Vector-borne Infectious Diseases and Climate Change

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Abstract

Climate change has a variety of impacts on human health including spread of infectious diseases. Vector-borne and water-borne infectious diseases are two main categories of diseases which are forecasted to be most affected.

It has been reported that climate change has altered the distribution of some infectious disease vectors such as mosquitoes and ticks. Many papers have also reported that the climate has influenced epidemics of vector-borne infectious diseases such as dengue fever and malaria. It is forecasted that epidemic and endemic regions of dengue fever and malaria will expand in many areas and probably increase the number of patients. It is also likely that the endemic region of Japanese encephalitis (JE) virus will expand northward and the activity of JE virus will increase in northern Japan. On the other hand, it should be noted that in addition to climate change, multiple biological and sociological factors also influence epidemics of vector-borne infectious diseases. Our current understanding of the effects of climate change on human health, including infectious diseases, is insufficient. Further extensive studies are warranted.

Key words: climate change, dengue fever, global warming, Japanese encephalitis, malaria, vector-borne infectious diseases

1. Introduction

Global warming is an unequivocal phenomenon today and is evident from observations of increases in global average air and ocean temperatures. Global warming is associated with other climate changes, *e.g.*, changes in rainfall, increases in storms. Climate change has a variety of impacts on human health. Many effects have been reported; however, many of the emerging and forecasted effects have yet to be clearly confirmed with scientific data. The emerging evidence of the effect of climate change/global warming on human health and projected trends are summarized in the 4th report of the Intergovernmental Panel on Climate Change (IPCC) (Confalonieri *et al*., 2007). This report states that climate change has altered the distribution of some infectious disease vectors (medium confidence), altered the seasonal distribution of some allergenic pollen species (high confidence), and increased heat wave-related deaths (medium confidence). The projected trends in climate change-related effects include: (1) an increase in malnutrition and consequent disorders, including those relating to child growth and development (high confidence), (2) an increase in the number of people suffering from mortality, disease or injury from heat waves, floods, storms, fires and droughts (high confidence), (3) a change of the range of some infectious disease vectors (high confidence), (4) mixed effects on malaria; in some places the geographical range will contract, elsewhere the geographical range will expand and the transmission season may be changed (very high confidence), (5) an increase in the burden of diarrheal diseases (medium confidence), (6) an increase in cardio-respiratory morbidity and mortality associated with ground-level ozone (high confidence), (7) an increase in the number of people at risk of dengue fever (low confidence), and (8) some benefits to health, including fewer deaths from cold, although it is expected that these will be outweighed by the negative effects of rising temperatures worldwide, especially in developing countries (high confidence). These effects on human health can be divided into direct and indirect ones (Table 1). The direct effects include an increase in mortality especially among those with cardiovascular and and/or respiratory diseases, and an increase in cases of heat stroke due to heat waves. The indirect effects include an increase in the number infectious disease patients, and possibly changes in the patterns of allergies.

Vector-borne and water-borne infectious diseases are two main categories of infectious diseases which are forecasted to be most affected (Fig. 1). There will be an increase in vector-borne infections as a result of an expansion of arthropod-infested areas, an increase in feeding behavior of mosquitoes, an increased rate of

Table 1 Some of the emerging and forecasted effects of climate change on infectious diseases and other human health conditions in the world.

Effects on infectious diseases
• Expansion of mosquito-infested areas and increase in mosquito activity: increase in the number of patients with mosquito-borne infectious diseases (*i.e.*, dengue and malaria) and expansion of epidemic areas.
• Contamination of water and foods with bacteria: increase in the number of patients with water-borne and food-borne infectious diseases.
• Deterioration of environmental and social conditions: increased risk of infectious diseases
Direct effects on other health conditions
• Heat waves: short-term increase in mortality especially among those with cardiovascular and/or respiratory diseases, and increase in heat-shock patients
• Co-effects with air pollution: increases in asthma and allergy patients
• Storms and floods: increases in morbidity and accidental deaths

