

Pathogens in an Anthropized World: A Geographical Perspective on Zoonotic and Vector-borne Diseases*

by

Sophie VANWAMBEKE**

KEYWORDS. — Medical Geography; *Aedes*-borne Virus; Biological Resources; Environmental Factors; Human Environment Interactions.

SUMMARY. — Infectious diseases have not been relegated to humankind's past, far from it. This is being strikingly illustrated by the ongoing Zika fever epidemic in South America. While interest for the links between infectious diseases and the environment, in particular for vector-borne and zoonotic diseases, has drawn the attention of scientists from various disciplines for a long time, the currently exploding data availability and modelling capacity are opening new avenues for a better understanding and prediction of such infections. We present a resource-based habitat concept, expanded to include human populations, as a framework for unifying knowledge and research in the field of vector-borne diseases, with a focus on *Aedes*-borne viruses such as Zika virus and dengue virus.

MOTS-CLÉS. — Géographie médicale; Virus transmis par l'aédès; Ressources biologiques; Facteurs environnementaux; Interactions humain-environnement.

RÉSUMÉ. — *Pathogènes dans un monde anthropisé: une perspective géographique sur les zoonoses et maladies à transmission vectorielle.* — Les maladies infectieuses n'ont pas été reléguées au passé de l'humanité, tant s'en faut, ce qu'illustre de manière frappante l'épidémie de fièvre Zika en cours en Amérique du Sud. Les liens existant entre les maladies infectieuses, en particulier les zoonoses et maladies transmises par les vecteurs, et l'environnement intéressent depuis longtemps les scientifiques issus de diverses disciplines. Aujourd'hui, toutefois, l'explosion des données disponibles et les possibilités offertes par la modélisation ouvrent de nouvelles voies pour une meilleure compréhension de telles infections. Nous présentons ici un cadre conceptuel d'habitat basé sur les ressources, élargi pour y inclure la population humaine, cadre destiné à unifier les connaissances et la recherche dans le domaine des maladies à vecteur, en donnant priorité aux virus transmis par les moustiques du genre *Aedes*, tels que le virus Zika et celui de la dengue.

* Paper presented at the meeting of the Section of Human Sciences held on 16 February 2016. Text received on 3 June 2016 and submitted to peer review. Final version approved by the reviewers received on 16 December 2016.

** Member of the Academy; Université catholique de Louvain, Earth & Life Institute, Georges Lemaître Centre for Earth and Climate Research, place Pasteur 3, B-1348 Louvain-la-Neuve (Belgium).

TREFWOORDEN. — Medische geografie; *Aedes*-overgedragen virus; biologische rijkdommen; Milieufactoren; Milieu-mens-interacties.

SAMENVATTING. — *Pathogenen in een geanthropiseerde wereld: een geografisch perspectief op zoönoses en vector-overgedragen ziekten.* — Infectieziekten behoren jammer genoeg niet tot het verleden. Dit wordt levendig geïllustreerd door de recente uitbraak van Zikakoorts die zich momenteel voltrekt in Zuid-Amerika. De verbanden die bestaan tussen besmettelijke ziekten, zoönoses en vector-overgedragen ziekten enerzijds, en omgevingsfactoren anderzijds, hebben al sinds lang de aandacht getrokken van wetenschappers uit diverse disciplines. Vandaag de dag stellen de enorme hoeveelheden aan gegevens alsook simulatiemodellen ons in staat om nieuwe pistes te verkennen die ons een beter inzicht kunnen geven in infectieziekten. We presenteren hier een conceptueel kader voor de studie van habitats dat uitgaat van bestaansmiddelen en dat op een expliciete manier rekening houdt met de menselijke bevolking. Deze benadering biedt een uniek framework om onze kennis van vector-overgedragen ziekten te vergroten. In deze paper richten we ons op de virussen die worden overgedragen door *Aedes* muggen, zoals het Zika- en denguevirus.

Introduction

News over the past few years have reminded us that, far from being in our past, infectious diseases are persisting and will persist. Infectious diseases were, and will be, companions of humankind (FAUCI & MORENS 2012, JONES *et al.* 2008). Most recently headlining the news is the mosquito-borne Zika fever, caused by Zika virus. After emerging in the Pacific in 2007, its first appearance in America was identified, retrospectively, in Brazil in late 2014 (MUSSO & GUBLER 2016). It is now estimated to have caused about thirty thousand cases in Brazil (FARIA *et al.* 2016). Known to virologists since its discovery in the Zika forest of Uganda in 1947, Zika virus had previously been recorded in Africa and Asia (FAUCI & MORENS 2016). Infection with Zika virus had been associated generally with mild, self-limiting symptoms prior to 2013, but this changed following the French Polynesia epidemic. Strong hypotheses exist concerning neurological complications (Guillain-Barré syndrome) (MUSSO & GUBLER 2016) and neurological complication in neonates (microcephaly) (CAUCHEMEZ *et al.* 2016, JOHANSSON *et al.* 2016). While still incomplete, the epidemiological and experimental evidence for the link between microcephaly and infection with Zika virus is mounting fast enough for the WHO to have declared an emergency on 1 February 2016 (World Health Organisation 2016), and for the CDC to recommend that pregnant women avoid travelling to areas where the virus is known to circulate (Center for Disease Control 2016). All ingredients for widespread worry amongst the general population and for major global concern are gathered: a virus likely to cause severe birth defect emerging on a continent where it was previously unrecorded, transmitted by mosquitoes that are at the moment expanding their distribution globally on a backdrop of global environmental change. In the meantime, dengue persists as a scourge of the tropics, causing an estimated

