

"EXOTIC" VIRUSES THAT THREATEN US

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EMERGING INFECTIOUS
DISEASE. A newly developed disease in humans transmitted by an infectious agent (microbe) from a known animal, the environment, or an infectious agent.

ARTHROPODS. A group of invertebrate animals characterized by an exoskeleton, a segmented body, and articulated appendages. Insects (such as mosquitoes and ticks), spiders, crustaceans, and myriapods are arthropods.

ARBOVIRUS. Virus transmitted by arthropod vectors, mainly mosquitoes and ticks. The term "arbovirus" is derived from the English "arthropodborn virus".

Since the beginning of the twenty-first century, we have observed the appearance or reappearance of multiple viral diseases, constituting a major challenge for human health. Viruses, called arboviruses because they are transmitted by arthropod vectors such as mosquitoes, are of particular concern because of their increasing expansion in various geographic regions. Among these arboviruses, the chikungunya, Zika, West Nile, and dengue viruses constitute a major and growing threat to human health in many countries. These viruses, once considered exotic because they are found in remote tropical regions, are now spreading beyond their usual areas and gaining ground globally. Europe is not spared from this threat as in recent years infection numbers have surged upwards.

VIRUSES FROM ANIMALS

Many emerging infectious diseases are transmitted to humans by a "vector" animal, which is often a blood-sucking arthropod, such as mosquitoes, flies or ticks. These diseases, when caused by viruses, are called "arboviruses", and the viruses involved are referred to as "arboviruses" (a term derived from the English "arthropod-born virus").

ZOONOSE. Infectious diseases transmitted from animals to humans. It can be caused by a variety of infectious agents, including bacteria, viruses, parasites and prions.

Most arboviruses infections are zoonoses, i.e. diseases initially present in domestic or wild animals carrying the infectious agent. The virus is then transmitted to humans by an arthropod vector, which has previously fed itself on the blood of an infected animal. Some arboviruses can spread from person to person exclusively via a vector, while others also use alternative modes of transmission (ex., Zika virus can be transmitted by both mosquitoes and sexually). Some arboviruses are not transmitted between humans, even by a vector. Humans are then considered an "epidemiological dead end" because they cannot spread the virus. This is likely related to the fact that for some of these viruses infected people, although developing the disease, do not have enough virus in their blood to transmit it effectively. This is the case, for example, with the West Nile virus. This virus spreads from one region to another either through infected humans moving (including by air transport) or through infected animals such as migratory birds.

MOSQUITOES AS THE MAIN VECTORS

Among the insects capable of transmitting viruses in Europe are ticks (transmitting the tick-borne encephalitis virus) and small biting flies called sandflies (transmitting the Toscana virus). However, mosquitoes, especially the tiger mosquito (whose scientific name is *Aedes albopictus*), play a major role in the spread of arboviruses. Native to Asia, this small black mosquito with white stripes on its body and legs was first detected in Europe in the late 70s; it arrived in France in 2004, in the South East of France, close to the Italian border.

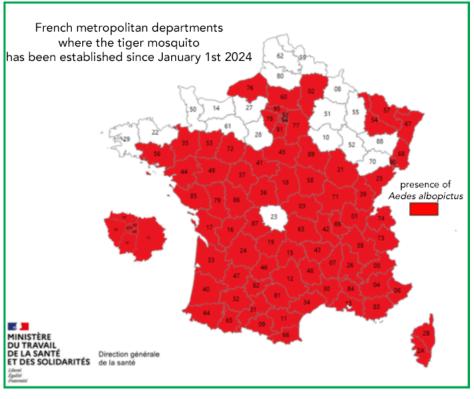


Figure 1. Since 2004, the tiger mosquito has colonized most of the French territory. Ministry of Solidarity and Health - Directorate-General for Health.

The rapid expansion of the tiger mosquito has been facilitated by international trade which has allowed it to be transported over long distances. In France, it has spread to 79 out of 96 metropolitan departments (compared to 71 in 2022 and 64 in 2021) (Figure 1). The extension of its territory over a large part of Europe seems inevitable in the years to come. One of the particularities of the tiger mosquito is its ability to efficiently transmit many viruses responsible for different diseases in humans. The most well-known viruses spread by this mosquito are the Zika virus, the chikungunya virus and the dengue virus.

Present throughout France, the common mosquito (called *Culex pipiens*) is also capable, although to a lesser extent, to transmit arboviruses, the best known of which is West Nile virus.

