Zika Virus & Pregnancy

Grand Rounds

Updated January 2017

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

First time in history…

"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

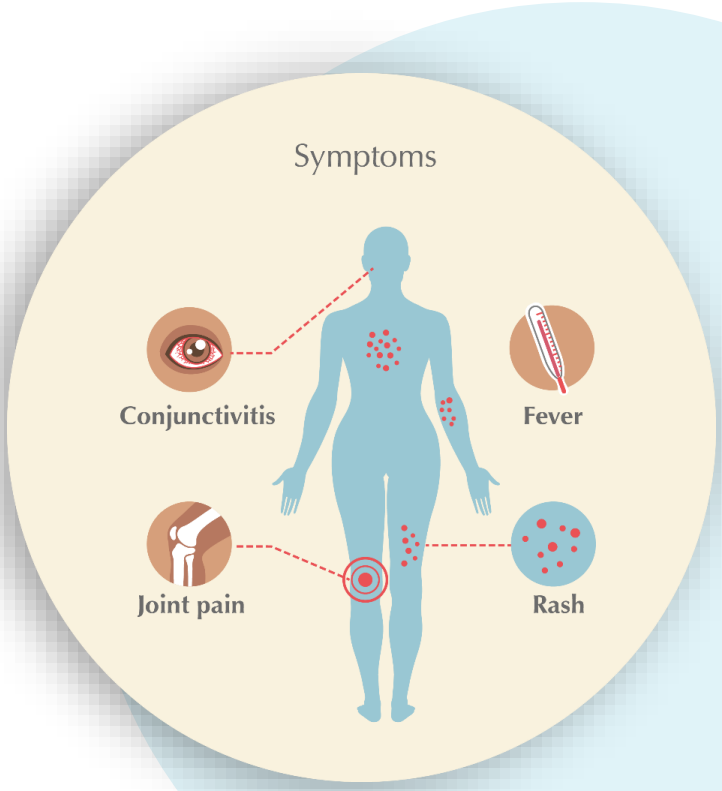
***Aedes aegypti* mosquito**

***Aedes albopictus* mosquito**

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

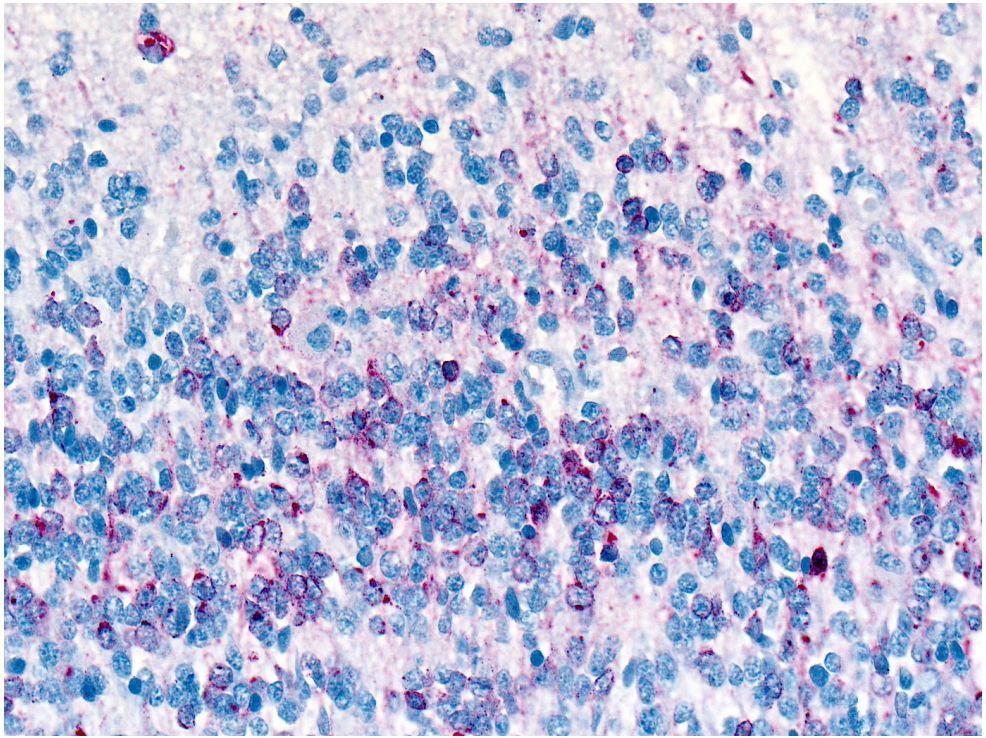
Centers for Disease Control and Prevention, *CDC Health Advisory: Recognizing, Managing, and Reporting Zika Virus Infections in Travelers Returning from Central America, South America, the Caribbean and Mexico*, 2016.

