



## RAPID RISK ASSESSMENT

# Autochthonous dengue cases in Madeira, Portugal

10 October 2012

### Source and date of request

ECDC internal decision, 4 October 2012.

### Public health issue

Risk for the EU associated with autochthonous transmission of dengue virus in the Autonomous Region of Madeira.

### Consulted experts

ECDC internal response team: Dragoslav Domanovic, Romit Jain, Lara Payne, Jas Mantero, Laurence Marrama, Emmanuel Robesyn, Herve Zeller, Denis Coulombier.

Portuguese team: Francisco George, Graça Freitas, Ana Nunes, Ana Clara Silva, Maurício Melim, Ana Leça, Kamal Mansinho, Paula Vasconcelos, Cristina Abreu Santos, Isabel Marinho Falcão.

World Health Organization: Jukka Pukkila (WHO EURO), Mikhail Ejov (WHO EURO), Raman Velayudhan (WHO HQ).

External experts: Paulo Almeida, Carla Sousa, Maria João Alves.

## Main conclusions and recommendations

- As the first known occurrence of autochthonous dengue infection in the Autonomous Region of Madeira, this is a significant public health event, although not entirely unexpected given the conclusions of a risk assessment undertaken for the EU in recent years. Due to the confirmed presence of the *Aedes aegypti* mosquito, a competent vector for dengue, additional cases may be expected in the coming weeks.
- The epidemiological situation does not imply any trade or travel restriction beyond the disinfestations currently being carried out.
- The Portuguese public health authorities are implementing control measures to limit the outbreak, reduce the risk of sustained transmission locally and the export of infected vectors from the island, and minimise the impact of dengue on the affected population.
- For residents, the risk can be lessened by reducing larval breeding sites inside and around households.
- Those intending to visit the island of Madeira are advised to take measures to prevent mosquito bites. Dengue is transmitted by a daytime mosquito and consequently protective measures must be applied during the day (unlike malaria).
- Travellers experiencing febrile symptoms with severe headache, retro-orbital pain, myalgia, arthralgia and maculo-papular rash within 14 days of visiting Madeira are advised to seek medical advice.
- Neighbouring areas (e.g. the Canary Islands) and other EU Member States need to assess the risk of *Aedes* mosquito populations establishing themselves and dengue being introduced. Surveillance activities will need to be implemented or enhanced on the basis of this risk assessment.
- In an affected area, confirmed cases and potential blood donors with fever or flu-like symptoms should not donate (bloods, tissues, cells or organs) for four weeks after recovery. Two other measures to consider are the quarantine of blood components and possibly pathogen reduction in platelets and fresh frozen plasma. Additional screening for asymptomatic infection of donors may be considered in specific situations (e.g. organ donation). The Portuguese authorities have implemented more stringent measures.

## Disease background information

### Dengue virus

Dengue is a mosquito-borne disease caused by viruses of the *Flaviviridae* family. There are four serotypes of dengue viruses (DEN1–4). The main mosquito vector is *Aedes aegypti* but other mosquitoes, including *Aedes albopictus*, have been implicated in disease transmission [1]. The infection is not transmitted directly from human to human, except in the case of blood transfusion, or organ and tissue transplantation.

The incubation period ranges from one to 12 days, with an average of three to seven days. Dengue infection can cause a wide clinical spectrum of illness. The majority of infections are either asymptomatic or result in a mild febrile illness. Symptoms include a sudden onset of fever, severe headache, retro-orbital pain, arthralgia and maculo-papular rash with a duration of up to seven days. The more severe and potentially deadly forms, classified as severe dengue, develop in less than 5% of patients. The symptoms include haemorrhages, thrombocytopenia, plasma leakage and circulatory failure. There is currently no vaccine available for dengue fever and treatment of the disease is symptomatic and supportive. Patients with severe dengue can recover without sequelae if diagnosed early and treated appropriately.

