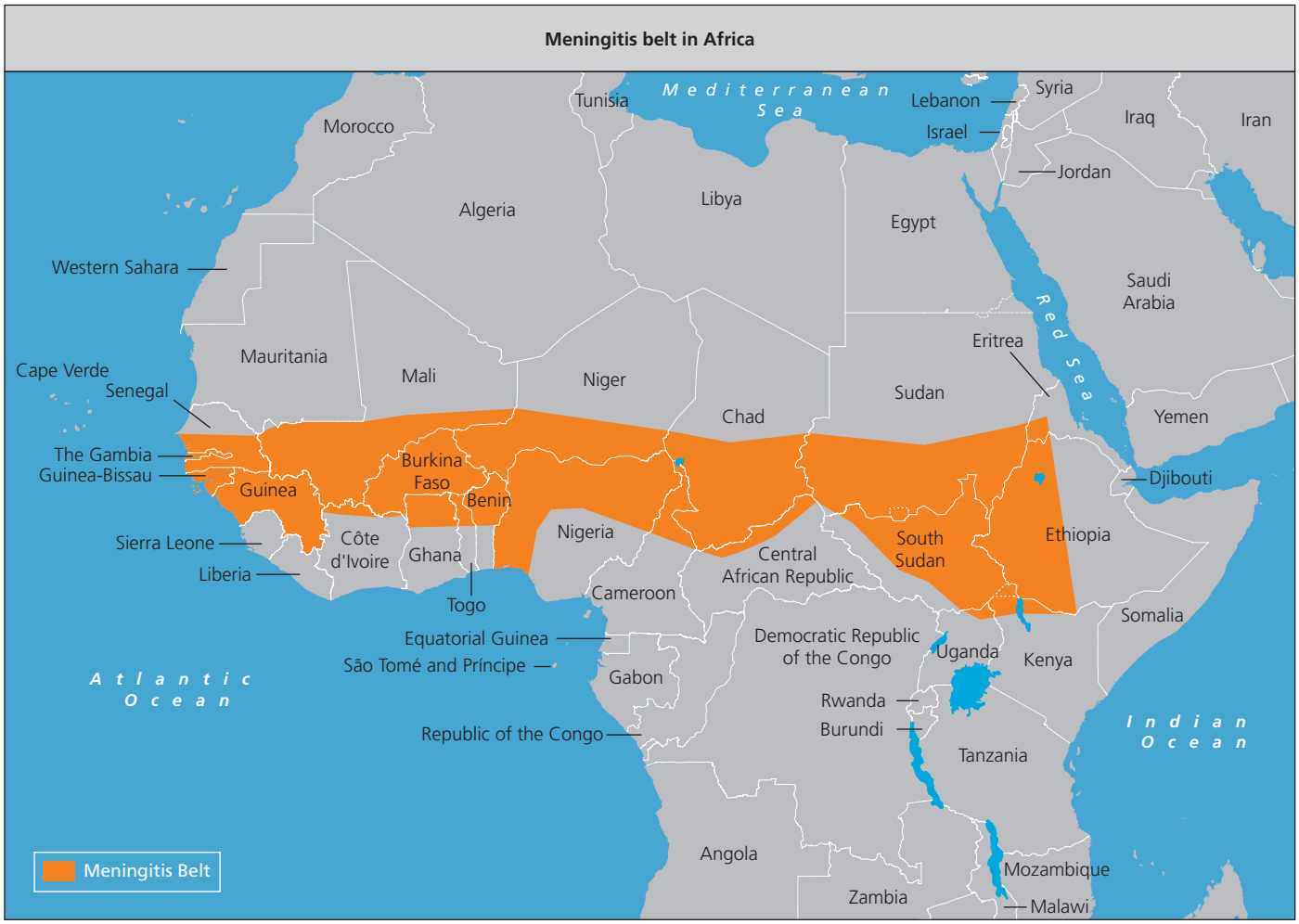

Figure 106-6 Meningitis belt in Africa. *(From Centers for Disease Control and Prevention: CDC Health information for international travel 2014. New York: Oxford University Press, 2014.)*

