CHAPTER 2

The Perfect Storm: Climate, Ecosystems and Infectious Diseases

Fernando J. Torres-Vélez • Corrie Brown

The studies of emerging diseases and environmental changes are linked together in a manner reminiscent of the old adage about the forest and the trees. Each new disease that occurs is studied in significant depth, that is, with an intense focus, as on a single tree. However, it is often the overall environmental changes, or the proverbial forest, that is the greatest influence on the actual emergence of that disease. In recent decades the world has experienced a plethora of new and reemerging pathogens – human immunodeficiency virus, Hantavirus, Nipah virus (NiV), severe acute respiratory syndrome, Rift Valley fever, and bluetongue among others. A common denominator in the appearance of these diseases has been some modification of the environment, intensification or regional variations of normal atmospheric phenomena such as El Niño-Southern Oscillation (ENSO), as well as more specifically human-induced environmental changes.[1] Some of these anthropogenic factors are habitat encroachment by the growing human population, putting humans in closer contact with animals harboring pathogens previously unknown to infect people. Other instances involve impacts that humans have been having on the environment for decades, brewing today's global climate changes. Over the last decade, the scientific investigations into climate change have expanded logarithmically and now comprehensive and elegant multidisciplinary studies are beginning to illuminate potential disease problems due to climate change.

Climate is usually defined in a specific area as the "average weather," the mean and variation of atmospheric components such as temperature, precipitation, and wind, over time, traditionally 30 years. The overall global climate is powered by a fraction of the total solar radiation reaching the planet. Approximately one-third of all the incoming solar energy never makes it to the Earth's surface but rather is reflected back to space by atmospheric components. Of the remaining two-thirds absorbed by the Earth, an equal amount must be radiated back to space, to prevent an ever-increasing surface temperature. Clouds and gases, such as water vapor and carbon dioxide (CO_2), absorb much of the thermal radiation emitted by land and oceans, retransmitting it to Earth in a desirable greenhouse effect. This natural greenhouse effect allows for temperatures that are compatible with life processes as we know them. Water vapor and CO_2 are the most important greenhouse gases and significant increases in either can cause an enhanced greenhouse effect which has an overall effect of climate warming. Oceans and plants serve as natural CO_2 buffers by absorbing a great deal of what is generated. However, human activity is offsetting this natural system by burning fossil fuels and clearing forests.[2]

In addition to the anthropogenic contribution to global warming, external factors such as volcanic eruptions can have a major impact on the global climate. This was clearly illustrated in 1991 after Philippine's Mount Pinatubo's eruption when a global cooling and drying of the atmosphere was recorded.[3] Also there are poorly understood, coupled air–sea climatic events, such as ENSO, which can alter the climate of vast geographical areas for extended periods of times. During the ENSO, there is a reversal of surface air pressures between the eastern and western tropical Pacific, bringing a weakening and often reversal of trade winds. This allows for warmer water from the western Pacific to flow toward the east and build up off the coast of South America. The change in trade winds brings rain to the dry eastern Pacific, leaving extensive drought in the western Pacific. Volcanic eruptions or ENSO can be influenced by or combined with anthropogenic-induced global warming to augment further climate changes or contribute to adverse climatic events.[4–7]

A global authority on climate change was established by the United Nations Environment Programme and the World Meteorological Organization in 1989 in the form of the Intergovernmental Panel on Climate Change (IPCC). The IPCC is composed of scientists from around the world who review and assess scientific and technical data relevant to the understanding of climate change. They are charged with providing the world with a clear scientific view on the current state of climate change and its potential environmental and socioeconomic consequences. This panel has concluded that the observed climate changes cannot be explained by just natural factors. There is agreement that disease incidence and distribution are likely to change, although the manner in which this will happen is complex and difficult to specify.[2]

Below are three examples of infectious diseases that have emerged as a result of some of the climatic changes described above. The first, bluetongue, and its spread into northern Europe may be the only clear example of disease spread directly related to global warming. The second, Rift Valley fever, has reemerged several times in Eastern Africa in recent years, largely as a result of expanded ENSO impacts. The third, NiV, emerged in Malaysia due to a combination of direct anthropogenic effects and socioeconomic pressures, combined with ENSO effects.

BLUETONGUE

Bluetongue virus extension into northern Europe is undoubtedly the best example of a livestock disease expanding its range based on climate change, although the intensive outbreaks experienced in the last 2 years demonstrate the multiplicity of factors that play a role.