Besnard, M., et al., Evidence of Perinatal Transmission of Zika Virus, French Polynesia, December 2013 and February 2014. Euro Surveill, 2014. 19(14): p. 1-5.

Oliveira Melo, A., et al., Zika Virus Intrauterine Infection Causes Fetal Brain Abnormality and Microcephaly: Tip of the Iceberg? Ultrasound in Obstetrics & Gynecology, 2016. 47(1): p. 6-7.

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



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.

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]

Zika is a Cause of Microcephaly

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

Zika Virus and Birth Defects — Reviewing the Evidence for Causality

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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

POTENTIAL RELATIONSHIP BETWEEN ZIKA VIRUS INFECTION AND BIRTH DEFECTS

Since the identification of the Zika virus in Brazil in early 2015, the virus has spread rapidly throughout the Americas (www.cdc.gov/zika/geo/active-countries.html). An increase in the

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

Baby with Severe Microcephaly

Potential Risk of Microcephaly

- **1 - 13%** estimated risk of microcephaly due to Zika virus infection in 1st 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

Johansson MA, Mier-Y-Teran-Romero L, Reefhuis J, Gilboa SM, Hills SL. Zika and the Risk of Microcephaly. N Engl J Med. 2016 May 25 [Epub ahead of print].

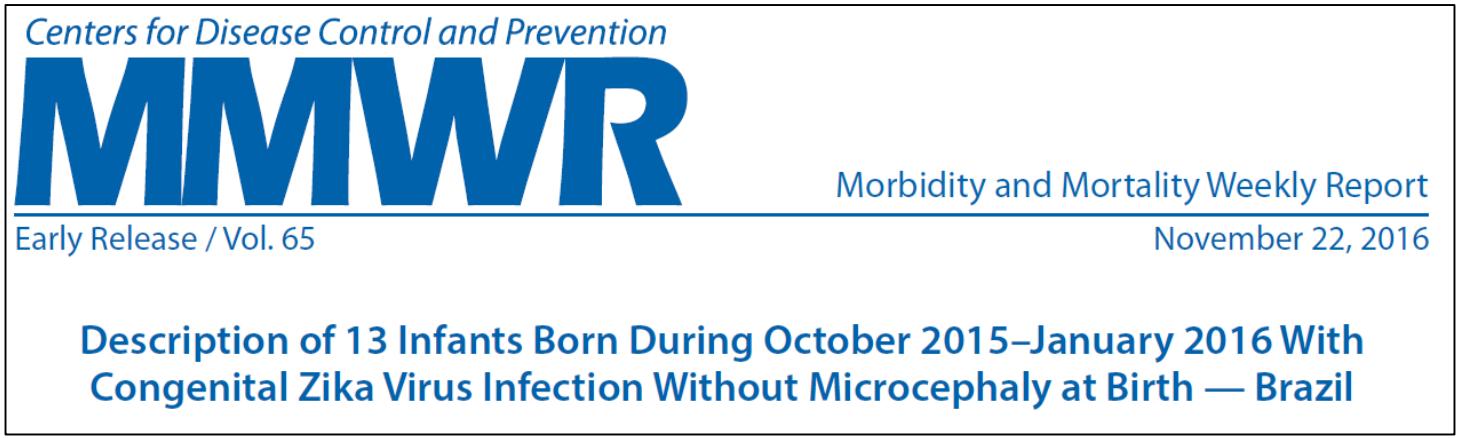
Potential Risk of Birth Defects Related to Zika

- 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 wome
  - Among women with infection in the 1st trimester of pregnanc birth defects were reported in **11%** of fetuses or infants

Honein MA, Dawson AL, Petersen EE et al. Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy. *JAMA.* 2016 Dec 15 [Epub ahead of print]

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 . . . MMWR. 22 Nov 2016.

