

## Cluster of autochthonous chikungunya cases in France

23 August 2017

### Main conclusions and options for response

The report of a cluster of autochthonous chikungunya cases in areas of Europe where *Aedes albopictus* is established is not unexpected during the summer months, when environmental conditions are favourable for mosquitoes. The risk of new clusters of local transmission emerging in the EU is currently considered moderate for chikungunya and dengue, as these diseases are endemic in large areas of the intertropical zone, repeated introductions occur through viraemic travellers returning from these areas, and weather conditions are currently suitable for *Aedes albopictus* activity in areas where it is established.

Early detection of imported cases is vital for preventing onward transmission through the introduction of the chikungunya virus by a viraemic traveller in an area where *Aedes albopictus* is established. Awareness among clinicians and information for travellers returning from areas with chikungunya transmission, combined with appropriate laboratory detection capacity, are essential during high mosquito activity season in areas where *Aedes albopictus* is established.

The detection of an autochthonous case should trigger epidemiological and entomological investigations to assess the potential of onward transmission and guide vector control measures aimed at lowering mosquito population density. In addition, personal protective measures against mosquito bites are recommended in affected areas to further reduce mosquito-borne transmission of chikungunya. Indoor and outdoor personal protective measures to reduce mosquito bites include the use of mosquito repellent in accordance with the instructions indicated on the product label; wearing long-sleeved shirts and long trousers, especially during the daytime when *Aedes albopictus* mosquitoes are most active; sleeping and resting in screened or air-conditioned rooms and using mosquito bed nets at night and during the day.

Travellers returning from areas where chikungunya transmission occurs should be advised to seek medical care if they develop symptoms consistent with chikungunya, in particular if they return to areas where the *Aedes albopictus* mosquito is established, in order to reduce the risk of the virus being introduced into the local mosquito population and to prevent further local transmission.

The prevention of chikungunya transmission through substances of human origin (SoHO) requires that preventive safety measures are applied to donors residing in or returning from affected areas. Based on epidemiological data, it is suggested that acute infection should be ruled out in SoHO donors living in or coming from affected areas using nucleic acid testing (NAT), or by temporarily interrupting donations in affected areas and excluding donations from travellers returning from such areas. The appropriate deferral period for donors with diagnosed chikungunya is unknown, but a period of at least four weeks after the resolution of symptoms should be considered, as suggested by data available on viraemia during and after chikungunya infection. If pathogen inactivation is applied, apheresis collection of platelets and plasma may continue in affected areas. Additionally, in all areas infested by *Aedes albopictus*, donors should be reminded to report any symptoms after giving blood. Organs from donors viraemic for chikungunya virus should not be used without consulting a transplant infectious disease expert.

The SOHO safety measures should be applied at a geographical level that takes into account the estimated zone of transmission and the daytime movements of the local population from the affected neighbourhood. EU blood safety authorities should consider the NUTS3 area where local transmission has been reported in the EU as the geographical criterion for deferring donation from travellers possibly exposed to chikungunya.

Preparedness regarding chikungunya in the EU requires the capacity to detect possible cases in areas with the presence of the competent vectors; strengthened surveillance systems (including clinician awareness, laboratory capacity for confirmation and rapid notification of cases); regular review of contingency plans for mosquito-borne outbreaks; education and collaboration of the general public on how to control mosquito breeding sites; strengthened vector surveillance systems and rapid implementation of vector control measures following each case.

## Source and date of request

ECDC internal decision, 14 August 2017.

## Public health issue

In the context of a cluster of four confirmed cases and one probable locally-acquired case of chikungunya in Var department, in southern France:

- What is the risk of onward vector-borne transmission?
- Is this cluster occurring at an unusually early time in the transmission season?
- If so, is this related to a change in vector capacity (climatic conditions) or a change in virus strain?

## Consulted experts

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External experts: Marie-Claire Paty, Henriette De Valk, Florian Franke and Clementine Calba (Public Health France).

Experts from WHO reviewed this risk assessment, however the views expressed in this document do not necessarily represent the views of WHO.

## Disease background information

Chikungunya is an *Aedes* mosquito-borne viral disease caused by a single-strand, positive-sense RNA virus (*Alphavirus* genus, *Togaviridae* family). The disease is widely distributed in tropical countries across Africa, Asia and the Americas. Chikungunya outbreaks in Europe have been previously reported in 2007 (Italy), and in 2010 and 2014 (France) [1].

