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WOMEN'S HEALTH CARE PHYSICIANS

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(Replaces Practice Advisory: Interim Guidance for Care of Obstetric Patients During a Zika Virus Outbreak, April 2019)

Immunization, Infectious Disease, and Public Health Preparedness Expert Work Group

The Society for Maternal-Fetal Medicine endorses this document. This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Immunization, Infectious Disease, and Public Health Preparedness Expert Work Group in collaboration with members Laura E. Riley, MD; R. Phillips Heine, MD; and with technical assistance from the Centers for Disease Control and Prevention's representative member Titilope Oduyebo, MD, MPH. The views do not necessarily represent those of the Centers for Disease Control and Prevention or the U.S. government.

Management of Patients in the Context of Zika Virus

ABSTRACT: Zika virus is a flavivirus with the potential to cause serious adverse pregnancy and infant outcomes. Although rates of Zika virus infection have decreased in the United States, obstetrician–gynecologists and other health care providers should continue to assess their patients for potential exposure based on travel or sexual history and test symptomatic patients with possible exposure and pregnant women with ongoing exposure regardless of symptoms in accordance with the Centers for Disease Control and Prevention recommendations. Pregnant women and those planning a pregnancy should talk to their health care providers about potential risks before traveling to an area where current or past Zika virus transmission has occurred. Testing recommendations for pregnant women with possible Zika virus exposure differ based on the presence or absence of symptoms of Zika virus infection and the circumstances of possible exposure. If obstetrician–gynecologists or other health care providers identify a patient who has possibly been exposed to the Zika virus and may require testing, they should contact their local or state health department for assistance. Consultation with a maternal–fetal medicine specialist or an infectious disease specialist with expertise in the management of infectious diseases in pregnancy may be useful for pregnant women with possible maternal Zika virus infection or concerning fetal findings. Zika virus identification and follow-up care of infants born to women with possible exposure to Zika virus during pregnancy are critical and can ensure that appropriate intervention services are available to affected infants. Obstetrician–gynecologists and other obstetric care providers should have a system to ensure relevant information regarding a woman's Zika infection status is communicated to pediatric care providers.

Recommendations

The American College of Obstetricians and Gynecologists makes the following recommendations:

- Pregnant women should avoid travel to areas where current Zika virus outbreaks are occurring because of the potential for major birth defects and developmental abnormalities among infected fetuses.
- Pregnant women and those planning a pregnancy should talk to their health care providers about potential risks before traveling to an area where current or past Zika virus transmission has occurred.
- To prevent possible infection during time periods near or around fertilization, women with possible exposure to Zika virus who want to get pregnant, regardless of symptom status, should consider waiting at least 8 weeks from symptom onset or exposure to attempt pregnancy. This includes women with diagnosed Zika virus infection.
- To prevent possible infection during time periods near or around fertilization, if a male partner has possible Zika virus exposure, regardless of his symptom status, the couple should consider waiting at least 3 months after the male's symptom onset or last possible Zika virus exposure to attempt pregnancy.

- Obstetrician–gynecologists and other health care providers routinely should ask pregnant women and other women of reproductive age about possible Zika virus exposure.
- Symptomatic pregnant women with possible Zika virus exposure or women who are pregnant with a fetus showing abnormalities consistent with congenital Zika virus syndrome should be tested as soon as possible. Asymptomatic pregnant women with ongoing possible exposure can be offered nucleic acid testing during pregnancy as part of routine obstetric care.
- Asymptomatic pregnant women with possible Zika virus exposure but without ongoing possible exposure are not recommended routinely to have Zika virus testing, but testing can be considered as part of a shared patient–provider decision-making model.
- Consultation with a maternal–fetal medicine specialist or an infectious disease specialist with expertise in the management of infectious diseases in pregnancy may be useful for pregnant women with possible maternal Zika virus infection or concerning fetal findings.
- For pregnant women with laboratory evidence of possible Zika infection, use of ultrasonography to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome is recommended.
- Obstetrician–gynecologists and other obstetric care providers should have a system to ensure relevant information regarding a woman’s Zika infection status is communicated to pediatric care providers.
- Obstetrician–gynecologists and other health care providers should counsel patients that although Zika has been detected in breast milk, based on the available data, the Centers for Disease Control and Prevention (CDC) and the World Health Organization currently recommend that infants born to women with suspected, probable, or confirmed Zika virus infection, or who live in or have traveled to areas with Zika, should continue to breastfeed according to established infant feeding guidelines.

