Climatic and geographic influences on arboviral infections and vectors

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Summary

Those components of climate that are likely to have major effects upon the geographical distribution, seasonal incidence and prevalence of vector-borne diseases are described. On the basis of existing and predicted climatic variations, examples are given of the types of changes that are to be expected, using several internationally important human and animal arboviral diseases including Rift Valley fever and African horse sickness.

Keywords


Introduction

In 430 BC Hippocrates said, "Whoever would study medicine aright must learn of the following subjects. First, he must consider the effect of the seasons of the year and the differences between them. Second, he must study the warm and cold winds, both those which are common to every country and those peculiar to a particular locality'.

From this, it can be seen that the influence of climate on infectious diseases has been a topic of some considerable interest for over 2,000 years. Recently an increase in that interest has been fuelled by the various global warming scenarios in circulation, and highlighted by the fact that eight of the warmest years on record have all occurred within the last decade or so, thereby seeming to support the concept of imminent climate change. Indeed, most authorities now accept that the balance of evidence suggests that human activities are warming the planet, and climate models predict an increase in global mean temperature of between 1°C and 3.5°C during the 21st Century (33, 34). Further predictions suggest that maximum warming will occur at high latitudes and during the winter, and that temperatures will increase more during the night than the day (40, 56). Accompanying changes in rainfall, wind patterns and seasonal weather variations are also expected.

Effect of climatic variables on vector biology

By definition, vector-borne diseases possess a vector stage, usually a crustacean, mollusc, insect or acarid, which is poikilothermic (cold blooded) and hence is especially sensitive to changes in climatic variables. Temperature and humidity are the components of the macroclimate which are likely to have the most important direct effect on vector biology and ecology (28, 44, 90, 110). However, many vectors demonstrate behavioural preferences for particular microclimates and the impact of climate change on microclimate environments has only occasionally been considered (68). Major macroclimatic variables with direct effects on vector biology are described below.

Temperature

A rise in temperature accelerates the metabolic rate of a vector, increases biting rates and will make bloodfeeding more frequent. This should lead to enhanced egg production and an increase in population size. However, the daily survival rate of individual vectors is likely to decrease as temperature rises and there will be an upper limit beyond which high temperature is positively detrimental. This is analogous to an extension of the hot dry season in many parts of the tropics, where vector activity is significantly reduced prior to the cooler rainy season in which the lower temperatures have an opposite effect. Temperature may also affect the geographical range or distribution (in terms of latitude and altitude) of vectors since this tends to be limited by minimum and maximum temperature (and humidity).

Humidity

High relative humidity favours most metabolic processes in vectors so that at higher temperatures, a high humidity (i.e. a low saturation deficit) will tend to prolong survival, although
increased susceptibility to fungal and bacterial pathogens may offset this to a variable degree. Low humidity (i.e. a high saturation deficit) causes a decrease in the daily survival rates of many arthropod vectors because of dehydration, but in some cases it may also cause an increase in the bloodfeeding rate, in an attempt to compensate for the high levels of water loss.

Rainfall
Rain is an important factor to most bloodfeeding groups of insects, including the blackflies (Simuliidae), biting midges (Culicoides), horse-flies (Tabanidae) and mosquitoes (Culicidae), because the immature larval and pupal stages are aquatic or semi-aquatic. Rainfall frequently limits the presence, absence, size and persistence of breeding sites. The precise level of impact on such sites will depend upon local evaporation rates, soil type, slope of terrain and the proximity of large bodies of water (e.g. rivers, lakes, ponds). However, since many insect vectors breed in seepage of water from irrigation pipe leaks, cattle trough overflows and residual water from previous rains, very heavy or prolonged rain may disrupt vector breeding sites and wash the immature stages away or kill them directly.

Wind
Since winds contribute to the passive dispersal of many species of flying insects, prevailing winds and wind speed may have a significant effect upon vector distribution. Some insect vectors, including species of mosquito, Simuliidae, sandflies (Phlebotominae) and Culicoides can be dispersed for hundreds of kilometres in this way.

In addition to these direct effects, climatic variables may also have important indirect effects upon vector abundance and distribution, and hence upon disease. One vector species may be displaced by another with a different vectoral capacity in an attempt to compensate for the high levels of water loss.

Effect of climate and other factors on the distribution of insect vectors
Palaeoclimatic records show that most shifts in the distribution of insect taxa have been associated with temperature change and that these shifts have occurred much more rapidly than changes in the distribution of vegetation and the higher animals (23, 24). Considering the high level of mobility of insects, especially winged insects, this should come as no surprise and strongly suggests that the current distribution of many insect vector species would change rapidly following any future climate change. In this context, a 1°C rise in temperature has been estimated to correspond to 90 km of latitude and 150 m of altitude (79).

