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Impact of global change on transmission of human infectious diseases

WU XiaoXu^{1†}, TIAN HuaiYu^{1††}, ZHOU Sen², CHEN LiFan¹ & XU Bing^{1,2*}

¹ College of Global Change and Earth System Science, Beijing Normal University, Beijing 100875, China; ² School of Environment, Tsinghua University, Beijing 100084, China

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Global change, which refers to large-scale changes in the earth system and human society, has been changing the outbreak and transmission mode of many infectious diseases. Climate change affects infectious diseases directly and indirectly. Meteorological factors including temperature, precipitation, humidity and radiation influence infectious disease by modulating pathogen, host and transmission pathways. Meteorological disasters such as droughts and floods directly impact the outbreak and transmission of infectious diseases. Climate change indirectly impacts infectious diseases by altering the ecological system, including its underlying surface and vegetation distribution. In addition, anthropogenic activities are a driving force for climate change and an indirect forcing of infectious disease transmission. International travel and rural-urban migration are a root cause of infectious disease transmission. Rapid urbanization along with poor infrastructure and high disease risk in the rural-urban fringe has been changing the pattern of disease outbreaks and mortality. Land use changes, such as agricultural expansion and deforestation, have already changed the transmission of infectious disease. Accelerated air, road and rail transportation development may not only increase the transmission speed of outbreaks, but also enlarge the scope of transmission area. In addition, more frequent trade and other economic activities will also increase the potential risks of disease outbreaks and facilitate the spread of infectious diseases.

global change, infectious disease, natural factors, human activities

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Since the 20th century, the global incidence of infectious diseases has had a series of ups and downs. At the beginning of the century, influenza pandemics were prevalent; in mid century, the incidence of all types of infectious diseases was relatively low. However, since the 1970s, new infectious diseases, including AIDS, severe acute respiratory syndrome (SARS), highly pathogenic avian influenza A (HPAI H5N1), Ebola hemorrhagic fever, legionellosis and Lyme disease, have emerged. Certain non-prevalent diseases, including tuberculosis, cholera, schistosomiasis, plague

and sexually transmitted diseases have reemerged, followed by biological attacks and infectious diseases caused by human activities. Various infectious diseases have unprecedented impacts on human health, social stability and economic development. Nearly 15 million people worldwide die from these diseases every year, accounting for 25% of all deaths (Morens et al., 2004). Morbidity and mortality bring heavy economic burdens to developing countries (Guerrant et al., 1999). Infectious diseases, together with war and famine, still rank first on the list of the greatest threats to human survival (Morens et al., 2004; Binder et al., 1999).

Under the influence of global change in both the natural

^{*}Corresponding author (email: bingxu@tsinghua.edu.cn)

[†]Equal contributor (email: wuxx@bnu.edu.cn)

^{††}Equal contributor (email: tianhuaiyu@gmail.com)

and social environment, the emergence and transmission patterns of infectious diseases have changed. Natural factors, especially global climate change, will directly or indirectly impact the transmission process of many such diseases. Global warming will also cause the rise of sea level and sea surface temperature, which increase the incidence of water-borne diseases including cholera and poisoning of shellfish products (McMichael et al., 1996; Patz et al., 1995). Research indicates that climate change, including increases of temperature and rainfall, more frequent deluges and storms, sea level rise, and environmental deterioration such as that caused by settlement in refugee camps, could cause outbreaks and prevalence of cholera (Tong et al., 2000). Global climate change will influence the spread of insect-borne infectious diseases, through its influence on the geographic distribution change of insect vectors, increase of propagation velocity, invasion strength of insect vectors and by shortening the incubation period of pathogens. Insect-borne infectious diseases strongly affected by climate change include malaria, schistosomiasis, dengue fever, viral encephalitis and others (McMichael et al., 1996; Patz et al., 1995). Extreme temperature, strong rainfall and natural disasters related to weather can directly cause death, adverse health effects and disease. Climate change indirectly affects human health through the following: Altering sources of infection, which causes increased emergence of infectious diseases and expansion of their geographic distributions; impacting grain yield, which causes emergence of dystrophic diseases; population movements, resulting from sea level rise that causes increasing incidence of infectious and mental diseases; by affecting air quality, which increases incidence of respiratory infectious diseases; by influencing society, the economy and population, which produces wide-ranging public health problems (http://www.unep.org/ annualreport/2011/).

Socioeconomic factors are important in emergence, development and variation of infectious diseases (Jones et al., 2008). First, land use, the human living environment, frequent trade and increased tourism are believed to be important drivers for the re-emergence and devastation of infectious diseases (Patz et al., 2004; Taylor et al., 2001; Weiss et al., 2004; Woolhouse et al., 2005), and create many social problems. For example, antibiotic abuse will lead to pathogen emergence of drug-tolerant persisters and variants (as in malaria, dengue, tuberculosis, cholera and influenza). Land cover change may induce prevalence of infectious diseases; for example, cultivating wastelands and deforestation has led to the emergence and spread of hemorrhagic fevers. Second, changes in the style of human activity have contributed to the spread of infectious diseases. These changes include frequent population migration, an increase in erotic services and multiple sex partners, illegal trade, industrialization of food, insufficient heat treatment in mechanized food production, and careless disinfection.

1 Natural environment and infectious diseases

Under the impetus of global natural and human activities, the emergence and transmission patterns of infectious diseases have changed (Figure 1). Natural factors, including temperature, humidity, rainfall, vegetation and land use directly or indirectly influence the outbreak and spread of many such diseases. Among these factors, the effects of climate change cover the widest range and have greater magnitude. Human activities are not only the major driver of climate change, but also indirect drivers of infectious disease spread.

