Zika Virus

An Update for Healthcare Providers on New Guidance and Testing in New York State

February 17, 2016

Elizabeth Dufort, MD, FAAP
Medical Director, Division of Epidemiology
New York State Department of Health
At the conclusion of this webinar, healthcare providers will be able to:

- Describe the epidemiology, transmission patterns, clinical manifestations, complications, and reporting of Zika virus
- Articulate NYSDOH’s recommendations for Zika virus testing
- Discuss diagnostic testing for Zika virus infection available through NYSDOH’s Wadsworth Center and interpretation of test results
Zika Virus – The Basics

- Single stranded RNA Virus
- Genus *Flavivirus*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
Zika Virus Vectors

- Transmitted by the *Aedes* species mosquitoes
  - *Aedes aegypti*: more efficient vectors for Zika (Yellow fever mosquito)
  - *Aedes albopictus*: possible vector for Zika (Asian tiger mosquito)
- Also transmit dengue and chikungunya viruses
- Lay eggs in domestic water-holding containers
- Live in and around households
- Aggressive and primarily daytime biters, but can also bite at night
Zika Virus

- Prior to 2015, Zika virus outbreaks occurred in areas of Africa, Southeast Asia, and the Pacific Islands
- In May 2015 - the first confirmed Zika virus infections in Brazil
- No local transmission to date in the continental United States
Zika Virus: Countries and Territories with Active Zika Virus Transmission

As of February 5, 2016

US Territories:
* Puerto Rico (Dec 2015)
* U.S. Virgin Islands
  - St. Croix
  - St. John
  - St. Thomas

Common travel destinations:
- Dominican Republic
- Mexico (Nov 2015)

Courtesy of the Centers for Disease Control and Prevention
Pregnant women in any trimester should consider postponing travel to areas where Zika virus is spreading.

Pregnant women who do travel to one of these areas should talk to their healthcare provider and strictly follow steps to avoid mosquito bites during the trip.

Women trying to get pregnant should discuss with their provider.

Warning Level 3, Avoid Nonessential Travel
Alert Level 2, Practice Enhanced Precautions
Watch Level 1, Practice Usual Precautions
WHO-Declaration of a Public Health Emergency of International Concern

- Given spread and broad geographic range of the mosquito species that transmits the virus
- Given the strong association with the rise in detected congenital malformations and neurological complications
- Lack of vaccines and rapid reliable tests
- Absence of population immunity

→ Urgent need to coordinate international efforts to address this threat

(February 1, 2016)
Zika Virus Imported Cases in the U.S.

• Approximately 50 cases of Zika virus diagnosed in the continental U.S.
  • All but one are travel-associated/imported
  • One report of sexual transmission
  • NO local vector-borne transmission
• New York State
  • 17 cases → All imported/travel-associated
• With outbreaks in the Americas, cases among U.S. travelers will likely increase
• Imported cases may result in virus introduction and local spread in some areas of U.S.
Aedes aegypti and Aedes albopictus Mosquitoes: Geographic Distribution in the United States
Laboratory experiments have shown that *Aedes albopictus* can transmit Zika virus from infected animals to uninfected animals. Its current involvement in transmission in the Americas is not known. *Aedes albopictus* has been implicated in transmission of other flavivirus outbreaks, such as a recent Dengue outbreak in Hawaii.
Modes of Transmission

• Mosquito Bite
  • From infected to uninfected humans and primates by bite of a mosquito
• Maternal-fetal
  • Intrauterine
  • Perinatal
• Other
  • Sexual Transmission
  • Blood transfusion
• Theoretical
  • Organ or tissue transplantation
  • Breast milk
Modes of Transmission

• Mosquito Bite
  • From infected to uninfected humans and primates by bite of a mosquito

• Maternal-fetal
  • Intrauterine
  • Perinatal

• Other
  • Sexual Transmission
  • Blood transfusion

• Theoretical
  • Organ or tissue transplantation
  • Breast milk
Maternal-Fetal Transmission of Zika Virus