Laboratory diagnosis of dengue infection relies on the identification of the virus, viral antigen or dengue-specific antibodies [1, 2]. Viral RNA can be detected using PCR up to day seven after fever onset. The detection of non-structural protein (NS1) of the dengue virus genome using ELISA is very specific for acute dengue infections up to day five after fever onset. Serological diagnosis can be performed by detecting dengue IgM antibodies five to six days after fever onset, or detecting a four-fold rise in specific IgG antibody titre on a pair of sera (acute and convalescent specimens). In a secondary dengue infection, dengue IgM antibodies usually appear earlier (from day two post fever onset) and with a shorter duration. Serological diagnosis also relies on an increase in dengue IgG titre. Serological cross-reactions between dengue viruses and closely-related flaviviruses are frequently reported.

Transmission of dengue infection through transfusion of erythrocytes, platelets and plasma, and the transplantation of solid organs and bone marrow has been reported [3–5].

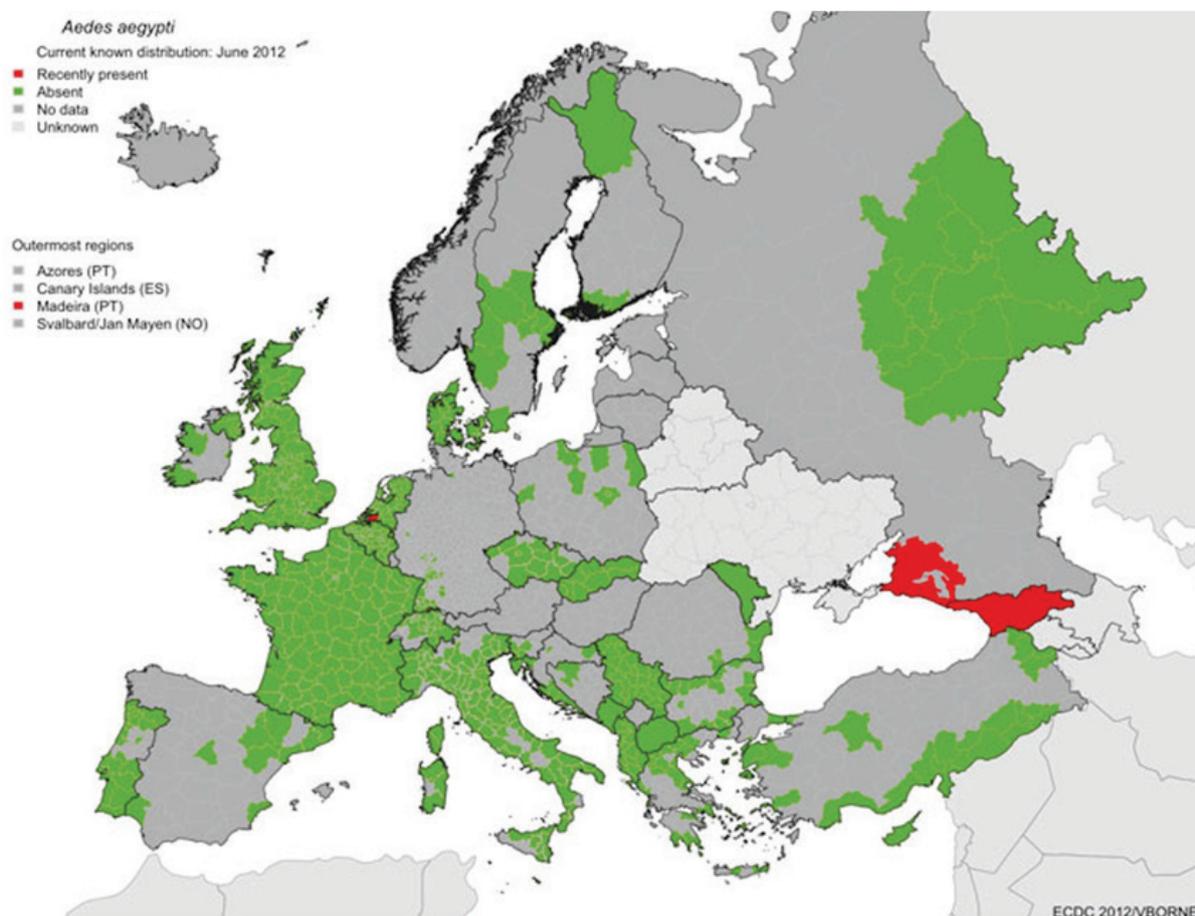
## Mosquito vectors

### *Aedes aegypti*

*Aedes aegypti* is considered the most competent mosquito vector for dengue transmission. The distribution of this mosquito in the EU is sporadic and localised. It has been reported in the Netherlands, where a low level of infestation with adult mosquitoes was found in two out of five used tyre companies in 2010. The mosquitoes were found to be genetically linked to those identified in a tyre company in Miami, Florida, USA [6]. In addition, *Aedes aegypti* is present in Georgia and the bordering southern Russian oblast.

