Zika Virus — What Clinicians Need to Know?

Clinician Outreach and Communication Activity (COCA) Call
January 26, 2016
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Objectives

At the conclusion of this session, the participant will be able to:

- Describe the epidemiology, clinical manifestations, management, and prevention of Zika virus disease
- Discuss diagnostic testing for Zika virus infection and interpretation of test results
- Articulate the importance of early recognition and reporting of cases
- State the recommendations for pregnant women and possible Zika virus exposure
- Discuss evaluation of infants with microcephaly and the relationship of Zika and microcephaly
TODAY’S PRESENTER

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TODAY’S PRESENTER

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Zika Virus
The latest emerging arbovirus in the Americas

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January 26, 2016
Zika Virus

- Single stranded RNA Virus
- Genus *Flavivirus*, Family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes (Stegomyia)* species mosquitoes
Zika Virus Vectors: Aedes Mosquitoes

- *Aedes* species mosquitoes
  - *Ae aegypti* more efficient vectors for humans
  - *Ae albopictus*
- Also transmit dengue and chikungunya viruses
- Lay eggs in domestic water-holding containers
- Live in and around households
- Aggressive daytime biters
Aedes aegypti and Aedes albopictus Mosquitoes: Geographic Distribution in the United States

Aedes aegypti

Aedes albopictus
Zika Virus Transmission Cycles

Sylvatic (jungle) cycle

Epidemic (urban) cycle
Other Modes of Transmission

- Maternal-fetal
  - Intrauterine
  - Perinatal
- Other
  - Sexual
  - Blood transfusion
  - Laboratory exposure
- Theoretical
  - Organ or tissue transplantation
  - Breast milk
Zika Virus:
Countries or Territories with Reported Local Transmission

as of January 23, 2016
Zika Virus Epidemiology

- First isolated from a monkey in Uganda in 1947
- Prior to 2007, only sporadic human disease cases reported from Africa and southeast Asia
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013–2014, >28,000 suspected cases reported from French Polynesia*

Zika Virus in the Americas

- In May 2015, the first locally-acquired cases in the Americas were reported in Brazil
- Currently, outbreaks are occurring in many countries or territories in the Americas, including the Commonwealth of Puerto Rico and the U.S. Virgin Islands
- Spread to other countries likely
Zika Virus in the Continental United States

- Local transmission of Zika virus has not been reported in the continental United States
- Since 2011, there have been laboratory-confirmed Zika virus cases identified in travelers returning from areas with local transmission
- With current outbreaks in the Americas, cases among U.S. travelers will most likely increase
- Imported cases may result in virus introduction and local spread in some areas of U.S.
Zika Virus Incidence and Attack Rates

- Infection rate: 73% (95%CI 68–77)
- Symptomatic attack rate among infected: 18% (95%CI 10–27)
- 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 Confirmed Zika Virus Disease Cases

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>N (n=31)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macular or popular 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
Zika Virus Clinical Disease Course and Outcomes

- Clinical illness usually mild
- Symptoms last several days to a week.
- Severe disease requiring hospitalization uncommon
- Fatalities are rare
- Guillain-Barré syndrome reported in patients following suspected Zika virus infection
  - Relationship to Zika virus infection is not known
Zika Virus and Microcephaly in Brazil

- Reports of a substantial increase in number of babies born with microcephaly in 2015 in Brazil; true baseline unknown
  - Zika virus infection identified in several infants born with microcephaly (including deaths) and in early fetal losses
  - Some of the infants with microcephaly have tested negative for Zika virus
- Incidence of microcephaly among fetuses with congenital Zika infection is unknown
Rates of Microcephaly Over Time: the Americas and the Caribbean

Comparison of the rates of microcephaly in the Americas and Caribbean from 2010-2014 and 2015

Updated as of Epidemiological Week 52 (December 27, 2015 – January 2, 2016)

Microcephaly rates by state in Brazil (cases per 1,000 live births)
- 0.1-1.0
- 1.1-15.0
- 15.1-30.0
- 30.1-45.0
- 45.1-88.6

Countries with Zika confirmed cases
- Epi Week 52 2015

Data Source:
Reported from the IHR National Focal Points and through the Ministry of Health websites.

