Review Article

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Factors affecting the emergence and prevalence of vector borne infections (VBI) and the role of vertical transmission (VT)

Francisco Miled Pherez

Department of Medicine, New York Medical College at Metropolitan Hospital Center, New York, U.S.A.

Abstract

Vector-borne infections (VBI) are very common around the globe and they account for many devastating diseases. They are not found exclusively in the third world or tropical regions but spread to every corner of the planet. The factors driving these infections are many and interact in very complex ways. This review attempts to put into perspective the external—climate change and demographics, as well as the internal factors that drive these infections with particular attention to the role that verticle transmission (VT) plays in the prevalence and emergence of these infections. VT has been widely demonstrated, its role in the maintenance of disease in nature has been suggested, but whether this role has a positive or negative effect seems to vary from species to species. The incorporation of this mechanism of transmission into the classic cycle of infection/maintenance of disease seems to explain important aspects of the epidemiology of VBI.

Key words Climate – cycle – environment – infection – mosquitoes – pathogen – reservoir – transmission – vectors – vertical

Introduction

Vector-borne infections (VBI) were first described in 1877 when lymphatic filariasis was found to be transmitted by mosquitoes from human to human[1]. For the past 128 years several VBI have been described involving a wide variety of infectious pathogens, together with a wide range of arthropods.

Vectors account for the transmission of malaria, lymphatic filariasis and leishmania, three of the most common infections on the planet (WHO) that affect millions of people worldwide with severe impacts on economic and social development. In the US, VBI are responsible for lyme disease (LD), babesia, tularaemia, ehrlichiosis, plague, rickettsial infections and west nile virus (WNV) among others[2].

The economic impact of these infections and the selection pressure that they exert on the human population justify the need for a greater understanding of their dynamics, and the factors influencing them.

The purpose of this review is to bring into context the role of verticle transmision (VT) in the arthropod cycle and its influence in the appearance and maintenance of VBI, while recognising that environmental and demographic factors play a central role in the dynamics of these diseases.

Environmental and demographic interactions

Environment: It has long been assumed that VBI must be influenced by climatic and seasonal changes in the same way as vectors are. However, the evidence sup-

porting this assumption is inconclusive. Data based on observation, have suggested that since the vector population changes given a change in climate, then VBI must also vary accordingly, however, this is a simplistic view. While mosquito populations and their activities increase during the rainy season, there are other variables that have to be taken into account when analysing the epidemiology of a certain infection and its relation with climate variations. A recent study[3] suggested that, while climate changes drive higher or lower rates of certain diseases, this is not the sole factor affecting the incidence of such diseases, but they also indicated that the increase in incidence of malaria on the African highlands was also the result of other environmental changes including a drop in the pesticide use, human migration and emergence of drug resistant strains, etc. In the US and Europe, in the last 20 years an increase in the incidence of LD and tick population density has been reported. This has been attributed, in the case of Europe, to climatic changes specifically to warmer climates, whereas in the US the changes have been attributed to increased awareness of the tick and an increase in reservoir population following reforestation[3] and hunting regulation.

Global warming has also been implicated as a possible driver of change in VBI. While this is very possible, at the local level, there are other important factors to be taken into account such as dam construction, wide use of pesticides, local incidence of resistant strains, availability of potable water, risk of flooding, etc[4]. Isolated climatic changes such as El Nino Oscillation Cycle (ENSO) phenomenon or other natural disasters, combined with severe poverty and poor access to health services have more predictable outcomes than long-term and slow climatic changes[4]. ENSO is a cyclic climatic event that is associated with heat waves and drought in southern Africa and Asia, while bringing floods to the coast of South America and Central Africa[3,5], these changes have been associated with changes in the pattern of transmission of some infections, many of which are transmitted by vectors[6]. An example of this is the outbreak of Rift Valley Fever in Kenya in 1997–98, after the worst flooding since 1961 and attributed to the ENSO event[7].

