

Zika Grand Rounds Facilitation Guide: Pregnancy

Intended audience: Obstetric Providers

Estimated time length: 20 minutes

CDC's Response to Zika

Zika Virus & Pregnancy

Grand Rounds
V2: Updated January 2017



- Good [morning/afternoon/evening]. Today I'd like to share with you what we've learned about Zika virus and pregnancy.

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 Zika outbreak is unprecedented. Although Zika was first identified almost 70 years ago, the potentially devastating effects on pregnancy are a recently recognized phenomenon.
- Some of you here today may remember that the last time an infectious pathogen (rubella virus) caused an epidemic of congenital defects was more than 50 years ago, before an effective vaccine became available.

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?

- My goal today is to share the most current information available, but I encourage you to stay up-to-date as the science advances. Here's a brief outline of my presentation.

Zika: The Basics

- First, let's start with some 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



- Zika is a single-stranded RNA virus that is closely related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses.
- It is primarily transmitted by the bite of two *Aedes* species mosquitoes, *Aedes aegypti* and *Aedes albopictus*.
- Zika is also transmitted through several other routes including
 - Intrauterine and perinatal transmission
 - Sexual transmission
 - Laboratory exposure
 - And probably blood transfusion

Where is Zika now?



Reported active Zika virus transmission
No reported active Zika virus transmission
As of 11 November 2016

The Pacific Islands
American Samoa
Fiji
Guam
Hawaii
Marshall Islands
Micronesia
Nauru
Palau
Papua New Guinea
Samoa
Tonga

Africa
Algeria
Angola
Cote d'Ivoire
DRC
Egypt
Ghana
Guinea
Kenya
Liberia
Mali
Mozambique
Nigeria
Senegal
Sierra Leone
South Africa
Tanzania
Togo
Zambia

Americas
Antigua and Barbuda
Bahamas
Barbados
Belize
Bonaire
Cuba
Curaçao
Dominican Republic
Ecuador
El Salvador
French Polynesia
Guatemala
Honduras
Jamaica
Mexico
Nicaragua
Panama
Paraguay
Peru
Puerto Rico
Trinidad and Tobago
United States
Uruguay
Venezuela

Map created by CDC/Univ. of Michigan/Johns Hopkins

- As of December 29, 2016, 61 countries and territories worldwide are reporting active Zika virus transmission. Check the CDC website for the latest numbers and locations.
- This map shows countries in which Zika virus is actively being transmitted by mosquitoes. Orange shading of a country doesn't mean that Zika virus is being spread across the entire country; it just means that Zika virus being spread by local mosquitoes has been reported in at least one area of that country. Visit the CDC website for more specific information about where Zika virus is being locally transmitted.
- To date, Florida and Texas have been the only states in the United States that have had local transmission. This occurred in small areas only in Miami-Dade County, FL and Brownsville, TX.

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

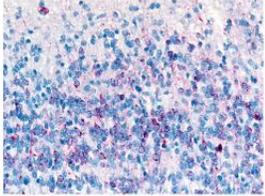


- Now I would like to switch gears and talk about some of the clinical aspects of Zika.
 - Many people infected with Zika virus won't have symptoms or will only have mild symptoms.
 - When symptoms do occur the most common ones are fever, rash, joint pain, and conjunctivitis (red eyes).
 - Symptoms typically last several days to a week.
 - Severe disease requiring hospitalization has been uncommon and fatalities have been rarely reported.
 - Based on similar infections, once a person has been infected with Zika and cleared the virus from their blood, it is believed that he or she is likely to be protected from future infections.

