Zika Virus & Pregnancy

Grand Rounds
“Never before in history has there been a situation where a bite from a mosquito could result in a devastating malformation.”

– Dr. Tom Frieden, CDC Director

Fortune, April 13, 2016

“...the last time an infectious pathogen (rubella virus) caused an epidemic of congenital defects was more than 50 years ago...”

– New England Journal of Medicine, April 13, 2016
Today’s Presentation

• Zika: The Basics
• Zika, Pregnancy, and Congenital Zika Syndrome
• CDC Guidance: Diagnosing and Testing for Zika
• Preventing Zika in Pregnant Women
• Standard Precautions to Prevent the Spread of Zika Virus and Other Infectious Agents During Healthcare Delivery
• What is CDC Doing?
• What Can You Do?
Zika: The Basics
What is Zika Virus?

• Single-stranded RNA virus
• Closely related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses
• Primarily transmitted by two *Aedes* species mosquitoes
  • *Aedes aegypti* and *Aedes albopictus* mosquitoes
• Additional modes of transmission
  • Intrauterine and perinatal transmission
  • Sexual transmission
  • Laboratory exposure
  • Probable: Blood transfusion
Where is Zika now?
Clinical Presentation

• Clinical illness usually mild
• Most common symptoms
  • Fever
  • Rash
  • Joint pain
  • Conjunctivitis
• Symptoms last several days to a week
• Severe disease uncommon
• Fatalities rare
• Once a person has been infected, likely to be protected from future infections
Clinical Management

• No vaccine or specific antiviral treatment
• Treat the symptoms
  • Rest
  • Drink fluids to prevent dehydration
  • Take medicine such as acetaminophen to reduce fever and pain
  • Avoid aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS) until dengue can be ruled out to reduce the risk of bleeding
Zika, Pregnancy, and Congenital Zika Syndrome
Zika Virus Infection in Pregnant Women

• Pregnant women can be infected
  • Through the bite of an infected mosquito
  • Through sex without a condom with an infected partner

• If infected around conception
  • Zika might present risk to fetus

• If infected during pregnancy
  • Zika can be passed to the fetus during pregnancy or around the time of birth
Zika Virus in Pregnancy

- Incidence of Zika virus infection in pregnant women is not known
- Infection can occur in any trimester
- No evidence of increased susceptibility
- The clinical course is similar in pregnant women and in non-pregnant people

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.
CDC Lab Confirms Zika In Fetal Tissues

- Zika virus has been shown to be present in fetal tissue
- Evidence of Zika virus has been detected in
  - Amniotic fluid
  - Placenta
  - Fetal brain tissue
  - Products of conception

Reference/attribution for image:
Ritter JM, Martines RB, Zaki SR. Zika Virus: Pathology From the Pandemic. Arch Pathol Lab Med. 2016 Oct 5. [Epub ahead of print]

Immunohistochemical staining of Zika virus antigen (red stain) in fetal brain tissue. This staining is present in the same areas where neuronal cell death/necrosis was identified by microscopic review of tissue morphology.
Zika Virus and Birth Defects — Reviewing the Evidence for Causality

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Margaret A. Honein, Ph.D., M.P.H., and Lyle R. Petersen, M.D., M.P.H.

SUMMARY

The Zika virus has spread rapidly in the Americas since its first identification in Brazil in early 2015. Prenatal Zika virus infection has been linked to adverse pregnancy and birth outcomes, most notably microcephaly and other serious brain anomalies. To determine whether Zika virus infection during pregnancy contributes to the observed increase in the number of infants with microcephaly in Brazil...
Congenital Zika Syndrome

• Pattern of congenital anomalies associated with Zika virus infection during pregnancy that includes:
  • Severe microcephaly (small head size) resulting in a partially collapsed skull
  • Thin cerebral cortices with subcortical calcifications
  • Eye anomalies, including macular scarring and focal pigmentary retinal mottling
  • Congenital contractures or limited range of joint motion
  • Marked early hypertonia, or too much muscle tone, and symptoms of extrapyramidal involvement
Potential Risk of Microcephaly

• **1 - 13%** estimated risk of microcephaly due to Zika virus infection in 1\textsuperscript{st} trimester
  • Modeling based on current outbreak in Bahia, Brazil

• *Important to remember*
  • Data are limited (infection rates unknown; microcephaly cases still being reported)
  • Microcephaly is difficult to detect prenatally
  • Microcephaly is only one of a range of possible adverse outcomes
Potential Risk of Birth Defects Related to Zika

- Among pregnant women in the United States with laboratory evidence of possible Zika virus infection:
  - Overall about 6% of fetuses or infants had birth defects potentially related to Zika virus
  - Similar proportion of pregnancies with birth defects (≈6%) among both symptomatic and asymptomatic pregnant women
  - Among women with infection in the 1st trimester of pregnancy, birth defects were reported in 11% of fetuses or infants