It was reported on Madeira island in the Autonomous Region of Madeira, Portugal, in 2004–2005. In 2006, *Aedes aegypti* mosquitoes were collected in six of the administrative divisions of the city of Funchal [7]. *Aedes aegypti* was present in continental Portugal until 1956 but has not been reported since. It was also common in Spain in the past, following introduction from North Africa. However, it has not been found since 1953 [8].

**Figure 1. Distribution of *Aedes aegypti* in Europe, June 2012**

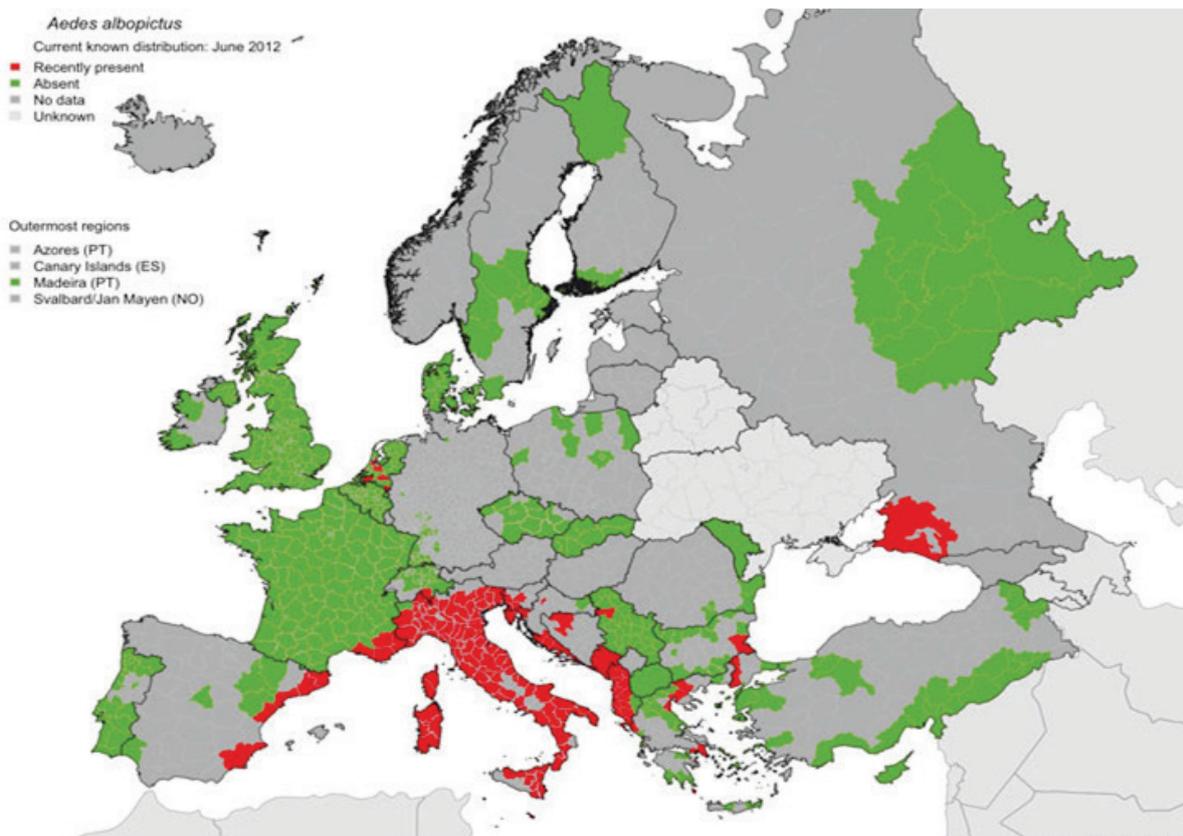


Source: [http://ecdc.europa.eu/en/activities/diseaseprogrammes/emerging\\_and\\_vector\\_borne\\_diseases/Pages/VBORNET\\_maps.aspx](http://ecdc.europa.eu/en/activities/diseaseprogrammes/emerging_and_vector_borne_diseases/Pages/VBORNET_maps.aspx)