## Clinical features

The incubation period ranges from two to 10 days, with an average of three days [2,3]. The disease usually results in high fever, myalgia, skin rash and arthralgia. The latter may persist for weeks or months, causing a significant disease burden in the affected community [4-7]. General complications, which are rare, include myocarditis, hepatitis, ocular and neurological disorders [8]. No specific treatment or licenced vaccine is currently available [9,10]. The medical management costs and productivity losses associated with a large chikungunya virus outbreak represent a significant economic burden [11].

The majority of infections are symptomatic (>75%) [12]. In humans, the viral load in the blood can be very high at the beginning of the infection and lasts 5–6 days after onset of fever [13].

## Diagnostics

Chikungunya virus can be identified using RT-PCR or viral isolation during the first week of illness. Serological diagnosis can be performed by detecting specific IgM antibodies in a serum specimen from day 4–5 after the onset of symptoms, preferably confirmed by sero-neutralisation assay. Diagnosis can also be confirmed by the detection of a four-fold rise in specific chikungunya antibodies titre in paired serum samples (acute and convalescent specimens). Genome sequencing of isolates can provide an indication of whether the virus has characteristics that increase the risk of its spread by *Aedes albopictus* mosquitoes. Differential diagnoses of dengue and Zika infection should be considered among travellers returning from tropical countries because of the wide circulation of these viruses in tropical areas and reports of co-infections [14-16].

## Transmission

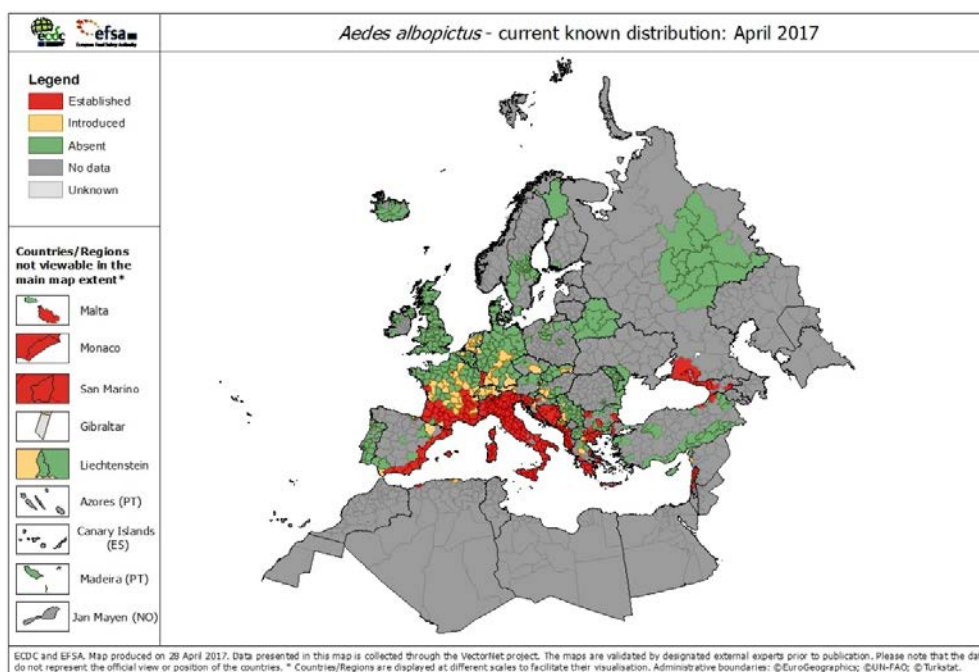
### Vector-borne transmission

Chikungunya is spread by the bite of *Aedes* mosquitoes, primarily *Aedes aegypti* and *Aedes albopictus*, two species which are active during the day and can also transmit other mosquito-borne viruses such as dengue and Zika.

Three main genotypes of chikungunya virus – Asian, West African and East/Central/South African (ECSA) – have been identified. The acquisition of an A226V mutation in the envelope protein E1 of the ECSA genotype, as initially observed in La Réunion in 2005, has increased the transmissibility of the virus through the widely distributed *Aedes albopictus* mosquitoes, in addition to the tropical main vector *Aedes aegypti* [17,18]. This mutated virus has spread from the Indian Ocean to East Africa and Asia (e.g. India, Sri Lanka, Singapore, Malaysia and China). In 2010 and 2014, the chikungunya virus strains responsible for the autochthonous cases in France belonged to the ECSA genotype but without the mutation A226V, while the genotype identified in the outbreak in Italy in 2007 had the mutation A226V (see Annex 1) [19-21].