1.1 Climate change and infectious diseases

1.1.1 Meteorological factors and infectious diseases

Meteorological factors affect infectious disease via three aspects: pathogen, host (Kuhn et al., 2005) and transmission route

(i) Effects of meteorological factors on pathogens. Temperature and humidity can directly impact reproduction of pathogens and their survival time in the environment (Zhang et al., 2008). Temperature has a significant effect on viruses. First, most viruses, bacteria and parasites have threshold temperatures to survive. For example, the threshold temperature for survival of the malaria parasite Plasmodium falciparum is 18°C (MacDonald, 1957), and the spread of malaria is limited to the range 16–33°C (otherwise the spore cannot reproduce). The optimal condition for malaria spread is high humidity and temperature, within 20-30°C (Khasnis et al., 2005). The threshold temperatures for the plasmodia P. falciparum and P. vivax to survive in malaria mosquitoes are 18°C and 15°C (Duane et al., 2001), respectively, whereas the threshold temperature for Japanese encephalitis virus survival is 20°C (Mellor et al., 2000). Many pathogens, such as Vibrio cholerae and hepatitis E virus are restricted to some tropical areas, also because of temperature limitation (Hunter, 2003). In addition, temperature can affect the evolution of viruses, thereby resulting in outbreaks of new infectious diseases. For example, global warming will cause the evolution of influenza virus and extensive outbreaks of influenza (Aimone, 2010; Brown, 2010; Gibbs et al., 2010; Tang et al., 2010). New influenza viruses are emerging, threatening the health and safety of human and other species. Studies have shown a certain correlation between global temperature and nucleoproteins. Global change would impact the evolution of arbovirus to some degree (Gould et al., 2009), and also affect change patterns of emerging diseases. Moreover, temperature can influence viral infectivity and risk. A study in Peru showed that 1°C rise in temperature would increase the probability of severe diarrhea by 5% (Checkley et al., 2000). Another study in Australia showed positive correlation between temperature and cases of Salmonella infection (D'Souza

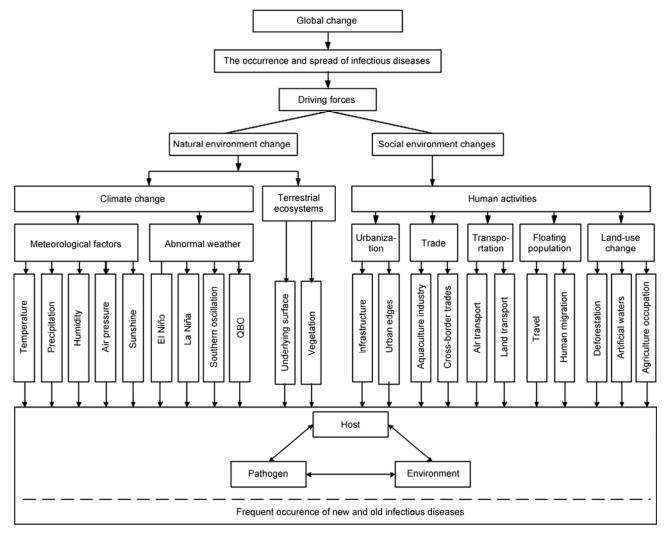


Figure 1 Relationship between global change and outbreak and transmission of infectious diseases.

et al., 2004).

(ii) Effects of meteorological factors on host. Climate change affects infectious disease hosts, via aspects including: (1) Spatiotemporal distribution of arthropods; (2) life cycle characteristics of arthropods; (3) spread pattern of related arboviruses; (4) spread efficiency from arthropod to vertebrate (Gould et al., 2009). Arthropod vectors are poikilothermic animals that are sensitive to change of climatic factors. Meteorological conditions influence the survival and reproduction rate of disease vectors, along with their habitat, distribution and quantity, spatiotemporal pattern of annual carrier activity and development, thus influencing pathogen survival and reproductive rate in disease vectors (Lafferty, 2009). Variations in carrier populations show positive correlation with temperature and humidity, and are also related to rainfall and sunshine, which are greater during periods of disease prevalence (Rogers et al., 2006). Geographic distribution and change of insect host species are closely related to patterns of temperature, rainfall and humidity. Temperature rise can accelerate entomic metabolism, increase spawning quantity and blood circulation frequency (Mellor et al., 2000). Global warming and climate change have the potential to significantly impact the hydrosphere and fragile atmosphere (Zell, 2004), and especially species diversity, human health and infectious disease distribution (Harvell et al., 1999; Intergovernmental Panel on Climate Change, 2001). One such threat is increasing contact between humans and vector- or water-borne diseases. Global warming is beneficial to the spread of malaria (Khasnis et al., 2005). The effect of rainfall is also significant; it indirectly modulates the life cycle of insects through influencing humidity. A wetter environment is much more beneficial for insect reproduction, which thereby increases the geographic distribution and abundance of seasonal insect vectors (Kuhn et al., 2005). Moreover, mosquito hosts are very sensitive to climate. Their reproductive and death rates are influenced by climate (Zell, 2004).

Mild meteorological conditions are favorable for reproduction of ticks, and modify the distribution of Crimea-Congo hemorrhagic fever (Ergonul, 2006). Outbreaks of this disease in Turkey are connected with mild temperatures in the preceding spring (Cazorla et al., 2003). Observations in recent years have shown that the number of rodents is also affected by climate, since warm and wet winters and springs can increase their number (Kausrud et al., 2007). Climate change aside, this number has the potential to grow in temperate areas, causing more contact between humans and rodents and greater risk of pathophoresis, especially in urban areas. In some European countries, damage to health infrastructure and the lack of health care knowledge among the public has increased the incidence of plague (Kausrud et al., 2007). A mild climate favors increase in the number of rodent species. However, harsh climate conditions such as heat waves may cause rodents to feed indoors, resulting in more contact with humans (Kausrud et al., 2007). Fluctuation in the number of main hosts is related to cases of plague (Davis et al., 2004). Climate change in central Asia is favorable for the spread of plague. According to prediction, 1°C temperature increase would heighten the number of diseases in hosts caused by Yersinia pestis by 50% (Stenseth et al., 2006). Plague epidemics in central Asia are common, and also impact European countries (Akiev et al., 1976). In Sri Lanka, drought has caused river to shift course and river water accumulation, which provides numerous breeding sites for local mosquito vectors and leads to frequent occurrence of malaria. Usually, in El Niño Southern Oscillation (ENSO) years, the northeast monsoon in that country brings sufficient rainfall, but not so the southwest monsoon. In recent years, the reemergence of malaria in certain locations may be related to ENSO. In recent decades, the longer propagation period of falciparum malaria in Pakistan has been connected with seasonal temperature increase in later parts of an ENSO year, which has a high temperature overall. Temperature can directly impact plasmodium growth and the mosquito life cycle. Sufficient rainfall is favorable for mosquito breeding, and suitable climate conditions can strengthen mosquito invasiveness. In 1987, malaria was very prevalent in Rwanda, mainly because of temperature increase (especially for temperature minima) and successional rainfall (Bouma et al., 1994). Temperature influences the growth, development, reproduction and death of Schistosoma and Oncomelania, and also contact between humans and infected water (Tong et al., 2000). In most cases, Schistosoma infection does not occur at low temperature (lower than 9°C). However, infection probability increases with temperature, maximizing within 24–27°C. However, temperatures in excess of 39°C can cause kill Oncomelania and reduce the Schistosoma infection rate (McMichael et al., 1996). The distribution of Oncomelania is also affected by rainfall (McMichael et al., 1996). Temperature has an important influence on the spread of dengue fever. With its increase, incubation of dengue virus in mosquitoes shortens, and these bite humans more frequently. Moreover, the geographic distribution of the mosquito that transmits dengue fever virus may be extended (McMichael et al., 1996; Patz et al., 1995). Global warming is likely to increase the incidence of food-borne diseases. For example, during the period 1982 to 1991, the incidence of food-borne disease in England was closely related to average temperature; this correlation had an average threshold temperature above 7.5°C (Tong et al., 2000).