<p>Clinical Management</p> <ul style="list-style-type: none"> • No vaccine or specific antiviral treatment • Treat the symptoms <ul style="list-style-type: none"> • 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. 	<ul style="list-style-type: none"> • Although research is underway, there is currently no vaccine or specific antiviral treatment for Zika. <ul style="list-style-type: none"> ○ The cornerstone of treatment is supportive care. Patients should be advised to treat the symptoms, including <ul style="list-style-type: none"> ○ Rest ○ Drinking fluids to prevent dehydration and ○ Taking medicine such as acetaminophen to reduce fever and pain ○ Aspirin and NSAIDs should be avoided until dengue can be ruled out to reduce the risk of bleeding. Pregnant women should talk with their doctor before taking NSAIDs or aspirin.
<p>Zika, Pregnancy and Congenital Zika Syndrome</p>	<ul style="list-style-type: none"> • When Zika virus is transmitted from a pregnant woman to her fetus, the effect on the health of the fetus and infant can be serious. We'll focus now on Zika, Pregnancy, and Congenital Zika Syndrome.
<p>Zika Virus Infection in Pregnant Women</p> <ul style="list-style-type: none"> • Pregnant women can be infected <ul style="list-style-type: none"> • Through a mosquito bite • Through sex without a condom with an infected partner • If infected around conception <ul style="list-style-type: none"> • Zika might present risk to fetus • If infected during pregnancy <ul style="list-style-type: none"> • Zika can be passed to the fetus during pregnancy or around the time of birth 	<ul style="list-style-type: none"> • Pregnant women can be infected with Zika through the same routes I discussed earlier, mainly <ul style="list-style-type: none"> ○ Through the bite of an infected mosquito or ○ Through sex without a condom with an infected partner • Zika may be passed to the fetus around the time of conception • If a women is infected during pregnancy, Zika can be passed to the fetus during pregnancy or around the time of birth.
<p>Zika Virus in Pregnancy</p>  <ul style="list-style-type: none"> • 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 in pregnant women is similar to non-pregnant people <p><small>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. Bennett, M., et al., Evidence of Perinatal Transmission of Zika Virus, French Polynesia, December 2013 and February 2014. Euro Surveill. 2014; 19(4): 1-5. Petersen, M., et al. Zika Virus Infections—Microcephaly and Other Neurologic Complications—French Polynesia, 2013-2014. JAMA. 2014; 312(23): 2551-61.</small></p>	<ul style="list-style-type: none"> • The incidence of Zika virus infection in pregnant women is not known. • However, infection can occur in any trimester. • There is no evidence that pregnant women are more susceptible to Zika than non-pregnant women, and • The clinical course of Zika is similar for pregnant women and non-pregnant women

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 has been shown to be present in fetal tissue.
- There is evidence of Zika virus detected in:
 - Amniotic fluid
 - Placenta
 - Fetal brain tissue
 - Products of conception
- This image shows 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.
- A CDC study released December 13, 2016, found that Zika virus can continue to replicate in infants' brains even after birth. This information could have important implications for babies born with microcephaly and for babies who are born seemingly healthy.
- Zika virus has also been found in the placenta.

Zika is a Cause of Microcephaly

IN: NEW ENGLAND JOURNAL OF MEDICINE

SPECIAL REPORT

Zika Virus and Birth Defects — Reviewing the Evidence for Causality

Sanja A. Rasmussen, M.D., Denise J. Jamison, M.D., M.P.H., 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

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/genetic-protective-cookies.html). An increase in the number of infants with microcephaly has been reported.

- In April 2016, in an article published in the New England Journal of Medicine, scientists at CDC concluded that enough evidence had accumulated to determine Zika virus is a cause of microcephaly and other brain anomalies.
- To reach this conclusion, the scientists conducted a systematic evaluation of the evidence, which supported a causal relationship between Zika virus infection and microcephaly and other serious brain anomalies.

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

- Congenital Zika syndrome is now a recognized 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
- A case series published in late November also demonstrated that microcephaly at birth is not a necessary feature of congenital Zika syndrome. Infants with head circumference in the normal range at birth can have brain abnormalities consistent with congenital Zika syndrome and can experience slowed head growth and develop microcephaly after birth.

Potential Risk of Microcephaly

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



Johnson ML, Muench FR, Ribeiro L, Beebe-Dubau J, Gilboa RM, Hillis SL. Zika and the Risk of Microcephaly. *NEJM*. 2016 May 20. [Epub ahead of print].