Human activity
The introduction of *Aedes albopictus*, an efficient vector of yellow fever and dengue viruses, into Italy in 1989, demonstrates that even winged insects do not always have to extend into new areas of suitable climate under their own power. This mosquito was probably introduced as drought-resistant eggs laid in second-hand car tyres that had been imported from the United States of America (USA). *Aedes albopictus* is now found in much of north and central Italy (38) and at several locations in Albania (3). Since the distribution of *Ae. albopictus* is bound, conservatively, by the mean 0°C isotherm in the coldest month of the year (77), this suggests that in Europe, where this isotherm encompasses most of the continent south of Scandinavia, *Ae. albopictus* may already be able to extend into most or all of these areas. In the USA, where the mosquito was introduced from Japan in 1985, *Ae. albopictus* now occupies 678 counties in 25 south-eastern States ranging as far north as Nebraska and Iowa (73). The species is also progressing southwards through Florida at the rate of 65 km per year, displacing *Ae. aegypti*. Should the projected temperature increases occur, then the range of this mosquito is likely to extend to include most of the populated areas of eastern USA, in addition to southern Canada (77).

Aspects of insect physiology

Diapause
It is of interest to note that both temperate and tropical geographical strains of *Ae. albopictus* are known. The temperate strains are physiologically competent to enter diapause (hibernation) during periods of cold weather by switching feeding behaviour from blood to plant juices, thereby producing large quantities of lipids from the ingested plant sugars. Tropical strains cannot make this switch and therefore have to remain within temperature ranges where activity is possible year-round. Thus, the southward spread of temperate *Ae. albopictus* in North America is already likely to be close to the upper thermal limit. As temperature increases still further, the current distribution of the species in Florida may become more limited.

Transovarial transmission
In temperate areas, many arboviruses are likely to be maintained over the cold winter periods by transovarial transmission through the virus vectors (41).

Effect of temperature on vector competence
When attempting to predict the effect of climate or climate-change on the distribution of vector-borne diseases, temperature-related vector and pathogen development rates must be considered simultaneously. In many cases, the successful completion of the developmental cycle of a pathogen within the vector may occur only within a clearly defined temperature band. Therefore, for each vector-pathogen combination, a limiting temperature range is likely to exist, outside which the pathogen will invariably fail to be transmitted, although the vector itself may be able to survive reasonably or very well. This band of 'permissive' temperatures may be unique to each pathogen. Within this band is likely to be a narrower set of temperatures within which the pathogen is transmitted most efficiently, usually...
become progressively less efficient due to a lower vector survival rate, a slower or defective pathogen developmental cycle or a combination of these factors.

The aim of this paper is to consider the above climatic effects upon vector-pathogen interactions and disease distribution, using appropriate examples of human, animal and zoonotic vector-borne diseases.

**Mosquito-borne encephalitides**

**Japanese encephalitis**

This mosquito-borne flavivirus is currently the most important cause of vector-borne encephalitis in humans, causing some 45,000 clinical cases and 11,000 deaths annually (14). Japanese encephalitis virus (JEV), was probably first identified clinically in Japan in the late 1800s with the first major epidemic recorded in that country in 1924. The virus was first isolated from humans (from the brain of a fatal case) in 1935, and from the principal mosquito vector, *Culex tritaeniorhynchus*, in 1938. Currently, the known distribution of the virus covers all areas extending westwards from Japan to the border areas of western Pakistan and India and from the Himalayan barrier in the north to a largely equatorial distribution including Sri Lanka, Malaysia, Indonesia and the Philippines in the south. Virus activity has also been reported from islands in the Torres Strait and JEV is therefore considered a threat to the mainland of Australia.

In general, recent epidemic activity has been reported across the northern part of the extensive range of JEV, with major epidemics occurring in Japan, the People’s Republic of China, Vietnam, Cambodia, north Thailand, north India and Nepal (42). Comparatively little activity has been reported from Myanmar (formerly Burma), Bangladesh and Laos, although this may be due to poor or under-reporting (42). In Japan and the Republic of Korea, extensive use of a commercially available vaccine has resulted in a dramatic decline in cases reported since the 1960s. However, the zoonotic transmission cycle of the virus is continuously maintained and represents an ever-present public health threat, requiring a continuous public health vaccination strategy.

Epidemic transmission of JEV is strongly influenced by climate. The peak transmission period is focused in a few weeks at the end of the tropical hot season. During this period, temperatures are typically 32°C or higher, allowing rapid virus replication in the vector, and the beginning of the rains provides numerous breeding sites leading to high vector productivity. As temperatures cool, epidemic activity invariably ceases. Closer to the equatorial regions, average peak temperatures are typically several degrees centigrade lower, and case reporting becomes much more sporadic.

Japanese encephalitis virus has a complex epidemiology, being maintained in a continuous mosquito-animal zoonotic cycle associated with rice-field ecosystems. The animals which act as virus-amplifying hosts are various species of ardeid water birds and domestic swine. The most important maintenance and epizootic/epidemic vectors over much of the range are thought to be a number of mosquito species in the Stitiens group of the subgenus *Culex*. The principal vector is *Cx. tritaeniorhynchus*, a species which is subjected to a wide range of climatic variation across an extensive geographic range. In maritime Siberia and north Japan, areas at the extreme edge of the range of JEV, the winters are very cold. This poses severe problems for the maintenance of both the virus and the vector. The population dynamics of *Cx. tritaeniorhynchus* are strongly linked to temperature in these areas (84), and individuals may hibernate over the winter as unfed adults. In such locations, therefore, species of floodwater *Aedes* mosquitoes, such as *Ae. japonicus*, are thought to maintain the virus over the winter by transovarial transmission in drought resistant eggs (86). In tropical climates, population patterns of *Cx. tritaeniorhynchus* are more closely associated with available moisture, either in the form of annual rainfall or rice-field irrigation, and adult activity usually continues throughout the year.