Congenital Zika Syndrome without Microcephaly at Birth

- Microcephaly from congenital infection can occur after birth
- The full spectrum of poor outcomes caused by Zika virus infection during pregnancy remains unknown

Linden V, Pessoa A, Dobyns WB, et al. Description of 13 Infants Born During October 2015–January 2016 With Congenital Zika Virus Infection Without Microcephaly at Birth — Brazil

Morbidity and Mortality Weekly Report

Centers for Disease Control and Prevention

Early Release / Vol. 65

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CDC Recommendations: Conception and Contraception
Clinical Guidance for Preconception and Sexual Transmission


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https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6539e1.pdf
## Women and Their Partners Thinking about Pregnancy

<table>
<thead>
<tr>
<th>Possible exposure via recent travel or sex without a condom with a partner infected with Zika</th>
<th>Women</th>
<th>Men</th>
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<tbody>
<tr>
<td>Wait <strong>at least</strong> 8 weeks after symptoms start or last possible exposure</td>
<td></td>
<td>Wait <strong>at least</strong> 6 months after symptoms start or last possible exposure</td>
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</tbody>
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<table>
<thead>
<tr>
<th>People living in or frequently traveling to areas with Zika</th>
<th>Women</th>
<th>Men</th>
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</thead>
<tbody>
<tr>
<td>Positive Zika test</td>
<td>Wait <strong>at least</strong> 8 weeks after symptoms start</td>
<td>Wait <strong>at least</strong> 6 months after symptoms start</td>
</tr>
<tr>
<td>No testing performed or negative test</td>
<td>Talk with doctor or healthcare provider</td>
<td>Talk with doctor or healthcare provider</td>
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Pregnancy Planning and Access to Contraception

• Preventing Zika infections during pregnancy
  • Includes supporting women who want to delay or avoid pregnancy to reduce Zika-related pregnancy complications
  • Preventing unintended pregnancy to avoid Zika-related adverse pregnancy and birth outcomes

• If couples decide to wait to conceive, healthcare providers should discuss
  • Strategies to prevent unintended pregnancy
  • Use of the most effective contraceptive methods (including long-acting reversible contraception) that meet their lifestyle needs and can be used correctly and consistently
  • Role of correct and consistent use of condoms, in addition to other birth control method used, in reducing the risk for sexually transmitted infections, including Zika
CDC Guidance: Diagnosing and Testing for Zika
Assessing for Zika During Pregnancy

- All pregnant women should be assessed for possible Zika exposure, signs, and symptoms at each prenatal care visit. They should be asked if they
  - Traveled to or live in an area with active Zika transmission
  - Had sex without a condom with a partner with potential exposure to Zika

Diagnostic Testing for Zika Virus

• Molecular method
  • Nucleic acid test (NAT, e.g., rRT-PCR) for viral RNA in body fluids or tissues

• Serologic method
  • Zika virus immunoglobulin M (IgM) enzyme-linked immunosorbent assay
  • Plaque reduction neutralization test (PRNT) to detect neutralizing antibodies in serum
Limitations of Zika Tests

- Presence of Zika virus RNA in serum and urine is relatively short-lived and negative results do not preclude infection.
- Testing for Zika virus IgM can result in false positive results because of cross-reacting antibodies against related flaviviruses and for nonspecific reasons.
- PRNT levels may not distinguish infecting virus in people previously infected with or vaccinated against a related flavivirus.
CDC Guidance: Pregnancy
Pregnant women with possible exposure to Zika virus and signs or symptoms should be tested for Zika virus infection.

Pregnant women with possible exposure to Zika virus who do not report symptoms also should be tested.

Pregnant women with ongoing risk of Zika virus exposure and who do not report symptoms should be tested in the 1st and 2nd trimesters of pregnancy.

http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e1.htm?s_cid=mm6529e1_e
Testing and interpretation recommendations for a pregnant woman with possible exposure to Zika virus — United States (including U.S. territories)

A

Assess for possible Zika virus exposure
Evaluate for signs and symptoms of Zika virus disease

- Symptomatic: <2 weeks after symptom onset, or
- Asymptomatic and NOT living in an area with active Zika virus transmission: <3 weeks after possible exposure

Zika virus Zika RNA NAT on serum and urine

Positive Zika virus Zika RNA NAT on serum or urine: Recent Zika virus infection

Negative Zika virus Zika RNA NAT on serum and urine

Zika virus IgM and dengue virus IgM on serum

- Symptomatic: Zika virus IgM and dengue virus IgM
- Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2-12 weeks after exposure

Zika virus IgM positive or equivocal and any result on dengue virus IgM: Presumptive dengue virus infection

