

# Chapter 4

## Urbanization and Infectious Diseases: General Principles, Historical Perspectives, and Contemporary Challenges

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### 4.1 Background

In 2009, a major demographic line was crossed: for the first time in history, the majority of the world population lived in cities rather than in towns and countryside (Fig. 4.1). This shift has been occurring over the past 100 years, with the most rapid rate of urban growth occurring over in the latter half of the twentieth century. Urban centers in the more developed regions of the world (i.e., North America, Australia, New Zealand, and Europe) experienced earlier growth in the 1920s–1950s, and since then, the rapid rate of urban growth has been concentrated in the cities and towns of developing nations [1].

According to the United Nations Population Division, the urban areas of the world are expected to absorb the entirety of the projected world population growth through 2050. The majority of this growth is expected to occur in less developed regions and countries such that by mid-century, 54% of the world's urban population will be concentrated in Asia and 20% in Africa. China and India together are

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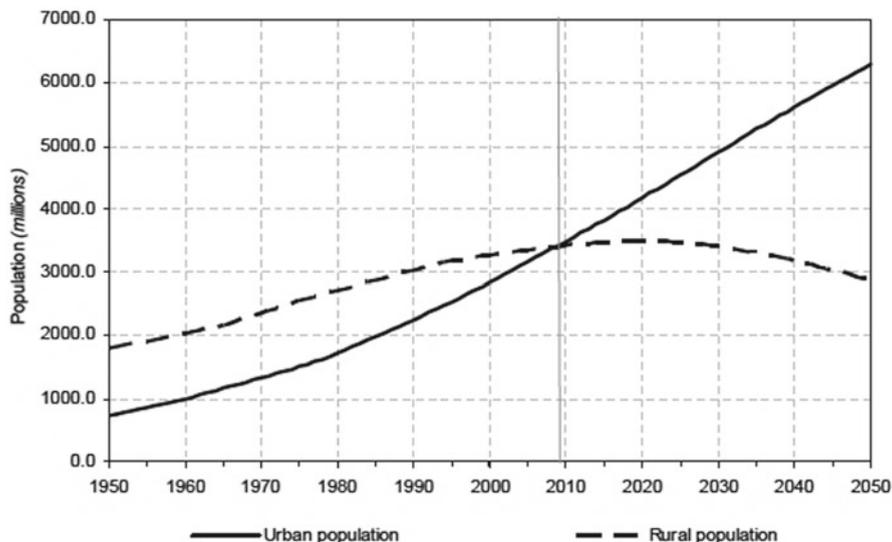
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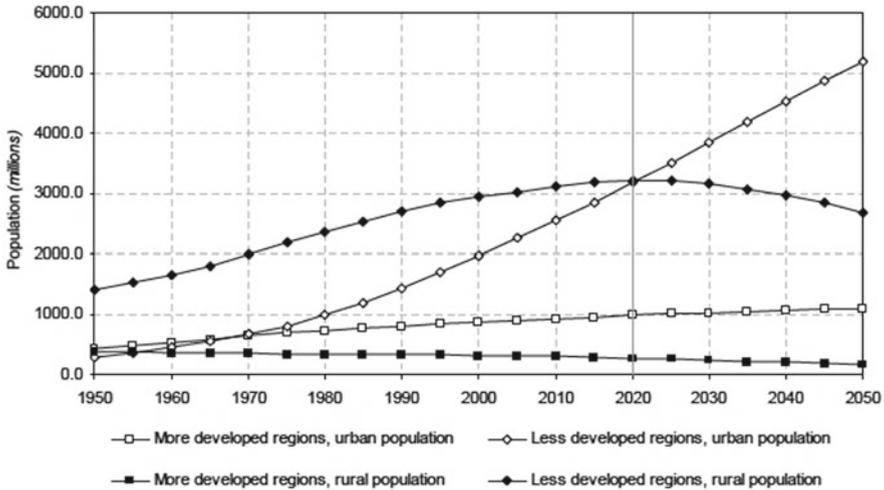


**Fig. 4.1** Urban and rural populations of the world, 1950–2050. *Source:* United Nations Department of Economic and Social Affairs, Population Division. *World Urbanization Prospects: The 2009 Revision.* New York 2010. Reprinted with permission of the United Nations

expected to account for approximately one-third of the increase in the world urban population in this timeframe [1] (Fig. 4.2).

This chapter will use the term “urbanization” to refer to this demographic shift. Urbanization is the result of migration from rural to urban locales as well as the imbalance between death and fertility rates in urban and rural locales—that is, the proportionally higher ratio of births vs. deaths in cities compared to countryside. It is important to recognize, however, that “urban” and therefore “urbanization” are terms that are not easily fixed. The United Nations Statistics Division recognizes that “because of national differences in the characteristics which distinguish urban from rural areas, the distinction between urban and rural population is not amenable to a single definition applicable to all countries” [2]. Nevertheless, for the purposes of this discussion, we will use the term “urbanization” to refer most basically to the demographic shift from less densely populated localities to more densely populated localities. Additional assumptions regarding the implications of urbanization will be explicitly addressed throughout this chapter.

The effect of urbanization on health trends, morbidity, and mortality are numerous. In more developed countries and industrialized centers, for example, violent crimes, drug abuse, and motor vehicle accidents are more common health problems than in rural areas. Environmental pollutants in industrialized centers across the spectrum of more and less developed nations have a deleterious impact on health.



