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Challenges in predicting climate and environmental effects on vector-borne disease episystems in a changing world

W. J. Tabachnick

Florida Medical Entomology Laboratory, Department of Entomology and Nematology, Emerging Pathogens Institute, University of Florida, IFAS, 200 9th Street, SE, Vero Beach, Florida

wjt@ufl.edu

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Summary

Vector-borne pathogens cause enormous suffering to humans and animals. Many are expanding their range into new areas. Dengue, West Nile and Chikungunya have recently caused substantial human epidemics. Arthropod-borne animal diseases like Bluetongue, Rift Valley fever and African horse sickness pose substantial threats to livestock economies around the world. Climate change can impact the vector-borne disease epidemiology. Changes in climate will influence arthropod vectors, their life cycles and life histories, resulting in changes in both vector and pathogen distribution and changes in the ability of arthropods to transmit pathogens. Climate can affect the way pathogens interact with both the arthropod vector and the human or animal host. Predicting and mitigating the effects of future changes in the environment like climate change on the complex arthropod–pathogen–host epidemiological cycle requires understanding of a variety of complex mechanisms from the molecular to the population level. Although there has been substantial progress on many fronts the challenges to effectively understand and mitigate the impact of potential changes in the environment on vector-borne pathogens are formidable and at an early stage of development. The challenges will be explored using several arthropod-borne pathogen systems as illustration, and potential avenues to meet the challenges will be presented.

Key words: vector-borne diseases, episystems, Bluetongue, West Nile.

Introduction

Vector-borne diseases continue to plague world health. The World Health Organization estimates the following global annual impact: 300 million malaria cases (WHO, 2009a), 50–100 million dengue cases (WHO, 2009b), and 120 million filariasis cases (WHO, 2000). The toll from other vector-borne diseases like trypanosomiasis, leishmaniasis, Japanese encephalitis, onchocerciasis and yellow fever add more millions of cases each year. It has been estimated these diseases represent 17% of the global disease burden due to all parasitic and infectious diseases recorded as disability-adjusted life years (Townson et al., 2005).

There has been enormous progress in medical entomology since arthropods were shown to transmit pathogens to humans over 120 years ago. It is now accepted that vector-borne disease cycles are complex systems due to the requisite interactions between arthropod vectors, animal hosts and pathogens that are under the influence of environmental factors that contribute to variation in disease transmission in complex ways.

This paper will explore the influence of a changing world, focusing on the influence of the environment with emphasis on the effects of climate change on vector-borne diseases. Climate is a major environmental driver influencing vector-borne disease epidemiology. Many papers have explored the potential consequences of global climate change, particularly the impact of global warming, on vector-borne diseases (Dobson and Carper, 1992; Epstein, 2000; Epstein, 2007; Githeko et al., 2000; Greer et al., 2008; Hay et al., 2002; Kobayashi, 2008; Linthicum et al., 2008; Sutherst, 2004; Toussaint et al., 2006). The Intergovernmental Panel on Climate Change (IPCC, 2001; IPCC, 2007) lists vector-borne diseases among the most likely consequences to change due to changes in climate. The sensitivity of vector-borne disease cycles to climate has resulted in the view that vector-borne diseases can serve as ‘the canary in the mine’ as a first alert of changes due to climate (Randolph, 2009).

Despite evidence that climatic patterns, including temperature and rainfall patterns, have direct effects on vector-borne diseases, there are reservations about the potential for predicting future effects of climate change on vector-borne diseases (Dobson, 2009; Fish, 2008; Gould and Higgs, 2009; Gould et al., 2006; Gubler, 2002; Gubler, 2008; Gubler et al., 2001; Lafferty, 2009; Randolph, 2009; Reiter, 2001; Reiter et al., 2004; Russell, 1998; Sutherst, 2004). These papers explore alternatives to climate-driven hypotheses for vector-borne disease epidemiology and generally point to the need for greater understanding of the ecology of vector-borne diseases in order to understand and predict the effects of future changes in the environment. For example, although climate change has been linked to changes in the epidemiology of malaria (i.e. Githeko et al., 2000; Pascual and Bouma, 2009; Watson and McMichael, 2001) and dengue (i.e. Benitez, 2009; Hales, 2003; Patz et al., 1998), others have focused on the complexity of vector-borne disease cycles and proposed alternative likely explanations for the observed patterns of malaria (Lafferty, 2009; Reiter, 2001) and dengue (Gubler, 2002).

Vector-borne diseases will continue to evolve in a changing world as they have done throughout history. For example, the evolution of the domestic form *Aedes aegypti aegypti* (L.) occurred after humans began storing water in containers. This type of water storage provided the niche for the evolution of this container-breeding mosquito and led to its urbanization and commensalism with humans, resulting in an increase in the level of transmission of both yellow fever virus (YFV) and dengue virus (DENV) (Tabachnick,

1991). We live in a rapidly changing world. We must be prepared for changes in the world in advance and prioritize health-related resources to prevent or reduce the impact of vector-borne diseases on human health. Unfortunately, our understanding of the underlying mechanisms that influence vectors, pathogens, hosts, interactions between all three, and vector-borne disease systems at all scales is rudimentary at best and hence forecasting the future of vector-borne diseases is fraught with uncertainty (Tabachnick, 1998; Tabachnick, 2003). This review will use the concept of an 'episystem' (Tabachnick, 2003) to (1) describe the complexity of vector-borne disease cycles, (2) explore the influence of climate on these systems, (3) explore our capability to assess the potential impact of changes in climate on these systems, (4) set the issue of climate in the broader context of environmental change in general, and (5) outline the kinds of information that will be necessary for accurately predicting future climatic or environmental effects on vector-borne disease systems.

