# The ongoing threat of arbovirosis in Europe

## Analysis related to dengue and chikungunya viruses and its vectors

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## Introduction

In the last ten years, numerous cases of outbreaks of dengue and chikungunya fever have been reported in the European region. The emerge of this arthropod-borne viral diseases has emphasised a serious and growing problem of public health that is affecting not only the EU but also the rest of the world. The introduction of this tropical illnesses to the European continent is principally due to the global expansion and establishment of its vectors, mosquito species *Aedes aegypti* and *Aedes albopictus*. Other possible factors driving its geographic spread are the increasing volume of trade and travel and environmental challenges including climate change. Therefore, surveillance and control methods of this invasive mosquitoes are fundamental to prevent future outbreaks and reduce the risk of local transmission in vector colonised areas.

## Arboviruses

**Dengue virus**
- Single-stranded positive sense RNA virus
- Family: *Flaviviridae*; genus: *Flavivirus*

**Chikungunya virus**
- Single-stranded positive sense RNA virus
- Family: *Togaviridae*; genus: *Alphavirus*

They have emerged from a **sylvatic/enzootic cycle** to an **urban/epidemic cycle**, where they are transmitted by vectors between humans without the requirement for amplification in wild animals. This can be considered an **'indirect' route** of **human-to-human transmission** (1).

### According to WHO

It is estimated that nearly **75%** of the **global population** is **exposed** to **dengue**, especially in the tropics and subtropics, where it is also considered the leading cause of ilness and death (2).

**Chikungunya virus** has also caused a series of epidemics involving **5-10 million people** and exposing hundreds of millions at risk (2).

## Drivers of the emergence of arboviruses

They are biotic and abiotic parameters that have allowed and promoted the large colonisation of invasive mosquitoes species (IMS) and consequently the introduction of several exotic pathogens in different ecological niches (temperate regions) (4).

### Extrinsic factors

They allow the physical proximity between virus-vector-human host (1).

- Climate change (temperature and rainfalls)
- Internacional trade and travel

### Intrinsic factors

They modulate infection of vector and human host and the efficiency of transmission (1).

**Breeding habitat choice and feeding behavior**
- Preferential for man-made water containers as breeding sites (3,4)
- Preferential for humans as a feeding host (3,4)

**Diapausing and dessication-resistant eggs**
- Eggs with an increased overwinter survival and enhanced passive dispersal (4)

**Vector competence**
- Capacity to orally acquire, maintain and transmit pathogens to another vertebrate host (1,4)
- Influenced by virus and vector genetics, among other factors

***Ae. albopictus* microbiome**
- Modulates different host traits (lifespan or vector competence) (3)
- Principally composed by *Wolbachia* species

**Vector and human immunity**
- RNAi-based antiviral responses in the mosquito (1)
- Innate and adaptive immunity in humans

## Competent vectors

*Aedes* mosquitoes are aggressive, daytime biting insects with a preference for human blood (anthropophily) and a high invasive potential (1,3). The principal species of this genus are the following:

### *Aedes aegypti*

- Strongly anthropophilic and endophilic (preference for being indoors)
- Commonly found in urban and sub-urban areas
- Confined within the tropics and sub-tropics
  - Re-established only in specific areas in the European continent (Madeira, Portugal)

### *Aedes albopictus*

- More opportunistic and exophilic (preference for being outdoors)
- Traditionally found in rural areas
- Globally spread (also in temperate regions)
- Established throughout Southern Europe (Figure 1)

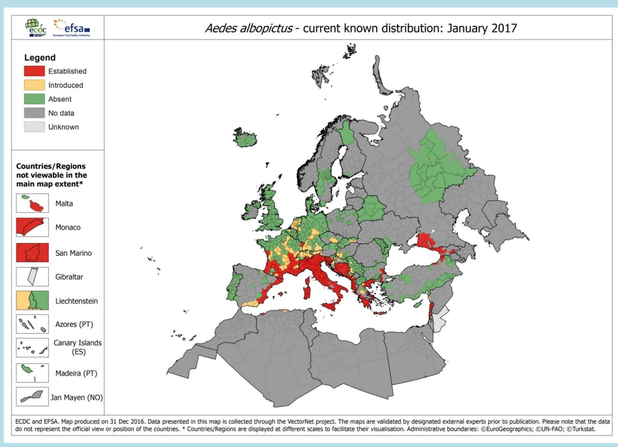


Figure 1: current known distribution of *Ae. albopictus* in Europe (January 2017) . Source: http://ecdc.europa.eu

