



NEW YORK CITY DEPARTMENT OF
HEALTH AND MENTAL HYGIENE
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Commissioner

2016 DOHMH Advisory #2: Management of Pregnant Women with Travel to Areas Affected by the Zika Virus Outbreak

Please share with your colleagues in Ob/Gyn and Family Medicine, Pediatrics, Infectious Disease, and Emergency Medicine:

- Advise patients who are pregnant or trying to become pregnant to postpone travel to areas with ongoing Zika virus transmission.
- Travelers should take precautions to prevent infection by avoiding mosquito bites.
- Laboratory testing for Zika virus is indicated for pregnant women who report compatible symptoms during or within 2 weeks of travel to an affected area.
 - Testing is not indicated for asymptomatic pregnant women or other asymptomatic patients.
 - Providers MUST report suspected cases to the NYC Department of Health (DOHMH) at 1-866-692-3641 BEFORE submitting specimens for Zika virus testing. DOHMH will determine whether testing is indicated and will assist with arranging testing and transportation of specimens to the laboratory.
- Providers, especially those caring for pregnant women, should call into a Centers for Disease Control and Prevention (CDC) clinical update conference call on Tuesday, January 26 at 2pm.
 - Details are forthcoming and will be posted at <http://emergency.cdc.gov/coca/calls/>

January 25, 2016

Dear Colleagues,

The Centers for Disease Control and Prevention (CDC) issued the attached guidance document; [Interim Guidelines for Pregnant Women During a Zika Virus Outbreak – United States, 2016](#). Included are recommendations for screening, testing and management of pregnant returning travelers. CDC has scheduled a conference call for providers wanting to learn more about Zika virus and issues surrounding the current outbreak. Providers are encouraged to call in and ask questions. The call is being held on Tuesday, January 26 at 2PM (details at <http://emergency.cdc.gov/coca/calls/>).

Pregnant women advised to postpone travel to affected areas

Advise your patients who are pregnant to postpone travel to areas with ongoing Zika virus transmission. For the most recent information on affected areas, visit <http://www.cdc.gov/zika/geo/index.html>. As the number of affected areas likely will increase, please check the site frequently.

If patients, particularly pregnant women, travel to affected areas, advise them to prevent mosquito bites. The mosquitoes that transmit Zika, dengue, and chikungunya viruses are aggressive biters and are present during the daytime and early evening. The Health Department has developed a *Travel Warning for Pregnant Women* available via 311 or at our website:

<http://www1.nyc.gov/assets/doh/downloads/pdf/cd/zika-travel-warning-012116.pdf> [English]

<http://www1.nyc.gov/assets/doh/downloads/pdf/cd/zika-travel-warning-012116-sp.pdf> [Spanish]

Translations in additional languages, such as Portuguese, French, and Haitian Creole, will be available soon.

Zika virus infections identified in New Yorkers

Zika virus infections have been and will continue to be identified in New Yorkers as long as the outbreak persists and people travel to affected areas. To date, there have been three confirmed New York City cases: 1 in 2013 and 2 in 2016. None of the New York City cases were in pregnant women. It is likely that there are other cases that were not reported, because testing is not commercially available, patients may not have sought medical care because their illness was mild, and providers have not historically attempted to test for Zika virus.

Who to test

- All testing must be coordinated by DOHMH.
- Testing will only be considered when there is:
 - A history of travel to a Zika-affected area during or within 2 weeks of illness onset in a pregnant women with compatible illness (two or more of any of the following; acute onset of fever, maculopapular rash, arthralgia or non-purulent conjunctivitis) **OR**
 - Women with fetuses who have ultrasound findings of fetal microcephaly or intracranial calcifications and a history of travel to an affected area while pregnant **OR**
 - A child diagnosed with microcephaly whose mother was pregnant while in an affected area since the outbreak began in 2015.
- Testing currently also is available for non-pregnant patients with compatible illness and travel. However, this service may be discontinued if the volume of specimens overwhelms laboratory testing capacity.
- Patients diagnosed with Guillain-Barre Syndrome (GBS) with a history of travel to a Zika-affected area may also be considered for testing after consultation with DOHMH.