## *Aedes albopictus*

*Aedes albopictus* can transmit dengue virus to humans but is considered a less competent mosquito vector than *Aedes aegypti*. Since the 1970s, this mosquito species has become increasingly established in EU countries, mainly through the global trade in tyres, notably in Bulgaria, France, Greece, Italy, the Netherlands, Slovenia and Spain [9]. It was introduced, but not established, in Belgium in 2000 and Germany in 2007 and 2011. This mosquito species has also established itself in neighbouring countries such as Albania, Bosnia-Herzegovina, Croatia, Monaco, Montenegro, San Marino, Serbia, Switzerland and the Vatican City (see map).

**Figure 2. Distribution of *Aedes albopictus* in Europe, June 2012**



Source: [http://ecdc.europa.eu/en/activities/diseaseprogrammes/emerging\\_and\\_vector\\_borne\\_diseases/Pages/VBORNET\\_maps.aspx](http://ecdc.europa.eu/en/activities/diseaseprogrammes/emerging_and_vector_borne_diseases/Pages/VBORNET_maps.aspx)

In continental EU, the only dengue epidemic ever reported occurred in 1927 and 1928 in Greece and resulted in a high mortality rate. The vector was *Aedes aegypti*. There are repeated reports of cases of dengue fever being imported into the EU area by travellers returning from countries with dengue epidemics in Asia, Africa and Latin America [10, 11].

In 2010, autochthonous sporadic cases of dengue were reported in southern France and the Dubrovnik area of Croatia. However, these cases occurred in areas where *Aedes albopictus* has been found and *Aedes aegypti* is not reported to be present [12, 13]. To date, no epidemics have been reported in the EU area.

## Event background information

On 3 October 2012, the Portuguese public health authorities reported two cases of dengue infection confirmed in patients residing on the island of Madeira in the Autonomous Region of Madeira, Portugal. Both patients had no recent travel history abroad and presented with a clinical picture of influenza-like symptoms, leucopenia, thrombocytopenia and hepatic dysfunction [14]. Neither of them has been admitted to hospital.

Within a short period of time, further cases have been identified in several patients presenting with febrile syndrome but no identified aetiology.

By 10 October, 18 cases had been confirmed and 191 probable cases were under investigation. Since the first two cases were identified, a total of 26 cases have been hospitalised (currently 11). No cases have been reported to date on Porto Santo, the other inhabited island within the Autonomous Region of Madeira, Portugal.



In the affected area

- Deferral of blood donors with fever or flu-like symptoms for 28 days after recovery.
- Laboratory screening of blood donors by RT-PCR.
- Information to blood donors to report any symptoms in the 15 days following donation.
- Quarantine of bloods products in stock for retrospective testing.
- Platelets supplied by Portuguese Blood and Transplantation Institute.
- Post transfusion haemovigilance.

Blood collection in non-affected areas

- Deferral of blood donors for a period of 28 days after leaving the affected area.
- Deferral of blood donors with fever or flu-like symptoms for 28 days after recovery.
- Deferral of confirmed cases of dengue infection for 120 days after diagnosis.

These recommendations have been made available on the website of Portugal's Directorate-General for Health [18].

## ECDC threat assessment for the EU

This is the first known occurrence of locally transmitted dengue infection in the Autonomous Region of Madeira, and consequently, a new geographical area reporting such autochthonous cases in the EU.

The risk for travellers and residents will depend on the course of the outbreak in the coming weeks and the effectiveness of the control measures currently being implemented.

The island of Madeira has an established mosquito vector population of *Aedes aegypti*. The climatic conditions in the archipelago will remain suitable for vector activities in the coming weeks and may therefore result in additional cases becoming infected in the future. During the winter months, as the temperature remains above 10°C, the conditions will remain suitable for vector presence, but at a much lower level of activity [19]. Vertical transmission of dengue virus from mosquitoes to their offspring is documented for *Aedes aegypti* [20, 21]. This phenomenon, even if limited, may contribute to renewed transmission in the spring next year, when climatic conditions will result in increased vector activity.