Infection confirmed in infants with microcephaly in Brazil
Zika virus RNA identified in specimens of fetal losses

- Infection confirmed in infants with microcephaly in Brazil
- Zika virus RNA identified in specimens of fetal losses

• Additionally:
  - Zika virus detected prenatally in amniotic fluid
  - In infant whose mother traveled to Brazil and delivered in the US

Modes of Transmission

- Mosquito Bite
  - From infected to uninfected humans and primates by bite of a mosquito
- Maternal-fetal
  - Intrauterine
  - Perinatal
- Other
  - **Blood transfusion**
  - **Sexual Transmission**
- Theoretical
  - Organ or tissue transplantation
  - Breast milk
Recommendations – Blood Donation

• February 16th, 2016

• FDA issues recommendations to defer blood donation if:
  • Individuals traveled to areas with active Zika transmission within the last four weeks
  • If symptoms of Zika virus infection
  • Those who had sexual contact with a person who traveled to an area with Zika in the last three months
FOR IMMEDIATE RELEASE

DCHHS Reports First Zika Virus Case in Dallas County
Acquired Through Sexual Transmission

DALLAS (Feb. 2, 2016) – Dallas County Health and Human Services (DCHHS) has received confirmation from the Centers for Disease Control and Prevention (CDC) of the first Zika virus case acquired through sexual transmission in Dallas County in 2016. The patient was infected with the virus after having sexual contact with an ill individual who returned from a country where Zika virus is present. For medical confidentiality and personal privacy reasons, DCHHS does not provide additional identifying information.
• Possible sexual transmission
  – Two case reports of sexual transmission in symptomatic men (although one transmission occurred before onset of symptoms)
  – One report in a symptomatic man of viable virus in semen for 2 to up to 10 weeks after symptom onset
• Of particular concern in relation to transmission to pregnant women
• Unknown
  – Currently no reports of transmission from infected women to partners
  – Whether asymptomatic men can transmit is unknown
  – Duration of shedding in semen is unknown
Sexual transmission

**CDC and NYSDOH**

- Men who reside in or have traveled to an area of active Zika virus transmission who have a pregnant partner should abstain or consistently and correctly use condoms during sex for the duration of the pregnancy.
- Pregnant women should discuss their male partner’s potential exposures to mosquitoes and history of Zika-like illness with their health care provider.
- Men who reside in or have traveled to an area of active Zika virus transmission who are concerned about sexual transmission of Zika virus might consider abstaining from sexual activity or using condoms consistently and correctly during sex.

**Public Health England**

- The risk of sexual transmission of Zika virus is thought to be very low.
- If a female partner is at risk of getting pregnant, or is already pregnant, condom use is advised for a male traveler:
  - for 28 days after his return from an active Zika transmission area if he has not had any symptoms compatible with Zika virus infection
  - for 6 months following recovery if a clinical illness compatible with Zika virus infection or laboratory confirmed Zika virus infection was reported

https://www.gov.uk/guidance/zika-virus
Clinical Presentation – Zika Virus Disease
Clinical Presentation – Zika Virus Disease

- Infection rate: 73%
- Symptomatic attack rate among infected: 18%
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths

Note: Rates based on serosurvey on Yap Island, 2007 (population 7,391)

# Reported Clinical Symptoms Among 31 Confirmed Zika Virus Disease Cases

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular or papular rash</td>
<td>28</td>
<td>90%</td>
</tr>
<tr>
<td>Subjective fever</td>
<td>20</td>
<td>65%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>20</td>
<td>65%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>17</td>
<td>55%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15</td>
<td>48%</td>
</tr>
<tr>
<td>Headache</td>
<td>14</td>
<td>45%</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>12</td>
<td>39%</td>
</tr>
<tr>
<td>Edema</td>
<td>6</td>
<td>19%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
<td>10%</td>
</tr>
</tbody>
</table>

