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## Questions and Answers for Healthcare Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure

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## Summary

CDC has updated its interim guidelines for US healthcare providers caring for pregnant women and women of reproductive age during ongoing transmission of Zika virus. These guidelines apply to healthcare providers caring for women of reproductive age in the United States including US territories and will be updated as more information becomes available.

### **What is different in these updated guidelines?**

Updated guidelines include a new recommendation to offer serologic testing to asymptomatic pregnant women (women who do not report clinical illness consistent with Zika virus disease) who have traveled to areas with ongoing transmission of Zika virus. Testing should be offered between 2 and 12 weeks after pregnant women return from travel to areas with ongoing Zika virus transmission. The updated guidelines also include recommendations for healthcare providers

caring for women who reside in areas with ongoing transmission of Zika virus, including recommendations for screening, testing; and management of pregnant women and recommendations for counseling women of reproductive age (15–44 years).

### **Why is CDC updating clinical guidelines?**

CDC continues to evaluate all available evidence and to update recommendations as new information becomes available. CDC's updated guidelines have been informed by our close collaboration with clinicians, professional organizations, state and local health departments, and many other stakeholders.

The updated guidance includes a recommendation to offer IgM antibody testing for Zika virus to asymptomatic pregnant women. Although we have limited information about antibody testing of asymptomatic patients, data from related viruses suggest that this testing may be useful when timeframe of exposure is known. Thus, testing may provide useful information for pregnant women and their healthcare providers. A negative IgM test result 2-12 weeks after known exposure suggests that a recent Zika virus infection did not occur, which may obviate the need for serial ultrasounds. Local health officials should determine when to implement testing of asymptomatic pregnant women on the basis of information about levels of Zika virus transmission and laboratory capacity. In addition, the updated guidance also provides recommendation for female residents in areas with ongoing transmission of Zika virus.

### **Why is CDC changing its recommendation for testing of asymptomatic pregnant travelers?**

Although we have limited information about antibody testing of asymptomatic patients, data from related viruses suggest that testing may be useful when the time frame of exposure is known. Interpretation of testing results can be challenging and complex. A negative IgM test result obtained 2 to 12 weeks after travel suggests that a recent infection did not occur and could obviate the need for serial ultrasounds.

## **General Questions**

### **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.

They can also bite at night. 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. Sexual transmission of Zika virus is possible.

### **Is there a risk of sexual transmission to a pregnant woman from a male partner with Zika virus infection?**

Sexual transmission of Zika virus can occur, although there is limited data about the risk. The risk for sexual transmission of Zika virus can be eliminated by abstinence and reduced by correct and consistent use of condoms. Additional studies are needed to characterize the risk of sexual transmission of Zika virus.

### **Who is at greatest risk of being infected?**

Persons living in or traveling to an area where Zika virus is found who have 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 [CDC's Zika Travel Information webpage \(http://wwwnc.cdc.gov/travel/page/zika-travel-information\)](http://wwwnc.cdc.gov/travel/page/zika-travel-information) for the most updated information.

### **What is the potential for Zika virus to spread to the United States?**

Currently, local transmission of Zika virus by mosquitoes has not been reported in the continental United States, but has been reported in the Commonwealth Puerto Rico and the US Virgin Islands. 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 becomes available, CDC will provide updates on its [Zika website \(http://www.cdc.gov/zika/index.html\)](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 complications of Zika virus infection?**

There have been cases of Guillain-Barré syndrome reported in patients following suspected Zika virus infection. The relationship between Zika virus infection and Guillain-Barré syndrome is not known.

### **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 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. Given the potential risks of maternal Zika virus infection, pregnant women whose male partners have or are at risk for Zika virus infection should consider using condoms or abstaining from sexual intercourse.

**Are there any special precautions for pregnant women on the use of insect repellents?**

EPA-registered insect repellents containing ingredients such as DEET, picaridin, and IR3535 are safe for use during pregnancy when used in accordance with product label.

## Sexual Transmission

**Is there a risk of sexual transmission to a pregnant woman from a male partner with Zika virus infection?**

Sexual transmission of Zika virus can occur, although there is limited data about the risk. The risk for sexual transmission of Zika virus can be eliminated by abstinence and reduced by correct and consistent use of condoms. Given the potential risks of maternal Zika virus infection, pregnant women whose male partners have or are at risk for Zika virus infection should consider using condoms or abstaining from sexual intercourse.

