



NEW YORK CITY DEPARTMENT OF
HEALTH AND MENTAL HYGIENE
Mary T. Bassett, MD, MPH
Commissioner

2016 DOHMH ADVISORY #11: New Zika Virus Clinical Guidance Available

Please share with your colleagues in Obstetrics/Gynecology, Maternal/Fetal Medicine, Internal Medicine, Family Medicine, Emergency Medicine, Urgent Care, Pediatrics, Neonatology, Infectious Disease and Neurology:

- **Clinical guidance materials are available from the NYC Health Department for evaluation of Zika virus infection in infants and counseling of pregnant women at risk for Zika virus infection.**
- **A conference call on Zika virus for prenatal providers will be held on Thursday, May 12, noon-1 PM.**

May 11, 2016

Dear Colleagues,

The New York City Health Department has developed guidance on clinical care for persons with or at risk for Zika virus infection. The following documents are attached, and are also available on our website:

- New: "[Congenital Zika Virus Infection: Interim Guidance for Clinical Evaluation.](#)"
- Updated: "[Interim Guidance on Counseling Pregnant Patients With or at Risk for Zika Virus.](#)"

We invite providers who care for pregnant women to participate in a conference call regarding Zika virus infection and pregnancy. The call will provide:

- Updated information on Zika virus infection and associated birth defects
- Details about who should be tested and how to obtain testing for these patients
- An opportunity to ask questions

DATE/TIME: Thursday, May 12, noon

CALL-IN NUMBER: (800) 611 1148

English Call Registration Link: (<https://www.surveymonkey.com/r/GD6VS2W>)

For additional information on Zika virus, visit:

<http://www1.nyc.gov/site/doh/health/health-topics/zika-virus.page>. You may also call the 866-692-3641 to discuss a specific case or ask questions about testing. We appreciate your continued diligence and cooperation as NYC responds to Zika virus.

Sincerely,

Jay K. Varma, MD
Deputy Commissioner
Division of Disease Control



Congenital Zika Virus Infection: *Interim Guidance for Clinical Evaluation*

I. INTRODUCTION

Congenital Zika virus infections result from intrauterine transmission of the virus from mother to fetus during pregnancy. Zika causes a wide range of adverse perinatal outcomes, including intrauterine fetal demise, microcephaly, other central nervous system (CNS) abnormalities, intrauterine growth retardation, and abnormal amniotic fluid volume.¹ The incidence of these adverse outcomes among infected women is unknown.

Infants with possible congenital Zika virus infection include those born to mothers who, while pregnant, either traveled to or resided in an area* with ongoing Zika virus transmission OR had condomless sex with a partner who traveled to or resided in an area with ongoing Zika virus transmission. The decision to evaluate and test such infants should be guided by:

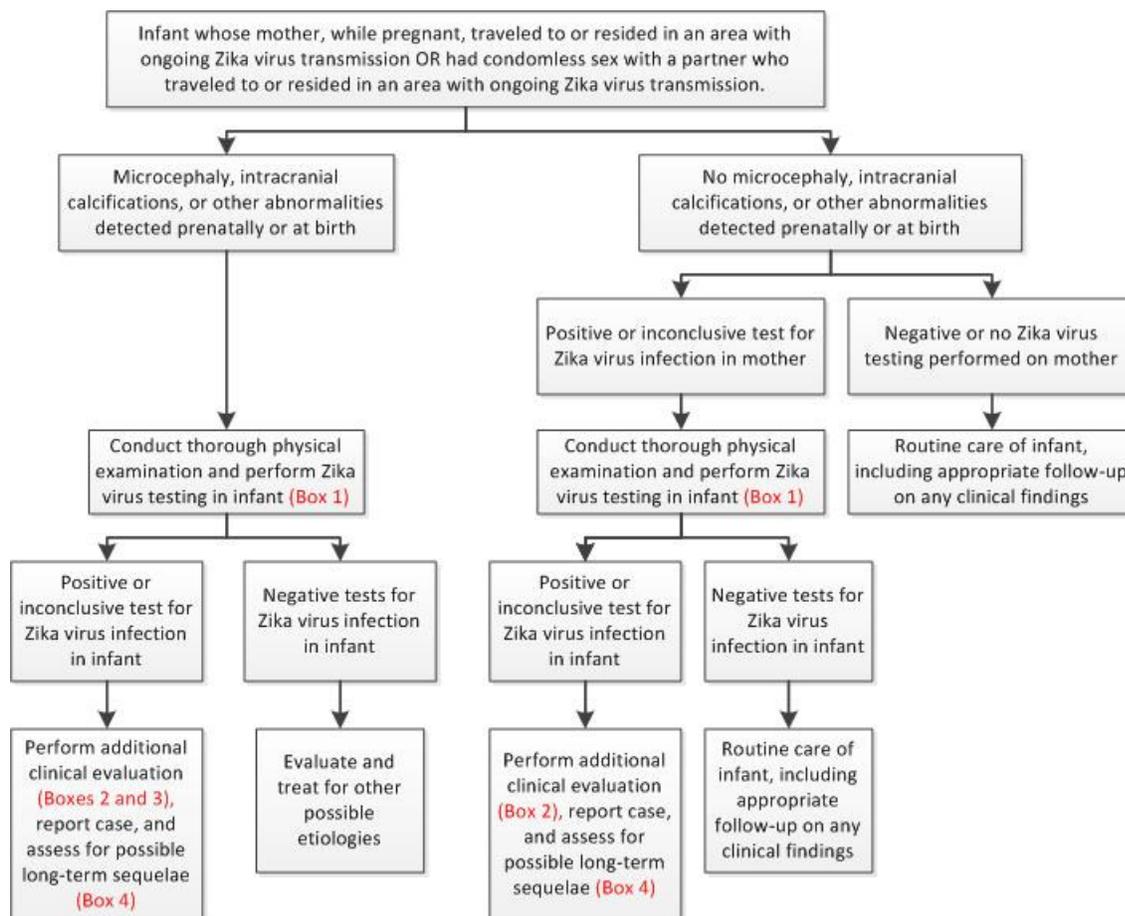
- i. Whether the infant had microcephaly, intracranial calcifications, or other abnormalities detected prenatally or at birth
- ii. The mother's Zika virus testing results