Yap Island, 2007

Distinguishing Zika from Dengue and Chikungunya

- Dengue and chikungunya viruses transmitted by same mosquitoes with similar ecology
- Dengue and chikungunya can circulate in same area and rarely cause co-infections
- Diseases have similar clinical features
- Important to rule out dengue, as proper clinical management can improve outcome*

## Clinical Features: Zika Virus Compared to Dengue and Chikungunya

<table>
<thead>
<tr>
<th>Features</th>
<th>Zika</th>
<th>Dengue</th>
<th>Chikungunya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Rash</td>
<td>++++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Myalgia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Shock</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
Differential Diagnosis for Zika Virus Disease in Returning Travelers

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Rickettsia
- Parvovirus
- Group A streptococcus
- Rubella
- Measles
- Adenovirus
- Enterovirus
Initial Assessment and Treatment

- No specific antiviral therapy
- Treatment is supportive (i.e., rest, fluids, analgesics, antipyretics)
- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infections
- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage
Zika Virus Outcomes

- Clinical illness usually mild, lasting for several days to a week
- Severe disease requiring hospitalization uncommon, fatalities rare
- Maternal-fetal transmission
- Guillain-Barré syndrome reported in patients following suspected Zika virus infection
  - Relationship to Zika virus infection is not clear, but under active investigation
Microcephaly

Microcephaly is the clinical finding of a small head when compared with infants of the same sex and age. The size of the head is considered a reliable assessment of the volume of the underlying brain.
Diagnosing Microcephaly

• **Prenatally:**
  - Can be detected prenatally by routine ultrasound at 18-20 weeks
  - However, best identified on prenatal US later in pregnancy (late second trimester, early third trimester)
  - Serial prenatal US helpful to detect microcephaly in utero

• **Infant:**
  - Most often defined as head circumference < 3rd percentile
  - Standard growth charts by gestation, sex, and age
  - Asymmetric more concerning than symmetric
Ascertainment of Microcephaly and Other Adverse Outcomes Related to Zika

- The NYS Congenital Malformations Registry will assist with rapid ascertainment of microcephaly and other adverse birth outcomes
- Assistance from healthcare providers will be essential for this effort
- CDC is developing webinars for guidance on microcephaly surveillance
- More guidance on reporting will be available soon
Zika Virus Disease Surveillance

- Consider in travelers with acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis within 2 weeks after return.

- Inform and evaluate women who traveled to areas with Zika virus transmission while they were pregnant.

- Evaluate fetuses/infants of women possibly infected during pregnancy for possible congenital infection and microcephaly.

- Be aware of possible local transmission in areas where Aedes species mosquitoes are active.
Reporting Suspect Zika Virus Cases

- As an arboviral disease, Zika virus disease is a nationally notifiable disease
  - Healthcare providers are required to report all suspected cases to their local health department where the patient resides
  - Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies

- Timely reporting allows NYSDOH and local health departments to assess and reduce the risk of local transmission or mitigate further spread
February 9, 2016

TO: Healthcare Providers, Hospitals, Local Health Departments (LHDs)
FROM: NYSDOH Bureau of Communicable Disease Control (BCDC) and Wadsworth Center (WC)

HEALTH ADVISORY: ZIKA VIRUS TESTING PROCESS

NYSDOH Zika Testing Eligibility

Identify a patient presenting for care who meets the following criteria:

1. Pregnant woman who traveled to an area with Zika virus transmission while pregnant (see http://www.cdc.gov/zika/geo/index.html) OR

2. Non-pregnant woman, man, or child who develops (or developed) compatible symptoms during or within 4 weeks of travel to an area with Zika virus transmission OR

3. A person who traveled to an area with active Zika virus transmission and who presents with Guillain-Barré syndrome OR

4. Infant with microcephaly, intracranial calcifications or other abnormality whose mother traveled during pregnancy (or born to mothers with positive or inconclusive test results)
Evaluation of Pregnant Women

