

## **Cover sheet**

### **Global Warming and Arboviral Infections**

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## Introduction

The earth is warming and there is almost universal consensus that human activities are contributing to this in an unprecedented way.[1] In view of this experts have proposed that we are now living in the Anthropocene epoch, an era where human activities are the dominant geophysical influence on the environment.[2] Climate change is accompanied by altered rainfall patterns, flooding and an increased likelihood of extreme weather events. These phenomena are potentially linked to the expansion of the range of permissive vectors and, thus, an expansion of the geographic range of a variety of arboviral threats.[3-5] In contrast, climate change may lead to changes in land use and alterations in human behaviour that may paradoxically reduce the risk of arboviral transmission. In this article we will consider the implications of climate change for a number of arboviruses.

## Dengue

Dengue is globally the most important arboviral infection and currently endangers half the world's population.[6] Dengue is a flavivirus and is transmitted by *Aedes* mosquitoes. Dengue infection results in a range of clinical presentations ranging from a self-limiting febrile illness through to life-threatening shock and haemorrhage. There is no specific therapeutic and currently available vaccine candidates have limited efficacy. The principal vector in tropical countries is the highly domesticated mosquito, *Aedes aegypti*. However the past few years has seen an expansion in the range of the competent dengue vector, *Aedes albopictus*, also known as the Asian tiger mosquito.[7] *Ae. albopictus* has been introduced into Europe and has become established in several countries raising the possibility of dengue transmission.[7, 8] Temperature and humidity are significant factors in influencing dengue transmission dynamics – an increase of these may lengthen the dengue

“season” in endemic areas and, potentially, promote the establishment of dengue transmission in new areas such as southern Europe or the southern United States. Furthermore, significant climate change may result in an expansion of the range of *Ae. aegypti* with an attendant increased risk of dengue transmission.[9] Interestingly, the vector implicated in the outbreak of dengue in Madeira in 2012 was *Ae. aegypti*, that despite vector control efforts has become established in this setting.[10] In addition, effects of climate change such as flooding may result in significant migration into urban environments.[11] This has the potential to further increase the population density in already overcrowded urban conurbations potentially enhancing the dengue transmission risk.

### **Tick-borne encephalitis**

Tick-borne encephalitis (TBE) is a flavivirus transmitted by *Ixodes* ticks, principally *Ixodes ricinus*. TBE typically causes a biphasic illness with an initial viraemic phase that is difficult to distinguish from other viral illnesses followed by a secondary phase where neurological features predominate.[12] TBE is endemic in Europe and it is likely that climate change has already impacted its transmission dynamics.[13] Higher temperatures result in faster tick development cycles and higher population densities. In addition, warmer climates lengthen the duration of tick-active periods and promote the expansion of the vector into higher altitudes. This has been seen in Sweden where there has been an increase in TBE cases since the mid-1980s – this increase correlates with shorter, warmer winters and, thus, an increase in the potential disease transmission season.[4] In addition, in the Czech Republic TBE transmission is occurring at higher altitudes – again, this is linked to increased temperatures that support the establishment of the vector in new, previously hostile areas.[14, 15]

## **Chikungunya**

Chikungunya is an alphavirus transmitted by *Aedes* mosquitoes.[16] Acutely, it causes a disease similar to dengue although haemorrhage and shock are not seen. Severe clinical manifestations have been described – these are more common in the elderly and in those with co-morbidities.[16] A striking feature of chikungunya is the development of severe and sometimes disabling joint symptoms after the resolution of the infection. Chikungunya is endemic in parts of West Africa and recent years have seen a striking expansion of the disease with Africa, Asia and the Americas.[17] Explosive outbreaks with a notably high attack rate have been described – the outbreak on Reunion Island in 2005/06 affected a third of the island's population.[18] There have been outbreaks of chikungunya in Italy, France and Croatia in recent years – in all these *Ae. albopictus* has been implicated.[7] *Ae. albopictus* appears to be firmly established in southern Europe and has expanded its range to include Belgium and the Netherlands raising the possibility of disease transmission in these areas.[7, 8]

## **West Nile virus**

West Nile Virus (WNV) is another Flavivirus that is transmitted by *Culex* mosquitoes.[19] In most cases WNV is asymptomatic or results in a self-limiting infection indistinguishable from other viral infections. Neuroinvasive infection occurs in a small percentage of cases but is associated with morbidity and a significant mortality rate.[20] As birds serve as amplifying hosts for WNV, it is possible that changes in migratory patterns secondary to climate change may result into changes to WNV epidemiology. WNV is already established in parts of Europe and competent vectors are present throughout the continent.[21]

## Conclusions

Successful arboviral transmission requires optimal environmental conditions for both vector and virus. Climate change is likely to contribute to the expansion of the outer limits of arboviral transmission. Using the most extreme climate scenarios modelling experiments suggest that there may be dengue transmission in the UK summer by 2100.[22] What is perhaps more likely is occasional autochthonous transmission events resulting from a viraemic individual travelling to a non-endemic area inhabited by permissive vectors. This has already been seen with outbreaks of dengue and chikungunya in parts of southern Europe. Additionally, climate change is likely to result in significant human movement with the increased emergence of “climate refugees”. This new phenomenon will have associated health challenges that will go beyond infectious diseases.

While “tropical” arboviruses are not likely to be seen frequently in routine UK medical practice in the near future the fact that we live in an interconnected and increasingly mobile world means it is important that UK medical professionals are aware of these diseases.

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