In the EU, *Aedes albopictus* is established primarily around the Mediterranean (see Figure 1). It has been confirmed as a competent vector for strains belonging to the ECSA genotype as well as the strain from the Asian genotype that spread in the Americas [22-24]. Population dynamics of *Aedes albopictus* are mainly driven by temperature (survival of adults and development of larvae) and rainfall favouring the presence of breeding sites either of natural origin (small natural water bodies), or man-made (artificial containers of any kind) [25]. The potential role of anthropogenic breeding sites (e.g. flowerpot plates, water containers) is considered a key factor for the maintenance of *Aedes albopictus* populations during the hot, dry summer in the French Riviera region of southern France [25]. More information on the vector is available in the *Aedes albopictus* ECDC factsheet for experts [26]. The extrinsic incubation period of chikungunya virus in *Aedes albopictus* is expected to be below 10 days, usually five to eight days under laboratory conditions, which can be shortened at higher temperatures in natural conditions, and in particular, when the mutated A226V ECSA strain is involved [17,27].

**Figure 1. Current known distribution of *Aedes albopictus* in the EU and neighbouring countries, April 2017**



*Aedes aegypti*, the main vector of chikungunya, is present around the Black Sea and in Madeira [23].

*Aedes albopictus* has not been incriminated as a vector in the large outbreaks of chikungunya caused by the Asian genotype. This seems to be linked to the presence of an amino acid in the E1-98 region that blocks the ability of the Asian genotype virus to adapt to *Aedes albopictus* by means of the E1-A226V mutation [28,29]. However laboratory studies have demonstrated that *Aedes albopictus* can transmit some strains to a varying degree, depending on the viral genome (including those from the Asian genotype which emerged in the Caribbean in 2013) and the environmental temperature [24,29].

In the Var department, *Aedes albopictus* was first detected in 2007 [30]. The dynamics of *Aedes albopictus* populations in the Provence-Alpes-Côte d'Azur region studied between 2008 and 2011 demonstrate a marked seasonality pattern [25]. In general, females of *Aedes albopictus* lay their first batch of eggs at the beginning of May. The maximal adult vector densities are then reported between early July and early September, followed by progressive decrease in populations, with limited egg-laying activity until November or December, depending on local climatic conditions.

## Non-vector-borne transmission

Transmission of chikungunya virus infection through transfusion and transplantation has not been reported in humans, although animal models have shown that such transmission is possible. Donated material may be infectious if taken from infected asymptomatic donors [31] or during a short viraemic period before symptom onset. Transmission through blood transfusion has recently been described in Australia for Ross River virus, an alphavirus closely related to chikungunya virus [32]. Chikungunya virus infection was detected in 0.54% (three out of 557) of the asymptomatic donors investigated in Puerto Rico in April–August 2014, with estimated viral loads ranging from  $2.9 \times 10^5$  to  $9.1 \times 10^7$  copies/ml. Two of the three donors remained asymptomatic after donation [33]. The estimated risk of a viraemic blood donation varied from 38.2–52.3 per 100 000 donations in Thailand [34] to 132.3 per 100 000 donations in La Réunion [35]. In Italy, the estimated number necessary to yield one viraemic blood unit was 95 599 donations [36]. The fact that infectious virus and RNA have been found in the cornea and sclera of deceased donors in La Réunion [37] suggests that there is a risk of chikungunya transmission through grafts of ocular tissues. The risk of chikungunya transmission through other cells, tissues and organs cannot be excluded.

## Disease distribution

Chikungunya is endemic in Africa, south-east Asia, the Indian subcontinent, the Pacific Region and in tropical regions of the Americas since its introduction in 2013.

In the region of the Americas and the Caribbean, as of 11 August 2017, PAHO had reported around 140 000 suspected and confirmed chikungunya cases in 2017. Brazil reported most cases (93%), followed by Bolivia (2.3%), Panama (1.1%) and Peru (1.0%) [38]. In Asia, Bangladesh, India and Pakistan have reported cases of chikungunya. Since May 2017 and as of 14 July, Bangladesh had reported 2 700 chikungunya cases in the capital Dhaka [39]. In 2017, as of 13 August, India had reported 21 340 chikungunya cases, compared with 64 057 cases during 2016 [40]. In 2017, as of 22 June, Pakistan had reported 3 190 chikungunya cases in Karachi [41]. Additionally, around 2 000 chikungunya cases had been reported in Gwadar district in the southern part of the country during the first half of 2017 [42].