Experimental studies with vectors of JEV, under controlled climatic conditions, have demonstrated that mosquitoes maintained under autumn or winter conditions carry only low concentrations of virus which are restricted to the posterior mid-gut cells. In contrast, high titres and disseminated infections occur under summer conditions (88). At 28°C, 60% of *Cx. tritaeniorhynchus* transmit virus nine days after infection, and 100% after fourteen days, whereas no transmission was detected at 20°C for up to twenty days post infection (100). A similar effect of temperature was also shown by Leake and Johnson who demonstrated positive salivary gland infections in inoculated *Cx. tritaeniorhynchus* after five days incubation at 32°C, but only after twenty-one days at 26°C (43). In a summary of vector competence studies, Burke and Leake demonstrated that the predominantly tropical mosquito species, *Cx. tritaeniorhynchus*, *Cx. gelidus* and *Cx. fuscocephalus*, are efficient vectors of JEV, whereas more temperate *Culex* species, such as *Cx. tarsalis* (a vector of equine encephalitides in North America) are significantly less efficient (14). The findings suggested that increases in environmental temperature could convert less efficient species into important vectors, thereby significantly expanding the potential range of JEV.

**Transmission of St Louis and western equine encephalitis virus in North America**

On the basis of field and laboratory studies performed in California, Reeves et al. forecast that a rise in environmental temperature of 3°C to 5°C would cause a significant northward shift of both St Louis encephalitis virus (SLEV) and western equine encephalitis virus (WEEV) (83). The latter is
moving northwards and is predicted to disappear from many regions in North America where it is currently endemic, while the range of SLEV will extend much further northwards into Canada, where sporadic outbreaks of disease already occur. These predicted changes are based partly on the fact that the lowest temperature at which WEEV transmission can occur via the vector Cx. tarsalis is 11°C while for SLEV the minimum temperature is 15°C (56). At temperatures above 30°C, Cx. tarsalis modulates WEEV infection so that the proportion of infected vectors decreases dramatically, thus reducing the overall transmission rates. However, SLEV infection is not modulated by the vector and so the transmission of the virus will not be similarly adversely affected at the higher temperatures.

African horse sickness virus

Introduction

African horse sickness virus (AHSV) is a double-stranded ribonucleic acid (RNA) virus that causes an infectious, non-contagious, arthropod-borne disease of equids and occasionally dogs (African horse sickness [AHS]). The disease is particularly severe in horses, killing 80% to 95% of naïve animals, but infection is virtually sub-clinical in zebra and donkeys. Although at least four human cases of severe disease have been documented, AHS is not a zoonosis (25, 101). Nevertheless, the principles involved in transmission of AHS by insect vectors are identical to those of many arthropod-borne zoonotic diseases and AHS can therefore serve as an instructive model to illustrate the effects of climatic variables upon the epidemiology and distribution of vector-borne viral diseases in general.

Distribution and epidemiology

Nine distinct serotypes of AHSV exist, and these are transmitted between vertebrate hosts almost entirely by species of Culicoides biting midge. As the name implies, AHSV originated in Africa and is enzootic in tropical and subtropical areas south of the Sahara in a band stretching from Senegal in the west to Ethiopia and Somalia in the east, and extending as far south as northern South Africa (31, 65). The Sahara desert seems to provide a geographical barrier which has prevented any permanent spread of the virus to North Africa, or beyond.

Until relatively recently, the virus was believed to be confined to continental Africa, except for occasional excursions into Yemen (70, 81). However, from 1959 to 1961, AHSV serotype 9 (AHSV-9) made a dramatic extension out of Africa and spread along a broad front, across the Arabian peninsula and the Middle East, reaching as far as Pakistan and India (31). Nevertheless, by the end of 1961, as the result of a massive vaccination campaign and the deaths of over 300,000 equids, the disease was eradicated in Asia (7). The failure of the virus to persist in Asia was probably due to a combination of factors, including vaccination, vector control and more particularly, adverse climatic conditions that reduced or prevented adult vector activity during the winter periods.

During 1965, AHSV-9 again spread beyond the enzootic zones in sub-Saharan Africa, appearing first in Morocco and then in Algeria and Tunisia, before crossing the Straits of Gibraltar into southern Spain (62). The virus persisted in North Africa until 1966, before finally disappearing from the area, but the extension into Spain lasted less than three weeks (19).