Asymptomatic pregnant women

- Testing of pregnant women is not recommended unless they have symptoms **OR** there is evidence of fetal microcephaly or intracranial calcifications.
- Current serologic testing methodologies have not been evaluated for persons who are not infected. The predictive value of the test is unknown, possibly leading to false positive test results.
- Pregnant women with a history of travel to an affected area and no symptoms should undergo serial ultrasound evaluation for microcephaly or intracranial calcifications. Details are available in the attached CDC guidance.

Where to test and how to make arrangements

- At this time, testing is not available through commercial laboratories.
- Testing can only be done at select laboratories, including the New York State Department of Health Public Health Laboratory at Wadsworth and the Centers for Disease Control and Prevention (CDC).
- Healthcare providers wishing to test for Zika virus **must first contact** DOHMH by calling the Provider Access Line (PAL) at 1-866-692-3641.
- If patients are *seen during non-business hours*, providers should collect specimens and store them until they discuss the case with DOHMH on the following business day.
 - Collect 2 tubes of serum, each with 2cc (use a red or speckled top tube)
 - Store specimens at -70 °C **OR**, if deep freezing is unavailable, store in a refrigerator (4 °C).
- Collect the following information for each patient:
 - Symptoms, onset of illness, travel dates, country of travel, week of gestation at time of illness onset, and history of previous infection with dengue, chikungunya, or West Nile virus or Yellow Fever vaccination.

Testing

- Patients meeting testing criteria will be tested for Zika, dengue, and chikungunya viruses.
- Available tests include RT-PCR (for patients with onset of symptoms up to one week prior to serum collection) and serology.
- DOHMH will advise providers on proper specimen collection, storage and shipping, as well as provide the appropriate submission forms.
- Test type for symptomatic patients will be dictated by the number of days between the onset of illness and the date of specimen collection:
 - If 0-7 days, both RT-PCR and serologic testing will be performed.
 - If more than 7 days, only serologic testing will be performed.
- Test type for patients meeting other testing criteria will be determined upon consultation with the DOHMH.
- Test results may be delayed due to the volume of requests.
- Providers seeking urgent dengue or chikungunya virus test results should also submit specimens to test for these viruses at a commercial laboratory.
 - If dengue is suspected, providers are reminded to avoid using aspirin or NSAIDs to avoid problems with clotting in patients who may go on to develop severe dengue disease.
 - For dengue and chikungunya testing, RT-PCR testing on specimens collected within 5 to 7 days of illness onset is the best method to confirm a positive diagnosis. A negative result does not rule out infection.
 - Serologic testing should be performed in addition to RT-PCR. Dengue and Zika viruses are both flaviviruses, and cross-reactivity may occur making it difficult to interpret serologic results.
- Symptomatic non-pregnant patients for whom illness is resolving may not warrant testing.
 - Providers should consider testing such patients at a commercial laboratory for dengue or chikungunya viruses.

Reporting

Clinicians and laboratories must report all cases of all arboviral diseases (e.g., Zika, chikungunya, dengue, and West Nile virus) to the DOHMH. Cases may be reported by telephone by calling the PAL (866-692-3641), or fax (347-396-2753) using the Universal Reporting form (URF), or the electronic URF. The URF and instructions may be downloaded from the Health Department website at <http://www1.nyc.gov/site/doh/providers/reporting-and-services/reporting-central.page>.

As always, we appreciate your continued collaboration with our efforts in New York City.

