ZIKA VIRUS AND PREGNANCY
Background

Zika belongs to the flavivirus family of viruses and is closely related to a number of other human pathogenic viruses, including the viruses that cause yellow fever, dengue fever, and chikungunya. These infections are spread via the bite of the *Aedes* species mosquito, which is found in many tropical and subtropical locations, including parts of the United States.1 Many people infected with the Zika virus will not exhibit any symptoms. Of those who do, most develop an acute febrile illness that lasts several days to a week and then resolves completely. Hospitalization is rare.1 The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis (red eyes).1

To date, the most critical clinical issue is the strong association between Zika infection in pregnancy and the development by the fetus of congenital abnormalities. The most concerning of these is microcephaly, in which an infant’s head is significantly smaller than children of the same age and gender.1 This condition is often associated with developmental delay and other neurological issues. Much is still unknown about the precise relationship between development of this condition and the preceding Zika infection. Additionally, in areas affected by Zika, the reports of Guillain-Barré syndrome (uncommon sickness of the nervous system) have increased.1

Researchers continue to work to understand more about the spread of the virus, as well as the impact to pregnant women and unborn fetuses.

Current Concern

Prior to 2015, there had been no outbreaks of Zika outside of Africa, Southeast Asia, and the Pacific Islands.1 In May 2015, the first confirmed case of infection was reported in Brazil, and cases have now been reported in numerous countries in Central and South America. The potential for local transmission in the United States exists and, indeed, has already been reported in Puerto Rico. The Centers for Disease Control and Prevention (CDC) is actively involved in monitoring the situation and developing improved case definitions and diagnostic test options. In addition, the CDC has issued a travel advisory recommending that pregnant women defer travel to areas where Zika transmission is ongoing.2

Zika Infection and Diagnosis

The diagnosis of Zika virus infection is made through molecular and serologic testing. Test methodologies include (1) reverse transcription-polymerase chain reaction (RT-PCR) for viral RNA and (2) immunoglobulin (IgG and IgM) ELISA and plaque reduction neutralization test (PRNT) for Zika virus antibodies.

Zika and Pregnancy

The CDC has issued interim guidelines for US health care providers who are caring for pregnant patients and women of reproductive age. Pregnant women who have travelled to areas with Zika virus infection and who are exhibiting Zika virus symptoms should be tested for Zika virus infection.1

Additionally, the CDC recommends that health care providers can be offered serologic testing for pregnant women with a history of travel to areas with Zika virus and who are asymptomatic (testing between 2 to 12 weeks after travel).1

The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine have also issued a Practice Advisory reiterating the CDC’s prevention strategies and current guidance for management of pregnant women who have been exposed and for women of reproductive age.4

What can pregnant patients do to prevent Zika infection?5

- Check CDC travel guidance; pregnant women should avoid travel to any area with Zika. www.cdc.gov/travel/page/zika-travel-information.
- Talk to her doctor or other health care provider first, if she must travel to an area with Zika.
- Prevent mosquito bites, including covering up arms and legs and using EPA-registered insect repellent, which is safe to use during pregnancy.
- Use latex condoms, the right way, every time or choose not to have any type of sex if the male partner has been in an area with Zika during the pregnancy.

What can health care providers do for pregnant patients?5

- Know the symptoms of Zika and ask patients about their travel history. The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis.
- Contact their state and local health departments for laboratory testing.
- Educate a pregnant woman and her partner on how to prevent Zika transmission.
- Call CDC and the state or local health department for clinical consultation. Notify state and local health departments when they have cases of Zika.
- Offer testing to pregnant women and others with symptoms of Zika who have traveled to areas with Zika. The CDC has made available testing algorithms and additional clinical guidance on their website for health care providers. Please visit www.cdc.gov for more information.
Testing for Zika infection: CDC Testing Algorithms

FIGURE 1. Updated interim guidance: testing algorithm*,†,§,¶ for a pregnant woman with possible Zika virus exposure,** not residing in an area with active Zika virus transmission#

* Testing is recommended for pregnant women with clinical illness consistent with Zika virus disease, including one or more of the following signs or symptoms: acute onset of fever, rash, arthralgia, or conjunctivitis during or within 2 weeks of travel or possible sexual exposure. Testing includes Zika virus reverse transcription-polymerase chain reaction (RT-PCR), and Zika virus immunoglobulin M (IgM) and neutralizing antibodies on serum specimens. More information is available at http://www.aphl.org/Materials/CDCMemo_Zika_Chik_Deng_Testing_011916.pdf. Because of the overlap of symptoms and areas where other viral illnesses are endemic, evaluate for possible dengue or chikungunya virus infection.

† Testing can be offered to pregnant women without clinical illness consistent with Zika virus disease. If performed, testing should include Zika virus IgM, and if IgM test result is positive or indeterminate, neutralizing antibodies on serum specimens. Testing should be performed 2–12 weeks after travel.

§ Laboratory evidence of maternal Zika virus infection: 1) Zika virus RNA detected by RT-PCR in any clinical specimen; or 2) positive Zika virus IgM with confirmatory neutralizing antibody titers that are ≥4-fold higher than dengue virus neutralizing antibody titers in serum. Testing is considered inconclusive if Zika virus neutralizing antibody titers are <4-fold higher than dengue virus neutralizing antibody titers.

¶ Fetal abnormalities consistent with Zika virus disease include microcephaly, intracranial calcifications, and brain and eye abnormalities. Fetal ultrasounds might not detect abnormalities until late second or early third trimester of pregnancy.

** Possible exposure to pregnant women without clinical illness consistent with Zika virus disease. If performed, testing should include Zika virus IgM, and if IgM test result is positive or indeterminate, neutralizing antibodies on serum specimens. Testing should be performed 2–12 weeks after travel.

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### LabCorp now offers a Zika virus RT-PCR test authorized by the FDA for emergency use.

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Zika Virus Comprehensive Profile, NAA, Serum and Urine</th>
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<tr>
<td>Test Number</td>
<td>139600</td>
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For more information about specimen collection, please refer to the online Test Menu at www.LabCorp.com.

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by authorized laboratories;
- This test has been authorized only for the detection of RNA from Zika virus and diagnosis of Zika virus infection, and not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.
Testing for Zika infection: CDC Testing Algorithms

FIGURE 2. Updated interim guidance: testing algorithm for a pregnant woman residing in an area with active Zika virus transmission, with or without clinical illness consistent with Zika virus disease.

* Tests for pregnant women with clinical illness consistent with Zika virus disease include Zika virus reverse transcription-polymerase chain reaction (RT-PCR), and Zika virus immunoglobulin M (IgM) and neutralizing antibodies on serum specimens. More information is available at http://www.aphl.org/Materials/CDCMemo_Zika_Chik_Deng_Testing_011916.pdf. Because of the overlap of symptoms and areas where other viral illnesses are endemic, evaluate for possible dengue or chikungunya virus infection. If chikungunya or dengue virus RNA is detected, treat in accordance with existing guidelines. Repeat Zika virus testing during pregnancy is warranted if clinical illness consistent with Zika virus disease develops later in pregnancy.

† Testing can be offered to pregnant women without clinical illness consistent with Zika virus disease. If performed, testing should include Zika virus IgM, and if IgM test result is positive or indeterminate, neutralizing antibodies on serum specimens. Results from serologic testing are challenging to interpret in areas where residents have had previous exposure to other flaviviruses (e.g., dengue, yellow fever) because of cross-reactivity with other flaviviruses.

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‖ Clinical illness is consistent with Zika virus disease if one or more signs or symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) are present.

References