See the **Figure** for more information on which infants require evaluation and testing. Infants who meet the criteria for evaluation require:

- Zika virus testing
- Review of previous prenatal ultrasounds and maternal Zika virus testing
- A thorough newborn physical examination, with assessment of head (occipitofrontal) circumference, length, and weight

¹ Rasmussen, S. et al., NEJM Apr 13, 2016 <http://www.nejm.org/doi/full/10.1056/NEJMSr1604338>

*Areas with Zika virus transmission are listed on the CDC website at <http://wwwnc.cdc.gov/travel/page/zika-travel-information>.

Figure. Interim guidelines for evaluating infants with possible congenital Zika virus infection. ^{†§¶}

[†]Microcephaly defined as occipitofrontal circumference less than the third percentile for gestational age and sex based on standard growth curves not explained by other etiologies.

[§]Laboratory evidence of Zika virus infection includes 1) detectable Zika virus, Zika virus RNA, or Zika virus antigen 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 or cerebrospinal fluid. Testing is considered inconclusive if Zika virus neutralizing antibody titers are < 4 -fold higher than dengue virus neutralizing antibody titers.

[¶]For infants, perform reverse transcription–polymerase chain reaction (RT-PCR) testing for Zika virus RNA and Zika virus IgM and neutralizing antibodies on serum collected from the umbilical cord or directly from infant within 2 days of birth, if possible. If cerebrospinal fluid is obtained for other reasons, test for Zika virus RNA, Zika virus IgM and neutralizing antibodies. Consider histopathologic evaluation of the placenta and umbilical cord with Zika virus immunohistochemical staining on fixed tissue and Zika virus RT-PCR on fixed and frozen tissue. More information on laboratory testing for Zika virus infection is available at <http://www.cdc.gov/zika/state-labs/index.html>.

Adapted from: Fleming-Dutra, K. et al., MMWR Feb 26, 2016 (<http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm>)

Because information on the effects of congenital Zika virus infection is limited, health care providers should exercise clinical judgment in the assessment of newborns with abnormalities other than microcephaly who were born to mothers exposed to Zika virus during pregnancy. For these infants, health care providers should consider testing the mother before testing the infant. Further clinical evaluation may also be indicated for infants born to Zika-exposed but untested mothers as well as for infants who test negative for Zika but are born to Zika-positive mothers.

These guidelines will be updated as additional information becomes available.

II. DIAGNOSTIC EVALUATION: Frequently Asked Questions

1. What are the current recommendations for laboratory testing of newborns and infants with possible congenital Zika virus infection?

Get Pre-Approval of Lab Testing from DOHMH. To test patients who are NYC residents, including newborns and infants with possible congenital Zika virus infection, providers must obtain pre-approval from DOHMH. To do so, providers must call 866-692-3641 (the DOHMH Provider Access Line), Monday to Friday, 9 a.m. to 5 p.m. Staff at this number can assist with determination of whom to test and which specimens are required. The Provider Access Line is available during non-business hours for urgent or emergent consultation with a DOHMH physician. For more information on this process, including links to relevant forms, please refer to the [quick reference guide](#) and [DOHMH Health Alert #7](#).

BOX 1. Recommended Zika virus laboratory testing for newborns and infants with possible congenital Zika virus infection:

- Test serum for Zika virus RNA, Zika virus immunoglobulin M (IgM), and neutralizing antibodies. Collect the initial sample either from the umbilical cord or directly from the infant within two days of birth, if possible.
- If cerebrospinal fluid is obtained for other studies, test for Zika virus RNA, Zika virus IgM and neutralizing antibodies.
- Consider histopathologic evaluation of the placenta and umbilical cord with Zika virus immunohistochemical staining on fixed tissue and Zika virus reverse transcription-polymerase chain reaction (RT-PCR) on fixed and frozen tissue.
- If not already performed during pregnancy, test mother’s serum for Zika virus IgM and neutralizing antibodies.

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR 2016; 65:63–7.
<http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm>

*Find more information on laboratory testing for Zika virus infection at cdc.gov/zika/state-labs

2. What does “laboratory evidence of Zika virus infection” include?

1) Detectable Zika virus, Zika virus RNA, or Zika virus antigen in any clinical specimen.

