Prevention of sexual transmission of Zika virus

Interim guidance update

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World Health Organization

1. Introduction

1.1 Background

This document is an update of guidance published on 7 June 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.

This review comprises recent evidence on sexual transmission of Zika virus which includes sexual transmission from

- Asymptomatic males to their female partners,
- Symptomatic female to her male partner,
- Longer shedding of Zika virus in semen.

Based on this new evidence, the recommended length of time for safer sex practices for asymptomatic males returning from areas with active Zika virus transmission was extended from 8 weeks to 6 months. This is the same length of time as is recommended for symptomatic males. This recommendation now also applies to females, whether or not they have had symptoms. The 6 month duration of safer sexual practice upon return has not changed. (Please see footnote c).

The current evidence on persistence of Zika virus in semen, its infectiousness and impact on sexual transmission 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 26 August 2016, a total of 17 studies or reports have been published on sexual transmission of Zika virus, including the following:

- Seven studies on symptomatic male to female transmission[2-8]
- One study on male to male transmission[9]
- One study on female to male transmission[10]
- Two studies on asymptomatic male to female transmission[11-12]
- Four case-reports reported by International Health Regulations National Focal Points[13-16]
- Two case-reports described through government/news media[17-18]

In addition, eight studies have been published on the presence of Zika virus in semen.[19-26]

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 26 August 2016, sexual transmission of Zika virus has been reported in eleven countries (United States of America[3], Italy[4], France[5], Germany[6], New Zealand[8], Argentina[13], Chile[14], Peru[15], Portugal[16], Canada[17], and Spain[18]) and referred mainly to vaginal intercourse. On 2 February 2016, the United States Centers for Disease Control and Prevention (CDC) announced the first documented case of a man infected with Zika virus through anal sex.[9] Soon after, a case report published in April 2016 raised the suspicion of Zika virus transmission through oral sex.[5] The case 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. Up to June 2016, cases of sexual transmission were reported only from

symptomatic males. At that date, for the first time, a possible man to woman sexual transmission between two asymptomatic cases was documented in Brittany, France.[11] In August 2016 a second case of sexually transmitted Zika virus from an asymptomatic man, returning from a Zika virus active area, to his non traveller female partner was published.[12] In July 2016 the first case of a female to male sexual transmission of Zika virus was reported.[10] The woman had returned to New York City, USA, from an area of Zika virus activity and engaged in a condomless vaginal intercourse with her non traveller partner. The longest duration between the onset of symptoms in the index case and sexual transmission of Zika virus is 41 days.[7]

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.[19] The virus was cultured in semen at least 14 days after symptom onset. In 2016, seven studies reported the presence of Zika virus in semen, detected by reverse transcription polymerase chain reaction (RT-PCR). One of the reports[20] 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[21], 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. After this report, equal viral permanence was detected in a case in the Netherlands[22] and longer shedding of the Zika virus in semen was documented in New Zealand (76 days)[8], France (80[23], 93 days[24]) and Italy (181 days[25]) through RT-PCR. Infectious virus, however, has been recovered in semen up to 24 days.[5] Up to date, the maximum documented time of Zika virus ribonucleic acid (RNA) detection in semen after the onset of symptoms is 188 days.[26] The case, an Italian man, was diagnosed in Haiti where he developed Zika virus infection symptoms 14 days before returning to Italy in February 2016.

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. The presence of Zika virus in the genital tract of a female with Zika virus infection was first reported in July 2016, suggesting potential risk of female to male transmission.[27] The patient's vaginal fluids and cervical mucous were found to be positive for Zika virus RNA through RT-PCR on days 3 and 11 respectively. Studies have also reported the presence of Zika virus by RT-PCR in saliva[28, 29] and urine [19, 20, 29-36]. The persistent shedding of Zika virus RNA in saliva and urine has been found up to 91 days[26] after the onset of infection. Culture of Zika virus in urine [19, 29, 31, 37] and saliva[29] 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 the following:

1. In regions with active Zika virus transmission, 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.
   b. Men and women also get counselling on safer sexual practices[a], and be offered condoms. The consistent use of condoms is essential to prevent sexually transmitted infections, including human immunodeficiency virus (HIV), and unwanted pregnancy.[39, 40]
   c. Sexually active men and women be correctly counselled and offered a full range of contraceptive methods to be able to make an informed choice about whether and when to become pregnant, in order to prevent possible adverse pregnancy and fetal outcomes.
   d. 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.[40]
   e. Pregnant women should practice safer sex[a] or abstain from sexual activity for at least the whole duration of the pregnancy. Their partners should also be informed about this recommendation.