Vector-borne disease episystems, scale and the influence of climate

The vector-borne disease episystem encompasses all of the biological and environmental components and aspects of the entire epidemiological vector-borne disease system within specified geographical and/or temporal scales. It has been used previously to define different epidemiological systems for the vector-borne animal pathogen Bluetongue virus (BTV) (Tabachnick, 2003). The episystem includes the vectors, the hosts, the pathogens, the biological controlling mechanisms and all of the environmental factors that have an effect on disease epidemiology within a defined spatio-temporal region. Episystems might occur at different levels of scale. For example, one might define the episystem for a specific pathogen at the local level of a village or town, which may be a different episystem with different components and influences than the same pathogen defined at the countrywide, continental wide or the global level. An episystem might be defined temporally if various controlling factors have different influences over time. For example, the West Nile virus (WNV) episystem in the northeast USA in 2000 may be different from the current episystem in the same region due to changes in vector populations, avian amplification host populations, human behavior and climate over the past decade.

Fig. 1 is modified from a concept developed by Sutherst (Sutherst, 2004) to emphasize the complexity of the interactions between some contributing factors, including the direct and indirect influences of many factors on vector-borne disease. The disease cycle, represented by the vector–pathogen–host relationship, has multiple influences that are interconnected and/or dependent on one another. Fig. 1 is a useful abstraction for visualizing vector-borne disease episystems. Climate has direct effects on the vector, pathogen and host, and their interactions with one another, yet climate also has direct influence on other environmental factors that in turn may also directly influence vector-borne disease transmission cycles. Poverty and human population size although likely to be influenced by climate also influence vector-borne disease cycles independent of climate. Although climate in the form of rising temperature has been proposed to influence the surge of increased dengue in the world in recent years, there is also good reason to believe that this surge may be due to the increases in the size and distribution of urban human populations, continuing poverty in many parts of the tropical world and an erosion of public health infrastructure in many regions (Gubler, 2002; Gubler, 2008).

Climate, i.e. temperature, precipitation, humidity, wind, etc. can influence various aspects of an arthropod vector's life cycle, including survival, arthropod population numbers, vector pathogen interactions, pathogen replication, vector behavior and of course vector distribution. Table 1 lists several possible influences of climate on vectors and shows the potential influence on vector-borne disease cycles. Understanding of the influence of climate on several current vector-borne disease episystems has provided knowledge about vector-borne disease epidemiology and has allowed greater ability to forecast vector-borne disease outbreaks in current episystems. For example, the influence of rainfall and drought periods on WNV epidemiology in North America has been integrated in surveillance and risk prediction for WNV in California

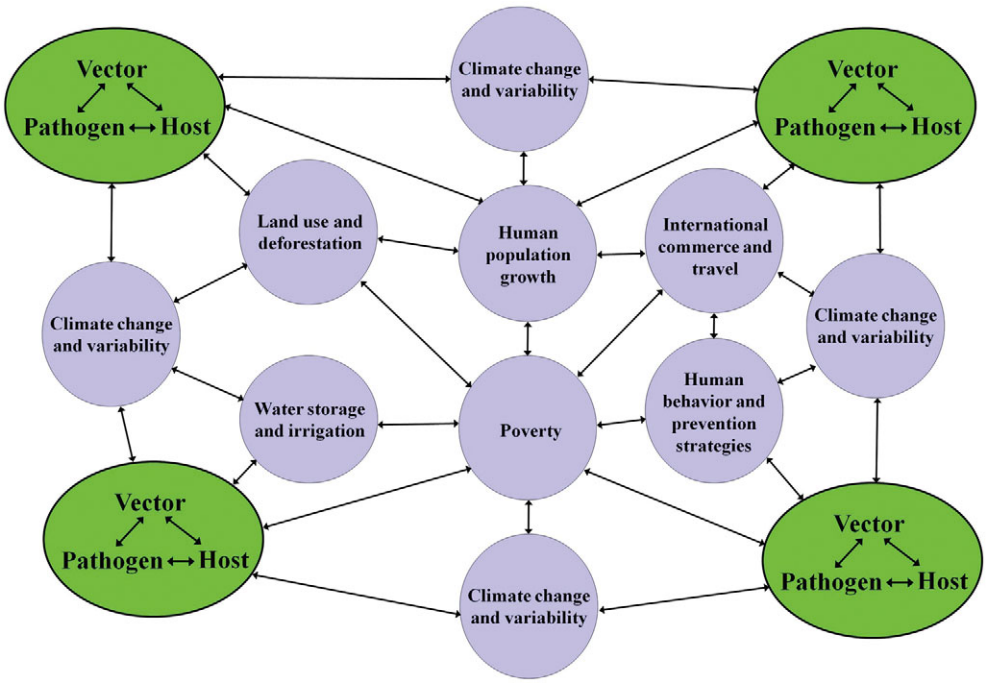

Fig. 1. The vector-borne disease episystem illustrating interactions between selected environmental factors with effects on the vector–pathogen–host epidemiologic cycle [modified from Sutherst (Sutherst, 2004)].