CDC Recommendations: Conception and Contraception

Clinical Guidance for Preconception and Sexual Transmission

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
September 30, 2016

Update: Interim Guidance for Preconception Counseling and Prevention of Sexual Transmission of Zika Virus for Persons with Possible Zika Virus Exposure — United States, September 2016

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https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6539e1.pdf

Women and Their Partners Thinking about Pregnancy

Possible exposure via recent travel or sex without a condom with a partner infected with Zika	
Women	**Men**
Wait ***at least*** 8 weeks after symptoms start or last possible exposure	Wait ***at least*** 6 months after symptoms start or last possible exposure

People living in or frequently traveling to areas with Zika		
	Women	**Men**
Positive Zika test	Wait ***at least*** 8 weeks after symptoms start	Wait ***at least*** 6 months after symptoms start
No testing performed or negative test	Talk with doctor or healthcare provider	Talk with doctor or healthcare provider

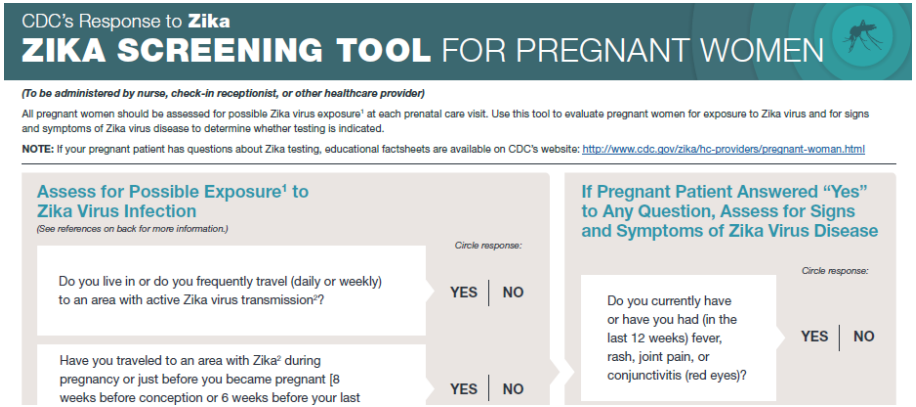
Pregnancy Planning and Access to Contraception

- 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



CDC's Response to **Zika**

ZIKA SCREENING TOOL FOR PREGNANT WOMEN

(To be administered by nurse, check-in receptionist, or other healthcare provider)

All pregnant women should be assessed for possible Zika virus exposure[1] at each prenatal care visit. Use this tool to evaluate pregnant women for exposure to Zika virus and for signs and symptoms of Zika virus disease to determine whether testing is indicated.

NOTE: If your pregnant patient has questions about Zika testing, educational factsheets are available on CDC's website: http://www.cdc.gov/zika/hc-providers/pregnant-woman.html

Assess for Possible Exposure[1] to Zika Virus Infection

(See references on back for more information.)

Circle response:

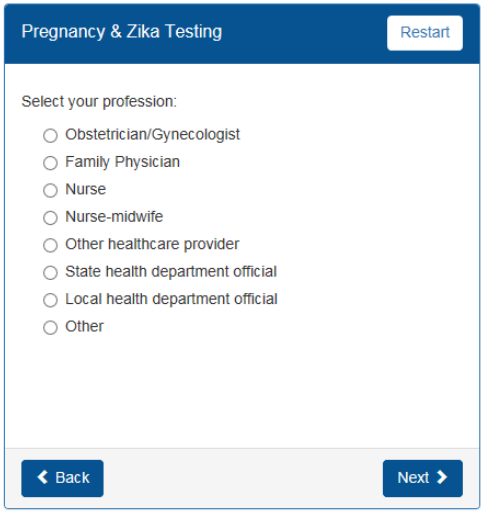
Do you live in or do you frequently travel (daily or weekly) to an area with active Zika virus transmission[2]? — YES | NO

Have you traveled to an area with Zika[2] during pregnancy or just before you became pregnant [8 weeks before conception or 6 weeks before your last — YES | NO

