Article
https://doi.org/10.61900/SPJVS.2023.04.01

IMPACT OF RECENT AND FUTURE CLIMATE CHANGE ON VECTOR-BORNE DISEASES: VIRUSES ANALYSES

Serban MOROSAN[1,2], Andreea COZMA[3], Anca DASCALU[3], Luciana CRIVEI[3]

Department of Public Health, Iasi University of Life Sciences, Romania[1]
Department of Exact Sciences, Iasi University of Life Sciences, Romania[3]
Regional Center of Advanced Research for Emerging Diseases, Zoonoses and Food Safety (ROVETEMERG), Iasi University of Life Sciences, Romania[3]
UMS28, Sorbonne Université /INSERM, Paris, France[2]

*E-mail: serban.morosan@uaiasi.ro

Abstract

Climate directly impacts health through climatic extremes, air quality, sea-level rise, and multifaceted influences on food production systems and water resources. Climate also affects infectious diseases, which have played a significant role in human history, impacting the rise and fall of civilizations and facilitating the conquest of new territories. This review highlights significant regional changes in vector and pathogen distribution, changes that have been anticipated by scientists worldwide. Further future changes are likely if we fail to mitigate and adapt to climate change. Many key factors affect the spread and severity of human diseases, including mobility of people, animals, and goods; control measures in place; availability of effective drugs; quality of public health services; human behavior; and political stability and conflicts.

Keywords: vector-borne viruses, climate change

Stade of art

Climate change is considered one of the greatest threats to human health by the World Health Organization. The rate of global warming which has occurred during recent decades has been unprecedented over the past millennium, and there is consensus in the scientific community that the cause is increasing anthropogenic emissions of greenhouse gases. Climate change directly impacts health through long-term changes in rainfall and temperature, climatic extremes (heatwaves, hurricanes, and flash floods), air quality, sea-level rise in low- land coastal regions, and multifaceted influences on food production systems and water resources . Climate has a direct impact on the dynamics of a subset of infectious diseases, including vector-borne diseases (VBDs), some water-borne diseases such as cholera, and other soil-borne and food-borne pathogens. Climate also has multiple indirect effects through socioeconomic factors; as one example, flooding can hamper disease control measures in place, including vector control.

In March 2022, the report delivered by intergovernmental panel on climate change (IPCC) warned that without swift climate action we would see an escalation of infectious diseases. Infectious diseases will spread to new regions, surge in areas where they were previously under control and new infectious diseases could infects humans from ‘spill over' from animals. In Europe, several arthropod-borne viruses (arboviruses) are of concern to public authorities, such as the chikungunya virus (CHIKV), the dengue fever virus (DENV), the zika virus (ZIKV) or the West Nile virus (WNV), all 4 transmitted by mosquitoes, but also the tick-borne encephalitis virus (TBEV) and the Crimean-Congo hemorrhagic fever virus (CCHFV) both transmitted by ticks. For some of these arboviruses (such as WNV, DENV and TBEV), several hundred human cases (imported or indigenous) are detected each year in Romania. For others (such as CCHFV, ZIKV, CHIKV), the risk of emergence is taken very seriously and should be actively monitored. The European Union has ranked WNV as high priority and CCHF-virus (CCHFV) has been one of the eight priority emergent pathogens for the last 3 years by the

World Health Organization (WHO), requiring urgent attention in research, development and innovation because of their expansion and epidemic potential in the near future.

The transmission cycles of vector-borne diseases are sensitive to climatic factors, but disease risks are also affected by factors such as land use, vector control, human behaviour, population movements and public health capacities. Climate change is regarded as the principal factor behind the observed move of the tick species *Ixodes ricinus* — the vector of Lyme borreliosis and tick-borne encephalitis in Europe — to higher latitudes and altitudes. A similar phenomenon is observed for *Hyalomma marginatum*, the main vector of the Crimean-Congo Hemorrhagic fever (CCHF). Climate change is projected to lead to further northwards and upwards shifts in the distribution of *Ixodes ricinus* and *Hyalomma marginatum*.

