

Prevention of sexual transmission of Zika virus

Interim guidance update

7 June 2016

WHO/ZIKV/MOC/16.1 Rev.2



1. Introduction

1.1 Background

This document is an update of guidance published on 18 February 2016 to provide advice on the prevention of sexual transmission of Zika virus.

The primary transmission route of Zika virus is via the *Aedes* mosquito. However, mounting evidence has shown that sexual transmission of Zika virus is possible and more common than previously assumed.¹ This is of concern due to an association between Zika virus infection and adverse pregnancy and fetal outcomes, including microcephaly, neurological complications and Guillain-Barré syndrome.

The current evidence base on Zika virus remains limited. This guidance will be reviewed and the recommendations updated as new evidence emerges.

1.2 Target audience

This document is intended to inform the general public, and to be used by health care workers and policy makers to provide guidance on appropriate sexual practices in the context of Zika virus.

2. Sexual transmission of Zika virus

2.1 Current evidence

2.1.1 Summary of publications

As of 19 May 2016, 12 studies or reports have been published on sexual transmission of Zika virus, including:

- Four studies on male to female transmission.²⁻⁵
- One study on male to male transmission.⁶
- Four case-reports reported by International Health Regulations National Focal Points.⁷⁻¹⁰
- Three case-reports described through government/news media.¹¹⁻¹³

In addition, three studies have been published on the presence of Zika virus in semen.¹⁴⁻¹⁶

2.1.2 Modes of sexual transmission

Zika virus transmission by sexual intercourse was first suggested by Foy et al.² Published in 2011, this study described the case of a male patient infected with Zika virus in south-eastern Senegal in 2008 who infected his wife via sexual intercourse upon return to the United States of America. Since then and up to 19 May 2016, sexual transmission of Zika virus has been reported in ten countries (United States of America³, France⁴, Italy⁵, Argentina⁷, Chile⁸, Peru⁹, Portugal¹⁰, New Zealand¹¹, Canada¹² and Germany¹³) and referred mainly to vaginal intercourse. On 2 February 2016 the United States Centers for Disease Control and Prevention announced the first documented case of a man infected with Zika virus through anal sex.⁶ Soon after, a case report published in April 2016 raised the suspicion of Zika virus transmission through oral sex. The case, identified in February 2016, had sexual contact with a partner with symptoms of Zika virus infection. Transmission via oral sex was suspected as the sexual activity involved vaginal intercourse, with no condom and no ejaculation, and oral sex with ejaculation.⁴

To date, all published cases of sexual transmission have been from symptomatic male, whose sexual activities may have occurred before, during or after Zika symptom onset, to their partner. It remains unknown if women or asymptomatic men can transmit the virus through sexual activity.

2.1.3 Presence of the virus in semen

Zika virus was first isolated in semen in a man in Tahiti who sought treatment for hematospermia during a Zika virus outbreak in French Polynesia in December 2013.¹⁴ The virus was cultured in semen at least 14 days after symptom onset. In 2016 two studies reported the presence of Zika virus in semen, detected by reverse transcription polymerase chain reaction (RT-PCR). One of the reports¹⁵ documented that the virus was cultured from the semen specimen 14 days after diagnosis (thus more than 2 weeks after illness onset); and the viral load detected was 100 000 times that of his blood. In the second report and most recent study, published in May 2016¹⁶, researchers reported the case of a 68 year-old man returning to the United Kingdom from the Cook Islands. His semen was positive for Zika virus 62 days after his symptoms began. This is the maximum documented time of Zika virus detection in semen. However, the full length of time that the virus can persist in semen after onset of symptoms remains unknown, as sequential samples were not collected.

3. Presence of Zika virus in other body fluids

Publications on the presence of Zika virus in other body fluids that may be involved in sexual transmission have also been considered. Studies have reported the presence of Zika virus by RT-PCR in saliva^{17, 18} and urine^{14, 15, 18-25}. The persistent shedding of Zika virus ribonucleic acid (RNA) in both fluids has been found up to 29 days after the onset of infection. Culture of Zika virus in urine^{14, 18, 20, 26} and saliva¹⁸ has also been reported, with the virus cultured at day six after symptom onset for both fluids.