Background

Zika virus is a flavivirus that is spread to humans primarily through bites by infected *Aedes* species mosquitoes (*Ae. aegypti* and *Ae. albopictus*) and is closely related to dengue virus, West Nile virus, Japanese encephalitis virus, and yellow fever virus. Transmission of Zika virus has been reported through sexual contact, blood transfusion, and from a woman to her fetus. *Possible Zika virus exposure* is defined as travel to or residence in an area of active Zika virus transmission (8) or sex without a condom with a partner

who traveled to or lives in an area with risk of Zika virus transmission. *Ongoing Zika virus exposure* is defined as currently living in or frequent (eg, daily or weekly) travel to areas with Zika virus transmission. The incubation period for the Zika virus is approximately 3–14 days (1). The signs and symptoms of Zika virus infection include fever, rash, arthralgia, and conjunctivitis.

In 2015 and 2016, Zika virus caused outbreaks across the Americas. However, since early 2017, the reported incidence of Zika virus disease has decreased, and in most countries the virus has become endemic with periodic outbreaks.

Although pregnant women are not at greater risk of Zika virus acquisition and personal sequelae than non-pregnant women, Zika virus has been identified as a teratogen with characteristic neurotropism (2, 3). Fetal Zika infection has been shown to result in a distinct pattern of birth defects including severe microcephaly with partially collapsed skull; thin cerebral cortex with calcifications noted in the subcortical region; macular scarring, focal pigmentary retinal mottling, and other abnormalities on ophthalmologic examination of the retina; congenital contractures (these can be in a single joint or in multiple joints) or arthrogryposis; and marked early hypertonia and symptoms of extrapyramidal involvement. Emerging data from case reports and case series have reported other abnormalities, such as cardiac anomalies and diaphragmatic hernia. Zika virus also has been linked with other adverse pregnancy outcomes, including miscarriage, preterm birth, growth restriction, and stillbirth (4).

Transmission of Zika virus from the woman to her fetus has been documented in all trimesters, and a diagnosis of Zika infection during any trimester may be associated with fetal or neonatal abnormalities, including growth delays. It is estimated that the risk of congenital Zika virus syndrome is 5–10%. These estimates are consistent across studies globally. Limited available data indicate that infection with Zika virus (confirmed by nucleic acid testing) during the first trimester and early second trimester of pregnancy is associated with a higher proportion of Zika-related birth defects (5, 6).

Prevention

Currently, there is no commercially available vaccine against, treatment for, or method to prevent vertical transmission of the Zika virus. Several Zika virus vaccines are in various stages of development, and some are undergoing clinical trials to evaluate their safety and immunogenicity.

Pregnant women should avoid travel to areas where current Zika virus outbreaks are occurring because of the potential for major birth defects and developmental abnormalities among infected fetuses. The CDC maintains and updates a list of areas where Zika virus transmission has been identified (for current locations, see the CDC’s

travel website at <https://wwwnc.cdc.gov/travel/page/zika-travel-information>). Pregnant women and those planning a pregnancy should talk to their health care providers about potential risks before traveling to an area where current or past Zika virus transmission has occurred. If travel to one of these areas is necessary, the following precautions to prevent mosquito bites should be performed: The mosquitos that transmit Zika virus are active all the time, particularly during daylight hours. Therefore, covering the skin throughout the day and night, using an insect repellent registered by the Environmental Protection Agency, and remaining in air-conditioned locations as much as possible are recommended. The safety of diethyltoluamide (known as DEET), an Environmental Protection Agency-registered insect repellent, during pregnancy has been established (7). A pregnant woman whose male partner has possible Zika virus exposure should use condoms or abstain from sex for the duration of the pregnancy.

