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  Passcode: 974205265
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Zika Virus: Updates to Clinical Guidance and Recommendations for Pregnant Women and Infants

Clinician Outreach and Communication Activity (COCA) Webinar
July 27, 2017
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National Center for Emerging & Zoonotic Infectious Diseases
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Duke Ophthalmology
Duke University School of Medicine
To Ask a Question

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Update: Interim Guidance for Healthcare Providers Caring for Pregnant Women with Possible Zika Virus Exposure—United States, July 2017

Titilope Oduyebo, MD, MPH
Lead, Clinical Team, Pregnancy & Birth Defects Task Force
CDC’s Zika Virus Response

July 27, 2017
Topics to be covered

• Updated interim guidance for pregnant women
  • Emerging data and current state of epidemic
  • Updated recommendations for testing and interpretation of results

• Pregnancy outcomes after maternal Zika virus exposure
  • Zika Pregnancy and Infant Registries
  • Findings from the Zika Pregnancy and Infant Registries and implications

• Pediatric ophthalmologic findings among infants following congenital Zika virus infection
  • Ocular findings among infants with congenital Zika virus infection
  • CDC guidance for ophthalmologic screening for infants with possible congenital infection
Emerging Data and Current State of Epidemic
Big Picture: Emerging Data and Implications for Zika Testing

- Declining trend in reported cases of Zika infection leads to lower pretest probability and a higher proportion of positive test results being false
- Zika virus IgM antibodies can persist for months in some people, which could make it difficult for healthcare providers to use Zika IgM test results to determine whether an infection occurred during the current pregnancy versus prior to conception
Declining Trends in Reported Zika Cases in the Americas

Confirmed and suspected Zika virus in the Americas, 2015–2017 (as of May 25, 2017)

Declining Trends in Reported Zika Virus Disease Cases in the US

Laboratory-confirmed Zika virus disease cases in US states and Washington, DC, 2016–2017 (as of July 5, 2017)
Example 1: Disease is common
- 40 out of 100 patients in this area have the disease
- Test specificity: 98% (high)
- Test sensitivity: 98% (high)
Hypothetical Example of Disease Prevalence and Implications for Test Performance: Disease is Rare

Example 2: Disease is rare
- 1 out of 100 patients in this area have the disease
- Test specificity: 98% (high)
- Test sensitivity: 98% (high)

67% false positive
Prolonged Zika Virus IgM

- Zika virus IgM can persist beyond 12 weeks in a subset of infected people

- Unpublished preliminary data from Zika Virus Persistence (ZiPer) Study of persons with NAT-confirmed Zika virus disease
  - Zika virus IgM detected in 100% of participants at 8-15 days after symptom onset
  - Detectable IgM levels decreased over time, however some participants remained IgM positive for more than 7 months after symptom onset

CDC HAN-00402: https://emergency.cdc.gov/han/han00402.asp
Pregnant woman with possible exposure to Zika virus before current pregnancy

A positive Zika IgM antibody test result could mean....

- Zika virus infection during current pregnancy, meaning pregnancy is likely at risk from Zika
- Zika virus infection before current pregnancy, meaning pregnancy is likely not at risk from Zika
- False positive result, meaning pregnancy is likely not at risk from Zika
Updated Guidance
Updated Guidance: Emphasis on Shared Decision-Making Model

• Updated guidance emphasizes a shared decision-making model for testing and screening pregnant women

• Clinical judgment is imperative
  • Decisions about testing should be informed by factors such as
    • Length of possible exposure
    • Type or location of travel
    • Intensity of Zika transmission
    • Presence of symptoms
    • Prevention measures
    • Preferences or concerns
    • Jurisdictional recommendations
Symptomatic Pregnant Women with Possible Zika virus Exposure

**UPDATED INTERIM PREGNANCY GUIDANCE:**
**SYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE**

**Testing Recommendations and Interpretation of Results for Healthcare Providers**

**ASK PREGNANT WOMEN ABOUT**
- Travel to or residence in any areas with risk for Zika virus transmission before and during the current pregnancy
- Possible sexual exposure before and during the current pregnancy
- A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy
- Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia)

Before testing, discuss testing limitations and potential risks for misinterpretations of test results.

