



RAPID RISK ASSESSMENT

Autochthonous cases of dengue in Spain and France

1 October 2019

Summary

On 16 September 2019, the Catalonian Public Health Agency confirmed an autochthonous case of dengue in a resident of Barcelonès county in Catalonia, Spain. The case had onset of symptoms on 6 September 2019, with no recent travel history outside of Spain. Dengue infection was confirmed by the Catalan reference laboratory for arboviruses and the Spanish national reference laboratory for arboviruses. Epidemiological investigations in Catalonia are ongoing, and further cases may be detected. According to national authorities, control measures are being implemented.

On 20 September 2019, the regional public health agency of Provence-Alpes-Côte d'Azur region reported a locally acquired confirmed case of dengue in a resident of the city of Vallauris in the department of Alpes-Maritimes. The case had onset of symptoms on 30 August and did not report any recent travel history outside of mainland France. This case was laboratory-confirmed by the French National Reference Centre for Arboviruses (NRC, Marseille). Door-to-door active case finding was implemented around the home of the autochthonous case on 19 September. Four additional cases in the direct vicinity were identified.

In addition, the regional public health agency of Auvergne-Rhône-Alpes reported a locally acquired probable dengue case in a resident of Caluire-et-Cuire – a suburban area of the city of Lyon – in the Rhône department. The case had onset of symptoms on 14 July 2019. For this case, NRC laboratory confirmation is still pending. The case did not report any recent travel outside of mainland France.

To date, these three events should be considered as independent because epidemiological investigations could not identify any epidemiological links between them.

Based on previous observations of autochthonous arbovirus transmission during the past decade, namely dengue and chikungunya, reports of sporadic autochthonous cases or limited clusters of dengue are expected in the Mediterranean region and southern parts of EU/EEA countries in the summer and autumn due to the presence of established populations of a competent vector (*Ae. albopictus*) and a large volume of travel-associated cases returning from epidemic/endemic tropical and subtropical countries favouring the introduction of dengue or chikungunya viruses.

The probability of further local sustained transmission remains very low, both in Spain and in France. Environmental conditions will become progressively less suitable for transmission over the autumn season. To date and based on ECDC's epidemiological assessment, the risk that visitors to the affected area will become infected and subsequently introduce the virus and thus initiate further local transmission in their country of residence cannot be excluded, but remains very low.

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Event background

Locally acquired dengue case in Spain

On 16 September 2019, the Catalonian Public Health Agency confirmed an autochthonous case of dengue in a resident of Barcelonès county in Catalonia, Spain [1]. The case is an adult female who presented with sudden general malaise, high fever, headache and a rash on 6 September 2019. Dengue infection was confirmed with both serology and molecular diagnostic tests by the Catalan reference laboratory for arboviruses and the Spanish national reference laboratory for arboviruses (18 September). The case did not report any travel outside of Spain during the past two years [2]. Following the detection of this autochthonous dengue case, the protocol for surveillance and control for arboviruses transmitted by mosquitos was activated in Catalonia in order to conduct epidemiological investigations and implement vector control activities [2].

The following actions were implemented by the public health authorities or will soon be initiated (in accordance with national recommendations):

- Epidemiological and entomological investigations.
- Active case finding in the probable places of transmission.
- Raising awareness of healthcare workers and laboratories in the area.
- Assessment of the need to implement safety measures on substances of human origin.
- Public communication.

To date, epidemiological investigations have not identified the primary travel-associated case.

Up until 2018, only imported dengue cases were detected in Spain, mainly in people returning from Latin America and Asia-Pacific [3]. In 2018, six autochthonous dengue cases were reported from Spain [4,5]. No case had a recent travel history to dengue-endemic areas. Three of the autochthonous cases, all with disease onset in August, travelled or resided in the Región de Murcia and other municipalities in the Province of Cádiz at the probable time of infection [3]. Two other autochthonous cases, with disease onset in September, were probably infected in the Región de Murcia [3]. The sixth confirmed case was reported in Catalonia, with onset of symptoms in mid-October. This case was attributed to the introduction of dengue virus (DENV). All cases were serotype 1 (DENV-1).

Locally acquired dengue cases in France

The case in Vallauris, department of Alpes-Maritimes, was diagnosed by serology (IgM+) on a sample processed in a local laboratory eight days after onset of symptoms on 30 August 2019. The epidemiological investigation immediately identified a potential primary case, with onset of symptoms on 11 July who stayed at the case's house while viraemic. The French NRC confirmed both the autochthonous case and the imported case with positive PCR for DENV-1. The locally acquired case did not report recent travel outside of mainland France.

Door-to-door active case finding was implemented on 19 September in the vicinity of the home of this locally acquired autochthonous case. During this investigation, four additional cases of locally acquired dengue fever were identified. For three of them, there is serological evidence of a recent flavivirus infection; the fourth case (PCR positive) was identified following the sensitisation of health workers.