(iii) Effects of meteorological factors on transmission. Climate change can influence the occurrence and spread of infectious diseases through its effect on transmission. For example, climate change can cause air pollution and shortages of food and clean water (Debono et al., 2012), leading to changes of high-incidence areas and outbreak patterns, thereby affecting the occurrence and spread of infectious disease.

Climate change can alter the spread of infectious diseases by influencing the water environment. Taking red tides as an example, global warming provides excellent conditions for algae growth. Algae in warm waters and sewage ditches contain many toxins, which may be related to an increased incidence of liver cancer in recent years. With the continuing rise in sea surface temperature, liver cancer has spread to coastal areas in high altitude and low temperature zones (Luber et al., 2009). Red tide outbreaks in drinking water sources present a huge threat to public health. Moreover, eating contaminated fish from red tide waters indirectly impacts human health (Morris et al., 1982). Climate change and over-exploitation of resources will aggravate the shortage of clean water in Africa and Southeast Asia (Intergovernmental Panel on Climate Change, 2007). Shortage of clean water may bring a series of waterborne infectious disease outbreaks. One study of children under the age of five from less developed and developing countries showed that low rainfall was closely related to outbreaks of illnesses such as diarrhea (Lafferty, 2009).

Climate change can alter the spread of infectious disease by influencing food. Climate change, including changes in temperature, rainfall and soil moisture, alter or relocate grain-producing areas (McMichael, 2001). People in such areas tend to be dystrophic, which is more common in developing countries. Thus, hunting wild animals to survive, along with poor health and sanitary conditions, increase risks of infectious disease in residents of these areas (U.S. Global Change Research Program, 2001). Model studies have also shown that decreased grain production caused by global climate change would increase the number of those living in poverty by 5%-10% (Parry et al., 2004); large number of refugees and increased transient populations would cause outbreaks of a series of infectious diseases (McMichael et al., 2006). Increases in average temperature will result in an obvious increase in the number of people infected with Salmonella and Campylobacter (D'Souza et al., 2004). Diseases caused by food sources can also kill vulnerable people (Hall et al., 2002). In 10 countries of mainland Europe, cases of Salmonella food poisoning have risen

to nearly 30% (Kovats et al., 2004). Investigations in England have also found a close connection between the incidence of food poisoning and temperature of the preceding 2–5 weeks (Bentham et al., 2001).

Climate change can alter the spread of infectious diseases by influencing air quality. One study focused on the potential effects of climate change on air pollution over the next 50 years in the eastern United States. The study stated that the ozone-related death toll would increase by 4.5% in 2050 relative to that in 1990 (Hogrefe et al., 2004). Climate change may alter geographic range and time of pollen and spore spread, thereby causing prevalence of anaphylactic diseases including hay fever and asthma (Beggs, 2004).

1.1.2 Abnormal weather events and infectious diseases

Abnormal weather events have significant effects on mosquito-borne, rat-borne and tick-borne diseases (Zell, 2004). Disease outbreaks rise significantly during El Niño events, such as incidence of diarrhea in Peru (Checkley et al., 2000), African horse sickness in South Africa (Baylis et al., 1999), and dengue fever in the South Pacific (Hales et al., 1996; Epstein, 1999). The increased hantavirus activity in the Four Corners region of the southwest United States in 1997 and 1998, as well as periodic epidemics of Rift Valley fever in Eastern Africa, are related to El Niño events (Epstein, 1999). Cases of human infection in Colorado of the U.S. are also related to EI Niño (Hjelle et al., 2000), so we may conclude that the increase of rainfall owing to EI Niño leads to a rise in the number of rodents. Such rise intensifies intraspecific competition, and increased contact between humans and rats strengthens hantavirus activity (Zell, 2004). EI Niño is also related to outbreaks of cholera. The most catastrophic flood disasters in a century occurred in 1991 and 1998 in China; cholera was extensively prevalent in 1998, but not in 1991. The flood of 1991 was caused by EI Niño, and it produced a decrease in sea surface temperature and seawater salinity in the southeastern waters of China, which is unfavorable for the prevalence of cholera. Flooding in 1998 was caused by La Niña, and it led to abnormal rise in sea surface temperature in southeastern waters, which was favorable for the growth and reproduction of comma bacillus (Wang et al., 2000). The outbreak and prevalence of malaria in Ecuador, Peru and Bolivia in 1983 were related to heavy rains and accompanying ENSO.

The quasi-biennial oscillation (QBO) of stratospheric westerly winds at the equator is associated with tropospheric weather patterns such as change of atmospheric pressure caused by the Southern Oscillation. Recently, it was proven that Ross River virus found in Queensland, Australia had significant seasonal change, with peaks in summer and autumn. Heavier summer rainfall in southeast Queensland had a strong relationship with occurrence of the QBO in the west. The QBO can affect virus activity by influencing the local environment (Zell, 2004).