Africa, where it caused a wave of epidemics in 1988 and 1989. The epidemic clone spread to several countries.[28] In 1996 in Africa, major outbreaks of meningococcal meningitis occurred (>185 000 reported cases with a case fatality rate of ~10%) caused by *N. meningitidis* serogroup A, clone III-1.[29] In Canada, a virulent group C, ET-15 strain of *N. meningitidis* was associated with an increased case fatality rate.[30] In these examples, the virulence of the microbe and travel and trade acted synergistically to change the epidemiology and burden of disease. In 2000, serogroup W135 *N. meningitidis* caused an outbreak of infection in pilgrims to the Hajj and spread to their contacts and others around the world. Studies using serotyping, multilocus sequence typing, multilocus DNA fingerprints and other techniques found identical W135 isolates in multiple countries. Before this outbreak, pilgrims from many countries received a vaccine that protected against serotype A but not W135. The polysaccharide meningococcal vaccine reduces risk of disease in the vaccinated individual but does not prevent oropharyngeal carriage or transmission of *N. meningitidis*.[31]

Factors Influencing Emergence of Disease

Travel of persons from tropical regions to major urban areas throughout the world raises concerns that unusual infections could be introduced into an environment where they could spread to large populations. A key factor that determines whether a pathogen can persist and spread in a new population is its basic reproductive rate, which is the number of secondary infections produced in a susceptible population by a typical infectious individual. To become established in a new host population, a pathogen must have a basic reproductive rate that exceeds one. The basic reproductive rate for a pathogen is affected by a range of biologic, social and environmental factors, so may vary by place and population. Also critical in determining how easily an infection can be controlled is the proportion of transmission that occurs before onset of symptoms or during asymptomatic infection.[32]

Multiple factors restrict the introduction and spread or persistence of infection in a region (Box 106-4). Nutrition determines susceptibility to and severity of many infections. A substantial proportion of disease burden in LMIC can be attributed to childhood and maternal weight and micronutrient deficiences.[33] Before measles vaccine was introduced, the epidemiology of measles exhibited marked periodicity in large populations, with peaks typically occurring every 2–3 years.[34] In small island communities (or other isolated populations), outbreaks typically occur only after periodic introductions from outside. It has been suggested that measles, as it has been known in the 20th century, could not have established itself much before 3000 BCE because before that time human populations had not achieved sufficient size to sustain the virus.

BOX 106-4 FACTORS THAT RESTRICT THE INTRODUCTION AND SPREAD OF INFECTIONS

- Geoclimatic factors that cannot support vector or intermediate host.
- Genetics of human population, making it genetically resistant or relatively resistant.
- Immunity of human population, making it not susceptible because of past infection with same or related microbe or via vaccination.
- Demographic factors (e.g. size and density of population will not support sustained transmission of diseases such as measles).
- Social and behavioral factors (e.g. absence of activities such as iv drug use and unprotected sex with multiple partners).
- Food preparation habits and local traditions (e.g. certain dishes not eaten, food always well cooked).
- High-quality housing, sanitation, public health infrastructure, good surveillance.
- High standard of living, good nutrition, lack of crowding, access to good medical care.
- Biologic characteristics of the microbe.

EXAMPLES OF EMERGING PATHOGENS

It is instructive to look at examples of infections that have recently undergone major shifts in distribution and to review the key factors that have influenced their geographic spread. A recurring theme is the movement of humans who introduce pathogens into a new region (see also Chapter 4) and human alteration of the landscape or ecology that permits contact with previously unrecognized microbes, often through interaction with animals or animal products. Many infections in humans have domestic or wild animals as their sources.[35]

Human Immunodeficiency Virus and Other Pathogens Carried by Humans

Organisms that survive primarily or entirely in the human host and are spread from person to person (e.g. by sexual or other close contact) can be carried to any part of the world. The spread of HIV in recent decades to all parts of the world is a reminder of the rapid and broad reach of travel networks. Although the infection has also spread via blood and shared needles, it has been the human host engaging in sex and reproduction who has been the origin for the majority of the infections worldwide. Person-to-person spread accounted for the rapid worldwide distribution of severe acute respiratory syndrome (SARS), a coronavirus infection, in the spring of 2003, after the virus emerged from an animal reservoir, most likely bats, and infected farmed civets.[36]