It is generally suspected that climate change has played (and will continue to play) a role in the expansion of other disease vectors, notably the Asian tiger mosquito (*Aedes albopictus*), which can disseminate several diseases including dengue, chikungunya and Zika, and phlebotomus sandfly species, which transmit leishmaniasis.

Vector-borne diseases represent 17% of infectious diseases causing 700,000 deaths each year and economic losses of around one billion euros (WHO, 2020). VMs are caused by infectious agents (mainly viruses but also bacteria and parasites) transmitted to vertebrates by the bite of a hematophagous arthropod vector. Among them, mosquitoes are the first vectors of pathogens in human health while ticks are the first vectors in animal health (and second in human health) ([1].

In Europe, several arboviruses (arthropod-borne virus) are of concern to public authorities, such as the chikungunya virus (CHIKV), the dengue fever virus (DENV), the zika virus (ZIKV) or the West Nile virus (West-Nile virus, WNV), all 4 transmitted by mosquitoes, but also the tick-borne encephalitis virus (TBEV) and the Crimean-Congo hemorrhagic fever virus (CCHFV) both transmitted by ticks. For some of these arboviruses (such as WN, DENV and TBEV), several hundred human cases (imported or indigenous) are detected each year in France, Romania and Moldova. For others (such as CCHFV, ZIKV, CHIKV), the risk of emergence is taken very seriously and should be actively monitored.

Ticks are a major risk factor for animal and human health by transmitting the greatest variety of pathogens (bacteria, parasites and viruses) compared to other groups of arthropod vectors ([2, 3]). They affect livestock as well as humans, as well as pets and leisure animals. The abundance and activity of ticks are very dependent on the movements of wild animals and changes in biotopes. In fact, on a global scale, the intensification of human and animal movements as well as environmental changes are among the main factors for the emergence and/or extension of the range of many pathogens. transmitted by ticks, often zoonotic and for some epizootic. Among the pathogens transmitted by ticks, there are bacteria including the agents responsible for borreliosis, rickettsiosis, anaplasmosis, bartonellosis, ehrliochiosis, but also parasites responsible for babesiosis and theileriosis, and finally viruses responsible for encephalitis and/or hemorrhagic fever. At European level, the two main diseases are ([4]) Lyme borreliosis with an estimate of nearly 65,000 new cases diagnosed each year (and 300,000 cases annually in the USA) ([5]), tick-borne encephalitis which represents the most important neuroinvasive disease transmitted by ticks in Europe and Asia with several thousand human cases per year, including a hundred in France since 1968, with a recent increase in their incidence (around 30 cases per year). The diseases induced are for some of them very difficult to diagnose and the control and prevention strategies remain very complicated to implement since they require the disruption of a complex chain of transmission involving vertebrate hosts and ticks that interact in a constantly changing environment.

<u>Viral vector borne diseases</u>

CCHF is a widespread tick-borne viral disease caused by an *Orthonairovirus* of the *Nairoviridae* family. CCHFV has been considered to be one of the eight priority emergent pathogens for the last 3 years by the World Health Organization (WHO), requiring urgent attention in research, development and innovation because of its epidemic potential in the near future.

While infected animals are usually asymptomatic, humans can develop a serious infection. In humans, CCHFV infection can lead to a severe, life-threating disease characterized by hemodynamic instability, hepatic injury, and neurological disorders, with a worldwide lethality rate from 5 to 40%.

This infection is a public health concern given the increase in its distribution area, particularly in Europe, and more particularly in Turkey and the Balkans. Currently, less than 20,000 cases of infection with this virus have been confirmed worldwide. In Turkey, no cases had been identified before 2002; since then, more than 9,700 cases have been diagnosed [6]). The CCHFV was ultimately found to be endemic in more than 50 countries across Africa, Asia, Europe, and the Middle East.