**Fig. 4.2** Urban and rural populations by development group, 1950–2050 *Source:* United Nations Department of Economic and Social Affairs, Population Division. *World Urbanization Prospects: The 2009 Revision*. New York 2010. Reprinted with permission of the United Nations

Rapid growth of urban centers with poor urban planning and little capacity to meet the needs of a rapidly growing population often leads to the development of slums and shantytowns. Sanitation and waste removal, safe drinking water, secure housing, and access to adequate nutrition are other important challenges of urbanization. This chapter focuses on the infectious diseases implications of urbanization, which interrelate with the other health concerns listed above.

Along with war and famine, infectious diseases have been a leading cause of death and disability in developing societies for as long as history has been recorded. The field of modern medicine emerged around the study of infections, understanding their transmission, and developing ways to treat them with antibiotics as well as to prevent them with vaccines.

Infectious diseases, by definition, persist and thrive depending on how and how easily they are transmitted, as well as how easily they evolve over time in response to medical intervention. Infectious diseases are propagated via different forms of exposure, including exposure of an uninfected individual to the infected droplets, feces, or bodily fluids of another individual or exposure of an uninfected host to the blood or saliva of an infected vector. In the case of skin flora that can lead to serious infections, the exposure may be touch alone. With greater contact between infected and uninfected individuals, the opportunity for infections to spread increases. Urbanization necessarily provides more opportunity for contact and exposure and therefore has great implications for the transmission and the evolution of infectious diseases around the world.

Drawing on both historical and contemporary perspectives, this chapter will discuss urbanization as it pertains to epidemics and pandemics, specific considerations for developing countries, and implications of urbanization and infectious disease in more developed countries.

## **4.2 Urbanization, Epidemiology, Epidemics, and Pandemics**

Among the most intuitive manifestations of the interrelatedness of population density and infectious diseases are epidemics and pandemics. Throughout recorded history, epidemics have changed the world and influenced the trajectory of nations as well as science, medicine, and health. From plague to smallpox to more recent outbreaks of influenza and SARS, population trends influence and are influenced by infectious disease. The next section lays a basic framework for understanding the importance of shifting population demographics to epidemics and pandemics through a brief review of critical epidemiological principles, followed by historical and contemporary case examples of epidemics and pandemics.

### ***4.2.1 Emergence of the Field of Epidemiology***

The field of epidemiology was born of the desire to understand how disease is spread and propagated, particularly during times of epidemics. The Centers for Disease Control defines epidemiology as “the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems” [3]. The recognition of the importance of population characteristics to spread of disease has informed the field of epidemiology from the outset, and modern epidemiologists develop statistical and mathematical models that incorporate population characteristics to predict disease transmission and evolution as well as to anticipate possible interventions to control them.

### ***4.2.2 Mathematics of Epidemics***

The field of epidemiology has burgeoned significantly since its origin in the early 1900s, and the mathematics involved can be extremely complex. Several variables are basic to the mathematics of epidemics [3, 4]. Models for describing epidemics are based upon the reproductive rate of a given disease—that is, the number of individuals infected directly by the primary case (the first infected person) during the time when she/he is infectious. The reproductive rate is itself determined by the attack rate of the disease (i.e., the risk of transmission in any given encounter), as well as the number of encounters the primary case would have, on average, during the infectious period of the disease. In other words, the greater the population

density, the greater the number of encounters and the greater the reproductive rate. There are other factors that determine how a disease will be spread, including acquisition of immunity during an outbreak, existing immunity, the rate at which infected and susceptible individuals enter and leave the community, as well as the different types of encounter required for disease spread (i.e., via droplets, fecal-oral route, vectors, etc.). Population density is one of the most basic variables that affects the duration and impact of an epidemic.

Another important factor, particularly when considering the implications of urbanization, is the rate of entry and exit from the community. A significant proportion of the increase in urban population is due to the migration of people from rural areas to urban areas. As we will discuss in more detail further on this chapter, this can allow for the importation of diseases that were formerly confined to rural areas to urban centers where there may be increased opportunity to spread. This can also allow for increased opportunity to spread if, due to lack of prior exposure, migrants to a given area are more susceptible to a disease that is endemic to that area. In addition, as globalization continues and travel increases among the major cities both nationally and internationally, diseases can be propagated between and among urban centers. This can lead to farther-reaching—even worldwide—outbreaks of disease. Historically, travel by boat or train has enabled the transmission of endemic diseases to novel populations, causing outbreaks of diseases such as measles and smallpox and contributing to the decimation of native peoples. More recently, however, air travel has expedited the movement of airborne pathogens [5]. Viruses can now travel across the world within 24 hours, rather than within days. This statistic becomes even more powerful when considered together with the fact that more than one billion individuals worldwide travel by airplane each year [6, 7].

Another important factor in the mathematics of disease spread, as mentioned above, is the level of susceptibility in a given community. Once a certain level of immunity against a given disease is achieved, either through the conferring of immunity to infected individuals who survive an exposure or through vaccination, the reproductive rate is necessarily reduced as the risk of transmission in a given encounter is decreased. Limits to the spread of disease and the propagation of an epidemic occur when enough individuals in a community are immune to the disease such that the likelihood of an infected individual encountering a susceptible individual is very low. This is the basis for the concept of “herd immunity.” The level of immunity required to prevent or interrupt a disease outbreak varies depending on the pathogen. Vaccination programs, which are discussed next, aim to reduce the percentage of individuals susceptible to a given disease and, ideally, achieve high enough rates of immunity to eradicate it.