- We don't yet know the risk of microcephaly in infants of mothers infected with Zika virus during pregnancy, but we are learning more information.
- Based on modeling data from the current outbreak in Brazil, the estimated risk of microcephaly was 1-13% when the infection occurred in the first trimester.
- Currently, there are not enough data to estimate the risk when the infection occurs in the 2nd or 3rd trimester.
- There are some limitations of this study, noted here, including that some pregnancies are ongoing, and microcephaly cases are still being reported and investigated.

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



Hesseltine M, Davidson AL, Peterson 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].

- A report from the US Zika Pregnancy Registry found that about 6% of women with laboratory evidence of possible recent Zika virus infection had birth defects potentially related to Zika virus.
- The proportion of pregnancies with birth defects was similar (around 6%) among pregnant women who experienced symptoms and pregnant women who were asymptomatic.
- This emphasizes the importance of screening pregnant women for Zika risk and testing them when indicated, because asymptomatic women are just as likely to have babies with birth defects.
- The report also found that among women with maternal symptoms OR laboratory evidence of possible Zika virus infection in the first trimester of pregnancy, birth defects were reported in 11% of completed pregnancies.

CDC Recommendations: Conception and Contraception

- Now, I will discuss CDC recommendations, first for preconception counseling.

Clinical Guidance for Preconception and Sexual Transmission



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

Frank E, Pearson MD, Chen M, Moore-Davis MD, Rubin N, Rubin R, Taylor TH, et al. 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. *MMWR*. 2016 Sep 30;65(39):1043-1048. doi:10.1093/mmwr.mm6509a1.

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6509a1.htm>

- CDC published updated interim guidance for preconception counseling and prevention of sexual transmission of Zika on September 30, 2016.

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 travelling 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

- This guidance includes recommendations to help healthcare providers discuss pregnancy planning with women and their partners after possible exposure to Zika. The table on this slide shows the suggested timeframes for waiting to get pregnant after possible exposure to Zika.
- Women should wait at least 8 weeks after last possible exposure or symptom onset before attempting conception. Men should wait at least 6 months after last possible exposure or symptom onset. The waiting period for men is longer because Zika virus can be found in semen longer than in other body fluids.

Pregnancy Planning and Access to Contraception

- Preventing Zika infections during pregnancy
 - Includes supporting women who want to delay or avoid pregnancy in order 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, HCPs 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 STIs, including Zika

- Preventing Zika infections during pregnancy is CDC's top priority for the Zika response. This includes supporting women who want to delay or avoid pregnancy to avert Zika-related adverse pregnancy and birth outcomes.
- Healthcare providers should discuss strategies to prevent unintended pregnancy among women who wish to avoid or delay pregnancy, including counseling on the use of the most effective contraceptive methods that meet couples' lifestyle needs, and can be used correctly and consistently.
- Additionally, healthcare providers should advise patients to consider using condoms correctly and consistently, in addition to other birth control methods, to reduce the risk of acquiring or transmitting Zika and other sexually transmitted infections.

CDC Guidance: Diagnosing and Testing for Zika

- Now, I will speak about the CDC's guidance about testing for and diagnosing Zika virus infection.

Assessing for Zika During Pregnancy

- All pregnant women should be assessed for 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

Link: <https://www.cdc.gov/zika/pdfs/zika-scr-screeningtool.pdf>

- In light of the adverse outcomes associated with Zika virus infection during pregnancy, all pregnant women should be assessed for Zika exposure, signs and symptoms at each prenatal visit.
- They should be asked if they
 - Traveled to or live in an area with Zika or
 - Had sex without a condom with a partner with potential exposure to Zika.
- CDC has developed a tool (shown here), which is available in both interactive and printable versions on CDC's website, to help healthcare providers determine if testing is needed.