Like many other viruses, the CCHFV circulates on several continents, depending on the distribution of its vector, the tick, and its different hosts which can be sedentary or migratory. With global warming, the distribution areas of its vector seems to change, thus modifying the circulation of the virus, with the effect of increasing the risk of emergence in new geographical areas ([7]). Climate changes of recent decades have recently led to a rise in the distribution of this virus.

West Nile virus (WNV), Usutu virus (USUV), and the tick-borne encephalitis virus (TBEV) are all arboviruses belonging to *Flaviviridae* family, characterized by vectorial transmission and sometimes associated with neuroinvasive infections. The circulation of these viruses is considered endemic in some parts of Europe with cases reported in many countries. Hematophagous arthropods such as mosquitoes (WNV, USUV) and ticks (TBEV) transmit the virus among hosts. Romania has a long history regarding the circulation of the WNV, the disease being first reported in 1955 [29]. In addition, during 1996, Romania also recorded the most important human outbreak reported in Europe at the time, in the south-eastern region of the country. Of the 393 human cases recorded, 352 were severe forms of meningoencephalitis [30]. A continued transmission was observed during the next years but with a lower number of clinical infections [31]. Another notable outbreak occurred during 2010, with 52 confirmed cases and a 10% mortality rate. Although most infections were located in the southern part of the country, new cases have also been reported inside the arch of the Carpathian Mountains [29]. Moreover, during 2016, another disease outbreak was recorded in Romania, this time registering 93 neurological human cases [32]. To date, the most severe outbreak registered in Europe in recent years took place in 2018, when Romania registered 277 clinical cases and 43 deaths out of a total of 2083 human clinical infections at the European level. A decrease in infections was observed in the following years[33-35]. Since 1997, a passive surveillance system has been implemented in Romania. Every year, from June to November, blood serum and cerebrospinal fluid from suspect cases of human WNV-associated central nervous system infections in patients over the age of 15 years old are screened using IgM WNV enzyme-linked immunosorbent assay (ELISA). A 28-day quarantine period is mandatory for all blood donors from localities where human cases have been detected. Nevertheless, a significant number of human viral encephalitis cases remain unconfirmed for WNV and are recorded as “viral encephalitis with unknown etiology”, as the current legislation does not require further confirmatory tests for other arthropod-borne arboviruses. As a consequence, the blood donors are not screened for other viruses although some, i.e., Toscana[36]and Usutu, were recently reported in Romania.

USUV, a member of the Japanese encephalitis serocomplex, is phylogenetically close to WNV [37-39]. USUV has spread to a large part of the European continent over the two decades, mainly leading to substantial avian mortalities with a significant recrudescence of bird infections recorded throughout Europe within the last few years[40]. In Europe, USUV was first reported in Austria and was associated with high mortality among blackbirds (*Turdus merula*)[41]. This event was followed by a retrospective study in Italy on bird tissue samples stored from 1996, which subsequently tested positive for USUV by molecular techniques[42]. Later, the virus was identified in mosquitoes and different vertebrate hosts in several European countries[43, 44]. USUV infection in humans is considered to be most often asymptomatic or to cause mild clinical signs[40]. The first human neuroinvasive infection in Europe was registered in 2009 in Italy in a patient with meningoencephalitis symptoms [45] followed by other reports[46]. Seroconversion in healthy blood donors was also registered[47]. In Romania, the first serological evidence of the presence of USUV was documented in a domestic dog, but its presence in humans has not yet been demonstrated.

TBEV is endemic in many European countries including Romania, being the most important neuroinvasive arbovirus vectored by ticks[48, 49]. Information on the tick- borne encephalitis (TBE) epidemiology in Romania is scarce and partly outdated. The most important outbreak in humans was recorded in 1999, when 38 infections were recorded, raw goat dairy products being incriminated as the source of infection. Seroprevalence rates varied between 0.0% and 41.5% in humans and between 0.0% and 27.7% in livestock [50]. Since 2008, TBE has been passively monitored in 11 north-western and central counties considered at risk out of the 41 counties of Romania. TBE is also notifiable at the EU level since 2012[51].