To prevent possible infection during time periods near or around fertilization, women with possible exposure to Zika virus who want to get pregnant, regardless of symptom status, should wait to attempt pregnancy using the timeframes shown in Table 1. Also, women with possible exposure to Zika virus who want to get pregnant, regardless of symptom status, should consider waiting at least 8 weeks from symptom onset or exposure to attempt pregnancy. This includes women with diagnosed Zika virus infection (Table 1) (8).

If a male partner has possible Zika virus exposure, regardless of his symptom status, the couple should

consider waiting at least 3 months after the male's symptom onset or last possible Zika virus exposure to attempt pregnancy. For those couples who are not planning to get pregnant but want to prevent sexual transmission, abstinence or the consistent proper use of condoms also is recommended for the above time frames.

Assessment

Anyone who lives in or travels to an area where Zika virus is found and who has not been infected with Zika virus already is at risk of contracting Zika virus. For current locations with Zika virus transmission, see the CDC's travel website at <https://wwwnc.cdc.gov/travel/page/zika-travel-information>. Once an individual has been infected, he or she is likely to be protected from future infections, although this finding is based on limited data and experience from other flaviviruses (9). Obstetrician-gynecologists and other health care providers routinely should ask pregnant women and other women of reproductive age about possible Zika virus exposure.

Zika Virus Testing

Nucleic acid tests and serologic tests are available to detect Zika virus infection, although each test has limitations. "Nucleic acid test" is a generic term referring to all molecular tests, including real-time reverse transcription polymerase chain reaction tests. Serologic tests to detect Zika virus infection include immunoglobulin M (IgM) and plaque reduction neutralization tests. Detection of Zika virus by polymerase chain reaction during acute infection is

Table 1. Recommendations to Prevent Sexual Transmission of Zika

Exposure Scenario	Recommendations
Couples who want to attempt pregnancy	
Only the female partner has possible Zika virus exposure.	<ul style="list-style-type: none"> Use of condoms or abstinence from sex for at least 8 weeks after the female partner's symptom onset or last possible Zika virus exposure (if asymptomatic) should be advised.
The male partner or both partners have possible Zika virus exposure.	<ul style="list-style-type: none"> Use of condoms or abstinence from sex for at least 3 months after the male partner's symptom onset or last possible Zika virus exposure (if asymptomatic) should be advised.
One or both partners have ongoing* possible Zika virus exposure.	<ul style="list-style-type: none"> Prepregnancy care should include a discussion of the signs and symptoms and the potential risks associated with Zika virus infection and strategies to prevent Zika virus infection. If either partner develops signs and symptoms or is diagnosed with Zika virus infection, the couple should follow the suggested timeframes listed above before attempting pregnancy.
Women who are pregnant	
A pregnant woman whose male partner has possible Zika virus exposure.	<ul style="list-style-type: none"> Use of condoms or abstinence from sex for the duration of the pregnancy should be advised.

*Ongoing Zika virus exposure is defined as currently living in or frequent (eg, daily or weekly) travel to areas with Zika virus transmission.

variable and depends on the type of sample, the timing of testing in relation to the onset of symptoms, and the type of test used. The IgM test has many limitations, including cross reactivity with antibodies to other flaviviruses such as dengue and yellow fever; persistence beyond 4 months in some who are infected, making it difficult to determine if an infection occurred during pregnancy (including periods near or around fertilization); and the fact that the IgM test's positive and negative predictive values significantly decline with the decreasing prevalence of Zika. Plaque reduction neutralization tests also have limitations because cross-reactive antibodies can be found in patients who have been vaccinated against or with a previous infection with other flaviviruses. Currently, there is no immunoglobulin G test for Zika approved in the United States. Efforts to develop and validate Zika virus serologic assays with improved specificity for Zika virus infection and the ability to distinguish a recent infection from a previous infection are ongoing.