**WHOM to test?**
- Pregnant women reporting possible exposure during current pregnancy and symptoms of Zika virus disease

**WHEN to test?**
- Test as soon as possible, through 12 weeks after symptom onset

**WHICH tests?**
- Zika virus NAT (serum and urine) AND Zika virus IgM serology (serum)

**RESULTS and ADDITIONAL tests**
- Positive Zika virus NAT (if Zika IgM negative, see footnote)
- Negative Zika virus NAT AND non-negative Zika virus IgM
- Plaque reduction neutralization test (PRNT)
- Zika virus PRINT >10 AND dengue virus PRINT <10
- Zika virus PRINT >10 AND dengue virus PRINT ≥10
- Zika virus PRINT <10

**INTERPRETATION**
- **ACUTE ZIKA VIRUS INFECTION**
- **ZIKA VIRUS INFECTION, TIMING OF INFECTION CANNOT BE DETERMINED**
- **FLAVIVIRUS INFECTION, SPECIFIC VIRUS AND TIMING OF INFECTION CANNOT BE DETERMINED**
- **NO EVIDENCE OF ZIKA VIRUS INFECTION**
Updated Guidance: Ask Pregnant Women

**ASK PREGNANT WOMEN** about
- Before and during current pregnancy:
  - Travel or residence in areas with risk for Zika virus transmission
  - Possible sexual exposure
  - Diagnosis of laboratory-confirmed Zika virus infection before the current pregnancy
  - Symptoms of Zika virus infection during the current pregnancy

If no symptoms reported, refer to asymptomatic algorithm.
Updated Guidance: When to Test Symptomatic Pregnant Women

WHEN to test?
Test as soon as possible; through 12 weeks after symptom onset
Updated Guidance: Which Tests for Symptomatic Pregnant Women

**WHICH tests?**
- Zika virus NAT* (serum and urine)
- Zika virus IgM serology (serum)

**NAT** = nucleic acid testing
RESULTS & INTERPRETATION

Positive Zika virus NAT on serum and urine specimens

\[\text{ACUTE ZIKA VIRUS INFECTION}\]
Interpretation of Results of Nucleic Acid and Antibody Testing for Suspected Zika Virus Infection

**TABLE 1. Interpretation of results of nucleic acid and antibody testing for suspected Zika virus infection**

<table>
<thead>
<tr>
<th>Zika IFT (serum)</th>
<th>Zika IFT (urine)</th>
<th>Zika virus and dengue virus IgM</th>
<th>Zika virus IgM</th>
<th>Dengue virus IgM</th>
<th>Interpretation and recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Any weak or positive IgM</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Positive evidence of Zika virus infection</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Positive or weak IgM</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Positive evidence of Zika virus infection</td>
</tr>
<tr>
<td>Negative or not performed</td>
<td>Positive</td>
<td>Negative or weak IgM</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Positive evidence of Zika virus infection</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative or not performed</td>
<td>Negative or weak IgM</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>Positive evidence of Zika virus infection</td>
</tr>
<tr>
<td>Negative or not performed</td>
<td>Negative or not performed</td>
<td>Any weak, negative or weak IgM</td>
<td>&lt; 100</td>
<td>&lt; 100</td>
<td>No evidence of Zika virus infection</td>
</tr>
<tr>
<td>Negative or not performed</td>
<td>Negative or not performed</td>
<td>Any non-negative or negative IgM</td>
<td>≥ 100</td>
<td>≥ 100</td>
<td>No evidence of Zika virus infection</td>
</tr>
<tr>
<td>Negative or not performed</td>
<td>Negative or not performed</td>
<td>Positive but negative antibody</td>
<td>Not performed</td>
<td>Not performed</td>
<td>No evidence of Zika virus infection</td>
</tr>
<tr>
<td>Negative or not performed</td>
<td>Negative or not performed</td>
<td>Positive but negative antibody</td>
<td>Not performed</td>
<td>Not performed</td>
<td>No evidence of Zika virus infection</td>
</tr>
</tbody>
</table>

Odushebo et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus — United States, July 2017. [https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w](https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w)
Updated Guidance: Test Results for Symptomatic Pregnant Women