CONCLUSIONS

There is a wealth of evidence that recent climate change has already affected pathogen–vector–host systems, in particular over temperate, peri-Arctic and Artic areas and high altitude regions in the tropics. There are now many examples of the early impacts of climate change on animal VBD bur- den, while the most severe VBD outbreaks affect- ing humans tend to be affected by a myriad of complex socioeconomic factors and climate. This review demonstrates that the spread of vectors and the pathogens they transmit worldwide has been anticipated by scientists.

REFERENCES

1. Rochlin, I. and A. Toledo, *Emerging tick-borne pathogens of public health importance: a mini-review.* J Med Microbiol, 2020. **69**(6): p. 781-791.
2. Halos, L., et al., *Defining the concept of 'tick repellency' in veterinary medicine.* Parasitology, 2012. **139**(4): p. 419-23.
3. Jongejan, F. and G. Uilenberg, *Ticks and control methods.* Rev Sci Tech, 1994. **13**(4): p. 1201- 26.
4. de la Fuente, J., et al., *Flying ticks: anciently evolved associations that constitute a risk of infectious disease spread.* Parasit Vectors, 2015. **8**: p. 538.
5. Estrada-Peña, A., et al., *Effects of environmental change on zoonotic disease risk: an ecological primer.* Trends Parasitol, 2014. **30**(4): p. 205-14.
6. Leblebicioglu, H., et al., *Crimean-Congo haemorrhagic fever in travellers: A systematic review.* Travel Med Infect Dis, 2016. **14**(2): p. 73-80.
7. Estrada-Peña, A. and J.M. Venzal, *Climate niches of tick species in the Mediterranean region: modeling of occurrence data, distributional constraints, and impact of climate change.* J Med Entomol, 2007. **44**(6): p. 1130-8.
8. Grech-Angelini, S., et al., *Crimean-Congo Hemorrhagic Fever Virus Antibodies among Livestock on Corsica, France, 2014-2016.* Emerg Infect Dis, 2020. **26**(5): p. 1041-1044.
9. Hoogstraal, H., *The epidemiology of tick-borne Crimean-Congo hemorrhagic fever in Asia, Europe, and Africa.* J Med Entomol, 1979. **15**(4): p. 307-417.
10. Xia, H., et al., *Transstadial Transmission and Long-term Association of Crimean-Congo Hemorrhagic Fever Virus in Ticks Shapes Genome Plasticity.* Sci Rep, 2016. **6**: p. 35819.
11. Grandi, G., et al., *First records of adult Hyalomma marginatum and H. rufipes ticks (Acari: Ixodidae) in Sweden.* Ticks Tick Borne Dis, 2020. **11**(3): p. 101403.
12. Shuaib, Y.A., et al., *Ixodid tick species and two tick-borne pathogens in three areas in the Sudan.* Parasitol Res, 2020. **119**(2): p. 385-394.
13. Pérez-Eid, C., *[Emergence of tick-borne diseases in temperate countries].* Ann Biol Clin (Paris), 2004. **62**(2): p. 149-54.
14. Pérez-Eid, C., *[New distribution of tick-borne diseases in temperate countries].* Ann Biol Clin (Paris), 2004. **62**(3): p. 253-5.
15. Vial, L., et al., *Strong evidence for the presence of the tick Hyalomma marginatum Koch, 1844 in southern continental France.* Ticks Tick Borne Dis, 2016. **7**(6): p. 1162-1167.