4. Interim recommendations

Based on growing evidence that Zika virus can be sexually transmitted, WHO recommends:

1. Country health programmes should ensure that:
 - a. All people (male and female) with Zika virus infection and their sexual partners (particularly pregnant women) receive information about the risks of sexual transmission of Zika virus, contraceptive measures and safer sexual practices^a, and are provided with condoms.
 - b. Women who have had unprotected sex and do not wish to become pregnant due to concerns about Zika virus infection have ready access to emergency contraceptive services and counselling.²⁷
 - c. In order to prevent adverse pregnancy and fetal outcomes, men and women of reproductive age, living in areas where local transmission of Zika virus is known to occur, be correctly informed and oriented to consider delaying pregnancy; and follow recommendations (including the consistent use of condoms) to prevent human immunodeficiency virus (HIV), other sexually transmitted infections, and unwanted pregnancies.^{27, 28}
2. Sexual partners of pregnant women, living in or returning from areas where local transmission of Zika virus is known to occur, should practice safer sex^a or abstinence from sexual activity for at least the whole duration of the pregnancy.
3. Couples or women planning a pregnancy^b who are returning from areas where transmission of Zika virus is known to occur, are strongly recommended to wait at least 8 weeks before trying to conceive to ensure that any possible Zika virus infection has cleared; and 6 months if the male partner was symptomatic.

^a Safer sexual practices include: postponing sexual debut; non-penetrative sex; correct and consistent use of male or female condoms; and reducing the number of sexual partners.³⁰

^b See separate WHO guidance on 'Pregnancy management in the context of Zika virus infection' for further details (available online at <http://www.who.int/csr/resources/publications/zika/pregnancy-management/en/>)

4. Men and women returning from areas where transmission of Zika virus is known to occur should adopt safer sex practices or consider abstinence for at least 8 weeks^c upon return.
 - a. If before or during that period Zika virus symptoms (rash, fever, arthralgia, myalgia or conjunctivitis²⁹) occur, men should adopt safer sex practices or consider abstinence for at least 6 months^d. Women should be correctly informed about this recommendation.
 - b. WHO does not recommend routine semen testing to detect Zika virus. However, symptomatic men can be offered semen testing at the end of the 8 week period after return, according to country policy.
5. Independently of considerations regarding Zika virus, WHO always recommends the use of safer sexual practices including correct and consistent use of condoms to prevent HIV, other sexually transmitted infections and unwanted pregnancies.²⁷

5. Guidance development

5.1 Acknowledgements

This document has been updated with new evidence appearing in the literature by a guideline development group composed of staff from the Departments of Reproductive Health and Research; and Pandemic and Epidemic Diseases, WHO Geneva (Ian Askew, Nathalie Broutet, Pierre Formenty, Bela Ganatra, Sami Gottlieb, Metin Gulmezoglu, Ronnie Johnson, Edna Kara, Rajat Khosla, James Kiarie, Qiu Yi Khut, William Perea Caro, Melanie Taylor; Teodora Wi), and the Department of Communicable Diseases and Health Analysis, (Sylvain Aldighieri, Maeve Brito de Mello, Massimo Ghidinelli, Rodolfo Gomez, Maria del Pilar Ramon Pardo) and the Knowledge Management, Bioethics and Research Office, WHO Regional Office for the Americas (Ludovic Reveiz).

^c As the exact incubation period for Zika virus is still unknown, this period is based on the estimated upper limit of the incubation period of 14 days for related flaviviruses.³¹ To this period, three times the longest published period of viremia after symptom onset (11 days)³² has been added, and additional time allowed for variability in individuals' immune systems. This was also the approach adopted by the United States Centers for Disease Control and Prevention.³³

^d The recommendation on condom use is a conservative measure based on evidence to date. Given the limited data on the duration of Zika virus in semen, the longest documented time period for the persistence of detectable Zika virus RNA particles in the semen (62 days) after symptom onset has been multiplied by three.¹⁶ This is in line with recommendations made by the United States Centers for Disease Control and Prevention.³³

5.2 Guidance development methods

This document was developed based on a review of relevant literature and guideline development group discussion and consensus. Relevant literature was sourced from MEDLINE using the following search terms: flavivirus; sexual transmission; transmission; and Zika. The guideline development group reached consensus on the recommendations through group discussion.