- Obtain recent travel history from all pregnant women
- NYSDOH recommends and will provide testing for all pregnant women who traveled to an area with ongoing Zika virus transmission during pregnancy (Feb. 4th)
  - Symptomatic OR Asymptomatic
    - Consistent with CDC guidance (Feb. 5th)
  - Any time after travel
  - To provide information to pregnant women and their provider to help inform clinical management and decision making
Pregnant woman with history of travel to an area with ongoing Zika virus transmission

Test for Zika virus infection

Positive or inconclusive for Zika virus infection
Consider serial fetal ultrasounds
Consider amniocentesis for Zika virus testing

Negative for Zika virus infection
Fetal ultrasound to detect microcephaly or intracranial calcifications

Microcephaly or intracranial calcifications present
Retest pregnant woman for Zika virus infection
Consider amniocentesis for Zika virus testing

Microcephaly or intracranial calcifications not present
Routine prenatal care
NYSDOH Zika Testing Eligibility

Identify a patient presenting for care who meets the following criteria:

1. Pregnant woman who traveled to an area with Zika virus transmission while pregnant (see http://www.cdc.gov/zika/geo/index.html) OR

2. Non-pregnant woman, man, or child who develops (or developed) compatible symptoms during or within 4 weeks of travel to an area with Zika virus transmission OR

3. A person who traveled to an area with active Zika virus transmission and who presents with Guillain-Barré syndrome OR

4. Infant with microcephaly, intracranial calcifications or other abnormality whose mother traveled during pregnancy (or born to mothers with positive or inconclusive test results)
Zika Testing (Non-pregnant Patient)

• Non-pregnant patient with compatible symptoms during or within 4 weeks of travel to an area with Zika virus transmission
• Few days to a week incubation period (up to 2 weeks)
• Compatible symptoms: (generally two of the four)
  – Fever
  – Maculopapular rash
  – Arthralgia
  – Conjunctivitis
  – *Other*: headache, myalgia, retro-orbital pain, vomiting
NYSDOH Zika Testing Eligibility

Identify a patient presenting for care who meets the following criteria:

1. Pregnant woman who traveled to an area with Zika virus transmission while pregnant (see http://www.cdc.gov/zika/geo/index.html) OR

2. Non-pregnant woman, man, or child who develops (or developed) compatible symptoms during or within 4 weeks of travel to an area with Zika virus transmission OR

3. A person who traveled to an area with active Zika virus transmission and who presents with Guillain-Barré syndrome OR

4. Infant with microcephaly, intracranial calcifications or other abnormality whose mother traveled during pregnancy (or born to mothers with positive or inconclusive test results)
NYSDOH Zika Testing Eligibility

Identify a patient presenting for care who meets the following criteria:


2. Non-pregnant woman, man, or child who develops (or developed) compatible symptoms during or within 4 weeks of travel to an area with Zika virus transmission OR

3. A person who traveled to an area with active Zika virus transmission and who presents with Guillain-Barré syndrome OR

4. Infant with microcephaly, intracranial calcifications or other abnormality whose mother traveled during pregnancy (or born to mothers with positive or inconclusive test results)
Diagnostic Testing for Zika Virus

• No commercially-available diagnostic tests at present
  • CDC is working with commercial laboratories to address this issue

• Testing is available at NYSDOH’s Public Health Laboratory – The Wadsworth Center
  • No cost for laboratory testing

• CDC is working to expand laboratory diagnostic testing to other state and large urban area public health laboratories
NYSDOH Zika Testing Procedures

• Verify that the patient meets testing criteria
  – For patients who do not meet testing criteria, they should be advised as such
  – If a provider wishes to discuss a specific case that does not meet criteria however is of concern, contact your LHD

• Call the local health department (LHD) where the patient resides

• Contact information for LHDs is available at https://www.health.ny.gov/contact/contact_information/

