

Supplementary Background Information

Potential Influence of Climate Change on Vector-Borne and Zoonotic Diseases:

A Review and Proposed Research Plan

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Vector-Borne and Zoonotic Diseases – Definitions and Importance

Vector-borne diseases are those for which the pathogen is transmitted to or among humans by an arthropod vector. The property of being borne by flying or otherwise motile vectors has contributed to the facility with which vector-borne diseases are introduced into and spread among human populations. Although most vector-borne diseases are zoonotic (caused by pathogens that are transmitted between vertebrate animals and humans), several that have been long-established in human populations (e.g. malaria, dengue) are transmitted from human to human by an arthropod vector and no longer require the participation of an animal reservoir in the transmission cycle. The distribution of these non-zoonotic vector-borne diseases is limited to the distribution of their vectors, although the vector is sometimes present where the disease is absent or rare (Reiter et al. 2003), suggesting the risk of re-emergence of some of these diseases. The incidence of non-zoonotic vector-borne diseases in humans is determined by the behavior and population dynamics of the vector, as well as human behavioral, cultural and land use factors. Arthropod vectors are especially sensitive to local climate. Because they are ectothermic, temperature profoundly affects their development, behavior and population

dynamics. Precipitation can affect the availability of breeding habitat for vectors with aquatic immature states and thereby can be an important determinant of their distribution.

The zoonotic diseases, those caused by pathogens that require a vertebrate host other than humans, are of increasing importance. One reviewer determined that 61% of infectious diseases are zoonotic, and of those infectious diseases considered to be “emerging”, 75% were zoonotic (Taylor et al. 2001). The zoonotic diseases include vector-borne and non-vector-borne zoonoses.

The distributions of the vector-borne zoonotic diseases are restricted to those areas where the range of the vector overlaps that of a competent host that serves as a source of infection for the vector and, in some instances, acts as a reservoir for the pathogen. The incidence of these diseases in humans is tied to the development, behavior, and abundance of both the arthropod vector and the vertebrate host, making understanding and predicting the response of these diseases to climate change more difficult. Many of these diseases are of tremendous importance to human health. Chagas disease affects 16 to 18 million people in Latin America and leishmaniasis affects 1.5 million persons per year worldwide. Lyme disease is the leading vector-borne disease in the United States and accounts for approximately 20,000 cases of human illness each year in the US alone (CDC 2007). West Nile Virus (WNV) is the leading cause of arboviral encephalitis in the US with approximately 1.5 million estimated infections in the US since the disease emerged in 1999.

The agents of the non-vector-borne zoonoses are transmitted from vertebrate animals to humans by direct or indirect contact and do not require the participation of a vector in the transmission cycle. Indirectly transmitted non-vector-borne zoonoses

include those caused by water-borne and food-borne agents. The potential impact of water-borne zoonoses in the context of climate change is important and has been reviewed (Dangendorf 2004). The line between directly and indirectly transmitted zoonotic pathogens often blurs because some pathogens may be transmitted by either direct or indirect mechanisms. The hantaviruses, for example are transmitted directly by rodent bite or other direct contact with an infected rodent. They are also transmitted via contact with contaminated environment or fomites, or via infectious aerosol. The pathogens responsible for these non-vector-borne zoonoses, many of which have existed unrecognized for thousands or millions of years in wildlife host populations, sometimes spill over into human populations that come into contact with wild animals. Many of the most newly discovered and, perhaps most lethal, emerging diseases are non-vector-borne zoonoses. In many cases humans are a dead-end host, but a few important pathogens (e.g., human immunodeficiency virus) have adapted to humans and contact with the original host is no longer required to cause human disease. The requirement for direct or indirect contact with an infected vertebrate host has likely resulted in the relative restriction of many non-vector-borne zoonoses within closely associated and relatively isolated host populations facilitating the coadaptation of specific host and pathogen populations. Although sporadic cases of spillover of these pathogens into closely associated human populations (e.g., isolated indigenous populations) likely has occurred for thousands of years, frequent and relatively large outbreaks of human disease only were recognized in recent decades, contributing to the concept of “emerging infectious diseases.” Such outbreaks include the South American hemorrhagic fevers (caused by arenaviruses), hantavirus pulmonary syndrome (hantaviruses), Ebola and Marburg

hemorrhagic fevers (filoviruses), Nipah virus encephalitis (henipaviruses), severe acute respiratory syndrome (SARS coronavirus), and monkeypox (monkeypox virus). Despite the importance of these diseases, even the most recent reviews of climate change and human disease have devoted only a few lines to non-vector-borne zoonotic diseases (Confalonieri et al. 2007; Khasnis and Nettleman 2005; Patz and Olson 2006). Recent forums on the ecology of climate changes and infectious diseases (Wilson 2009) and on climate change and public health (Frumkin et al. 2008) have largely overlooked them; a few have treated them in more detail, especially in Europe (Semenza and Menne 2009; Vorou et al. 2007).

The ecology and transmission of all of the pathogens causing the above groups of VBZD are influenced by climate and there is a large body of evidence suggesting that climate change has and will continue to affect the incidence and distribution of these diseases in human populations.

Rodents and Bats – Pandora’s Box of Zoonoses?