### 4.2.3 *Vaccines*

Edward Jenner is credited as the inventor of the vaccine against smallpox (derived from cowpox lesions) in the late 1700s, although several sources credit a Chinese

Buddhist nun with the earliest recorded practice (as early as the year 1,000) of inoculating people with smallpox for protection from the disease through use of ground scabs inhaled intranasally [8]. Inoculation, also called variolation, was likely also practiced in Africa, Turkey, and India long before the 1700s when the practice became more common in England and the rest of Europe and ultimately led to modern vaccination [9]. Louis Pasteur was the next to develop a successful vaccine, against rabies, in 1885. The late 1800s and 1900s subsequently saw the development of vaccines against plague (1897); cholera (1917); typhoid (1917); diphtheria (1923); pertussis (1926), tuberculosis (BCG, 1927); tetanus (1927); yellow fever (1935); influenza (1945); polio (1955); measles (1963); combined measles, mumps, and rubella (1971); hepatitis B (1982); *Haemophilus influenzae* type B (1990); varicella (1995); hepatitis A (1995); and rotavirus (1998) [10, 11].

The success of vaccination programs is exemplified by the end of smallpox; the last indigenous case of smallpox occurred in 1977 in Somalia, and in 1980, the Global Health Assembly declared smallpox eradicated. Other successes include the elimination of wild-type polio from most countries in the world. In 2003, measles was declared to no longer be endemic in the Americas [12].

The importance of vaccination to the prevention of epidemics cannot be overstated. To maintain these successes moving forward, vaccination programs will have to be expanded to meet the needs of a growing population. Failure to do so will likely lead to resurgence of vaccine-preventable diseases, as in the recent urban outbreaks of yellow fever in several West African cities including Abidjan, Ivory Coast (2001 and 2008), Dakar, Senegal (2002), and Bobo-Dioulasso, Burkina Faso (2004). These outbreaks were likely catalyzed by lower vaccination rates in conjunction with increasing population density and overcrowding conditions favorable for the *Aedes* spp. mosquitoes that carry the virus [13]. Even in developed countries like the USA, vaccination remains an issue. Measles resurged in Southern California between 1988 and 1990, predominantly in urban young adults and children under 5 years of age who had not yet been vaccinated. Outbreaks occurred within schools, colleges, detention facilities, and other institutions in urban areas. In order to control these outbreaks, schools required immediate immunization of non-immunized children and many re-immunization programs were launched [14]. Finally, vaccination is not only a key to prevention of epidemics but is also a cornerstone of curtailing the spread of disease during epidemics and pandemics.

#### 4.2.4 Case Examples of Pandemics

To illustrate the principles described above, the following section describes pandemics from the fourteenth century to the twenty-first century, including plague, Spanish flu, severe acute respiratory syndrome (SARS), and modern influenza pandemics. The critical role and context of the urban environment in each of these historical and contemporary pandemics is also described.

#### 4.2.4.1 Plague

The plague has been responsible for numerous outbreaks and three pandemics in recorded history, most infamously, perhaps, during the fourteenth century in Europe where it was subsequently referred to as “The Black Death.” Most estimates are that 50–75 million people worldwide, including about one-third to one-half of all fourteenth century Europeans, succumbed to the plague [15]. The plague was transmitted along trade routes by fleas carried on vermin and other animals infected with different biovars of the bacillus *Yersinia pestis*. There has been some debate over the exact numbers of the infected, and even whether *Yersinia pestis* was the true, sole pathogen responsible [16, 17], but it is widely agreed that “The Black Death” changed European history.

Transmission of plague is dependent on the interaction among vectors (fleas) and hosts (rats, humans, other animals). Although most plague is transmitted in the bubonic form, evolution to pneumonic plague can lead to direct transmission from person to person. Early globalization, such as trade routes from China along the Silk Road into Europe and from seaport to seaport, allowed for the rapid propagation of plague, with up to thousands of people newly infected every day [18]. Recognition of the importance of the migration of traders and their wares into urban centers of trade and industry led to early attempts at outbreak control including quarantines, movement restriction, and closure of ports to ships coming from affected countries [18]. The risk of spread from rats to humans is now known to be related to the population density of rats, the level of flea infestation per rat, as well as the level of bacteria in both the rats and their fleas [19–21]. Although the epidemiology and ecology of ancient plague are certainly more complex than this, the importance of early urbanization in early plague pandemics is clear if not clearly understood.

#### 4.2.4.2 “Spanish” Influenza

The Spanish influenza pandemic of 1918–1919 killed millions of people worldwide, with recent estimates as high as 50 million and some evidence to suggest that urban areas had higher mortality [22]. By that point in history, the field of epidemiology was taking shape. Alongside improved ability to identify microscopic pathogens as well as greater understanding of pathogen transmission and immunologic defense mechanisms, there was greater focus on public health interventions. The influenza vaccine would not be developed until 1945, however, and quarantine was still the mainstay of prevention during influenza outbreaks [23].

Non-pharmacologic interventions to reduce transmission of influenza were based on reducing points of contact among infected and noninfected individuals. These interventions included “social distancing” policies such as closings of schools, churches, and theaters, as well as prohibitions on large public gatherings. Recent analyses of historical data have demonstrated that such interventions, when implemented early, were associated with approximately 50% lower peak death rates and lower cumulative excess mortality [24]. The duration of these interventions also had

an effect; when cities relaxed these restrictions, the epidemic returned with a rebound in morbidity and mortality [24–26]. Another study used mathematical models to demonstrate that the number of infected individuals to which a healthy individual is exposed also may correlate with mortality—that is, the greater the exposure, the more severe the illness and the higher the case fatality rate [27]. These studies have led many public health experts to argue in favor of a multipronged approach including early, sustained non-pharmacologic interventions alongside use of antivirals and vaccine development in the event of another influenza pandemic.