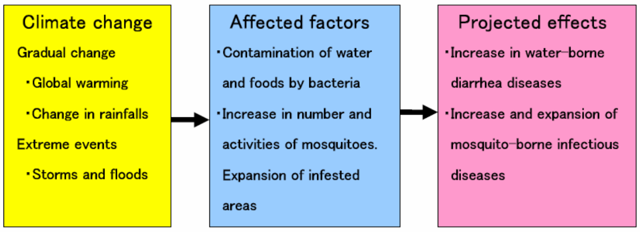

Fig. 1 Projected effects of global warming on infectious diseases.

larval development and an increased speed of virus replication in infected mosquitoes. There will be an increase in diarrheal diseases from bacterial infections due to contamination of water and foods.

2. Effects of Climate Change on Vector-borne Infectious Diseases

Vector-borne infectious diseases are transmitted by infected arthropods. The vectors include mosquitoes, ticks, sandflies, blackflies and triatomid bugs. Major mosquito-borne infectious diseases include dengue fever/dengue hemorrhagic fever, Japanese encephalitis, West Nile fever, Murray Valley encephalitis, Ross River fever, Rift Valley fever and yellow fever, which are caused by viruses, and malaria caused by protozoa. Tick-borne infectious diseases include tick-borne encephalitis, which is caused by tick-borne encephalitis viruses. There is evidence suggesting that some of these vector-borne infectious diseases are affected by climate change.

2.1 Dengue fever (DF) and dengue hemorrhagic fever (DHF)

Dengue fever and dengue hemorrhagic fever are the most important vector-borne viral infectious diseases in the world (Kurane & Takasaki, 2001; Kurane, 2007). There are four serotypes of dengue virus, dengue virus types 1, 2, 3 and 4. Although these are called the four serotypes of the dengue virus, it is generally accepted that these four dengue viruses are antigenically-related different species. Humans are natural hosts of dengue viruses, and dengue viruses are maintained between mosquitoes and humans in nature. Dengue viruses are transmitted to humans by infected mosquitoes, mainly *Aedes aegypti* and *Aedes albopictus*. Dengue virus infection can be asymptomatic or cause two forms of illness, dengue fever and dengue hemorrhagic fever, although the majority of dengue viral infections are asymptomatic. Dengue fever is a self-limited febrile illness accompanied by retro-orbital or frontal headache, etc. Myalgia and bone pain occur soon after the onset of the fever. A small percentage of patients infected with the dengue virus demonstrate plasma leakage into interstitial spaces, thrombocytopenia and also hemorrhagic manifestation. This severe life-threatening syndrome is called dengue hemorrhagic fever. Dengue fever and dengue hemorrhagic fever are a serious cause of morbidity and mortality in most tropical and subtropical areas of the world: mainly Southeast and South Asia, Central and South America, and the Caribbean (Fig. 2). There are approximately 2.5 billion people at risk in the world for infection with dengue viruses. Nearly 100 countries and areas are at risk for domestic dengue virus infections. Dengue cases are estimated to occur in up to 100 million people annually. A total of approximately 500,000 cases of DHF occur annually. Large epidemics of DF/DHF are usually caused by *Aedes aegypti*, while *Aedes albopictus* causes only small outbreaks.

It has been reported that there is an association between epidemics of dengue fever and climate (Hales *et al*., 1999; Hales *et al*., 2002; Corwin *et al*., 2001; Gagnon *et al*., 2001; Cazelles *et al*., 2005). However, these reported associations are not always consistent, probably due to the complexity of climatic effects on transmission, and also due to the presence of other factors. Heavy rainfall or high temperature can lead to an increase in transmission; however, there are reports that drought can also be a cause of an increase in dengue epidemics, when household water storage increases the number of suitable mosquito breeding sites (Pontes *et al*., 2000; Depradine & Lovell, 2004; Guang *et al*., 2005). It has been reported that density maps of *Aedes aegypti* based on temperature, rainfall, cloud cover are consistent with the distribution of dengue fever (Hopp & Foley, 2003). The model of vector abundance has demonstrated a good agreement with the distribution of reported dengue cases in some areas of the world (Hopp & Foley, 2003).