Currently, there are no reports of established populations of *Aedes aegypti* in continental Europe. However, the risk of *Aedes aegypti* spreading to the neighbouring islands and into the Mediterranean basin cannot be excluded. The potential spread of the infection through *Aedes albopictus* is limited. Therefore, the risk of further spread of dengue virus to continental Europe is considered very low during the coming winter months. However, should dengue transmission become entrenched in Madeira, the risk of spread to continental Europe in the summer of 2013 would need to be assessed carefully.

As dengue infection is mild or asymptomatic in a large proportion of infected persons, it poses a safety risk to substances of human origin if asymptomatic viraemic carriers of dengue viral infection make donations.

## Conclusions and recommendations

As the first known occurrence of autochthonous dengue infection in the Autonomous Region of Madeira, this is a significant public health event, although not entirely unexpected given the conclusions of a risk assessment undertaken for the EU in recent years [22]. Due to the confirmed presence of the *Aedes aegypti* mosquito, a competent vector for dengue, additional cases may be expected in the coming weeks.

The epidemiological situation does not imply any trade or travel restriction or other measure beyond the disinfestations currently being carried out.

The Portuguese public health authorities are implementing control measures to limit the outbreak, reduce the risk of sustained transmission locally and the export of infected vectors from the island, and minimise the impact of dengue on the affected population.

For residents, the risk can be lessened by reducing larval breeding sites inside and around households and educating residents in affected communities.

Travellers experiencing febrile symptoms with severe headache, retro-orbital pain, myalgia, arthralgia and maculo-papular rash within 14 days of visiting Madeira are advised to seek medical advice.

Travellers visiting the island of Madeira are advised to take individual protective measures to prevent mosquito bites. Dengue is transmitted by a daytime mosquito and consequently protective measures must be applied during the day (unlike malaria).

Entomological surveillance and control activities targeting possible importation channels for *Aedes aegypti* mosquitoes from the island of Madeira should be considered within the EU [2].

Neighbouring areas (e.g. the Canary Islands) and other EU Member States need to assess the risk of *Aedes* mosquito populations establishing themselves and dengue being introduced. Surveillance activities will need to be implemented or enhanced on the basis of this risk assessment [23].

In an affected area, confirmed cases and potential blood donors with fever or flu-like symptoms should defer from donating (bloods, tissues, cells or organs) for four weeks after recovery. Two other measures to consider are the quarantine of blood components and possibly pathogen reduction in platelets and fresh frozen plasma. Additional screening for asymptomatic infection of donors may be considered in specific situations (e.g. organ donation). The Portuguese authorities have implemented more stringent measures.