Testing of Pregnant Women

Interpretation of Zika virus testing is complicated given the nature of the infection as well as limitations of the available tests. If obstetrician-gynecologists or other health care providers identify a patient who has possibly been exposed to the Zika virus and may require testing, they should contact their local or state health department for assistance. Testing recommendations for pregnant women with possible Zika virus exposure differ based on the presence or absence of symptoms of Zika virus infection and the circumstances of possible exposure (10).

Symptomatic pregnant women with possible Zika virus exposure or women who are pregnant with a fetus showing abnormalities consistent with congenital Zika virus syndrome should be tested as soon as possible (10). For more details on specific tests for symptomatic pregnant women, see the CDC's *Update: Interim Guidance for Health Care Providers Caring for Pregnant Women With Possible Zika Virus Exposure—United States (Including U.S. Territories)*, July 2017, Figure 1, at <https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm>.

Asymptomatic pregnant women with ongoing possible exposure can be offered nucleic acid testing during pregnancy as part of routine obstetric care. Frequency of testing may be dependent on location, and health care providers are encouraged to use a shared decision-making model with their patients. Currently, IgM testing is not recommended routinely because of the limitations of the tests and the difficulty in interpreting results (10). For more detail on specific tests for asymptomatic pregnant women with ongoing exposure see the CDC's *Update: Interim Guidance for Health Care Providers Caring for Pregnant Women With Possible Zika Virus Exposure—United States (Including U.S. Territories)*, July 2017, Figure 2, at <https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm>.

Asymptomatic pregnant women with possible Zika virus exposure but without ongoing possible exposure are not recommended routinely to have Zika virus testing, but testing can be considered as part of a shared patient-provider decision-making model (10). For more detail on specific tests for asymptomatic pregnant women without ongoing exposure, see the CDC's *Update: Interim Guidance for Health Care Providers Caring for Pregnant Women With Possible Zika Virus Exposure—United States (Including U.S. Territories)*, July 2017, Figure 2, at <https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm>.

Testing of Nonpregnant Women

Zika virus testing of serum and urine is recommended for nonpregnant women who have had possible exposure to Zika virus and who develop signs or symptoms consistent with Zika virus disease. Currently, testing of nonpregnant asymptomatic women is not recommended (10).

Clinical Management of Possible Zika Virus Infection in a Pregnant Woman

The continued uncertainties surrounding Zika virus highlight the challenges of providing appropriate management and counseling about exposure and infection during pregnancy. Laboratory evidence of recent flavivirus infection for which a specific Zika infection cannot be excluded is particularly challenging. Pregnant women with laboratory evidence of recent flavivirus infection should be managed the same way as women with confirmed Zika virus infection because Zika virus infection cannot be ruled out given the challenges with interpretation of Zika virus serology. Consultation with a maternal-fetal medicine specialist or an infectious disease specialist with expertise in the management of infectious diseases in pregnancy may be useful for pregnant women with possible maternal Zika virus infection or concerning fetal findings.

Fetal Evaluation

For pregnant women with laboratory evidence of possible Zika infection, use of ultrasonography to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome is recommended. Ultrasonographic examinations can be used to assess fetal anatomy, particularly neuroanatomy, and to monitor growth (11).

However, ultrasonographic examinations, particularly if obtained soon after onset of infection, may not identify prenatal features of congenital Zika syndrome. Delays as long as 29 weeks from infection onset and the presentation of fetal abnormalities have been observed (12–15). There are insufficient data to define the optimal timing between exposure and initial ultrasonographic screening or frequency of ultrasonography in pregnant women with Zika virus infection.