Multidrug-resistant (MDR) tuberculosis has continued to increase. The World Health Organization estimated that 450 000 cases and 170 000 deaths from MDR tuberculosis occurred in 2012.[18] Extensively drug-resistant (XDR) tuberculosis, which is virtually untreatable, has been reported by 92 countries. Almost 10% of MDR-TB cases are XDR-TB.[18] Humans also carry resistance genes and virulence factors that can be transferred to and exchanged with other microbes.[37]

Dengue Fever

Dengue fever is a mosquito-borne viral infection found in most tropical and subtropical regions globally. An estimated 96 million people have symptomatic infection each year.[38] Viremic humans regularly enter regions infested with *Aedes aegypti*, the principal vector of dengue, transporting the virus for new outbreaks. Because four serotypes of dengue virus exist and infection with one serotype does not confer lasting immunity against other serotypes, a person can be infected more than once. One study found the risk of developing severe dengue after repeat infection was 82–103 times greater than after primary infection.[39] In an outbreak in Cuba, 98.5% of cases of dengue shock syndrome (DSS) or dengue hemorrhagic fever (DHF) were in persons with a prior dengue infection.[40] Risk factors for severe dengue identified in epidemiological studies include young age, virus strain, and host genetics.[41]

Factors that have aided the spread of dengue include increasing travel to and from tropical regions; expansion of the regions infested with *Aedes aegypti* and *Aedes albopictus*; population growth and increasing urbanization in tropical areas; the use of nonbiodegradable and other containers that make ideal breeding sites for the mosquito; inadequate vector control programs and increasing resistance of vectors to insecticides.

In 2001 the vector that was implicated in an outbreak of dengue in Hawaii[42] was *Aedes albopictus*, a mosquito species that has been introduced into new regions in recent decades, probably primarily by shipping used tires and other items.[43] The virus responsible for the Hawaii outbreak was similar to dengue isolates from Tahiti, suggesting that viremic travelers introduced the virus from the South Pacific.

Although large dengue epidemics occurred in the USA in the 20th century, few cases have been acquired in the USA in recent years, despite the presence of epidemic disease in adjacent areas of Mexico and the presence of a competent vector (*Aedes aegypti*) in southeastern USA (Figure 106-7).[26] *Aedes albopictus* has even broader distribution in continental USA. The presence of screened dwellings and air conditioning may make an area relatively resistant to spread of infection, even if a competent vector infests a region. Since 2009 a few cases of local dengue transmission have occurred in Key West, Florida,[43] and

