Letter to the Editor

# Usutu Virus: An emerging Flavivirus in silent expansion

## Virus Usutu: un flavivirus emergente en expansión silenciosa

Amauri Lázaro Noda Albelo[1,2] https://orcid.org/0009-0002-3250-613X

Roberto Cañete Villafranca[2*] https://orcid.org/0000-0002-6490-4514

[1]Servicio Médico Integral (SMI). Montevideo, Uruguay.

[2]Universidad de Ciencias Médicas de Matanzas. Cuba.

[*]Corresponding author: canete.villafranca@gmail.com

Dear Editor,

We read with interest the first documented case of a fatal autochthonous Usutu virus (USUV) infection in an immunocompromised patient in Hungary and the reports of Usutu virus circulation across Europe.(1,2) The Usutu virus, a zoonotic flavivirus closely related to West Nile virus (WNV), went virtually unnoticed by global public health authorities for decades. However, in the last twenty years, it has demonstrated a remarkable capacity for geographic expansion, ecological adaptation, and the ability to cause human disease.

USUV was initially isolated in 1959 from a *Culex neavei* mosquito captured near the Usutu River in Eswatini (formerly Swaziland) and has also spread to Europe, primarily affecting birds and having a limited impact on human health. Over the following decades, the virus circulated widely, almost silent, in sub-Saharan African countries, including South Africa, Nigeria, Senegal, Uganda, the Central African Republic, and Côte d'Ivoire, facilitated by factors such as climate change, leading to increased human exposure.(3) Early serological studies showed frequent exposure in human populations, but without a clear description of clinical symptoms. Essentially, USUV was considered an avian virus with little impact on humans.

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The real turning point occurred in the late 1990s and early 2000s, when the Usutu virus was detected in Austria after causing unusually high mortality in blackbirds (*Turdus merula*).[4] This event, similar to the 1999 West Nile virus (WNV) outbreak in North America, revealed that USUV could produce severe epizootics in European birds. The virus spreads rapidly to Germany, Switzerland, and Hungary (2002-2005), Italy (since 2006), Spain and France (since 2012), and Belgium, Netherlands, and United Kingdom (2016–2018).[2]

Similar to West Nile Virus, USUV is maintained in a bird-mosquito cycle, with the predominant participation of *Culex pipiens*, *Culex modestus*, *Culex neavei*, *Aedes albopictus*, and other local mosquitoes and the key involvement of passerine birds, especially blackbirds, owls, robins, sparrows, and warblers acting as its main reservoirs or amplifiers. Humans, bats, and other mammals are accidental hosts. Vector's ecological plasticity, which has allowed the virus to establish itself in temperate climates and participate in urban cycles, facilitating human exposure.[5]

The first USUV confirmed case was reported in Italy in 2009, in an immunocompromised patient with neuroinvasive infection. Since then, sporadic cases of meningoencephalitis have been notified in Italy, Croatia, Germany, France, and Spain. High regional seroprevalence, suggesting intense undetected circulation.

USUV clinical presentations can overlap with other flavivirus infections such as WNV, dengue, and Zika) making diagnosis difficult. The increase of human cases is close link to the geographic expansion of the vector, the increased surveillance and screening of blood banks, the increased epidemic peaks in birds, which act as sentinels, and other climate factors, prolonging transmission seasons and facilitating the winter survival of mosquitoes.[6]

The absence of vaccines or specific antiviral therapies further amplifies the importance of preventive strategies, particularly vector control and integrated one health surveillance. As mentioned, climate change is accelerating the northward spread of mosquito-borne viruses, creating niches for arboviruses previously restricted to warner regions. It is very important the detection of diverse USUV linages in new territories suggesting ongoing viral adaptation and genetic diversification, which may increase the risk of zoonotic spillover.

We urge public health authorities worldwide to expand molecular surveillance, integrate USUV monitoring into existing arbovirus programs, and promote interdisciplinary collaboration. The emergence of USUV infections is a reminder that arboviruses, once considered marginal, can rapidly evolve into significant health threats. Early recognition, sustained research, and coordinated action are essential

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to prevent USUV from becoming the next major arboviral epidemic in European countries and beyond.

## Bibliographic references

1. Szabó BG, Nagy A, Nagy O, Koroknai A, Csonka N, Korózs D, *et al*. First documented case of a fatal autochthonous Usutu virus infection in an immunocompromised patient in Hungary: a clinical-virological report and implications from the literature. Virol J. 2025;22(1):261. DOI: https://doi.org/10.1186/s12985-025-02890-9

2. Simonin Y. Circulation of West Nile Virus and Usutu Virus in Europe: Overview and Challenges. Viruses. 202;16(4):599. DOI: https://doi.org/10.3390/v16040599

3. Leal Filho W, Ternova L, Parasnis SA, Kovaleva M, Nagy GJ. Climate Change and Zoonoses: A Review of Concepts, Definitions, and Bibliometrics. Int J Environ Res Public Health. 2022;19(2):893. DOI: https://doi.org/10.3390/ijerph19020893

4. Weidinger P, Kolodziejek J, Bakonyi T, Brunthaler R, Erdélyi K, Weissenböck H, *et al*. Different dynamics of Usutu virus infections in Austria and Hungary, 2017-2018. Transbound Emerg Dis. 2020;67(1):298-307. DOI: https://doi.org/10.1111/tbed.13351

5. Nikolay B. A review of West Nile and Usutu virus co-circulation in Europe: how much do transmission cycles overlap? Trans R Soc Trop Med Hyg. 2015;109(10):609-18. DOI: https://doi.org/10.1093/trstmh/trv066

6. Agliani G, Giglia G, Marshall EM, Gröne A, Rockx BHG, van den Brand JMA. Pathological features of West Nile and Usutu virus natural infections in wild and domestic animals and in humans: A comparative review. One Health. 2023;16:100525. DOI: https://doi.org/10.1016/j.onehlt.2023.100525

### Conflict of interest

The authors declare no conflict of interests.

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