OR

2) Positive results of serologic testing consisting of IgM and neutralizing antibodies in serum or cerebrospinal fluid

III. CLINICAL EVALUATION: Frequently Asked Questions

1. How do I evaluate newborns and infants with positive or inconclusive Zika virus test results?

BOX 2. Recommended clinical evaluation for newborns and infants with positive or inconclusive Zika virus test results:

- Perform a comprehensive physical examination, including careful measurement of head circumference, length, weight and assessment of gestational age.
- Evaluate for neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly and rash or other skin lesions. Perform full-body photographs and photographic documentation of any rash, skin lesions or dysmorphic features. If an abnormality is noted, consult with an appropriate specialist.
- Perform a cranial ultrasound, unless prenatal ultrasound results from the third trimester demonstrated no abnormalities of the brain.
- Evaluate hearing by evoked oto-acoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth. Refer infants with abnormal initial hearing screens to an audiologist for further evaluation.
- Perform an ophthalmologic evaluation, including examination of the retina, either before discharge from the hospital or within 1 month after birth. Refer infants with an abnormal initial eye evaluation to a pediatric ophthalmologist for further evaluation.
- Perform other evaluations specific to the infant's clinical presentation.

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. *MMWR* 2016; 65:63–7.
<http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm>

2. What additional evaluation is recommended for newborns and infants with possible congenital Zika virus infection and [microcephaly](#), intracranial calcifications, or other abnormalities?

Box 3. For Zika-exposed infants with microcephaly, intracranial calcifications or abnormal neurologic findings, additional evaluation includes:

- Consult with a clinical geneticist or dysmorphologist.
- Consult with a pediatric neurologist to determine appropriate brain imaging and additional evaluation (e.g., ultrasound, computerized tomography scan, magnetic resonance imaging or electroencephalogram).
- Test for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection and herpes simplex virus infections. Consider consulting a pediatric infectious disease specialist.
- Perform a complete blood count with platelet count and liver function and enzyme tests, including alanine aminotransferase, aspartate aminotransferase and bilirubin.
- Consider genetic and other teratogenic causes based on additional congenital anomalies that are identified through clinical examination and imaging studies.

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. *MMWR* 2016; 65:63–7.
<http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm>

3. How is microcephaly diagnosed?

Microcephaly is diagnosed when an infant's head is smaller than expected as compared to infants of the same age (or gestational age) and sex. Microcephaly, as defined by CDC in the setting of evaluating for possible congenital Zika virus infection, is a **head circumference less than the third percentile**, based on standard growth charts (e.g., Fenton, Olsen, CDC, or WHO growth curves) for sex, age and gestational age at birth. For a diagnosis of microcephaly, the head circumference should be disproportionately small in comparison with the length of the infant and not explained by other etiologies (e.g., other congenital disorders).

4. When should head circumference (HC) be measured?

The optimal time to measure HC is 24 to 36 hours after birth, when molding of the head by the birth canal has subsided. Measuring the HC earlier may not accurately reflect brain volume.

5. What is the recommended long-term follow up for infants with possible congenital Zika virus infection (as defined on page 1)?

Box 4: For all infants with possible congenital Zika virus infection, recommended long-term follow-up:

- Report case to DOHMH and monitor for additional guidance. To report, call DOHMH’s Provider Access Line at 1-866-692-3641.
- Consider conducting **additional hearing screen at age 6 months**. Refer any child with developmental delay for an audiologic evaluation. Ensure that appropriate follow-up of abnormal newborn hearing screening has occurred.
- Carefully evaluate head circumference and developmental characteristics and milestones throughout the first year of life, in consultation with appropriate medical specialists (e.g., pediatric neurology, developmental-behavioral pediatrics, physical and speech therapy).

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR 2016; 65:63–7.
<http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm>

6. If a mother had Zika virus infection during pregnancy but her newborn tests negative for Zika virus, what is recommended for additional follow-up?

In the absence of abnormal findings on examination, the infant should receive routine pediatric care, including measurement of growth and development and appropriate evaluation and follow-up for any clinical findings that arise. If the newborn has abnormal findings on examination, perform diagnostic testing for other causes of the newborn’s conditions, including testing for other congenital viral infections if indicated. Guidance for following infants born to Zika virus-infected mothers is below (Table).

Table. Congenital Zika Virus Infection Monitoring Assessments.

Assessments	Age 0-28 days		Age ≥28 days		
	No microcephaly, intracranial calcifications, or other abnormalities	Microcephaly, intracranial calcifications, or other abnormalities	2 months	6 months	12 months
Measurements					
Weight	+	+	+	+	+
Length	+	+	+	+	+
Head Circumference	+	+	+	+	+
Gestational Age Assessment	+	+	+	+	+
Physical Exam	+	+	+	+	+
Neurological					
Dysmorphisms*					
Hepatosplenomegaly					
Rash/Skin Lesions*					
Cranial Ultrasound§	+	+			
Hearing Evaluation (OAE or ABR)	+	+		+	
Ophthalmology	+	+			
Genetics Consultation		+			
Pediatric Neurology Consultation		+			
Pediatric Infectious Disease Consultation		+			
Tests					
CBC with Platelets		+			
Liver Functions		+			
Other Congenital Infections/TORCH		+			
Developmental Assessment	+	+	+	+	+

*Photographs should be obtained.

§Unless third trimester showed no abnormality.

Adapted from: Fleming-Dutra, K. et al., MMWR Feb 26, 2016 (<http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm>) and Staples, J.E. et al., MMWR Jan 29, 2016 (<http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm>).

IV. OUTCOME/PROGNOSIS: Frequently Asked Questions

1. What is the prognosis for newborns/infants with congenital Zika virus infection?

The prognosis for newborns/infants with congenital Zika virus infection is not known.