After 1966, reports of AHSV were limited to sub-Saharan Africa for over 20 years. However, in July 1987, an outbreak of AHS due to serotype 4 (AHSV-4) was confirmed in central Spain (50). The most likely source was a number of zebra which were imported from Namibia into a safari park where horses were present, approximately 45 km south-west of Madrid (50). Zebra are susceptible to infection with AHSV, but unlike horses, usually show no clinical signs. This safari park subsequently became the site of the first twenty-seven cases of AHS in Spain in 1987. The epizootic continued for three to four months in central Spain, apparently ending in October (20).

The 1987 outbreak in Spain caused alarm because AHS is a notifiable disease and Madrid was the furthest north that the virus had ever been recorded. However, concern was moderated because all previous information suggested that the virus is incapable of overwintering in Europe. Consequently, the apparent end of the epizootic in October 1987 was in line with expectations and no further outbreaks were expected. Unfortunately, this was not the case, additional severe outbreaks followed in Spain from 1988 to 1990, in Portugal in 1989 and in Morocco from 1989 to 1991, before vaccination and zoosanitary measures eliminated the virus from the area. All of these outbreaks were due to AHSV-4, a serotype that had never previously been recorded outside southern Africa. During the course of the outbreaks no other evidence was found of any serotype of AHSV within 3,000 km of Spain and northern Morocco. Consequently, it seems certain that there was only one introduction of the virus into the area and that was via the imported zebra in 1987. Subsequent to this introduction, the virus had persisted in the area for at least five years, overwintering four times in the process.

This situation was unprecedented; nowhere else and at no other time had any serotype of AHSV succeeded in overwintering more than twice outside sub-Saharan Africa. Much speculation ensued as to how and why the situation had changed.

African horse sickness virus causes a viraemia in horses and zebra that may extend for 18 and 40 days, respectively, though in both species the duration of viraemia is usually much shorter. The virus is transmitted between equid hosts...
virtually entirely by Culicoides biting midges, which are biological vectors. These insects are only able to transmit the virus by biting; no evidence of transovarial transmission exists. In much of sub-Saharan Africa, the climate allows the adult vector Culicoides to be active throughout the year. Consequently, AHSV survives in these enzootic areas, through continuous and uninterrupted cycles of transmission between the vertebrate and invertebrate hosts. Outside sub-Saharan Africa, the failure of AHSV to persist had been attributed mainly to an absence of efficient vector species of Culicoides or, if such vectors were present, to their seasonal incidence due to the relatively harsh winters experienced in such areas. However, for the virus to have been able to survive in the western Mediterranean basin for five consecutive years, efficient vector species of Culicoides must be present in Spain, Portugal and Morocco, and in at least some areas of these countries, the climate must be sufficiently mild for adult vectors to be active throughout the year. In these areas, any vector-free periods that do occur, must be shorter than the maximum duration of viraemia in the local susceptible vertebrate population (i.e. 18 days in this case), otherwise the last infected equid will have died or recovered before new vectors arrive to continue the cycle.

**Culicoides imicola: the only proven field vector of African horse sickness virus**

The only proven field vector of AHSV is *Culicoides imicola* (61). This is an Afro-Asiatic species which is common throughout Africa and much of South-East Asia. Until recently, the species was thought to be absent from Europe but it is now known to be widely distributed throughout south-west Spain and most of Portugal, ranging as far north as 41°5'N and including all of the areas in which AHS has been recorded (82). *Culicoides imicola* also has a wide distribution in northern Morocco (9). Furthermore, in central Spain, in the area of the 1987 AHS outbreak, *C. imicola* has a seasonal incidence; the adults disappear during autumn, not to reappear until the following April, three to four months later (64). Given that the maximum duration of viraemia in horses is 18 days, this is far too long for the virus to survive in vertebrates alone. Therefore, under existing climatic conditions, AHSV would not be expected to be able to overwinter in central Iberia, and indeed it did not persist there. The virus arrived in the area in July 1987 and disappeared in October the same year, never to reappear (64). However, further south in Spain, and also in southern Portugal and northern Morocco, the situation is different, particularly in those areas that are bordered by the 12.5°C isotherm for the average daily maximum temperature in the coldest month of the year (January). Adult *C. imicola* are present and active throughout the year and as a direct result, these areas are potential enzootic zones for AHSV (9, 64).

The expansion of *C. imicola* from North Africa into Spain and Portugal, although apparently a recent occurrence, appears to be permanent, and Rawlings et al. have suggested that a northwards expansion may still be continuing (82). It is not known whether this northwards extension is the result of some general climatic change or whether the recent series of exceptionally warm years is merely providing a preview of the possible effects of such a change.

**'New' vectors of African horse sickness virus**

Although *C. imicola* is the only confirmed field vector of AHSV, during the outbreaks in Spain, isolations of this virus were also made from mixed pools consisting almost entirely of *C. obsoletus* and *C. pulicaris*, but excluding *C. imicola* (63). Neither of these two species had previously been connected with AHSV but given that the distribution of both species is more northerly than the usual range of AHSV, this is not surprising, since presumably they have had little opportunity to become infected. Therefore, the northerly extension in range of AHSV into southern Europe, facilitated by the earlier expansion in the distribution of its traditional vector, *C. imicola*, could have brought the virus into contact with new, unsuspected vectors. Had the virus not been eliminated from the area by the implementation of vaccination and zoosanitary measures, this could have resulted in the spread of the virus even further northwards, rather like passing on a baton in a relay race. The involvement of novel vectors is always a possibility and is to be suspected whenever the distribution of a vector-borne pathogen alters significantly.