If maternal testing does not suggest infection, women should receive the same ultrasonographic screening as any other pregnant woman as part of standard routine prenatal care.

Amniocentesis

Although Zika virus RNA has been detected in amniotic fluid specimens, the usefulness of amniocentesis is unknown. A negative amniotic fluid test result cannot rule out congenital Zika virus infection. The results of serial amniocentesis tests have demonstrated that Zika virus RNA may be present only transiently (16).

Postnatal Management

Testing placental tissue specimens from pregnancies with possible Zika virus exposure may be considered for diagnostic purposes in certain scenarios, but it is not recommended routinely (10).

Testing of placental and fetal tissues (or autopsy tissue in the event of an infant death) may be considered in selected scenarios for pregnancies resulting in a miscarriage or fetal loss to provide insight into the potential etiology of the fetal loss or infant death, which could inform a woman's future pregnancy planning.

Neonatal Outcomes and Evaluation

Obstetrician–gynecologists and other obstetric care providers should have a system to ensure relevant information regarding a woman's Zika infection status is communicated to pediatric care providers. Newborns should be tested and evaluated for congenital Zika virus infection in accordance with CDC guidelines (17). Zika virus identification and follow-up care of infants born to women with possible exposure to Zika virus during pregnancy are critical and can ensure that appropriate intervention services are available to affected infants. Health care providers can check for updates on caring for infants and children affected by Zika virus on the CDC's web page "Zika and Pregnancy, Caring for Infants and Children" at <https://www.cdc.gov/pregnancy/zika/testing-follow-up/infants-children.html>.

Breastfeeding

Although Zika virus has been detected in breast milk by polymerase chain reaction (18), there are no reports of confirmed transmission of Zika virus infection through breastfeeding. Obstetrician–gynecologists and other health care providers should counsel patients that although Zika has been detected in breast milk, based on the available data, the CDC and the World Health Organization currently recommend that infants born to women with suspected, probable, or confirmed Zika virus infection, or who live in or have traveled to areas with Zika, should continue to breastfeed according to established infant feeding guidelines (19–22).

Reporting and the U.S. Zika Pregnancy and Infant Registry

Because of the diminishing number of cases of Zika virus infection, the CDC closed the mainland U.S. pregnancy registry on March 31, 2018, but the Zika active pregnancy surveillance system in Puerto Rico remains open. Zika infection remains a reportable condition, and all laboratory-confirmed cases should continue to be reported to local and state health officials so that they can report them to the CDC-managed national arbovirus surveillance system ArboNET. For updates on Zika surveillance and reporting, health care providers are encouraged to check the CDC's web page "U.S. Zika Pregnancy and Infant Registry" at <https://www.cdc.gov/pregnancy/zika/research/registry.html>.

Infection Control Considerations

The CDC, the American College of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine recommend standard precautions in health care settings to protect obstetrician–gynecologists and other health care providers and patients from infection with Zika virus as well as from other blood-borne pathogens. Minimizing exposure to body fluids is important because Zika virus has been detected in many body fluids, including blood, urine, semen, saliva, breast milk, vaginal fluid, and amniotic fluid.

Conclusion

Zika virus is a flavivirus with the potential to cause serious adverse pregnancy and infant outcomes. Although rates of Zika virus infection have decreased in the United States, obstetrician–gynecologists and other health care providers should continue to assess their patients for potential exposure based on travel or sexual history and test symptomatic patients with possible exposure and pregnant women with ongoing exposure regardless of symptoms in accordance with CDC recommendations. Information and recommendations regarding Zika virus screening and testing are evolving, and obstetrician–gynecologists and other health care providers should check guidance for updates routinely.

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for obstetrician–gynecologists, other health care providers, and patients. You may view these resources at: www.acog.org/zika.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's website, or the content of the resource. The resources may change without notice.

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American College of Obstetricians and Gynecologists
409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920

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