#### **4.2.4.3 Severe Acute Respiratory Syndrome (SARS)**

Severe acute respiratory syndrome (SARS) was the first worldwide outbreak of the new millennium and perhaps the most impressive demonstration of the interrelatedness of urbanization, globalization, and viral spread. SARS is now known to be caused by a novel coronavirus, thought most likely to have been carried in animals prior to introduction to humans. The first people infected with SARS lived outside of the city of Guangzhou, China. It was subsequently spread from an infected patient to hospital staff, one of whom traveled to Hong Kong and stayed in a hotel where he infected 16 other people, who then went on to carry it to other hospitals and other countries around the world. In Hong Kong, nearly half of SARS infections were acquired in health centers [28]. In Toronto, health centers were also epicenters of nosocomial spread [29, 30].

The SARS pandemic began outside of a major city, was brought to a major city, and from there was spread to other major cities around the world. As was highlighted above in reference to the bubonic plague, globalization and urbanization tend to go hand in hand. In modern times, international travel via aircraft allows for transmission from one major urban center to other major urban centers across the world within hours, catalyzing the process and allowing regional epidemics to become global pandemics within a matter of weeks or even days.

#### **4.2.4.4 Avian and Swine Influenza**

Earlier in this chapter, the epidemiology and lessons learned during the 1918 influenza outbreak were reviewed. This section will briefly discuss the ways that urbanization influences modern outbreaks of influenza. As with SARS, such factors include rapid spread via infected droplets in crowded centers (including health facilities), increased international travel, and animal to human to human transmission. Shifting animal demographics related to urbanization may also play a role in the evolution of viral outbreaks.

Influenza strains infect a variety of birds, both wild and domestic. Although relatively little is understood regarding the mechanisms by which cross-species transmission occurs, infected poultry, pigeons, and swine tend to play a role in the outbreak of novel strains of influenza that can subsequently cause significant morbidity

and mortality among humans [31]. H5N1 Avian influenza is now epidemic among poultry and likely some migratory birds as well. When H5N1 is transmitted to humans, the route appears to be via direct contact with infected birds rather than via contact with other infected humans. This explains why the H5N1 virus did not become epidemic or pandemic among people. In the era of urbanization and globalization, however, once genetic reassortment does allow for efficient human to human transmissibility, a handful of infections can lead to a worldwide pandemic.

The most recent H1N1 influenza pandemic, for example, was caused by an influenza virus that was a reassortment among human, avian, and swine strains of the virus [32, 33]. The index case was in Mexico, and the virus rapidly spread from there throughout the world via air travel. Unlike seasonal flu, such influenza pandemics are rare. There were only three influenza pandemics in the twentieth century, in 1918, 1957, and 1968. This is because in order for an influenza virus to cause a pandemic, three conditions must be met: first, the viral strain must be antigenically novel such that the population has little or no preexisting immunity; second, the strain must be transmitted to humans; and third, the strain must be efficiently transmitted from person to person [34, 35]. Once these conditions are met, particularly in the age of urbanization and globalization, worldwide spread occurs rapidly. As with SARS, all of the index cases in the early weeks of the H1N1 pandemic of 2009–2010 could be traced to air travel from the index city [36].

Changing human population dynamics also influence animal population dynamics. In more remote and rural areas, localized farming is common. As populations shift, however, large agribusinesses are developed in order to supply urban populations with meat, poultry, and produce. As a consequence, animals are often kept in crowded conditions that may allow for rapid transmission of disease. These large animal farms are also points of multiple, sustained contact between humans and birds or swine, which may increase the opportunity for viral mutation to take place. Similarly, transport of live animals to large markets in urban centers can be a potential point of ignition.

### 4.3 Urbanization and Specific Infectious Diseases

Urbanization affects the spread of infectious diseases in both developed and developing countries, in wealthy enclaves as well as informal settlements. However, as the World Health Organization has described, disease threats disproportionately affect the urban poor and socioeconomic gradients are evident across many diseases [37]. The following section provides examples of major diseases—that is, those that affect large numbers of people—with a special emphasis on these diseases' impacts on urban residents. It is intended to provide an overview of selected diseases and evidence of their importance in the age of urbanization; however, it does not purport to provide exhaustive coverage of infectious diseases related to urbanization, which are numerous and varied. Furthermore, it is important to note that these diseases affect all countries, regardless of countries' stages of economic development.

### 4.3.1 *Water and Sanitation-Related Diseases*

Approximately one-third of the world's population lacks access to clean water, and nearly 40% lacks access to "improved sanitation facilities" for safe disposal of human waste [38]. While people living in rural areas have the least access to clean water and adequate sanitation, urban dwellers, especially those in developing countries, still face major water and sanitation challenges. For example, sanitation rates differ substantially between urban areas of developing countries (71%) and urban areas of developed countries (100%) [38]. Furthermore, some health experts posit that urbanization will bring wild animals—and their waste—into closer contact with drinking supplies for humans, thereby increasing the risk for waterborne zoonotic infectious diseases [39].