Diagnostic Testing for Zika Virus

- Molecular method
 - Nucleic Acid Amplification Test (NAT) 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

- Before going through the Zika diagnostic tests, I would like to make the point that there are no licensed Zika tests in the US. Rather, all currently available Zika tests – at CDC, health departments, and commercial labs – are being used under an FDA Emergency Use Authorization. This mechanism allows unlicensed tests to be used in a public health emergency.
- Diagnostic testing for Zika virus infection can be accomplished using both molecular and serologic methods.
- The molecular method - called RNA nucleic acid testing, also referred to as NAT, detects viral RNA in body fluids including serum and urine. rRT-PCR is a type of nucleic acid testing. Anytime Zika RNA is detected, Zika virus infection is confirmed.
- The serologic tests, usually done through a simple blood draw, detect antibodies to Zika virus. This includes the Zika virus immunoglobulin M (IgM) assay to detect [anti-Zika virus] IgM antibodies in serum.
- An additional serologic test is the plaque reduction neutralization test, or PRNT, which measures virus-specific neutralizing antibodies, and can be helpful to differentiate Zika from other flavivirus infections.

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

- There are a number of limitations to keep in mind when interpreting both Zika molecular and serologic assays. First, since Zika virus RNA in serum and urine are short-lived, negative results do not preclude infection.
- Second, testing for Zika virus IgM can result in false positive results because of significant cross-reactivity with other flaviviruses such as dengue and for other non-specific reasons.
- Third, PRNT may not distinguish the type of infecting virus in people previously infected with or vaccinated against a related flavivirus.

CDC Guidance: Pregnancy

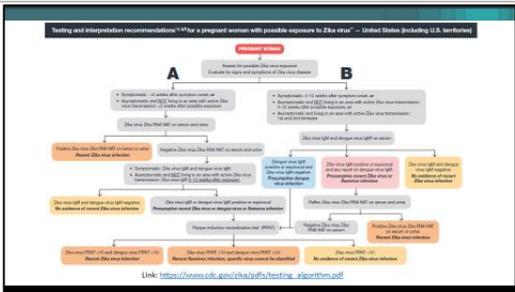
- Next, I will discuss CDC's current guidance regarding Zika and pregnant women.

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 should be offered testing
- 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/35/wr/mm3524a1.html>

- CDC recommends Zika testing for all pregnant women with possible exposure to Zika virus **and** signs or symptoms of Zika virus infection.
- In addition, pregnant women with possible exposure to Zika virus who do not report symptoms should also be tested.
- Testing recommendations for asymptomatic pregnant women with possible Zika virus exposure differ based on the circumstances of possible exposure (i.e., ongoing versus limited exposure) and the elapsed interval since the last possible Zika virus exposure.



- The specific testing plan for a pregnant woman depends on several factors, including whether she had symptoms of Zika and how much time has elapsed since her symptoms or last possible Zika exposure. This is described in the CDC guidance.
 - This flow chart was published in the updated pregnancy guidance in CDC’s Morbidity and Mortality Weekly Report on July 29, 2016. In the next few slides, I will briefly describe the updated guidance.

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

- Symptomatic pregnant women evaluated within two weeks after symptom onset should receive Zika virus testing of their serum and urine using NAT testing. A positive result confirms a diagnosis of a recent Zika virus infection. A negative result does not rule out infection. Therefore if the NAT tests on both serum and urine are negative, then Zika virus IgM and dengue virus IgM antibody testing should be immediately performed.
- If evaluated within 2-12 weeks after symptom onset, a pregnant woman should first have a Zika virus IgM test, and if the test is positive or equivocal, NAT should be performed on serum and urine.

Updated Guidance: Asymptomatic Pregnant Women

- Living in areas without active 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 active 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 active 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 asymptomatic pregnant women who live in an area without Zika but who may have been exposed to Zika
 - If evaluated within 2 weeks after last possible exposure, NAT testing should be performed on serum and urine. If negative, Zika virus IgM testing should be performed 2-12 weeks after exposure.
 - If evaluated 2-12 weeks after last possible exposure, Zika virus IgM testing should be performed. If positive or equivocal, NAT testing should be performed on serum and urine.
- Asymptomatic pregnant women who live in an area with Zika should receive Zika virus 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.