## References

1. ECDC. Dengue factsheet for health professionals. European Centre for Disease Prevention and Control; 2010 [04.10.2012]. Available from: [http://ecdc.europa.eu/en/healthtopics/dengue\\_fever/basic\\_facts/Pages/Factsheet\\_health\\_professionals.aspx](http://ecdc.europa.eu/en/healthtopics/dengue_fever/basic_facts/Pages/Factsheet_health_professionals.aspx).
2. WHO. Dengue Guidelines for diagnosis, treatment, prevention and control. New Edition. World Health Organisation; 2009 [04.10.2012]. Available from: <http://www.who.int/rpc/guidelines/9789241547871/en/>.
3. PAHO. Eligibility for Blood Donation: Recommendations for Education and Selection of Prospective Blood Donors. Washington D.C.: Pan American Health Organization; 2009 [05.10.2012]. Available from: <http://www2.paho.org/hq/dmdocuments/2009/EligiBlood09EN.pdf>.
4. Tambyah PA, Koay ES, Poon ML, Lin RV, Ong BK. Dengue hemorrhagic fever transmitted by blood transfusion. *N Engl J Med*. 2008 Oct 2;359(14):1526-7.
5. Linnen JM, Vinelli E, Sabino EC, Tobler LH, Hyland C, Lee TH, et al. Dengue viremia in blood donors from Honduras, Brazil, and Australia. *Transfusion*. 2008 Jul;48(7):1355-62.
6. Brown JE, Scholte EJ, Dik M, Den Hartog W, Beeuwkes J, Powell JR. *Aedes aegypti* mosquitoes imported into the Netherlands, 2010. *Emerg Infect Dis*. 2011 Dec;17(12):2335-7.
7. Almeida AP, Goncalves YM, Novo MT, Sousa CA, Melim M, Gracio AJ. Vector monitoring of *Aedes aegypti* in the Autonomous Region of Madeira, Portugal. *Euro Surveill*. 2007 Nov;12(11):E071115 6.
8. Eritja R, Aranda C, Padros J, Goula M, Lucientes J, Escosa R, et al. An annotated checklist and bibliography of the mosquitoes of Spain (Diptera: Culicidae). *European Mosquito Bulletin*. 2000;8:10-8.
9. Straetemans M. Vector-related risk mapping of the introduction and establishment of *Aedes albopictus* in Europe. *Eurosurveillance*. 2008;13(7).
10. Gautret P, Simon F, Hervius Askling H, Bouchaud O, Leparc-Goffart I, Ninove L, et al. Dengue type 3 virus infections in European travellers returning from the Comoros and Zanzibar, February-April 2010. *Euro Surveill*. 2010 Apr 15;15(15):19541.
11. Jelinek T. Trends in the epidemiology of dengue fever and their relevance for importation to Europe. *Euro Surveill*. 2009 Jun 25;14(25).
12. G La Ruche YS, A Armengaud, F Peloux-Petiot, P Delaunay, P Desprès, A Lenglet et al. First two autochthonous dengue virus infections in metropolitan France, September 2010. *Eurosurveillance*. 30 September 2010 15(39).
13. I Gjenero-Margan BA, D Krajcar, V Lesnikar, A Klobučar, I Pem-Novosel, S Kurečić-Filipović et al. Autochthonous dengue fever in Croatia, August–September 2010. *Eurosurveillance*. 03 March 2011;16(9).
14. Directorate-General of Health. Casos de dengue na Regiao Autonoma da Madeira. 2012 [03.10.2012]; Available from: <http://www.dqs.pt/?mid=0&cr=23048>
15. National Institute of Health Dr. Ricardo Jorge. Febre de dengue na Madeira, Diagnóstico laboratorial. 9 October 2012. Available from: <http://www.insa.pt/sites/INSA/portugues/ComInf/Noticias/Paginas/DengueMadeiraDiaglab.aspx>
16. Instituto Nacional de Estatística Portugal. Population census of Madeira. 2011 [05.10.2012]. Available from: <http://www.citypopulation.de/php/portugal-admin.php?adm1.id=MA>.
17. Autonomous Region of Madeira. Personal protective measures. Available from: [http://www.sesaram.pt/index.php?option=com\\_content&view=article&id=1069%3Aamosquito-&catid=192%3Ainformacoes&Itemid=417&lang=pt](http://www.sesaram.pt/index.php?option=com_content&view=article&id=1069%3Aamosquito-&catid=192%3Ainformacoes&Itemid=417&lang=pt).
18. Directorate-General of Health. Abordagem para casos de dengue. 2012 [10.10.2012]; Available from: <http://www.dqs.pt/?f=3&id=23047>
19. Gonçalves Y, Silva J, Biscoito M. (2008). On the presence of *Aedes* (*Stegomyia*) *aegypti* Linnaeus, 1762 (Insecta, Diptera, Culicidae) in the Island of Madeira. *Bol.Mus.Funchal*, 58 (322):53-59
20. Joshi V MD, Sharma RC. Persistence of dengue-3 virus through transovarial transmission passage in successive generations of *Aedes aegypti* mosquitoes. *Am J Trop Med Hyg*. 2002 Aug(67(2)):158-61.
21. Le Goff G RJ, Guerra M, Cruz M, Barja Simon Z, Roca Y, Vargas Florès J, et al. Natural vertical transmission of dengue viruses by *Aedes aegypti* in Bolivia. *Parasite*. 2011 Aug(18(3)):277-80.
22. ECDC. Consultation on mosquito-borne disease transmission risk in Europe. Paris, 26 November 2010. Meeting report. February 2011
23. ECDC. Guidelines for the surveillance of invasive mosquitoes in Europe. Technical report. Stockholm, 5 October 2012; Available from: <http://ecdc.europa.eu/en/publications/Publications/TER-Mosquito-surveillance-guidelines.pdf>