According to the World Health Organization, nearly two million diarrhea-related deaths are reported each year [38]. Fecal matter in water consumed by households can lead to diseases such as cholera, cryptosporidiosis, giardiasis and typhoid, among others [40]. The urban slum environment is fertile ground for these diseases, due in large part to overcrowded housing conditions, lack of availability of treated water, and lack of adequate sanitation facilities. Cholera outbreaks, for example, have been reported in urban slums in various parts of the world, ranging from Kolkata, India, and Jakarta, Indonesia, to Nairobi, Kenya, and Kampala, Uganda [41, 42]. Specific studies have implicated factors such as the construction of pit latrines in close proximity to wells (from which people draw their drinking water) in the fecal contamination of water sources [43]. Similarly, researchers investigating a 2007 typhoid outbreak in a West Bengal, India, slum suggested that *Salmonella typhi* bacteria in the fecal matter from victims were carried via open sewage drains, which then contaminated nearby unchlorinated drinking water sources [44].

Several studies have examined the water storage practices of urban residents in resource-poor areas. A study of the Parque Universitario slum in Fortaleza, Brazil, found a higher likelihood of fecal matter presence in household tap water stored in clay pots rather than in capped plastic bottles. The authors posit several explanations for the modes of transmission of fecal matter in these "wide mouth" clay pots: "scooping with contaminated hands in the container, manually clearing blocked filters and inadvertently contaminating [water storage] vessels during cleaning" [45]. Overall, it is notable that 30% of the water samples in the study contained fecal material.

Strategies to reduce the incidence of waterborne infectious diseases are numerous and varied. The World Health Organization has adopted a "household water treatment and safe storage" (HWTS) framework for preventing diarrheal disease. Water treatment techniques include the use of bleach, chlorine, and filters and the boiling of water, among other simple, cheap methods [46]. In terms of water storage, a study of urban dwellers in South India found that the practice of storing water in brass containers significantly decreased the presence of *E. coli* compared to other types of storage containers [47]. Other scientists have argued for a holistic approach to addressing the water and sanitation needs of slums. A study in Ahmedabad, India, demonstrated that "slum upgrading" could significantly reduce incidents of waterborne illness. Slum upgrading was defined as creating "connections to a water

supply for individual households, underground sewage for individual households, toilets for individual households, storm water drainage, stone paving of internal and approach roads, solid waste management, and street lighting” [48].

Reducing diarrheal illness related to urbanization will require not only addressing the current problems borne of rapid migration with virtually no urban planning—that is, “slum upgrading”—but also curtailing the development of slums in the first place.

### 4.3.2 *Vector-Borne Diseases*

As demographics shift from rural to urban, and as urban centers increasingly encroach on adjacent deserts, forests, and fields, human hosts may be newly exposed to diseases spread by fleas (plague), flies (leishmaniasis), mosquitoes (malaria, yellow fever, dengue, Japanese encephalitis), and ticks (Lyme, Babesia). When migrants from rural areas bring livestock with them to urban centers (often in slums or shantytowns on the outskirts of cities), vector ecology is also affected.

For example, over the latter half of the last century, the incidence and worldwide distribution of dengue has been increasing [49]. Dengue is spread by the same *Aedes* spp. mosquitoes that also carry yellow fever. Interestingly, dengue fever, in contrast to many of the other vector-borne illnesses, is primarily an urban problem. The *Aedes* mosquitoes live in and around houses. When a dengue epidemic occurs, it begins in cities and spreads centrifugally outward to neighboring city areas, suburbs, and towns [50]. The increasing incidence of dengue and dengue hemorrhagic fever has been tied to population growth, urbanization, and poor urban planning leading to poor water sanitation and human solid waste reservoirs for the mosquitoes that transmit the infection (e.g., tires, plastic containers) [13, 49].

Other vector-borne illnesses such as yellow fever and leishmaniasis have also been affected by urbanization. As discussed earlier, the recent epidemics of yellow fever in West Africa are most likely due to a combination of inadequate vaccination coverage, increasing population density, as well as the environmental factors just described that allow for proliferation of *Aedes* spp. mosquitoes. A combination of shifting population dynamics, deforestation, and expansion of nonimmune human populations into endemic areas has been correlated with increased transmission of visceral leishmaniasis around the world [51].

Finally, we turn our attention to malaria. The problem of resistant malaria is described elsewhere in this book. The remainder of this section discusses the impact of urbanization on malaria.

Malaria, which is a vector-borne disease caused by selected *Plasmodium* species, is a leading global killer, especially of children. In Africa, 20% of all child deaths are due to malaria [52]. According to the World Health Organization, there were nearly 250 million cases of malaria in 2008, in 100 countries [53]. However, the majority of the estimated one million deaths due to malaria each year occur in Africa [54].

Data from sub-Saharan Africa suggests an increased risk for malaria in rural areas when compared with urban areas. For example, the *Plasmodium falciparum* entomological inoculation rate, defined as the number of “infective bites per person per annum,” [55] is considerably lower in sub-Saharan African urban areas than in rural ones [56]. There may be several reasons for this. First, unlike for *Aedes* spp. mosquitoes, urban areas are inhospitable environments for *Anopheles* mosquito development, the major vectors of the *Plasmodium* parasites that cause malaria [57]. City pollution is thought to inhibit larval development of *Anopheles* mosquitoes [58]. In addition, city dwellers have increased access to insecticide-treated nets (ITNs). Urban residents have a rate of ITN use three times higher than that of rural residents in sub-Saharan Africa. Finally, urban residents live in closer proximity to health-care facilities compared to their rural counterparts, affording them greater access to treatment for malaria once infected [54].

