



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.² 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. On July 29, 2016, the Centers for Disease Control and Prevention (CDC) reported the first cases of local mosquito-borne Zika virus transmission in the continental US (Florida). The 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 of the world 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 (IgM) ELISA and (3) plaque reduction neutralization test (PRNT) for Zika virus antibodies.

Zika and Pregnancy

On July 25, 2016, the CDC updated its interim guidelines for US health care providers who are caring for pregnant patients with possible exposure to Zika virus. The CDC noted that "All pregnant women in the United States and U.S. territories should be assessed for possible Zika virus exposure at each prenatal care visit."³ "Possible exposures to Zika virus include travel to or residence in an area with active Zika virus transmission, or sex with a partner who has traveled to or resides in an area with active Zika virus transmission without using condoms or other barrier methods to prevent infection."^{3**}

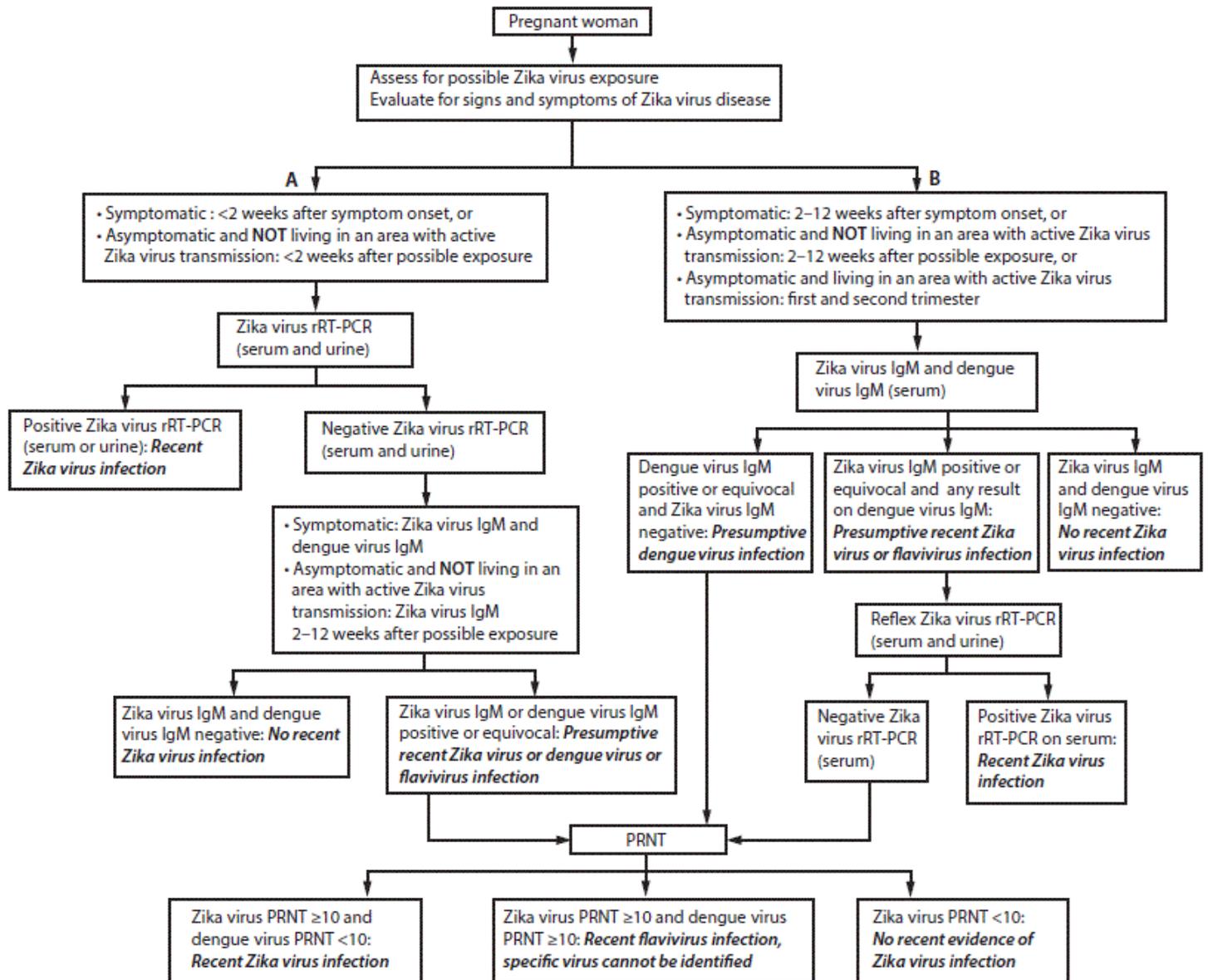
The clinical guidance also focuses on key points related to testing for symptomatic and asymptomatic pregnant women with exposure to Zika. Please see Figure 1 for "updated interim guidance: testing and interpretation recommendations" from the CDC for pregnant women with possible exposure to Zika virus.³

What can health care providers do for pregnant patients?⁴

- 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 about 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 Algorithm³

FIGURE 1. Updated interim guidance: testing and interpretation recommendations^{*,†,§,¶} for a pregnant woman with possible exposure to Zika virus — United States (including U.S. territories)³**



Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported. A pregnant woman is considered asymptomatic if these symptoms are NOT reported.