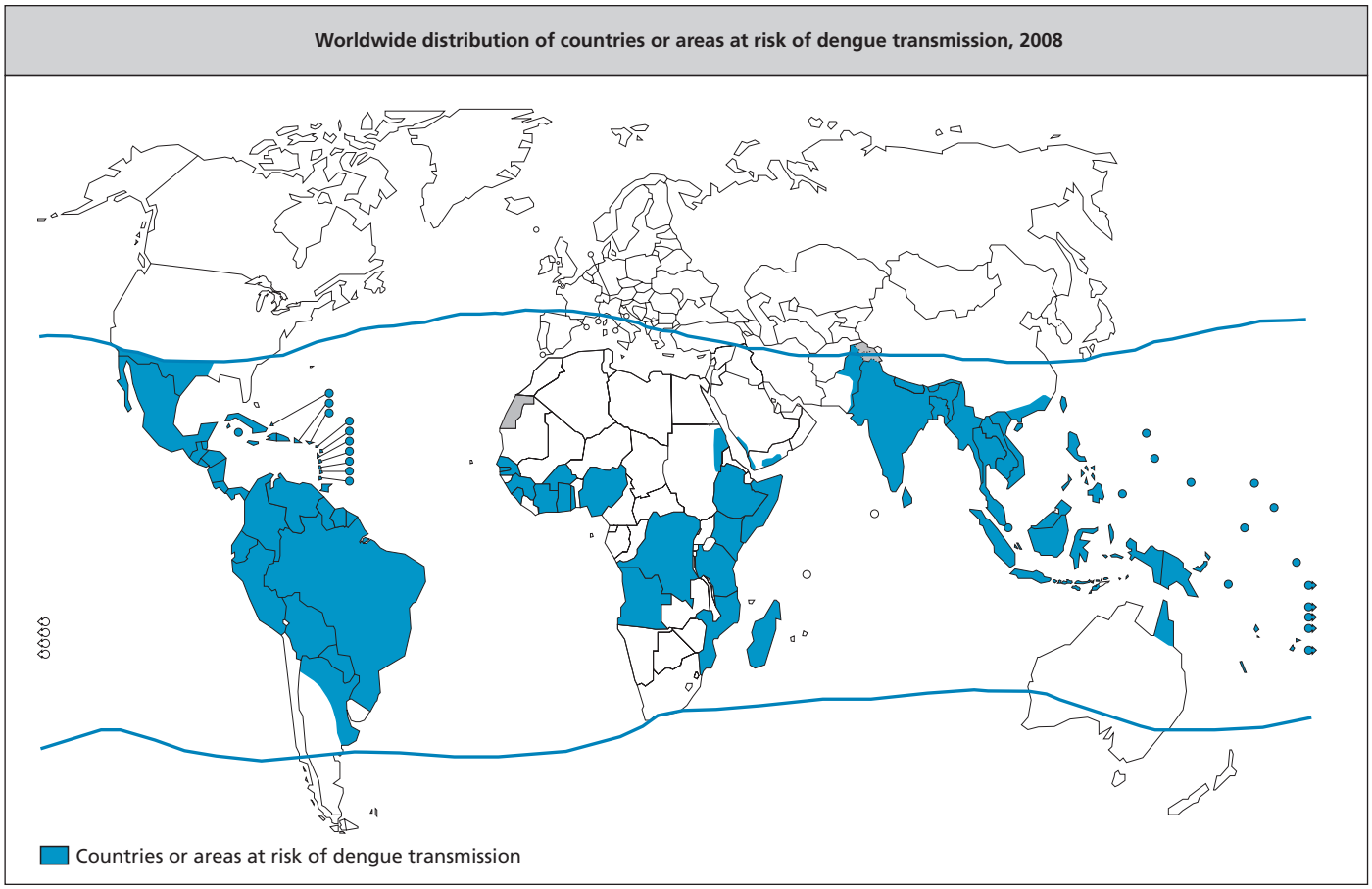

Figure 106-7 Worldwide distribution of countries or areas at risk of dengue transmission, 2008. Many areas with a competent vector do not report dengue epidemic activity. *(Copyright ©World Health Organization, 2014.)*

serologic studies have also documented that dengue infections are occurring in Texas.[44]

Chikungunya Virus

Chikungunya, a mosquito-borne alphavirus originally isolated in Tanzania in 1953, has spread from Africa, causing massive outbreaks in the Indian Ocean islands, India, and other parts of Asia since 2005. In the summer of 2007 an outbreak caused hundreds of cases (175 laboratory confirmed) in north-eastern Italy. The index case was a visitor from India. The vector implicated was *Aedes albopictus*, postulated to have been introduced via used tires.[45] Mutations in the virus may have enabled it to replicate more efficiently in *Aedes albopictus* mosquitoes, the Asian tiger mosquito, which is now widely distributed outside of Asia.[46] It can survive cooler temperatures than *Aedes aegypti*.

Beginning in late 2013 local chikungunya transmission was documented in the Caribbean islands. The virus has now spread widely in Central and South America.[47] Chikungunya virus is introduced into new areas by viremic travelers and can cause high attack rates in susceptible populations; persistent and disabling joint pain can follow acute illness, especially in older individuals.[48]

Cholera

Cholera illustrates the complex interactions between microbe, environment and host.[49] *Vibrio cholerae* lives in close association with marine life, binding to chitin in crustacean shells and colonizing surfaces of algae, phytoplankton, zooplankton and water plants. *V. cholerae* can persist within the aquatic environment for months or years, often in a viable but dormant state, noncultivable by usual techniques. Environmental factors, including temperature, salinity, pH and seawater nutrients, affect the persistence, abundance and viability of the organisms, and hence influence human epidemics.

