Commentary

Re-emergence of Chikungunya and other scourges: the role of globalization and climate change

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Summary. Globalization and climate change are important phenomena in a changing world. To date, only the effect of globalisation on infectious diseases, from vector-borne to respiratory infections, has been well established. The influence of cyclic natural climatic events and local variations in temperature and precipitation has also been recognised; however, there is still no conclusive evidence of an effect of global warming on infectious disease patterns.

Key words: globalization, climate change, infectious diseases, Chikungunya.

The transition to the new millennium has been marked by a series of events that may affect the health of human beings. Among them, globalization and environmental change, including climate change, have the potential to influence the emergence and re-emergence of infectious diseases.

GLOBALIZATION AND INFECTIOUS DISEASES: A HISTORICAL PERSPECTIVE

Human concentration is a key factor in the persistence of infectious diseases. The historian W.H. McNeill accurately described how infectious diseases began to constitute a threat for humanity when, after the early agricultural settlements, overcrowded towns began to arise [1]. Actually, the appearance of viral diseases (*i.e.*, those diseases that McNeill referred to as "diseases of civilization", which are today known as standard childhood diseases) was due to the transition from small hunting-gathering tribes to larger agriculture-based communities, and the appearance of these disease perhaps lagged no more than 1000 years behind the emergence of human populations large enough and in sufficient communication with one another to sustain these diseases [2]. It is now estimated that a minimum population size of about 400 000 inhabitants is needed to sustain the circulation of infectious agents. The first known examples date back to around 2000 BC, in particular, in Mesopotamia, where a dozen towns were interconnected, and in the Nile Delta in Ancient Egypt.

With the emergence of other civilizations, human movement and trade favoured the spread of infectious diseases from one area to another. In fact, globalization is by no means a new phenomenon: the movement of people through Eurasia dates back at least 2000 years, to the era of the ancient Silk Road trade route, with the global spread of infectious diseases following a parallel course. In fact, the emergence and spread of infectious disease can, in a sense, be considered to be the epitome of globalization, with the world becoming one giant breeding ground for microbes. By Roman times, between 165 and 180 AD, smallpox had reached Rome, during the Plague of Antoninus, and three centuries later the bubonic plague hit Europe for the first time (542-543 AD) as the Plague of Justinian, via world trade routes [3].

Another example of the effect of partial globalisation is represented by the "black death" pandemic, which ravaged Italy and Europe in 1347 at the height of the Mongol Empire. The major determinant of this global plague was probably the opening of northern routes throughout the Asian prairies, which, along with the old silk routes connecting China to Siria, were covered by Mongol horsemen,

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caravanserai, postal couriers and soldiers. Infected mice and their fleas, hidden in grain sacks, transported *Pasteurella pestis* from east to west, through a globalised Euro-Asian human network which connected the Mongol headquarters in Karakorum with Kazan' and Astrachan' on the Volga River, Caffa in Crimea with Khanbaliq in China, and with numerous caravanserai, up to Aleppo. From the Aegean ports, rats, fleas and bacteria then spread to the Mediterranean coasts and to the rest of Europe [1].

The discovery of America provided further opportunities to germs to spread beyond old borders. A classical example of that is represented by the spread of measles and smallpox from the Old World to the Americas, which probably favoured the conquest of the Aztec and Incas lands by the Spaniard conquerors Cortés and Pizarro. Whether the epidemic of syphilis, which appeared at the time of the discovery of the New World, was due to germ migration in the opposite direction is still a matter of debate. What is certain is that, during the following years, several agents started to "migrate" and to colonise the Americas via the transoceanic routes, such as the yellow fever virus and *Plasmodium malariae*, which were unwittingly introduced by African slaves.

Faster ship, train, airplane: technological development changed human lifestyle during the last century, favouring the occurrence of global pandemics. The "Spanish" flu epidemic, which occurred at the time of the "Great War" is probably one of the first examples of the consequences of the spread of an infectious agent through an interconnected world. Other flu pandemics, like those of the "Asian" and "Hong Kong" influenza viruses, are now considered as paradigms of the global threat of emerging infectious diseases in the modern world.

Today, human pathogens are experiencing yet another bonanza from a new era of globalization, characterized by faster travel over greater distances and worldwide trade. The emergence and increased utilization of high-speed transportation, in particular, has further transformed the experience of distance and space and contributed to creating the conditions for the spread of infectious agents throughout the largest global community that has ever existed. A "global village" of billions of people creates fertile ground for the spread of a variety of germs, and the AIDS pandemic is the demonstration that a new virus may silently spread from the centre of Africa to all parts of the world, causing devastating pandemics within a few decades. However, acute infections with a short incubation period may do even better. Only a few years ago, in early 2003, the World Health Organisation launched a global alert after a number of fatal cases of pneumonia were reported in Hong-Kong [4]. The outbreak of Severe Acute Respiratory Syndrome (SARS), due to a "new" human coronavirus (SARS-CoV) that had emerged in the southern Chinese province of Guangdong in November 2002, was successfully under control by June 2003, after a series of outbreaks in the Far East, from Hong-Kong to Hanoi and from Singapore to Beijing, as well as in distant locations such as Toronto. For the first time, air transportation was considered to be the cause of an unprecedented global crisis which threatened the right to human mobility.