2. What is the link between Zika virus and microcephaly?

Zika causes microcephaly and other serious brain anomalies.²

3. If a mother infected with Zika virus near the time of delivery passes the virus to her newborn at birth, can the baby develop microcephaly?

We do not know whether a newborn who gets Zika virus at birth will develop microcephaly after birth. There have been no reports of Zika virus infection around the time of birth leading to microcephaly in infants.

We do know that babies can develop microcephaly after birth, if their head growth slows or their brain fails to develop after birth. Such cases of microcephaly may not be linked to Zika.

4. Is there any information on neurocognitive outcomes in neonates if they are exposed to Zika virus during labor and delivery or after birth?

There is currently no information on neurocognitive outcomes in neonates exposed to Zika virus peripartum, such as during labor and delivery or after birth. Based on evidence from other flaviviruses, such as West Nile virus and dengue virus, a range of poor outcomes have been observed.

5. What birth defects have been reported in infants with *confirmed* congenital Zika virus infection?

Brain abnormalities reported in infants with laboratory-confirmed congenital Zika infection include microcephaly and disrupted brain growth. Two recent publications of maternal Zika cases from French Polynesia³ and Brazil⁴ indicate a wide range of risk for abnormal perinatal outcomes, including intrauterine growth restriction, cerebral calcifications, abnormal cerebral and umbilical arterial blood flow, oligohydramnios, anhydramnios, and third-trimester fetal death.

6. What birth defects have been reported in infants with *suspected* congenital Zika virus infection?

A [report of 35 infants with microcephaly](#) who were born during a 2015 outbreak of Zika virus infection in Brazil described the following brain abnormalities: intracranial calcifications, ventriculomegaly and neuronal migration disorders (lissencephaly and pachygyria). Other anomalies included congenital contractures and clubfoot. Some infants with possible Zika virus infection have been found to have intracranial calcifications and abnormal eye findings. An important distinction is that neither these infants nor their mothers had laboratory-confirmed Zika virus; however, 75 percent of the mothers reported symptoms consistent with Zika virus.

² Rasmussen, S. et al., NEJM Apr 13 <http://www.nejm.org/doi/full/10.1056/NEJMSr1604338>

³ Cauchemez, S et al., Lancet Mar 12 2016 [http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)00651-6.pdf](http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)00651-6.pdf)

⁴ Brazil P., et al NEJM Mar 4, 2016 <http://www.nejm.org/doi/full/10.1056/NEJMoa1602412>

7. What is the CDC Pregnancy Registry?

The CDC's **U.S. Zika Pregnancy Registry** collects information on Zika-infected pregnant women and their infants to better understand the range of pregnancy and infant outcomes. DOHMH will participate in this effort by collecting information about women infected during pregnancy and will follow up with the women through pregnancy outcome and the first 12 months of their infants' lives. DOHMH will collect this information from obstetric and pediatric healthcare providers and submit these data, without identifying information, to CDC. To report cases of suspected congenital Zika infection to DOHMH, call the Provider Access Line at 1-866-692-3641. Information on the registry can be found at www.cdc.gov/zika/hc-providers/registry.



NEW YORK CITY DEPARTMENT OF

HEALTH AND MENTAL HYGIENE

Mary T. Bassett, MD, MPH

Commissioner

Interim Guidance on Counseling Pregnant Patients With or at Risk for Zika Virus

(Last edited April 22, 2016)

Background

An outbreak of Zika virus is currently expanding in South and Central America, Mexico, Pacific Islands and the Caribbean. Although illness due to Zika virus infection is usually mild, congenital infection with Zika virus can cause microcephaly and other severe fetal brain defects.¹ The full spectrum of Zika virus infection in the fetus and infant has not yet been determined, but is under study.

To date, there has been no vector-borne local transmission of Zika virus in the continental United States, though this may change in the spring and summer when mosquitoes are more active. Mosquito surveillance in New York City will be conducted to learn if Zika virus circulates within local mosquito populations.

Because travel between Zika-affected areas and New York City is common, New York City health care providers will continue to encounter patients who have, or are at risk for, Zika virus infection. We recommend that providers ask **ALL** pregnant patients about travel during pregnancy, and plans for future travel, to identify patients at risk for Zika infection during pregnancy, and to provide guidance on prevention and testing. In addition, because Zika virus can be transmitted by an infected male to their sexual partner, we recommend asking about travel among male sexual partners of pregnant women. The Centers for Disease Control and Prevention (CDC) recommend that pregnant women with male partners infected with or potentially exposed to Zika virus either abstain from sex or use condoms correctly and consistently for the duration of their pregnancy during vaginal, anal, or oral sex.

This document includes information that providers can use when counseling pregnant patients on prevention of Zika virus infection, diagnostic testing for infection, and the possible effects of infection during pregnancy. The most recent information on Zika virus infection is summarized.

We recognize that it is challenging to counsel patients when the full spectrum of effects of Zika virus infection during pregnancy remains unknown. However, providing the latest information available will enable patients to make the best decisions possible, taking into account their own values, beliefs, and personal considerations.

Because information on the epidemiology and clinical spectrum of Zika virus infection is changing rapidly, providers should check the links below for updated information. This document will be updated periodically as new information becomes available.