Bluetongue is an arthropod-borne disease, capable of infecting all ruminants, but with most severe clinical disease in sheep, in which there is severe depression, lameness, and often facial and tongue swelling, and abortion in pregnant animals. In cattle there is usually minimal clinical disease, but these animals can remain viremic for months, and so serve as the main reservoir of infection.[8] Bluetongue virus (BTV) is a segmented dsRNA virus in the Orbivirus genome, family *Reoviridae*. The disease is endemic in much of Africa and over large segments of the Americas, with distribution coinciding with the range of *Culicoides* spp., the responsible insect vector. The main Asian-African vector is *Culicoides imicola*. The disease has occurred in North Africa and the Middle East, making sporadic incursions into southern Europe, as *Culicoides* are easily transported on wind. The "envelope" or range of usual *C. imicola* distribution includes the southernmost parts of Europe, which are the regions that have been

sporadically affected by bluetongue over the last few decades. Farther north in Europe, there are other *Culicoides* species known as the Palearctic species, *C. pulicaris* and *C. obsoletus.* Although both had been proven to be capable of transmitting bluetongue experimentally, they were not functioning in the natural epidemiology of infection prior to 2008.

Over the last several years, there have been documented increases in nighttime and winter temperatures and also changes in moisture conditions.[9] Warming trends in Europe created an environment for enhanced replication and survival of all of these *Culicoides* species, and, in some cases, shortened cold periods allowed for the vectors to persist throughout the winter. The range of *C. imicola* has expanded in recent years with the expansion shown to be coincident with warming.[10] The warming not only improved and expanded the populations of *Culicoides*, but also enabled enhanced viral replication within the vector.

Several strains of BTV have made incursions into Europe since the late 1990s. One of these, BTV-8, came from Africa and moved through Italy and up into Germany and the United Kingdom, affecting areas that had never before experienced bluetongue disease. It is hypothesized that the enhanced *C. imicola* population in southern Europe helped to fuel an outbreak. With expanding populations of *C. imicola* and the Palearctic species, there was more extensive overlap of these different species. A "handover" event occurred probably multiple times, in which the new host species picked up the virus from the endemic host. Once the virus was established within the Palearctic species, it was able to move to more northerly climes.[11] The increased temperatures in these more northerly areas, especially the shortened winter period, ensured that the Palearctic species would survive through the season during which BTV would have otherwise been expected to die back. As a result, there was sustained transmission of the disease in new areas.

This extension of BTV into northern Europe resulted in disease in many countries that had never before experienced the disease. More than 3000 outbreaks of bluetongue were reported to the World Organization for Animal Health in 2008 from northern European countries, and hundreds of thousands of ruminants died or were euthanized to prevent spread.[12]

RIFT VALLEY FEVER

Rift Valley fever virus is a segmented, enveloped, single-stranded RNA virus in the genus *Phlebovirus*, family *Bunyaviridae*. It has a wide variety of hosts but severe disease is seen most commonly in ruminants, especially sheep and goats, where it can present as an "abortion storm," death of neonates, and hepatic disease. It is also zoonotic and in humans presents as a febrile, flu-like illness, with some experiencing severe liver pathology or vascular complications. Mortality in humans ranges from 1% to 5% but in some outbreaks has been much higher.[13,14]

The virus is transmitted transovarially in mosquitoes and, under dry climatic conditions, can survive in *Aedes* mosquito eggs for years and maybe decades. With excessive rainfall, the mosquito eggs will hatch, and carry virus to susceptible ruminants, which experience a high viremia. Then *Culex* mosquitoes serve to transport the infection from animal to animal and, occasionally, animal to human.

The disease was first described around Lake Naivasha, in the Kenyan portion of Africa's Rift Valley, in 1930, and remained confined to the larger geographic zone of the Rift Valley for more than 40 years, with sporadic outbreaks occurring, usually associated with heavy rainfall.[15]

However, since 1977, Rift Valley fever has been recorded outside this zone on multiple occasions, all of which are associated with increases in flooding allowing for extensive mosquito replication. In 1977, Rift Valley fever surfaced in Egypt, and there was an extensive outbreak involving thousands of human and animal cases. Building of the Aswan dam in the years prior to this outbreak was probably an important factor as this hydrological project permitted controlled flooding of agricultural lands and subsequent enhanced mosquito habitats.[16] Then, in 1987, there was another outbreak, this time across the continent to West Africa, in Mauritania. In this case, Rift Valley fever occurred subsequent to completion of the Diama dam on the Senegal river, another project that created increased standing water for mosquito amplification.[17] In both of these cases, Egypt and Mauritania, there were human-induced changes to the environment, in the form of dam-building which created more standing water and therefore greater habitat possibilities for vectors of disease.