three hundred and ninety million infections and ninety-six million symptomatic cases yearly (BHATT *et al.* 2013).

Being mosquito-borne, arboviruses such as dengue virus and Zika virus have strong relationships with the environment: their transmission cycle relies on exothermic vectors and, often, wild reservoir hosts. All these organisms have specific habitat requirements that environmental conditions affect. The idea that mosquito-borne diseases, and more generally vector-borne diseases, are tightly associated to environmental conditions is not novel, and has been formulated in diverse fields such as medicine (MAY 1952), biogeography (PAVLOVSKY 1966), and geography (SORRE 1933). Their studies looked closely at various vector and pathogen systems and established the foundations of what can now be found under the broad field of landscape epidemiology. In geography, work has expanded greatly in the second half of the 20th century, applying emerging quantitative methods and dealing with diverse topics ranging from AIDS to health care (VERHASSELT 1993).

Interest for the connections between vector population distribution, pathogen circulation, and the environment has, however, soared for the past twenty years (KITRON 1998, OSTFELD *et al.* 2005, REISEN 2010), and two major reasons can be highlighted for this. First, as emphasized by recent epidemics, many aspects of ongoing global environmental changes have a significant impact on the risk of infectious disease emergence and re-emergence. This goes clearly well beyond the climatic aspects of global change (JONES *et al.* 2013, McMICHAEL 2004). Changes in animal populations (domestic and wild), in human populations, in interactions between animal and human populations, land use and cover change, global travel of goods and people, all have been related to notable events related to infectious diseases. Second, our capacity to analyse the associations between environmental and epidemiological factors is greater than ever. Key to this is the data availability: we can now map with high spatial and temporal resolution many environmental factors relevant to zoonotic and vector-borne diseases (ESTRADA-PEÑA *et al.* 2016, HERBRETEAU *et al.* 2007, ROGERS *et al.* 2002). The efforts allocated to monitor and model the global environment and its changes are benefitting efforts to better understand and predict the distribution and dynamics of vectors and vector-borne diseases. Data concerning vectors, pathogens, and diseases are also getting more widely available thanks to increase in reporting, better data publication and compilation (PURSE & GOLDING 2015), as well as the appearance of novel digital tools (MADDER *et al.* 2012) and citizen science projects (GARCIA-MARTÍ *et al.* 2016). These data can be fed to ever more elaborate yet more accessible models of the effect of the environment on vector distribution, pathogen distribution, and disease risk (CIANCI *et al.* 2015, DE CLERCQ *et al.* 2015). Expanding data and model elaboration together offer a world of possibilities as well as needs. Despite this broad availability, the data often represent keyholes onto complex ecological systems. Environmental data are often proxies of the actual factors considered (ESTRADA-PEÑA *et al.* 2016),

and most epidemiological data only ever monitor a part of the transmission system (RANDOLPH 2001). This leads to a plethora of results that are incomparable, either because proxies are not directly comparable, because the part of the transmission system is different, or because the spatial or temporal scales considered differ. We propose that a strong conceptual background focused on the ecology of the pathogen would help consolidate knowledge already acquired in previous modelling efforts, and elaborate more coherent models even if they answer diverse needs.

In this paper we elaborate a resource-based habitat concept as drawn from conservation ecology, focused on the case of *Aedes*-borne flaviviruses such as Zika virus and dengue virus, two viruses of global public health concern. We detail the concept as adapted to such pathogens, all the way to their human niche, then discuss how it could help identify and formulate ecological hypotheses, and guide modelling and monitoring efforts.

Pathogens as Organism of Focus: *Aedes*-borne Flaviviruses

As can be seen, our proposed resource-based habitat concept focuses ultimately on the pathogen. In this paper, we focus on two *Aedes*-borne flaviviruses of public health importance: Zika virus and dengue virus. Other *Aedes*- or mosquito-borne flaviviruses include Yellow Fever virus, West Nile virus and Japanese encephalitis virus (GRARD *et al.* 2010). Dengue virus usually causes asymptomatic or mildly symptomatic disease, but can cause dengue haemorrhagic fever. Dengue fever is found across the tropics, but incidence is difficult to estimate as most cases present mild symptoms. According to the WHO, dengue fever causes about fifty to one hundred million cases annually (Special Programme for Research and Training in Tropical Diseases and World Health Organization 2009) but others place this figure at about ninety million (BHATT *et al.* 2013). Both viruses appear to be principally vectored by *Aedes aegypti* and *Aedes albopictus* mosquitoes. These two species are extremely well adapted to anthropized landscapes.