16. Grech-Angelini, S., et al., *Tick-borne pathogens in ticks (Acari: Ixodidae) collected from various domestic and wild hosts in Corsica (France), a Mediterranean island environment.* Transbound Emerg Dis, 2020. **67**(2): p. 745-757.
17. Morel, P.C., *[Relations of animal viruses and Rickettsia with their vector ticks].* Ann Parasitol Hum Comp, 1971. **46**: p. Suppl:179-96.
18. Xiao, X., et al., *Identification of a putative Crimean-Congo hemorrhagic fever virus entry factor.* Biochem Biophys Res Commun, 2011. **411**(2): p. 253-8.
19. Cikman, A., et al., *Seroprevalence of Crimean-Congo Hemorrhagic Fever Virus in Erzincan Province, Turkey, Relationship with Geographic Features and Risk Factors.* Vector Borne Zoonotic Dis, 2016. **16**(3): p. 199-204.
20. Papa, A., et al., *Recent advances in research on Crimean-Congo hemorrhagic fever.* J Clin Virol, 2015. **64**: p. 137-43.
21. Fajs, L., et al., *Prevalence of Crimean-Congo hemorrhagic fever virus in healthy population, livestock and ticks in Kosovo.* PLoS One, 2014. **9**(11): p. e110982.
22. Gergova, I. and B. Kamarinchev, *Seroprevalence of Crimean-Congo hemorrhagic fever in southeastern Bulgaria.* Jpn J Infect Dis, 2014. **67**(5): p. 397-8.
23. Gergova, I. and B. Kamarinchev, *Comparison of the prevalence of Crimean-Congo hemorrhagic fever virus in endemic and non-endemic Bulgarian locations.* J Vector Borne Dis, 2013. **50**(4): p. 265-70.
24. Németh, V., et al., *Serologic evidence of Crimean-Congo hemorrhagic fever virus infection in Hungary.* Vector Borne Zoonotic Dis, 2013. **13**(4): p. 270-2.
25. Ceianu, C.S., et al., *First serologic evidence for the circulation of Crimean-Congo hemorrhagic fever virus in Romania.* Vector Borne Zoonotic Dis, 2012. **12**(9): p. 718-21.
26. Mertens, M., et al., *Crimean-Congo Hemorrhagic Fever Virus in Bulgaria and Turkey.* Vector Borne Zoonotic Dis, 2016. **16**(9): p. 619-23.
27. Schuster, I., et al., *Detection of Crimean-Congo hemorrhagic fever virus-specific IgG antibodies in ruminants residing in Central and Western Macedonia, Greece.* Ticks Tick Borne Dis, 2017. **8**(4): p. 494-498.
28. Bratuleanu, B., et al., *Seroprevalence of Crimean-Congo Hemorrhagic Fever Among Small Ruminants from Southern Romania.* Vector Borne Zoonotic Dis, 2022. **22**(7): p. 397-401.
29. Sirbu, A., et al., *Outbreak of West Nile virus infection in humans, Romania, July to October 2010.* Euro Surveill, 2011. **16**(2).
30. Tsai, T.F., et al., *West Nile encephalitis epidemic in southeastern Romania.* Lancet, 1998. **352**(9130): p. 767-71.
31. Cernescu, C., et al., *Continued transmission of West Nile virus to humans in southeastern Romania, 1997-1998.* J Infect Dis, 2000. **181**(2): p. 710-2.
32. Dinu, S., et al., *West Nile virus circulation in South-Eastern Romania, 2011 to 2013.* Euro Surveill, 2015. **20**(20).