• Ideally, the patient should be available to you (or your staff) during the call to the LHD
NYSDOH Zika Testing Procedures

1. The LHD will complete the NYSDOH Zika virus testing authorization questionnaire with the patient/yourself/your staff

2. The LHD will provide a list of specimen collection sites and the patient can choose the site most convenient for them
   - Not limited to these sites if a site can appropriately process and ship the specimen
   - A list of specimen collection sites and telephone numbers is available at:
NYSDOH Zika Testing Procedures

3. If testing is approved by the LHD, an **authorization form** will be emailed to the patient to present at the collection site
   - Collection sites will accept a printed ticket or an image on a smartphone
   - If patient does not have an email address, LHD can fax the form to the patient, provider, or directly to the specimen collection site

4. Provide the patient with a **written order/prescription for Zika virus testing** for both serum and urine for polymerase chain reaction (PCR) and serum for serology

5. Advise patients to call the collection site to find out if an appointment is required
NYS DOH - Authorization for Zika Virus Testing

Thank you for registering with us. Please print the Registration Ticket below and bring it with you to your selected hospital. This ticket will help to reduce wait time at your event.

Recipient

Jane Doe

Event Information

Campaign: MatD - Zika test Campaign
Form: MatD Zika Form
County: NYS DOH
Zika Registration
Selected Hospital: Albany Memorial Hospital

Public Notes - Additional information to share with people want to be tested for the Zika virus.

ID#: 3184
NYSDOH Zika Testing Procedures

• Wadsworth’s Infectious Diseases Requisition (IDR) form to go with the specimen:

• Provider to fill out the IDR
  – However, use normal processes if a pre-existing process with the specimen collection site exists
Patient name and address

Physician name and address

Specimen details

Test request

Travel history – location and dates

Pregnant & trimester

Clinical symptoms
NYSDOH Zika Testing Procedures

In summary, patient needs three things:

1. Lab order (PROVIDER)
2. Infectious Disease Requisition Form (IDR) (PROVIDER)
3. LHD authorization form (Local Health Department)
NYC Residents - Zika Testing Process

• NYCDOHMH is using a different specimen collection and transportation procedure for NYC residents only
• If the patient resides in NYC, see NYCDOHMH guidance
• Providers should contact the New York City Department of Health and Mental Hygiene’s (NYCDOHMH) Provider Access Line for questions and other assistance at:
  – 1-866-692-3641

NYSDOH Zika Testing Procedures

- All providers, including NYC based providers/facilities caring for patients who reside outside of NYC, must follow this process and obtain LHD approval
Specimen Collection Information

• Serum:
  – At least six milliliters (ml) of blood in a serum tube (red top, serum separator tube, tiger top, speckle top, gold top)
  – Do NOT use blood tubes that contain anti-coagulants such as green top, yellow top or purple top
  – Centrifuge

• Urine:
  – Collect urine in a sterile cup with a minimum volume of 3 ml and a maximum volume of 20 ml.
  – (Urine does NOT need to be sterile collection)
Specimens

**Serum**
Collect whole blood in red top tubes
minimum 6ml

Centrifuge and remove serum
minimum 3ml

Freeze serum and
urine -70 to -80°C

**Urine**
Minimum 3ml
Packaging, Shipping, and Certification

IATA
DOT
Certification
Specimen Transport for Non-NYC Residents

- Follow shipping regulations for UN 3373 Biological Substance, Category B and UN 1875, Class 9 for dry ice

- Specimens must be shipped on dry ice to the Wadsworth Center, David Axelrod Institute, 120 New Scotland Avenue, Albany, NY 12208. Label the outside of the package with storage conditions (-70 to -80°C)
Zika Virus Testing in Infants

- Maternal blood and urine
- Infant blood and urine
- Placental PCR and immunohistochemical testing
- Umbilical blood
- CSF (if done for another reason)