In relation to climate change and zoonotic diseases we emphasize the potentially very important role of two taxa of vertebrate animals (rodents and bats) and one geographic area (the tropics). Because of our kinship, mammals are the most likely group of animals to share pathogens with humans. The rodents and bats constitute 63% of mammal species. Their numbers, combined with aspects of their life history and their likelihood of coming into close proximity to humans makes the rodents (Mills 2005) and the bats (Calisher et al. 2006) excellent hosts for a wide variety of potential zoonotic pathogens. Important rodent-borne directly transmitted zoonotic pathogens include the hemorrhagic fever viruses [hantaviruses and arenaviruses (Mills and Childs 2001)]. The

hantaviruses cause two diseases: hemorrhagic fever with renal syndrome (HFRS) affects about 100,000 people per year in Asia and hantavirus pulmonary syndrome (HPS) is caused by autochthonous New World hantaviruses. The existence of the New World hantaviruses and HPS was unrecognized until 1993. Although the incidence of HPS in the Americas (about 3300 HPS cases recognized since 1993) appears to be much lower than for HFRS in Asia and Europe, we have yet to recognize the full extent of the disease, and the case fatality can be as high as 50%. The arenaviruses include the agents of the South American hemorrhagic fevers. Before the recent introduction of an effective vaccine, Junín virus was responsible for 500 to 3500 cases of Argentine hemorrhagic fever each year in a small area of the Argentine pampas (Enria et al. 2006). Large outbreaks of Bolivian hemorrhagic fever (caused by Machupo virus) have been associated with increases in rodent host populations (Kuns 1965).

Our appreciation for the role of bats as hosts for agents of VBZD is increasing. Important diseases such as those caused by the filoviruses relatively rarely spill over into human populations. Nevertheless, the frequency of outbreaks of some of these diseases, such as Ebola and Marburg hemorrhagic fevers, seems to be increasing (Groseth et al. 2007). Evidence suggests that the filoviruses are hosted by tropical bats (Towner et al. 2009). Other zoonotic diseases hosted by tropical or sub-tropical bats have recently emerged. Nipah virus, which first appeared in Malaysia in 1999, caused an outbreak of 265 human cases of febrile encephalitis with a mortality of 38% and ended with the destruction of more than a million pigs which acted as amplifying hosts after introduction from bat populations (Chua et al. 2000). Recent outbreaks of Nipah virus encephalitis have affected India and Bangladesh (Hsu et al. 2004). Related bat-borne henipaviruses

including Hendra and Menangle viruses are associated with human disease in Australia, as is the rabies-like Australian bat lyssavirus (Field and Lunney 2003). Other lyssaviruses from Europe and Africa are associated with human fatalities (Calisher et al. 2006). The SARS coronavirus, now thought to be hosted by bats (Lau et al. 2005; Li et al. 2005), was responsible for an outbreak in 2003 that caused more than 8000 human cases and 774 deaths worldwide (WHO 2010).

Studies of the incidence of some rodent-borne hemorrhagic fevers in humans show clear links to climatic factors acting through their influence on host population dynamics (Mills et al. 1992; Mills and Childs 1998; Yates et al. 2002). Links between climate and bat population dynamics are poorly studied. It has been suggested that Ebola hemorrhagic fever outbreaks may be associated with specific climatic triggers (Pinzon et al. 2004) but the mechanisms are unknown.

The Tropical Connection

The greatest burden of VBZD is in the tropics (Confalonieri 2005). The most important vector-borne diseases (e.g., malaria, dengue fever, leishmaniasis, Chagas disease, chikungunya and yellow fever) are largely tropical. Most of the directly transmitted emerging pathogens mentioned above (hantaviruses, arenaviruses, filoviruses, henipaviruses, SARS coronavirus) are primarily tropical. Most arenaviruses and pathogenic New World hantaviruses are hosted by a group of rodents traditionally referred to as the family Muridae, subfamily Sigmodontinae (Musser and Carleton 1993) whose center of diversity is the New World tropics. Although HPS was first recognized in temperate areas (the United States and Patagonia), by far the greatest number of cases and the greatest geographic diversity of New World hantaviruses are now reported from

the tropics. As surveillance and phylogenetic studies improve and continue in these areas, the recognized diversity of hantaviruses and arenaviruses in the New World tropics is expected to become much greater.

For hundreds of years naturalists have recognized latitudinal gradients in diversity, the most prominent of which is the increase in species richness from the poles to the tropics. This increased richness also applies to pathogens (Guernier et al. 2004). In fact, one of the explanations advanced for increased diversity of animals in the tropics is increased pressure by predators and pathogens (Begon et al. 2006; Rohde 1992). Although we may have described the majority of vertebrate species on earth, new species, including rodents and bats (Csorba et al. 2007; Mares et al. 2000) are described regularly. Although nearly 875,000 species of arthropods are known in the world, specialists believe that as many as 30,000,000 species remain to be described in the tropics alone (Wilson 1992). Some of these are likely to be vectors of various pathogens and could expand their ranges as climatic conditions change. Estimates of numbers of pathogen species range up to one million for viruses and three million for bacteria, only a tiny fraction of which have been described (United Nations Environment Program 1995). For example, recent studies have identified numerous previously unrecognized species of the bacterial genus *Bartonella* in rodents and other non-human hosts (Bai et al. 2007; Inoue et al. 2009; Kosoy et al. 2003; Stevenson et al. 2003; Ying et al. 2002). Some of these bartonellae also have been isolated from human patients suffering from a variety of illnesses, suggesting they could represent previously unrecognized human pathogens (Bai et al. 2007; Kosoy et al. 2003; Kosoy et al. 2008).

Despite intensive research, the explanation(s) for the latitudinal gradient in biodiversity is still unclear. What *is* clear is that the tropics are home to a vast pool of known and potential human pathogens and their hosts and vectors. In the face of climate change and the potential introduction of many of these hosts, vectors, and pathogens to more northern latitudes, our profound lack of knowledge about the diversity, identity, and natural history of the tropical biota represents a significant impediment to understanding and predicting the effects of climate change on VBZD.

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