Nevertheless, malaria remains a major urban health concern. Malaria experts have estimated that 200 million city dwellers in Africa are at risk for malaria [59]. Some experts note that characteristics of rapid urban development (e.g., open wells, poor sanitation in slum areas) may provide opportunities for water to pool and, consequently, for malarial vectors to breed [55, 60]. This may be especially true among poorer sections of cities: urban malaria prevalence rates in Africa have been shown to be inversely correlated with individuals’ socioeconomic status [61]. Furthermore, there is an emerging concern that many city residents lack sufficient immunity to malaria [58] and that urban children in endemic countries who regularly visit rural areas may be at increased risk for malarial anemia [62]. In cities where farming activities exist, so, too, does the potential for the urban environment to support anopheline mosquito development [58]. Lastly and particularly concerning is recent evidence from slum areas in sub-Saharan African cities that suggests that various *Anopheles* species are beginning to adapt to polluted city water sources [13, 57, 58].

### **4.3.3 Respiratory Infections: Highlight on Tuberculosis**

The epidemic and pandemic potential of viral respiratory infections such as influenza and SARS in the age of urbanization and globalization was reviewed previously. This section focuses on the bacterial airborne disease tuberculosis (TB), which is caused by *Mycobacterium tuberculosis*. 1.7 million people died from TB in 2009; 85% of all global TB cases occurred on the African and Asian continents [63]. TB is also an urbanization and health issue; high rates of TB have been reported in large cities throughout the world [64, 65], prompting concerns of possible urban TB epidemics in the future as more people migrate into cities [64].

Experts posit various explanations for the proliferation of TB in urban settings. First, overcrowding is known to be positively correlated with the incidence of TB [64, 66]. For example, one study of neighborhoods in Harare, Zimbabwe, found that living in a home with two or more people per room was a significant risk factor for TB [67].

Dubbed by WHO as a “disease of poverty,” the urban poor are particularly at risk for TB infection due not only to overcrowding but also to higher rates of underlying malnutrition and comorbidities including HIV [66, 68]. One study in Mexico documented that neighborhoods with low socioeconomic status (SES) had higher TB morbidity and mortality rates compared to higher SES neighborhoods [69].

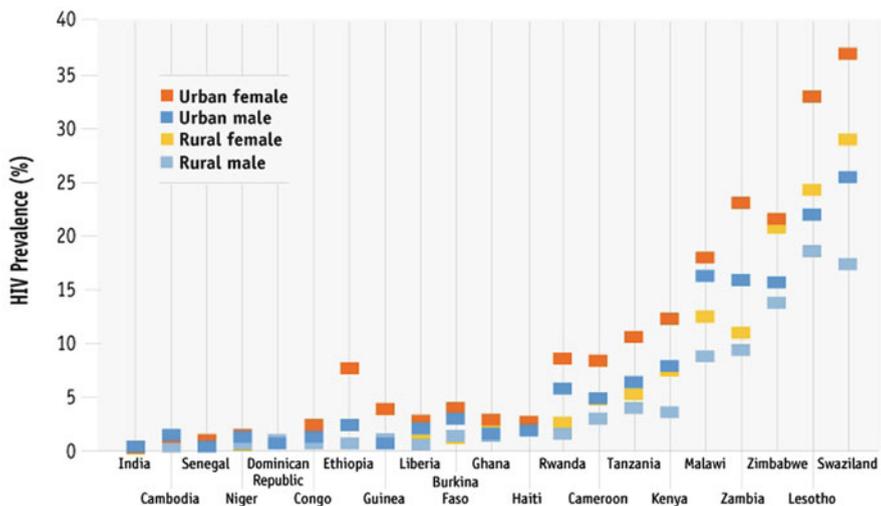
Numerous other studies underscore the dilemma of poor urban dwellers who, due to lack of knowledge about TB and lack of access to quality health-care services, often remain undiagnosed or, once diagnosed, are not able to complete TB treatment [68, 70, 71]. A recent study of 106 private physicians in Mumbai found that these physicians prescribed more than 60 different treatment regimens for TB, and less than 10% of these physicians prescribed regimens meeting the study authors’ definition of a “correct prescription” for TB drug treatment [72].

The dangers of TB are compounded by the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), discussed in detail elsewhere in this book. MDR-TB accounted for 440,000 cases worldwide in 2008 [63]. MDR-TB has been reported in many large cities, such as Mumbai, Sao Paulo, and Shanghai [13, 71, 73, 74] and in smaller numbers, XDR-TB cases have been documented in many cities around the world [75, 76]. New York City alone reported 19 cases of XDR-TB between 1993 and 2006 [77]. Data from Mumbai, India, found much higher rates of MDR-TB in Mumbai, compared to rural areas of India [78]. In China, there is concern that workers from rural areas infected with TB are migrating to the cities in search of work, consequently transmitting TB and possibly contributing to TB drug resistance [71, 79]. There is concern that these Chinese migrants are neither seeking nor receiving appropriate, timely TB treatment [80]. The case fatality rate associated with MDR-TB is much higher than for nonresistant TB, especially if left untreated. Researchers studying TB in a poor section of Sao Paulo, Brazil, for example, reported a 60% mortality rate among the non-HIV-infected MDR-TB patients in the study sample [74].

#### ***4.3.4 HIV/AIDS (and Other Sexually Transmitted Infections)***

HIV/AIDS is by far the most widespread epidemic in the world, with the greatest morbidity and mortality. A chapter in this book focuses on the HIV pandemic; this section will briefly highlight some ways that urbanization may impact on the propagation and evolution of the virus.