(Reisen et al., 2004) and Florida (Shamen and Day, 2005). El Niño/Southern Oscillation and satellite imagery that included temperature and rainfall information was used successfully to predict a Rift Valley fever outbreak in the Horn of Africa (Anyamba et al., 2009). Climate has influenced vector-borne diseases and in the future will continue to influence vector-borne disease at local, regional and continental scales.

Predicting future vector-borne disease episystems

Gauging the direct influence of the environment on vectors, pathogens, hosts and vector-borne disease episystems is a difficult challenge. Predicting the consequences of future environments and future climate changes on current episystems or the potential for the development of new episystems is much more difficult. Tabachnick explored the issues and challenges to predicting emerging vector-borne pathogen transmission in different regions of the world and the consequences associated with the purposeful introduction of modified vectors to prevent pathogen transmission (Tabachnick, 1998; Tabachnick, 2003). The difficulty in making successful predictions about disease transmission due to potential environmental changes is the paucity of available information on the mechanisms controlling and influencing specific components of the complex vector–pathogen–host cycle. This is illustrated by the lack of information about mechanisms controlling vector competence for specific pathogens. Vector competence is the susceptibility of the vector to infection with the pathogen and the ability of the infected vector to transmit the pathogen to a host during blood feeding. Vector competence is a key component in the vector–pathogen cycle. There are many examples of both genetic and environmental variation causing variation in vector competence between vector species, populations and between individual vectors (Beerntsen et al., 2000; Tabachnick, 1994). However, the complexity of genetic and environmental effects on vector competence has hardly been explored. The specific genes influencing vector competence in nature are virtually unknown. The array of vector competence phenotypes produced by various genotypes in different environments, the norm of reaction of the genotype, have yet to be thoroughly characterized (Tabachnick, 2003).

The complexity of the effects of the environment on a vector-borne pathogen is illustrated by *Culex pipiens quinquefasciatus* Say competence for WNV. *Culex p. quinquefasciatus* infection with WNV increases with temperature. However, the influence of temperature changes due to the age of the adult, due to the virus dose or viremia, and the effect of these factors on the effect of temperature were non-linear (Richards et al., 2007). The effects on vector infection also differed between two strains of the species, demonstrating that different genotypes respond completely differently to complex environments (Richards et al., 2007). *Culex p. quinquefasciatus* vector competence for WNV was also different from its vector competence for the related virus St Louis encephalitis virus (SLEV). These studies illustrate that norms of reaction under different environments were not linear, and one could not predict vector competence under different environmental conditions (Richards et al., 2007; Richards et al., 2009).

There are no examples of specific genes that control vector competence in natural populations for any vector–pathogen system nor is there information about environmental influences on a specific controlling genotype, the norms of reaction, under interacting arrays of environmental factors. There are complex environmental effects on vector genotypes that are not fully known. We do not yet understand the genetic systems controlling vector competence, the full array of environmental factors influencing genotypes nor how environmental factors interact with one another within any vector-borne disease episystem on a local, regional or higher level. Therefore, it is not surprising that we have little ability to predict the future behavior of episystems under changing environmental conditions.

There is much to be learned by exploring these issues with current vector-borne disease episystems. In the last 10 years two new vector-borne disease episystems came into being. The first is the North American WNV episystem after the entry of WNV into the USA in 1999. The second is the BTV European episystem, which developed following the entry of BTV into Europe in 1998. I will use these two episystems to explore evidence that climate change or other environmental factors influenced their development.

Examples of climatic and environmental influences on the formation of new episystems

Bluetongue virus in Europe

Bluetongue, a disease of ruminants, is caused by BTV. Bluetongue provides useful lessons concerning difficulties with climate-driven hypotheses for vector-borne disease episystems. The virus causes clinical signs and significant mortality in sheep and infects cattle, although cattle rarely develop clinical signs. Other animals, including deer, buffalo, elephants, zebra and even lions can be infected with BTV. As a result of its impact on livestock, non-tariff trade barriers restrict livestock trade between Bluetongue-endemic countries and

Table 1. Selected influences of climate conditions on vectors of disease

Climate condition	Influence on vectors
Increasing temperatures	
Higher transmission potential	
	Decreasing vector generation time
	Increasing vector population growth rate
	Decreasing pathogen extrinsic incubation period
	Increasing length of transmission period
Lower transmission potential	Decreasing vector longevity
	Decreasing life expectancy
Increasing abundance of water	
Higher transmission potential	Increase in vector larval habitats
	Increase in vector population sizes
	Increase in animal host populations over time
Lower transmission potential	Decrease vector host interactions with increase in water sources and dispersion of animal hosts
	Some vector-borne disease cycles require periods of drought for pathogen amplification

Both water and temperature will influence host and vector distributions in unknown complex ways.

Bluetongue-free countries. Bluetongue is confined to specific geographical regions where BTV vector competent species in the genus *Culicoides* are found. The virus is considered endemic in parts of the northern hemisphere, Australia, Africa and parts of Asia where one or more of the 24 different BTV serotypes occur. There have been a few reported sporadic outbreaks of Bluetongue in Europe, i.e. Iberian Peninsula in 1956 and 1960, a few Greek Islands in 1979–1980. In 1998 BTV-9 entered Europe for the first time (Wilson and Mellor, 2008). Between 1999 and 2006, Italy (Sardinia, Sicily and mainland Italy) had outbreaks of BTV 1, 2,16. In 2006 BTV-8 caused major outbreaks in Belgium, The Netherlands, Germany, France, Luxembourg and in 2007–2009 it entered the Czech Republic, Hungary, Sweden, Switzerland and the United Kingdom. The spread of BTV throughout northern Europe was unprecedented and represented the appearance of a new BTV episystem. More than a million domestic and wild animals were infected with BTV. In response, several countries initiated BTV vaccination programmes for their livestock to curtail the impact of the disease. Of great alarm were the reports that BTV-8 in northern Europe had caused clinical signs in cattle. Previously BTV was not known to cause substantial clinical signs in cattle.

