

Sexual transmission of dengue in Spain

18 November 2019

Summary

Spanish authorities have reported the likely sexual transmission of dengue between two men. One of the men travelled to Cuba and the Dominican Republic (both countries where dengue is endemic) and returned to Spain on 4 September 2019. He developed symptoms of dengue on 5 September. In the days following his return, the man had unprotected sex with his partner, who had not travelled outside of Spain in the previous 45 days. His partner developed dengue symptoms on 15 September. According to the Spanish authorities, the comorbidities of both patients were assessed by clinicians responsible for their follow-up and were not considered relevant for the risk assessment.

Semen samples from both cases tested positive for dengue virus (DENV). Molecular investigations identified identical viral sequences between the two cases. Entomological investigations around the residence of the cases in the municipality of Madrid, Spain did not find any *Ae. albopictus* mosquitoes, a known vector for DENV.

In the absence of data supporting infection through other possible routes, it appears likely that the secondary case acquired DENV infection through sexual contact. This is the first case of dengue described in an area without the presence of vector mosquitoes that has been attributed to sexual transmission, and the first sexual transmission described between men who have sex with men (MSM). This mode of transmission is consistent with what has been observed for other flaviviruses such as Zika virus.

Despite the large numbers of imported cases, sexual transmission of DENV had not been previously reported in the EU/EEA.

Based on the current limited evidence, sexual transmission of dengue appears to be a rare route of transmission and the risk (both among MSM and heterosexuals), is considered extremely low. More research is needed to quantify the risk of sexual transmission and to identify risk factors. However, the risk of transmission by those returning from dengue-endemic areas with symptoms compatible with dengue infection, or with confirmed dengue infection, can be minimised by abstaining from sex or practicing safe sex using condoms until all symptoms are resolved.

Infectious disease clinicians should be informed that sexual transmission is a potential, but apparently rare mode of transmission for dengue and that they should: 1) consider it in patients with dengue in the absence of a compatible travel history; and 2) advise all patients with dengue on the potential risks of sexual transmission, and that those risks can be mitigated through abstinence from sexual contact, or practicing safe sex using condoms, during the course of their disease. This particularly applies if their partner is pregnant to prevent adverse pregnancy outcomes related to dengue infection during pregnancy.

Event background

At the end of September 2019, Spanish health authorities confirmed two cases of dengue reported in two men residing in the municipality of Madrid, Spain [1]. The first case, who was classified as imported, travelled to Cuba from 28–30 August 2019 and to the Dominican Republic from 2–4 September 2019 [2]. He developed symptoms of dengue on his return on 5 September 2019 and had unprotected anal sexual intercourse with his male partner during the following three days.

His partner developed symptoms (fever, headache, back pain, myalgia, diarrhoea and rash) on 15 September 2019. On 18 September 2019, he tested positive for dengue virus (DENV) by a rapid test and PCR. Since the partner had not travelled outside of Spain in the 45 days prior to the onset of symptoms, he was classified as an autochthonous case. The imported case tested positive for dengue (urine sample) on 19 September 2019 [2]. Both cases were confirmed with DENV infection by the national reference laboratory Centro Nacional de Microbiología del Instituto de Salud Carlos III [3]. Semen samples from both cases tested positive for dengue by PCR. Partial sequencing and phylogenetic analysis revealed DENV type 1 (DENV-1) in both cases, with identical viral sequence in all samples sequenced, including semen from the imported case [2]. The sequence was also similar to DENV detected in other cases imported from Cuba. According to the Spanish authorities, the comorbidities of the patients were assessed by the clinicians responsible for their follow-up and were not considered relevant for the risk assessment.

Entomological investigations at the place of residence of the men, and places they visited during the incubation period in Madrid were negative; no adult *Aedes albopictus* mosquitoes were detected. Ongoing entomological surveillance carried out in the Community of Madrid since 2017 has detected the presence of *Ae. albopictus* mosquitoes in only one municipality, Velilla de San Antonio, [4] which is far from any area visited by the men.