Map Production:
PAHO-WHO AD CHA IR ARO

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>
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<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>
</tbody>
</table>
Diagnostic Testing for Zika Virus

- Reverse transcriptase-polymerase chain reaction (RT-PCR) for viral RNA in serum collected ≤7 days after illness onset
- Serology for IgM and neutralizing antibodies in serum collected ≥4 days after illness onset
- Plaque reduction neutralization test (PRNT) for ≥4-fold rise in virus-specific neutralizing antibodies in paired sera
  - Only available at CDC
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues
Zika virus serology (IgM) 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 primary flavivirus infections

Difficult to distinguish infecting virus in people previously infected with or vaccinated against a related flavivirus

Healthcare providers should work with state and local health departments to ensure test results are interpreted correctly
Laboratories for Diagnostic Testing

- No commercially-available diagnostic tests
- Testing performed at CDC and a few state health departments
- CDC is working to expand laboratory diagnostic testing in states
- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infections
- Healthcare providers should contact their state health department to facilitate diagnostic testing
Initial Assessment and Treatment

- No specific antiviral therapy
- Treatment 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
Differential Diagnosis for Zika Virus Disease

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Rickettsia
- Parvovirus
- Group A streptococcus
- Rubella
- Measles
- Adenovirus
- Enterovirus

* Similar clinical presentations
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 infected during pregnancy for possible congenital infection and microcephaly.
- Be aware of possible local transmission in areas where Aedes species mosquitoes are active.
Reporting Zika Virus Disease Cases

- Zika virus is a nationally notifiable disease
  - Healthcare providers encouraged to report suspected cases to their state health department
- State health departments are requested to report laboratory-confirmed cases to CDC
- Timely reporting allows health departments to assess and reduce the risk of local transmission or mitigate further spread
Zika Virus Preventive Measures

- No vaccine or medication to prevent infection or disease
- Primary prevention measure is to reduce mosquito exposure
- Pregnant women should consider postponing to areas with ongoing Zika virus outbreaks
- Protect infected people from mosquito exposure during first week of illness to prevent further transmission
Possible Future Course of Zika virus in the Americas

- Virus will continue to spread in areas with competent vectors
  - Transmission increasing in Central America, Mexico, and Caribbean
  - Anticipate further spread in Puerto Rico and U.S. Virgin Islands

- Travel-associated cases will introduce virus to U.S. states
  - Imported cases will result in some local transmission and outbreaks
  - Air conditioning may limit the size and scope of outbreaks
  - Colder temperatures will interrupt and possibly stop further spread

- Experience from dengue might be predictive
  - From 2010–2014, 1.8 million dengue cases reported per year to PAHO
  - 558 travel-related and 25 locally transmitted cases in U.S. states
Zika Virus and Pregnancy

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CDC Zika Response Team
Centers for Disease Control and Prevention

January 26, 2016
Zika Virus and Pregnancy

- Limited information is available
- Existing data show:
  - No evidence of increased susceptibility
  - Infection can occur in any trimester
  - Incidence of Zika virus in this population is not known
  - No evidence of more severe disease

Centers for Disease Control and Prevention, *CDC Health Advisory: recognizing Managing and reporting Zika Virus Infections in Travelers Returning from Central America, South America, the Caribbean and Mexico*, 2016.


Maternal-Fetal Transmission of Zika Virus

- Evidence of maternal-fetal transmission
  - Zika virus infection confirmed in infants with microcephaly in Brazil and in infants whose mothers have traveled to Brazil but delivered in the US
  - Zika virus RNA identified in specimens of fetal losses
  - Zika virus detected prenatally in amniotic fluid
    - Two women at ~30 weeks gestation with a history of symptoms consistent with Zika infection
    - Fetal microcephaly and intracranial calcifications detected on ultrasound
    - Amniotic fluid testing positive for Zika virus RNA by RT-PCR

Maternal-Fetal Transmission of Zika Virus

- Evidence of perinatal transmission (during time of delivery)
  - Zika outbreak in French Polynesia 2013-2014
    - Two pregnant women with signs and symptoms consistent with Zika infection around the time of delivery
    - Both mothers tested positive for Zika virus RNA by RT-PCR
    - Zika virus infection was confirmed in the neonates, 1-3 days after delivery
    - Unlikely that neonates were exposed to mosquitoes
    - Outcomes regarding microcephaly was not reported

CDC Recommendations: Pregnant Women Considering Travel

- Pregnant women in any trimester should consider postponing travel to areas where Zika is present.