The significance of the 1988 AHSV isolations from *C. obsoletus* and *C. pulicaris* in Spain is emphasised further through the implications of recent research on a northern European midge, *C. nubeculosus*. This species has an oral susceptibility rate for AHSV of less than 1% when the immature stages of the midge are reared at 25°C and when the adults are fed upon a standard titre of virus. Furthermore, this rate of oral susceptibility cannot be enhanced by selective breeding from susceptible parents (66). However, if the rearing temperature of the immature stages of the midge is raised to between 30°C and 35°C, not only does the developmental time from egg to adult decrease dramatically to produce significantly smaller adults, but the oral susceptibility rate increases to over 10%, and virus replicates to levels suggesting that transmission is possible (67). Similar results have been obtained using *C. nubeculosus* and bluetongue virus, a major pathogen of ruminants (111). Since selective breeding had no effect upon the *C. nubeculosus* oral susceptibility rate, this is clearly not a genetically controlled, heritable trait, as is usually exhibited by biological vectors. Instead, it may be that the increase in development temperature not only gives rise to smaller adults but more 'fragile' adults with an increased incidence of the so-called 'leaky gut' phenomenon (11). In such a situation, virus is able to pass directly from the ingested blood meal in the gut lumen, into the haemocoel without having to first infect and replicate in the gut wall cells. Once in the haemocoel, it is well documented that most arboviruses will replicate and then be transmitted, even by insects that do not normally act as vectors. Such a sequence of events may be envisaged as a hybrid mechanism whereby infection is initiated by a
mechanical event (passage of virus from the gut lumen into the haemocoel without replication), but transmission is the result of a series of subsequent biological events (infection of and replication in the salivary glands, and release of progeny virus particles into the salivary ducts). This research with *C. rubeculonius* suggests that under the appropriate environmental conditions (i.e. elevated temperature), species of *Culicoides* not normally considered to be vectors, may be able to transmit AHSV, a premise that presumably can be extended to other insect groups and other viruses. Indeed, the isolations of AHSV from mixed pools of *C. obsoletus* and *C. pulicaris* in Spain during 1988 may be an example of the leaky gut phenomenon in operation, potentiated by the unusually warm conditions prevailing in the area at the time. Increasing temperature due to climate change or even to more ephemeral climatic variations will tend to increase the likelihood of such 'unusual' isolations.

**Effect of temperature on African horse sickness virus infection in vector species of *Culicoides***

The infection rates and rates of virogenesis of AHSV within vector species of *Culicoides* are temperature dependent (109). At elevated temperatures, infection rates tend to be higher, rates of virogenesis faster and transmission earlier. However, individual midges survive for a shorter period of time. As ambient temperature is reduced, the reverse is true for each of these four variables. Furthermore, AHSV replication does not occur below 15°C and at temperatures less than or equal to 15°C, the apparent infection rate rapidly falls to zero (109). However, when midges are maintained for extended periods at temperatures of 10°C to 15°C, and then transferred to temperatures within the virus permissive range (>20°C), 'latent' virus that has persisted in some individuals, commences replication and rapidly reaches a high titre.

Concurring with these studies, other researchers have demonstrated that adults of *C. imicola*, the major vector of AHSV, are active in the field at temperatures up to 3°C lower than the minimum required for AHSV replication (92). In practical terms, this suggests that AHSV transmission may occur only over the warmer parts of the range of *C. imicola*. In the cooler areas of *C. imicola* distribution (e.g. further north or at higher altitudes), even if the virus were introduced, transmission would be impossible or restricted to certain times of the year (e.g. high summer) or climatically favourable localities. These findings suggest that even if *C. imicola* were to continue expansion in range northwards, the ability to transmit AHSV will progressively decrease with increasing latitude, unless accompanied by climate moderation. Nevertheless, an additional aspect must be considered, namely: extended midge survival at low temperatures, up to 90 days in some cases (12), and replication of latent virus in some of these individuals once the temperature rises to permissive levels (e.g. in spring). These phenomena could constitute a viral overwintering mechanism in the absence of vertebrate involvement, and also in the apparent absence of infected vectors (Table 1). Although the precise 'trigger' temperatures may vary, this is a general mechanism that is likely to be applicable to a wide range of arboviruses and vectors.

