Q and A's for Obstetrical Healthcare Providers: Pregnant Women and Zika Virus Infection

Summary
CDC has developed interim guidelines for healthcare providers in the United States caring for women during a Zika virus outbreak. These guidelines include recommendations for pregnant women considering travel to an area with Zika virus transmission and recommendations for screening, testing, and management of returning pregnant travelers. These guidelines will be updated as more information becomes available.
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What is Zika virus?
Zika virus is a mosquito-borne single-stranded RNA virus related to dengue virus. In the Americas, Zika virus is primarily transmitted by *Aedes aegypti,* but *Aedes albopictus* mosquitoes can also transmit the virus.

How is Zika virus transmitted?
Zika virus is transmitted to humans primarily through the bite of an infected *Aedes* species mosquito. *Aedes* mosquitoes are aggressive daytime biters and feed both indoors and outdoors. Zika virus can be transmitted from a pregnant mother to her fetus during pregnancy or around the time of birth. We do not know how often Zika perinatal transmission occurs.

Who is at risk of being infected?
Anyone who is living in or traveling to an area where Zika virus is found who has not already been infected with Zika virus. Specific areas where Zika virus transmission is ongoing are often difficult to determine and are likely to change over time. Please visit http://wwwnc.cdc.gov/travel/notices/ for the most updated information.

What is the potential for Zika virus to spread to the United States?
Currently, local transmission of Zika virus has not been reported in the continental United States but has been reported in the Commonwealth Puerto Rico. With the current outbreaks in the Americas, the number of cases among U.S. travelers is expected to increase. As the number of returning travelers with Zika virus disease increases, viral introduction and local spread in the U.S. may occur. As more information before available, CDC will provide updates: http://www.cdc.gov/zika/index.html

What are symptoms of Zika virus infection?
About 1 in 5 people infected with Zika virus become symptomatic. Characteristic clinical findings are acute onset of fever with maculopapular rash, arthralgia, or conjunctivitis. Other commonly reported symptoms include myalgia and headache. Clinical illness is usually mild with symptoms lasting for several days to a week.

Are there known complications of Zika virus infection?
There have been cases of Guillain-Barré syndrome reported in patients following suspected Zika virus infection.

What types of testing for Zika virus are available to test pregnant women?
During the first week of illness, Zika virus disease can often be diagnosed by performing reverse transcriptase-polymerase chain reaction (RT-PCR) on serum. Serology assays can also be used to detect Zika virus-specific IgM and neutralizing antibodies, which typically develop toward the end of the first week of illness. Plaque-reduction neutralization testing (PRNT) can be performed to measure virus-specific neutralizing antibodies to confirm primary flavivirus infections and differentiate from other viral illnesses

How can I order a Zika virus test for a patient that has traveled to an area with Zika virus transmission?
There are no commercially available tests for Zika virus. Zika virus testing is performed at the CDC Arbovirus Diagnostic Laboratory and a few state health departments. Healthcare providers should contact their state and local health department to facilitate testing. See the Diagnostic Testing webpage for information on how to obtain Zika testing.

How is maternal Zika virus infection diagnosed?
Laboratory evidence of maternal Zika virus infection can include Zika virus RNA detected by RT-PCR in any clinical specimen; or positive Zika virus IgM with confirmatory neutralizing antibody titers that are ≥4-fold higher than dengue virus neutralizing antibody titers in serum. Testing would be considered inconclusive if Zika virus neutralizing antibody titers are < 4-fold higher than dengue virus neutralizing antibody titers.

What are the challenges in interpreting Zika virus testing?
RT-PCR test may not demonstrate Zika virus RNA in a woman with Zika virus infection if the period of viremia has passed. Serum serologic testing can be performed, however, cross-reactivity with related flaviviruses (e.g., dengue and yellow fever viruses) is common. Plaque-reduction neutralization testing (PRNT) can be performed to measure virus-specific neutralizing antibodies to Zika virus, but neutralizing antibodies may still yield cross-reactive results in persons who were previously infected with another flavivirus, such as dengue, or has been vaccinated against yellow fever or Japanese encephalitis. It is important to work closely with your state or local health department to ensure the appropriate test is ordered and interpreted correctly.

How can Zika virus infection be prevented?
There is no vaccine to prevent Zika virus infection. Travelers can protect themselves by taking steps to prevent mosquito bites. Use insect repellent; wear long-sleeved shirts and long pants; and stay in places with air conditioning or with window and door screens. Pregnant women can and should choose an EPA-registered insect repellents and use it according to the product label. See http://wwwnc.cdc.gov/travel/page/avoid-bug-bites

What is known about the effects of Zika virus on pregnant women?
We expect that the course of Zika virus disease is similar to that in the general population. No evidence exists to suggest that pregnant women are more susceptible or experience more severe disease during pregnancy. It is not known if pregnant women are more susceptible to Guillain-Barré syndrome.

Is there any association between Zika virus infection and congenital microcephaly?
There have been reports of congenital microcephaly in babies of mothers who were infected with Zika virus while pregnant. Zika virus infections have been confirmed in several infants with microcephaly; it is not known how many of the microcephaly cases are associated with Zika virus infection. Studies are under way to investigate the association of Zika virus infection and microcephaly, including the role of other contributory factors (e.g., prior or concurrent infection with other organisms, nutrition, and environment).

Is there any known association between maternal Zika virus infection and other adverse pregnancy outcomes?
The full spectrum outcomes that might be associated with Zika virus infections during pregnancy is unknown and requires further investigation.

