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Perspective

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Can dengue virus be sexually transmitted?

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Non-mosquito-borne transmission is well described for dengue virus (DENV), with many routes reported, including mucocutaneous exposure, needle-stick injuries and laboratory accidents, blood transfusion, bone marrow transplant, organ transplant, intrapartum and perinatal transmission and breastfeeding, although such reports remain rare.[1] International travellers returning to non-dengue-endemic countries have often unmasked such non-vector transmission. Sexual transmission for Zika virus (ZIKV), a flavivirus closely related to DENV, was first reported in a traveller even before the explosive ZIKV outbreak in the Americas and is thought to have contributed to about 1% of all Zika cases in travellers.[2] Zika virus RNA can frequently be detected in the semen of men for up to 3 months after Zika virus infection.[3] The question then arises whether dengue virus can also be found in human semen.

The first prospective study which studied semen obtained from consecutively recruited male patients with laboratory-confirmed dengue was published in early 2018.[4] The authors were able to enrol only five patients at a hospital in Singapore, a dengue-endemic country. Semen was collected at a median of 5 days post fever onset (range 3–6 days). However, DENV was not detected by PCR in any of the semen, suggesting the absence of DENV shedding into the semen.

A few months later, the first case report of DENV PCR-positive semen was published in a Caucasian traveller returning to Italy with primary dengue infection acquired in Thailand.[5] At the patient's admission in an Italian hospital on Day 9 from symptom onset, he was still symptomatic (arthralgia, asthenia and nausea). The diagnosis of dengue was made by the detection of dengue virus (DENV)-specific antibodies (IgM and IgG, titre 1:160 and 1:40, respectively) and viral RNA using real-time RT-PCR in samples from different body fluids. DENV Type 2 was confirmed. Semen was found to be positive for 37 days post symptom onset, even when viraemia and viruria became undetectable. No onward sexual transmission was reported. However, some features are unusual in this case. This patient was still dengue PCR positive on Day 9 in serum samples, which is unusual, as PCR positivity disappears by Days 4–6 of illness.[6] The PCR in their laboratory may have been ultrasensitive or cross-contaminated. Long-term prospective studies recruiting large number of males are needed that take into account all the variables needed to fully understand the shedding of DENV into semen and its implications. Virus titres, strain, human genetics, sample timing, sensitivity of PCR assay and potential contamination and virology testing of PCR-positive samples will be necessary. The scientific community was successful in conducting large-scale prospective semen studies for Zika-infected men. It should, therefore, also be possible to perform such studies for dengue, given that dengue continues to widely circulate. Recruiting dengue patients for conducting semen studies may, however, be more difficult compared to Zika patients, as dengue patients are usually symptomatically more ill than Zika patients.

Regarding DENV shedding in vaginal secretions and women-to-men transmission, the shedding of DENV-RNA was demonstrated in vaginal secretions in one woman till date, measured by the same laboratory in Italy as the above case.[7] This female traveller had acquired dengue in Sri Lanka and returned to Italy in April 2017. Laboratory testing demonstrated detectable DENV-RNA in plasma, urine, saliva and vaginal secretions. Persistent shedding of DENV-RNA was demonstrated in vaginal secretions, and DENV-RNA was detectable in the pelleted fraction for up to 18 days from symptom onset. Again, no onward sexual transmission was documented.

However, in late 2018, the first case report of probable female-to-male sexual transmission of DENV was published in a Letter to the Editor.[8] Here, a male South Korean man who had not travelled became ill with laboratory-confirmed dengue which was identical to DENV of a woman traveller who had acquired a dengue infection while travelling to Indonesia. The female traveller started feeling ill on her day of return to South Korea and had sexual intercourse with the non-travelling male

partner on the first day after return. Nine days later the non-travelling Korean partner developed laboratory-confirmed dengue. South Korea is not dengue endemic, and public mosquito surveillance has never identified DENV-carrying mosquitoes. The timing of this infection in the non-travelling sexual partner is highly suggestive of female-to-male sexual transmission.

Sexual transmission of DENV is hence plausible, with this first report of a probable female-to-male sexual transmission. No other reports of sexual transmission exist. Given that in the past decade hundreds of travellers with dengue viraemia have returned to Europe or other non-endemic countries,[9–12] and with only one probable case, sexual transmission of DENV remains a negligible problem.

In conclusion, even if dengue PCR can occasionally be found in semen or vaginal secretions, reports on sexual transmission are extremely rare. Sexual transmission of DENV has no public health significance.

Conflict of interest: None declared.

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