With regard to the anthropogenic effects on the environment, it has been proposed that urban development, deforestation, wide use of pesticides, increased international trade and travel, increase in farming, use and development of irrigation, and increase in the emissions of green house gases, in particular CO_2 and methane, could together and individually change breeding patterns in vectors, prolong exposure, to accelerate development of pathogens, shift in endemic areas, to increase exposure of non-immunised individuals, etc. The increase in emissions of gases will change climatic conditions more specifically by reducing the minimum temperatures giving narrower diurnal and nocturnal ranges, and, therefore, better conditions for the development of vectors[4]. It has been observed that in the last 100 years, the emission of CO_2 and methane have increased their atmospheric concentrations by one-third and 100% respectively, this in turn affects plant biology by reducing the amount of water lost and increasing plant foliage. Increase in foliage produces a suitable microenvironment for vectors. The soil also gets saturated faster with water leading to the formation of water reservoirs where mosquitoes can breed[5].

Not all the changes in climate favour vectors. More extreme temperatures can work both ways, for example increased flooding and rain fall have a positive effect on vectors by providing the adequate microenvironments for the breeding of mosquitoes. But it also means colder and longer winters, which most likely have a negative effect[3,4].

Demographics: The effects of demographics on disease transmission have been evident for many centuries, as a species adopts a gregarious behaviour; it becomes susceptible to disease transmission and instrumental to the life cycle of pathogen and vector.

Historical records show evidence of such a relationship, where the epidemics of plague and flu in Europe and Smallpox in Mesoamerica[8,9] exemplify the effect of increased trade and travel in the amplification and globalisation of an infection. If we add to that the dynamics of vectors, the results can prove devastating to immunologically naïve individuals[10].

The expected growth of the human population for the year 2050 is four billion—ten billion humans will be inhabiting the earth[5]. Although a higher proportion of those people will live in cities, the extreme poverty in regions of the world that have the greatest concentration of people would still allow for the perfect conditions for the transmission of disease.

There is also increased invasion of wild habitats with resulting changes in land use and biodiversity. Increase in transport networks and modes allow more people to travel around the world in ever-shorter time. The above conditions make for non-immune individuals to be exposed to infections and for infections to appear in new places.

The movement of reservoir livestock from one area to another or the importation of vectors[2] can bring with it new diseases with great adaptability in the part of the pathogen and the vector. An example of this is the shipment of livestock infested with ticks over great distances that brought African tick bite fever from sub-Saharan Africa to the West Indies, making this endemic disease in one region an emerging infection in another[11]. Another example is the import of *Aedes albopictus* (Asian tiger mosquito) into the US, first found in Texas in 1985[2,12] and now widespread in the mid-Atlantic and midwest regions, capable of potentially transmitting diseases like dengue, yellow fever (YF), WNV and La Crosse (LAC) encephalitis virus[2,12]. Migration of infection is not only the result of human movement. The genetic similarities between WNV found in Kenya and Romania suggests that this virus was brought into Europe by migrating birds from Africa[7]. The outbreak of WNV in New York in 1999 is closely linked to a virus found in a dead goose in Israel in 1998[13].

Our relationship with other species is also a factor that promotes the transmission of VBI, as exemplified by the risk for contact with the dog tick *Rhipicephalus sanguineus,* known vector for *Rickettsia conori* and alternative vector for *R. rickettsi*[14].

The vector-pathogen relation

The vector and pathogen interactions greatly affect the dynamics of VBI and explain many of the particular characteristics of each infection and its epidemics. Vectors require certain environmental characteristics that are unique for each type of organism. Mosquitoes for instance require humid conditions, whereas ticks can live in warm dry climates[14]. On the other hand, pathogens require a vector and a reservoir, in many instances the vector can serve as both, like in *B. burgdorferi/Ixodes scapularis*[11]. Some pathogens need an enzootic cycle, whereas others are exclusive to humans and are capable of maintaining their cycle by human–vector–human transmission like dengue and malaria[2]. Pathogen versatility has been exemplified by field evidence pointing at *R. sanguineus* as a viable alternative vector for the transmission of Rocky Mountain Spotted Fever in cases reported in Arizona, where this infection is not typically found[14]. This versatility, amplifies the possibilities for VBI to emerge in regions where they traditionally are not encountered.