Autochthonous transmission has previously occurred in continental Europe, with the first autochthonous outbreak in Emilia Romagna, Italy involving 205 cases of chikungunya infection between 4 July and 27 September 2007 [18,43]. This was the first outbreak reported outside of a tropical region where a competent vector (*Ae. albopictus*) for the chikungunya virus was present. In France, autochthonous cases linked to imported cases were detected in the Var department in September 2010 (two laboratory-confirmed cases) and in the city of Montpellier, Hérault department in October 2014 (12 cases, including 11 confirmed) [20,21]. A table summarising dengue and chikungunya transmission events in Europe is available in Annex 1.

## Event background information

On 11 August 2017, France notified an autochthonous case of chikungunya virus infection, diagnosed in the Var department (Provence-Alpes-Côte d'Azur region) of south-eastern France through the Early Warning and Alert System (EWRS). The case lives in Cannet-des-Maures in the Var department. The onset of symptoms was on 2 August 2017. The infection was confirmed by RT-PCR and validated by the National Reference Centre. On 14 August, a second case was confirmed in a neighbour of the first case, with onset of symptoms on 8 August 2017. As of 22 August 2017, two additional confirmed cases and one probable case have been identified. Among the confirmed and probable cases, one lives in the same household as the second case and two live in the same neighbourhood as the other confirmed cases [44].

The dates of onset of these four confirmed and probable cases range from 2 August to 17 August 2017.

French authorities activated the chikungunya/dengue national response plan at risk level 3, corresponding to a single localised cluster of chikungunya cases in an area with established *Aedes albopictus* vector populations. As a result, French authorities implemented the following measures:

- Vector control measures around the houses of the cases in weeks 32 and 33, as well as at the place of employment of the first confirmed case.
- Active case finding (door-to-door, as well as by contacting the health professionals in the area) and laboratory investigation of suspected cases. So far, these investigations have not identified a case among anyone with a travel history who could have introduced the virus into the area (primary case).
- Blood donation deferral in the area and improved post donation information.
- Local communication, coordinated by the regional health agency.

## ECDC threat assessment for the EU

The report of a cluster of autochthonous chikungunya cases in areas of Europe where *Aedes albopictus* is established is not unexpected during the summer months, when environmental conditions are favourable for mosquitoes. Similar limited clusters of autochthonous transmission of dengue and chikungunya have been occurring since 2010 in southern France during this period [45,46] (see Annex 1) and in Italy in 2007. This is consistent with modelling studies in the European context [47].

This cluster is currently limited to cases infected within a 200-metre radius during a period of two and half weeks, suggesting possible involvement of two mosquito generations in the transmission. The identification of additional cases associated with this cluster through active surveillance is possible, in particular since the primary case who may have introduced the virus into the area has not been identified.

Further transmission in the area is unlikely following the implementation of vector control measures, and the risk of a significant expansion of the transmission area is very low. The absence of new cases in the affected area within the next two weeks will provide evidence of the effectiveness of the local vector control measures.

The risk of new clusters of local transmission emerging in the EU is currently considered moderate for chikungunya and dengue, as these diseases are endemic in large areas of the intertropical zone, repeated introductions occur through viraemic travellers returning from these areas, and weather conditions are currently suitable for *Aedes albopictus* activity in areas where it is established.

Further characterisation of chikungunya virus genotype is important because the presence of mutations such as the E1-A226V might favour the increased fitness of chikungunya virus in *Aedes albopictus* and enhance its epidemic potential [48]. The epidemic potential of this cluster will be reassessed if new information of significance is obtained from the genetic sequencing of locally acquired cases together with new epidemiological information.

The seasonal forecast issued in August for the period September to November 2017 predicts the absence of temperature anomalies and a higher probability of a drier climate in south-eastern France [49], which would not favour prolongation of vector activity beyond the normal seasonal range. However, weather conditions are expected to remain suitable for high vector activity until the end of September [25].

As France has cancelled mobile blood collection in the affected area and improved post-donation information to donors in the Var department, the risk of further transmission through substances of human origin (SOHO) is very low.

## Conclusions and options for response

Early detection of imported cases is the key to preventing onward transmission through the introduction of the chikungunya virus by a viraemic traveller into an area where *Aedes albopictus* is established. Awareness among clinicians and information for travellers returning from areas with chikungunya transmission, combined with appropriate laboratory detection capacity, are essential during high mosquito activity season in areas where *Aedes albopictus* is established.

The detection of an autochthonous case should trigger epidemiological and entomological investigations to assess the potential of onward transmission and guide vector control measures aimed at lowering mosquito population density [50]. In addition, personal protective measures against mosquito bites are recommended in affected areas to further reduce mosquito-borne transmission of chikungunya. Indoor and outdoor personal protective measures to reduce mosquito bites include the use of mosquito repellent in accordance with the instructions indicated on the product label; wearing long-sleeved shirts and long trousers, especially during the daytime when *Aedes albopictus* mosquitoes are most active; sleeping and resting in screened or air-conditioned rooms and using mosquito bed nets at night and during the day.

