Guidance for Providers Caring for Women and Men Of Reproductive Age with Possible Zika Virus Exposure

(Modified from CDC[*ξ], FDA[†] and WHO[#] Published Guidance)

Planning Pregnancy for Infected, Exposed, or Possibly Exposed Individuals

1. **Women and men who have Zika virus disease** should wait at least **6 months** after onset of illness to attempt reproduction. The temporal relationship between the presence of viral RNA and infectivity is not known definitively and, thus, the absolute duration of time to wait before attempting pregnancy is unknown. Male and female partners who become infected should avoid intimate sexual contact or use condoms for the same 6 months. Intimate sexual contact includes vaginal, anal and oral sex and the sharing of sex toys.

2. **Women and men with possible exposure to Zika virus but without clinical illness** consistent with Zika virus disease should consider testing for Zika viral RNA within 2 weeks of suspected exposure and wait at least 8 weeks after the last date of exposure before being re-tested. They then should consider attempting pregnancy only if the test is negative. Ideally, if the rRT-PCR results were negative one would obtain antibody testing if and when available. This testing paradigm will not necessarily guarantee lack of Zika virus infectivity.

3. **Women and men** who **reside** in **areas** of **active Zika virus transmission** should talk with their health care providers about attempting reproduction and avoid exposure to mosquito bites. Patients desiring pregnancy should be counseled about the risks of infection during pregnancy and methods to avoid infection. Ideally, these patients would delay attempts at pregnancy until the risk of infection during pregnancy is minimal.

4. Currently, there is no evidence that Zika virus will cause congenital infection in pregnancies initiated after the resolution of maternal Zika viremia.

5. Providing preconception counseling is challenging because currently available data are limited. Discussions about **pregnancy timing should be individualized** and should include information about the signs and symptoms of Zika virus disease and the potential adverse outcomes associated with Zika virus infection in pregnancy. If the male or female partner of a pregnant woman becomes infected or tests positive for Zika virus, he or she should avoid intimate sexual contact as described above or use condoms for the duration of the pregnancy.

6. In areas of active Zika virus transmission, health care providers should discuss strategies to **prevent unintended pregnancy**, including use of the **most effective contraceptive methods**. In addition, patients should be counseled that correct and consistent use of condoms reduces the risk for sexually transmitted infections.

7. **Infertility treatment centers caring for patients at risk of infection** during the course of treatment or subsequent pregnancy should develop strategies to mitigate the risk of viral transmission to the patient, the fetus, and health care workers. Strategies should incorporate sufficient counseling about the challenges of interpreting test results, even from direct viral RNA testing, e.g., rRT-PCR. The primary challenges are the occurrence of false negative and positive results and the possibility of infection at any time after blood sampling. Moreover, any testing performed at a time other than the time of treatment might not reflect true viral status, particularly in areas of active Zika virus transmission. Any patient who proceeds with attempted pregnancy after negative testing should be counseled about the possible presence of virus with a negative test, the risks of subsequent infection, the possible viral effects on the fetus, and testing during pregnancy as per national guidance.

   At present, possible strategies for dealing with these challenges in women and men with possible exposure or who reside in areas of active virus transmission include:

   - For males or females with a positive viral rRT-PCR test result, treatment of infertility should be halted immediately. Defer treatment until 1) a subsequent rRT-PCR re-test is negative on both the male and female **and** 2) at least 6 months have passed for them from the time of the last positive result.

- For males or females without testing or with a negative rRT-PCR test result, consider gamete or embryo cryopreservation and quarantine until 1) a subsequent rRT-PCR re-test is negative on both the male and female **and** 2) at least 8 weeks have passed from the time of the gamete collection.
- For males not previously infected with the Zika virus who are planning travel to an area of active virus transmission, consider semen cryopreservation before travel. Ideally they should be tested for viral RNA by rRT-PCR at the time of semen collection and within 1 week after return.

