Zika Virus in New York State: An Update for Obstetric and Neonatal Providers and the Birth Facility

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New York State Department of Health
September 20, 2016
Zika Virus – The Basics

• Single stranded RNA Virus of the Genus *Flavivirus*
• Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
• Arthropod-borne virus (arbovirus)
• Transmitted by the *Aedes* species mosquitoes
  • *Aedes aegypti* (Yellow fever mosquito): efficient vectors for Zika
  • *Aedes albopictus* (Asian tiger mosquito): possible vector for Zika
• Zika virus can be sexually transmitted and may persist in semen beyond the period of acute illness
• Outbreaks are occurring in many countries
• Zika virus can cause a congenital syndrome characterized by microcephaly and other abnormalities

*Courtesy of the Centers for Disease Control and Prevention*
Zika Virus Cases in the United States

As of September 14, 2016

• 3,176 cases of Zika virus diagnosed in the U.S. States and the District of Columbia
  • 43 (1.4%) are locally acquired mosquito-borne cases (Miami, Florida)
  • 3,132 (98.6%) are travel-associated/imported
  • 26 sexual transmission
  • 1 laboratory transmission
  • 8 Guillain-Barré syndrome
• New York (685 – 22%) and Florida (639 – 20%) have highest number of cases in the states
• Puerto Rico has 17,315 locally acquired cases

## Zika Virus Cases in New York State

### As of September 10, 2016

- 749 cases of Zika virus diagnosed in New York State
- New York City and Nassau and Suffolk Counties had the highest case burden
- No cases of local mosquito-borne transmission (LMBT)

### Table: Zika Virus Cases in New York State

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Human Cases</th>
<th>Zika</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Travel associated</td>
<td>LMBT**</td>
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</tbody>
</table>

### Notes
Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection

US States and the District of Columbia*

731

*Includes aggregated data reported to the US Zika Pregnancy Registry as of September 8, 2016

Pregnancy Outcomes in the United States and the District of Columbia

<table>
<thead>
<tr>
<th>Liveborn infants with birth defects*</th>
<th>Pregnancy losses with birth defects**</th>
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</thead>
<tbody>
<tr>
<td>18</td>
<td>5</td>
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</table>

Includes aggregated data reported to the US Zika Pregnancy Registry as of September 8, 2016

Objectives

• Risks of mother-to-child Zika virus transmission
• Prevention of congenital Zika syndrome
• Diagnostic testing of pregnant women potentially exposed to Zika virus
• Management of pregnant women potentially infected with Zika virus
• Labor & Delivery concerns
• Evaluation of the newborn
Zika and Neural Tissue

- Zika virus is neurotrophic
- Zika virus efficiently infects neural progenitor cells, producing cell death and abnormal growth
- Live Zika virus has been cultured from the brain of a fetus with severe anomalies after maternal infection
- Zika virus RNA has been identified in brain tissue of affected fetuses and infants
Zika Virus and Pregnancy Outcomes

• Causal relationship between prenatal Zika virus infection and certain severe brain anomalies, including microcephaly

• Evaluation of symptomatic women in Brazil (N=72 Zika virus positive)
  – Fetal ultrasound N=42
    • Fetal abnormalities (12/42; 29%)
  – Outcomes: fetal death (2), in utero growth restriction (5), ventricular calcification/CNS abnormalities (7)

• A retrospective analysis of the 2013–2014 Zika virus outbreak in French Polynesia
  – 8 fetuses and infants with microcephaly, representing an estimated 1% of fetuses or infants born to women infected with Zika virus during 1st trimester
  – Risk of other anomalies not assessed

Congenital Zika Syndrome

- Surveillance case definition under review
- Clinical
  - microcephaly, intracranial calcifications, or other central nervous system abnormalities
    - ventriculomegaly, abnormalities of the corpus callosum, cerebrum, and cerebellum, brain atrophy, hydranencephaly
    - features of brain disruption sequence may be seen (severe microcephaly, overlapping cranial sutures, prominent occipital bone, redundant scalp skin, neurologic impairment)
  - also described: eye findings, seizures, hypertonia, arthrogryposis, clubfoot
- Laboratory evidence (definitive or probable)
Microcephaly

• **Prenatally:**
  • Can be difficult to diagnose
  • May be detected by routine ultrasound at 18-20 weeks
  • However, best identified on ultrasound later in pregnancy (late second trimester, early third trimester)