In the absence of evidence supporting a possible vector transmission or other routes of transmission, sexual transmission is considered the most likely route of transmission in this case. This is the first case of dengue described in an area without the presence of vector mosquitoes that has been attributed to sexual transmission, and the first sexual transmission described between MSM.

Disease background

Disease characteristics

Dengue is primarily 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 DENV infection is available in the [ECDC dengue factsheet](#), and detailed information on laboratory diagnostics is presented in the previous rapid risk assessment '[Local transmission of dengue in France and Spain – 2018](#)' [5,6]. A comprehensive overview of DENV diagnostic capacity in the EU/EEA can be found in the [EVD-LabNet directory](#) [7].

Vector-borne transmission of DENV depends, among other factors, on the presence of active competent vectors and suitable temperatures. In the southern part of Europe, in areas with established populations of *Ae. albopictus* mosquitoes (see *Ae. albopictus*, [current known distribution](#), August 2019 [8]), environmental conditions during summer and early autumn can support vector abundance at a level that is sufficient for autochthonous transmission. This could then lead to sporadic cases or localised cluster/outbreaks after importation of the virus; however, the risk of dengue establishing in Europe is considered low [9]. *Ae. albopictus* is a competent vector for all four DENV serotypes, but considered a less competent vector for DENV than the primary tropical and subtropical vector *Aedes aegypti* (see [ECDC factsheet for experts](#)) [11,12]. *Ae. aegypti*, is not present in the continental EU.

The primary mode of transmission of DENV between humans is through vectors, however there is evidence of other modes of transmission though these remain rare. Documented additional modes of transmission include mucocutaneous exposure to blood, needle-stick injuries and laboratory accidents, blood transfusion, bone marrow transplant, organ transplant, intrapartum and perinatal transmission and breastfeeding [12]. Vertical transmission of DENV has been described at low rates [13]. Depending on the timing of the infection during pregnancy, it may lead to adverse pregnancy outcomes (e.g. preterm birth, low birthweight, foetal distress) [13,14].

Disease surveillance for dengue in the EU

Dengue is a notifiable disease in the EU [15]. From 2011 to 2018, EU/EEA countries reported case-based data on 14 856 dengue cases to The European Surveillance System, of which 27 cases were locally acquired. During the same time period, Spain reported 560 dengue cases, of which six were locally acquired. All locally-acquired cases in EU/EEA countries were related to vector-borne transmission and are listed in the overview of [autochthonous transmission of dengue virus in EU/EEA, 2010-2019](#) [16].

Further information on dengue surveillance in EU/EEA countries can be found in [ECDC's Annual Epidemiological Report 2017](#) [17] and in the online [surveillance atlas of infectious diseases](#) (up to 2018) [18].

Risk assessment questions

This risk assessment addresses the public health significance of the report of an autochthonous dengue case who was probably infected through sexual transmission.

ECDC risk assessment for the EU/EEA

Risk of vector-borne transmission

Reports of locally-acquired dengue cases in areas with established populations of *Ae. albopictus* and favourable environmental conditions for vector activity are not unexpected. Several autochthonous transmission events of DENV have been reported in Croatia, France and Spain between 2010 and 2019 [16,19]. *Aedes albopictus* mosquitoes were first detected in Catalonia, Spain, in 2004 [20,21] and have since been spreading southward along the coast, with recent detections in western and central Spain [4,21]. Given that entomological investigations around the residence of the cases in the current event did not identify any *Ae. albopictus*, and that the mosquito was only recently detected in one municipality of Madrid far from any area visited by the cases (and not in other areas despite surveillance), it is unlikely that the autochthonous case was mosquito-transmitted. Other routes of non-mosquito-borne transmission for DENV were excluded in this event. Hence, the most likely route of infection of the autochthonous dengue case was through sexual transmission.