In 1997, there was a large outbreak in the Horn of Africa, beginning in northern Kenya and eventually moving to affect five different countries in the region, with large losses of domestic ruminants and extensive human infection.[18] This outbreak was attributed to excessive rainfall, which was brought about by the ENSO effect.[19] Then again in 2006–2007 there was another less extensive outbreak in the Horn of Africa, also attributed to heavy rainfall due to ENSO. However, by the time of this outbreak, climatic prediction models had been developed, and so sufficient warnings of a potential outbreak were distributed 2–6 weeks before the outbreak, dampening the overall impact because of preparedness and mitigation efforts, involving prompt suspicion and documentation of the diagnosis with aborted or ill animals and selected use of the available vaccine, isolation, and mosquito precautions and control.[20]

NIPAH

NiV is a newly described virus belonging in the *Henipavirus* genus of the *Paramyxoviridae* family. It emerged in Malaysia in the late 1990s in both humans and swine. In pigs, the disease occurred primarily as a respiratory ailment, with severe coughing, and was initially called "barking pig syndrome." The virus replicated in the respiratory tract of pigs and presumably was disseminated by aerosol to humans who developed a multisystemic disease, with predominant encephalitis and high case-fatality rate. During the course of the outbreak, there were 105 human deaths, almost all of which were closely associated with pig rearing or slaughter. To control the disease approximately one million pigs were slaughtered. The disease has reappeared, on a much smaller scale, in small clusters in humans in India and Bangladesh, but without any associated swine disease.[21–24]

Early molecular characterization of NiV revealed its relatedness to Hendra virus (HeV), another novel *Paramyxovirus* previously discovered in Australia only a few years before.[25,26] As HeV was shown to have a reservoir in pteropid bats (large fruit bats called flying foxes), these animals were studied for a possible role in NiV epidemiology. Approximately 3 years after the initial outbreak in Malaysia, NiV was isolated from the urine of these bats as well as from partially eaten fruits consumed by the animals.[27] Subsequent detection of NiV antibodies and RNA in bats' saliva and urine in Thailand, Cambodia, and India further strengthened the hypothesis that flying foxes of the genus *Pteropus* were the natural reservoir.[28–30]

With subsequent outbreaks taking place without pigs as the intermediate host, the ecologic and epidemiologic picture of NiV became more intricate and complex than originally thought. What was the role of pigs during its first emergence? What factors promoted infection of pigs during the first emergence?

During the 1990s, swine production in Malaysia moved to a more intensive system with high turnover of piglets. In addition, most farms were often combining fruit production with the use of pig waste as fertilizer, resulting in many trees overhanging pigpens. Extensive slash and burn practices in the region and an extended dry season brought up by the ENSO promoted changes in migration patterns of the *Pteropus* bats to areas of plentiful food availability, the pig/fruit farms.[31] It is believed that the combination of these production techniques, land use, and climate changes provided the ideal conditions for NiV's emergence in swine, from which it was aerosolized easily to humans. A unique set of factors brought two species with historically distinct ecological niches into close contact. Furthermore, the intense production practices allowed for a subtle introduction, circulation, and establishment of the virus into a new amplifying host, the pig. Retrospective serologic studies indicate that the first human cases in Malaysia predated the 1997 outbreak, indicating that the virus may have been circulating at low levels prior to the known emergence. The intensive management (high turnover of piglets) likely

allowed a small amount of virus in select pigs to be widely circulated through transport and extensive sales associated with the rapidly developing intensive swine industry. As more animals became infected, there was increased possibility for transmission to people, and an outbreak occurred in the human population.[32] Recent outbreaks in India and Bangladesh have been attributed to direct contact with the bat's body fluids.[24,33]

CONCLUSION

As we continue contributing to global climate changes, modifying and encroaching into new habitats, there will undoubtedly be new instances of disease emergence and modifications of existing epidemiologic patterns.

To pinpoint emerging problems at their source and help to prevent their spread, it will be critical that health professionals become aware of the potential for novel or unexpected infections and to work more closely with veterinary, agricultural, and climate experts to understand better and control these emerging and expanding global health threats.

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