Dengue virus and Zika virus transmission relies on at least three species (pathogen, vector, and host). Often, both *Ae. aegypti* and *Ae. albopictus* are implicated in transmission. When sylvatic transmission takes place, involving non-human primates and monkeys, several host species also need to be considered. This means that examining the ecological functions and resources required for the various species involved in transmission will be necessary to represent the habitat of the virus. It also means that most monitoring efforts will only document a section of the transmission cycle.

A Resource-based Habitat for *Aedes*-borne Flaviviruses

The resource-based habitat concept (RBHC) finds its origin in conservation ecology primarily (HARTEMINK *et al.* 2015) and adopts a functional ecology perspective, with a focus on the organism and its needs, rather than on habitat characteristics such as vegetation classes (DENNIS *et al.* 2003, 2006). The functions that the organism of focus — here, the pathogen — needs to carry out are identified (*e.g.* feeding, mating, oviposition, ...). These functions are then associated to specific resources found in the environment. The resources can be either a consumable (*e.g.* host plant for an herbivorous insect), or utility (*e.g.* suitable micro-climate). A bottom-up approach is thus adopted here, in line with the classical ecological niche concept. Furthermore, the resource-based habitat concept explicitly accounts for the movement capacity of the organism; so, its capacity to make use of diverse, multiple resources in the landscape, provided they are within reach. Contrary to a habitat-focused approach, which often tends to associate a single land cover class to an organism, combinations of landscape elements or land cover types that offer all the required resources can be identified and mapped (HARTEMINK *et al.* 2015). Here we bring this ecological perspective towards the geographical perspective by including human hosts and their own relevant functions and resources (fig. 1). We focus here on fine-scale environmental features and ecological interactions at the landscape level, and assume climatic conditions favourable to pathogen, vectors, and hosts.

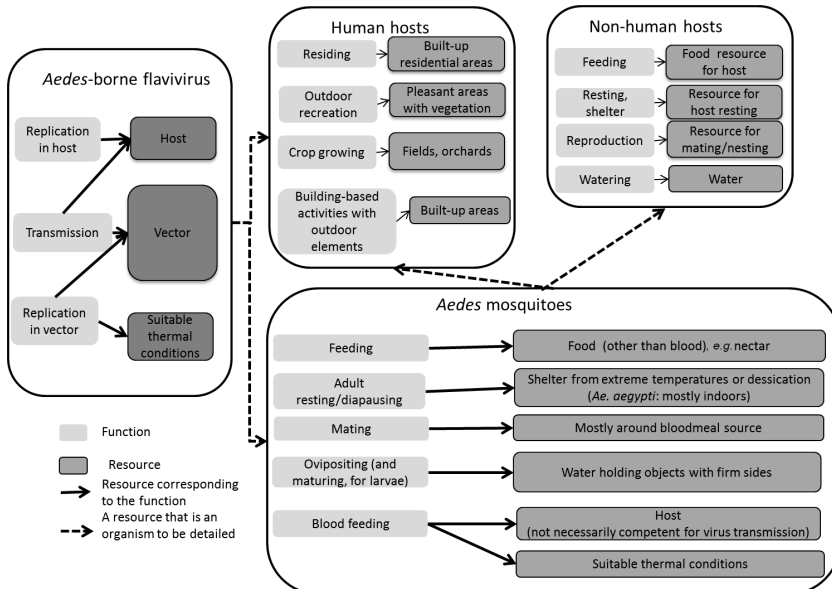


Fig. 1. — A resource-based habitat concept adapted to *Aedes*-borne viruses.

PATHOGEN LEVEL

We can identify three essential functions for *Aedes*-borne flaviviruses: replication in the host, replication in the vector, and transmission. This leads us to identify two resources necessary for the pathogen: vectors and hosts. Vectors are here identified as mosquitoes of the genus *Aedes*, and we focus here on the two species of primary interest for public health: *Ae. aegypti* and *Ae. albopictus*. The host species of interest will vary according to whether the virus considered circulates in non-human hosts in a sylvatic cycle, or whether the virus has adapted to circulate, at least in part, in humans.