Fig. 2 as modified from elsewhere (Tabachnick, 2003) shows the worldwide distribution of the BTV serotypes and the different primary *Culicoides* BTV vector species. The BTV endemic regions have specific BTV serotypes associated with different *Culicoides* species. These regions with different *Culicoides* vectors and serotypes are probably different BTV episystems (Tabachnick, 2003). The western hemisphere BTV episystems illustrate the concept of episystems associated with specific vector species. In the USA the primary vector is *Culicoides sonorensis* Wirth and Jones, and the historic BTV serotypes in the USA are BTV-2, 10, 11, 13, 17. In South America, *Culicoides insignis* Lutz is the primary vector, and there is a different suite of BTV serotypes in BTV-1, 3, 6, 8, 12, 14, 17.

The unprecedented rapid expansion of BTV in Europe has been linked to climate change (Purse et al., 2006). The initial phases of BTV entry to southern Europe in 1998–2000 have been attributed to an expansion in the range of the historic primary African vector *Culicoides imicola* Kieffer. This range expansion was believed possible due to higher temperatures in Europe from 1998 to 2006 where seven of the 10 warmest years from 1958 to 2007 occurred and the winter of 2006–2007 was the warmest on record (Wilson and Mellor, 2008). Once BTV entered Europe, several European *Culicoides* species were found to be efficient BTV vectors involved in BTV transmission, i.e. *Culicoides dewulfi* Goetghebuer, *Culicoides pulicaris* (Linnaeus), members of the *Culicoides obsoletus* complex and of course *C. imicola*.

Why did BTV spread to Europe? Is there evidence for the role of climate change? Are other environmental, biological and/or ecological factors responsible? Is it plausible that higher temperatures may have allowed *C. imicola* into southern Europe? Did higher temperatures allow other *Culicoides* to increase their vector competence for BTV (Purse et al., 2005; Wilson and Mellor, 2008)? The influence of the change in Europe's climate as the cause of the expansion of BTV into Europe is plausible. However, there is no objective conclusive evidence for this hypothesis. Although the hypothesis is plausible, plausibility is not proof, and other explanations might be similarly plausible. Several alternative explanations for the change in Europe's BTV epidemiology were dismissed as unlikely (Purse et al., 2005). However, Gould and Higgs stated that although the climate hypothesis has merit they could not dismiss other environmental factors as possible contributing factors (Gould and Higgs, 2008). Other plausible explanations expose the lack of evidence for climate as the main driver.

Bluetongue viruses are known to move with infected livestock or other animals and any change in livestock and/or exotic animal movements in parts of Europe would serve to spread the virus. For example, an increase in animal theme parks in Europe with an increase in exotic wildlife imported from BTV-endemic regions could have increased the likelihood of the entry of BTV, its spread and epidemiology. Between 1965 and 1995 Europe's animal theme parks increased in France (200%), Germany (30%), Italy (130%),

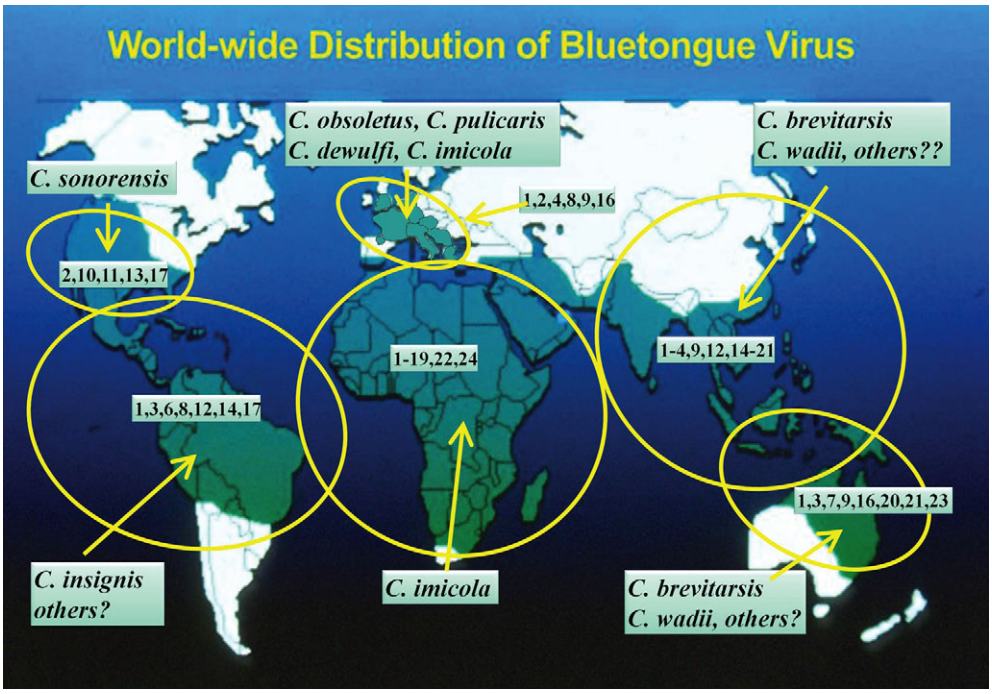

Fig. 2. The worldwide distribution of Bluetongue virus (BTV) serotypes and the primary *Culicoides* vectors in different geographical regions denoting six predominant BTV episystems [modified from Tabachnick (Tabachnick, 2004)].