1.1.3 Meteorological disasters caused by abnormal weather and infectious diseases

Drought is found to have a close relationship with outbreaks of some infectious diseases. In 1993, an abnormal occurrence of deadly SARS broke out in New Mexico, Colorado, Utah and Arizona in the United States. A Bunyaviridae Hantavirus pathogen was named Sin Nombre virus (Nichol et al., 1993; Wenzel, 1994). Later, it was found that this virus was spread by the deer mouse. During previous outbreaks of hantavirus in spring and summer of 1993, locally abnormal winter rainfall caused a long drought, which resulted in a dramatic 10-fold increase in rodent numbers in the early part of the outbreak (Engelthaler et al., 1999). Owing to shortages of food, deer mice invaded human settlements to forage, thus introducing the virus and causing the outbreak of Hantavirus pulmonary syndrome (Engelthaler et al., 1999). Severe drought can lead to a shortage of water supply, so residents use water from pools with no streamflow, secondary supplied water and water from long-term storage. Once the water resources are contaminated, outbreaks of intestinal infectious diseases can readily occur (Yang, 2007; Feng, 2000). Drought can cause pollutants to accumulate in dams and blue-green algae to massively propagate, releasing toxins in dams and lakes.

Rainstorms are also connected with the occurrence of some infectious diseases. The bunyavirus Rift Valley Fever Virus (RVFV) shows symptoms in humans, including fever and encephalitis accompanied by retinal inflammation, and first broke out in 1912 (Gonzalez-Scarano et al., 1996). This virus mainly harbors on the body surface of mosquitoes, primarily Aedes and Culex (Wilson et al., 1994). Rift Valley fever occurs after downpours, with abnormal sea temperatures in the eastern equatorial Pacific and western equatorial Indian Ocean (Linthicum et al., 1999). In addition to rise in sea surface temperature, rainfall causes many grassland depressions in East Africa, which provide breeding sites for immature mosquitoes. There are large numbers of infected grain-sized eggs in these floodplain grasslands, which are the origin of Rift Valley fever outbreaks. Rift Valley fever disappears with ending of the rainy season and decrease in number of mosquitoes (Zell, 2004). Research into the effects of flood disasters on infectious diseases has been carried out domestically. After these disasters, deterioration of environmental hygiene and increased hazardous exposure in crowds always causes outbreaks and prevalence of many infectious diseases. Xianning in Hubei Province suffered flooding in 1998. Investigation of this showed that respiratory infectious disease was the principal disease during the early and late flood stage and effector phase after flooding, while intestinal infectious disease was the main one during the flood period (Zhou, 2000). Insect-borne disease mainly occurs in the disaster period, whereas natural focus infection disease occurs during the later flood stage and effector phase after flood. Effects of flood disaster on infectious diseases include: (1) Effects on schistosomiasis related to

the spread of snails to surrounding areas via floodwater, flotage and other means, causing an increased incidence of schistosomiasis infection (Xie et al., 1999; Zhang et al., 2003, 2004); (2) effects on leptospirosis related to the fact that it is a zoonotic disease caused by pathogenic *Leptospira*, with rats and pigs as principal sources of infection. Most scholars believe that the prevalence of Leptospira in disaster areas after flooding depends on the carrier rate of infection sources (Ren et al., 2005). It has been shown that rat density is positively correlated to leptospirosis incidence (Pan et al., 2003); (3) effects on hemorrhagic fever with renal syndrome (HFRS) related to the fact that it is a natural focus infection disease, with rats as the major disease host. When humans and rats cohabitate, the likelihood of contact and infection increases. Local outbreaks or prevalence of HFRS readily occur. Sometimes, flooding may reduce the number of rats and thereby HFRS incidence. Since there is not enough time or no place for rats to move or escape to in flood disaster areas, some rats drown, which results in reduced numbers of hosts and disease incidence. However, some rats move to unaffected high altitudes or bordering land, where the number of infection sources increases, resulting in more contact between humans and rats and increased incidence of disease (Chen et al., 1999; Chen, 1999); (4) effects on intestinal infectious disease related to the fact that water supply facilities and sanitary fixtures like lavatories are flooded or inundated during flood disasters, leading to pollution of these and other water sources by garbage, excrement and the like. This directly produces outbreaks and prevalence of many intestinal infectious diseases, among which infectious diarrhea has a high-frequency (Chen et al., 1998; Cheng et al., 1999); (5) effects on malaria related to the connection between its incidence and rainfall (Wen et al., 2003). Flooding can increase epidemics in malarious areas (Zhang et al., 2004). In addition, torrential rains or rainstorms may transport sewage and waste water into sources of drinking water and dams, thereby causing diseases (Thomas et al., 2006). Recent focuses of model studies are on simulating variations of safety and usability of drinking water caused by climate change (Ferguson et al., 2007).

Heat waves are also frequently related to infectious diseases. Outbreaks of such diseases in southeast Romania from 1996 to 1997 were very similar to those that broke out in Israel in 2000. Both were related to heat waves caused by high temperature in early summer (Rogers et al., 2006).

1.2 Terrestrial ecosystem and infectious diseases

The outbreak of infectious diseases is related to types of underlying surfaces. Previous studies have indicated that appearance of seasonal wetlands is associated with outbreaks of HPAI H5N1 on the Indian subcontinent (Adhikari et al., 2009). The first case of avian influenza in Romania was in the Danube Delta, the largest wetland in Europe. One

of the most important factors sustaining transmission of avian influenza virus is that it may survive in water without a host. Water can increase the spread of excrement and saliva, propagate virus even lacking hosts, and redistribute viruses among different hosts (Gilbert et al., 2008). The occurrence of HPAI H5N1 is closely related to the distribution of water and wetlands in China, India and Pakistan (Adhikari et al., 2009; Fang et al., 2008; Biswas et al., 2009). Global transmission of H5N1 through wild bird migration, poultry transport and the interface of interaction between wild and domestic birds, has been determined for improved understanding (Liang et al., 2010).

The occurrence of infectious disease is associated with the vegetation ecosystem. In the Middle East and northeast Africa, HPAI H5N1 has occurred in areas with greater seasonal variation of Normalized Difference Vegetation Index (NDVI) values (Williams et al., 2009). In Europe, HPAI H5N1 occurrence is also closely related to NDVI (Si et al., 2010). Based on NDVI time series data, this occurrence in Africa and the Middle East is correlated with differences in phenological characteristics of plants (Williams et al., 2008, 2009). This results from the fact that plant distribution affects the food sources of waterfowl, thereby altering their distribution and movement.

Many kinds of natural factors together influence the occurrence and spread of infectious diseases. Research indicates that influences on HPAI H5N1 occurrence among wild birds in Europe were increased NDVI in December, intermediate NDVI in March and at lower elevations, increased minimum temperatures and decreased precipitation in January (Si et al., 2010). It is believed that this occurrence is mainly impacted by food sources, increased temperature and decreased precipitation (Si et al., 2010). Global warming and climate change may significantly modify the hydrosphere through heavy rainfall, floods, storms, heat waves and droughts. Research found that falciparum malaria in northwest Pakistan is related to continuous rainfall in September and October, and continuing high temperatures in November and December (Bouma et al., 1996).