- 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	<ul style="list-style-type: none"> Consider serial ultrasounds every 3-4 weeks to assess fetal anatomy and growth† Discussions regarding amniocentesis should be individualized for each clinical circumstance† 	<p>LAB TESTING:</p> <ul style="list-style-type: none"> Infant serum and urine should be tested for Zika virus (Zika RNA, NAT). Infant serum should be tested for Zika IgM. If IgM is obtained by other means, it can also be tested. Zika virus (Zika RNA NAT and IgM) staining of umbilical cord and placenta is recommended† <p>PERINATAL LOSS:</p> <ul style="list-style-type: none"> Zika virus (Zika RNA NAT and IgM) staining of fetal tissues is recommended†
Recent flavivirus infection, specific virus cannot be identified		
Presumptive recent Zika virus infection**	<ul style="list-style-type: none"> 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† 	<p>LAB TESTING:</p> <ul style="list-style-type: none"> Infant serum and urine should be tested for Zika virus (Zika RNA, NAT). Infant serum should be tested for Zika IgM. If IgM is obtained by other means, it can also be tested. Zika virus (Zika RNA NAT and IgM) staining of umbilical cord and placenta is recommended† <p>PERINATAL LOSS:</p> <ul style="list-style-type: none"> Zika virus (Zika RNA NAT and IgM) staining of fetal tissues should be considered†
Presumptive recent flavivirus infection**		
Recent dengue virus infection	<ul style="list-style-type: none"> Clinical management in accordance with existing guidelines (CDC/110682, WHO/107034, WHO/109144, WHO/113813, WHO/114707, WHO/115105) 	
No evidence of Zika virus or dengue virus infection	<ul style="list-style-type: none"> Provide ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome† Fetal abnormalities present: recent Zika virus (Zika RNA NAT and IgM) test, based clinical management on corresponding laboratory results. Fetal abnormalities absent: base obstetric care on the ongoing risk of Zika virus exposure to the pregnant woman. 	

- This tool is also available online at CDC.gov/Zika and provides information on the prenatal and postnatal management of pregnant women based on their laboratory test results.

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/ur/ur6502a1.htm?_r=0&cid=mm6502a1_a

- Prenatal management is similar for pregnant women with *confirmed* recent Zika or flavivirus and *presumptive* recent Zika virus or flavivirus infection.
- Clinical management includes serial fetal ultrasounds every 3-4 weeks to assess fetal anatomy and monitor growth. Amniocentesis should be individualized for pregnant women with confirmed recent Zika virus or flavivirus infection and can be considered for pregnant women with presumptive recent Zika virus or flavivirus infection.

Preventing Zika in Pregnant Women

- As I mentioned, Zika virus infection has serious potential health implications for pregnant women and their fetuses. Let's continue to discuss how to prevent Zika virus infection.

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://www.cdc.gov/travel/page/zika-information>

- First, CDC recommends that pregnant women not travel to areas with Zika.
- If a pregnant woman **must** travel to an area with Zika, she should talk to her healthcare provider before departing and strictly follow steps to avoid mosquito bites and prevent sexual transmission during her trip.
- Upon her return, she should talk to her healthcare provider, even if she doesn't feel sick.

<p>Prevent Mosquito Bites</p> <p>If a pregnant woman lives in or travels to an area with Zika, she should:</p> <ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> • DEET, picaridin, IR3535, oil of lemon eucalyptus or 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 	<ul style="list-style-type: none"> • All pregnant women should prevent mosquito bites by wearing long sleeved shirts and long pants. • Whenever possible, pregnant women should also stay and sleep in air-conditioned places or places that have window and door screens. • The use of insect repellants with EPA-registered ingredients is important. Insect repellents should contain one of the following active ingredients listed on this slide. When used as directed, these insect repellants are proven safe and effective, even for pregnant and breastfeeding women. • Finally, items that hold water such as tires, planters, and birdbaths should be emptied and scrubbed, turned over, covered, or thrown out once a week since mosquitoes lay eggs near water.
<p>Prevent Sexual Transmission of Zika Virus</p> <p>A pregnant woman whose partner lives in or has traveled to an area with Zika should</p> <ul style="list-style-type: none"> • use condoms correctly every time they have sex, or • abstain from sex <p>For the duration of the pregnancy, even if the pregnant woman's partner does not have symptoms or feel sick.</p> 	<ul style="list-style-type: none"> • Pregnant women should also take actions to prevent Zika infection through sex. • If a pregnant woman's partner lives in or has traveled to an area with Zika, healthcare providers should advise that the couple use condoms from start to finish every time they have sex or not have sex during the entire pregnancy. • It is important that these actions are taken for the duration of the pregnancy, even if the woman's partner does not have symptoms or feel sick.
<p>Standard Precautions to Prevent the Spread of Zika Virus and Other Infectious Agents During Healthcare Delivery</p>	<ul style="list-style-type: none"> • Next, we'll switch gears again and discuss infection control in the healthcare setting through use of Standard Precautions in the context of Zika virus.
<p>Zika Virus Disease in Healthcare Settings</p> <ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • To date, there have been no reports 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), so standard infection prevention precautions are still necessary.