If Pregnant Patient Answered "Yes" to Any Question, Assess for Signs and Symptoms of Zika Virus Disease

Circle response:

Do you currently have or have you had (in the last 12 weeks) fever, rash, joint pain, or conjunctivitis (red eyes)? — YES | NO



Link: http://www.cdc.gov/zika/pdfs/zikapreg_screeningtool.pdf

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

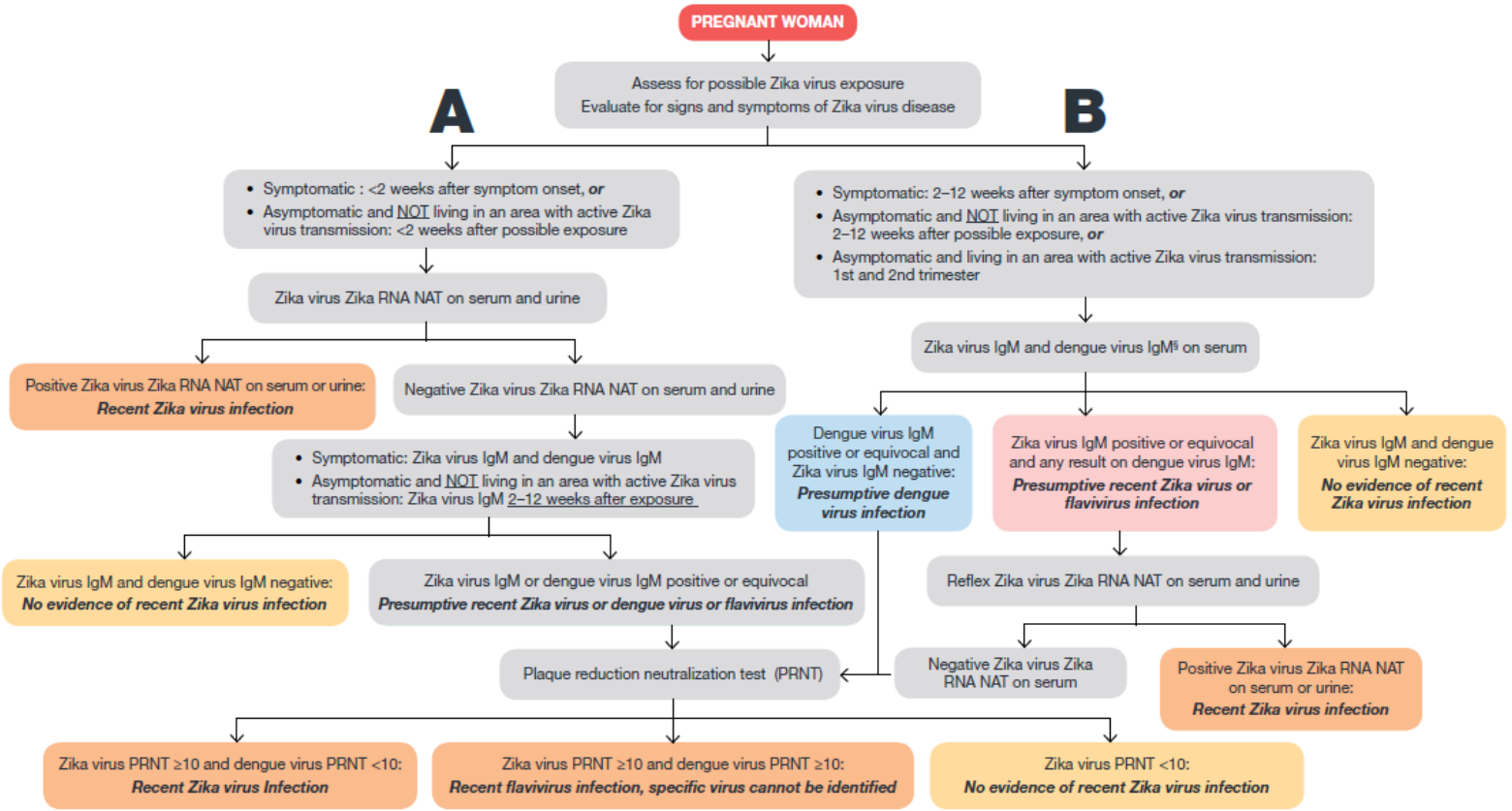
CDC Guidance: Pregnancy

CDC Recommendations: Who Should be Tested

- **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 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)



Link: https://www.cdc.gov/zika/pdfs/testing_algorithm.pdf

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.