2 Human activity and infectious disease

Human activities influence the emergence and transmission of infectious diseases via the following aspects (Figure 1).

2.1 Growing population mobility

2.1.1 International travel

With the development of transportation over almost a century, human travel has transitioned from interzonal to international. Over the last 50 years, the number of international travelers has risen by 1300% (Mavroidi, 2008). According to statistics, there are nearly one million international travelers daily and one million per week traveling between de-

veloped and developing countries (Garrett, 1996), representing nearly 700 million trips annually (Gossling, 2002). Ecotourism and adventure tourism have seen the highest growth rate at 10% each year since 1985, and often involve activities with high risk of disease transmission (Chomel et al., 2007). Increased tourism, business travel, and immigration have contributed to the dissemination of pathogens (Arguin et al., 2009). Existing reported diseases include HIV, legionellosis, Cyclospora cayetanensis, cholera, viral hemorrhagic fevers, transmissible spongiform encephalopathies, dengue, malaria, schistosomiasis, leptospirosis, tuberculosis, dysentery and others (Ostroff et al., 1998). According to transmission media, infectious diseases basically can be divided into water-borne, food-borne (Swaminathan et al., 2009), airborne and zoonotic diseases. Based on the Geosentinel Surveillance Network, statistics of 17353 infected travelers visiting developing countries indicated that tourism, visits with family and friends, and business travel respectively accounted for 59%, 15% and 14% of all trips. In such travel, malaria is the disease with the highest mortality rate and diarrhea is the most frequent, followed by dengue and typhoid fever (Freedman et al., 2006; Hill, 2006). African tick bite fever has been reported to have caused 350 cases attributed to intercontinental travel (Jensenius et al., 2004). Dengue is a tropical infectious disease, transmitted by Aedes aegypti and Aedes albopictus, which has spread globally by infected travelers becoming a new infection source. Leishmaniasis rapidly spread in developed and non-epidemic countries over the last two decades of the 20th century, for which one important factor was rapidly growing international travel (Antinori et al., 2005; Pavli et al., 2010; Pérez-Ayala et al., 2009). Furthermore, global crowd-gathering events, such as the Olympic Games, World Expo or World Cup, not only increase the number of travel destinations, but also attract many travelers and accordingly increase the disease risk. For instance, according to evaluation of cumulative disease trend from the Geosentinel Surveillance Network, the Beijing Olympic Games was considered to have potential risks for disease outbreaks.

2.1.2 Population migration from rural areas to cities

With the accelerated development of urbanization, a shift in population migration from rural areas to cities and suburbs has changed global patterns of infectious diseases. It is estimated that nearly 40% of the increased urban population in developing countries come from rural areas (Leon, 2008). The "floating population" often suffers poor health care situations and high residential densities, which readily cause infectious disease outbreaks and further spread disease during large population movements. Taking China as an example, there were only 6.57 million who were considered floating in the third census, representing 0.65% of the total population. In the fifth census in 2000 and a 1% population sampling survey in 2005, the floating population reached 121 million and 147 million, respectively, constituting

9.55% and 11.26% of total population. During the SARS event in 2003 and influenza A (H1N1) pandemic in 2009, the floating population was the vulnerable group, easily susceptible to infection and difficult to monitor (Zeng et al., 2009; Zeng, 2009). Research on health surveys of the floating population in Beijing indicated that there was a higher risk of disease and greater mental stress for people migrating from rural areas to cities than for other groups (Chen, 2011). Similar surveys showed that the incidence of viral hepatitis, syphilis, measles, dysentery, mumps and infectious diarrhea in floating populations is higher than in local residents (Yang et al., 2007). China's Ministry of Health, the WHO and UNICEF conducted a baseline survey of children's health care conditions in Hangzhou and Beijing at the end of 2006. The survey showed that the incidence of diarrhea in children in the floating population was 16.5% and 13.3%, and that of cough was 34.2% and 30.4% in the respective cities. These rates are all higher than those in poor rural areas in 1998 (Huang et al., 2008). There were similar situations in other developing countries, such as Africa, Asia, and Latin America. Outbreaks of leishmaniasis, which used to be confined to rural areas, occurred in many cities as a result of tremendous rural population immigration (Jeronimo et al., 1994; Werneck et al., 2002). Other forms of cutaneous leishmaniasis broke out in densely populated cities in western and central Asia (Ashford, 2000). In recent years, cholera outbreak in the Tanzanian capital of Dar es Salaam has resulted from large floating poor populations and outdated health care support facilities (Penrose et al., 2010).

2.2 Rapid urbanization

Urbanization and health is another focus of current research on socioeconomic factors, and it is one of six research issues of global environmental change and health in the Earth System Science Partnership (ESSP; Confalonieri et al., 2006). Since the beginning of the 20th century, England became the first country with urban population exceeding rural population; by 2007, over half the global population was living in cities. Moreover, according to a UN forecast, urban population in 2050 will reach 6.3 billion (Alirol et al., 2011). The 20th and 21st centuries represent an important stage of urbanization, and an era with obvious problems of infectious disease and health in cities. With urbanization development, cities expand outward, floating populations increase and urban populations concentrate. Rapid urbanization is often accompanied by poverty and deterioration of living environment, and people's needs exceed the service capacity. The shift in population from rural to urban has been altering global patterns of infectious diseases and mortality (Hay et al., 2005).

2.2.1 Lagging urban infrastructure

The rapid expansion of cities has greatly modified the living

environment for various sources of infection. Sudden changes of environment increase biological attacks and the possibility of infection events, thus augmenting the probability of spreading infectious disease (Wu et al., 2010). Moreover, poor infrastructure, water supply, drainage, and sewage treatment systems facilitate breeding for some vectors (Sutherst, 2004). For example, rapid urbanization caused a global outbreak of dengue fever in the late 20th century. Su et al. (2005) found that urbanization may change types and dominance of major vectors of dengue fever. In addition, Lin et al. (2005) believed that urbanization may cause vectors to breed indoors. Water pollution caused by urban sewage often provides good breeding areas for Culex, causing outbreaks of diseases such as lymphatic filariasis (Maciel et al., 1996), systemic lupus erythematosus, Rift Valley fever and other diseases. Taking China as an example, in the next 20 years there will be 400 million peasants migrating to cities. This implies huge demand for health care and related facility construction along with potentially huge risks, as inferred from lessons in Asian, African and Latin American countries.