For updated information:

- Patient information and educational materials <http://www1.nyc.gov/site/doh/health/health-topics/zika-virus.page>
- CDC Zika and pregnancy page <http://www.cdc.gov/zika/hc-providers/index.html>
- Information for Health Care Professionals on the Health Department's Zika Virus website: <http://www1.nyc.gov/site/doh/providers/reporting-and-services.page>
- Diagnostic testing and specimen collection: <http://www1.nyc.gov/site/doh/providers/reporting-and-services.page> .

- Reporting to the Health Department: Providers should report the following to the New York City Health Department (1-866-692-3641) within 24 hours:
 - Microcephaly or intracranial calcifications diagnosed prenatally or at birth in an infant or fetus whose mother may have been exposed to Zika virus during pregnancy (through travel or sex).
 - Persons with Guillain-Barré syndrome (GBS) who traveled to an area with Zika virus transmission within 4 weeks of GBS onset.

Providers can also call the Provider Access Line at 1-866-692-3641 with questions.

Providers should monitor the New York City Health Department’s Health Alerts and check www.nyc.gov/health and www.cdc.gov for updates as they become available. To sign up for the New York City Health Alert Network as a new user, go to <https://a816-healthpsi.nyc.gov/FIM/signup.aspx>.

Prevention of Zika virus infection

1. How can infection of pregnant women be prevented?

Zika virus is primarily transmitted to humans by *Aedes* mosquitoes. Other documented modes of transmission include sexual transmission, intrauterine and intrapartum transmission, and, theoretically, blood transfusions and tissue transplants. However, the vast majority of cases result from mosquito-borne transmission.

Since Zika virus is primarily transmitted by mosquitoes and there is currently no vaccine or medication to prevent infection, the most important means of prevention is avoiding mosquito bites. **Therefore, CDC recommends that all pregnant women consider postponing travel to areas where Zika virus is spreading.** If that is not possible, encourage patients to prevent mosquito bites during travel by using an Environmental Protection Agency-approved insect repellent, staying in air-conditioned or well-screened environments (or if that is not possible, using a permethrin-treated bed net), and covering up exposed skin as much as possible when outdoors. Importantly, *Aedes* mosquitoes bite all day and not only at dusk/nighttime. Many effective repellents are safe during pregnancy. Additional information on mosquito repellents and other ways of preventing mosquito bites may be found at: <http://wwwnc.cdc.gov/travel/page/avoid-bug-bites>.

Because sexual transmission of Zika virus is also possible, steps to prevent transmission from an infected partner to a pregnant woman should be taken. Pregnant women whose male partners live in or have traveled to a Zika-affected area should consider abstaining from sex for the duration of the pregnancy, or, alternatively, using a condom correctly and consistently for every episode of vaginal, anal, or oral sex for the entire pregnancy.

2. How long after traveling to areas with ongoing Zika transmission should a woman wait before trying to become pregnant?

CDC recently published detailed guidance on timing of pregnancy for both men and women who traveled to Zika-affected areas.² CDC recommends that women who have Zika virus infection wait at least 8 weeks after symptom onset to attempt conception, and men with Zika virus infection wait at least 6 months after symptom onset to attempt conception. Women and men with possible exposure to Zika virus (through travel or sex), but without clinical illness, should wait at least 8 weeks after exposure to attempt conception.

After viremia has resolved in a woman attempting to conceive, there is no evidence to suggest that the pregnancy will be affected. However, data to answer this question for Zika are limited. (See **latest guidance from CDC** at: <http://www.cdc.gov/mmwr/volumes/65/wr/mm6512e2.htm>).

Testing for Zika virus infection

1. Who should be offered testing for Zika virus?

The New York City Health Department recommends that providers offer testing to all pregnant women, whether or not they had symptoms compatible with Zika (fever, maculopapular rash, non-purulent conjunctivitis, or arthralgias) who traveled to an area with Zika virus transmission while pregnant, and all pregnant women who have had any act of unprotected sex (vaginal, anal, oral) with a male partner who lives in or has traveled to an area with Zika virus transmission. Testing should also be offered to nonpregnant persons who develop Zika-compatible symptoms within 4 weeks of travel to an area with Zika virus transmission. For information on how to obtain testing for a patient, see: <http://www1.nyc.gov/site/doh/providers/reporting-and-services.page>.

2. Why should providers offer Zika virus testing for pregnant women?

It is important to diagnose Zika virus infection during pregnancy because the information may guide monitoring and clinical decision-making for the remainder of the pregnancy. Negative testing may also offer some reassurance for a pregnant woman who has traveled to a Zika affected area or has had possible sexual exposure, though the level of reassurance will depend on when the specimens were collected in relation to the exposure. Not all patients who are tested will have a definitive result, since positive results may be due to exposure to other flavivirus infections (e.g., dengue, West Nile), and negative results could be due to obtaining specimens too soon after exposure.

3. How can I arrange for my patient to get the Zika test?

Providers must call the Health Department through the Provider Access Line (1-866-692-3641) to arrange testing. Submitters must follow laboratory guidelines (See the Zika Virus Provider page at <http://www1.nyc.gov/site/doh/providers/reporting-and-services.page>).

Providers will be asked to collect 2 serum specimens and a urine specimen from all pregnant patients with a travel history to a Zika-affected area or with possible sexual exposure. Testing will include serological testing for Zika virus for all patients, and reverse transcriptase-polymerase chain reaction (RT-PCR) testing of serum and urine for Zika virus for patients whose specimens were obtained within 4 weeks of symptom onset (if symptomatic) or within 6 weeks of last possible exposure (if asymptomatic). Also, a follow-up serum specimen, collected approximately 3 weeks after the first serum, will be necessary to complete testing for many patients.