VECTOR LEVEL

Vectors are a necessary resource for the pathogen functions of transmission and replication in the vector. They have of course their own functions and resources that need to be accounted for, which include hosts. For *Aedes* mosquitoes, we can identify the functions of feeding, adult resting and diapausing, mating, ovipositing (and maturing, for larvae), and blood feeding (*cf.* fig. 1). Feeding here refers to nectar feeding, which requires plant, either nectar or honeydew, possibly also from fruit and sap from wounds. The importance of this varies between males and females (STONE & FOSTER 2013), as only females feed on blood. The importance of nectar feeding for females appears to vary between sites, possibly in relation to availability, and may affect vectorial capacity. *Ae. aegypti* females, highly adapted to the human indoor environment, largely rely on multiple blood feeding to get energy (SCOTT & TAKKEN 2012). For *Ae. aegypti*, resting largely relies on the human built-up environment, with a strong preference for those buildings where humans are found (RITCHIE 2014). In *Aedes* mosquitoes, mating does not necessarily take place in swarms, as males usually seek females around blood meal sources (OLIVA *et al.* 2014). Oviposition takes place in water-holding objects with firm sides (RITCHIE 2014). This includes artificial containers made up of a diversity of materials, as well as some natural containers such as tree holes, bamboo, open coconuts, leaves. *Ae. aegypti*, now fully adapted to the urban environment, relies mostly on artificial containers (RITCHIE 2014), while *Ae. albopictus* relies on both artificial and natural containers (VANWAMBEKE *et al.* 2007). Such objects suitable for *Aedes* breeding can also be found in cultivated areas such as orchards (VANWAMBEKE *et al.* 2007), so their role as an area providing ovipositing resources may need to be considered. These mosquito species may have adapted to artificial containers as early as the 17th century in the case of *Ae. aegypti*. This has allowed them to travel from continent to continent, during the slave trade for *Ae. aegypti* (GUBLER 2014), and more recently with trade of goods for *Ae. albopictus* (KRAEMER *et al.* 2015, REITER & SPRENGER 1987). Blood feeding resources, *i.e.* hosts, are essentially found in humans for *Ae. aegypti*, emphasizing its current full reliance on the anthropized

environment as highlighted for ovipositing sites. While *Ae. albopictus* is known to be more opportunistic (PAUPY *et al.* 2009), if humans are available it will largely feed on them, or on animals associated to humans such as dogs and pigs (PONLAWAT & HARRINGTON 2005). Possibly a better way to describe the feeding behaviour of *Aedes* mosquitoes is their plasticity in relation to circumstances (FARAJI *et al.* 2014).

HOST LEVEL: NON-HUMAN HOSTS

In the case of the viruses of focus here, non-human hosts do not always intervene. Dengue virus mostly circulates as an urban, entirely human transmission cycle. In Asia, where dengue virus originates from, all four dengue virus serotypes have been identified in sylvatic cycles, *i.e.* a transmission cycle relying on non-human primates and monkeys (GUBLER 2014). The move-out of the forest and into rural villages is estimated to have taken place about 2,000-4,000 years ago (GUBLER 2014). When these viruses are introduced into new areas, it is most importantly related to the travel of infected humans bringing the virus into a new area (*e.g.* for Zika: FARIA *et al.* 2016, MUSSO & GUBLER 2016). However, the role of non-human hosts may be significant in those areas where an urban cycle is not established yet or where control efforts reduce virus circulation in humans. The current epidemic of Zika fever in Brazil illustrates these issues. Preliminary results indicate that the virus may circulate in non-human primates (FAVORETTO *et al.* 2016). In circumstances where possible non-human hosts are found, it may be useful to include them. Because focusing on a specific species is not relevant here, we do not detail the functions and associated resources beyond the general indications of figure 1.

HOST LEVEL: HUMAN HOSTS

A full list of functions of human hosts would be challenging, but is not necessary. Only those functions or human activities that may expose them to mosquito bites, thus exposing them to be infected, or to serve as a host and infect mosquitoes, need to be pinpointed. Indeed, this may still include a broad diversity of elements when considering the fact that *Aedes* mosquitoes are day-biters, but keeping in mind that the purpose is eventually to map human hosts in relation to the vector (and possibly of non-human hosts), the list can be kept manageable. For the purpose of this overview of the conceptual framework, we mention residing, recreation, crop growing, and building-based activities associated to outdoor surroundings (*e.g.* schooling). Local contexts may help to identify the most relevant landscape elements: while it is clear that *Aedes* mosquitoes are extremely well adapted to the urban environments, not all built-up areas or human-frequented areas equally support transmission, depending on how well they support human-vector contact. This has been illustrated for example across the border between

Mexico and the United States of America where, despite similar climatic conditions, dengue prevalence differs greatly. This relates to human behaviour and living conditions (REITER *et al.* 2003). In a study of dengue transmission potential on the island of Oahu (Hawaii), residential areas and outdoor recreation were selected to map areas of greatest exposure to mosquito bites (VANWAMBEKE *et al.* 2011). If cultivated areas provide mosquito oviposition sites, they may need to be considered here in relation to the human activity of crop growing.