**RESULTS & INTERPRETATION**

Negative Zika virus NAT  
**AND**  
Negative Zika virus IgM  
↓  
**NO EVIDENCE OF ZIKA VIRUS INFECTION**
Updated Guidance: Symptomatic Pregnant Women -- PRNT

RESULTS & ADDITIONAL TESTS
Negative Zika virus NAT
AND
Non-negative* Zika IgM
↓
Plaque reduction neutralization test (PRNT)

*Non-negative terms include positive, equivocal, presumptive positive, or possible. Terms listed here are only examples of assay interpretation terminology because nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. [https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika](https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika)
Updated Guidance: Symptomatic Pregnant Women

### RESULTS & INTERPRETATION

- Zika virus PRNT >10
- And
dengue virus PRNT <10

**ZIKA VIRUS INFECTION, TIMING OF INFECTION CANNOT BE DETERMINED**

For pregnant women without Zika virus exposure before the current pregnancy, a **positive IgM result represents recent Zika virus infection.**

*For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.
Updated Guidance: Symptomatic Pregnant Women

RESULTS & INTERPRETATION
Zika virus PRNT >10 AND dengue virus PRNT >10
↓
FLAVIVIRUS INFECTION, SPECIFIC VIRUS AND TIMING OF INFECTION CANNOT BE DETERMINED

For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent unspecified flavivirus infection.

*For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.
Updated Guidance: Symptomatic Pregnant Women

RESULTS & INTERPRETATION
Zika virus PRNT <10

NO EVIDENCE OF ZIKA VIRUS INFECTION
Asymptomatic Pregnant Women with Possible Zika Virus Exposure

**UPDATED INTERIM PREGNANCY GUIDANCE: ASYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE**

Testing Recommendations and Interpretation of Results for Healthcare Providers

**ASK PREGNANT WOMEN ABOUT**
- Travel to or residence in **areas with risk for Zika virus transmission** before and during the current pregnancy
- Possible sexual exposure before and during the current pregnancy
- A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy
- Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia)
- If symptoms are reported, refer to symptomatic algorithm.

Before testing, discuss testing limitations and potential risks of misinterpretations for test results.

**WHOM to test?**
- Asymptomatic pregnant women with ongoing possible Zika virus exposure
- Asymptomatic pregnant women with recent possible Zika virus exposure, without ongoing exposure:
  - Testing not routinely recommended, but should be considered.
  - If considering testing, base decisions on patient preferences and values, clinical judgment, a balanced assessment of risks and expected outcomes, and jurisdiction’s recommendations.
  - If testing is conducted, follow algorithm for symptomatic pregnant women using timeframe from last possible exposure.

**WHEN to test?**
- Three times during pregnancy:
  - First test at initiation of prenatal care.

**WHICH tests?**
- Zika virus NAT (serum and urine)

**RESULTS**
- Positive Zika virus NAT
- Negative Zika virus NAT

**INTERPRETATION**
- **ACUTE ZIKA VIRUS INFECTION**
- **NO ZIKA VIRUS RNA DETECTED. ZIKA VIRUS INFECTION DURING PREGNANCY CANNOT BE RULED OUT.**
Updated Guidance: Asymptomatic Pregnant Women with Ongoing Possible Exposure

**ASK PREGNANT WOMEN** about
- Possible Zika exposure before and during current pregnancy
- Diagnosis of laboratory-confirmed Zika virus infection before pregnancy
- Presence of symptoms during current pregnancy

**COUNSEL PATIENTS** on Zika testing

If symptoms are reported, refer to symptomatic algorithm.
Updated Guidance: Asymptomatic Pregnant Women with Ongoing Possible Exposure

**WHEN to test? WHICH tests?**
Test with Zika virus NAT on serum and urine three times during pregnancy
# Updated Guidance: Asymptomatic Pregnant Women with Ongoing Possible Exposure

## Refer to Table 1 for Interpretation

### Table 1: Interpretation of results of nucleic acid amplification testing for suspected Zika virus infection

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>RNA/ct/mL</th>
<th>Zika virus IgM</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>&gt;5,000</td>
<td>Any</td>
<td>Positive Zika virus infection</td>
</tr>
<tr>
<td>Negative</td>
<td>&lt;5,000</td>
<td>Any</td>
<td>Negative Zika virus infection</td>
</tr>
</tbody>
</table>

### Interpretation Guide

**WHOM to test?**
- Asymptomatic pregnant women with ongoing possible Zika virus exposure
- Testing not routinely recommended, but should be considered.
- If considering testing, base decisions on patient preferences and values, clinical judgment, a balanced assessment of risks and expected outcomes, and jurisdictional recommendations.
- If testing is conducted, follow algorithm for asymptomatic pregnant women using timeline from last possible exposure.