† Testing includes Zika virus rRT-PCR on serum and urine samples, Zika virus and dengue virus IgM, and PRNT on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (<http://www.cdc.gov/zika/laboratories/lab-guidance.html>). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

§ Dengue virus IgM antibody testing is recommended only for symptomatic pregnant women.

¶ If Zika virus rRT-PCR testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of an rRT-PCR negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (<http://wwwnc.cdc.gov/travel/notices/>), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission).

Note from LabCorp: Please contact your LabCorp representative about the dengue virus IgM test. Per the CDC, dengue virus IgM antibody testing is recommended only for symptomatic pregnant women.

Testing for Zika infection: CDC Clinical Management

TABLE. Clinical management of a pregnant woman with suspected Zika virus infection³

Interpretation of laboratory results*	Prenatal management	Postnatal management
Recent Zika virus infection	Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth. [†] Decisions regarding amniocentesis should be individualized for each clinical circumstance. [§]	Live births: Cord blood and infant serum should be tested for Zika virus by rRT-PCR, and for Zika IgM and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. Zika virus rRT-PCR and IHC staining of umbilical cord and placenta are recommended. [¶] Fetal losses: Zika virus rRT-PCR and IHC staining of fetal tissues are recommended. [¶]
Recent flavivirus infection; specific virus cannot be identified		
Presumptive recent Zika virus infection**	Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth. [†] Amniocentesis might be considered; decisions should be individualized for each clinical circumstance.	Live births: Cord blood and infant serum should be tested for Zika virus by rRT-PCR, and for Zika virus IgM and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. Zika virus rRT-PCR and IHC staining of umbilical cord and placenta should be considered. [¶] Fetal losses: Zika virus rRT-PCR and IHC staining of fetal tissues should be considered. [¶]
Presumptive recent flavivirus infection**		
Recent dengue virus infection	Clinical management in accordance with existing guidelines. ^{††}	
No evidence of Zika virus or dengue virus infection	Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome. [†] Fetal abnormalities present: repeat Zika virus rRT-PCR and IgM test; base clinical management on corresponding laboratory results. Fetal abnormalities absent: base obstetric care on the ongoing risk for Zika virus exposure risk to the pregnant woman.	

Abbreviations: CSF = cerebrospinal fluid; IgM = immunoglobulin M; IHC = immunohistochemical; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* Refer to the previously published guidance for testing interpretation (<http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm>).

† Fetal abnormalities consistent with congenital Zika virus syndrome include microcephaly, intracranial calcifications, and brain and eye abnormalities.

§ Health care providers should discuss risks and benefits of amniocentesis with their patients. It is not known how sensitive or specific rRT-PCR testing of amniotic fluid is for congenital Zika virus infection, whether a positive result is predictive of a subsequent fetal abnormality, and if it is predictive, what proportion of infants born after infection will have abnormalities.

¶ Refer to pathology guidance for collection and submission of fetal tissues for Zika virus testing for detailed information on recommended specimen types (<http://www.cdc.gov/zika/laboratories/test-specimens-tissues.html>).

** rRT-PCR or PRNT should be performed for positive or equivocal IgM results as indicated. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (<http://www.cdc.gov/zika/laboratories/lab-guidance.html>). Because of the overlap of symptoms and areas where other viral illnesses are endemic, evaluate for possible dengue or chikungunya virus infection.

†† http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf

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

Test Name	Zika Virus Comprehensive Profile, NAA, Serum and Urine	Test Name	Zika Virus MAC-ELISA, IgM, Serum
Test Number	139600	Test Number	163049
For more information about specimen collection, please refer to the online Test Menu at www.LabCorp.com .		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 Emergency Use Authorization (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.

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by authorized laboratories;
- This test has been authorized only for the 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.



www.LabCorp.com

References

1. Centers for Disease Control and Prevention (CDC). Zika: The Basics of the Virus and How to Protect Against it. Available at: www.cdc.gov/zika. Accessed May 23, 2016.
2. Centers for Disease Control and Prevention (CDC). Zika Virus. Available at: www.cdc.gov/zika/geo/index.html. Accessed May 23, 2016.
3. 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*. ePub: 25 July 2016. DOI: <http://dx.doi.org/10.15585/mmwr.mm6529e1>.
4. Centers for Disease Control and Prevention (CDC). CDC's Response to Zika: What can be done. Available at: www.cdc.gov/zika. Accessed May 23, 2016.