This broad overview of the RBHC for *Aedes*-borne flaviviruses clearly shows that this framework can only be of use if including human environment. Indeed, these transmission systems are now nearly exclusively relying on human populations, and the vectors are highly adapted to the urban or built-up environment.

Discussion: Moving Forward with a RBHC for *Aedes*-borne Flaviviruses in an Anthropized World

The RBHC framework offers an integrated perspective of human-environment interactions in the context of zoonotic and vector-borne diseases. It allows to identify precisely the habitat of a pathogen in relation to the habitat of the species necessary to its transmission cycle. Furthermore, it includes aspects of movement capacity. This may appear of limited interest for the fully-urbanized transmission of dengue by *Ae. aegypti*. However, in the case of emerging viruses such as Zika virus, or in areas where the more rural *Ae. albopictus* is prevalent, the movement capacity of vectors and non-human hosts may be more important to consider. Also, the depth of the association between the functional resources of this virus (vectors and hosts) is made striking by the model, as humans appear both as the host and as the (unwilling) providers of many of the vector's resources. There could hardly be a more glaring illustration of the importance for health of the issue of human-environment interactions. Regardless, most other conceptual frameworks that focus on human-environment interactions to understand vector-borne disease transmission, such as One Health (HARTEMINK *et al.* 2015, ZINSTAG *et al.* 2011) or Ecohealth (WILCOX *et al.* 2004), do not offer such a structured approach to pathogen habitat and interactions between the species involved. Only the RBHC framework allows to strictly identify all environmental resources needed for the system to function, allowing thus to formalize the search for the best environmental proxies to the transmission systems. As such, it will be an important complement to broad concepts such as One Health and Ecohealth, and has great potential to contribute to bridging mechanistic and statistical modelling approach (HARTEMINK *et al.* 2015).

In this paper we have focused on the landscape scale. Clearly, the landscape scale is the main entry point for understanding the contacts between vectors and hosts in a way that opens up possibilities for control measures. It is the scale at which relevant human activities take place and where land management decisions,

including those that can affect disease risk, are taken. Other, broader scales of study can, however, also be approached usefully by the RBHC, and offer for example insight into apparent differences in habitat between environmentally different regions. This has been found for the grayling butterfly (*Hipparchia semele*), which occupies structurally different habitats in different regions in Europe (heathland or forest). The habitats are, however, similar when considering their correspondence to a functional requirement (VAN DYCK 2012).

One major attraction of the RBHC in the context of *Aedes*-borne flaviviruses may be their usefulness in identifying knowledge gaps and structuring formal questions on the ecology of the organism under study. Considering the current situation with Zika virus, and reflecting ongoing preoccupation, several such questions can be highlighted. The risk of introduction in areas that are currently virus-free is a major cause of concern, in particular in relation to international travel, a concern that was raised particularly in the context of the Olympics held in Brazil. Current models deal with this question relatively poorly: empirical statistical models require data to be computed but we are faced here with scenarios never encountered before, and mechanistic models deal poorly with environmental factors in a spatially-explicit context (HARTEMINK *et al.* 2015). If confirmed, the presence of the virus in non-human primates in contexts where humans, non-human primates, and mosquitoes interact closely may interfere with control efforts. The functional ecology considered in the RBHC would be useful for this question.

When considering humans, it may appear challenging to identify and map the relevant functions to consider. Indeed, as we are here considering day-biting mosquitoes that live in close association with human populations, it may appear irrelevant and unfeasible to distinguish between diverse human activities. However, not all activities equally expose people: desk work in an air-conditioned office would relate to a very low degree of exposure, and a central business district could therefore be excluded in a map of risk. On the other hand, areas where people gather for outdoor social and sport activities are not necessarily found in built-up areas but may provide mosquito habitat as well as intense exposure (VANWAMBEKE *et al.* 2011). As suggested above, thanks to the focus on functional aspects of habitats, the RBHC may help to compare existing empirical studies that do not appear coherent or identify differences related to plasticity of the organisms involved.

Conclusion

Due to the persisting importance of zoonotic and vector-borne diseases in today's world, a thorough understanding of the effect of human-environment interactions on pathogen transmission is indispensable. The RBHC offers a robust perspective to formalize existing knowledge, structure research questions

and data collection, and bridge modelling approaches. By expanding it to humans, we make it useful beyond ecology and for public health. We believe it can be a very useful support to existing, more general conceptual frameworks of environment and health.