33. López-Ruiz, N., et al., *West Nile virus outbreak in humans and epidemiological surveillance, west Andalusia, Spain, 2016.* Euro Surveill, 2018. **23**(14).
34. Papa, A., *West Nile virus infections in Greece: an update.* Expert Rev Anti Infect Ther, 2012. **10**(7): p. 743-50.
35. Rizzo, C., et al., *West Nile virus transmission: results from the integrated surveillance system in Italy, 2008 to 2015.* Euro Surveill, 2016. **21**(37).
36. Popescu, C.P., et al., *Emergence of Toscana Virus, Romania, 2017-2018.* Emerg Infect Dis, 2021. **27**(5): p. 1482-1485.
37. Best, S.M., *Flaviviruses.* Curr Biol, 2016. **26**(24): p. R1258-r1260.
38. Ishikawa, T. and E. Konishi, *[Flaviviruses].* Uirusu, 2011. **61**(2): p. 221-38.
39. Yoshii, K., *[Pathogenic mechanisms of Tick-borne Flaviviruses].* Uirusu, 2018. **68**(1): p. 78-88.
40. Clé, M., et al., *Usutu virus: A new threat?* Epidemiol Infect, 2019. **147**: p. e232.
41. Weissenböck, H., et al., *Emergence of Usutu virus, an African mosquito-borne flavivirus of the Japanese encephalitis virus group, central Europe.* Emerg Infect Dis, 2002. **8**(7): p. 652-6.
42. Weissenböck, H., et al., *Usutu virus, Italy, 1996.* Emerg Infect Dis, 2013. **19**(2): p. 274-7.
43. Ashraf, U., et al., *Usutu virus: an emerging flavivirus in Europe.* Viruses, 2015. **7**(1): p. 219-38.
44. Vilibic-Cavlek, T., et al., *Epidemiology of Usutu Virus: The European Scenario.* Pathogens, 2020. **9**(9).
45. Pecorari, M., et al., *First human case of Usutu virus neuroinvasive infection, Italy, August-September 2009.* Euro Surveill, 2009. **14**(50).
46. Santini, M., et al., *First cases of human Usutu virus neuroinvasive infection in Croatia, August-September 2013: clinical and laboratory features.* J Neurovirol, 2015. **21**(1): p. 92-7.
47. Zaaijer, H.L., et al., *Usutu virus infection in Dutch blood donors.* Transfusion, 2019. **59**(9): p. 2931-2937.
48. Stefanoff, P., et al., *Virus detection in questing ticks is not a sensitive indicator for risk assessment of tick-borne encephalitis in humans.* Zoonoses Public Health, 2013. **60**(3): p. 215-26.
49. Martin, L.J., et al., *Investigating novel approaches to tick-borne encephalitis surveillance in Sweden, 2010-2017.* Ticks Tick Borne Dis, 2020. **11**(5): p. 101486.
50. Molnár, G.B., et al., *[Epidemiological assessment of morbidity and natural foci of TBE-CEE virus infection in Transylvania].* Rev Med Chir Soc Med Nat Iasi, 2008. **112**(2): p. 471-7.
51. Steffen, R., *Epidemiology of tick-borne encephalitis (TBE) in international travellers to Western/Central Europe and conclusions on vaccination recommendations.* J Travel Med, 2016. **23**(4).
52. Michelet, L., et al., *High-throughput screening of tick-borne pathogens in Europe.* Front Cell Infect Microbiol, 2014. **4**: p. 103.
53. Gondard, M., et al., *Ticks and Tick-Borne Pathogens of the Caribbean: Current Understanding and Future Directions for More Comprehensive Surveillance.* Front Cell Infect Microbiol, 2017. **7**: p. 490.
54. Boularias, G., et al., *High-Throughput Microfluidic Real-Time PCR for the Detection of Multiple Microorganisms in Ixodid Cattle Ticks in Northeast Algeria.* Pathogens, 2021. **10**(3).
55. Shimada, S., et al., *Tofla virus: A newly identified Nairovirus of the Crimean-Congo hemorrhagic fever group isolated from ticks in Japan.* Sci Rep, 2016. **6**: p. 20213.
56. de Vos, C.J., et al., *Assessing the introduction risk of vector-borne animal diseases for the Netherlands using MINTRISK: A Model for INTegrated RISK assessment.* PLoS One, 2021. **16**(11): p. e0259466.