2.2 Malaria

Malaria is considered to be the most important vector-borne infectious disease in the world. There have been many reports which suggest climate change affects malaria. Climate has had an influence on the distribution, intensity of transmission and seasonality of malaria in sub-Saharan Africa (Hay *et al*., 2002; Craig *et al*., 2004). The El Niño Southern Oscillation (ENSO) phenomenon

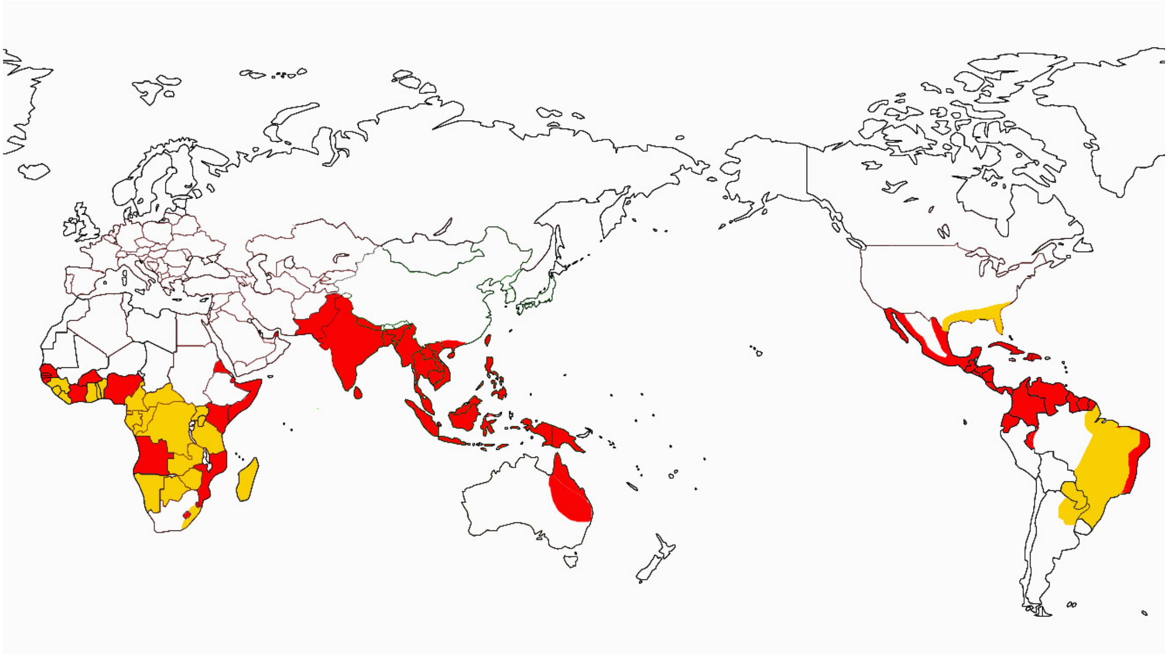

Fig. 2 Distributions of dengue epidemics worldwide. Red: areas where dengue epidemics have been reported. Yellow: areas where presence of *Aedes aegypti* is confirmed. (from the Website of Center for Disease Control and Prevention, U.S.A.)