**Table 1**

African horse sickness virus: overwintering mechanism

<table>
<thead>
<tr>
<th>No.</th>
<th>Sequence of events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>The virus seems to require temperatures ≥15°C in order to replicate in, and be transmitted by, the vector <em>Culicoides</em></td>
</tr>
<tr>
<td>2.</td>
<td>Adults of the AHSV vector, <em>Culicoides imicola</em>, are active at temperatures as low as 12°C and can survive even cooler temperatures in an inactive state.</td>
</tr>
<tr>
<td>3.</td>
<td>Since the virus requires a higher minimum temperature than the vector, this suggests that replication and transmission may be possible over any part of the range of the vector.</td>
</tr>
<tr>
<td>4.</td>
<td>However, during cold periods, virus can survive for extended periods at 'undetectable' levels in adult vectors, the lifespan of which is extended at these temperatures, up to 90 days in some cases.</td>
</tr>
<tr>
<td>5.</td>
<td>When temperatures rise to permissive levels (≥15°C), virus replication in the vector commences and transmission becomes possible.</td>
</tr>
<tr>
<td>6.</td>
<td>This situation provides an overwintering mechanism for AHSV in the absence of vertebrate involvement and also in the absence of detectable virus in the vectors.</td>
</tr>
</tbody>
</table>

AHSV: African horse sickness virus

**African horse sickness and El Niño/Southern oscillation in South Africa**

In South Africa, major epizootics of AHS occur every ten to fifteen years, although the reason for this pattern has been unclear. However, a strong link between the timing of these epizootics and the warm (El Niño) phase of the El Niño/Southern oscillation (ENSO) has recently been discovered. Baylis et al. suggest that the association is mediated by the combination of heavy rainfall and drought brought to South Africa by ENSO (10). The link between this climatic phenomenon and AHS is via the vector, *C. imicola*, which breeds in saturated soil. In years of heavy rain, populations of this insect can increase by over 200-fold. Baylis and his co-workers showed that since 1803, thirteen of the fourteen major epizootics of AHS in South Africa have coincided with a warm-phase ENSO. However, since 1803, forty-two ENSOs have also occurred which were not marked by epizootics of AHS. Baylis et al. explain this apparent anomaly by showing that in South Africa, warm phase ENSOs typically bring heavy rain followed by drought; no AHS epizootics occurred during these years. However, a sub-set of ENSO years exists where the pattern is reversed, i.e., pronounced drought is followed by heavy rain. These were the years when the thirteen AHS epizootics occurred. The reasons why this pattern of drought followed by heavy rain is conducive to AHS, remain unclear, but recognition of the pattern means that prediction of future AHS epizootics in South Africa will be made significantly easier. Similar links between the excessive rainfall brought to certain areas of the globe by El Niño or other climatic variation, and vector-borne disease prevalence, have been reported for many diseases including the zoonosis, Rift Valley fever (RVF) (112).
Rift Valley fever virus

Introduction

An acute and highly fatal disease of lambs, associated with heavy rains and accompanied by reports of illness in humans, was first recognised in the Rift Valley of Kenya at the beginning of the 20th Century, although the cause was not identified until 1930 (16, 72, 95). The agent, Rift Valley fever virus (RVFV) is an arbovirus and is now known to be a typical member of the genus Phlebovirus of the family Bunyaviridae (75).

A wide variety of animals can be infected by RVFV, ranging from rodents to the hippopotamus. However, disease seems to be limited to domestic ruminants and humans (60). Clinical signs can range from inapparent to peracute, depending upon the strain of virus and the species of host infected. Disease is most severe in sheep, cattle and goats, producing high mortality rates in new-born animals and abortion in pregnant females. Infection in humans is usually associated with a mild to moderately severe influenza-like illness, although severe ocular sequelae, encephalitis and haemorrhagic disease occur in a small proportion of patients, occasionally leading to death (99).

Major outbreaks and distribution of the virus

Major outbreaks of RVF, affecting sheep and cattle, have been recorded in Kenya from 1930 to 1931, in 1968 and from 1978 to 1979, with minor outbreaks at irregular intervals during the intervening years (18, 60). The disease was first recognised in southern Africa when a major epizootic occurred in sheep-rearing areas in north-eastern South Africa, in 1950. In the affected regions, an estimated 100,000 sheep died and 500,000 sheep aborted, with smaller losses in cattle and some cases of human disease (74, 89). Severe outbreaks also occurred in Namibia in 1955, and, following heavy rains, in South Africa from 1974 to 1976 (99). Additionally, sporadic outbreaks of RVF were seen in South Africa in 1952-1953, 1955-1959, 1969-1971, 1981 and 1999 (8, 51, 53, 55, 98, 104, 108). Further extensive outbreaks of the disease occurred in southern Africa, involving mainly cattle, in Zimbabwe in 1955, 1957, 1969-1970 and 1978 (15, 94, 96, 97), in Mozambique in 1969 (51, 52, 80, 103), and in Zambia in 1973-1974, 1978 and 1985 (4, 32). During the 1978 epizootic in Zambia, an estimated 60,000 abortions occurred and almost 10,000 cattle died. Similar losses were thought to have occurred in the earlier epizootic from 1969 to 1970 (97). Serological evidence of RVFV or isolations of the virus have also been reported in at least twenty other countries of Africa, including Madagascar. However, the virus has, as yet, not been recorded outside the African continent (60, 99).