Zika Testing Limitations

8. **Testing for Zika has been complicated.** Testing is not universally available for use in those individuals for whom testing is recommended and the cost is not universally covered by insurance. Reproductive health care providers should identify the tests that are available in their community, the limitations and interpretation of the results of these tests, which patients will be allowed testing by these testing facilities, and whether testing is covered by insurance. Ideally this information would be obtained before patients who are infected or at-risk for infection present for care.
9. **Routine testing** for Zika viral RNA by rRT-PCR should be made available for women or men who are attempting reproduction and who have possible exposure to Zika virus but no clinical illness. Evidence suggests that a positive test for Zika viral RNA in serum is likely associated with the presence of virus in semen or other bodily fluids. A negative serum test result by RT-PCR would not necessarily preclude the presence of the virus in semen or other bodily fluids. Patients should be provided counseling regarding interpretation of the test results.
10. Although Zika virus can be present in semen and cervical and vaginal secretions and sexual transmission of the virus has occurred between partners of the same and opposite sex, **testing of semen and cervical and vaginal fluids is not recommended** until methods for detecting Zika virus in semen or bodily fluids other than serum or urine are validated.

Fertility Treatments Using Autologous or Donated Gametes

11. **Fertility treatment for sexually intimate couples** using their own gametes and embryos should follow the timing recommendations for persons attempting reproduction.
12. The Food and Drug Administration (FDA) guidance states that living donors of sperm, oocytes and embryos will be deemed ineligible for anonymous donation if they have any of the following risk factors:

    - medical diagnosis of Zika virus infection in the past 6 months;
    - residence in or travel to an area with active Zika virus transmission within the past 6 months; or
    - within the past 6 months had sex with a male partner who, during the 6 months before this sexual contact, received a diagnosis of or experienced an illness consistent with Zika virus disease, or had traveled to an area of active Zika virus transmission.

13. **Directed (or known) donors** must undergo the same evaluation and eligibility determination as anonymous donors.
14. **Fertility treatment using a gestational carrier** should follow timing recommendations for gestational carriers as for persons attempting reproduction.
15. When using **donated embryos**, consideration should be given as to the potential exposure of the embryos to Zika virus, particularly if the embryos were frozen at a time before these screening processes were in effect.
16. It is tempting to assume that the use of techniques for sperm preparation that have been shown to be effective for minimizing the risk of HIV transmission should be similarly effective for minimizing risk of Zika virus transmission. However, **these procedures have not yet been demonstrated to be effective in preventing transmission of the Zika virus nor has cryopreservation been demonstrated to destroy the Zika virus.**
17. Data involving Zika, its transmission and infectivity, and its adverse effects on fetuses and adults is changing daily. **Guidance based on current knowledge is iterative** as our understanding of this virus rapidly changes. Any guidance published today may not be accurate for counseling and treatment of individuals tomorrow.

18. It is suggested that until more data are available about asymptomatic males and females potentially exposed to Zika, practitioners providing treatment that involves use of gametes in these potentially infected individuals **develop language to be added to their consent** forms that conveys this gap in knowledge to these individuals.

References

[*] Oduyebo T, Igbinosa I, Petersen EE, et al. *Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016.* MMWR Morb Mortal Wkly Rep 2016;65:739–744. DOI: http://dx.doi.org/10.15585/mmwr.mm6529e1

[ξ] Centers for Disease Control and Prevention. *Preconception Counseling: For Women and Men Living in Areas with Ongoing Spread of Zika Virus Who Are Interested in Conceiving*. https://www.cdc.gov/zika/pdfs/preconception-counseling.pdf. Accessed September 12, 2016.

[†] Food and Drug Administration. *Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products.* *http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*. *Accessed September 12, 2016.*

[#] World Health Organization. *Prevention of sexual transmission of Zika virus Interim guidance.* WHO reference number: WHO/ZIKV/MOC/16. 1 Rev. 3, September 6, 2016.

This report was developed under the direction of the Zika Virus Guidance Task Force of the American Society for Reproductive Medicine as a service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Executive Committee of the American Society for Reproductive Medicine has approved this report.*

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