2.2.2 Disease spread risks in suburbs

With the expansion of cities, both developed and developing countries face the same problems, in that city edges or suburbs are often the first to impinge on undeveloped areas, such as forests and wastelands. Humans often lack immunity when moving into a new area or environment. Moreover, human impacts may bring new pathogens and vectors into such areas (McMichael et al., 2006; Ashford, 2000; Charrel et al., 2007; Harrus et al., 2005; Patz et al., 2000). Diseases related to this that have been reported include yellow fever, trypanosomiasis, Kyasanur Forest disease, malaria and leishmaniasis (Patz et al., 2000; Molyneux, 2003).

2.3 Continuous changes in land use

Land use change, including agricultural encroachment, deforestation, road and dam building, wetland transformation, mining and urban expansion, has led to a series of disease outbreaks and changed the transmission pattern of many endemic diseases (Patz et al., 2004). Land use change can influence diseases indirectly by changing the habitats and behavioral habits of wild animals and livestock. This increases the possibility of human exposure to pathogens and vectors, reduces regional biodiversity, increases the dominance of infected species, and provides breeding areas for vector-borne disease hosts.

2.3.1 Deforestation

Deforestation has accelerated since the early 20th century, with $101724~\rm km^2$ of forest cleared each year. Forest disappears gradually at a rate of 0.3%, and tropical forests disappear at 23% annually (Wolfe et al., 2000). This disappearance destroys the original ecosystem, and the land is trans-

formed into pastures, farmland, plantations or wasteland, which are low-biodiversity environments. Further, the formation of many fragmented habitats has a "marginal" (edge) effect, which increases the opportunity for human contact with new pathogens or wild animals (Patz et al., 2004). For example, cases of malaria (Yasuoka et al., 2007), onchocerciasis (Wilson et al., 2002), Lyme disease (Killilea et al., 2008), cutaneous leishmaniasis (Chaves et al., 2008) and other vector-borne diseases and corresponding vector populations are rising. Population dominance of vectors in forests is also changing. With the effects of increased light, enlarged wasteland areas and increased surface ponding, the population of photophilic vectors has increased in forests. Recent studies indicate an increase in cases of SARS, Ebola virus, Nipah virus and some bat-host viral pathogens (Leroy et al., 2005; Looi et al., 2007). There is a growing sense that HIV, falciparum malaria and other zoonotic diseases are results of increased human exposure to wild animals (Keele et al., 2009; Rich et al., 2009).

2.3.2 Artificial waters

Dams, paddy field irrigation and other water conservancy facilities furnish breeding areas for vector-borne infectious disease hosts, and increase risks of expanding the habitats of intermediate hosts for schistosomiasis (Seto et al., 2002; Xu et al., 2004). With population movement, extensive development of new irrigated areas, and dam building, the incidence and geographic distribution of schistosomiasis is shifting (Chitsulo et al., 2000). Neighborhood relationships and hydrologic connectivity has been quantified to assess the effect of inter-village parasitic transport on disease transmission and control (Xu et al., 2006). After completion of the Aswan Dam in Egypt, local Schistosoma haematobium was gradually replaced by Schistosoma mansoni as a result of ecological changes. The completion of the Jama dams on the Senegal River and a dam on the Bafing River exacerbated an S. mansoni epidemic in North Senegal (Southgate et al., 2001). The Three Gorges Dam is also believed to enlarge the snail habitat and further spread schistosomiasis in southern China (Li et al., 2000). Furthermore, changes to surface water bodies can impact the regional ecological environment and dominance of vectors of certain vector-borne diseases. Artificial waters have flooded breeding areas of Simuliidae, which transmit onchocerciasis, but provided breeding areas for Anopheles and Planorbis, which respectively transmit malaria and schistosomiasis. Dam spillways become new breeding areas of Simulium, which have triggered epidemics of onchocerciasis in West Africa.

2.3.3 Large-scale agricultural encroachment

Nearly half of the world's land is used for agricultural production, which consumes two-thirds of fresh water resources (Horrigan et al., 2002). The low biodiversity and fragile ecosystems of agricultural land contribute to the occurrence of vector-borne diseases. In developing countries,

traditional agricultural irrigation and intensive irrigation canals have become ideal habitats for *Culex* and snails. Typical irrigated farming generates breeding areas for *Culex* (in particular *Culex tritaeniorhynchus*, a vector of Japanese encephalitis virus) and snails. In western Kenya, *Anopheles arabiensis* is common during rice growing season, whereas *Anopheles funestus* is common in the mature rice season. *Anopheles gambiae* appears after the rainy season, whereas in the dry season, *Anopheles arabiensis* dominates. Research in Tanzania and Kenya found that excessive agricultural encroachment and resistance vectors are keys for outbreak and reemergence of malaria (Bodker et al., 2000; Shanks et al., 2000).

2.4 Rapid development of transportation

2.4.1 Air transportation

Currently, the speed of cross-regional spread of infectious diseases is faster than at any time in history because of rapid and efficient air transportation, which has been significant in boosting long-distance epidemic transmission. In a study of the SARS event of 2003, Olsen et al. believed that the epidemic was transmitted by SARS patients who were in the incubation period and was spread globally by air transport (Breugelmans et al., 2004; Olsen et al., 2003). Wilder-Smith et al. analyzed records of flights to Singapore and believed that the spread of SARS on airplanes was overestimated (Wilder-Smith, 2003a; 2003b; 2004). Vogt et al. (2006) collected information on the passengers and crew on seven flights heading to the U.S. carrying SARS patients, and the results of their retrospective study indicated that the risk of SARS transmission on aircraft has not been overestimated. Although risk of the spread of SARS by air transport remains controversial, a consensus has been reached that epidemic diseases can be effectively spread in aircraft (Roy et al., 2004). This has attracted attention from scholars for taking epidemic prevention and control measures at airport customs and immigration centers (Wilder-Smith, 2003b; 2004). Similarly, in a study on the 2009 H1N1 pandemic, Khan found that in almost all countries accessible to Mexicans, confirmed cases of H1N1 have emerged, and the rate of spread is astonishingly high (Khan et al., 2009). Based on an investigation of H1N1 cases on a airplane flight, Baker found that close contact with symptomatic patients poses a higher risk of infection. After the passengers departed the aircraft, subsequent exposure measurement became inefficient and difficult (Baker et al., 2010). Thus, in-flight measurement of the potential risks of H1N1 transmission was proposed (Wagner et al., 2009). As an efficient means for spreading infectious diseases, air transport is also of concern regarding its influence on risks of transmission of other infectious diseases, including tuberculosis (Abubakar, 2010; Dowdall et al., 2010; Kornylo-Duong et al., 2010), malaria (Bradley, 1989; Tatem et al., 2006), plague (Pascali, 1982), yellow fever