- 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.
Zika Virus Disease Prevention: Pregnant Women

- Avoid mosquito bites:
  - Use EPA-registered insect repellent
    - EPA-registered repellents including DEET are considered safe to use in pregnant and lactating women
  - Wear long-sleeved shirts and long pants to cover exposed skin
  - Wear Permethrin-treated clothes
  - Stay and sleep in screened-in or air-conditioned rooms
- *Aedes* mosquitoes bite mostly during the daytime
  - Practice mosquito prevention strategies throughout the entire day
Evaluation of Pregnant Women

- Healthcare providers:
  - Obtain recent travel history from pregnant women
  - If history of travel to an area with ongoing Zika transmission during pregnancy is present:
    - Evaluate for symptoms of Zika virus and other related viruses (dengue and chikungunya) during or within 2 weeks of travel
    - Refer to the “Interim Guidelines for Pregnant Women During a Zika Virus Outbreak — United States, 2016”

http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1er.htm?s_cid=mm6502e1er_e
Interim guidance:
Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman reports clinical illness consistent with Zika virus disease during or within 2 weeks of travel

Test for Zika virus infection

Positive or inconclusive test for Zika virus infection

Fetal ultrasound to detect microcephaly or intracranial calcifications
Offer amniocentesis for Zika virus testing

Negative test(s) for Zika virus infection

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding is present

Consider amniocentesis for Zika virus testing

No findings present

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding is present

Consider amniocentesis for Zika virus testing

No findings present

Pregnant woman does NOT report clinical illness consistent with Zika virus disease during or within 2 weeks of travel

Test for Zika virus infection

Negative test(s) for Zika virus infection

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding is present

Consider amniocentesis for Zika virus testing

No findings present

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding develops

Consider serial ultrasounds to detect development of microcephaly or intracranial calcifications
Recommendations for Testing

- Pregnant women should be tested:
  - History of travel to an area with Zika virus transmission during pregnancy AND:
    - Presence of two or more of the following symptoms (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) during travel or within 2 weeks of travel
    OR
    - Presence of fetal microcephaly or intracranial calcification by ultrasound
Interim guidance: 
Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman reports symptoms* consistent with Zika virus disease during or within 2 weeks of travel

Test for Zika virus infection**

Positive or inconclusive test for Zika virus infection

Fetal ultrasound to detect microcephaly or intracranial calcifications
Offer amniocentesis for Zika virus testing
Recommended ≥15 weeks

*Two or more of the following symptoms:
• Acute onset of fever
• Maculopapular rash
• Arthralgia
• Conjunctivitis

**RT-PCR test should be performed during the first week after onset of symptoms
Interim guidance:
Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman reports symptoms consistent with Zika virus disease during or within 2 weeks of travel

Test for Zika virus infection

Positive or inconclusive test for Zika virus infection:
- Fetal ultrasound to detect microcephaly or intracranial calcifications
- Offer amniocentesis for Zika virus testing
  Recommended ≥15 weeks

Negative test(s) for Zika virus infection:
- Fetal ultrasound to detect microcephaly or intracranial calcifications
- Either finding is present
  Consider amniocentesis for Zika virus testing
Interim guidance: Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman reports symptoms consistent with Zika virus disease during or within 2 weeks of travel

Test for Zika virus infection

Positive or inconclusive test for Zika virus infection

Fetal ultrasound to detect microcephaly or intracranial calcifications
Offer amniocentesis for Zika virus testing
Recommended ≥15 weeks

Negative test(s) for Zika virus infection

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding is present
Consider amniocentesis for Zika virus testing