**WHEN to test?**
- Three times during pregnancy:
  - First test at 1st trimester, then at 28-32 weeks, then at delivery.

**Which tests?**
- Zika virus NAT (serum and urine)

**Results**
- Positive Zika virus NAT
- Negative Zika virus NAT

**Interpretation**
- Positive Zika virus infection
- No Zika virus RNA detected. Zika virus infection during pregnancy cannot be ruled out.
Updated Guidance: Asymptomatic Pregnant Women with Recent Possible Exposure, but without Ongoing Possible Exposure

ASK PREGNANT WOMEN ABOUT
- Travel to or residence in *any areas with risk for Zika virus transmission* before and during the current pregnancy.²
- Possible sexual exposure before and during the current pregnancy.
- A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy.³
- Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia).
- If symptoms are reported, refer to symptomatic algorithm.

Before testing, discuss testing limitations and potential risks of misinterpretations for test results.

WHOM to test?
- Asymptomatic pregnant women with ongoing possible Zika virus exposure.
- Asymptomatic pregnant women with recent possible Zika virus exposure, without ongoing exposure:
  - Testing not routinely recommended, but should be considered.
  - If considering testing, base decisions on patient preferences and values, clinical judgment, a balanced assessment of risks and expected outcomes, and jurisdiction's recommendations.
  - If testing is conducted, follow algorithm for symptomatic pregnant women using timeframe from last possible exposure.

WHEN to test?
- Three times during pregnancy:
  - First test at initiation of prenatal care.

WHICH tests?
- Zika virus NAT (serum and urine)

RESULTS
- Positive Zika virus NAT:
  - ACUTE ZIKA VIRUS INFECTION
- Negative Zika virus NAT:
  - NO ZIKA VIRUS RNA DETECTED. ZIKA VIRUS INFECTION DURING PREGNANCY CANNOT BE RULED OUT.
Updated Guidance: Asymptomatic Pregnant Women with Recent Possible Exposure, but without Ongoing Possible Exposure

WHOM to test
Testing is no longer routinely recommended. Testing should be considered using:

- A shared decision-making model based on patient preferences and values
  - Clinical judgment
- A balanced assessment of risks and expected outcomes
- Jurisdiction’s recommendations

If testing is conducted, follow algorithm for symptomatic pregnant women using timeframe from last possible exposure.
Initial Evaluation Of Infants Whose Mothers Had Possible Zika Virus Exposure During Pregnancy But Were Not Tested

- Comprehensive physical exam
  - Head circumference, weight, height measurements
  - Neurologic assessment
- Standard newborn hearing assessment
- Based on level of possible exposure, consider
  - Head ultrasound
  - Ophthalmologic exam
- Based on evaluation, consider Zika virus laboratory testing of infant

Updated Guidance: Asymptomatic Pregnant Women with Possible Zika Virus Exposure

Jurisdictions may recommend testing of asymptomatic pregnant women for clinical decision-making or as part of Zika virus infection surveillance.
Updated Guidance: Testing of Placental and Fetal Tissues

Testing of placental tissues not routinely recommended for asymptomatic women without ongoing possible exposure when infant or fetus does not have Zika-associated birth defects.
Recommendations to Prevent Zika Virus Infection Have not Changed

- **Do Not Travel**
  - Pregnant women should **not** travel to areas with risk for Zika virus transmission

- **Prevent Mosquito Bites**
  - If a pregnant woman lives in or travels to an area with risk for Zika virus transmission, she should take steps to prevent mosquito bites

- **Prevent Sexual Transmission**
  - Take steps to prevent sexual transmission of Zika from a partner who lives in or traveled to an area with risk for Zika virus transmission
Clinical Tools for Implementing Guidance

PRETEST COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS FOR ASYMPTOMATIC PREGNANT WOMEN WITH ONGOING EXPOSURE TO ZIKA

1. The purpose is to educate patients on the importance of Zika testing and counseling.
2. The guide provides recommendations for healthcare providers on how to communicate with patients about Zika testing and counseling.
3. The guide includes a script for healthcare providers to follow during conversations with patients.

COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS FOR ASYMPTOMATIC PREGNANT WOMEN WHO WERE RECENTLY EXPOSED TO ZIKA

1. The purpose is to educate patients on the importance of Zika testing and counseling.
2. The guide provides recommendations for healthcare providers on how to communicate with patients about Zika testing and counseling.
3. The guide includes a script for healthcare providers to follow during conversations with patients.

PRETEST COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS FOR PREGNANT WOMEN WITH SYMPTOMS OF ZIKA

1. The purpose is to educate patients on the importance of Zika testing and counseling.
2. The guide provides recommendations for healthcare providers on how to communicate with patients about Zika testing and counseling.
3. The guide includes a script for healthcare providers to follow during conversations with patients.

CDC Response to Zika

WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING

For Pregnant Women Who Have Ongoing Exposure to Zika but No Symptoms

Zika testing is complex. In general, testing for Zika requires looking for both Zika genetic material (DNA or RNA) and antibodies to the virus that would allow a Zika infection. 

- Testing for Zika genetic material is recommended for you because it can tell your doctor if you were recently infected with Zika.
- Testing for Zika antibodies is not recommended for pregnant women who have ongoing exposure to Zika but no symptoms, because the results cannot be interpreted. We know that Zika antibodies can stay in the body for several months. If you lived or traveled to an area where local mosquito-borne Zika was circulating, you may have been infected before pregnancy. This means you have already developed antibodies against Zika before you became pregnant. Because of this, Zika antibody testing may not tell your doctor if you were infected more recently during your current pregnancy. This means that Zika antibodies would not tell you if you were pregnant before Zika infection.
Sharing Up-to-Date Information

• Providing updated clinical guidance
• Responding to your inquiries:
  » Email: ZikaMCH@cdc.gov
  » Zika Pregnancy Hotline: 770-488-7100
  » CDC-INFO: (800-232-4636)

http://www.cdc.gov/zika

US Zika Pregnancy Registry and Puerto Rico Zika Active Pregnancy Surveillance System

Dana Meaney-Delman, MD, MPH
Co-Lead, Pregnancy and Birth Defects Task Force
Centers for Disease Control and Prevention
Zika Pregnancy and Infant Registries: US Zika Pregnancy Registry and Zika Active Pregnancy Surveillance System (ZAPSS)

Purpose of registries

- To monitor pregnancy and infant outcomes in pregnancies with laboratory evidence of possible Zika virus infection
  - Estimate number of infants with birth defects
  - Provide data to inform phenotype of congenital Zika syndrome
  - Help ensure infants are linked to care
Zika Pregnancy and Infant Registries: Who is Included

- Pregnant women in the 50 US states and US territories.
- Pregnant women with laboratory evidence of possible Zika virus infection (regardless of whether they have symptoms) and their exposed infants.
- Infants with laboratory evidence of congenital Zika virus infection (regardless of whether they have symptoms) and their mothers.
# Zika Pregnancy and Infant Registries: A Comparison

<table>
<thead>
<tr>
<th>Registry Feature</th>
<th>US Zika Pregnancy Registry</th>
<th>Zika Active Pregnancy Surveillance System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>50 States and District of Columbia, US territories and Freely Associated States excluding Puerto Rico</td>
<td>Puerto Rico</td>
</tr>
<tr>
<td>Maternal Eligibility</td>
<td>Pregnant women with laboratory evidence of Zika</td>
<td>Pregnant women with laboratory evidence of Zika</td>
</tr>
<tr>
<td>Infant Follow-Up</td>
<td>Through 1&lt;sup&gt;st&lt;/sup&gt; year of life</td>
<td>Through 3&lt;sup&gt;rd&lt;/sup&gt; year of life</td>
</tr>
</tbody>
</table>
Pregnancy Outcomes Following Zika Virus Infection during Pregnancy in US Territories