4. How long will it take to get test results?

Results of RT-PCR testing should be available within approximately 1 week of the specimen arriving at the laboratory. Serological test results may take several weeks and, for many patients, will need to be repeated (i.e., convalescent specimen) to determine whether infection was due to Zika or another flavivirus, such as dengue or West Nile. It will take several additional weeks to obtain results of the second blood specimen, which should be

collected at least 3 weeks after the first specimen. If serological test results are not received after 5-6 weeks, providers should call the Provider Access Line (1-866-692-3641) for follow-up.

5. How will I receive results for Zika testing?

The New York City Health Department will immediately report all Zika positive RT-PCR or serological results by phone to the submitting provider. Zika test results will also be faxed to the provider or facility listed as the submitter when performed in the city public health laboratory, and results will be mailed when testing occurs at the state public health laboratory. Each test result (RT-PCR on serum, RT-PCR on urine, MAC ELISA, MIA, and, if performed, PRNT) is forwarded to the provider as soon as it is available; thus, ordering providers may receive a series of multiple individual test results from both the city and state public health laboratories.

6. What do the results mean?

See 2016 DOHMH Advisory #5: Diagnostic Testing for Zika Virus and Interpretation of Results at <http://www1.nyc.gov/assets/doh/downloads/pdf/cd/zika-advisory5.pdf>.

7. What if testing is equivocal or inconclusive?

Due to the limitations of currently available tests for Zika, it is possible to have an equivocal result. Additional testing may be required to distinguish whether positive results are due to Zika infection, infection with another flavivirus (e.g., dengue or West Nile), or previous vaccination against flavivirus infection (i.e., yellow fever or Japanese encephalitis viruses). The timing of infection may be difficult to ascertain in some cases, further complicating interpretation of results. Pregnant women with equivocal results should be considered potentially infected and offered the same follow-up during the course of their pregnancy as pregnant women with positive results.² The NYC Health Department is available for consultation on interpretation of test results by calling the Provider Access Line (1-866-692-3641).

Inconclusive results may include patients who are tested several months or more after last exposure, when RT-PCR and IgM would likely be negative, or in cases when serological cross-reactivity occurs with other flaviviruses (e.g., if the patient had a previous dengue infection).

8. If Zika testing has not occurred or test results are pending at the time of delivery, what additional steps should be taken?

Please call the NYC Provider Access Line at 1-866-692-3641 to obtain further guidance. In some instances, depending on whether the mother had symptoms compatible with Zika or whether there were concerning prenatal findings, the Health Department may recommend collection of additional specimens (e.g., serum from cord blood, placental tissue, and/or fetal specimens in cases of fetal demise) to test for congenital infection.

9. What happens if I have a patient who meets criteria for Zika virus testing over the weekend or during evening hours?

Routine requests for approval of Zika testing (e.g., asymptomatic pregnant woman or person with Zika-like symptoms after travel to an affected area) can only be processed during regular business hours. Call the NYC Provider Access Line at 1-866-692-3641 Monday-Friday, 9am-5pm. Consultation with the Health Department for urgent matters (e.g., infant born with microcephaly to a mother who traveled to a Zika-affected area while pregnant) is available at all times, via the same number (1-866-692-3641).

Management of Pregnant Patients Following Zika Virus Testing

1. What is known about the effect of Zika virus infection during pregnancy?

There is no evidence that pregnant women are more susceptible to Zika virus infection, or experience more severe symptoms during pregnancy. However, Zika virus is a cause of microcephaly and other severe fetal brain and eye defects. The full spectrum of effects of congenital Zika virus infection has not yet been described but is under study. Severe congenital neurological complications have been documented in fetuses infected throughout pregnancy; it is unknown whether the risk to the fetus changes if Zika infection occurs at different times during pregnancy.

2. What type of follow-up should be offered for a pregnant woman following a Zika virus test?

A pregnant woman with positive or equivocal Zika virus diagnostic test results does not necessarily have an infected fetus; the proportion of fetuses with congenital infection is unknown. The virus may also cause transient infection of the fetus, or have a teratogenic effect, even if congenital infection does not occur. Referral to a maternal fetal medicine (MFM) specialist is recommended in all cases of possible maternal Zika virus infection. The specialist to whom the patient is referred should be informed that the patient is Zika positive or Zika inconclusive so that recommended follow-up testing can be performed. Ongoing clinical evaluations, such as with serial ultrasounds, interpretation of laboratory test results, and guidance from the MFM specialist enable patients to arrive at appropriately informed decisions about how best to manage their pregnancies.

