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Investigating the sexual transmission of Zika virus

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The sexual transmissibility of Zika virus, a pathogen that is transmitted primarily by aedes mosquitos, has important implications,[1] particularly for women because infection during pregnancy causes adverse pregnancy and fetal outcomes, including microcephaly.[2] WHO has included transmission through sexual intercourse and bodily fluids as a priority in its Zika Virus Research Agenda, which was a crucial component of the public health response to the 2015–16 Zika virus outbreak in South America. However, in the absence of methodologically rigorous population-based studies, the epidemiology of sexually transmitted Zika virus remains poorly understood. To help to understand and quantify aspects of sexual transmission, the WHO Zika Sexual Transmission Research Group developed a sexual transmission framework (appendix). The proposed framework describes seven variables and their inter-relationships: incubation period, serial interval, duration of infectiousness, probability of transmission per sex act, reproductive number, transmission rate through sexual contact, and susceptibility to Zika virus infection through sexual contact.[3] Through a combination of empirical research and modelling, this framework aims to determine the transmission dynamics of sexually transmitted Zika virus and thereby establish its epidemic potential.

To discuss the applicability of the framework and to address the dearth of data and research related to sexually transmissible Zika virus, a meeting of experts was convened in Geneva, Switzerland, on March 20–21, 2017. Experts in the fields of sexually transmitted infections, mathematical modelling, reproductive health, public health, and arboviral biology from public health and academic institutions reviewed the existing evidence about sexual transmission of Zika virus, identified critical research gaps, and discussed methods for

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investigation of sexual transmission. This Comment summarises the main findings of the meeting.

Evidence from epidemiological, biological, and animal studies was reviewed. First, a systematic review of 18 observational studies and case reports summarised evidence of sexual transmission of Zika virus in 27 sexual partnerships.[4] No studies of sexual transmission in endemic areas have been identified to date; the cases of sexual transmission were identified in sexual partners of travellers returning from areas affected by Zika virus. Second, a prospective cohort study in Puerto Rico[5] showed more frequent and longer persistence of Zika virus RNA in semen than in vaginal fluid when detected by quantitative reverse transcription PCR (qRT-PCR). Experimental studies in a mouse model have shown that the virus persists in the testis and can infect vaginal mucosa, yet only male-to-female, not female-to-male, sexual transmission has been documented in this model.[6] Third, animal studies have provided additional insights into the role of immunity and the correlation between the detection of Zika virus RNA through RT-PCR and infectiousness as determined by culture.[6] A review of the pathophysiology of the virus noted that the limited understanding of the identity of cellular receptors that mediate Zika virus entry[7] might have implications for research on sexual transmissibility and diagnostics.

The Zika virus sexual transmission framework served as a springboard for discussion to highlight existing gaps in the evidence for sexual transmission and to identify research questions. Key questions include: how can episodes of sexual transmission be differentiated from vector transmission? Is RT-PCR positivity a predictor of infectiousness? Do coexisting sexually transmitted infections and HIV affect duration of viral persistence or the susceptibility to acquisition? Is there a difference between sexual and mosquito-borne acquisition of infection regarding effects on fetal development? Furthermore, as viral persistence studies include mostly male participants, more data are needed to understand viral localisation and persistence in the female reproductive tract.[7] Investigation of these research questions is complicated by the asymptomatic nature of many Zika virus infections and the need for more accurate diagnostic tests.

Methodological approaches to address the research gaps were also discussed. In Zika-virus-endemic areas, studies of the risk of sexual transmission should require enrolment of couples who live, work, or travel in distinct geographical areas with or without risk of mosquito-borne Zika virus transmission (eg, in areas with the vector or at elevation and without the vector). Observational epidemiological studies should be conducted among discordant couples with Zika virus infection, household contacts of people with diagnosed Zika virus infection returning to areas where there is no mosquito-borne transmission of Zika virus, and groups at high risk of sexually transmitted infections and HIV. A working group has been established to develop a standardised protocol to address the methodological challenges of this issue that could be easily adapted and implemented should new epidemics of Zika virus arise. Particular attention will be given to methods for the valid and consistent collection of sensitive information about sexual practices between partners. Finally, experimental animal and basic science studies were also identified as essential to determine whether the presence of distinct genital mucosal receptors, viral RNA signatures, or immune responses correlates with the mode of transmission.

The expert group underlined the complementary roles of basic science, animal, epidemiological, and mathematical modelling studies. They also highlighted the importance of mobilising adequate funds to move this research agenda forward. A multidisciplinary research approach and adaptation of the sexual transmission framework will not only inform the current questions on Zika virus, but can serve as a template to study and to anticipate the sexual transmission of other emerging pathogens.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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