REFERENCES

- BHATT, S., GETHING, P. W., BRADY, O. J., MESSINA, J. P., FARLOW, A. W., MOYES, C. L., DRAKE, J. M., BROWNSTEIN, J. S., HOEN, A. G., SANKOH, O., MYERS, M. F., GEORGE, D. B., JAENISCH, T., WINT, G. R. W., SIMMONS, C. P., SCOTT, T. W., FARRAR, J. J., & HAY, S. I. 2013. The global distribution and burden of dengue. — *Nature*, **496**: 504-507.
- CAUCHEMEZ, S., BESNARD, M., BOMPARD, P., DUB, T., GUILLEMETTE-ARTUR, P., EYROLLE-GUIGNOT, D., SALJE, H., VAN KERKHOVE, M. D., ABADIE, V., GAREL, C., FONTANET, A. & MALLET, H.-P. 2016. Association between Zika virus and microcephaly in French Polynesia, 2013-15: A retrospective study. — *The Lancet*, **387**: 2125-2132.
- Center for Disease Control 2016. How to Protect Yourself. — <http://www.cdc.gov/zika/pregnancy/protect-yourself.html>
- CIANCI, D., HARTEMINK, N. & IBAÑEZ-JUSTICIA, A. 2015. Modelling the potential spatial distribution of mosquito species using three different techniques. — *Int. J. Health Geogr.*, **14**: 10.
- DE CLERCQ, E. M., LETA, S., ESTRADA-PEÑA, A., MADDER, M., ADEHAN, S. & VANWAMBEKE, S. O. 2015. Species distribution modelling for *Rhipicephalus microplus* (Acari: Ixodidae) in Benin, West Africa: Comparing datasets and modelling algorithms. — *Prev. Vet. Med.*, **118**: 8-21.
- DENNIS, R. L. H., SHREEVE, T. G. & VAN DYCK, H. 2003. Towards a functional resource-based concept for habitat: A butterfly biology viewpoint. — *Oikos*, **102**: 417-426.
- DENNIS, R. L. H., SHREEVE, T. G. & VAN DYCK, H. 2006. Habitats and resources: The need for a resource-based definition to conserve butterflies. — *Biodivers. Conserv.*, **15**: 1943-1966.
- ESTRADA-PEÑA, A., ALEXANDER, N. & WINT, G. R. W. 2016. Perspectives on modelling the distribution of ticks for large areas: So far so good? — *Parasit. Vectors*, **9**.
- FARAJI, A., EGIZI, A., FONSECA, D. M., UNLU, I., CREPEAU, T., HEALY, S. P. & GAUGLER, R. 2014. Comparative host feeding patterns of the Asian Tiger Mosquito, *Aedes albopictus*, in urban and suburban northeastern USA and implications for disease transmission. — *PLoS Negl. Trop. Dis.*, **8**: e3037.
- FARIA, N. R., AZEVEDO, R. d. S. d. S., KRAEMER, M. U. G., SOUZA, R., CUNHA, M. S., HILL, S. C., THEZE, J., BONSALE, M. B., BOWDEN, T. A., RISSANEN, I., ROCCO, I. M., NOGUEIRA, J. S., MAEDA, A. Y., VASAMI, F. G. d. S., MACEDO, F. L. d. L., SUZUKI, A., RODRIGUES, S. G., CRUZ, A. C. R., NUNES, B. T., MEDEIROS, D. B. d. A., RODRIGUES, D. S. G., NUNES QUEIROZ, A. L., SILVA, E. V. P. d., HENRIQUES, D. F., TRAVASSOS DA ROSA, E. S., DE OLIVEIRA, C. S., MARTINS, L. C., VASCONCELOS, H. B., CASSEB, L. M. N., SMITH, D. d. B., MESSINA, J. P., ABADIE, L., LOURENCO, J., ALCANTARA, L. C. J., LIMA, M. M. d., GIOVANETTI, M., HAY, S. I., DE OLIVEIRA, R. S., LEMOS, P. d. S., OLIVEIRA, L. F. d., DE LIMA, C. P. S., DA SILVA, S. P., VASCONCELOS, J. M. d., FRANCO, L., CARDOSO, J. F., VIANEZ-JUNIOR, J. L. d. S. G., MIR, D., BELLO, G., DELATORRE, E., KHAN, K., CREATORE, M., COELHO, G. E., DE OLIVEIRA, W. K., TESH, R., PYBUS, O. G., NUNES, M. R. T. & VASCONCELOS, P. F. C. 2016. Zika virus in the Americas: Early epidemiological and genetic findings. — *Science*, **352**: 345-349.