5.3 Declaration of interests

Interests have been declared in-line with WHO policy and no conflicts of interest identified from any of the contributors.

5.4 Review date

Unless important changes are urged by new evidence, these recommendations will remain valid until November 2016 if no new data become available before this date. The Department of Reproductive Health and Research at WHO Geneva will be responsible for reviewing this guideline at that time in light of new and available evidence, and updating it as appropriate.

6. References

- WHO Media Center WHO Director General addresses media after Zika Emergency Committee. 08/03/2016 <http://www.who.int/mediacentre/news/statements/2016/zika-ec/en/>. Accessed 14 May 2016
- Foy BD, Kobylinski KC, Chilson Foy JL, et al. 'Probable non-vector-borne transmission of Zika virus', Colorado, USA. *Emerg Infect Dis.* 2011;17(5):880–88
- Hill SL, Russell K, Hennessey M, et al. Transmission of Zika virus through sexual contact with travellers to areas of ongoing transmission — continental United States, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:215–216
- D'Ortenzio E, Matheron S, de Lamballerie X, Hubert B, Piorkowski G, Maquart M, Descamps D, Damond F, Yazdanpanah Y, Leparce-Goffart I. Evidence of sexual transmission of Zika virus. *N Engl J Med.* 2016 Apr 1
- Venturi G, Zammarchi L, Fortuna C, Remoli M, Benedetti E, Fiorentini C, Trotta M, Rizzo C, Mantella A, Rezza G, Bartoloni A. An autochthonous case of Zika due to possible sexual transmission, Florence, Italy, 2014. *Euro Surveill.* 2016;21(8):pii=30148. DOI: <http://dx.doi.org/10.2807/1560-7917.ES.2016.21.8.30148>. Accessed 27 April 2016
- Deckard DT, Chung WM, Brooks JT, et al. Male-to-Male Sexual Transmission of Zika Virus — Texas, January 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:372–374. DOI: <http://dx.doi.org/10.15585/mmwr.mm6514a3>. Accessed 27 April 2015
- WHO Zika virus infection - Disease Outbreak News (07/03/2016). <http://www.who.int/csr/don/7-march-2016-zika-argentina-and-france/en/>. Accessed 27 April 2016
- WHO Zika virus infection - Disease Outbreak News (15/04/2016). <http://www.who.int/csr/don/15-april-2016-zika-chile/en/>. Accessed 27 April 2016
- WHO Zika virus infection - Disease Outbreak News (21/04/2016). <http://www.who.int/csr/don/21-april-2016-zika-peru/en/>. Accessed 27 April 2016
- WHO Zika virus, microcephaly and Guillain-Barré syndrome. Situation Report 21/04/2016. http://apps.who.int/iris/bitstream/10665/205505/1/zikasitrep_21Apr2016_eng.pdf?ua=1. Accessed 27 April 2016
- Possible case of sexual transmission of Zika virus - Ministry of Health Manatu Hauora. <http://www.health.govt.nz/news-media/media-releases/possible-case-sexual-transmission-zika-virus>. Accessed 27 April 2016
- Government of Canada News. Statement from the Chief Public Health Officer of Canada and Ontario's Chief Medical Officer of Health on the first positive case of sexually transmitted Zika Virus. 26/04/2016. <http://news.gc.ca/web/article-en.do?nid=1056379>. Accessed 14 May 2016
- ABC News Germany reports 1st sexual transmission of Zika virus. <http://abcnews.go.com/Health/wireStory/germany-reports-1st-sexual-transmission-zika-virus-39093203>. Accessed 19 May 2016
- Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus; *Emerg Infect Dis.* 2015, Feb;21(2):359-61
- Mansuy JM, Dutertre M, Mengelle C, et al. Zika virus: high infectious viral load in semen, a new sexually transmitted pathogen? *Lancet Infect Dis* 2016;16:405-405.
- Atkinson B, Hearn P, Afrough B, Lumley S, Carter D, Aarons EJ, et al. Detection of Zika virus in semen [letter]. *Emerg Infect Dis.* 5 May 2016
- Musso D, Roche C, Nhan TX, Robin E, Teissier A, Cao-Lormeau VM. Detection of Zika virus in saliva. *J Clin Virol.* 2015;68:53-5. DOI: 10.1016/j.jcv.2015.04.021 PMID: 26071336
- Barzon L, Pacenti M, Berto A, et al. Isolation of infectious Zika virus from saliva and prolonged viral RNA shedding in a traveller returning from the Dominican Republic to Italy, January 2016. *Euro Surveill* 2016;21
- A.C. Gourinat, O. O'Connor, E. Calvez, C. Goarant, M. Dupont-Rouzeyrol. Detection of Zika virus in urine. *Emerg. Infect. Dis.*, 21 (2015), pp. 84–86
- Fonseca K, Meatherall B, Zarra D, Drebot M, MacDonald J, Pabbaraju K, et al. First case of Zika virus infection in a returning Canadian traveler. *Am J Trop Med Hyg.* 2014;91(5):1035-8. Available from: DOI: 10.4269/ajtmh.14-0151 PMID: 25294619
- Shinohara K, Kutsuna S, Takasaki T, Moi ML, Ikeda M, Kotaki A, Yamamoto K, Fujiya Y, Mawatari M, Takeshita N. Zika fever imported from Thailand to Japan, and diagnosed by PCR in the urines., Hayakawa K, Kanagawa S, Kato Y, Ohmagari N. *J Travel Med.* 2016 Jan 18;23(1). pii: tav011. doi: 10.1093/jtm/tav011
- Korhonen EM, Huhtamo E, Smura T, Kallio-Kokko H, Raassina M, Vapalahti O. Zika virus infection in a traveller returning from the Maldives, June 2015. *Euro Surveill.* 2016;21(2). doi: 10.2807/1560-7917.ES.2016.21.2.30107.
- Campos GS, Bandeira AC, Sardi SI. Zika Virus Outbreak, Bahia, Brazil. *Emerg Infect Dis.* 2015 Oct;21(10):1885-6. doi: 10.3201/eid2110.150847. PMID: 26401719
- de M Campos R, Cirne-Santos C, Meira GL, Santos LL, de Meneses MD, Friedrich J, Jansen S, Ribeiro MS, da Cruz IC, Schmidt-Chanasit J, Ferreira DF. Prolonged detection of Zika virus RNA in urine samples during the ongoing Zika virus epidemic in Brazil. *J Clin Virol.* 2016 Apr;77:69-70. doi: 10.1016/j.jcv.2016.02.009
- Rozé B, Najjioullah F, Fergé JL, Apetse K, Brouste Y, Cesaire R, Fagour C, Fagour L, Hochedez P, Jeannin S, Joux