Presumptive recent Zika virus or flavivirus infection

Zika virus IgM negative: No evidence of recent Zika virus infection

Zika virus IgM and dengue virus IgM negative: No evidence of recent Zika virus infection

B

- Symptomatic: 2-12 weeks after symptom onset, or
- Asymptomatic and NOT living in an area with active Zika virus transmission: 2-12 weeks after possible exposure, or
- Asymptomatic and living in an area with active Zika virus transmission: 1st and 2nd trimester

Zika virus RNA NAT on serum

Positive Zika virus RNA NAT on serum or urine: Recent Zika virus infection

Zika virus RNA NAT on serum

Plaque reduction neutralization test (PRNT)

Zika virus PRINT ≥10 and dengue virus PRINT <10: Recent Zika virus infection

Zika virus PRINT <10 and dengue virus PRINT ≥10: Recent flavivirus infection, specific virus cannot be identified

Zika virus PRINT <10: No evidence of recent Zika virus infection

Updated Guidance: Symptomatic Pregnant Women

• Evaluated <2 weeks after symptom onset
  • Should receive Zika virus NAT testing of serum and urine
    • Positive NAT result confirms diagnosis: recent maternal Zika virus infection
    • Negative NAT result does not rule out Zika virus infection
      • Zika IgM and dengue IgM antibody testing should be performed immediately on the same specimen or a subsequently collected specimen

• Evaluated 2–12 weeks after symptom onset
  • Should first have a Zika virus immunoglobulin (IgM) test
    • If positive or equivocal, serum and urine NAT should be performed
Updated Guidance: Asymptomatic Pregnant Women

- Living in areas without Zika, evaluated <2 weeks after last possible exposure
  - NAT testing should be performed
    - If the NAT test is negative, Zika IgM test should be performed 2–12 weeks after exposure
- Living in areas without Zika, evaluated 2–12 weeks after last possible exposure
  - Should receive a Zika virus IgM antibody test
    - If positive or equivocal, serum and urine NAT should be performed
- Living in areas with Zika
  - Asymptomatic pregnant women who live in an area with Zika should receive Zika IgM testing at the start of prenatal care and again during the 2nd-trimester.
For symptomatic and asymptomatic pregnant women with possible Zika virus exposure who seek care >12 weeks after symptom onset or possible exposure

- IgM antibody testing might be considered
  - A negative IgM antibody test or NAT result >12 weeks after symptom onset or possible exposure does not rule out recent Zika virus infection because IgM antibody and viral RNA levels decline over time.

- Given the limitations of testing beyond 12 weeks after symptom onset or possible exposure, serial fetal ultrasounds should be considered.
### Clinical management of a pregnant woman with suspected Zika virus infection

<table>
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<tr>
<th>Interpretation of Laboratory Results*</th>
<th>Prenatal Management</th>
<th>Postnatal Management</th>
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</table>
| Recent Zika virus infection          | Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth† | LIVE BIRTHS: Infant serum and infant urine should be tested for Zika virus Zika RNA NAT. Infant serum should be tested for Zika IgM. If CSF is obtained for other reasons, it can also be tested.**  
FETAL LOSSES: Zika virus Zika RNA NAT and IHC staining of umbilical cord and placenta is recommended.³ |
| Recent flavivirus infection; specific virus cannot be identified | Decisions regarding amniocentesis should be individualized for each clinical circumstance§ | | |
| Presumptive recent Zika virus infection*** | Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth†  
Amniocentesis might be considered; decision should be individualized for each clinical circumstance§ | LIVE BIRTHS: Infant serum and infant urine should be tested for Zika virus Zika RNA NAT. Infant serum should be tested for Zika IgM. If CSF is obtained for other reasons, it can also be tested.**  
FETAL LOSSES: Zika virus Zika RNA NAT and IHC staining of umbilical cord and placenta should be considered.⁴ |
| Presumptive recent flavivirus infection*** | | | |
| Recent dengue virus infection        | Clinical management in accordance with existing guidelines (http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf) | | |
| No evidence of Zika virus or dengue virus infection | Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.⁷  
Fetal abnormalities present: repeat Zika virus Zika RNA NAT and IgM test; base clinical management on corresponding laboratory results.  
Fetal abnormalities absent: base obstetric care on the ongoing risk of Zika virus exposure to the pregnant woman. | | |

Prenatal Management: Confirmed or Presumptive Recent Zika Virus or Flavivirus Infection

• Consider serial ultrasounds every 3-4 weeks to assess fetal anatomy and growth
• Amniocentesis
  • Individualized for pregnant women with confirmed recent Zika virus or flavivirus infection
  • Can be considered for pregnant women with presumptive recent Zika virus or flavivirus infection

http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e1.htm?s_cid=mm6529e1_e
Preventing Zika in Pregnant Women
Do Not Travel to Areas with Active Zika Transmission