• **Infant:**
  • CDC defines as head circumference < 3\textsuperscript{rd} percentile
  • CDC recommends INTERGROWTH-21\textsuperscript{st} standards
    [http://intergrowth21.ndog.ox.ac.uk/](http://intergrowth21.ndog.ox.ac.uk/)
    • Standard growth charts by gestation, sex, and age
What We Need to Know

- Relative and absolute risk among infants born to mothers infected at different times during pregnancy
- Other factors that might affect a woman’s risk of adverse pregnancy or birth outcomes
  - Co-infection with another virus
  - Preexisting immune response to another flavivirus
  - Genetic background of mother and fetus
  - Severity of maternal infection
- Validated birth prevalence estimates of microcephaly in Brazil or other countries in recent outbreak
- Full spectrum of defects caused by prenatal Zikavirus infection (ocular, hearing, joint, developmental …)

Goal: Prevent Congenital Zika Virus Syndrome

- No protective medication or vaccine exists
- Prevent maternal Zika exposure 8 weeks before conception and during the entire pregnancy
  - Prevent travel to area with active mosquito-borne Zika transmission by woman and her sexual partner(s)
  - Prevent mosquito bites
  - Prevent sexual transmission to pregnant woman or woman planning to conceive
## Suggested Timeframe to Wait Before Trying to Get Pregnant

**CDC, April 1, 2016**

<table>
<thead>
<tr>
<th>Possible exposure via recent travel or sex without a condom with a man infected with Zika</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zika symptoms</td>
<td>Wait at least 8 weeks after symptoms start</td>
<td>Wait at least 6 months after symptoms start</td>
</tr>
<tr>
<td>No Zika symptoms</td>
<td>Wait at least 8 weeks after exposure</td>
<td>Wait at least 8 weeks after exposure. Talk with your healthcare provider</td>
</tr>
</tbody>
</table>

**World Health Organization, September 6, 2016**

For regions with no active transmission of Zika virus, WHO recommends practising safer sex or abstinence for a period of six months for men and women who are returning from areas of active transmission to prevent Zika virus infection through sexual intercourse.

The couple should consistently practice safe sex with vaginal, oral and anal sex during the waiting period to prevent sexual transmission to the woman planning to conceive.

CDC:MMWR/ April 1, 2016 / 65(12);315–322
Care during Pregnancy: Management of Symptomatic Infection

- Approximately 80% of cases are asymptomatic
- Common symptoms include macular or papular rash, fever, arthralgias/myalgias, and conjunctivitis
- Clinical disease usually mild
- Supportive care
Care during Pregnancy: Diagnostic Testing (1)

- Zika virus testing is recommended for travel or sexual risk anytime during pregnancy inclusive of the 8 weeks prior to conception
  - Travel to an area of concern / emigration from an area of concern
  - Unprotected sex (oral, vaginal, anal) with a partner that lives in or has traveled in an area of concern
  - Test irrespective of the presence or absence of symptoms
Care during Pregnancy: Diagnostic Testing (2)

- Testing through Wadsworth Center, the New York State Department of Health (NYSDOH) Public Health Laboratory, is recommended for pregnant women living in NYS outside of New York City (NYC)
  - Comprehensive testing available inclusive of PCR and serology
  - Consistent approach to testing (PCR followed by serology as indicated) irrespective of estimated timing of exposure
  - Testing can be arranged by the Local Health Department through previously announced procedures

- Testing through the New York City Department of Health and Mental Hygiene (NYCDOHMH) Public Health Laboratory is recommended for pregnant women residing in NYC. Testing should be arranged in consultation with the NYCDOHMH.
  - Laboratory testing is conducted by the NYCDOHMH laboratory in conjunction with the NYSDOH Wadsworth Center
  - NYC Provider Access Line (PAL): 1 (866) 692-3641, Monday to Friday, 9 a.m. to 5 p.m.
Commercial Laboratories and Zika Virus Testing

• Commercially available testing varies by laboratory
  • Serum PCR only
  • Serum PCR, urine PCR, and/or IgM
  • Serum PCR, Plasma PCR, Urine PCR, and/or Zika IgM

• Negative predictive value of a given test is highly dependent on timing since exposure

• Zika IgM titers can be affected by cross-reactivity with other flaviviruses (ex. Dengue virus)