How should pregnant patients who are considering travel to an area with Zika virus transmission be counseled?
Until more is known, and out of an abundance of caution, CDC recommends special precautions for pregnant women, pregnant women in any trimester should consider postponing travel to an area where Zika virus transmission is ongoing. If a pregnant women is considering travel to one of these areas, she should talk to her healthcare provider. If she travels, she should strictly follow steps to avoid mosquito bites during the trip.

How should women trying to become pregnant who are considering travel to an area with Zika virus transmission be counseled?
They should consult with their healthcare provider before traveling to these areas and strictly follow steps to prevent mosquito bites during the trip.

Which pregnant women should be tested for Zika virus infection?
Obstetrical providers should obtain a travel history from all pregnant women and use recent travel history to guide decisions about testing. Testing is not indicated for pregnant women without a travel history to an area with Zika virus transmission.

Pregnant women with a history of travel to an area with Zika virus transmission and who report two or more symptoms consistent with Zika virus disease (including acute onset of fever, maculopapular rash, arthralgia or conjunctivitis) during or within two weeks of travel should be tested. In addition, pregnant women with a history of travel to an area with Zika virus transmission and who have ultrasound findings of fetal microcephaly or intracranial calcifications should also be tested for Zika virus infection. Testing should be performed in consultation with state or local health departments.
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Why is Zika virus testing not recommended for all pregnant women who have travelled to an area with Zika virus transmission?
As with all tests, healthcare providers must carefully weigh the risks and benefits of testing. CDC would not recommend testing for asymptomatic pregnant women with a travel history unless there is fetal ultrasound finding of microcephaly or intracranial calcifications. Serologic testing results are difficult to interpret. False positives due to cross-reactivity may lead to undue concern and clinical management based on inaccurate information (i.e. false positives or inconclusive tests).

What specimens can be tested for Zika virus?
Zika virus RT-PCR and serology assays can be performed on maternal serum or plasma. Zika virus RT-PCR can also be performed on amniotic fluid. Other testing that can performed includes the following: 1) histopathologic examination and immunohistochemical staining of the placenta and umbilical cord, 2) Zika virus testing of frozen placental tissue and cord tissue, and 3) IgM and neutralizing antibody testing of cord blood.

Why is fetal ultrasound recommended?
Fetal ultrasound is generally performed in pregnancies between 18-20 weeks of gestation to assess fetal anatomy as part of routine obstetrical care. Microcephaly and intracranial calcifications can be detected during routine ultrasounds, as well as during ultrasounds performed later in pregnancy. Microcephaly and intracranial abnormalities have been demonstrated in pregnancies with known Zika virus disease. Abnormal ultrasound findings in women with recent travel to an area with Zika virus transmission can provide an opportunity to identify findings consistent with fetal Zika virus infection and offer pregnant women the option of amniocentesis to test for Zika virus RNA. In addition, a normal ultrasound can provide reassurance to pregnant women who have travelled to an area of Zika virus transmission who are concerned about fetal microcephaly.

What ultrasound findings would be expected in association with a fetal Zika virus infection?
The full spectrum outcomes that might be associated with Zika virus infections during pregnancy is not known. Congenital microcephaly and intracranial calcifications have been detected on ultrasound as early as 18-20 weeks

When should a screening fetal ultrasound be performed?
If a pregnant woman has symptoms consistent with Zika virus disease during or within 2 weeks of travel, she should be seen by her healthcare provider. If a pregnant woman does not experience clinical symptoms consistent with Zika virus disease during or within 2 weeks of travel, ultrasound evaluation is recommended. Serial ultrasound screening (every 3-4 weeks) may be considered at the discretion of the provider. The optimal time to perform ultrasound screening for fetal microcephaly and other neurologic abnormalities is not known.

Who should be offered amniocentesis?
Amniocentesis should be offered to pregnant women with recent travel to an area with Zika virus transmission and a positive or inconclusive maternal serum test. For pregnant women with recent travel to an area with Zika virus transmission and ultrasound findings of microcephaly or intracranial calcifications, amniocentesis may also be considered. Consultation with a maternal-fetal medicine specialist should be considered.

Why is amniocentesis offered?
While amniocentesis is a relatively safe test, risk and benefits of amniocentesis should always be considered. An amniocentesis can be used to provide additional clinical information. For example, a positive RT-PCR result on amniotic fluid would be suggestive of intrauterine infection and potentially useful to pregnant women and their health care providers to guide decisions about timing of delivery and the level of neonatal care at delivery sites.

When should amniocentesis be performed?
Timing of amniocentesis should be individualized based on the patient's clinical circumstances. Amniocentesis is not recommended until after 15 weeks of gestation. Amniocentesis performed ≥15 weeks of gestation is associated with lower rates of complications than those performed at earlier gestational ages, and early amniocentesis (≤14 weeks of gestation). However, the exact timing of amniocentesis should be individualized based on the patient's clinical circumstances. Referral to maternal-fetal medicine or infectious disease specialist with expertise in pregnancy management may be warranted. Risk and benefits of performing the amniocentesis should be discussed with the patient.

How would results of Zika virus RT-PCR amniotic fluid test results inform clinical management of pregnant women?
A positive Zika virus RT-PCR result from amniotic fluid would be suggestive of intrauterine infection. This information would be useful for pregnant women and their health care providers to assist in determining clinical management (e.g., antepartum testing, delivery planning). A negative Zika virus RT-PCR result from amniotic fluid may prompt a work up for other causes of microcephaly (e.g., other infections, genetic disorders).

For more information, please visit:
CDC travel alert
CDC Zika Virus Home Page
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