Sincerely,

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NYC HEALTH DEPARTMENT REFERENCE GUIDE FOR ZIKA TESTING

WHO TO TEST

Pregnant woman or non-pregnant patient with any two or more of the following symptoms:

- Acute fever
- Maculopapular rash
- Arthralgia(s)
- Conjunctivitis

AND whose onset of illness occurred during or within 2 weeks of travel to an affected area

OR

Woman found to have a fetus with microcephaly or intracranial calcifications and who traveled to an affected area while pregnant

OR

Child diagnosed with microcephaly whose mother was pregnant while in an affected area

OR

Patients diagnosed with Guillain-Barre Syndrome (GBS) and a history of travel to an affected area (Providers should consult with the NYC Health Department to determine if testing is appropriate)

Providers caring for pregnant women not meeting testing requirements should refer to the CDC [Interim Guidelines for Pregnant Women During a Zika Virus Outbreak – United States, 2016](#)

CONTACT THE NYC HEALTH DEPARTMENT TO OBTAIN APPROVAL FOR LABORATORY TESTING

During regular business hours call the Provider Access Line (PAL) at 1-866-692-3641. If you are seeing patients after regular business hours, or weekends, collect the appropriate specimens and contact the PAL the next business day. *Specimens not approved in advance will be rejected by the laboratory.*

Have the following information available:

- Patient Name
- Date of birth
- Symptoms
- Onset of illness
- Travel dates
- Country of travel
- Week of gestation at time of illness
- History of previous infection with dengue, chikungunya, West Nile virus
- Vaccination with Yellow Fever vaccine

WHAT TO COLLECT

- For RT-PCR, collect 2 cc serum
- For serology, collect 2 cc serum
- If doing both RT-PCR and serology, collect 2 tubes of serum

TEST TYPE

Test type will be dictated by the number of days between the onset of illness and the date of specimen collections

- If 0-7 days, both RT-PCR and serologic testing will be performed.
- If more than 7 days, only serologic testing will be performed.

FORMS

All specimens submitted for testing must be accompanied by the appropriate forms. The NYC Health Department will provide all necessary forms following consultation.

STORAGE AND SHIPPING

- Specimens should be stored at -70 °C and shipped on dry ice.
- If deep freezing is unavailable specimens should be kept in a refrigerator
- Facilities capable of shipping specimens directly to CDC or Wadsworth will be given the appropriate instructions
- Facilities unable to ship directly will work with the Health Department to have specimens picked up by a courier and brought to the NYC Public Health Laboratory for shipping.

IT IS VERY IMPORTANT that all submission forms be completed in full, contain information that is consistent across forms, and accompany the specimens in a bag. Specimen tubes must be labeled properly with the patient's name, date of birth, and date of collection. If the information on the forms is incomplete or if the name does not match the name on the tube, the specimens cannot be tested.

NOTES ABOUT LABORATORY TESTING

- At this time, testing is not available through commercial laboratories and can only be done at select laboratories including the New York State Public Health Laboratory at Wadsworth and the Centers for Disease Control and Prevention (CDC).
- All specimens will be tested for Zika, dengue and chikungunya viruses
- Test results may be delayed due to the volume of requests
- Providers seeking dengue or chikungunya virus test results in a timely manner are encouraged to also submit specimens to test for these viruses to a commercial laboratory.
 - For dengue and chikungunya testing, RT-PCR testing on specimens collected within 5 to 7 days of onset of illness is the best method to confirm a positive diagnosis. However, a negative result does not rule out infection, and serologic testing should be done in addition to RT-PCR.
 - Providers should keep in mind that dengue and Zika viruses are both flaviviruses, and cross-reactivity may occur making it difficult to interpret serologic results.
 - If dengue is suspected, providers are reminded to avoid using aspirin or NSAIDs to avoid problems with clotting in patients who may go on to develop severe dengue disease.
- Symptomatic non-pregnant patients for whom illness is resolving may not warrant testing. Providers should consider testing the patient at a commercial laboratory for dengue or chikungunya.