has had an impact on the risk of malaria epidemics in southern Asia and South America (Kovats *et al*., 2003). Associations between interannual variability in temperature and malaria transmission were reported in Africa. It has also been reported that the minimum temperature at the start of the transmission season accounted for the variability in malaria epidemics between years in Madagascar (Bouma, 2003). The number of cases admitted with malaria was associated with rainfall and high maximum temperatures 3-4 months previously in Kenya (Githeko & Ndegwa, 2001). Malaria morbidity data from the late 1980s to the early 1990s in Ethiopia indicated that epidemics were associated with high minimum temperatures in the preceding months (Abeku *et al*., 2003). On the other hand, there has been no clear evidence that malaria has been affected by climate change in South America (Confalonieri *et al*., 2007) or in the Russian Federation (Semenov *et al*., 2002). Although many reports have indicated a relationship between climate and malaria transmission dynamics, it should be stressed that there is still much uncertainty about the potential impact of climate change on malaria at local and global levels (Confalonieri *et al*., 2007)

2.3 Japanese encephalitis (JE)

2.3.1 Epidemiology of JE in Japan

Japanese encephalitis (JE) is a serious viral encephalitis with a high mortality rate and a high percentage of neuro-psychiatric sequelae. JE occurs endemically and in annual epidemics in many Asian countries (Oya & Kurane, 2007). Approximately 50,000 cases are reported annually worldwide. The disease is caused by the bite of JE virus-infected mosquitoes. JE is an especially important disease in East, Southeast and South Asia (Fig. 3). The endemic regions have expanded recently to New Guinea and northern Australia. JE virus is the only mosquito-borne virus that is endemic and causes human disease in Japan at this point.

JE virus is maintained in nature between vector mosquitoes and domestic pigs in endemic regions. The principal vector of JE virus is *Culex tritaeniorhynchus* in most endemic areas of Asia, including Japan. *C. tritaeniorhynchus* reproduces in rice paddies and the connecting canals. Pigs are also considered an amplifier for JE virus in the temperate zone. Thus, pigs are the amplifier as well as the natural host of JE virus in the transmission cycle of JE virus in human residential areas. In temperate areas, the vector mosquitoes start to be detected in May, then seroconversion of pigs occurs and occurrence of human cases follows.

It is understood that the number of JE patients is affected by multiple factors; the activity and numbers of JE virus-infected mosquitoes, location of pig farms, immune status of humans, preventive measures against mosquitoes, etc. Especially in countries like Japan where JE vaccination has been strongly implemented and most of the people have protective immunity against JE virus, the threat of JE is not reflected by the number of patients. Pigs are not immunized with JE vaccine except for sows expected to give birth. Pigs are usually killed to be shipped to market before six months of age in Japan. Most pigs are born after the JE season is over in the previous year; thus, they are naïve to JE virus before the current year's epidemic season starts. Naïve pigs are highly susceptible to JE virus and easily infected with it by the bite of infected mosquitoes. Pigs develop high and sustained levels of viremia after infection, and high levels of specific antibodies. These indicate that the seroconversion rate among sentinel sero-negative pigs reflects the prevalence of JE virus in the

Fig. 3 Distribution of Japanese encephalitis (JE) worldwide.

area. In Japan, seroconversion rates of sentinel pigs have been checked in most prefectures every year. Seroconversion usually starts in May or June in Okinawa, the southernmost prefecture, and in July in other southern prefectures. The sero-positive area gradually moves up north. Seroconversion is detected in most prefectures by the end of October. Thus, the sentinel pig system is useful for estimating the JE risk in humans and activity of JE virus-infected mosquitoes.

2.3.2 Effects of climate change on the seroconversion rate to JE virus in pigs

JE surveillance was implemented in 1965 under the National Epidemiological Surveillance of Vaccine Preventable Diseases program by the Ministry of Health and Welfare (currently the Ministry of Health, Labour and Welfare) in Japan (Arai *et al.*, 2008). This surveillance includes (i) confirmation of notified JE cases, (ii) prevalence of JE antibodies among the general population, and (iii) seroconversion rates of sentinel pigs nationwide. Seroconversion rates to JE virus among sentinel pigs are assessed by measuring specific antibodies to JE virus approximately 2-3 times a month from May or June to October. Seroconversion rates in sentinel pigs of the year are shown for each participating prefecture from 1972 to 1995 (Fig. 4). Although seroconversion rates differed year by year especially in northern Japan, high levels of seroconvertion rates were observed every year in southern Japan.