Continued care with a general prenatal care provider is needed in close coordination with this specialty care. The currently recommended follow-up for a pregnant woman who is continuing her pregnancy and has a positive or equivocal Zika test results includes:

- Referral to an MFM specialist
- Serial fetal ultrasounds every 3-4 weeks, and
- Test maternal and infant specimens upon delivery, or of fetal tissues in the event of spontaneous or elective termination of pregnancy, to determine if congenital infection was present

3. What are the recommendations regarding amniocentesis?

Much remains unknown: the sensitivity and specificity of RT-PCR testing of amniotic fluid for congenital Zika virus infection; whether a positive maternal PCR result is predictive of subsequent fetal abnormality; and, if predictive, the proportion of infants that will have abnormalities following intrauterine exposure. For pregnant women with a positive travel history or possible sexual exposure; those with positive or equivocal Zika testing; or those with ultrasound findings consistent with Zika-related effects, such as microcephaly or calcifications, amniocentesis for Zika RT-PCR testing can be considered on a case-by-case basis.¹ Amniocentesis should not be performed before 15 weeks gestation. If amniocentesis is done for other reasons, amniotic fluid should also be sent for Zika virus RT-PCR testing.¹ For testing of amniotic fluid, providers should contact the NYC Provider Access Line at 1-866-692-3641 for guidance on how to collect and submit specimens to the NYC Public Health Laboratory.

4. What does a positive result of RT-PCR testing on amniotic fluid mean?

It is not yet known what a positive RT-PCR test on amniotic fluid means. The sensitivity and specificity of RT-PCR test for amniotic fluid is currently unknown. It is also unknown whether pregnancies with PCR-positive amniotic fluid are more likely to have serious fetal anomalies or other poor outcomes, compared with Zika virus infected pregnant women who have PCR-negative amniotic fluid tests.²

5. What are the recommendations for ultrasound?

Ultrasound imaging is recommended to detect possible fetal anomalies that may be associated with Zika virus infection, including brain abnormalities. In addition to routine ultrasounds during prenatal care, serial ultrasounds are recommended to assess fetal growth and anatomy every 3-4 weeks in pregnant women testing positive for Zika virus.² Establishing accurate dating with early ultrasound and date of last menstrual period is particularly important because Zika virus infection may affect growth of the fetal head, and microcephaly is one anomaly caused by Zika virus infection. Women who have traveled to an area with Zika virus transmission but have negative Zika virus testing are advised to have an ultrasound, and if normal, to continue with routine testing.

Microcephaly is a difficult diagnosis to make, and referral to an MFM specialist to evaluate for this diagnosis is recommended for pregnant women testing positive for Zika virus.² The current definition for microcephaly is a head circumference ≥ 2 standard deviations below the mean for sex and gestational age at birth.³ The accuracy of ultrasound to diagnose microcephaly in the setting of Zika infection is not known.⁴ Fetal brain magnetic resonance imaging (MRI) may be considered for further evaluation of suspected brain abnormalities seen on ultrasound. If brain abnormalities are noted on imaging, referral to a neurologist experienced in prenatal evaluations may provide additional guidance and help interpreting the impact of these abnormalities. Other findings on ultrasound may include intrauterine growth restriction, abnormal amniotic fluid volume, and/or abnormal cerebral or umbilical artery flow.⁵ Ultrasound imaging and MRI should be performed where expertise is available for such studies and under the guidance of an MFM specialist. Continued care with a patient's general prenatal provider is needed in close coordination with this specialty care.

6. How should providers arrange for testing of the fetus or neonate from a Zika virus positive or inconclusive pregnancy?

The Health Department will actively follow up with providers of pregnant women who have had positive or inconclusive tests for Zika virus to determine the outcome of the pregnancy and whether the fetus or infant has any diagnosed abnormalities. DOHMH will also work with providers to ensure proper collection and testing of infant or fetal specimens at the end of the pregnancy.

Please notify the Health Department by calling the Provider Access Line (1-866-692-3641) so that the Health Department can help coordinate collection, proper storage, labeling and submission of specimens at the end of the pregnancy. In all cases, you **must** contact the Provider Access Line before sending the tissue to the New York City Public Health Laboratory.

- i. If a live birth—collect cord blood, umbilical cord tissue and placental tissue, as directed by the Health Department.
- ii. If a spontaneous or induced abortion—collect placental, cord and/or fetal tissue, as directed by the Health Department.²
- iii. Both formalin-fixed and fresh-frozen tissue should be collected. If this is not possible, formalin-fixed tissue should be prioritized.

Additional information on testing in New York City may be found at:

<http://www1.nyc.gov/assets/doh/downloads/pdf/cd/zika-advisory7.pdf>.

Additional information on testing fetal tissues may be found at: <http://www.cdc.gov/zika/hc-providers/tissue-collection-submission.html>.

7. What information can I provide my pregnant patients with Zika virus infection if ultrasound results are normal?

Normal results from fetal ultrasounds may be used to reassure a patient that no gross anatomical defects were likely to be present at the time of the ultrasound. However, the sensitivity of fetal ultrasound for microcephaly and other birth defects is limited, particularly during early pregnancy. Therefore, serial fetal ultrasounds are recommended to increase the likelihood of detecting abnormalities.

8. What guidance can I provide pregnant patients with Zika virus infection who are considering pregnancy termination?

A woman may consult her provider, partner, or other trusted persons while making the decision to continue or terminate a pregnancy. Providers should avoid making assumptions about the woman's pregnancy intentions and should offer the most updated information available about the possible effects of Zika virus infection on pregnancy and provide timely referrals. It is critical to communicate that we do not know much about the short- and long-term effects of Zika virus infection on fetal development or pregnancy outcomes. We do not know the proportion of Zika-affected pregnancies that will result in adverse outcomes for the fetus or neonate.