- Pregnant women should **not** travel to areas with Zika
- If a pregnant woman **must** travel, she should
  - Talk with her healthcare provider before she goes
  - Strictly follow steps to prevent mosquito bites during the trip
  - Take steps to prevent sexual transmission
  - Talk with her healthcare provider after she returns, even if she doesn’t feel sick

Prevent Mosquito Bites

If a pregnant woman lives in or travels to an area with Zika, she should:

• Wear long-sleeved shirts and long pants
• Stay and sleep in places with air conditioning or that use window and door screens
• Use insect repellents with one of the following EPA-registered active ingredients:
  • DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, or 2-undecanone
• Once a week, empty and scrub, turn over, cover, or throw out items that hold water, such as trash containers, tires, buckets, toys, planters, flowerpots, birdbaths or pools
Prevent Sexual Transmission of Zika Virus

A pregnant woman whose partner lives in or has traveled to an area with Zika should

• Use condoms correctly every time they have sex, or
• Not have sex

For the duration of the pregnancy, even if the pregnant woman’s partner does not have symptoms or feel sick.
Standard Precautions to Prevent the Spread of Zika Virus and Other Infectious Agents During Healthcare Delivery
Zika Virus Disease in Healthcare Settings

• No reports to date of transmission of Zika virus from infected patients to healthcare personnel or other patients in healthcare settings

• Zika virus has been detected in blood, amniotic fluid, urine, saliva, and genital fluids (including semen and vaginal fluids)
Standard Precautions

- Basic measures to prevent infections that apply to all patient care
- Based on principle that all blood, body fluids, secretions, excretions (except sweat), non-intact skin, and mucous membranes may contain transmissible infectious agents

- Goals
  - Prevent direct contact between a patient’s body fluids and healthcare provider (HCP) mucous membranes or broken skin
  - Protect HCP and prevent them from transmitting potentially infectious material from one patient to another
  - Avoid percutaneous exposure to contaminated sharp implements
Standard Precautions: Personal Protective Equipment (PPE)

• Healthcare personnel education and training in the use of PPE is an Occupational Safety and Health Administration (OSHA) requirement

• Gloves, gowns, face masks, face shields, goggles

• Facilities should assure availability and accessibility of PPE to HCP

• Educate all HCP on proper selection and correct use of PPE
  • HCPs must assess their risk for exposure and select appropriate PPE

• Examples of obstetric procedures that require increasing amount of PPE
  • Vaginal exam particularly during amniotomy
  • Vaginal delivery including manual removal of placenta
  • Operative procedures
What is CDC Doing?
Many Questions Remain

• What is the level of risk from a Zika virus infection during pregnancy?
• When during pregnancy does Zika virus infection poses the highest risk to the fetus?
• What is the full range of potential health problems that Zika virus infection may cause?
• What other factors (e.g., co-occurring infection, nutrition, symptomatic vs. asymptomatic) might affect the risk for birth defects?
Collecting Data for Action

Surveillance of Zika and its Effects on Pregnant Women, Infants, & Children

US Zika Pregnancy Registry
Zika Active Pregnancy Surveillance System (Puerto Rico)
Proyecto Vigilancia de Embarazadas con Zika (Colombia)
US Zika-Related Birth Defects Surveillance
ArboNET Surveillance of Children with Postnatal Zika
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
Developing Tools for Healthcare Providers

www.cdc.gov/Zika

*Free materials available in English, Spanish and other languages
What Can You Do?
Report Cases

• Zika virus infection and disease are nationally notifiable conditions

• The following cases should be reported to your state health department
  • Symptomatic and asymptomatic cases with laboratory evidence of Zika virus infection
  • Babies born with or without abnormalities consistent with congenital Zika syndrome and laboratory evidence of Zika virus infection
Report Information to US Zika Pregnancy Registry

• Purpose of registry
  • To monitor pregnancy and infant outcomes following Zika virus infection during pregnancy and to inform clinical guidance and public health response

• More information
  • To contact CDC Registry staff, call the CDC Emergency Operations Center watch desk at 770-488-7100 and ask for the Zika Pregnancy Hotline or email ZIKApregnancy@cdc.gov
  • For non-urgent requests, call 800-CDC-INFO (800-232-4636)
In Summary

• Know the basics about Zika transmission in your community
• Understand the assessment and management of Zika among pregnant women and protect them from exposure
• Counsel couples on how to avoid Zika infection as they plan for pregnancy
• Provide access to effective contraception to those not planning pregnancy
• Inform your local or state health department and the US Zika Pregnancy Registry as indicated
More Information about Zika

More information on caring for pregnant women, infants, or children with Zika virus infection is available at CDC's Zika website.

www.cdc.gov/zika
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.