<p>Standard Precautions</p> <ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Healthcare personnel must adhere to Standard Precautions in all healthcare settings. • This is already-existing guidance, but Zika provides an opportunity to emphasize the importance of following these existing protective recommendations. • Standard precautions are basic measures to prevent infection and are a group of practices that apply to all patients, regardless of suspected or confirmed infection status, in any setting in which healthcare is delivered. • The goals of implementing standard precautions are to <ul style="list-style-type: none"> ○ Prevent direct contact between a patient's body fluids and the healthcare provider's mucous membranes or broken skin ○ To protect healthcare providers and prevent them from transmitting potentially infectious material from one patient to another; ○ And to avoid percutaneous exposure to contaminated sharp implements.
<p>Standard Precautions: Personal Protective Equipment (PPE)</p> <ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> • HCPs must assess their risk for exposure and select appropriate PPE • Examples of obstetric procedures that require increasing amount of PPE <ul style="list-style-type: none"> • Vaginal exam particularly during amniotomy • Vaginal delivery including manual removal of placenta • Operative procedures 	<ul style="list-style-type: none"> • One component of Standard Precautions is the use of personal protective equipment (or PPE), such as gloves, gowns, face masks, face shields, and goggles. • Facilities should assure that sufficient and appropriate PPE is available and readily accessible to healthcare personnel. In addition, healthcare personnel should be educated on the proper selection and correct use of PPE. • Examples of high-risk obstetric procedures that require increasing amounts of PPE in the labor and delivery setting include: <ul style="list-style-type: none"> ○ Vaginal examinations, particularly during amniotomy, when exposure to fluids would be expected; ○ Performing a vaginal delivery or manual removal of a placenta when exposure to larger volumes of fluids would be anticipated; and ○ Procedures in an operating room setting.
<p>What is CDC Doing?</p>	<ul style="list-style-type: none"> • So, what is CDC doing to learn more about Zika and respond?

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?



- Our understanding of Zika virus continues to evolve. Although we have learned about the association of Zika and poor pregnancy outcomes in a short amount of time, many questions remain. For example:
 - 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?
 - What is the risk for later health problems in an infant who is infected or who has had exposure to Zika virus but is born without abnormalities?
- Answering these critical questions is a focus of our ongoing research and ultimately may help reduce the effects of Zika infection during pregnancy and anticipate the needs of women infected with Zika virus during pregnancy, children with congenital Zika infections, and their families.

Collecting Data for Action

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



- This slide lists some of what CDC is doing to learn more about Zika infection during pregnancy.
 - CDC established the US Zika Pregnancy Registry in collaboration with state, tribal, local, and territorial health departments in the United States and territories (excluding Puerto Rico). The registry collects information about women with laboratory evidence of possible Zika virus infection during pregnancy, whether or not they have symptoms, and their infants.
 - CDC helped develop a similar system in Puerto Rico, the Zika Active Pregnancy Surveillance System.
 - Additionally, enhanced surveillance of pregnant women with Zika in Colombia has been established.
 - CDC supports 45 jurisdictions in the US to conduct Zika-related birth defects surveillance to better understand Zika exposure during pregnancy and adverse outcomes.
 - ArboNET, an existing national arboviral surveillance system managed by CDC and state and territorial health departments, collects information on laboratory-confirmed Zika virus disease cases reported from US states and territories. The data from this system will help us understand the effects of postnatal Zika infection.
- Data will be used to update recommendations for clinical care, plan for services for pregnant women, their infants and families affected by Zika, and improve prevention of Zika infection during pregnancy.