- FAUCI, A. S. & MORENS, D. M. 2012. The perpetual challenge of infectious diseases. — *N. Engl. J. Med.*, **366**: 454-461.
- FAUCI, A. S. & MORENS, D. M. 2016. Zika Virus in the Americas – Yet another arbovirus threat. — *N. Engl. J. Med.*, **374**: 601-604.
- FAVORETTO, S., ARAUJO, D., OLIVEIRA, D., DUARTE, N., MESQUITA, F., ZANOTTO, P. & DURIGON, E. 2016. First detection of Zika virus in neotropical primates in Brazil: A possible new reservoir (No. biorxiv; 049395v1).
- GARCIA-MARTÍ, I., ZURITA-MILLA, R., SWART, A., VAN DEN WIJNGAARD, K. C., VAN VLIET, A. J. H., BENNEMA, S. & HARMS, M. 2017. Identifying environmental and human factors associated with tick bites using volunteered reports and frequent pattern mining: Environmental and human factors associated with tick bites. — *Trans. GIS*, **21** (1): 277-299.
- GRARD, G., MOUREAU, G., CHARREL, R. N., HOLMES, E. C., GOULD, E. A. & DE LAMBALLERIE, X. 2010. Genomics and evolution of *Aedes*-borne flaviviruses. — *J. Gen. Virol.*, **91**: 87-94.
- GUBLER, D. J. 2014. Dengue viruses: Their evolution, history and emergence as a global public health problem. — In: GUBLER, D. J., OOI, E. E., VASUDEVAN, S. & FARRAR, J. (Eds.), *Dengue and Dengue Hemorrhagic Fever*. Wallingford, CABI, pp. 1-29.
- HARTEMINK, N., VANWAMBEKE, S. O., PURSE, B. V., GILBERT, M. & VAN DYCK, H. 2015. Towards a resource-based habitat approach for spatial modelling of vector-borne disease risks: Resource-based habitats for vector-borne diseases. — *Biol. Rev.*, **90**: 1151-1162.
- HERBRETEAU, V., SALEM, G., SOURIS, M., HUGOT, J.-P. & GONZÁLEZ, J.-P. 2007. Thirty years of use and improvement of remote sensing, applied to epidemiology: From early promises to lasting frustration. — *Health Place*, **13**: 400-403.
- JOHANSSON, M. A., MIER-Y-TERAN-ROMERO, L., REEFHUIS, J., GILBOA, S. M. & HILLS, S. L. 2016. Zika and the risk of microcephaly. — *N. Engl. J. Med.*, **375**: 1-4.
- JONES, K. E., PATEL, N. G., LEVY, M. A., STOREYGARD, A., BALK, D., GITTLEMAN, J. L. & DASZAK, P. 2008. Global trends in emerging infectious diseases. — *Nature*, **451**: 990-993.
- JONES, B. A., GRACE, D., KOCK, R., ALONSO, S., RUSHTON, J., SAID, M. Y., MCKEEVER, D., MUTUA, F., YOUNG, J., McDERMOTT, J. & PFEIFFER, D. U. 2013. Zoonosis emergence linked to agricultural intensification and environmental change. — *Proc. Natl. Acad. Sci.*, **110**: 8399-8404.
- KITRON, U. 1998. Landscape ecology and epidemiology of vector-borne disease: Tools for spatial analysis. — *J. Med. Entomol.*, **35**: 435-445.
- KRAEMER, M. U., SINKA, M. E., DUDA, K. A., MYLNE, A. Q., SHEARER, F. M., BARKER, C. M., MOORE, C. G., CARVALHO, R. G., COELHO, G. E., VAN BORTEL, W., HENDRICKX, G., SCHAFFNER, F., ELYAZAR, I. R., TENG, H.-J., BRADY, O. J., MESSINA, J. P., PIGOTT, D. M., SCOTT, T. W., SMITH, D. L., WINT, G. W., GOLDING, N., HAY, S. I. 2015. The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*. — *eLife*, **4**.
- MADDER, M., WALKER, J. G., VAN ROOYEN, J., KNOBEL, D., VANDAMME, E., BERKVEN, D., VANWAMBEKE, S. O. & DE CLERCQ, E. M. 2012. e-Surveillance in animal health: Use and evaluation of mobile tools. — *Parasitology*, **139**: 1831-1842.
- MAY, J. M. 1952. History, Definition, and Problems of Medical Geography: A General Review. — Washington, International Geographic Union, XVIIth International Geographical Congress.