No findings present
Interim guidance: Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman does NOT report symptoms consistent with Zika virus disease during or within 2 weeks of travel

Fetal ultrasound to detect microcephaly or intracranial calcifications
Interim guidance:
Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman does NOT report symptoms consistent with Zika virus disease during or within 2 weeks of travel

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding is present

Test** pregnant woman for Zika virus infection
Consider amniocentesis for Zika virus testing

**Serology assay should be used
Interim guidance:
Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman does NOT report symptoms consistent with Zika virus disease during or within 2 weeks of travel

Fetal ultrasound to detect microcephaly or intracranial calcifications

No findings present

Consider serial ultrasounds to detect development of microcephaly or intracranial calcifications
Interim guidance:
Testing Algorithm for a Pregnant Woman with History of Travel to an Area with Zika Virus Transmission

Pregnant woman does NOT report symptoms consistent with Zika virus disease during or within 2 weeks of travel

Fetal ultrasound to detect microcephaly or intracranial calcifications

Either finding is present
- Test** pregnant woman for Zika virus infection
  - Consider amniocentesis for Zika virus testing

No findings present
- Consider serial ultrasounds to detect development of microcephaly or intracranial calcifications

Either finding develops

**Serology assay should be used
Zika and Pregnancy: Clinical Management

- Confirmed maternal or fetal infection:
  - Antepartum:
    - Consider serial ultrasounds every 3-4 weeks
    - Consider referral to specialist with expertise in pregnancy management
  - Peripartum:
    - Histopathologic examination of the placenta and umbilical cord;
    - Testing of frozen placental tissue and cord tissue for Zika virus RNA
    - Testing of cord serum for Zika and dengue virus IgM and neutralizing antibodies
Zika Virus and Microcephaly

Cynthia Moore, MD, PhD
Pregnancy and Birth Defects Team
CDC Zika Response Team
Centers for Disease Control and Prevention

January 26, 2016
What is Microcephaly?

- Clinical finding of a small head when compared to infants of same sex and age
- Measured by head circumference (HC) or occipitofrontal circumference (OFC)
- Reliable assessment of intracranial brain volume
- Often leads to cognitive and/or neurologic issues
- Mechanisms
  - primary due to abnormal development (often with a genetic etiology)
  - secondary due to arrest or destruction of normally-forming brain tissue (by infection, vascular disruption)
- Difficult birth defect to monitor because of inconsistent definition and use of terminology
Infants with Microcephaly

AP Photos/Felipe Dana

Typical newborn head CT scan

scattered intracranial calcifications
enlarged ventricles and volume loss
Range of Microcephaly Severity

Baby with Typical Head Size

Baby with Microcephaly

Baby with Severe Microcephaly
Fetal Brain Disruption Sequence

- First described in 1984 but noted in earlier literature
- Brain destruction resulting in collapse of the fetal skull, microcephaly, scalp rugae and neurologic impairment
- Images below from 1990 series; phenotype appears to be present in some affected babies in Brazil (2015—present)

Moore et al., J Peds, 1990
Microcephaly and Zika

What we know

• Small number of positive test results for Zika virus infection in infants with microcephaly
• Microcephaly pattern consistent with Fetal Brain Disruption Sequence
  • Based on photos/scans of a small number of affected infants from Brazil
  • Retrospective investigation in French Polynesia outbreak in 2013-2014
  • Infants with other intrauterine infections such as cytomegalovirus (CMV)

What we don’t know

• Causal relation between Zika virus and microcephaly or other adverse pregnancy outcomes
• Full spectrum of phenotypes in affected infants
• Impact of timing of infection during pregnancy
• Impact of severity of maternal infection
• Magnitude of the possible risk of microcephaly and other adverse pregnancy outcomes
**Zika Virus Laboratory Testing of Infants***

- **Recommended for**
  1. Infants with microcephaly or intracranial calcifications born to women who traveled to or resided in an area with Zika virus transmission while pregnant
  2. Infants born to mothers with positive or inconclusive test results for Zika virus infection