THE EFFECTS OF CLIMATE AND CLIMATIC CHANGES ON INFECTIOUS DISEASES

Climate change (*i.e.*, global warming) is also a factor that may potentially increase the infectious-disease burden in a rapidly changing world. Human societies have a long history of experience with naturally-occurring climatic vicissitudes consequent to climatic cycles. More acute events include disasters and disease outbreaks, which have often occurred in response to extreme regional climatic cycles, such as the El Niño Southern Oscillation (ENSO) cycle. Today, in addition to natural cycles, human activities are altering the world's climate by increasing the atmospheric concentration of energy-trapping gases, thereby amplifying the natural "greenhouse effect" that makes the Earth habitable. Global temperature has increased by around 0.4 ºC since the 1970s and now exceeds the upper limit of natural (historical) variability. Moreover, climate change is represented by changes not only in temperature but also in the pattern of other climatic factors, such as humidity and precipitation; these might also be affected by changes, accordingly. Whether, and in which direction, changes in world climate have an impact on human health remains largely undefined. Some aspects of the impact would be beneficial. For example, milder winters would reduce the seasonal winter-time peak in deaths that occurs in temperate regions, whereas in tropical regions a further increase in temperatures might reduce the viability of disease-transmitting mosquito populations. Overall, however, scientists consider that most of the health impact of climate change would be adverse [5].

Disease outbreaks are often known to be influenced by local weather, yet the way in which changes in disease trends are affected by long-term global warming is more difficult to establish [6].

The influence of climatic factors on the activity of some vector-borne infections is well known. For example, in a study conducted in northern Sardinia, we found an association between in-

cidence peaks in Spotted Mediterranean Fever, a tick-borne infection due to Rickettsia conorii, and temperature peaks one year earlier [7]. Warm ENSO events that increase precipitation in East African regions (and that may result in droughts in southern Africa) have also been associated with the occurrence of Rift Valley Fever outbreaks in Kenya [8]. Apparently, this finding is somewhat inconsistent with those of a study on Chikungunya infection, which showed an association between drought and the emergence of the viral infection along coastal East Africa [9].

Evidence of the possible effects of long-term warming is even weaker. A study on Tick-borne encephalitis (TBE) in Europe did not reveal any obvious differences between sites where TBE did or did not emerge, and in Sweden increases in TBE pre-dated the onset of warmer springs and winters [10]. In African highlands, where the incidence of malaria had been increasing since 1976, no significant change in long-term climate was detected [11]. However, these results were disputed by other authors [12]. Moreover, based on the assumption that the parasite develops much more quickly in the mosquito when temperatures exceed 19 °C, other authors implicated increases in temperature in the return of malaria to Kenya's highlands, where a combination of insecticide and cool temperatures had eradicated the diseases in the 1960s [13].

Respiratory infections might also be influenced by climate change. In fact, the seasonality of these infections in temperate areas is well known. Furthermore, strong cold ENSO phases, which have been associated with lower temperatures and higher humidity in winters in Europe, have been associated with larger and more severe influenza epidemics in France [14]. Regarding the possible effect of global warming, there is already some evidence that, because of milder winters, the incidence of some of these infections is decreasing; in particular, a decrease in the incidence of Respiratory Syncytial Virus infections has been reported in England in recent years [15]. Thus, as demonstrated by these findings, the possible effects of global warming are unpredictable and may drive to opposite outcomes.

A TROPICAL VIRUS REACHES ITALY: GLOBALIZATION OR CLIMATE CHANGE?

An event that is exemplary of the possible effects of globalization and climate change is the Chikungunya outbreak in Italy in the summer of 2007, when a tropical virus introduced by a man from Kerala (an Indian district affected by a large outbreak) infected local mosquitoes (*Aedes albopictus*, also defined as "tiger mosquito"), which transmitted the infection to other persons [16]. Although the role of climate change was emphasised in the scientific debate following the event [17], the Italian climate has always been suitable for *Ae. Albopictus* to flourish during the warm season. It appears, rather, that the epidemic was the result of the globalisation of vectors and humans [18-20], which occurred through a two-step process: i) the introduction and adaptation of *Ae. albopictus* to a new environment (*i.e.*, an area with a temperate climate); and ii) the introduction of CHIKV in a previously infection-free country as a product of population movement. However, the epidemic was limited in space and time, probably because of appropriate control measures and the time-limited capacity of the vector to sustain infection transmission beyond the hot season in a country with a temperate climate.

CONCLUSIONS

Globalization and climate change are important phenomena in a changing world. Although both may play a role in changing patterns of infectious diseases, to date only the effect of globalisation has been well established. With regard to climate, its influence on infectious diseases patterns has been recognised (*i.e.*, different disease distribution for temperate and tropical areas, seasonality of respiratory infections in temperate climates, etc.), as well as the effects of cyclic events like ENSO and local variations in temperature and precipitations; however, there is still no conclusive evidence of an effect of global warming, though whether this will continue to be the case in the future cannot be predicted.

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