Sharing Up-to-Date Information

- Providing updated clinical guidance
- Responding to your inquiries:
 - Email ZikaMCH@cdc.gov
 - CDC-INFO



Center for Disease Control and Prevention
MMWR
 Morbidity and Mortality Weekly Report
 Early Release / Vol. 65 July 25, 2016

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

Talbot TR, Hensley ML, Lopez-Gatell H, et al. Centers for Disease Control and Prevention. 2016. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016. *Morbidity and Mortality Weekly Report*. 65(27):500-504. doi:10.1182/1098-2745.65.27.500

- Every new finding from a published study, each new data point collected –all this information feeds into what is known about Zika and directs our public health action. CDC is rapidly translating new findings into messages for the public and updated clinical guidance, and is committed to sharing what we know when we know it.
- CDC maintains a 24/7 Zika Pregnancy Hotline for healthcare providers of pregnant patients with possible Zika virus infection. Through this service, CDC scientists and clinicians are available for any concerns about clinical management and to answer questions about the US Zika Pregnancy Registry by telephone or email consultation. Providers and the general public can also ask questions through CDC INFO at 800-CDC-INFO (800-232-4636) or www.cdc.gov/cdc-info.

Developing Tools for Healthcare Providers



- CDC has also developed a number of communication materials for healthcare providers and their patients.
- These materials, available on the CDC website in a variety of languages, help translate CDC’s clinical guidance into tools for use in a clinical setting.

What Can You Do?

- All of us, as healthcare professionals or members of the community, can work together to help improve our understanding of the effects of Zika and to improve awareness of how to prevent Zika.

Report Cases

- Zika virus disease and Zika virus infection without disease, including congenital Zika virus infection, are nationally notifiable conditions.
- Report all cases of Zika virus infections and Zika disease to your state health department.



- Zika virus disease and Zika virus congenital infection are nationally notifiable conditions that should be reported to the National Notifiable Diseases Surveillance System (NNDSS).
- The following cases should be reported to your state health department:
 - Symptomatic and asymptomatic cases with laboratory evidence of Zika virus infection
 - Infants born with or without abnormalities consistent with CZS and laboratory evidence of Zika virus infection
- Reporting to the US Zika Pregnancy Registry, as described in next slide, is voluntary.

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 [U.S. 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)



- As we discussed briefly, CDC established the US Zika Pregnancy Registry to monitor pregnancy and infant outcomes to help inform clinical guidance and direct public health action.
- The registry casts a wider net than ArboNET and National Notifiable Diseases Surveillance System as it pertains to Zika, because the registry includes symptomatic and asymptomatic pregnant women with positive, equivocal, or inconclusive Zika test results with or without symptoms. It also includes **all** infants born to these women, not only those with identified congenital infection, and they will be followed for 1 year.
- As a healthcare provider, you can support the registry by spreading the word about its importance, and working with your health department to report cases and collect clinical and follow-up information.
- If you have clinical questions or questions about reporting to the pregnancy registry, you can go to the CDC website for information or contact CDC via email or phone.

In Summary

- Know the basics about Zika transmission in your community
- Diagnose and test for Zika for those with symptoms 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

- To summarize, as a healthcare provider, here's what you can do:
 - Know the basics about Zika transmission and prevention
 - Understand the assessment and management of Zika among pregnant women and protect them from exposure,
 - Counsel couples on Zika prevention if they are planning a pregnancy
 - Provide access to effective contraception for those not planning pregnancy, and
 - Inform your state or local 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

- Additional information and resources can be found on the CDC website.

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

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.