Under conditions of population crowding, poor sanitation and lack of clean water, cholera can have a devastating impact, as was shown by the massive outbreak of El Tor cholera in Rwandan refugees in Goma, Zaire, which caused 12 000 deaths in July 1994.[50]

Toxigenic *Vibrio cholerae* O1 was introduced into Haiti in 2010 in the aftermath of the earthquake.[51] As of March 2013, it had caused >650 000 illnesses and >8000 deaths. Studies suggest that it was introduced by UN mission personnel who lacked sanitary disposal of their waste. Subsequently a tributary of the Artibonite River was contaminated with a pathogenic strain of South Asian type *Vibrio cholerae*.

The organism can be carried by humans who can introduce it into new regions. Trade probably also plays a critical role. Ballast water, picked up by boats in multiple locations and discharged at another time and place, carries a wide range of species.[52,53] In earlier studies of the ballast and bilge of cargo ships in the USA Gulf of Mexico, researchers were able to identify *V. cholerae* identical to the strains causing epidemic disease in Latin America.[54]

Food-Borne Disease

The globalized food market moves pathogens from one region to another. An outbreak of cholera in Maryland, USA, was traced to imported, contaminated commercial frozen coconut milk.[55] Alfalfa sprouts grown from contaminated seed sent to a Dutch shipper caused outbreaks of *Salmonella* spp. on two continents, the USA and Finland.[56] Commercial movement of fruits and vegetables redistributes resistance factors along with the microbes.

Travel and trade are key features in the epidemiology of the infection *Cyclospora*, a cause of gastroenteritis. For many years cases were often associated with living in or travel to areas where sanitary facilities were poor. In the summer of 1996, a large US outbreak occurred in persons who had not traveled. Over a period of a few months, 1465

cases of cyclosporiasis were reported from 20 states. The outbreak was linked to raspberries imported from Guatemala.[57]

Visceral Leishmaniasis

In the past, visceral leishmaniasis in Brazil was primarily a rural disease. Recently, however, several cities have reported large outbreaks of visceral leishmaniasis.[58] Reasons for the change in epidemiology include geoclimatic and economic factors (drought, lack of farm land, famine), leading to migration of large numbers of persons, who settle in densely populated peri-urban areas that lack basic sanitation. Domestic animals, such as dogs and chickens, are sources of blood meals for the sand fly vector of leishmaniasis. Outbreaks, affecting especially children and young adults, have occurred in many cities in Brazil. Malnutrition contributes to disease severity.

Disease–disease interactions also alter the epidemiology of infections. Visceral leishmaniasis has become an important infection in HIV-infected people in Spain and other areas where the two infections coexist.[59] The presence of HIV leads to increased risk of progression of infection; disease can also appear years after exposure.

MOVEMENT OF VECTORS AND OTHER SPECIES

Movement of nonhuman species can affect infections in humans. Importation of wild animals from Ghana into the USA led to an outbreak of monkeypox, an infection previously known to exist in Africa. Humans became infected by handling domestic prairie dogs (sold as pets) that had been housed with the imported wild animals from Africa.[60] *Aedes albopictus* introduced into the USA via used tires shipped from Asia[61] has since become established in at least 21 contiguous states of the USA and in Hawaii. *Aedes albopictus* can transmit dengue and chikungunya viruses and is a competent laboratory vector of La Crosse, yellow fever and other viruses. Multiple strains of eastern equine encephalitis virus have been isolated from *Aedes albopictus* in Florida.

Current transportation systems regularly carry all forms of life, including potential vectors, along with people and cargo. In an experiment conducted several years ago, mosquitoes, house flies and beetles in special cages were placed in the wheel bays of a Boeing 747 aircraft and carried on flights lasting up to 7 hours. Temperatures were as low as −62°F (−52°C) outside and ranged from 46°F to 77°F (8–25°C) in the wheel bays. Survival rates were greater than 99% for the beetles, 84% for the mosquitoes and 93% for the flies.[62] Occasional cases of so-called airport malaria – cases of malaria near airports in temperate regions – attest to the occasional transport and survival of an infective mosquito.