**How should pregnant women with male partners with Zika virus infection be counseled?**

Given the potential risks of maternal Zika virus infection, pregnant women whose male partners have or are at risk for Zika virus infection should consider abstaining from sexual intercourse or using condoms. Recommendations will be updated as more information becomes available.

## Laboratory Testing

**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.

**Is an immunoglobulin G (IgG) test commercially available?**

No. There is currently no commercially available FDA-cleared test

**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  $\geq 4$ -fold higher than dengue virus neutralizing antibody titers in serum by PRNT. 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.

### **Does a positive Zika virus IgM always indicate Zika virus infection?**

No, a positive IgM result can be difficult to interpret since cross-reactivity can occur with related flaviviruses (e.g., dengue, Japanese encephalitis, West Nile, yellow fever). A positive Zika virus IgM result may reflect: previous vaccination against a flavivirus (e.g., yellow fever); previous infection with a related flavivirus; or current infection with a flavivirus, including Zika virus.

### **Does a negative Zika virus RT-PCR always rule out Zika virus infection?**

No. During the first 7 days of symptom onset, viral RNA can often be identified in serum, and RT-PCR is the preferred test. However, viremia decreases over time, and a negative RT-PCR on serum collected 5-7 days after symptom onset does not preclude Zika virus infection. Serologic testing should be performed.

### **What should providers consider when ordering a test for Zika virus infection?**

Each clinical scenario is unique, and healthcare providers should consider all available information when ordering a test for Zika virus infection including patient travel history, history of flavivirus infection, vaccination history, ultrasound findings, and the presence of symptoms. They should work with their state, local, and territorial health departments for assistance interpreting test results.

### **How can providers order a Zika virus test for a patient who 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 \(http://www.cdc.gov/zika/hc-providers/diagnostic.html\)](http://www.cdc.gov/zika/hc-providers/diagnostic.html) webpage for information on how to obtain Zika testing.

### **Who should providers contact to facilitate testing and interpretation of results?**

For this information, healthcare providers should contact their state, local or territorial health department.

## **Zika and Pregnancy**

### **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 microorganisms, nutrition, and environment).

### **Is there any known association between maternal Zika virus infection and other adverse pregnancy outcomes?**

The full spectrum of 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?**

CDC recommends that pregnant women in any trimester should consider postponing travel to an area where Zika virus transmission is ongoing. If a pregnant woman 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.

### **How should pregnant women with male partners with Zika virus infection be counseled?**

Given the potential risks of maternal Zika virus infection, pregnant women whose male partners have or are at risk for Zika virus infection should consider abstaining from sexual intercourse or using condoms for the duration of pregnancy. Recommendations will be updated as more information becomes available.

### **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 be 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.

### **Who should be offered amniocentesis?**

Amniocentesis should be offered to pregnant women with recent travel to an area with Zika virus transmission, reporting 2 or more symptoms within two weeks of travel 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 healthcare 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  $\geq 15$  weeks of gestation is associated with lower rates of complications than those performed at earlier gestational ages ( $\leq 14$  weeks of gestation). However, the exact timing of amniocentesis should be individualized based on the patient's clinical circumstances. Referral to a 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 healthcare 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).

## **Asymptomatic Pregnant Travelers**

### **When should asymptomatic pregnant women with a history of travel be tested for Zika virus infection?**

Testing should be offered from 2 to 12 weeks after pregnant women return from travel to areas of ongoing Zika virus transmission. Information about serologic testing of asymptomatic persons is limited; on the basis of experience with other flaviviruses, we expect that antibodies will be present from 2 weeks after virus exposure and can persist for up to 12 weeks.

### **What does a negative Zika virus IgM mean?**

Although data on the performance of IgM serologic testing in asymptomatic persons is limited, on the basis of experience with other flaviviruses, when performed from 2 to 12 weeks after travel to areas of ongoing Zika virus transmission, a negative (IgM) result suggests that infection did not occur and could obviate the need for serial ultrasounds.