2. In regions with NO active Zika virus transmission health programmes should ensure that:
   a. 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 6 months[c] upon return to prevent Zika virus infection through sexual transmission.
   b. Couples or women planning a pregnancy[b], who are returning from areas where transmission of Zika

[a] Safer sexual practices include correct and consistent use of male or female condoms, non-penetrative sex, reducing the number of sexual partners, and postponing sexual debut. [37] http://www.unaids.org/sites/default/files/media_asset/2015_terminology_guidelines_en.pdf

[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/)

virus is known to occur, are advised to wait at least 6 months[c] before trying to conceive to ensure that possible Zika virus infection has cleared.

c. Sexual partners of pregnant women, returning from areas where transmission of Zika virus is known to occur, should be advised to practice safer sex[a] or abstain from sexual activity for at least the whole duration of the pregnancy.

Note: WHO does not recommend routine semen testing to detect Zika virus. However, symptomatic or asymptomatic men could be offered semen testing after returning from areas where transmission of Zika virus is known to occur, according to country policy. Two tests performed at different days (e.g.one week interval) should be performed because of false negative results or intermittent shedding. However, more evidence is necessary to determine the exact interval between two tests.

3. 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.[39]

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, Edna Kara, Pierre Formenty, Bela Ganatra, Sami Gottlieb, Metin Gulmezoglu, Ronnie Johnson, Rajat Khosla, James Kiarie, Qiu Yi Khut, William Perea Caro, Melanie Taylor, Teodora Wi); the Department of Communicable Diseases and Health Analysis, and the Knowledge Management, Bioethics and Research Office, WHO Regional Office for the Americas (Sylvain Aldighieri, Maeve Brito de Mello, Massimo Ghidinelli, Rodolfo Gomez, Maria del Pilar Ramon Pardo, Ludovic Reveiz); the Centers for Disease Control and Prevention (CDC), Division of Global Migration Task Force; the CDC National Center for HIV/AIDS, viral Hepatitis, STD and TB Prevention (John Brooks), the CDC National Center for Emerging and Zoonotic Infectious Diseases (Susan Hills), and the European Centre for Disease Prevention STI/HIV and Viral Hepatitis (Otilia Mardh).

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 were 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

1. 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 14/05/2016
2. 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
3. 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
4. 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
5. D'Ortenzio E, Matheron S, de Lamballerie X, Hubert B, Piorkowski G, Maquart M, Descamps D,Damond F, Yazdanpanah Y, Leparc-Goffart I. Evidence of sexual transmission of Zika virus. *N Engl J Med.* 2016 Apr 1
6. Frank C, Cadar D, Schlaphof A, Neddersen N, Günther S, Schmidt-Chanasit J, Tappe D. Sexual transmission of Zika virus in Germany, April 2016. *Euro Surveill.* 2016;21(23):pii=30252. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.23.30252

[c] The recommendation on adoption of safer sex practices or considering abstinence for 6 months is a conservative measure. Although documented cases have shown persistence of ZIKV RNA in semen longer than the 62 days (and up to 188 days) adopted for the calculation of 6 months (3 times 62 days), we are maintaining the recommendation given 1) that sexual transmission of ZIKV has not been reported after 41 days of symptom onset; 2) the limited data on the duration of ZIKV in semen; and 3) the lack of knowledge on whether ZIKV is infectious after it is found in semen following a long period after symptom onset (24 days is the maximum period up to which the virus has been cultured).