Spain (230%) and United Kingdom (110%) (from http://www.infoparks.com/flashan/zhistory/frameset.htm). More parks probably mean greater numbers of imported, exotic, potentially BTV-infected animals like elephants, zebra, water buffalo, lions, etc. An estimated 75% of animals in parks and zoos are from the wild purchased from dealers (Encyclopedia Britannica online, http://www.britannica.com/EBchecked/topic/657894/zoo). The movement of animals from the wild to zoos and parks is substantial and there are guidelines for transportation (Linhart et al., 2008). However, there are no restrictions to exclude BTV-infected animals. Unrestricted animal movement remains a plausible explanation for the entry of BTV into Europe (Mintiens et al., 2008). The majority of imported animals are not tested for BTV and would not exhibit clinical signs of disease although they would be sources to infect wild *Culicoides*. Exotic wild animals are also being introduced onto private properties, including hunting preserves and private zoos with little attention to the potential for introducing and/or facilitating the spread of BTV.

There have been changes in wildlife populations in Europe that could influence BTV epidemiology. Wild deer populations have increased substantially in western Europe during the last 20 years. For example, 5.7% of the roe deer sampled in Germany showed BTV antibody indicating previous infection (Ruiz-Fons, 2008). There was little evidence for the role of climate change in the increase in infections due to another vector-borne pathogen, tick-borne encephalitis (TBE) in northern Italy from 1996 to 2006. However, support was found for the influence on TBE increases due to changing forest landscapes and that both red and roe deer, essential hosts in maintaining and amplifying tick populations, had increased 10% from 1996 to 2000 in the region and over 300% in the last 50 years (Rizzoli et al., 2009). Changes in livestock management practices in parts of Europe could also influence BTV transmission. The initial entry of BTV to Italy resulted in the widespread use of modified live attenuated vaccines for several BTV serotypes that may have influenced BTV epidemiology. Further, from 2003 to 2008, there has been a *ca*. 46% increase in the number of cows per herd in Italy (Cavirani, 2008). Changing practices associated with vaccinations, changing practices due to managing larger herds, larger numbers of BTV wildlife animal hosts such as deer, changing animal practices due to higher temperatures and changes in the habitats of *Culicoides* could all contribute or cause changes in BTV epidemiology. There are a host of alternative explanations for the new BTV episystem in Europe in addition to climate-driven hypotheses, and few of the alternative hypotheses have been adequately explored.

Although the range expansion of *C. imicola* was thought essential for BTV entering Europe, other *Culicoides* species in northern Europe turned out to be efficient BTV vectors. The proposed connection between *C. imicola* expansion and BTV expansion is unnecessary. If elevated temperatures are essential to maintain a longer transmission season in northern Europe and/or to allow the resident vectors to transmit, this is not consistent with the western USA BTV episystem where *Culicoides* maintain annual BTV transmission despite long seasons with subzero temperatures. If one assumes that Europe's *Culicoides* are less competent than USA or African vectors, poor vector competence can be offset by large vector population sizes. What are the vector population sizes, and what are the features of the environment that influence Europe's *Culicoides* populations? Baylis et al. showed the difficulty in using temperature alone to model *Culicoides* populations, observing that failures of their model to predict *C. imicola* in Europe indicates temperature was less important than other unknown drivers (Baylis et al., 2004). The entry of BTV into Europe may not have been dependent on the expansion of the range of *C. imicola* and was probably due to the movement of infected animals not infected *Culicoides* (EFSA, 2007). Although climate change, i.e. higher temperature, more precipitation, more frost-free days, may have played a role, it is premature to ignore other alternatives. There is little real evidence that climate change in Europe from 1999 to 2006 played a direct or indirect role on BTV in Europe. Other factors may have been important in initiating and sustaining the European BTV episystem.

Among the 1254 species of *Culicoides* in the world only *ca*. 30 have been incriminated to varying degrees in BTV transmission and all are members of four (*Avaritia* Fox, *Culicoides* Latreille, *Monoculicoides* Khalaf, *Hoffmania* Fox) of the eight known subgenera (Meiswinkel et al., 2004). Tabachnick pointed out that *Culicoides* BTV vector species are unrelated phylogenetically, comprising only selected members of different *Culicoides* subgenera (Tabachnick, 2003). For example *C. sonorensis*, the North American BTV vector, has two closely related sister species that are not BTV vectors whereas *C. insignis*, in a different subgenus, is the primary BTV vector in South America. Hence, *Culicoides* vector capacity and competence between such phylogenetically disparate species did not evolve from a common ancestor (Tabachnick, 2003).