For further analysis, the average percentages of seroconversion rates among sentinel pigs were calculated for each participating prefecture in 1982, 1990, and 1993-2000. Meteorological data at multiple sites in each prefecture are available from the 1980s. The data of (1) average day temperature, (2) highest temperature of the day, (3) number of days with the highest temperature being 30^{o}C or higher and (4) average amount of rainfall, were collected for 47 prefectures during three summer months including July, August and September in 1982, 1990 and 1993-2000. The meteorological data obtained at the same or closest sites to the pig farms or slaughterhouses were used for the analyses along with the final seroconversion data in pigs.

The relationship between the seroconversion rate to JE virus and categories of meteorological data during the summer season were examined by linear regression analysis. There were positive relationships between seroconversion rates in pigs and each of three categories of meteorological data: the highest daytime temperature, average temperature during the three months and the number of days with the highest day temperature being 30^{o}C or higher. No significant positive relationship was found between the seroconversion rate and average rainfall. These results indicate that in years when the temperature is high during summer, seroconversion rates in sentinel pigs are higher and high levels of seroconversion in sentinel pigs are observed even in prefectures located in northern Japan. Thus, if global warming continues, it is possible that the activity of JE virus, *i.e.*, activity of JE virus-infected mosquitoes, will become constantly high even in northern Japan, probably including Hokkaido, the northernmost island. These trends, however, will not directly increase the number of JE patients if appropriate countermeasures are taken, *i.e.*, strong implementation of JE vaccination.

2.4 Other vector-borne infectious diseases

There is some evidence of climate-related shifts in the distribution of tick vectors. Northern or altitudinal shifts in tick distribution have been reported in Sweden and Canada (Lindgren & Talleklint, 2000; Lindgren & Gustafson, 2001; Barker & Lindsay, 2000), and also altitudinal shifts in the Czech Republic (Daniel *et al.*, 2004). Geographical changes in tick-borne infections