7. Turmel JM, Abgueguen P, Hubert B, Vandamme YM, Maquart M, Le Guillou Guillemette H, et al. Late sexual transmission of Zika virus related to probable long persistence in the semen. *Lancet*. 2016 Jun 18;387(10037):2501. DOI: 10.1016/S0140-6736(16)30775-9
8. Harrower J, Kiedrzynski T, Baker S, Upton A, Rahnama F, Sherwood J, et al. Sexual transmission of Zika virus and persistence in semen, New Zealand, 2016. *Emerg Infect Dis*. 2016 Oct. DOI: 10.3201/eid2210.160951 http://dx.doi.org/10.3201/eid2210.160951 Accessed 19/08/2016
9. 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 27/04/2016
10. Davidson A, Slavinski S, Komoto K, Rakeman J, Weiss D. Suspected Female-to-Male Sexual Transmission of Zika Virus — New York City, 2016. MMWR Morb Mortal Wkly Rep. ePub: 15 July 2016. DOI: http://dx.doi.org/10.15585/mmwr.mm6528e2 Accessed 19/08/2016
11. Fréour T, Mirallié S, Hubert B, Splingart C, Barrière P, Maquart M, Leparc-Goffart I. Sexual transmission of Zika virus in an entirely asymptomatic couple returning from a Zika epidemic area, France, April 2016. *Euro Surveill.* 2016;21(23):pii=30254. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.23.30254 Accessed 18/08/2016
12. Brooks RB, Carlos MP, Myers RA, et al. Likely Sexual Transmission of Zika Virus from a Man with No Symptoms of Infection — Maryland, 2016. MMWR Morb Mortal Wkly Rep. ePub: 26 August 2016. DOI: http://dx.doi.org/10.15585/mmwr.mm6534e2 Accessed 26/08/2016
13. 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 27/04/2016
14. WHO Zika virus infection - Disease Outbreak News (15/04/2016). http://www.who.int/csr/don/15-april-2016-zika-chile/en/ Accessed 27/04/2016
15. WHO Zika virus infection - Disease Outbreak News (21/04/2016). http://www.who.int/csr/don/21-april-2016-zika-peru/en/ Accessed 27/04/2016
16. 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 27/04/2016
17. 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 14/05/2016
18. Spain records first case of sexually transmitted Zika virus http://www.reuters.com/article/us-health-zika-spain-idUSKCN0ZH5QI Accessed 16/08/2016
19. 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
20. 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.
21. Atkinson B, Hearn P, Afrough B, Lumley S, Carter D, Aarons EJ, et al. Detection of Zika virus in semen [letter]. *Emerg Infect Dis*. 5/052016
22. Reusken C, Pas S, GeurtsvanKessel C, Mögling R, van Kampen J, Langerak T, Koopmans M, van der Eijk A, van Gorp E. Longitudinal follow-up of Zika virus RNA in semen of a traveller returning from Barbados to the Netherlands with Zika virus disease, March 2016. *Euro Surveill.* 2016;21(23):pii=30251. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.23.30251 Accessed 17/08/2016
23. Matheron S, D'Ortenzio E, Leparc-Goffart I, Hubert B, de Lamballerie X, and Yazdanpanah Y. Long Lasting Persistence of Zika Virus in Semen. *Clinic Infect Dis* 2016 : ciw509v1-ciw509
24. Mansuy JM, Pasquier C, Daudin M, Chapuy-Regaud S, Moinard N, Chevreau C, Izopet J, Mengelle C, Bujan L. Zika virus in semen of a patient returning from a non-epidemic area. *The Lancet Infect Dis* 2016;16:894-895. DOI: http://dx.doi.org/10.1016/S1473-3099(16)30153-0 Accessed 16/08/2016.
25. Barzon L, Pacenti M, Franchin E, Lavezzo E, Trevisan M, Sgarabotto D, Palù G. Infection dynamics in a traveller with persistent shedding of Zika virus RNA in semen for six months after returning from Haiti to Italy, January 2016. *Euro Surveill.* 2016;21(32):pii=30316. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.32.30316 Accessed 17/08/2016
26. Nicastri E, Castilletti C, Liuzzi G, Iannetta M, Capobianchi MR, Ippolito G. Persistent detection of Zika virus RNA in semen for six months after symptom onset in a traveller returning from Haiti to Italy, February 2016. *Euro Surveill.* 2016;21(32):pii=30314. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.32.30314 Accessed 20/08/2016
27. Prisant N, Bujan L, Benichou H, Hayot PH, Pavili L, Lurel S, et al. Zika virus in the female genital tract. *Lancet Infect Dis*. 2016; pii: S1473-3099(16)30193-1. DOI: http://dx.doi.org/10.1016/S1473-3099(16)30193-1 Accessed 18/08/2016
28. 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
29. Barzon L, Pacenti M, Berto A, Sinigaglia A, Franchin E, Lavezzo E, Brugnaro P, Palù G. 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(10):pii=30159. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.10.30159
30. Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine.*Emerg. Infect. Dis.*, 21 (2015), pp. 84–86
31. 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
32. 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
33. 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.

34. 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

35. 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

36. Rozé B, Najioullah 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

37. 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).

38. UNAIDS Terminology Guidelines 2015 page 11. http://www.unaids.org/sites/default/files/media_asset/2015_terminology_guidelines_en.pdf Accessed 16/08/2016

39. World Health Organization, 'Women in the context of microcephaly and Zika virus disease', 2016. http://www.who.int/features/qa/zika-pregnancy/en/ Accessed 12/05/2016

40. 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 20/04/2016