DENGUE VIRUS: THE MOST REPRESENTED

The dengue virus, like all viruses transmitted to humans by insects, has a genome made of RNA, unlike our genome which is made up of DNA (Figure 2). It was first isolated in 1940 from blood samples from infected patients in Japan. Nevertheless, clinical descriptions of this disease date back several centuries without the virus involved being identified at the time. According to studies, dengue fever is **asymptomatic** in 50% to 90% of cases. In symptomatic people, the symptoms (fever, headache, muscle aches) can easily be confused with other viral diseases such as the flu or Covid-19. Although dengue fever is most often mild, in about 1% of cases, it can lead to a life-threatening form called "hemorrhagic" dengue fever characterized by bleeding from multiple organs [1]. Damage to the brain, sometimes with serious consequences, has also been reported.

ASYMPTOMATIC. An asymptomatic individual is a person infected with an infectious agent (such as a virus or bacteria) who has no symptoms of the disease. Nevertheless, asymptomatic carriers can often transmit the infection

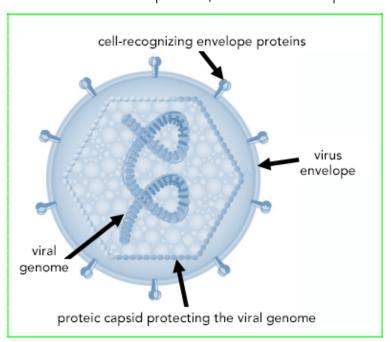


Figure 2. Schematic representation of the Dengue virus. The genome of the virus (formed from RNA) is enclosed in a protein shell called a capsid. This capsid is surrounded by an envelope in which some proteins of the virus are located, allowing it to attach to the cells it will infect.

INDIGENOUS CASES. Locally acquired infections, which means that the person has contracted the disease in the area where they reside.

IMPORTED CASES. Infections acquired by people who have traveled to an area where the disease is present and then brought the infection back to their country or region of origin.

The dengue virus seems to have found a favorable ground in the southern regions of Europe. Indeed, although the number of dengue cases in Europe remains limited, with less than a hundred cases recorded in Europe before 2022, an upward trend is confirmed, mainly over the past 2 years. This increase is illustrated by the multiplication of indigenous cases, i.e. infections contracted on the metropolitan territory, unlike the imported cases contracted abroad or in the French overseas departments. France is the European country reporting the most cases of dengue. The departments of southern and south-eastern France, such as Hérault, Gard, Var, and the Alpes-Maritimes, are particularly exposed due to the high density of tiger mosquitoes and highly urbanized areas. In 2022, 66 cases of autochthonous dengue were identified, marking a turning point for the circulation of the virus in France. In 2023, 45 new cases were identified. 2024 is another record year with at least 85 local cases identified and more than 2000 imported cases. These three years each represent significantly more cases than the cumulative number of cases in the last 20 years.

ZIKA: THE MOST MYSTERIOUS

Like the majority of arboviruses, a significant proportion of people infected with the Zika virus do not develop symptoms. Symptoms are usually mild. They begin between 3 and 14 days after infection, and lasts from a few days to a week. The most common symptoms are a fever, rash, headache, or conjunctivitis (red eyes). Most infected people do not require hospitalization and recover completely from infection. However, the Zika virus is particularly dangerous for pregnant women because it can cause serious malformations of the fetus, including microcephaly, which corresponds to a reduction in the diameter of the brain [2].

The Zika virus was discovered in 1947 in a monkey inhabiting the Zika forest in Uganda. Responsible only for isolated cases in Africa, it was considered unlikely dangerous until a major epidemic appeared in Latin America, probably due to a mutation of the virus, infecting more than a million people in 2015-2016. In Europe, two autochthonous cases were suspected in France in 2019 in the Var department (the chains of transmission, particularly vectorial, have not been clearly established). Although the virus is still on the World Health Organization's list of the 10 most at-risk diseases, it has mysteriously almost disappeared from the radar in recent years. However, its comeback remains a serious possibility because it circulates quietly in various countries, especially in Asia and Africa. Thus, the surveillance of the Zika virus requires particular vigilance on the part of the scientific community.

CHIKUNGUNYA: QUITE DISCREET IN RECENT YEARS

Unlike other arboviruses, chikungunya is largely symptomatic. "Bent-over man's disease" (translation of the term "chikungunya" from Makondé, a

Bantu language spoken in Tanzania) most often manifests itself as fever and severe, often disabling joint pain, frequently affecting the hands, wrists, ankles and feet. Other symptoms include headaches, muscle aches, and bleeding from the gums or nose. Recovery can last several weeks, and pain can sometimes persist for years [3].

The chikungunya virus, first identified in Tanzania in 1952, has been circulating for several decades in Africa, India, and Asia, as well as in the Indian Ocean. The first two autochthonous cases of chikungunya in France were detected in 2010 in the Var. Since then, about thirty indigenous cases have been recorded in France. Although the chikungunya virus has been discreet in recent years in Europe with, for example, only 3 cases imported into France in 2021 and 5 cases in 2022, it remains closely monitored because it can be transmitted very efficiently by the tiger mosquito.