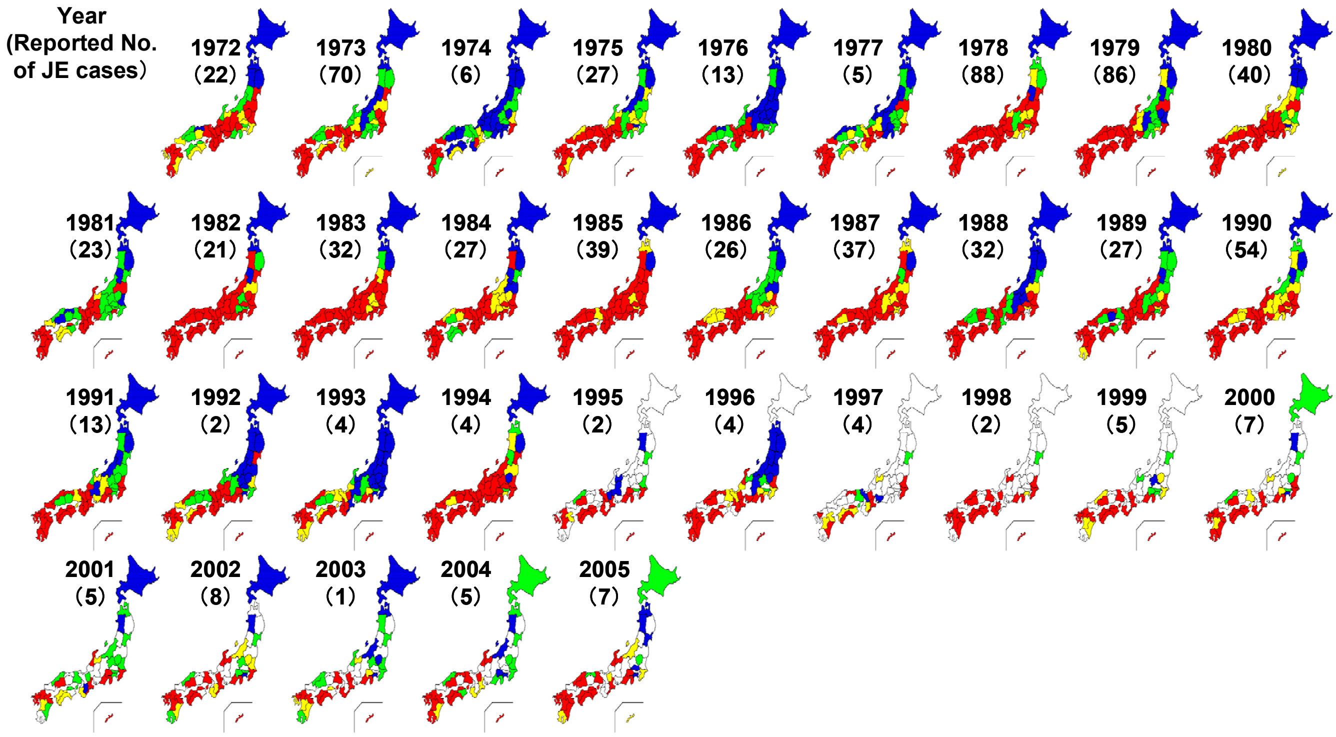

Fig. 4 Seroconversion rates to Japanese encephalitis virus in sentinel pigs in each prefecture from 1972 to 2005. The numbers in parentheses indicate reported human JE cases. Red: 80%, yellow: 50%-80%, green: <50%, blue: no seroconversion, white: not tested. (Data from National Epidemiological Surveillance of Vaccine Preventable Diseases program, the Ministry of Health, Labour and Welfare, Japan)

were also observed in Denmark (Skarphedinsson *et al.*, 2005). A severe outbreak of Murray Valley encephalitis reportedly occurred after heavy rainfall and flooding in southern Australia, and ENSO has been proposed as a predictive tool (Nicholls, 1986). Heavy rain or floods can cause outbreaks of Ross River fever, due to increased breeding of mosquitoes (Mackenzie, J. *et al.*, 2000)

3. Some Considerations to be Addressed

It is expected that research on the effects of climate change on infectious diseases will become much more active. There are some concerns to be addressed in this research. The number of patients with infectious diseases can be affected by multiple factors. It is generally agreed that infection with pathogens does not always lead to disease. The asymptomatic infection rate is often greater than the symptomatic one with many pathogens. There are differences in virulence among strains in each species of pathogen. Thus, the number of symptomatic infections can vary depending on the level of virulence of the dominant strains within each pathogen. Furthermore, changes in human disease can be modified by levels of accuracy of surveillance and reporting systems, disease control measures, the immune status of the affected population, population changes and other factors such as changes in land-use and agricultural techniques (Kovats *et al.*, 2001; Rogers & Randolph, 2006). Thus, in the studies of the effects of climate change on infectious diseases, multiple biological and sociological factors should be taken into account.

4. Conclusions

It is expected that the levels of impacts of climate change on infectious diseases will differ among regions, depending on their infrastructure. In Japan, we cannot say that the impacts of global warming on infectious diseases are apparent at this point yet. However, it is expected that these impacts will appear in one form or another if climate change/global warming continue to progress in the future. Although studies of the effects of climate change on vector-borne infectious diseases have made much progress in recent years, there is still a lack of evidence rather than an absence of effects (Kovats *et al.* 2001). At the present time as well, research on the impacts of climate change/global warming on infectious diseases and on future prospects should be conducted in a wide range of research fields.

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