In summary, five autochthonous dengue cases, all living within a 100-meter radius, were identified by 26 September 2019. In addition, an imported case was diagnosed – probably the primary case. The onset of symptoms of the five autochthonous cases was between 1 August and 21 September.

The case in Caluire-et-Cuire (department of Rhône) was diagnosed by serology in a local laboratory on a sample taken 55 days after onset of symptoms. Confirmatory test results from the NRC are pending (second sample to assess antibody kinetics). The patient had no recent travel history outside of mainland France. The epidemiological investigation identified an imported primary case, with onset of symptoms on 30 June 2019 and residing within the vicinity of the locally acquired probable case.

The following actions were implemented by the public health authorities or will soon be initiated (in accordance with national recommendations):

- Epidemiological and entomological investigations.
- Active case finding in the probable places of transmission.
- Raising awareness of healthcare workers and laboratories in the area on dengue diagnosis and notification of cases.
- Safety measures for substances of human origin, e.g. blood donations.
- Public communication.

Since 2010, and prior to the five autochthonous cases mentioned above, nine events of autochthonous transmission of dengue have been recorded in France [6].

Disease background

Dengue is a mosquito-borne disease caused by viruses of the Flaviviridae family. There are four antigenically distinct serotypes of dengue viruses (DENV 1–4). General information on dengue virus infection is available in the <u>ECDC dengue factsheet</u>, and detailed information on laboratory diagnostics is presented in the previous rapid risk assessment 'Local transmission of dengue in France and Spain – 2018' [7,8]. A comprehensive overview of DENV diagnostic capacity in the EU/EEA can be found in the <u>EVD-LabNet directory</u> [9].

The mosquito *Ae. albopictus* is a competent vector for all four dengue virus serotypes, but considered a less competent vector for DENV than the primary tropical and subtropical vector *Ae. aegypti* (see <u>ECDC factsheet for experts</u>) [10,11]. Population dynamics of *Ae. 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 (containers of any kind) [12]. Transmission of DENV depends, among other factors, on the presence of active competent vectors and suitable temperatures. Laboratory experiments with *Ae. albopictus* from Shanghai with DENV-2 suggest that transmission is unlikely below 18 °C [13]. In the southern part of Europe in areas with established populations of *Ae. albopictus* (see *Ae. albopictus*, <u>current known distribution</u>, August 2019 [14]); environmental conditions during summer and early autumn can support vector abundance at a level that is sufficient for autochthonous transmission of DENV, which could then lead to sporadic cases or localised cluster/outbreaks after importation of the virus.

Aedes albopictus mosquitoes were first detected in Catalonia, Spain, in 2004, 15 km northeast of Barcelona [15,16] and have since been spreading southward along the coast, with recent detections in western Spain [17]. There is evidence from Murcia, 370 km southwest of Barcelona, that *Ae. albopictus* may be active during winter but at low density [18]. Entomological surveillance in the region shows that populations start increasing in April or May, reaching a peak in July or August, sometimes followed by a second peak in September [19-21]. *Ae. albopictus* from Catalonia was found to be susceptible to both DENV-1 and DENV-2. It was also able to transmit DENV-1 in a laboratory study under simulated environmental conditions mirroring the mean temperature and humidity recorded in July on the Catalonian coast [22].

Aedes albopictus were first detected in France in 2004 in Menton, 50 km east of Vallauris, and have since been spreading westward and northward [23]. *Aedes albopictus* reached the Rhône department in 2013 [24]. *Aedes albopictus* is normally active in southeast France from May until the beginning of November [25,26].

Aedes aegypti, another competent vector, is not present in the continental EU.

Disease surveillance for dengue in the EU

Dengue is a notifiable disease in the EU [27].

According to data retrieved from RENAVE, the Spanish National Surveillance Network, on 6 September 2019, Spain reported 580 confirmed imported cases of dengue between 2015 and 2018; 180 cases were reported in 2015, 199 cases in 2016, 52 cases in 2017 and 149 cases in 2018. Probable country of infection is available for 345 of 580 confirmed imported cases, e.g. 57/345 (16.5%) cases reported exposure in Thailand, 44/345 (12.75%) were exposed in Paraguay, 34/345 (9.9%) in Indonesia, and 24/345 (7%) in India.

According to data retrieved from The European Surveillance System (TESSy) on 6 September 2019, France reported 759 confirmed imported dengue cases between 2015 and 2018; 71 cases were reported in 2015, 159 in 2016, 240 in 2017, and 289 in 2018. Seventeen percent of the confirmed cases with known place of infection were reported from Thailand, 10% from Indonesia, and 8% from French Polynesia.

Further information on dengue surveillance in the EU/EEA countries can be found in ECDC's Annual Epidemiological Report 2017 [28] and in the online <u>surveillance atlas of infectious diseases</u> (up to 2018) [29].