- Provides data from women and infants living in American Samoa, the Commonwealth of Puerto Rico, the Federated States of Micronesia, the Republic of the Marshall Islands, and the US Virgin Islands

- Data reported to the US Zika Pregnancy Registry and the Puerto Rico Zika Active Pregnancy Surveillance System from January 1, 2016- April 25, 2017
Zika-Related Pregnancy Outcomes in US Territories

3,930 pregnancies with possible Zika infection

2,549 completed pregnancies

122 fetuses or infants with birth defects
## Results from Zika Pregnancy and Infant Registries

<table>
<thead>
<tr>
<th>Findings</th>
<th>US States and DC</th>
<th>US Territories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>USZPR(^1) % (95% CI)</td>
<td>USZPR/ZAPPS(^2) % (95% CI)</td>
</tr>
<tr>
<td><strong>Symptomatic vs. Asymptomatic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Symptomatic with birth defects</td>
<td>8 (4-13)</td>
<td>5 (4-6)</td>
</tr>
<tr>
<td>% Asymptomatic with birth defects</td>
<td>12 (7-19)</td>
<td>7 (4-11)</td>
</tr>
<tr>
<td><strong>Birth Defects by Trimester of Infection at DX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First trimester</td>
<td>15 (8-26)</td>
<td>8 (5-12)</td>
</tr>
<tr>
<td>Second trimester</td>
<td>--</td>
<td>5 (4-7)</td>
</tr>
<tr>
<td>Third trimester</td>
<td>--</td>
<td>4 (3-6)</td>
</tr>
</tbody>
</table>


Impact of Third Trimester Infections

• 34% of 3rd trimester infections were symptomatic

• Among mothers diagnosed with infection in the 3rd trimester, 4% had an infant or fetus with Zika virus-associated birth defects

Birth defects observed among pregnancies with symptom onset or positive laboratory testing during any trimester
Infant Follow-up in US Territories

<table>
<thead>
<tr>
<th>Recommended infant screening and testing reported to Zika pregnancy and infant registries</th>
<th>Live-born infants with birth defects %</th>
<th>Live-born infants without birth defects %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant Zika virus testing</td>
<td>55%</td>
<td>59%</td>
<td>59%</td>
</tr>
<tr>
<td>Postnatal neuroimaging</td>
<td>59%</td>
<td>52%</td>
<td>52%</td>
</tr>
<tr>
<td>Hearing screening</td>
<td>91%</td>
<td>78%</td>
<td>79%</td>
</tr>
</tbody>
</table>
Public Health Implications

• Highest proportion of Zika-associated birth defects among those with Zika virus infection during first and early second trimester of pregnancy
  » More data are needed to explore whether women infected in the third trimester are at risk for:
    • having a baby with birth defects
    • other adverse pregnancy outcomes

• Identification and follow-up care of infants can facilitate timely and appropriate clinical intervention services and assessment of future needs

• Monitoring of affected pregnancies and continued follow-up care for infant is critical to elucidating the impact of congenital Zika virus infection
What You Can Do to Help

- Educate families on Zika virus prevention
- Ask about possible Zika virus exposure
- Provide all needed tests and follow-up care
- Support infants and families
- Report to the Zika virus pregnancy and infant registries
Summary

- Zika virus infection diagnosed during any trimester of pregnancy poses a risk to the fetus.

- The absence or presence of symptoms in patients with confirmed Zika virus infection does not appear to affect the risk of birth defects.

- Healthcare providers can educate patients, follow CDC recommendations for screening and testing, support infants and families, and report to the Zika pregnancy and infant registries.
CDC’S Response to Zika

Zika Virus Infection: Pediatric Ophthalmologic Findings

S. Grace Prakalapakorn, MD, MPH
Assistant Professor of Ophthalmology and Pediatrics
Duke University
Ophthalmology 101
Normal Retina
Ocular Findings in Congenital Zika Infection
Ocular Findings Associated with Congenital Zika Virus Infection

- Ocular abnormalities have been identified in infants with and without microcephaly.
- Abnormalities have been found in the anterior and posterior ocular structures.
- Cortical visual impairment might be the most common cause of blindness among children with congenital Zika syndrome.
Macular and Optic Nerve Findings