(Oliva, 1979), cholera (Rondle et al., 1978), dengue fever, Norwalk virus (Kirking et al., 2010), and epidemic meningococcal diseases (Rachael et al., 2009). Modes of transmission during air travel and transport include via droplet transmission, interpersonal contact, vector-borne and zoonotic disease hosts entering the cabin, water and food contamination, and others. There were an estimated 36 billion air travelers in 2010. This means that an outbreak or epidemic of disease anywhere in the world could spread to other regions in only a few hours.

2.4.2 Highway and railway transportation

Highways are the main conduits for interregional and regional traffic. Highways carry more passengers and transport to more destinations than any other mode of transport. Taking China as an example, in 2009 its highways carried 2779081 passengers, more than 100 times the number by water transport and civil aviation combined, and about 18 times that of railway traffic (Bureau of Statistics of China, 2010). H1N1 pandemics spread in cities of all sizes in China, with an initial epidemic stage featuring the spread of imported cases, followed by secondary cases from initial imported cases, and a late stage in which the pandemic spreads from metropolitan areas to small cities and from eastern to western areas (Zeng et al., 2009). In the epidemic process, rapid movement of large populations is mainly realized through road traffic, so this traffic is an important risk factor for the secondary spread of infectious disease in various countries. Further, long-term freight is mainly transported by road traffic. Highway freight volume in 2009 was 21278.34 million tons, accounting for 75.3% of total freight (China Statistics Bureau, 2010). Some zoonoses are readily diffused to larger areas via shipping. For example, highly pathogenic avian influenza (HPAI) virus can generate increased human and animal infection in more areas, via agricultural products shipped from other areas. Fang et al. (2009) showed that during a SARS event, the transportation network of highways and railways is important in spreading an epidemic across mainland China. Close correlation between SARS distribution and a ring road in the Beijing urban area has been reported (Wang et al., 2006; Wang et al., 2008). Fang and Cao found a close association between HPAI outbreaks and minimum distance to the nearest national highway in China (Fang et al., 2008; Cao et al., 2010). However, results of similar studies in Europe did not show this association (Si et al., 2010).

2.5 Global trade and economy

At the start of the 20th century, with development of the transport network, strengthening of international cooperation and division of labor, the rise of the World Trade Organization (WTO) and other trade organizations, global trade increased tremendously. International merchandise trade increased 3- to 4-fold from 1980 to 2000, with the

main contribution from Asia (up to a 5-fold increase) (Sutherst, 2004). For nearly a century, Asia has been considered the epidemic focus of new and old infectious diseases, with repeated devastating events (Guan et al., 2002; Li et al., 2004; Smith et al., 2006). Frequent economic and trade exchange increases the possibility of infectious disease outbreaks. Both Asian and other countries are likely to face the problem of long-distance spread of pathogens and diffusion of new viruses along livestock trade routes.

2.5.1 Aquaculture industry

Since 1997, HPAI H5N1 epidemics have broken out in poultry in Asia (Li et al., 2004; Smith, et al., 2006; Chen et al., 2006), and this has resulted in enormous damage to the poultry industry in Southeast Asia (Gilbert et al., 2008). According to WHO statistics, as of March 2011, HPAI H5N1 has spread to more than 63 countries, resulting in 535 people infected and 316 deaths (http://www.who.int/csr/ disease/avian_influenza/country/cases_table_2011_03_25/ en/index.html).According to technical documents published by the United Nations Environment Programme Convention on Migratory Species (UNEP/CMS), the source of HPAI H5N1 was intensively-fed poultry, and virus mutation resulted from these extreme rearing environments. Poultry production in Asian countries can be classified into four categories, namely, backyard farming, free range, greenhouse cultivation and enclosure breeding. According to an investigation by Songserm et al. (2006) in Thailand, all the above methods, except for enclosure breeding, pose risks of H5N1 viral infection. A follow-up study by Biswas and Gilbert showed a higher risk of infection in backyard farming and free range breeding, and infected migratory birds and water containing the virus may have infected poultry (Biswas et al., 2009; Gilbert et al., 2006). According to statistics, about 80% of poultry production is by backyard farming in Asian and African countries (Aini, 1990; Permin et al., 2002). Through 2005, there were 140 million birds infected with the H5N1 virus, resulting in about a \$10 billion loss in Asian countries (Gilbert et al., 2008; Food and Agriculture Organization, 2005). Effective epidemic control methods include large-scale containment killings. As of 2010, more than 260 million chickens and other poultrybirds have been killed worldwide, producing economic losses totaling about \$20 billion (http://www.fao.org/ news/story/en/item/41287/icode/). The poultry industry in China has an annual output of nearly 15 billion birds, including about 5.6 billion chickens, 760 million ducks and 300 million geese (Martin et al., 2011). These are all sensitive to HPAI H5N1 (Keele et al., 2009), and the mortality rate is near 100% upon infection (Alexander, 2000, 2007; Webster et al., 1987). Losses from an epidemic outbreak over a large area would be immeasurable.