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

- **Recommended tests**
  - Zika virus RNA (RT-PCR), IgM, and neutralizing antibodies
  - Dengue virus IgM and neutralizing antibodies

- **Clinical specimens**
  - Serum (umbilical cord or direct, within 2 days of birth if possible)
  - Cerebrospinal fluid, if obtained for other studies

- **Consider histopathologic evaluation (placenta and umbilical cord)**
  - Zika virus immunohistochemical staining (fixed tissue)
  - Zika virus RT-PCR (fixed and frozen tissue)

- **Additionally, if not already performed, test mother’s serum**
  - Zika virus IgM and neutralizing antibodies
  - Dengue virus IgM and neutralizing antibodies

*When indicated, including: 1) infants with microcephaly or intracranial calcifications born to women potentially exposed to Zika virus during pregnancy, or 2) infants born to mothers with positive or inconclusive test results for Zika virus infection.
Interim Guidelines: Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection

Among infants with microcephaly or intracranial calcifications

Microcephaly or intracranial calcifications detected prenatally or at birth

Perform Zika virus testing and other clinical evaluation of infant

Positive or inconclusive test for Zika virus infection in infant
- Report case and assess infant for possible long-term sequelae

Negative tests for Zika virus infection in infant
- Evaluate and treat for other possible etiologies
Interim Guidelines: Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection

Among infants without microcephaly or intracranial calcifications

- No microcephaly or intracranial calcifications detected prenatally or at birth

  - Positive or inconclusive test for Zika virus infection in mother prior to delivery
    - Conduct thorough physical examination and perform Zika virus testing in infant
      - Positive or inconclusive test for Zika virus infection in infant
        - Perform additional clinical evaluation, report case, and assess for possible long-term sequelae
      - Negative tests for Zika virus infection in infant
  
  - No Zika virus testing performed on mother prior to delivery
    - Test mother if she reported clinical illness consistent with Zika virus disease during pregnancy
      - Positive or inconclusive test for Zika virus infection in mother
      - Negative tests for Zika virus infection in mother
        - No testing indicated if mother did not report clinical illness consistent with Zika virus disease during pregnancy
        - Negative tests for Zika virus infection in mother prior to delivery

  - Negative tests for Zika virus infection in mother prior to delivery
    - Routine care of infant, including appropriate follow-up on any clinical findings
Interim Guidelines: Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection

Among infants **without** microcephaly or intracranial calcifications

1. **Positive or inconclusive test for Zika virus infection in mother prior to delivery**
   - Conduct thorough physical examination and perform Zika virus testing in infant
     - **Positive or inconclusive test for Zika virus infection in infant**
       - Perform additional clinical evaluation, report case, and assess for possible long-term sequelae
     - **Negative tests for Zika virus infection in infant**
       - Routine care of infant, including appropriate follow-up on any clinical findings
Interim Guidelines: Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection

Among infants without microcephaly or intracranial calcifications

No microcephaly or intracranial calcifications detected prenatally or at birth

Positive or inconclusive test for Zika virus infection in mother prior to delivery

Conduct thorough physical examination and perform Zika virus testing in infant

Positive or inconclusive test for Zika virus infection in infant

Negative tests for Zika virus infection in infant

Perform additional clinical evaluation, report case, and assess for possible long-term sequelae

No Zika virus testing performed on mother prior to delivery

Test mother if she reported clinical illness consistent with Zika virus disease during pregnancy

Positive or inconclusive test for Zika virus infection in mother

Negative tests for Zika virus infection in mother

Routine care of infant, including appropriate follow-up on any clinical findings

No testing indicated if mother did not report clinical illness consistent with Zika virus disease during pregnancy
Interim Guidelines: Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection

Among infants without microcephaly or intracranial calcifications

No microcephaly or intracranial calcifications detected prenatally or at birth

Positive or inconclusive test for Zika virus infection in mother prior to delivery
- Conduct thorough physical examination and perform Zika virus testing in infant
  - Positive or inconclusive test for Zika virus infection in infant
    - Perform additional clinical evaluation, report case, and assess for possible long-term sequelae
  - Negative tests for Zika virus infection in infant
    - Routine care of infant, including appropriate follow-up on any clinical findings