If a woman is considering terminating her pregnancy and her regular provider does not perform induced abortions, referral to physicians who perform pregnancy termination should be provided. Pregnancy termination is legal, safe and available in NYC up to 23 6/7 weeks of pregnancy. You can refer her to <http://www.bookofchoices.org/> for information on abortion services across New York State. Pregnancy termination after 24 weeks is available for specific circumstances. For more information on where to refer patients for abortions past 24 weeks, call the National Abortion Federation (NAF) hotline 1-877-257-0012.¹² Providers should call the NYC Provider Access Line at 1-866-692-3641 to arrange testing of the fetal tissue/products of conception after an elective abortion in a Zika-positive or inconclusive pregnant woman.

9. Are there potential risks to the pregnancy for women who have traveled to areas with ongoing Zika transmission right before or right after they became pregnant?

It is not known how timing of Zika infection during or immediately before pregnancy affects an embryo.²

10. Is there any evidence that Zika infection during pregnancy will pose a risk for future pregnancies?

Currently, there is no evidence that previous, resolved Zika virus infection poses a risk for future pregnancies. However, data to answer this question for Zika are limited.

11. Is breastfeeding recommended with Zika virus infection?

The CDC currently recommends breastfeeding for mothers with Zika virus infection. No cases of Zika virus infection associated with breastfeeding have been reported.⁷

12. Are there any infection control guidelines for prevention of Zika virus transmission during labor and delivery?

The CDC urges use of Standard Precautions in any health care setting including this scenario (see http://www.cdc.gov/mmwr/volumes/65/wr/mm6511e3er.htm?s_cid=mm6511e3er_e).

13. What follow-up is recommended for infants of mothers with Zika virus infection?

Counsel mothers to obtain appropriate follow-up for infants, including hearing and vision screening in the neonatal period along with routine pediatric and specialty developmental follow-up individualized to the infant.⁷ The follow-up care for affected neonates and children will evolve as more data are collected on short- and long-term outcomes. Updated recommendations based on these data will further guide care.

To better understand the effects of Zika virus during pregnancy, CDC has established the U.S. pregnancy registry for Zika virus infection. This registry will provide information about the effects of Zika virus on pregnant women and their children. Information about the registry can be found at: <http://www.cdc.gov/zika/hc-providers/registry.html>.

Checklist: What services do I offer a pregnant woman at risk for having Zika virus infection?

- ◇ Review patient’s travel history and ask about her sexual activity and travel by her sex partners, and other potential exposures to Zika virus.
- ◇ Offer and arrange testing for Zika virus for all pregnant women who traveled to areas with Zika virus transmission while pregnant or who may have had sexual exposure.
- ◇ Report test results to patients as they are received and assist patients in interpreting these results using the most up-to-date information available.
- ◇ If Zika positive, equivocal, or inconclusive:
 - Arrange additional laboratory testing, as warranted.
 - Counsel regarding the current knowledge and data on Zika and pregnancy.
 - Provide counseling and timely referrals based upon your patient’s decision to continue or terminate the pregnancy.
 - Offer and arrange serial fetal ultrasounds every 3-4 weeks during pregnancy, and refer to a maternal-fetal medicine specialist.
 - Call the Health Department at 1-866-692-3641 to arrange for testing of maternal, fetal, or infant specimens for Zika upon delivery, or of fetal and maternal tissues in the event of spontaneous or elective termination of pregnancy .

References

1. Rasmussen SA, Jamieson DJ, Monein MA, and Petersen LR. Zika virus and birth defects – reviewing the evidence for causality. NEJM 2016; Apr 13. Available at http://www.nejm.org/doi/full/10.1056/NEJMs1604338?query=featured_zika
2. Petersen EE, Polen KN, Meaney-Delman D, et al.. Update: Interim guidelines for healthcare providers caring for women of reproductive age with possible Zika virus exposure—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:315-322.
3. Schuler-Faccini L, Ribeiro EM, Feitosa IML, et al. Possible Association between Zika Virus Infection and Microcephaly – Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65:59-62.
4. <http://www.acog.org/About-ACOG/News-Room/Practice-Advisories/Practice-Advisory-Interim-Guidance-for-Care-of-Obstetric-Patients-During-a-Zika-Virus-Outbreak>, accessed February 12, 2016.

5. Brasil P, Pereira JP, Gabaglia CR, et al. Zika Virus Infection in Pregnant Women in Rio de Janeiro – Preliminary Report. NEJM 2016, March 4. DOI: <http://www.nejm.org/doi/full/10.1056/NEJMoa1602412> Accessed March 8, 2016.
6. http://apps.who.int/iris/bitstream/10665/204421/1/WHO_ZIKA_MOC_16.1_eng.pdf?ua=1, accessed February 19, 2016.
7. Fleming-Dutra KE, Nelson JM, Fischer M, et al. Update: Interim Guideline for Health care Provider Caring for Infants and Children with Possible Zika Infection – United States, February 2016. MMWR Morb Mortal Wkly Rep 2016;65:182-187.
8. Foy BD, Kobylinski KC, Chilson Foy JL, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 2011;17:880–2.
9. Oster AM, Brooks JT, Stryker JE, et al. Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:120–121. DOI: <http://dx.doi.org/10.15585/mmwr.mm6505e1>
10. M McCarthy. Zika virus was transmitted by sexual contact in Texas, health officials report. BMJ. 2016 Feb 4;352:i720. doi: 10.1136/bmj.i720.
11. <http://www.cdc.gov/Zika/hc-providers/qa-pregnant-women.html>, accessed February 19, 2016.
12. <http://prochoice.org/think-youre-pregnant/find-a-provider/>, accessed March 16, 2016.