WEST NILE VIRUS: A COMPLEX TRANSMISSION CYCLE

About 20 to 30% of people infected with West Nile virus have symptoms. The most common symptoms are fatigue and headaches, often associated with a flu-like syndrome known as "West Nile fever." About 1% of human cases are characterized by brain disorders, including encephalitis (inflammation of the brain), meningitis (inflammation of the meninges), or meningoencephalitis (inflammation of the meninges and brain). In neurological forms, the mortality rate is around 10%, mainly affecting vulnerable people such as the elderly or immunocompromised patients [4].

reservoir susceptible species

Culex (vector) (vector)

Figure 3. The West Nile virus transmission cycle involves birds (virus amplifier hosts) and mosquitoes (vectors). The infection can spread to humans and a diverse range of vertebrates, generally considered accidental hosts or "dead ends" (not able to transmit the disease, but can develop it).

The West Nile virus was first isolated in 1937 from the West Nile district of northern Uganda. It has the particularity of having **reservoirs** in birds that allowed the virus to arrive In Europe via migratory birds, the common mosquito *Culex pipiens* can then transmit the virus from birds to humans

IMMUNOCOMPROMISED. A person whose immune system is weakened by an illness (AIDS) or who has received a transplant and is taking an antirejection drug.

RESERVOIR. A living being that, without developing symptoms of disease, harbors the survival and multiplication of an infectious agent that can be transmitted to other species.

(Figure 3). This virus is now well established in Europe where it is responsible for isolated cases but also for sometimes significant epidemics. A major outbreak hit Europe in 2018, with more than 2,000 cases identified and more than 180 deaths. In 2022, southern Europe was again impacted, particularly Italy, with 723 cases and 51 associated deaths. In France, in 2023, more than 40 cases have also been identified.

CLIMATE CHANGE IN THE BACKGROUND

Environmental changes have a significant impact on the emergence and re-emergence of infectious diseases [5]. The World Health Organization has identified climate change and ecosystem modifications, caused by biodiversity loss and land-use changes, such as environmental threats to human and animal health. Emerging infectious diseases, particularly those transmitted by insects, are closely linked to environmental changes. For example, climate change, urbanization and land use are changing the distribution of vectors (especially mosquitoes) as well as animal reservoir populations of these viruses. All this promotes the transmission of these viruses. In southern Europe, rising temperatures in spring encourage the proliferation of Culex mosquitoes, particularly in agricultural and urban areas. In addition, the alternation of dry periods and heavy rainfall promotes the proliferation of other mosquitoes, such as the tiger mosquito. Climate changes also influence many vertebrate hosts of viruses. For example, the migratory behavior of birds and the diversity of species in a specific area are highly dependent on anthropogenic factors. Although cases of arbovirus disease in Europe remain sporadic for the time being, they have been increasing in recent years. The fight against mosquito vectors and the strengthening of surveillance networks for circulating viruses remain the best strategy to fight against these new threats, which are often difficult to anticipate.

ANTHROPOGENIC FACTORAn element caused by human activity, directly or indirectly.

SPORADIC. A disease that affects only a few individuals and appears here and there in an irregular manner.

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ORIGINAL ARTICLE (ENGLISH VERSION)

EDITION: Catherine Braun-Breton, Association Jeunes Francophones et la Science.

SCIENTIFIC MENTORS: Catherine Braun-Breton

CITATION: Simonin Y. (2025). « Exotic » viruses that threaten us. https://www.jeunesfrancophonesetlascience.fr/.

CONFLICT OF INTEREST

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YOUNG REVIEWERS

CYRIL, AGE:10

Hi, I am Cyril! I am highly interested by sciences, enjoy Legos, Star wars and Jurassic world movies and love to play Mine Craft and soccer.

ANAÏS, AGE:14

Hello, I'm Anaïs. I grew up loving rocks, horses, and all other animals. I ride at least 2-3 times a week and love spending time at the barn. I don't enjoy talking to people that much and prefer the company of animals. I have written a novel, started to write a new one and have completed short stories.

AUTHOR

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Yannick Simonin is a professor of virology at the University of Montpellier. He leads a research group that focuses on emerging viruses, taking a holistic approach that takes into account the interdependence between human, animal and environmental health, within the framework of the "One Health" concept. His team is particularly interested in mosquitoborne viruses, including West Nile virus (WNV) and Usutu virus (USUV). In addition to the study of these arboviruses, his group explores the mechanisms of their transmission, their impact on public health and the development of innovative surveillance and control strategies. *yannick.simonin@umontpellier.fr