Vectors are not exclusive to any particular pathogen, and can, not only transmit more than one disease but they can do so at the same time. As in the case where, a patient was found to have both LD and human granulocytic anaplasmosis (formerly Ehrlichiosis), suggesting a transmission of both *B. burgdorferi* and *E. equi* by the same *Ixodes scapularis* tick[15]. This co-infection has been confirmed in up to 5.5% of nymphal ticks at Westchester County[15]. Also there is suggestion of

dual infection by *Babesia microti* and *B. burgdorferi*, which may result in a more severe illness[15].

Vertical transmission

Since 1906, it was suggested that transovarial transmission occurred in the *Ae. aegypti*/YF pair, but the evidence was indirect and multiple failures to confirm this left the issue unresolved until the 1970s when reports of transovarial transmission of La Crosse and Japanese encephalitis virus were published[16].

Transmission of infection to humans from mosquito bites occurs when the female takes a blood meal. This would suggest that, epidemics of infections transmitted by mosquitoes could only occur after the eggs hatch and the female mosquito is mature enough to take its blood meals. This fails to explain why epidemics sometimes occur early in the rainy season, why infections can remain in relatively limited areas with apparently not enough factors to sustain them, or the overwintering, in which infections disappear during the cooler months and then reappear in the warmer moister months.

The dynamics of VBI are largely dictated by factors that influence vectors directly, but the pathogen can change this dynamic and shorten the cycle of infection, this is accomplished by two mechanisms of VT: one, via the transovarial route; and the other by infection of eggs from female arthropods after oviposition, both leading the way to venereal transmission from male to female mosquitoes (Fig. 1).

As in the case of the YF epidemic in Para state, Amazon in 1998–99[17], this would explain how the virus remained in the region probably because of a transgenerational vertical transmission; from the female mosquito to the eggs that hatch in the next rainy season[17]. This mechanism of transmission has been demonstrated in the wild[18–20] and in the laboratory, VT has been shown to be sustainable[21]. This means

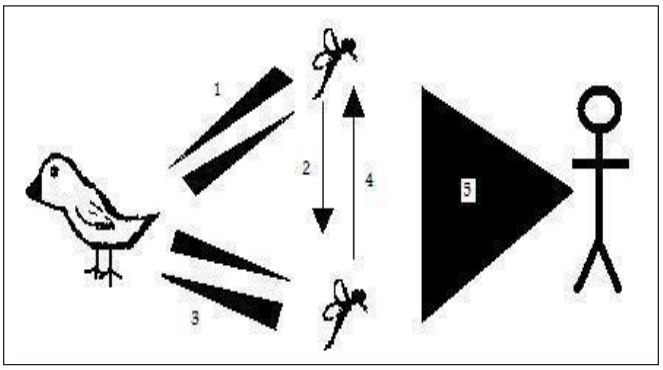

Fig. 1: Cycle of infection taking into account the consequences of vertical and venereal transmission (1—Classic wild cycle and maintenance of disease in nature; 2—Vertical transmission from mother vector to offspring; 3—Maintenance of wild cycle from vertically infected vectors; 4—Venereal transmission from vertically infected male vectors to non-infected female vectors; and 5—Transmission to dead-end host from orally, vertically and sexually infected female vectors)

that the virus can be transmitted earlier increasing horizontal transmission to humans[19,22,23]. In the epidemics of YF in Peru, it seems that a likely explanation for the overwintering and maintenance of the disease is found on the possible VT, in view of the lack of a wild vertebrate host to maintain the disease in nature[24]. Another way of amplifying the horizontal transmission of infections, is the venereal transmission of viruses form vertically infected males to naïve mature females, shortening the incubation period within the mosquito, and hastening the human infection[25–29]. The rate of VT is also influenced by climatic conditions, as is vector efficiency[18]. For some vector-pathogen complexes higher temperatures mean more infectiousness and vertical transmission rates as in *Aedes*-dengue, whereas for *Culex*-Western Equine Encephalitis, cooler climates seem to exert a favourable effect[27,30]. There also seems to be certain susceptibility in the part of the *Aedes* to YF, and this is dictated by geographical distribution and genetic control[27].