Updated Guidance: Testing Pregnant Women After 12 Weeks

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

Interpretation of Laboratory Results*	Prenatal Management	Postnatal Management
Recent Zika virus infection	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth† • Decisions regarding amniocentesis 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.** • Zika virus Zika RNA NAT and IHC staining of umbilical cord and placenta is recommended.¶ **FETAL LOSSES:** • Zika virus Zika RNA NAT and IHC staining of fetal tissues is recommended.¶
Recent flavivirus infection; specific virus cannot be identified		
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. ** • Zika virus Zika RNA NAT and IHC staining of umbilical cord and placenta should be considered.¶ **FETAL LOSSES:** • Zika virus Zika RNA NAT and IHC staining of fetal tissues should be considered.¶
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.† ◆ 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.	

Link: https://www.cdc.gov/zika/pdfs/testing_algorithm.pdf

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

http://wwwnc.cdc.gov/travel/page/zika-information

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

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
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July 25, 2016

Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016

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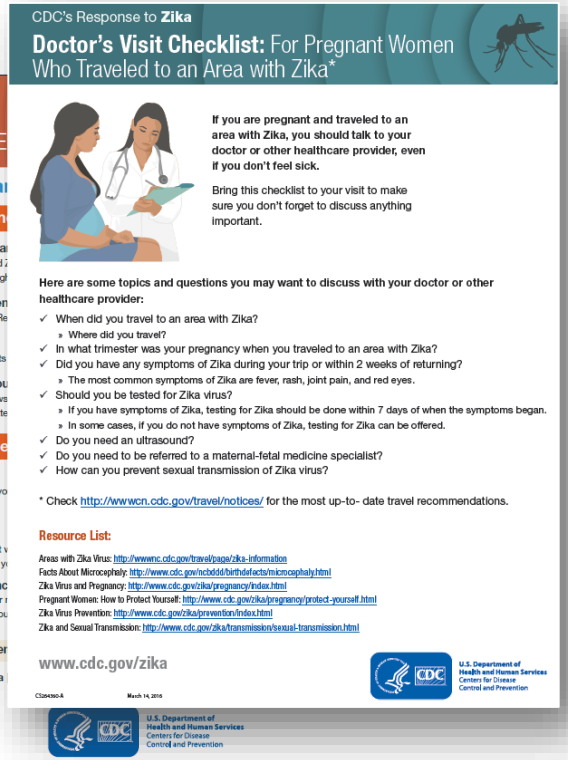
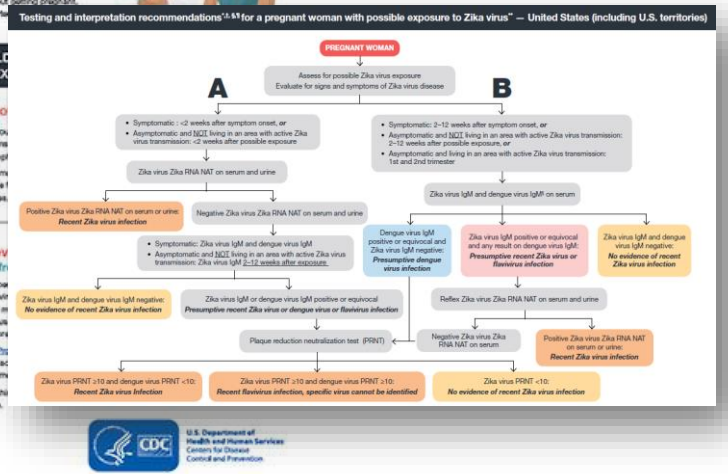
Developing Tools for Healthcare Providers





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
  - Available on the US Zika Pregnancy Registry website
  - 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).

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)
TTY: 1-888-232-6348 www.cdc.gov