Vector capacity for BTV probably evolved independently, perhaps as a result of different adaptations in these species to other aspects of each species niche. Tabachnick (Tabachnick, 2003) referred to traits that are adaptations for one purpose but also serve a different unrelated function or purpose as exaptations. However, exaptations are also beneficial traits for the organisms that are under natural selection (Gould and Vrba, 1982). There is little evidence that various traits involved in vector capacity are affected by natural selection for their vector capacity functions; hence, these are not adaptations or exaptations. A more correct interpretation based on our current knowledge of vector capacity traits is that these are likely to be the effects of adaptations but the effect is not necessarily adaptive, e.g. has an effect on fitness. Williams used the term 'effect' to describe a function that is a coincidental byproduct of an adaptation but is not the result of natural selection (Williams, 1966). For example, although vector longevity is an adaptation likely to be under selection, the role of longevity in vector capacity is not under natural selection and is a byproduct much like playing chess is a byproduct or an effect of the adaptation of the human brain. I will explore the significance of this view of vector capacity traits in understanding the consequences of environmental change elsewhere under Conclusions.

Culicoides vector capacity is not a phylogenetic ancestral trait, and apparently some vector capacity traits arose independently in disparate species. Hence, it is unlikely that the different *Culicoides* vector species share similar controlling mechanisms for selected vector capacity traits. Unfortunately without knowing the specific controlling mechanisms, without being able to explore environmental influences on genotypes (norms of reaction), without understanding pleiotropic fitness effects of vector capacity traits and with the possibility of different mechanisms in diverse species, there is little possibility of predicting the future consequences of a changing environment on these complex episystems.

Aside from the recent expansion of BTV to Europe, other BTV episystems have remained remarkably stable during the past 50 years. However, the finding of new BTV serotypes, i.e. BTV-3, 5, 6, 14, 19, 22 in Florida between 2004 and 2006 demonstrates how little we know about BTV episystems (Gibbs et al., 2008). The spread and impact of BTV on USA livestock in this changing

episystem is uncertain. There is little predictability what the consequences of a changing world will be for BTV episystems. Information is needed on the causes, influences and dynamics of the BTV episystems, on vector–pathogen–host interactions and information on the complexity of environmental interactions to understand how BTV episystems evolve in a dynamic and ever changing world.

WNV in the USA

The entry of WNV into New York City in 1999 and its spread in the ensuing five years throughout the USA illustrates episystem complexity and difficulty in predicting the consequences of an introduction of a vector-borne pathogen. Prior to 1999, WNV was found in the Palearctic, Afrotropical and Oriental regions where it periodically caused infections and outbreaks transmitted by species of *Culex*, including *Culex univittatus* Theobold, *Culex pipiens* Linnaeus and members of the *Culex vishnuii* Theobold complex to name a few (Hayes, 1989).

Fig. 3 shows the progression of WNV transmission throughout the USA after its introduction. As WNV spread it encountered new environments and new vector species. The figure only approximates the ranges of the primary USA vectors of WNV illustrating that there are probably at least four different episystems for WNV in the USA represented by the ranges of *Cx. p. pipiens*, *Cx. p. quinquefasciatus*, *Culex nigripalpus* Theobold and *Culex tarsalis* Coquillet. These ranges overlap and probably interact and influence one another. More accurate range distribution maps can be found elsewhere (Darsie and Ward, 2005).

Throughout its range WNV is dependent on avians as the primary hosts for amplification, as reservoirs for the virus and for spreading WNV by the migration of infected birds. Climate, particularly high summer temperatures and exceptionally heavy rainfall, was thought to influence WNV transmission in South Africa (McIntosh et al., 1976). However, the establishment of the North American WNV episystems was unexpected and the consequences were not entirely predicted. Prior to 1999, the following information was available for predicting the consequences of a WNV introduction into the USA: (1) as in most of the world the USA vectors would probably be species of *Culex* mosquitoes, and (2) because SLEV was already present in large portions of the USA, and transmitted by *Cx. p. pipiens*, *Cx. p. quinquefasciatus*, *Cx. nigripalpus* and *Cx. tarsalis*, it was likely these would also play a role in transmitting WNV. At the time of introduction in 1999 it was not yet then known that: (1) *Cx. tarsalis* was a more efficient vector of WNV than SLEV, (2) WNV would cause higher bird viremias, greater bird mortality and greater infectiousness compared with SLEV, and (3) aspects of SLEV episystems and WNV episystems are both influenced by cycles of drought and precipitation. The *Cx. nigripalpus* episystem in Florida illustrates this last point. A major driver of the *Cx. nigripalpus* episystems in Florida is the same for both WNV and SLEV (Day and Shamen, 2008; Shamen et al., 2005). Increased transmission in these episystems is dependent on the correct timing between increasing *Cx. nigripalpus* populations coinciding with the nesting bird populations. This may occur when Florida spring and summer drought conditions force bird and mosquito populations into contact around the few remaining sources of fresh water resulting in an initial round of viral amplification. Heavy precipitation events begin in Florida during mid-summer allowing the virus, mosquitoes and birds to become more widely distributed. The essential climatic conditions then necessary for efficient viral amplification is a secondary drought period, forcing mosquitoes and birds together again, increasing the amplification of the virus, followed by a large rainfall event resulting in the distribution of infected vectors and the involvement of humans and other host animals. These cycles are the signature conditions in Florida for both SLEV and WNV, although this was not known for WNV prior to it entering Florida in 2001.