- McMICHAEL, A. J. 2004. Environmental and social influences on emerging infectious diseases: Past, present and future. — *Philos. Trans. R. Soc. B Biol. Sci.*, **359**: 1049-1058.
- MUSSO, D. & GUBLER, D. J. 2016. Zika Virus. — *Clin. Microbiol. Rev.*, **29**: 487-524.
- OLIVA, C. F., DAMIENS, D. & BENEDICT, M. Q. 2014. Male reproductive biology of *Aedes* mosquitoes. — *Acta Trop.*, **132**: S12-S19.
- OSTFELD, R., GLASS, G. & KEESING, F. 2005. Spatial epidemiology: An emerging (or re-emerging) discipline. — *Trends Ecol. Evol.*, **20**: 328-336.
- PAUPY, C., DELATTE, H., BAGNY, L., CORBEL, V. & FONTENILLE, D. 2009. *Aedes albopictus*, an arbovirus vector: From the darkness to the light. — *Microbes Infect.*, **11**: 1177-1185.
- PAVLOVSKY, E. 1966. Natural Nidality of Transmissible Diseases in Relation to the Landscape Epidemiology of Zooanthroponoses. — Moscow, Peace publishers.
- PONLAWAT, A. & HARRINGTON, L. C. 2005. Blood feeding patterns of *Aedes aegypti* and *Aedes albopictus* in Thailand. — *J. Med. Entomol.*, **42**: 844-849.
- PURSE, B. V. & GOLDING, N. 2015. Tracking the distribution and impacts of diseases with biological records and distribution modelling. — *Biol. J. Linn. Soc.*, **115**: 664-677.
- RANDOLPH, S. E. 2001. The shifting landscape of tick-borne zoonoses: Tick-borne encephalitis and Lyme borreliosis in Europe. — *Philos. Trans. R. Soc. B Biol. Sci.*, **356**: 1045-1056.
- REISEN, W. K. 2010. Landscape epidemiology of vector-borne diseases. — *Ann. Rev. Entomol.*, **55**: 461-483.
- REITER, P. & SPRENGER, D. 1987. The used tire trade: A mechanism for the worldwide dispersal of container breeding mosquitoes. — *J. Am. Mosq. Control Assoc.*, **3**: 494-501.
- REITER, P., LATHROP, S., BUNNING, M., BIGGERSTAFF, B., SINGER, D., TIWARI, T., BABER, L., AMADOR, M., THIRION, J., HAYES, J., SECA, C., MENDEZ, J., RAMÍREZ, B., ROBINSON, J., RAWLINGS, J., VORNDAM, V., WATERMAN, S., GUBLER, D., CLARK, G. & HAYES, E. 2003. Texas lifestyle limits transmission of dengue virus. — *Emerg. Infect. Dis.*, **9**: 86-89.
- RITCHIE, S. A. 2014. Dengue vector bionomics: Why *Aedes aegypti* is such a good vector. — In: GUBLER, D. J., OOI, E. E., VASUDEVAN, S. & FARRAR, J. (Eds.), *Dengue and Dengue Hemorrhagic Fever*. Wallingford, CABI, pp. 455-480.
- ROGERS, D. J., RANDOLPH, S. E., SNOW, R. W. & HAY, S. I. 2002. Satellite imagery in the study and forecast of malaria. — *Nature*, **415**: 710-715.
- SCOTT, T. W. & TAKKEN, W. 2012. Feeding strategies of anthropophilic mosquitoes result in increased risk of pathogen transmission. — *Trends Parasitol.*, **28**: 114-121.
- SORRE, M. 1933. Complexes pathogènes et géographie médicale. — *Ann. Géographie*, **42**: 1-18.
- Special Programme for Research and Training in Tropical Diseases 2009. *Dengue: Guidelines for Diagnosis, Treatment, Prevention, and Control*. — Geneva, World Health Organization.
- STONE, C. M. & FOSTER, W. A. 2013. Plant-sugar feeding and vectorial capacity. — In: TAKKEN, W. & KOENRAADT, C. J. M. (Eds.), *Ecology of Parasite-Vector Interactions*. Wageningen, Wageningen Academic Publishers, pp. 35-79.
- VAN DYCK, H. 2012. Changing organisms in rapidly changing anthropogenic landscapes: The significance of the “Umwelt”-concept and functional habitat for animal conservation: Perception and habitat in anthropogenic landscapes. — *Evol. Appl.*, **5**: 144-153.

- VANWAMBEKE, S. O., BENNETT, S. N. & KAPAN, D. D. 2011. Spatially disaggregated disease transmission risk: Land cover, land use and risk of dengue transmission on the island of Oahu. — *Trop. Med. Int. Health*, **16**: 174-185.
- VANWAMBEKE, S. O., SOMBOON, P., HARBACH, R. E., ISENSTADT, M., LAMBIN, E. F., WALTON, C. & BUTLIN, R. K. 2007. Landscape and land cover factors influence the presence of *Aedes* and *Anopheles* larvae. — *J. Med. Entomol.*, **44**: 133-144.
- VERHASSELT, Y. 1993. Geography of health: Some trends and perspectives. — *Soc. Sci. Med.*, **36**: 119-123.
- WILCOX, B. A., AGUIRRE, A. A., DASZAK, P., HORWITZ, P., MARTENS, P., PARKES, M., PATZ, J. A. & WALTNER-TOEWS, D. 2004. EcoHealth: A transdisciplinary imperative for a sustainable future. — *EcoHealth*, **1**: 3-5.
- World Health Organisation 2016. WHO statement on the first meeting of the International Health Regulations (2005) (IHR 2005) Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations (WHO statement).
- ZINSSTAG, J., SCHELLING, E., WALTNER-TOEWS, D. & TANNER, M. 2011. From “one medicine” to “one health” and systemic approaches to health and well-being. — *Prev. Vet. Med.*, **101**: 148-156.