## **Pregnant Women Residing in Areas with Ongoing Transmission of Zika Virus**

### **Why is testing recommended for all pregnant women in areas with ongoing transmission of Zika virus?**

Pregnant women who reside in areas with ongoing transmission of Zika virus have an ongoing risk of maternal Zika virus infection throughout their pregnancy; therefore, symptomatic pregnant residents should be tested for Zika virus infection. Asymptomatic pregnant residents may be offered screening with serologic testing at the initiation of prenatal care and mid-second trimester. Local health officials should determine when to implement testing of asymptomatic pregnant women on the basis of information about levels of Zika virus transmission and laboratory capacity.

### **When should pregnant women in areas with ongoing transmission of Zika virus be tested?**

For pregnant women with symptoms consistent with Zika virus disease, testing is recommended during the first week of illness. For asymptomatic pregnant women, IgM testing is recommended at the initiation of prenatal care with follow-up IgM testing mid-second trimester.



**Does a prior negative Zika virus test result obviate the need for repeat testing if new symptoms consistent with Zika virus develop later on?** No. If new symptoms develop, a prior negative test for Zika virus does not rule out current infection. If new symptoms develop, a pregnant woman should be retested. During the first 7 days after symptom onset, viral RNA can often be identified in serum, and RT-PCR is the preferred test. However, viremia decreases over time, and a negative RT-PCR on serum collected 5-7 days after symptom onset does not exclude Zika virus infection. Serologic testing should be performed.

## Reproductive Age women in Areas of Ongoing Zika Virus

### **How should women of reproductive age who reside in areas of ongoing Zika virus transmission be counseled?**

Healthcare providers should discuss reproductive life plans, including pregnancy intentions and timing with women of reproductive age in the context of the potential risks of Zika virus transmission.

### **What is a reproductive life plan?**

A reproductive life plan helps a woman think about her goals for having or not having children and how to achieve these goals. A woman's plan depends on her personal goals and dreams.

Reproductive life plan worksheets are available online:

<http://www.cdc.gov/preconception/reproductiveplan.html>

(<http://www.cdc.gov/preconception/reproductiveplan.html>).

## Women in Areas of Ongoing Zika Virus Transmission Who Do Not Desire Pregnancy

### **What should health providers include in discussions with women who do not want to become pregnant?**

Healthcare providers should discuss strategies to prevent unintended pregnancy, including counseling on family planning and the correct and consistent use of effective contraceptive methods. Additionally, when choosing a contraceptive method, the prevention of sexually transmitted infections should also be considered, including the correct and consistent use of condoms.

## Women in Areas of Ongoing Zika Virus Transmission Who Desire Pregnancy

### **How should women living in areas with ongoing Zika virus transmission who plan to become pregnant be counseled?**

Healthcare providers should emphasize strategies to prevent mosquito bites and provide

preconception care, which should include a discussion about the potential risk of Zika virus infection in pregnancy, the signs and symptoms associated with Zika virus disease, and when to seek care.

### **Where can I find more information about preconception care?**

Preconception care aims to promote the health of women of reproductive age before conception and thereby improve pregnancy-related outcomes. More information about preconception care is available at: <http://www.cdc.gov/preconception/index.html>  
(<http://www.cdc.gov/preconception/index.html>)

## **Women with Laboratory-Confirmed Zika Virus Infection**

### **How should providers counsel women with current or previous laboratory-confirmed Zika virus infection about future pregnancy?**

Women of reproductive age with current or previous laboratory-confirmed Zika virus infection should be counseled that there is no evidence that prior Zika virus infection poses a risk of birth defects in future pregnancies. This is because the viremia is expected to last approximately one week in patients with clinical illness. There is no evidence that a fetus conceived after maternal viremia has resolved would be at risk for fetal infection.

## **Prenatal Diagnosis of Microcephaly**

### **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. Although microcephaly and intracranial calcifications are typically detected during ultrasounds in the late second and early third trimester of pregnancy, these findings might be detected as early as 18-20 weeks gestation. Microcephaly and intracranial abnormalities have been demonstrated in pregnancies with known Zika virus disease. Hence, additional ultrasounds might 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.