No Zika virus testing performed on mother prior to delivery
- Test mother if she reported clinical illness consistent with Zika virus disease during pregnancy
  - Positive or inconclusive test for Zika virus infection in mother
    - Routine care of infant, including appropriate follow-up on any clinical findings
  - Negative tests for Zika virus infection in mother
    - Routine care of infant, including appropriate follow-up on any clinical findings
- No testing indicated if mother did not report clinical illness consistent with Zika virus disease during pregnancy
  - Negative tests for Zika virus infection in mother prior to delivery

Negative tests for Zika virus infection in mother prior to delivery

Flowchart:
- Positive or inconclusive test for Zika virus infection in mother prior to delivery
- Conduct thorough physical examination and perform Zika virus testing in infant
- Test mother if she reported clinical illness consistent with Zika virus disease during pregnancy
- No testing indicated if mother did not report clinical illness consistent with Zika virus disease during pregnancy
- Negative tests for Zika virus infection in mother prior to delivery
- Routine care of infant, including appropriate follow-up on any clinical findings
Evaluation and Testing for All Infants with Possible Congenital Zika Virus Infection

For all infants with possible congenital Zika virus infection, perform the following:

- Thorough physical examination, including careful measurement of the head circumference, length, weight, and assessment of gestational age*
- Cranial ultrasound, unless prenatal ultrasound results from third trimester demonstrated no abnormalities of the brain
- Further evaluation
  - neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions*
  - hearing by evoked otoacoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth*
  - eye exam to include visualization of the retina, optic nerve, and macula either before discharge from the hospital or within 1 month after birth*
- Other evaluations specific to the infant’s clinical presentation

*If any abnormalities are noted, consultation with the appropriate specialist is recommended.
Additional Evaluation for Infants with Microcephaly or Intracranial Calcifications

- For infants with microcephaly, consultations are recommended with
  - A clinical geneticist or dysmorphologist
  - A pediatric neurologist to determine appropriate brain imaging and additional evaluation (e.g., US, CT scan, MRI, and/or EEG)
  - A pediatric infectious disease specialist should be considered after testing for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus, lymphocytic choriomeningitis virus, and herpes simplex viruses

- Further testing includes
  - Complete blood count, platelet count, and liver function tests including alanine aminotransferase, aspartate aminotransferase, and bilirubin

- Consideration of genetic and other teratogenic causes based on additional congenital anomalies that are identified through clinical examination and imaging studies
Recommended Long-Term Follow-up of Infants with Possible Congenital Zika Virus Infection

- Report case to state, territorial, or local health department and monitor for additional guidance as it released
- Conduct additional hearing screen at age 6 months, plus any appropriate follow-up of hearing abnormalities detected through newborn hearing screening
- Carefully evaluate head circumference and developmental characteristics and milestones throughout the first year of life
  - Use of appropriate consultations with medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy)
CDC Activities and Plans

- Coordinate response with PAHO and other regional partners
- Assist with investigations of microcephaly and Guillain-Barré syndrome
- Continue to evaluate and revise guidance as new data emerge
- Distribute guidance through health advisories, MMWR publications and the CDC website
- Communicate regularly with clinicians (COCA calls), professional organizations and state and local partners
Zika Virus Remaining Questions

- Incidence of maternal- fetal transmission by trimester
  - Factors that influence (e.g., severity of infection, maternal immune response)
- Risk of microcephaly and other fetal and neonatal outcomes
- Risk of Guillain-Barré syndrome
- Potential for long-term reservoirs of Zika
Summary

- Zika virus continues to circulate and cause locally-transmitted disease in the Americas
- Consider the possibility of Zika virus infection in travelers with acute fever, rash, arthralgia, or conjunctivitis within 2 weeks after return
- A substantial increase in rates of congenital microcephaly have been reported in Brazil
  - Studies are underway to characterize the relationship between Zika and congenital microcephaly
- Pregnant women in any trimester should consider postponing travel to areas of Zika virus transmission
Zika Virus Remaining Questions

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CDC Activities and Plans

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Additional Resources

Selected References

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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