• Comprehensive serologic evaluation (ie, evaluation of total antibodies against specific flaviviruses by microsphere immunofluorescence assay and plaque reduction neutralization testing) is not available through commercial laboratories
# Zika Virus: Diagnostic Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose</th>
<th>Results</th>
<th>Next steps</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POLYMERASE CHAIN REACTION:</strong> (serum or urine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--PCR</td>
<td>Detect Zika virus genetic material</td>
<td>Detected or not detected (indeterminate, equivocal)</td>
<td>If Zika virus detected, infection is confirmed. No further testing needed</td>
</tr>
<tr>
<td><strong>SEROLOGY:</strong> (serum)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--Zika IgM ELISA antibody</td>
<td>Screening test for IgM antibodies to flaviviruses</td>
<td>Presumptive positive, negative (inconclusive, equivocal)</td>
<td>Results interpreted in conjunction with MIA and exposure history to determine if convalescent titers and PRNT needed</td>
</tr>
<tr>
<td>--Arbovirus Total Antibody Microsphere Immunofluorescence Assay (MIA)</td>
<td>Screening test for total antibodies to flaviviruses</td>
<td>Reactive, nonreactive</td>
<td>Results interpreted in conjunction with IgM and exposure history to determine if convalescent titers and PRNT needed</td>
</tr>
<tr>
<td>--Plaque Reduction Neutralization Testing (PRNT)</td>
<td>Quantifies amount of neutralizing antibody to viruses of interest</td>
<td>Positive, negative (for each flavivirus tested)</td>
<td>Usually conducted on paired sera in follow-up of possible IgM presence and/or reactive MIA. May be done on single specimen to provide preliminary information in pregnant women</td>
</tr>
</tbody>
</table>


Persistent Viremia in Pregnant Woman

- Prior data suggested that viremia lasted approximately one week after symptom onset
- Case report: pregnant woman with serum PCR positivity at 4 weeks and 10 weeks after symptom onset
  - But not after delivery
  - Fetal infection confirmed
  - Brain abnormalities on fetal MRI
- Prognostic significance of prolonged viremia unknown
- No restriction by NYSDOH Wadsworth Center on PCR testing in pregnant women based on timing after exposure

Integrating Laboratory Results with Exposure History to Assess Risk: Case Example 1

No potential Zika exposure

Conception

Potential Zika exposure

Acute and Convalescent Testing: PCR (serum and urine) Zika IgM, MIA PRNT

No potential Zika exposure

Delivery
Integrating Laboratory Results with Exposure History to Assess Risk: Case Example 2

Residence in an area of ongoing mosquito-borne Zika transmission, or potential ongoing sexual exposure

<table>
<thead>
<tr>
<th>Conception</th>
<th>Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>No potential Zika exposure</td>
<td></td>
</tr>
</tbody>
</table>

Acute and Convalescent Testing:
- PCR (serum and urine)
- Zika IgM
- MIA
- PRNT
Care during Pregnancy: Management of Pregnant Women with Incomplete or Inconclusive Testing

- Available testing may not distinguish between past Zika virus and other flavivirus infections
- Women with a history of potential pregnancy-related exposure and any laboratory evidence of Zika virus infection should be managed as if they have been exposed to Zika virus
• CDC recommendations for care of pregnant women with possible Zika virus exposure
• NYSDOH testing algorithm is simpler and more expansive than CDC’s algorithm
Care during Pregnancy: Fetal Imaging and Amniocentesis

- Women with pregnancy-associated exposure history and any laboratory evidence of possible Zika infection should be followed with serial fetal ultrasounds every 3-4 weeks to assess fetal anatomy, particularly neuroanatomy, and to monitor growth.
- Decisions about amniocentesis should be individualized:
  - Amniotic fluid can be tested for Zika virus with PCR.
  - The predictive value of PCR results (either detectable or undetectable) is unknown.

MMWR, July 29, 2016
Fetal Loss or Stillbirth

- Women with fetal loss or stillbirth and laboratory evidence of possible Zika virus may benefit from information about the potential role of Zika virus
- PCR and immunohistochemical testing on fixed tissue and/or PCR on fresh frozen tissue available
- For information about testing, contact
  - **New York State outside of New York City** – Zika Information Line 1-888-364-4723 - Monday – Friday (9 a.m. to 5 p.m.)
Care during Labor and Delivery (L&D) and Care of the Newborn: Coordination of Care

- Routine procedures should be developed to convey Zika related history and laboratory assessment from prenatal care site to birthing facilities
- Routine assessment of travel history of pregnant woman and her sexual partner(s)
- Establishing communication and procedures for care within the birth facility prior to presentation for delivery is important
  - L & D staff
  - Infection Control
  - Laboratory: pathology, send-out
  - Electronic medical record capacity
  - Newborn pediatric care provider
  - Outpatient pediatric care provider
Management of Infants with Abnormalities Consistent with Congenital Zika Syndrome