As *Ae. albopictus* mosquitoes were not found in the area where the cases resided, and environmental conditions are not suitable for significant vector activity, there is most likely no risk of mosquito-borne transmission for other residents or for visitors to the affected area.

Risk of sexual transmission

This is the first time probable sexual transmission of dengue has been reported in an area without the presence of vector mosquitoes. Sexual transmission of DENV has only been reported once before in the peer-reviewed literature. This concerned the probable sexual transmission of DENV from a woman to a man in South Korea in 2013 [22]. The pair had unprotected vaginal sexual intercourse the day after the woman's return from a visit to Indonesia and while she was symptomatic. The male partner developed the illness nine days after sexual intercourse.

No cases of sexual transmission of DENV from heterosexual men to women or between MSM have been reported so far.

Despite this, there is some evidence that DENV can be present in the semen of infected men. A publication from Italy described persistence of DENV-RNA in the semen of a man returning from Thailand for 37 days following onset of symptoms. Antigenomic DENV-RNA, an indirect marker of ongoing viral replication, was also detected [24]. In contrast, a publication from Singapore reported that DENV-RNA was not detected in the semen of five symptomatic men tested three to six days after onset of fever [24]. DENV-RNA has also been detected in vaginal secretions of an infected woman up to 18 days after symptom onset [26].

For Zika virus (ZIKV), a flavivirus closely related to DENV, sexual transmission was reported even before the explosive ZIKV outbreak in the Americas and is thought to have contributed to about 1% of all ZIKV disease cases in travellers [12]. In addition, transmission of ZIKV among MSM has also been reported [26]. Between 2015 and week 45 of 2019, 22 EU/EEA Member States reported case-based data on 2 414 travel-associated ZIKV disease cases through The European Surveillance System, of which 22 were sexually transmitted. By comparison, 8 545 travel-associated dengue cases were reported to the European Surveillance System during a similar time period between 2015 and 2018. Given that many more travellers returned to the EU/EEA with DENV compared with ZIKV and no event of sexual transmission of DENV in the EU/EEA was reported until now, the risk for sexual transmission of DENV in the EU/EEA is considered to be extremely low.

Based on the evidence above, sexual transmission of dengue appears to be a rare route of transmission and the risk, both among MSM and heterosexuals is extremely low. More evidence is needed to quantify the risk of sexual transmission, and to identify possible risk factors.

Pregnant women

There is no evidence so far that the risk of sexual transmission of DENV is different for pregnant women. However, transmission of DENV to pregnant women (irrespective of the mode of transmission) might lead to poorer pregnancy outcomes such as preterm birth, low birthweight and foetal distress [13].

Risk of dengue transmission via substances of human origin

Detailed information on the risk of dengue transmission via substances of human origin is presented in the previous rapid risk assessment '[Local transmission of dengue fever in France and Spain – 2018](#)' [6].

Limitations

This assessment is undertaken based on facts known to ECDC at the time of publication. In particular, very limited evidence is available on the frequency of sexual transmission of dengue, persistence, and significance of DENV-RNA in semen and vaginal secretions.

Options for response

The options for response regarding sporadic vector-borne 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 [6].

Infectious disease clinicians should be informed that sexual transmission is a potential mode of transmission and consider it when patients present with symptoms of dengue and a lack of travel history to areas with ongoing dengue transmission.

Considering the extremely low (according to current knowledge) risk of sexual transmission of DENV, general advice to travellers to and returning from endemic areas should be to follow standard safe sex practices.

Persons returning from dengue endemic areas with symptoms of dengue and patients diagnosed with dengue (irrespective of sexual orientation) should be made aware of the potential risks of sexual transmission of dengue, and that those risks can be mitigated through abstinence from sexual contact, or practicing safe sex and using condoms during the course of their disease. This applies particularly if their partner is pregnant, to prevent adverse pregnancy outcomes related to dengue infection during pregnancy.

Source and date of request

ECDC internal decision, 8 November 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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