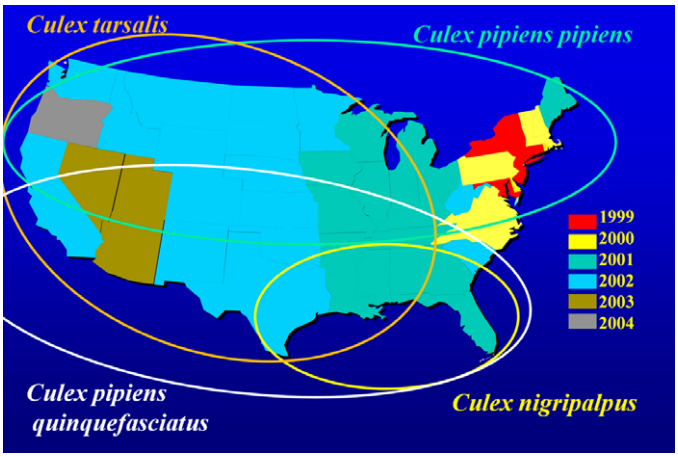

Fig. 3. The progression of West Nile virus (WNV) through the USA from 1999 to 2004, and general approximate ranges of the principal USA WNV vectors denoting the four major USA WNV episystems. Accurate range maps are described elsewhere (Darsie and Ward, 2005).

Several conclusions can be drawn from the USA WNV episystem(s). (1) There is little evidence that the entry and establishment of WNV in the USA was influenced by climate change. The WNV vectors were present in the USA, and entry of WNV was not contingent on climate change in North America (Gould and Higgs, 2009). (2) There was little predictability about the extent of transmission of WNV and risk to humans. (3) The various WNV North American episystems are influenced by factors specific to the individual systems. For example, in the southeast USA where *Cx. p. quinquefasciatus* broadly overlaps with *Cx. nigripalpus*, the epidemiology of WNV transmission by *Cx. nigripalpus* is strongly influenced by the timing of drought and rainfall events that are less important to WNV transmission by *Cx. p. quinquefasciatus*. This situation is analogous to the western USA where *Cx. tarsalis* WNV transmission is also influenced by cycles of drought and rainfall. There is evidence that *Cx. tarsalis* WNV transmission in California was influenced by higher summer temperatures (Reisen et al., 2006). (4) All four primary USA vector species are in the subgenus *Culex* but this subgenus also includes 10 other species in the USA (Darsie and Ward, 2005) that are not prominent in WNV epidemiology. *Culex p. pipiens* and *Cx. p. quinquefasciatus* in the USA are subspecies. Hence, their shared ancestry may have resulted in shared vector traits, common by descent. Accordingly their vector capacity for WNV may be due to similar controlling mechanisms. The other USA WNV vector species and other WNV vectors elsewhere in the world, i.e. *Culex univittatus* and *Culex vishnuii*, are also in the subgenus *Culex* although the remaining 212 species in the subgenus in the world are not considered WNV vectors. Therefore, similar to the *Culicoides* Bluetongue episystems, it is unlikely that the traits and mechanisms making an efficient WNV vector are shared between disparate species through a common ancestor of *Cx. tarsalis*, *Cx. univitattus*, *Cx. vishnui* and the two *Culex pipiens* forms. (5) Because there are probably few shared traits by descent one must assume that controlling mechanisms for vector–pathogen–host interactions also

differ between the episystems and that there are differences in the environmental factors that affect different episystems. (6) The influence of environmental factors on vector–pathogen–host interactions is complex and interacts with one another in complex unpredictable ways.

The impact of WNV on human populations in the USA far exceeded predictions based on the experience with the closely related SLEV and the WNV transmission patterns in other parts of the world. The estimated 1,000,000 people who have been infected with WNV in the USA from 1999 to 2009 exceed the numbers of SLEV human infections in the USA during the past 60 years. Has climate change influenced WNV transmission in the USA? Will changes in temperature, rainfall, patterns and seasonal shifts influence WNV transmission in the USA? Although there is evidence that climate has influenced WNV transmission in the USA, predicting future changes in WNV epidemiology due to climate change is problematic. Will transmission be increased? Will it be reduced? What types of environmental, epidemiological and ecological information are required to make accurate predictions about worldwide WNV episystems?

Conclusions

Vector-borne diseases, as represented by episystems, are dynamic systems adjusting continually in complex ways to changes in the environment. Climate change will certainly impact these episystems, as will changes in other environmental factors. Unfortunately, the ability to predict the consequences resulting from even specific environmental changes, were these changes known with assurance, requires an understanding that is still lacking. The consequences of climate change are not predictable with assurance, only that there will be likely changes.

The ability to predict future consequences of a changing environment on vector-borne diseases demands greater understanding of the array of biological and environmental features that comprises specific episystems. This will be a daunting challenge because episystems probably will show dramatic spatio-temporal differences requiring biological, environmental and ecological details for a specific episystem. One conclusion from this brief survey is that it is unlikely that vector capacity traits generally evolved from shared common ancestors in phylogenetically disparate vector taxa. It is important to note that this observation leads to the conclusion that many of the controlling features and mechanisms differ between episystems. This adds to the difficulty of predicting future consequences and applying information from one episystem to other episystems. The four North American *Culex* (*Culex*) vectors of WNV have many related non-vector species, as do the *Culicoides* BTV vectors. How did vector capacity traits that allow transmission of specific pathogens evolve? Are there factors that influence the evolution of vector capacity? What are such factors? Although the discussion here leads to the conclusion of convergent evolution illustrated by diverse *Culicoides* species independently having a suite of traits that permit them to be BTV vectors, all known BTV vectors are in different subgenera within the genus *Culicoides*. The North American WNV vectors are all in the same subgenus of *Culex*.