Risk assessment questions

This risk assessment addresses the public health significance of locally acquired dengue cases in areas with established populations of *Ae. albopictus* in the southern part of the EU. It also covers the risk for EU/EEA citizens residing in, or visiting, affected regions.

ECDC risk assessment for the EU/EEA

The recent reports of locally acquired dengue cases in France and Spain in late summer and autumn were not unexpected. Given the presence of established populations of *Ae. albopictus* and favourable environmental conditions for vector activity, infections with the dengue virus are possible. The establishment of *Ae. albopictus* in the southern continental EU has led to several similar autochthonous transmission events of DENV in Croatia, France and Spain between 2010 and 2018 [6].

In the past decade, all reported events of DENV transmission refer to sporadic cases or limited clusters of locally acquired dengue cases. In previous years, autochthonous DENV transmission occurred between August and October in Spain and between July and October in France. This demonstrates that sporadic transmission in both countries may occur up to late autumn. The period of transmission is dependent on the vector population and environmental conditions. Environmental conditions may remain suitable for significant vector activity until the middle of October [12,19-21,25] but are expected to become progressively less suitable during October and November. The detection of further cases in the affected regions/departments remains possible. To date, there is no established epidemiological or microbiological link between the three cases that were reported in Spain and France.

Catalonia is a popular tourist destination in the EU, with 83 million nights spent in tourist accommodations (2017) [30]. Introduction of DENV by travellers coming or returning from endemic areas can occur. Based on a modelling study using the air traveller volume coming from active dengue areas in 2010, the cities of Milan, Rome and Barcelona were predicted to be at higher risk of dengue importation, notably during August, September and October [31]. In France, both Provence-Alpes-Côte d'Azur and Rhône-Alpes are very popular tourist destinations in the EU, with 55 and 51 million nights spent in tourist accommodations, respectively, in 2017 [30]. Therefore, introduction of DENV by travellers coming or returning from areas with active dengue transmission is possible, even if considered a rare event.

Although a limited number of described dengue outbreaks were sustained by *Ae. albopictus*, the vector may act as a driver of epidemics in areas where *Ae. aegypti* is absent or where its population is too small to have epidemiological importance [32-36]. *Ae. albopictus* is also the vector responsible for the large seasonal DENV-2 outbreak in Réunion in the last two years [37]. The size of the Réunion outbreak demonstrated the considerable vectorial capacity of the *Ae. albopictus* population for transmitting DENV-2. Despite a lack of evidence of genetic adaptation of the virus to the *Ae. albopictus* population in Réunion, autochthonous dengue transmission events may warrant molecular investigations to better assess the epidemic potential of DENV, or when the primary case responsible for the virus introduction is unknown, point towards the possible origin of the introduction based on phylogenetic assessment.

To date and based on ECDC's epidemiological assessment, the risk that visitors to the affected areas become infected and subsequently introduce the virus and initiate further local transmission in their country of residence cannot be excluded, but remains very low. By comparison, there is a higher risk of virus introduction from travellers coming or returning from epidemic and endemic tropical and subtropical countries where DENV is circulating [38].

Limitations

This risk assessment is based on information available at the time of publication. While the epidemiological investigation is ongoing, there is a substantial uncertainty regarding the extent of potential circulation of the virus; further cases might be detected through active case finding. The level of risk should be re-assessed when significant new facts become available.

Options for response

The options for response with regard to sporadic cases of dengue among EU/EEA Member States as published in the ECDC rapid risk assessment 'Local transmission of dengue fever in France and Spain – 2018' (22 October 2018) remain valid [8].

Dengue and safety of substances of human origin

DENV is transmissible through substances of human origin (SoHO). Therefore, EU/EEA Member States should consider applying safety measures, according to an assessment of risk, to prevent the transmission of DENV through donations of SoHO. The SoHO safety interventions specified in the rapid risk assessment of dengue outbreaks in France and Spain in 2018 remain the same [8]. In relation to this sporadic autochthonous case of dengue in Barcelona and based on the epidemiological data, the Spanish Scientific Committee for Transfusion Safety (CCST) has considered that no special measures have to be implemented in response to this event, except for reinforcing the request to all donors to report any symptoms that appear post-donation and continuing with the corresponding epidemiological surveillance. Should new cases appear, this decision would be reassessed. As an additional surveillance measure, the Blood Bank of Catalonia (BST), according to the Public Health Institute, has decided to perform a screening for dengue detection (NAT) for the next two months.

Source and date of request

ECDC internal decision, 19 September 2019.

Consulted experts

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All experts have submitted declarations of interest, and a review of these declarations did not reveal any conflict of interest.

Disclaimer

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This report was written with the coordination and assistance of an Internal Response Team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. 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.

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