The furthest north that RVF has been reported to date, is Egypt, where from 1977 to 1978, a major epidemic occurred in the Nile delta and valley, causing an unprecedented number of human infections and deaths, in addition to numerous deaths and abortions in sheep, cattle, goats, water buffalo and camel (99). Estimates of the number of human cases ranged from 18,000 to over 200,000, with almost 600 deaths occurring from encephalitis and/or haemorrhagic fever (57, 58, 60, 78, 93). From 1987 to 1988, a severe epidemic of RVFV occurred in West Africa, in the Senegal River basin in southern Mauritania and northern Senegal. In Mauritania alone, an estimated 224 people died and a high rate of abortion in sheep and goats was also reported (35, 36, 39). More recently, following rainfall of 60 to 100 times the seasonal average, an exceptionally severe outbreak of RVF in humans (and domestic livestock) commenced in Kenya in mid-December 1997, and rapidly spread into Somalia and Tanzania. The number of human cases was estimated to be in the region of 89,000, which suggests that this may be one of the largest outbreaks of RVFV on record (3, 87). However, the epidemic was short-lived and by February/March 1998, the floods had receded, rainfall had returned to normal and the outbreak was considered to be over (5). Nevertheless, the virus has remained active elsewhere in Africa, and human deaths and animal abortions from RVF were again reported from Mauritania in September 1998 (6).

Transmission and epidemiology

The enzootic/epizootic transmission cycle of RVFV is exceedingly complex. The virus has been isolated in Africa from twenty-three species of mosquito from five genera, a pool of mixed Culicoides spp., a Simulium sp. and a Rhipicephalus tick (60). This wide diversity of arthropod vectors is in direct contrast to most other arboviruses which tend to have very limited numbers of vector species, and serves to emphasise the complex nature of the transmission cycle of RVFV. Nevertheless, the vector findings demonstrate that mosquitoes are by far the most important arthropod vectors of the virus and that different species of mosquito are the major vectors to livestock in the various areas of Africa where the virus is enzootic or epizootic.

Many researchers have observed that epizootics of RVFV appear to follow periods of excessive rain (2, 60, 99). However, the disease does not have a regular yearly or seasonal distribution. For instance, in South Africa, rainfall appears to follow an 18 to 20 year cycle, with 9 to 10 years of above average precipitation alternating with a similar period of low rainfall (60, 99). The epizootics of RVF tend to cluster during years of high rainfall. In northern Africa, RVF outbreaks occur in ecologically drier areas than further south and appear to be centred near irrigated areas around the River Nile. The rationale is that wetter conditions are usually those that favour the increased breeding of vector species of mosquito and hence more intense virus transmission. An increase in numbers of mosquitoes has been noted during times of RVF epidemics and epizootics (1, 2, 58). However, the central enigma in the epidemiology of RVF concerned the fate of the virus during inter-epizootic periods. The virus was thought to be enzootic in indigenous forests where it circulated in mosquitoes and unknown vertebrates, extending into
livestock rearing areas when heavy rains favoured the breeding of the vector. However, an unknown vertebrate reservoir has never been identified and it is unclear how virus could spread from such cryptic foci, to simultaneously infect livestock over wide geographic areas separated by hundreds of kilometres (60). A breakthrough occurred in 1985 when Linthicum et al. isolated RVFV during an inter-epizootic period from both male and female floodwater-breeding aedine mosquitoes that had been collected as larvae in the field and reared to adults in the laboratory (48). These workers thus demonstrated that transovarial transmission is the most likely mechanism for maintenance of RVFV during times when environmental conditions are unsuitable for active transmission between vector and vertebrate hosts. Floodwater aedine mosquitoes lay eggs on vegetation at the edge of an expanse of water, frequently in pans or ‘dambos’ in Africa (low-lying grassy areas that are inundated after heavy rains). Since these dambos often dry out rapidly, the aedine eggs are adapted to undergo an obligatory period of drying before being able to hatch on rewetting (during subsequent flooding). Thus, floodwater aedine mosquitoes can ‘overwinter’ as eggs, and the eggs can survive for long periods, possibly several seasons, if the dambos remain dry (99).

The suggestion is, therefore, that during inter-epizootic periods, RVFV is maintained principally via transovarial transmission of the virus in aedine mosquitoes, possibly aided by venereal transmission from males to females, and with a low level of transmission to livestock. Epizootics are precipitated by abnormally heavy rains which flood dambas or pans and lead to an explosive increase not only in the numbers of aedine mosquitoes but also of non-aedine species that breed in large rivers and dams, rather than floodwater aedines. Indeed, floodwater mosquito species are not represented at all in Egypt where the evidence suggests that the major vector was likely to have been Cx. pipiens, a species that breeds in polluted water and has been shown to be an efficient laboratory vector of RVFV (26, 59, 102). However, neither this species, nor any other mosquito present in Egypt, has been shown to be capable of transovarially transmitting RVFV. Thus, the survival of the virus in Egypt from 1977 to 1978, and in isolated foci until 1980, may be due to the hibernation of infected adults over the winter periods (99).