- J, Mehdaoui H, Valentino R, Signate A, Cabié A; GBS Zika Working Group. Zika virus detection in urine from patients with Guillain-Barré syndrome on Martinique, January 2016. *Euro Surveill.* 2016;21(9). doi: 10.2807/1560-7917.ES.2016.21.9.30154. PMID: 26967758
26. Bonaldo MC, Ribeiro IP, Lima NS et al. Isolation of infective Zika virus from urine and saliva of patients in Brazil. bioRxiv The preprint server for biology. doi: <http://dx.doi.org/10.1101/045443> (preprint).
 27. World Health Organization, 'Women in the context of microcephaly and Zika virus disease', 2016. <http://www.who.int/features/qa/zika-pregnancy/en/> Accessed 12 May 2016
 28. UNFPA, WHO and UNAIDS, 'Position statement on condoms and the prevention of HIV, other sexually transmitted infections and unintended pregnancy', 2015. http://www.unaids.org/en/resources/presscentre/featurestories/2015/july/20150702_condoms_prevention. Accessed 20 April 2016
 29. World Health Organization Regional Office for the Americas. Case Definitions. 1 April 2016.
 30. UNAIDS Terminology Guidelines October 2011 page 25. http://www.paho.org/hq/index.php?option=com_content&view=article&id=11117&Itemid=41532&lang=en
 31. Rudolph KE, Lessler J, Moloney RM, Kmush B, Cummings DA. Incubation periods of mosquito-borne viral infections: a systematic review. *Am J Trop Med Hyg.* 2014;90:882–91
 32. Lanciotti RS, Kosoy OL, Laven JJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. *Emerg Infect Dis.* 2008;14:1232–9
 33. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. Update: Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016. Accessed 11 May 2016.

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