Commonly reported macular findings

- Macular mottling
- Chorioretinal atrophy

Commonly reported optic nerve findings

- Hypoplasia
- Increased cup to disk ratio
- Pallor

Macular mottling, chorioretinal atrophy, and optic nerve hypoplasia

Subretinal hemorrhages, vascular tortuosity, abnormal vessel termination, and focal area of dilation

Other Ocular Findings

- Congenital glaucoma
- Iris colobomas
- Microphthalmia
- Subluxation of the lens
- Cataract
- Intraocular calcification

Risk Factors for Ocular Findings

- Smaller head circumference
- Microcephaly
- Other CNS abnormalities
- Earlier trimester infection in pregnancy
- Arthrogryposis
Infants with Possible Zika Virus Infection WITHOUT Microcephaly

Eye findings in Infants Without CNS Abnormalities

Optic nerve hypoplasia, chorioretinal atrophy, and macular mottling

Optic nerve hypoplasia and chorioretinal atrophy

# Eye Findings in Congenital Infections

<table>
<thead>
<tr>
<th></th>
<th>Zika</th>
<th>Toxoplasmosis</th>
<th>Rubella</th>
<th>CMV</th>
<th>Herpes Simplex</th>
<th>Syphilis</th>
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<tbody>
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<td>Conjunctivitis</td>
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<tr>
<td>Macular Mottling</td>
<td></td>
<td>+ focal pigmentary clumping</td>
<td>+ granular (Salt-and-pepper retinopathy)</td>
<td>+ granular (Salt-and-pepper retinopathy)</td>
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<td>Chorioretinal Atrophy</td>
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<tr>
<td>Optic Nerve abnormalities</td>
<td>Hypoplasia, cupping, pallor</td>
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<td>pallor</td>
<td>pallor</td>
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<tr>
<td>Cataract</td>
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<td>Microphthalmia</td>
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<td>Iris Coloboma</td>
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<td>Active inflammation:</td>
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CDC Recommendations: Ophthalmic screening
Who should be referred for screening and when?

- **Before hospital discharge:**
  - Infant whose mother has risk factors for maternal Zika virus infection (travel to or residence in an area with risk of Zika or sex with a partner who traveled to or resided in such an area)
  - Maternal test results are not available
  - There is a concern about infant follow-up care

- **Before 1 month of age:**
  - All infants with laboratory evidence of congenital Zika virus infection
  - Abnormal findings consistent with CZS

- **Follow up should occur**
  - If the ophthalmologic examination within the first month of age is normal
  - Another complete examination at 3 months of age

Screening should include

- Ophthalmologic assessment:
  - Visual acuity assessment
  - Intraocular pressure measurements
  - Slit lamp examination
  - Dilated fundus examination

- Resources for children with vision impairment or loss
  - Low vision specialist
  - Early intervention
How can primary care providers help?

- For infants without laboratory evidence of Zika virus infection but for whom suspicion for congenital Zika virus infection remains
  - Consider referral to an ophthalmologist before hospital discharge or within 1 month of birth
- Outpatient management of infants with possible congenital Zika exposure but without abnormalities consistent with CZS
  - During routine infant follow-up with primary care providers, at each well child visit
    - Vision screening, including assessment of visual regard
    - Referral to an ophthalmologist for any caregiver or provider concern
- Tips for screening vision in young infants
  - For very young infants (1-2 months of age): test wince to light
  - At about 3 months of age: fix and follow
  - Test vision with both eyes open first, then try one eye at a time

Summary

- Declining transmission and new data on Zika virus persistence increase complexity of testing
- Updated guidance places emphasis on shared decision-making based on patient preferences, clinical judgment, and in line with jurisdictional recommendations
- Zika virus infection poses a risk to all pregnancies, regardless of timing of possible exposure and symptoms
- Congenital Zika virus infection can lead to poor ophthalmologic outcomes in the presence and absence of other birth defects
Thank you!

More information on Zika: www.cdc.gov/zika

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

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Today’s webinar will be archived

When: A few days after the live call

What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

https://emergency.cdc.gov/coca/calls/2017/callinfo_072717.asp
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