### **Is ultrasound safe in pregnancy?**

Ultrasound is performed during pregnancy when medical information is needed. It has been used during pregnancy for many years and has not been associated with adverse maternal, fetal, or neonatal outcomes. Ultrasound operators are trained to use the lowest power for the minimum duration of time to obtain the needed information. There is consensus among various national and international medical organizations (American College of Radiology, American College of Obstetricians and Gynecologists, and the Society of Maternal and Fetal Medicine) that ultrasound is safe for the fetus when used appropriately.

## **What prenatal ultrasound findings have been observed among infants with confirmed Zika virus infection?**

Brain abnormalities reported in infants with laboratory-confirmed congenital Zika infection include microcephaly and disrupted brain growth. Some infants with possible Zika virus infection have been found to have intracranial calcifications and abnormal eye findings. It is not known if Zika virus infection caused any of these abnormalities.

In one published report of two infants with Zika virus RNA detected by PT-PCR, brain anomalies detected on ultrasound included corpus callosal and vermian dysgenesis, enlarged cisterna magna, severe unilateral ventriculomegaly, agenesis of the thalami, cataracts, intracranial and intraocular calcifications.

## **How is microcephaly diagnosed prenatally?**

Microcephaly can be diagnosed during pregnancy with ultrasound (<http://www.cdc.gov/ncbddd/birthdefects/diagnosis.html>). Microcephaly is most easily diagnosed by ultrasound late in the second trimester or early third trimester of pregnancy.

## **How early can microcephaly be diagnosed during pregnancy?**

Microcephaly might be detected as early as 18-20 weeks of gestation however, detection by prenatal ultrasound can be challenging at this gestational age due to fetal position and fetal motion artifact. The optimal time to perform ultrasound screening for fetal microcephaly is not known. In the absence of microcephaly, the presence of intracranial calcifications before 22 weeks gestation might suggest a risk for the future development of microcephaly.

## **How accurately can ultrasound detect microcephaly with maternal Zika virus?**

The accuracy of ultrasound to detect microcephaly in the setting of maternal Zika virus is not known and will depend on many factors such as the timing of maternal infection relative to the timing of screening, severity of microcephaly, patient factors (e.g., obesity), gestational age, the equipment used, and the expertise of the person performing the ultrasound. Because the absence of fetal microcephaly and intracranial calcifications on ultrasound at one point in pregnancy does not exclude future microcephaly, additional ultrasounds may be considered at the discretion of the health care provider. As we get more information specifically related to Zika virus infection and microcephaly, we expect that more specific guidance for women and their healthcare providers will be developed.

## **If a prenatal ultrasound demonstrates microcephaly, how well does it predict microcephaly in the infant?**

The sensitivity of prenatal ultrasound for detection of microcephaly depends on a range of factors

(e.g., timing of screening, severity of microcephaly, patient factors). In a study of fetal microcephaly not caused by Zika virus infection, prenatally diagnosed microcephaly correlated with neonatal microcephaly approximately 57% of the time.

### **Can fetal MRI be used to detect microcephaly?**

Fetal MRI is not a screening tool and should be used only to answer specific questions raised by ultrasound or used in occasional specific high-risk situations. Interpretation of fetal MRI requires specialized expertise and has limited availability in the United States.

## **Dengue and Chikungunya**

### **Where can I find more information on dengue virus?**

Information on dengue is available online: <http://www.cdc.gov/dengue/>  
(<http://www.cdc.gov/dengue/>).

### **Where can I find more information on chikungunya?**

Information is available online: <http://www.cdc.gov/chikungunya/>  
(<http://www.cdc.gov/chikungunya/>).

For more information, please visit:

[CDC travel notice \(http://wwwnc.cdc.gov/travel/notices/\)](http://wwwnc.cdc.gov/travel/notices/)

[CDC Zika Virus Home Page \(http://www.cdc.gov/zika/prevention/index.html\)](http://www.cdc.gov/zika/prevention/index.html)

[CDC Zika Virus Health care Provider Q&A \(http://www.cdc.gov/zika/hc-providers/index.html\)](http://www.cdc.gov/zika/hc-providers/index.html)

[MMWR Clinical Guidance for Obstetrical Provider](http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1er.htm)

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National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) (<http://www.cdc.gov/ncezid>)

Division of Vector-Borne Diseases (DVBD) (<http://www.cdc.gov/ncezid/dvbd/index.html>)