Interim Guidelines for Pregnant Women During a Zika Virus Outbreak — United States, 2016

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CDC has developed interim guidelines for health care providers in the United States caring for pregnant women during a Zika virus outbreak. These guidelines include recommendations for pregnant women considering travel to an area with Zika virus transmission and recommendations for screening, testing, and management of pregnant returning travelers. Updates on areas with ongoing Zika virus transmission are available online (<http://wwwnc.cdc.gov/travel/notices/>). Health care providers should ask all pregnant women about recent travel. Pregnant women with a history of travel to an area with Zika virus transmission and who report two or more symptoms consistent with Zika virus disease (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) during or within 2 weeks of travel, or who have ultrasound findings of fetal microcephaly or intracranial calcifications, should be tested for Zika virus infection in consultation with their state or local health department. Testing is not indicated for women without a travel history to an area with Zika virus transmission. In pregnant women with laboratory evidence of Zika virus infection, serial ultrasound examination should be considered to monitor fetal growth and anatomy and referral to a maternal-fetal medicine or infectious disease specialist with expertise in pregnancy management is recommended. There is no specific antiviral treatment for Zika virus; supportive care is recommended.

Zika virus is a mosquito-borne flavivirus transmitted primarily by *Aedes aegypti* mosquitoes (1,2). These vectors also transmit dengue and chikungunya virus and are found throughout much of the Americas, including parts of the United States. An estimated 80% of persons infected with Zika virus are asymptomatic (2,3). Symptomatic disease is generally mild and characterized by acute onset of fever, maculopapular rash, arthralgia, or nonpurulent conjunctivitis. Symptoms usually

last from several days to 1 week. Severe disease requiring hospitalization is uncommon, and fatalities are rare. Guillain-Barré syndrome has been reported in patients following suspected Zika virus infection (4–6).

Pregnant women can be infected with Zika virus in any trimester (4,7,8). The incidence of Zika virus infection in pregnant women is not currently known, and data on pregnant women infected with Zika virus are limited. No evidence exists to suggest that pregnant women are more susceptible to Zika virus infection or experience more severe disease during pregnancy.

Maternal-fetal transmission of Zika virus has been documented throughout pregnancy (4,7,8). Although Zika virus RNA has been detected in the pathologic specimens of fetal losses (4), it is not known if Zika virus caused the fetal losses. Zika virus infections have been confirmed in infants with microcephaly (4), and in the current outbreak in Brazil, a marked increase in the number of infants born with microcephaly has been reported (9). However, it is not known how many of the microcephaly cases are associated with Zika virus infection. Studies are under way to investigate the association of Zika virus infection and microcephaly, including the role of other contributory factors (e.g., prior or concurrent infection with other organisms, nutrition, and environment). The full spectrum of outcomes that might be associated with Zika virus infections during pregnancy is unknown and requires further investigation.

Recommendations for Pregnant Women Considering Travel to an Area of Zika Virus Transmission

Because there is neither a vaccine nor prophylactic medications available to prevent Zika virus infection, CDC recommends that all pregnant women consider postponing travel