In the case of dengue, *Ae. albopictus* has been shown to be a very infectious vector for this virus and is

also capable of VT at higher rates than *Ae. aegypti*. This gives it a role in the maintenance of the disease in nature, helping in overwintering and keeping virus levels even years before an outbreak occurs[31–33].

LAC virus has been shown to be capable of transovarial transmission in nature in *Ae. albopictus* collected in Tennessee, a fact that may give the mosquito an alternate role in the transmission and prevalence of the disease in the wild[12]. Another form of VT is exhibited by WNV, it occurs during oviposition by the female mosquito. This mechanism of VT seems to be a characteristic of Flaviviruses and although this mode of infection is not as efficient as the transovarial route, it may provide the means for a sustained source of WNV infection in a setting where an amplifying host is absent[13].

There are those who believe that VT and the "edge" it gives to the infection is relatively unimportant when it comes to mosquitoes like those of the genus *Culex*, since its eggs hatch immediately following embryonation, in contrast with *Aedes* eggs which are desiccation resistant[13]. It seems also that the ability to diapause (mechanism for overwintering) is largely dictated by the geographical distribution, and may have an effect on the rate of VT[34]. Transovarial transmission has also been described in ticks and other vectors, with a long list of bacteria transmitted by them[11,35,36].

Vectors like Ixodes ticks also show transtagial and co-feeding transmission of the bacteria and they feed on each step of their life cycle, therefore, multiplying the chances for transmission of disease.

While VT may be present in all arthropods, it does not seem to be an important factor for all VBI[35,17]. For some tick borne infections like LD, factors such as the mice population, tick behaviour and chances for human contact, seem to be more important in maintaining the disease[35]. The rate of VT may be different for the same pathogen depending on the vector that it is associated with, for example Rift Valley Fever has higher VT rates when paired with *A. lineatopennis* as compared to *A. juppi*[35]. While VT plays an important role in maintaining some of the spotted fever group of *Rickettsia*[37,38], the vector/pathogen relationship is not always beneficial. It has been shown that ticks and other vectors infected with rickettsial bacteria sometimes exhibit increased mortality and infertility rates[11,17,37–39]. Other pathogens, like Densovirus, do not appear to affect vector fecundity when transmitted by this mechanism[40]. Also, like in the case of *Borrelia duttonii*, pathogens can loose their pathogenicity after several transovarial transmissions[11].

Conclusion

It is evident that the interplay of mechanisms influencing the presence and emergence of VBI is very complex. There is not one single "most important" factor but rather a constellation of them that together influence both positively and negatively these infections, depending on how and in what combination they come together. There are factors, often related to human behaviour, which could be modified. Others remain beyond our control.

VT is one of those many factors and although it may be important for the maintenance of some VBI, for others it does not seem to play a crucial role, or its role is yet to be determined.

The mounting knowledge of the vector-pathogen relationship and in particular, the increasing evidence that the pathogens exert intrinsic and sometimes deleterious effects on the vector, as well as the better understanding of how cycles are maintained in nature, will surely bring with it alternative ways to target these epidemics that take a high toll on human lives and pose a great threat to society at large.

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Corresponding author: Dr. Francisco Miled Pherez, Department of Medicine, New York Medical College at Metropolitan Hospital Center, 1901 First Avenue, New York, NY 10029, U.S.A.
E-mail: milopherezd@hotmail.com

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