The appearance of RVFV in Egypt apparently represented the extension of the virus into a new area, possibly from the Sudan, which in 1976 was the nearest source of infection (22). The route of entry is uncertain but it has been suggested that the virus could have been introduced via infected humans travelling by air. However, the human infection rate in the Sudan is reported as having been extremely low at that time (99). Alternatively, the virus could have been introduced through the shipment of infected sheep and/or cattle, via the Nile or overland from northern Sudan, or by sea from other countries of Africa. This seems to be a strong likelihood (99), although a third route has been proposed. In general, flying insects including mosquitoes, tend to have rather limited flight ranges. However, strong evidence exists to suggest that under certain atmospheric conditions, flying insects are capable of being carried on the wind, as ‘aerial plankton’, over very long distances, possibly hundreds of kilometres (13, 29, 69, 76, 85). Such conditions were apparently present just prior to the start of the RVF epidemic in Egypt and could have facilitated the translocation of infected mosquitoes from disease foci in northern Sudan to southern Egypt, in association with northerly movements of the inter-tropical convergence zone (ITCZ) (90, 91, 93). The seasonal incidence of bluetongue virus in north-central Sudan, has similarly been attributed to carriage of the vector on the ITCZ, in this case a biting midge, C. imicola (71).

In West Africa, presence of RVF had long been reported without the occurrence of serious disease. However, the massive epidemic of 1977, in Egypt, which was probably associated with an increase in mosquito breeding sites, brought about by developments such as the Aswan Dam, prompted an increased monitoring of RVF activity between 1983 and 1987 in those countries in West Africa affected by similar constructions (21, 27). On the basis of this work, the threat of an epidemic of RVF was predicted in southern Mauritania and northern Senegal (21). Consequently, the RVF
epidemic that commenced in these countries in October 1987 was the first to have been predicted in an area where no similar outbreak had previously been recorded (99).

The recent series of epidemics of RVF in Senegal, Mauritania and Egypt show that the virus can not only extend rapidly beyond its usual range, but also suggest that the virus has the potential to occur outside Africa (39, 58, 93).

**Rift Valley fever in humans**

Humans become infected with RVFV either by mosquito bite or through contact with virus-infected animal tissues. In Egypt, the major mosquito vector is likely to have been *Cx. pipiens*. This is a peri-domestic species which readily bites man, so many human cases probably arose from mosquito bite. However, in southern Africa, the major mosquito vectors of RVFV are zoophilic and sylvatic, so the majority of human cases originate through contact with infected animals during food preparation, laboratory work, slaughter or necropsy. People involved in occupations leading to such contacts (livestock workers, veterinarians, abattoir workers, laboratory workers, housewives dealing with fresh meat, etc.) are therefore most at risk in these areas (99). The virus presumably gains entry to the human host via abraded skin, wounds or mucus membranes, but aerosol and intranasal infection have also been demonstrated (99). Low concentrations of RVFV have been found in milk and other body fluids of infected livestock, and consequently some authorities believe that human infections may sometimes result from the consumption of raw milk (99).

**Conclusion**

The influence of climatic variables on the distribution and seasonal incidence of arboviral diseases is of fundamental importance. In particular, temperature-dependent interactions between vectors and the arboviruses that they transmit are highly complex, and the outcomes can be difficult to predict. Furthermore, these interactions are likely to be profoundly influenced by climate change, whether or not this is induced by humans. Should the predicted alterations in climate over the first part of the 21st Century be confirmed, then the changes that have been outlined in this paper, particularly in relation to the distribution of AHSV and its vectors, may serve as an indication of impending changes in the epidemiology of a wide range of other vector-borne diseases of man and animals.

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**Influence du climat et de l’environnement sur les arboviroses et leurs vecteurs**

P.S. Mellor & C.J. Leake

**Résumé**

Les auteurs décrivent les facteurs climatiques susceptibles d’avoir une influence significative sur la répartition géographique, l’incidence saisonnière et la prévalence de maladies transmises par des vecteurs. En se fondant sur les variations climatiques observées et sur des prévisions, ils donnent quelques exemples des types de changements susceptibles de se produire pour plusieurs arboviroses humaines et animales majeures au plan international, notamment la fièvre de la Vallée du Rift et la peste équine.

**Mots-clés**

Arbovirus — Répartition — Santé publique — Température — Variables climatiques — Vecteurs — Zoonoses.
Efectos del clima y la geografía sobre las infecciones arbovirales y sus vectores

P.S. Mellor & C.J. Leake

Resumen

Los autores indican los componentes del clima más susceptibles de ejercer un efecto notorio sobre la distribución geográfica, la incidencia estacional y la prevalencia de enfermedades transmitidas por vectores. A partir de las variaciones climáticas, reales o predichas, los autores ofrecen ejemplos del tipo de cambios que cabe esperar en esos parámetros, aplicándolos a varias enfermedades arbovirales animales o humanas de importancia internacional, entre ellas la fiebre del Valle del Rift y la peste equina.

Palabras clave

References