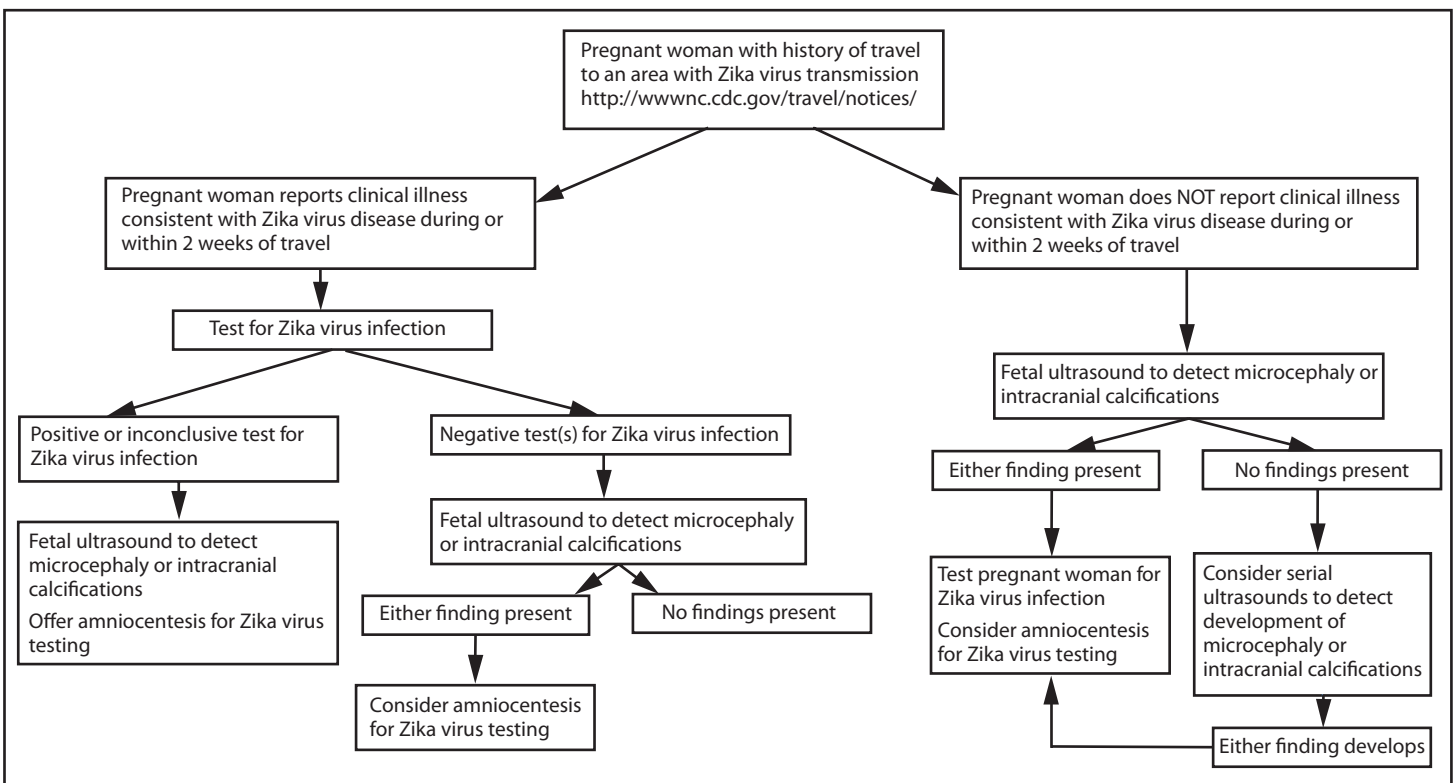
to areas where Zika virus transmission is ongoing (10). If a pregnant woman travels to an area with Zika virus transmission, she should be advised to strictly follow steps to avoid mosquito bites (11,12). Mosquitoes that spread Zika virus bite both indoors and outdoors, mostly during the daytime; therefore, it is important to ensure protection from mosquitoes throughout the entire day (13). Mosquito prevention strategies include wearing long-sleeved shirts and long pants, using U.S. Environmental Protection Agency (EPA)–registered insect repellents, using permethrin-treated clothing and gear, and staying and sleeping in screened-in or air-conditioned rooms. When used as directed on the product label, insect repellents containing DEET, picaridin, and IR3535 are safe for pregnant women (14,15). Further guidelines for using insect repellents are available online (<http://wwwnc.cdc.gov/travel/page/avoid-bug-bites>) (11,15).

Recommendations for Pregnant Women with History of Travel to an Area of Zika Virus Transmission

Health care providers should ask all pregnant women about recent travel. Women who traveled to an area with ongoing Zika virus transmission during pregnancy should be evaluated for Zika virus infection and tested in accordance with CDC Interim Guidance (Figure). Because of the similar geographic distribution and clinical presentation of Zika, dengue, and chikungunya virus infection, patients with symptoms consistent with Zika virus disease should also be evaluated for dengue and chikungunya virus infection, in accordance with existing guidelines (16,17).