Travellers returning from areas where chikungunya transmission occurs should be advised to seek medical care if presenting with symptoms consistent with chikungunya, particularly if returning to areas where *Aedes albopictus* mosquito is established, in order to reduce the risk of the virus being introduced into the local mosquito population and to prevent further local transmission.

The prevention of chikungunya transmission through SoHO requires that preventive safety measures are applied to donors residing in or returning from affected areas. Based on epidemiological data, it is suggested that acute infection should be ruled out in SoHO donors living in or coming from affected areas using nucleic acid testing (NAT), or by temporarily interrupting donations in affected areas and excluding donations from travellers returning from such areas. The appropriate deferral period for donors with diagnosed chikungunya is unknown, but a period of at least four weeks after the resolution of symptoms should be considered, as suggested by data available on viraemia during and after chikungunya infection. If pathogen inactivation is applied, apheresis collection of platelets and plasma may continue in affected areas. Additionally, in all areas infested by *Aedes albopictus*, donors should be reminded to report any symptoms after giving blood. Organs from donors viraemic for chikungunya virus should not be used without consulting a transplant infectious disease expert.

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Preparedness regarding chikungunya in the EU requires the capacity to detect possible cases in areas with the presence of the competent vectors; strengthened surveillance systems (including clinician awareness, laboratory capacity for confirmation and rapid notification of cases); regular review of contingency plans for mosquito-borne outbreaks; education and collaboration of the general public on how to control mosquito breeding sites; strengthened vector surveillance systems and rapid implementation of vector control measures following each case.

## Disclaimer

ECDC issued this risk assessment document on the basis of an internal decision according to Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 853/2004 establishing a European centre for disease prevention and control. In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter with their respective advantages and disadvantages. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA Member States. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written under coordination of an Internal Response Team (IRT) at the European Centre for Disease Prevention and Control (ECDC). All data published in this risk assessment are correct to the best of our knowledge on 22 August 2017. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

**Annex 1. Autochthonous transmission of dengue and chikungunya in Europe, 2007 to August 2017**

Year	Country, region, municipalities	Disease	Number of cases	Period	Origin of primary case	CHIKV genotype DENV serotype	Reference
2007	Italy, region of Emilia Romagna, main transmission areas in Castiglione di Cervia and Castiglione di Ravenna villages.	CHIKV	≈ 330 suspected and confirmed cases	July-September	India	ESCA E1-V226 CHIKV strain	[18,43]
2010	Croatia, Korčula Island and the Pelješac peninsula.	DENV	One case imported (DE) and two acute local cases. Additional suspected case by serology (<20).	August-October	Unknown	DEN-1	[51-53]
2010	France, Alpes-Maritimes department, Nice (city).	DENV	Two cases	End August-September	Unknown	DEN-1	[54]
2010	France, Var department, Fréjus.	CHIKV	Two cases	September	India	ESCA E1-A226 CHIKV	[20,22]
2012	Portugal, Madeira island, Funchal city and surroundings.	DENV	≈ 2100 cases	September-January	Unknown*	DEN-1	[55,56]
2013	France, Bouches du Rhône department, in the vicinity of Aix-en-Provence.	DENV	One case	October	Guadeloupe	Most probably DEN-2	[57]
2014	France, Hérault department, Montpellier	CHIKV	Eleven cases	September-October	Cameroon	ESCA E1-V226 CHIKV	[21]
2014	France, Var department, Toulon.	DENV	One case	Early August	Unknown	DEN-1	[58]
2014	France, Var department, Toulon	DENV	One case	Early September	Unknown	DEN-2	[58]
2014	France, Bouches du Rhône department, Aubagne.	DENV	Two cases	Late August-September	Unknown	DEN-2	[58]
2015	France, Gard department, Nîmes.	DENV	Six cases	September-October	Possibly French Polynesia	DEN-1	[59]
2017	France, Var department.	CHIKV	Four confirmed cases and one probable case	August	Unknown	Unknown	[44,60]

*Explanatory note:**DENV: Dengue virus**DEN-1 and DEN-2: Dengue serotype 1 and 2 respectively**CHIKV: Chikungunya virus**ESCA: East-South-Central Africa CHIKV lineage.**\* Genetic analysis supports an importation from Venezuela [61]*

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