2.5.2 Disease spread risks of international trade Globally, there were about 350 million live plants and wild-

life species traded yearly (Karesh et al., 2007). Approximately 4 million live birds are transported annually, and most of these are from Southeast Asian countries (Karesh et al., 2005). It is generally agreed that the main mode of transmission for avian flu is via various forms of poultry trade, which includes legitimate trade and illegal transactions (Alexander, 2000; Capua et al., 2006; Olsen et al., 2006; Van et al., 2005; Wang et al., 2006). Studies have shown that the major risk of avian flu in Europe is from bird migration, and the main risk in Asia is from the poultry trade (Kilpatrick et al., 2006). There are greater risks in wildlife trade, including induced epidemic outbreaks in areas with crowds of people, livestock epidemics, and strong negative impacts on international economies, trade, the livestock industry, and national wildlife ecosystems (Karesh et al., 2005). Since the mid-1990s, outbreaks of infectious diseases, including mad cow disease (BSE), foot-and-mouth disease (FMD), avian flu, swine flu and others, have caused losses of about \$80 billion to the global economy and trade industries (Karesh et al., 2005). At the beginning of 2003, the UN Food and Agriculture Organization stated that more than a third of meat traded was embargoed worldwide. Wild animals are considered the source of more than 70% of emerging infectious diseases (Kuiken et al., 2005), and diffusion of a series of new viruses has been triggered by various forms of trade. HIV is believed to be derived from human feeding on non-human primates (Gao et al., 1999). The Ebola virus is transmitted via human contact with great apes (Leroy et al., 2004), SARS coronavirus is induced by international trade in small carnivores (Bell et al., 2004), and monkeypox in the U.S. originates from imports of exotic pet rodents from Ghana (Guarner et al., 2004). Chytridiomycosis, derived from the African clawed frog that has been commercially traded, has eliminated nearly 30% of amphibians worldwide (Weldon et al., 2004).

2.6 Other human activities

Emergence and reemergence of a given type of infectious disease may be related to socioeconomic pressures, such as collapse of the public health system, lack of disease control strategies, and disturbances resulting from ecological and demographic changes (Taubes, 1997; Gubler, 1998; Reiter, 2001). Other human activities, including population growth, intensive agricultural development and changes in vaccine technology, are likely to alter the evolution and spread of influenza virus (Vandegrift et al., 2010). In addition, population age and size, and demographic components, such as numbers of workers or students, can affect the spread of influenza (Stefano et al., 2010). Influenza is closely related to age structure of the population. Avian and seasonal flu have different features across the population age distribution. Specifically, victims tend be the young and the elderly. Children and young adults are major flu victims. Statistics on influenza A (H5N1) virus infection in February 2008 indicated that the average age of cases is 18 years.

3 Discussions and conclusions

3.1 Discussion

3.1.1 Interaction between natural and human factors

Natural factors affect human activities; climate change can directly influence human behaviors such as by seasonal and other migration, and summer and winter lifestyles. Human behavior directly affects disease transmission. Seasonal outbreaks of avian influenza in Europe show that people are spending more time on outdoor activities in winter (Halstead, 1996). Alternately, in temperate regions, a growing number of summer gastroenteritis cases in developing countries have been connected with the fact that people prefer to picnic or cook outdoors because of increasingly higher temperatures (Altekruse et al., 1998). Rainfall, especially of the heavy variety, can increase the frequency and intensity of drinking water contamination. Climate can affect water sources and sanitation, water shortages can increase the probability of people using contaminated water sources, and these factors may add to cases of intestinal infectious diseases (Zhang et al., 2008). Human activities also change natural factors, which indirectly influence the occurrence and transmission of infectious diseases. Research (Zell, 2004) shows that the spread of infectious disease is affected by the spread or location change of pathogen-infected hosts or insects, and sometimes by both; the role of human activity cannot be ignored in this process. Tang and colleagues analyzed climate change and health statistics of 45 countries in Africa and 113 countries elsewhere. Their research shows that income level can regulate the negative influence of climate change over an average life span. With increased income, the impact of climate change on average life expectancy is gradually decreased. This impact is greater in African or developing countries than in others (especially developed ones), and the effect of climate change on health is much greater than on economic levels (Tang et al., 2010).

3.1.2 Human adaptation activities and infectious diseases

Long-distance travel, such as to escape heat or cold, acts as an efficient carrier of pathogens. Upon entering a new area or environment, people often become vulnerable to pathogens because of a lack of immunity. In addition, human intervention introduces new pathogens and vectors to the area, disturbs ecological systems, and causes certain endemic diseases to become epidemic across continents and oceans. Population migration caused by extreme weather or meteorological disasters is often accompanied by infectious disease outbreaks. For example, heavy rain and storms can contaminate drinking water sources, expand the habitats of vector-borne infectious disease hosts, or increase frequency

of contact with humans. During weather-related disasters, low population immunity levels and poor health conditions, along with the gathering of large numbers of people, readily cause outbreaks of epidemics and infectious diseases. It is believed that climate change can put tremendous pressure on worldwide supplies of food and clean water, particularly in Africa and Southeast Asia. This would further stimulate farmland encroachment, deforestation, dam building and other activities, thereby reducing local biological diversity, destroying the ecological environment, and producing rampant vector-borne diseases and zoonosis.

3.2 Conclusions

Under the impetus of global change in both natural and human activities, the occurrence and spread of infectious disease have been altered. Natural factors, especially climatic forcing, influence the outbreak and spread of many infectious diseases. Climate factors, including temperature, precipitation, humidity and sunshine, can affect pathogens, hosts and disease vectors, thereby influencing the occurrence and spread of disease. Furthermore, extreme weather events, such as El Niño/La Niña-Southern Oscillation and the QBO, are related to the transmission of infectious diseases. Droughts, floods and other meteorological disasters are also closely related to the occurrence and spread patterns of various such diseases. The spread of these diseases is associated with land cover type; for example, the first cases of avian influenza are often associated with wetlands and water. Further, vegetation distribution can modify outbreaks, through influencing the food sources of host animals. Many natural factors often work together to affect disease transmission. For example, global warming may significantly impact the hydrosphere via heavy rainfall, floods, storms, heat waves and droughts.

Human activity is an indirect driving force affecting the spread of infectious diseases. Among these activities, international travel and population migration from rural areas to cities are root causes of disease spread. Rapid urbanization accompanied by lagging urban infrastructure, and high risks of infectious disease resulting from urban land use change will alter the pattern of disease and death. Land use changes including agricultural encroachment, deforestation, road and dam building, wetland transformation, mining and urban expansion, have triggered a series of disease outbreaks and changed the transmission pattern of many endemics. Rapid development of aviation, road and railway transportation, not only speeds up the rate of disease spread, but also expands its range. In addition, frequent trade increases the possibility of outbreaks of infectious diseases, and provides the means for long-distance spread of pathogens and diffusion of new pathogens along livestock trade routes. Human activities, including demographic characteristics and health systems, can affect the spread of infectious diseases.

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