In the USA, transportation of raccoons in the late 1970s from Florida to the area between Virginia and West Virginia (in order to stock hunting clubs) unintentionally introduced a rabies virus variant into the animals of the region. From there, the rabies enzootic spread for hundreds of miles, reaching raccoons in suburban and densely populated regions of the north-east USA. Spill-over of the rabies virus variant into cats, dogs and other animal populations and direct raccoon–human interactions have had costly consequences.[63]

Highly pathogenic avian influenza A (H5N1) is a global concern.[64] It is entrenched in poultry populations in Asia and Africa and has caused outbreaks in Europe and the Middle East. Although the virus causes high mortality in infected humans, thus far H5N1 has not been able to establish sustained transmission from person to person. Most humans appear to have been infected via close contact with poultry or their products. Although the virus can be carried by migratory birds,[65] most introductions appear to have been related to movement of poultry and poultry products. In South East Asia risk was associated with duck abundance, human population and rice cropping intensity.[66]

Geographic Influences on Differential Diagnosis

Geographic exposures influence how one thinks about probable diagnoses in a given patient. In Mexico, for example, more than 50% of patients with late-onset seizures have computed tomography (CT) evidence of the parasitic infection, neurocysticercosis.[67] In Peru, 29% of persons born outside Lima who had onset of seizures after 20 years of age had serologic evidence of cysticercosis.[68] In northern Thailand, melioidosis is a common cause of sepsis, accounting for 40% of all deaths from community-acquired sepsis.[69]

In considering the consequences of exposures in other geographic regions, relevant data in assessing the probability of various infections include the duration of visit, activities and living conditions during the stay and the time lapsed since the visit. Among British travelers to West Africa, the relative risk of malaria was 80.3 times higher for persons staying for 6–12 months than among those staying 1 week.[70] In Malawi, the risk of schistosome infection increased directly with duration of stay. Seroprevalence was 11% for those present for 1 year or less, but this increased to 48% among those present for 4 years or longer.[71] In a study of persons with cysticercosis, the average time between acquisition of infection and onset of symptoms was about 7 years.[72]

For malaria, it is necessary to know not only whether infection can be acquired in a specific location but also the species of parasites present and the patterns of resistance to antimalarial agents. Figure 106-8 shows the distribution of malaria. Analysis of data from the GeoSentinel Surveillance network, a network that uses travelers as a sentinel population, finds marked differences in the spectrum of disease in relation to the place of exposure.[22,73]

Expression of disease may vary depending on age of first exposure, immunologic status of the host, genetic factors and the number and timing of subsequent exposures. Temporary residents of endemic regions have different patterns of response to a number of helminths from those of long-term residents. In cases of loiasis, temporary residents have immunologic hyperresponsiveness, high-grade eosinophilia and severe symptoms that are not seen in long-term residents of the same area.[74] Genetic factors can affect susceptibility to infection or expression of disease. Some persons, for example, are genetically resistant to infection with parvovirus because they lack appropriate receptors on their erythrocytes.[75] Persons lacking Duffy factor cannot be infected with the malarial parasite, *P. vivax*.

Conclusion

Knowledge about the geographic distribution of diseases is essential for informed evaluation and care of patients, who increasingly have had exposures in multiple geographic regions. Recent travel and trade patterns have led to more frequent contact with populations from low latitude areas, regions with greater species richness.[76] Infectious diseases are dynamic and will continue to change in distribution, and access to real time epidemiologic outbreak surveillance data such as that provided by ProMED (www.promedmail.org) is a vital tool for clinicians. Changes in virulence and shifts in resistance patterns will also require ongoing surveillance and communication to healthcare providers. Multiple factors favor even more rapid change, perhaps in unexpected ways, in the future: rapidity and volume of travel, increasing urbanization (especially in developing regions), the globalization of trade, multiple technologic changes that favor mass processing and broad dispersal, and the backdrop of ongoing microbial adaptation and change, which may be hastened by alterations in the physicochemical environment.

References available online at expertconsult.com.