Zika virus testing of maternal serum includes reverse transcription-polymerase chain reaction (RT-PCR) testing for symptomatic patients with onset of symptoms within the

FIGURE. Interim guidance: testing algorithm^{*,†,§} for a pregnant woman with history of travel to an area[¶] with Zika virus transmission, with or without clinical illness^{} consistent with Zika virus disease**



* Availability of Zika virus testing is limited; consult your state or local health department to facilitate testing. Tests include Zika virus reverse transcription–polymerase chain reaction (RT-PCR) and Zika virus immunoglobulin M (IgM) and neutralizing antibodies on serum specimens. Given the overlap of symptoms and endemic areas with other viral illnesses, evaluate for possible dengue or chikungunya virus infection.

† 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 would be considered inconclusive if Zika virus neutralizing antibody titers are <4-fold higher than dengue virus neutralizing antibody titers.

§ Amniocentesis is not recommended until after 15 weeks of gestation. Amniotic fluid should be tested for Zika virus RNA by RT-PCR.

¶ Updates on areas with ongoing Zika virus transmission are available online (<http://wwwnc.cdc.gov/travel/notices/>).

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

previous week. Immunoglobulin M (IgM) and neutralizing antibody testing should be performed on specimens collected ≥ 4 days after onset of symptoms. Cross-reaction with related flaviviruses (e.g., dengue or yellow fever) is common with antibody testing, and thus it might be difficult to distinguish Zika virus infection from other flavivirus infections. Consultation with state or local health departments might be necessary to assist with interpretation of results (18). Testing of asymptomatic pregnant women is not recommended in the absence of fetal microcephaly or intracranial calcifications.

Zika virus RT-PCR testing can be performed on amniotic fluid (7,9). Currently, it is unknown how sensitive or specific this test is for congenital infection. Also, it is unknown if a positive result is predictive of a subsequent fetal abnormality, and if so, what proportion of infants born after infection will have abnormalities. Amniocentesis is associated with an overall 0.1% risk of pregnancy loss when performed at less than 24 weeks of gestation (19). Amniocentesis performed ≥ 15 weeks of gestation is associated with lower rates of complications than those performed at earlier gestational ages, and early amniocentesis (≤ 14 weeks of gestation) is not recommended (20). Health care providers should discuss the risks and benefits of amniocentesis with their patients. A positive RT-PCR result on amniotic fluid would be suggestive of intrauterine infection and potentially useful to pregnant women and their health care providers (20).

For a live birth with evidence of maternal or fetal Zika virus infection, the following tests are recommended: histopathologic examination of the placenta and umbilical cord; testing of frozen placental tissue and cord tissue for Zika virus RNA; and testing of cord serum for Zika and dengue virus IgM and neutralizing antibodies. CDC is developing guidelines for infants infected by Zika virus. If a pregnancy results in a fetal loss in a woman with history of travel to an area of Zika virus transmission with symptoms consistent with Zika virus disease during or within 2 weeks of travel or findings of fetal microcephaly, Zika virus RT-PCR and immunohistochemical staining should be performed on fetal tissues, including umbilical cord and placenta.

There is no commercially available test for Zika virus. Testing for Zika virus infection is performed at CDC and several state health departments. Health care providers should contact their state or local health department to facilitate testing and for assistance with interpreting results (4).

How to Treat Pregnant Women with Diagnoses of Zika Virus Disease

No specific antiviral treatment is available for Zika virus disease. Treatment is generally supportive and can include rest, fluids, and use of analgesics and antipyretics (4). Fever should

be treated with acetaminophen (21). Although aspirin and other nonsteroidal anti-inflammatory drugs are not typically used in pregnancy, these medications should specifically be avoided until dengue can be ruled out to reduce the risk for hemorrhage (4,9,17).

In pregnant a woman with laboratory evidence of Zika virus in serum or amniotic fluid, serial ultrasounds should be considered to monitor fetal anatomy and growth every 3–4 weeks. Referral to a maternal-fetal medicine or infectious disease specialist with expertise in pregnancy management is recommended.

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