*Refer to the “Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection” – MMWR, 2016
Diagnostic Testing for Zika Virus

1. **PCR assay** to detect viral RNA in serum and urine

2. **Two-step antibody testing:**
   1. **Screening antibody test**
   2. **Confirmatory antibody test (Plaque reduction neutralization test - PRNT)** to detect a ≥4-fold rise in Zika virus-specific neutralizing antibodies in paired sera
Zika PCR Testing

• PCR will be performed on specimens collected either:
  – within one month of onset of symptoms or
  – within 6 weeks of travel
• PCR resulted the evening of the same weekday specimen is received by Wadsworth Lab
• If positive, no further testing required
• If negative, follow up with serology
Polymerase Chain Reaction (PCR)

PCR will be performed for chikungunya, dengue, and Zika virus on all travelers returning from areas with Zika virus activity. PCR tests for genetic material of viruses and generally detects infection within one week of onset of symptoms.

- If any of these are positive (DETECTED), results indicate current infection with the virus identified.
- Positive results are confirmatory.
- If results are negative (NOT DETECTED), await serology results.
Zika Screening Serology

1. CDC Zika/Dengue Specific IgM
2. Wadsworth Center Flavivirus IgM ELISA
3. Wadsworth Center Flavivirus Total Antibody Test
Serology Cross-Reactions with Other Flaviviruses

- Zika virus screening serology can be positive due to antibodies against related flaviviruses (e.g., dengue and yellow fever viruses)
- Neutralizing antibody testing may discriminate between cross-reacting antibodies in individuals who have never had a flavivirus infection before
- But, it may still be difficult to distinguish infecting virus in people previously infected with or vaccinated against a related flavivirus
Zika Screening Serology Testing

• If results are ‘Nonreactive’ → suggest that there was no evidence of flavivirus exposure
  – Unless early in illness, then need repeat testing with convalescent serum specimen ≥ 3 weeks later (paired acute and convalescent serum will be tested by PRNT)

• If results are ‘Reactive’
  – Can be false positives → some need a convalescent serum specimen ≥ 3 weeks later

• FOR PREGNANT WOMEN ONLY: PRNT will be performed on the original specimen received however collection of a convalescent specimen may still be required
Arbovirus Plaque Reduction Neutralization Test (PRNT)

- More specific diagnostic assay

- This assay measures the titer of the antibodies in the serum of the infected individual

- It is a biological assay based on the principle of interaction of virus and antibody resulting in inactivation of virus such that it is no longer able to infect and replicate in cell culture

http://www.cdc.gov/dengue/clinicalLab/laboratory.html
Zika Serology Testing

- Serology may be negative early in illness
- CDC IgM test expected to be positive approximately 2-12 weeks after infection
- Screening serology takes up to 7 days from specimen receipt
- Some patients will need confirmatory testing (PRNT) takes an additional 10-14 days
  - This is dependent on the length of time it takes for virus to grow in culture
- Some patients will need a convalescent specimen drawn 3 weeks after the first to look for a rise in antibodies
NYSDOH Zika Testing Results

• Results of Zika virus testing will be made available to providers

• Providers can access public health consultation for assistance with interpretation of results by calling the NYSDOH Zika Information Line at:

  NYSDOH Zika Information Line at: 1-888-364-4723

  Weekdays between 9AM and 6PM
Zika Resources

- CDC’s Zika Virus Information Page
  - Q&As for Obstetricians and Pediatricians

- NYSDOH’s Zika Virus Information Page
  - Testing process advisory
  - Webinars will be posted
  - Testing process one page information sheet for the public will be posted
  - Testing algorithm and interpretation will be posted

- PAHO’s Zika Virus Information Page
Acknowledgements

• The Centers for Disease Control and Prevention

• The NYSDOH Wadsworth Center

• The NYSDOH Congenital Malformations Registry
Questions?

Contact the NYSDOH Zika Information Line at:
1-888-364-4723
9AM-6PM weekdays