## Autochthonous cases in the EU

Table 1: Most relevant outbreaks in Europe in the last decade. Adapted from (5)

| | Outbreak | Reported cases | | | Index case (viraemic traveller returning from: ) | Vector | Virus |
|---|---|---|---|---|---|---|---|
| | | Confirmed | Probable | Hospitalized | | | |
| Chikungunya fever | Emilia-Romagna (Italy, July-Sep 2007) | 229 | 30 | 25 (11,6%) | India | *Ae. albopictus* | E1-226V (genotype) |
| | Frejús (France, Sept 2010) | 2 | - | 0 (0%) | India | | E1-226A (genotype) |
| | Montpellier (France, Oct 2014) | 11 | 1 | 12 (100%) | Cameroon | | E1-226V (genotype) |
| Dengue fever | Nice (France, Sept 2010) | 2 | - | 2 (100%) | île de la Martinique | *Ae. albopictus* | DENV-1 (serotype) |
| | Pelješac (Croatia, Aug-Oct 2010) | 17 | - | 3 (18%) | Croatia | | |
| | Madeira (Portugal, Oct 2012) | 18 | 256 | 26 (14%) | Not known | *Ae. aegypti* | |

## Prevention/surveillance/control measures for invasive mosquitoes (6)

### Personal protection methods

- Effective in bite prevention.
- **Repellents**, **mosquito screens** or **treated clothes**.

### Chemical methods

- Chemical insecticides.
- **Insect growth regulators** (larvacides) and **pyretroids** (adulticides) are the unique chemicals used in Europe.

### Enviromental methods (source reduction)

- Consists in removing or turning over water containers that could be used as potencial mosquito breeding sites.

### Mechanical methods

- Based on using different types of traps with odour baits as monitoring tools of mosquito populations.
- Two available trapping methods for *Aedes* mosquitoes are **ovitraps** and **BG-Sentinal traps**.

### Biological methods

**Entomopathogenic fungi:**
- Used for its adulticides, larvacides and ovicides effects.
- Most commonly employed: *Beauveria bassiana* and *Metarhizium anisopliae*.

**Copepods:**
- Used as natural predators of mosquito larvae.

***Bacillus thuringiensis* var. *israelensis* (*Bti*):**
- Used as a microbial larvacide due to its toxin effects.

**Paratransgenesis:**
- Based on the introduction of genetically modified bacteria in mosquitoes where they express effector molecules causing different damaging effects in the insects.

***Wolbachia*-induced cytoplasmic incompatibility:**
- Based on a reproductive alteration causing embryonic mortality in matings between *Aedes* species with different *Wolbachia* infection status.

### Genetic methods

**Sterile insect technique (SIT)**
- Relies on the release of large numbers of sterile males to supress natural populations of mosquitoes.

**Release of insects with Dominant Lethality (RIDL)**
- Consists in the generation of transgenic males with a dominant lethal gene expressed by a female-specific promoter.

## Future prospects & conclusions

- Nowadays, outbreaks of severe exotic pathogens, such as dengue and chikungunya viruses, have dangerously increased their frequency in Europe, facilitated by the establishment and adaptation of their competent mosquito vectors *Aedes aegypti* and *Aedes albopictus* in the region. Travellers returning from disease-endemic environments have also contributed to the introduction of this new viruses. Thus, in vector colonised areas where this arboviruses are also present, there is a genuine risk of local transmission of dengue and chikungunya fever.
- Knowing the factors of this phenomenon is essential to understand the epidemic dynamics, assess and predict the potential risk of transmission of this tropical diseases in new zones and implement control measures.
- There is no effective vaccine for chikungunya and dengue fever yet, therefore, vector-control measures are indispensable to reduce the abundance of this invasive mosquito species and prevent further incursions and outbreaks of the diseases they can transmit.
- Finally, there are still a lot of questions that remain unclear and need to be answered, such as: a better understanding of the biology of both vectors and the ecology and evolution of DENV and CHIKV in their original sylvatic cycle; the identification of other factors that could influence the transmission between humans and the determination whether autochthonous mosquito species could be a competent vector for DENV and CHIKV and others arboviruses as well.

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