HIV is distinct from the other examples discussed in this chapter in that it is transmitted via infected bodily fluids—that is, through blood exposure, sexual exposure, and during pregnancy, delivery, and breastfeeding—rather than via droplets, vectors, or fecal-oral contamination, which are perhaps more intuitively and directly related to urbanization. Urbanization may, however, influence behaviors that affect the risk of acquiring HIV, including alcohol and drug use as well as sexual behavior. Migrants to urban centers are often young people who are separated from their families and traditional social structures. In addition, the disparity



**Fig. 4.3** HIV prevalence by gender and area of residence 2003–2008. *Source:* WHO calculations based on data from Demographic and Health Surveys (DHS) 2003–2008. Reprinted with permission from WHO

between the rich and poor in urban environments can be stark. Migrants are typically seeking opportunity, coming to the city from a less privileged socioeconomic background. The confluence of these factors may lead to higher-risk behaviors.

According to the U.N., there were 2.6 million new cases of HIV infection in the world in 2009, and 1.8 million of these new cases were in sub-Saharan Africa alone [81]. In many sub-Saharan African countries, such as Zambia and Kenya, HIV prevalence rates among 15–49 year olds are higher in urban areas than in rural areas [82] (Fig. 4.3).

Considerable attention has been paid to the issue of high-risk sexual behaviors among workers who migrate to cities in search of work [13, 83, 84]. Much of this literature focuses on Asian countries. In China, where an estimated 140 million migrants reportedly exist, studies have described risky sexual practices and poor knowledge about HIV among male migrant workers [85], and even among migrant workers' school-aged children [86]. A study of male taxi drivers from rural Bangladesh who migrated for work to the capital, Dhaka, reported that approximately 60% of respondents had recently engaged in sex with commercial sex workers without using condoms [87]. Several studies of commercial sex workers in cities of India have documented the elevated risk of HIV infection among this population [88]. The phenomenon of young women and girls migrating to cities, becoming engaged in commercial sex work, and contracting HIV is well documented. A recent study of 287 Nepalese women and girls who had been sex-trafficked into urban brothels in India and then returned to Nepal revealed a 38% HIV-positive rate among these victims [89]. Seventeen of these women and girls were also found to have TB [90]. It appears that sexual behaviors of migrant workers will help fuel the

spread of HIV in cities—but also in the rural communities to which these workers will return.

Similar factors likely contribute to the transmission of HIV in sub-Saharan Africa, which has seen an impressive redistribution of populations and rise of rural-to-urban migration. Between 1960 and 1980, the crude population density more than doubled across sub-Saharan Africa and there was a nearly tenfold increase in the number of cities with populations exceeding 500,000 [91].

Linkages between urban slums/informal settlements and HIV have been described in the literature. In Kenya, an analysis of the Nairobi Cross Sectional Slum Survey found that slum residents who had either migrated from economically poor rural villages or from other slums were more likely to engage in risky behaviors with respect to HIV/AIDS (i.e., condom use and number of sexual partners) than other slum residents [83]. These findings are consistent with a recent study of five African cities—Accra, Dar es Salaam, Harare, Kampala, and Nairobi—which reported that living in a slum predicted riskier sexual behaviors [92]. Some researchers have posited that in migrating from rural areas to cities, individuals no longer find themselves bound to traditional values, resulting in increased promiscuity and an increased vulnerability to HIV infection [93].

Finally, when discussing HIV and urbanization, it is important to consider opportunistic infection and comorbidities. Tuberculosis infection tends to be both more severe and more difficult to treat among patients with HIV. Opportunistic infections, including infections with molds and fungus, may be influenced by movement between rural and urban environments. The high-risk sexual behaviors that lead to HIV transmission also place individuals at risk of acquiring other sexually transmitted infections, including syphilis. Additionally, because injection drug use has primarily been an urban health issue, urbanization may lead to an increase in injection drug use and thus further the spread of HIV. Injection drug use with shared needles can transmit many other viruses in addition to HIV. Approximately one in five injection drug users (approximately 16 million worldwide) is HIV-positive [94]. HIV also increases the risk of hepatitis C virus (HCV)—almost a third of individuals with HIV are co-infected with HCV [95, 96].

These trends are not only a problem of the developing world. During the early stages of the HIV epidemic in the United States, for example, the first patients diagnosed with HIV and those at highest risk were white men who had sex with men living in urban areas. The HIV epidemic in the USA continues to be primarily an urban problem, with more than 80% of HIV diagnoses occurring in major metropolitan areas [97].

## 4.4 Conclusions and Future Directions

The world's population continues to grow exponentially, and more people are living in cities and megacities. This population growth, coupled with the interconnectedness of the entire world, has significant implications for disease. This chapter

described major infectious disease threats in the urban environment, past and present, and illustrated several mechanisms by which urbanization can affect the epidemiology of infectious diseases (Table 4.1).

Urbanization disproportionately impacts the poor. Hence, not only “slum upgrading” but also prevention of slums will be important in order to mitigate the harmful effects of rapid urbanization. Further development of health systems in parallel with improved housing, sanitation, and access to clean water is necessary. Anticipating continued growth and expansion should prompt governments to dedicate additional resources to urban planning. Vaccination, monitoring and reporting of new cases, and ring chemoprophylaxis are critical for curtailing epidemics and pandemics. Disease surveillance systems and systems for communication and reporting are crucial [98]. Rapid innovations in information technology may inform the development of such systems.

Systems for epidemic response also must be strengthened. Rapid, early detection and diagnosis are keys to addressing any disease outbreak. Clinical diagnostic algorithms must be identified early and health providers educated about them, as laboratory diagnostic tools often take time to become available and affordable. Health-care workers should be targeted to receive treatment and prophylaxis as soon as possible. The manufacture and distribution of sufficient quantities of vaccine, treatment, and chemoprophylaxis during outbreaks is also a major challenge. Finally, processes for effective coordination of efforts among agencies involved in epidemic response must be developed in advance.