Tabachnick discussed the possibility of associations between phylogenetically related vectors and pathogens, and did not find significant evidence for co-evolution between mosquitoes and arboviruses in the strict sense (Tabachnick, 1998; Tabachnick, 2003). The observation that distantly related species share vector status for the same pathogen is consistent with the possibility that many vector capacity related traits are not adaptations under natural selection for their role in vector capacity. Vector capacity traits may arise incidentally due to shifts in function of traits that are adaptive for other reasons. Could there be some common capacity blueprint, shared by *Culicoides*, which provides the potential for traits that can shift to new functions required to be a BTV vector by selected species? Could a similar blueprint exist in the subgenus *Culex* allowing vector capacity through shifts to a suite of traits needed to be a WNV/SLEV vector? This would be analogous to the concept of the bauplan or blueprint (Mayr, 1982). Although more widely used to refer to a general body plan, here I use bauplan to encompass a fundamental blueprint for the suite of traits needed to be a vector of a pathogen. For example, the ancestral bauplan of the genus *Culicoides* provides a fundamental blueprint from which certain species within the genus evolve into different niches. As a byproduct of evolving into a specific niche some species will possess traits and mechanisms that can shift or be co-opted to enable them to be a vector of a pathogen purely as a byproduct of evolving into the specific niche. For example, this occurred when BTV came into contact with European *Culicoides* that could transmit BTV, and when WNV came into contact with North American *Culex* that could transmit WNV. The suite of traits required to be a vector are derived independently due to shifts to new functions in only selected *Culicoides*, excluding other taxa and dependent on a *Culicoides* species evolving in a particular niche. In this view, the vector species is a byproduct of a variety of adaptations. The vector simply occupies an ecological niche that encompasses traits allowing it to vector a specific pathogen. The bauplan in the genus *Culicoides* or subgenus *Culex* provides the potential for only some of the derived species in certain niches to evolve traits that will allow shift in function and potential for vector capacity. Accordingly vector status is the result of a convergence of different traits resulting in similar vector capacity phenotypes among *Culicoides* for BTV, subgenus *Culex* for SLEV and WNV, *Anopheles* for malaria and among *Aedes* subgenus *Stegomyia* for YFV and DENV to name a few. Identification of the characteristics that comprise the bauplan in the genus *Culicoides* or in the subgenera *Stegomyia or Culex*, and which traits in the bauplan have effects on vector capacity would help in identifying shared mechanisms between taxa, and help to understand and predict future changes in vector status. Understanding the adaptations that also play a role in vector capacity provides information on the fitness effects of the adaptations, and hence of the vector capacity traits. Information concerning the effects of adaptations on vector capacity would be useful in establishing how vector capacity evolves and provide insight into how vector capacity traits are maintained in vector populations. The fitness consequences of the adaptations is essential to how vector capacity will respond to future environmental change including climate and changes in vector population genotypes that are the result of strategies to reduce vector capacity through release of genetically modified vectors.

Aedes albopictus (Skuse) and *Aedes aegypti* (Linnaeus) may share common mechanisms derived from their common ancestor enabling them to transmit YFV and DENV. However, *Ae. aegypti aegypti,* recently evolved from sylvan *Ae. aegypti formosus* (Walker) (Tabachnick, 1991). Therefore, the extreme anthropophily of *Ae. aegypti aegypti*, and one of the reasons it is so efficient as a vector of human pathogens, is probably recently derived since the divergence from its common ancestor with the sylvan *Aedes aegypti formosus*. Are there different YFV episystems? Are there different DENV episystems? *Aedes aegypti* is distributed worldwide and different regions have *Ae. aegypti* populations with differences in their genetic structure and vector competence (Tabachnick, 1991). Accordingly for example, there is no reason to assume that the YFV

episystem in South America has the same characteristics, mechanisms and influences compared with YFV episystems in Africa. What of smaller episystems in local villages, towns, cities, regions? What of temporal episystems over time, seasons, years? Analogous questions can be asked for malaria and *Anopheles* species and for all other vector-borne diseases.

Although models of specific episystems provide the ability to assess the effect of changes on the model outcome, models are generally simple tools that cannot be used to predict realistic future consequences in natural systems. Unfortunately efforts along these lines have been used to make dire predictions concerning the spread and impact of vector-borne diseases due to changes in climate.

There is no doubt that vector-borne disease episystems will continue to evolve in a changing world. However, although we can study the causes of changes after the change occurs, predicting the effects of future environmental changes on complex episystems is problematic. Much more knowledge is needed about specific episystems. This includes knowledge of controlling mechanisms of the essential vector–pathogen–host interactions, characterization of the environmental impacts to explore norms of reactions for specific genotypes and causes controlling episystem evolution. This will lead to greater predictability and better assessments of the risk of disease in different regions (Tabachnick, 1998; Tabachnick, 2003).

As we proceed to fully understand these complex systems, mankind can reduce the impact of these diseases now. The following are some priorities that can significantly reduce vector-borne diseases: (1) ensure better health care to include improving the health care infrastructure in developing countries, (2) institute better surveillance protocols for these diseases throughout the world to quickly bring to bear resources to reduce epidemics, and (3) eliminate the poverty in the world that allows exposure to the vectors and makes it difficult to garner the resources to reduce the misery associated with these diseases (Beaty and Eisen, 2008). There are great challenges ahead to better understand vector-borne disease episystems. We must develop this information to be able to predict the consequences of a changing world on these complex disease systems. Mankind can reduce the burden of vector-borne disease now through a commitment to address the above priorities no matter the future impact of a changing world.

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