- Zika virus testing
  - Maternal testing, if not previously completed
  - Infant urine for PCR
  - Infant serum for PCR and serology
  - Placenta/umbilical cord
    - Fixed tissue for PCR and IHC
    - Fresh frozen tissue for PCR
- Evaluation for other causes of microcephaly
- Consultation and evaluation as indicated, with attention to neurologic, ophthalmologic and auditory status

Consultation with:
- Neurologist for determination of appropriate neuroimaging and additional evaluation.
- Infectious disease specialist for diagnostic evaluation of other congenital infections (e.g., syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus infection).
- Ophthalmologist for comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from the hospital or within 1 month of birth.
- Endocrinologist for evaluation for hypothalamic or pituitary dysfunction.
- Clinical geneticist to evaluate for other causes of microcephaly or other anomalies if present.

Consider consultation with:
- Orthopedist, physiatrist, or physical therapist for the management of hypertonia, club foot or arthrogryposis-like conditions.
- Pulmonologist or otolaryngologist for concerns about aspiration.
- Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist for the management of feeding issues.
- Perform auditory brainstem response to assess hearing.
- Perform complete blood count and metabolic panel, including liver function tests.
- Provide family and supportive services.
Management of Infants Born to Mothers with Laboratory Evidence of Zika Virus Infection: No Evidence of Infant Abnormalities

Before hospital discharge

Routine newborn care: PE, HC, weight/length, and neurologic exam
Hearing screen
Head US
Infant Zika virus testing (Table 1)

Table 2 Excerpt
MMWR, August 19, 2016

• Zika virus testing
  – Infant urine for PCR
  – Infant serum for PCR and serology
  – Placenta/umbilical cord
    • Fixed tissue for PCR and IHC
    • Fresh frozen tissue for PCR
Management of Infants Born to Mothers with Risk of Zika Virus Exposure not Previously Evaluated: No Evidence of Infant Abnormalities

Before hospital discharge

- Maternal Zika virus testing
- Consider Zika virus placental testing
- Routine newborn care: PE, HC, weight/length and neurologic exam
- Hearing screen
- Head US

• Zika virus testing
  - Maternal testing
  - Consider infant testing, especially if follow-up uncertain
  - Consider storing placental sections for further testing to be conducted if maternal testing provides laboratory evidence of possible Zika virus infection

Table 2 Excerpt
MMWR, August 19, 2016
Laboratory Testing through the NYSDOH or NYCDOHMH Public Health Laboratories:
Placenta and Newborn Testing

• New York State outside of New York City
  – Testing through Wadsworth Center, the NYSDOH Public Health Laboratory, is recommended
  – Testing can be arranged by contacting the Zika Information Line 1-888-364-4723 - Monday – Friday (9 a.m. to 5 p.m.). Urgent after hours inquiries can be directed to 1-866-881-2809.

• New York City
  – Consult NYCDOHMH for criteria for testing. Provider Access Line (PAL): 1-866-692-3641, Monday to Friday, 9 a.m. to 5 p.m.
  – Additional information is available for NYC providers at nyc.gov/zka/provider
Breast Feeding

• Zika virus RNA has been identified in breast milk
• No reports of Zika virus infection associated with breastfeeding
• Current evidence suggests that the benefits of breastfeeding outweigh the theoretical risks of Zika virus transmission.
• Current recommendations from both the CDC and the WHO are that women should be encouraged and supported to breastfeed their infants, regardless of maternal or infant Zika virus testing results.
Future Pregnancies

No evidence Zika virus will cause congenital infection in subsequent pregnancies conceived after resolution of maternal Zika viremia
CDC Zika Pregnancy Registry

• Goals
  – To collect information about pregnancy and infant outcomes following Zika virus infection during pregnancy.
  – To update recommendations for clinical care, plan for services for pregnant women and families, and improve prevention of Zika virus infection during pregnancy.

• Infants of women who meet inclusion criteria will be followed at regular intervals for the first year of life.
Reporting **Suspect Zika Virus Cases**

- Healthcare providers are required to report all **suspected** cases to their **local health department where the patient resides**

- Timely reporting allows NYSDOH and local health departments to assess and reduce the risk of local transmission or mitigate further spread
Zika Resources

• CDC Zika Virus Information Page
  – Q&As for Obstetricians and Pediatricians

• NYSDOH Zika Virus Information Page
  – Advisories and webinars
  – Testing process one page information sheet for the public
  – Statewide mosquito-borne disease weekly report

• NYC DOHMH Zika virus Information Page
Acknowledgements

- NYC DOHMH
- 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-5PM weekdays

lou.smith@health.ny.gov