In terms of future directions, three topics merit further consideration on the urbanization and global health agenda: (1) bioterrorism, (2) nosocomial infections and the development of resistant organisms, and (3) noninfectious diseases (i.e., chronic diseases) in urbanizing areas. First, there is a need to address the looming threat of bioterrorism, which capitalizes on the epidemiologic principles discussed in this chapter. Four diseases are recognized to have significant bioterrorism potential in urban settings. This chapter has discussed two disease agents—plague and smallpox virus—which can spread from person to person. The other two are anthrax (spores) and botulism (toxin), which are not spread from person to person but could cause mass infection and death if released in aerosolized form into a crowded area or, in the case of botulinum toxin, into the food supply. Outbreak preparedness requires identification of vaccines and treatments for these potential threats, developers who would be able to produce vaccines and treatments should need arise, and a sophisticated system of targeted, efficient diagnosis, isolation, treatment, and, where necessary, vaccination, to curtail further spread.

Second, to the extent that urbanization influences the development of medical centers and affects the use of broad-spectrum antibiotics, nosocomial infections such as *Clostridium difficile* and resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) bear mentioning. MRSA is now found fairly widely in the community and may be more common in urban residents compared to rural residents [99]. Less common but of great concern is the emergence of vancomycin-resistant *Staphylococcus aureus* (VRSA). Only a few cases of VRSA have been reported in the USA to date [100],

**Table 4.1** Influences of urbanization on selected infectious diseases.

Influences of migration, urbanization, and globalization	
Infection	More developed areas
<i>Diarrheal illness</i>	
Cholera	More developed areas
Salmonella including typhii	Reliance on large agribusinesses can lead to wide-spread outbreaks of food-borne illness.
<i>E. coli</i>	
Cryptosporidia	
<i>Vector-borne</i>	
Leishmaniasis	
Yellow fever	Migrants from rural areas bring livestock with them to urban centers, influencing vector ecology.
Dengue	<i>Aedes</i> mosquitoes thrive in urban environments; <i>Anopheles</i> mosquitoes do not.
Malaria	Rapid increases in population density can overwhelm vaccination programs, decrease herd immunity, and render a population more susceptible to outbreaks.
Rickettsial	Access to prevention, diagnosis, and treatment is greater in urban areas.
	Urban centers increasingly encroach on adjacent wilderness, bringing human hosts into closer contact with vectors.
<i>Sexually-transmitted &amp; blood-borne</i>	
HIV	
Syphilis	Migrants separated from their social networks may have higher rates of risk-taking behaviors, leading to higher rates of acquisition and transmission of STIs.
Hepatitis B and C	STIs are prevalent among commercial sex-workers.
	Access to prevention, diagnosis and treatment is higher in urban areas.
<i>Respiratory/droplet</i>	
Influenza	Rapid increases in population density can overwhelm vaccination programs, decrease herd immunity, and render a population more susceptible to outbreaks.
SARS	Air-travel connects urban centers around the world and can facilitate spread of highly contagious illness in minimal time.

(continued)

Table 4.1 (continued)

Influences of migration, urbanization, and globalization	
Infection	Less developed areas
Tuberculosis	<p>More developed areas</p> <p>As population increases, incarceration and homelessness increase, both of which are risk factors for TB.</p> <p>Immigration and globalization bring diseases from the developing world to the developed world.</p>
<i>Bioterrorism</i>	
Plague ( <i>Yersinia pestis</i> )	Highly-contagious infections can spread rapidly among a non-immune population, facilitated by high population density.
Smallpox	
Anthrax	Inhalation of anthrax spores could cause mass morbidity and mortality if released in a crowded urban center.
Botulism	Mass reliance on large agribusiness could allow for significant morbidity and mortality if <i>C. botulinum</i> were released into the canned food supply.
<i>Nosocomial &amp; drug resistant bacteria</i>	
<i>C. difficile</i>	Large medical centers with access to broad-spectrum antibiotics tend to be located in urban centers.
MRSA	Broad-spectrum antibiotic use can lead to the development of resistant organisms.
VRE	
ESBL organisms	
VRSA	

but they highlight the importance of judicious use of antibiotics as well as adherence to contact precaution protocols for hospitalized patients with suspected or confirmed resistant bacterial colonization.

Finally, it is important to acknowledge that a growing proportion of the global burden of disease is noncommunicable. Pollution, trauma, violence, and obesity all are major causes of death and disability that are on the rise with urbanization and globalization. Cardiovascular disease has been the leading cause of morbidity and mortality in both the developed and the developing world for the past 15 years [101]. This in part is due to improved control of infectious diseases and increasing lifespan (i.e., people are living long enough for cardiovascular disease to become salient) coupled with persistent, relatively higher rates of cigarette smoking in the developing world. More research in all aspects of chronic disease and urbanization processes need further elucidation.

Overall, urban centers pose great challenges in terms of disease, but they also present unique opportunities for health promotion and disease prevention. For example, the concentration of human and financial resources in cities can translate into greater capacity to carry out health campaigns in order to reduce the risk of transmission of diseases like HIV/AIDS and TB. Access to health education, condoms, disease diagnosis and treatment also may be greater in the urban centers compared to rural areas.

Urban centers have the potential to bring together a critical mass of people from multiple disciplines and sectors (e.g., medicine, health, economics, engineering, sociology, social work, architecture), harness collective knowledge, and foster an environment that promotes the development of innovative, integrative solutions to health problems. Ultimately, such holistic solutions are desperately needed to address the world's emerging urbanization and health threats.

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