Figure 106-8 (a, b) Worldwide distribution of malaria. *(Data from Centers for Disease Control and Prevention: CDC Health information for international travel 2014. New York: Oxford University Press, 2014.)*

Continued

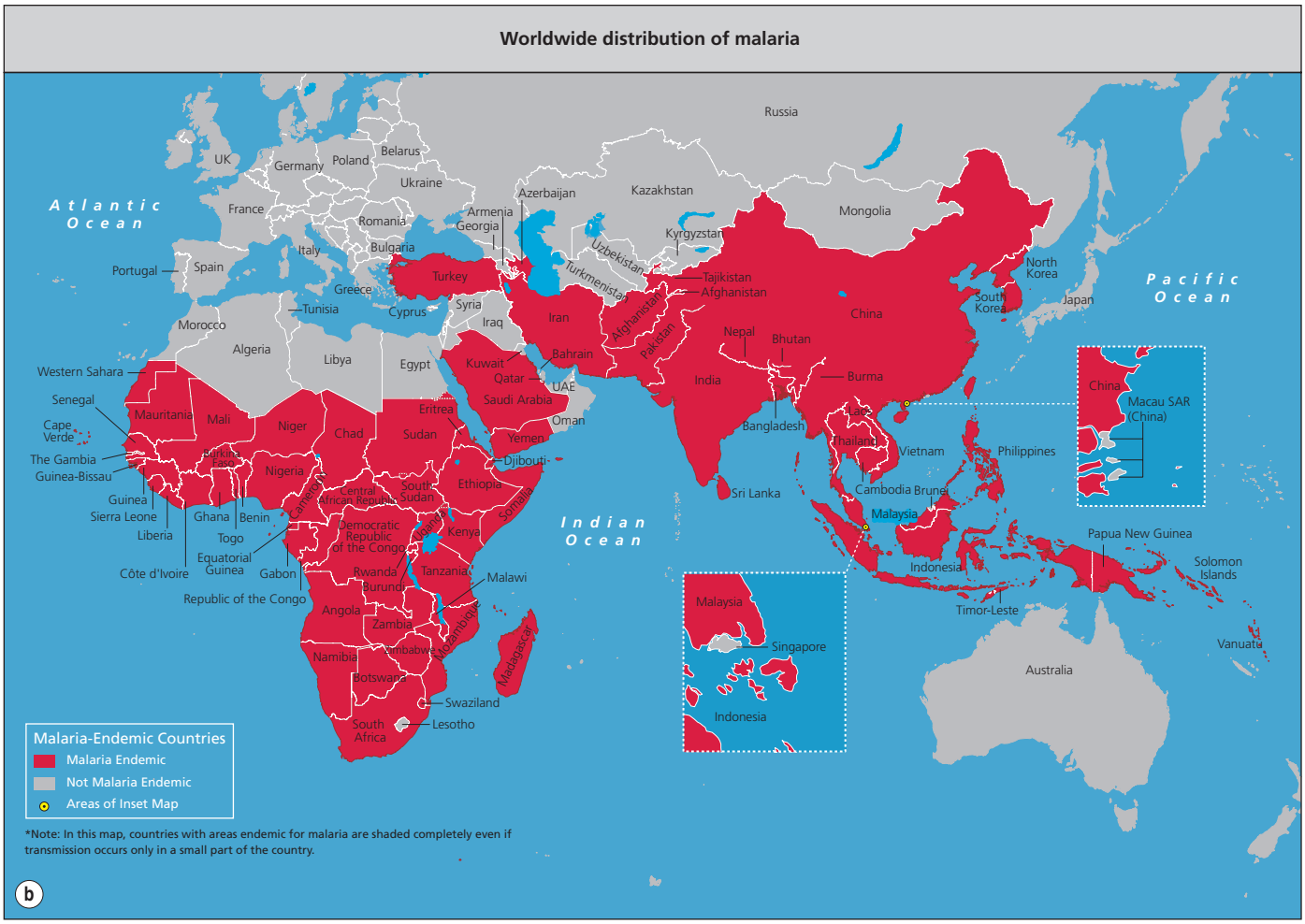

Figure 106-8, cont'd Worldwide distribution of malaria.

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