- All of this is the work of many people. Many thanks to all of our collaborators, and thank you all for listening today.

Frequently Asked Questions

What are the suggested timeframes for waiting to get pregnant after possible exposure to Zika?

- Regardless of whether they have symptoms, men with possible Zika exposure who do not live in areas of active transmission but who are considering pregnancy with their partner should wait at least 6 months after last possible exposure (without symptoms) or symptom onset (with symptoms) before trying to conceive.
- Women with possible Zika virus exposure who do not live in areas of active transmission but who are thinking about becoming pregnant should wait at least 8 weeks after symptoms start or last possible exposure before trying to conceive; this recommendation remains unchanged from the previous guidance.
- Women with possible Zika virus exposure who are not pregnant and do not plan to become pregnant and their male partners who want to minimize their risk of sexual transmission should use condoms in addition to their chosen birth control method, or they should not have sex for the same timeframes listed above. Correct and consistent use of condoms also reduces the risk for other sexually transmitted infections.
- Women of reproductive age and their partners should use the most effective contraceptive methods that meet their lifestyle needs and can be used correctly and consistently.

Where can I find information about areas with Zika?

This information is available online at [Areas with Zika](#)

How is Zika spread?

- Zika virus is spread to people primarily through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*).
- A pregnant woman can pass Zika virus to her fetus during pregnancy or around the time of birth. We do not know how often this happens.
- A person with Zika virus can pass it to his or her sex partners.
- Zika may be spread through blood transfusion.
- One case of Zika has been confirmed in a person in Utah with no known risk factors; however, the person did provide care to another person who had very high amounts of Zika virus in his blood. Although the route of transmission is not certain, family contacts should be aware that blood and body fluids of severely ill patients might be infectious.
- Transmission of Zika virus infection through breastfeeding has not been documented.

How should pregnant patients who are considering travel to an area with active Zika virus transmission be counseled?

CDC recommends that pregnant women not travel to an area with Zika. If a pregnant woman is considering travel to one of these areas, she should talk to her healthcare provider. If she travels, she should be counseled to strictly follow steps to avoid mosquito bites during the trip, and use condoms to

reduce exposure to possible sexual transmission of the virus. If a pregnant woman has a partner who lives in or has traveled to an area with Zika, she should be counseled to either use condoms from start to finish every time she has sex, or not have sex (vaginal, anal, and oral sex, and sharing of sex toys) during her pregnancy to prevent sexual transmission.

What types of testing for Zika virus are available to diagnose pregnant women?

The type of testing recommended varies depending on the time of evaluation relative to symptom onset or last date of possible exposure.

- Testing of serum and urine by RNA nucleic acid testing (NAT; e.g., rRT-PCR) is recommended for pregnant women who seek care up to 2 weeks after symptom onset or last date of possible exposure. A positive NAT test confirms the diagnosis of recent maternal Zika virus infection.
- For pregnant women who seek care 2-12 weeks after symptom onset or last date of possible exposure, serologic assays can be offered to detect Zika virus-specific IgM antibodies.
- Immediate NAT testing is now recommended for women who have a positive or equivocal Zika virus IgM result, because it provides the potential for a definitive diagnosis of Zika virus infection.
- Negative NAT results should be followed up with plaque reduction neutralization testing to measure virus specific neutralizing antibodies to confirm the presence of an immune response to a flavivirus infection and to differentiate Zika infection from other similar illnesses. Interpretation of serologic results has been described and published [elsewhere](#).

Does a positive Zika virus IgM always indicate Zika virus infection?

No; a positive IgM result can be difficult to interpret since cross-reactivity can occur with related flaviviruses (e.g., dengue, Japanese encephalitis, West Nile, yellow fever). A positive Zika virus IgM result may reflect: previous vaccination against a flavivirus (e.g., yellow fever); previous infection with a related flavivirus; or recent or current infection with a flavivirus, including Zika virus.

Is testing the semen of men with possible exposure to Zika virus recommended?

No, testing the semen of men with possible exposure to Zika virus is not currently recommended. Testing of semen has not yet been validated and interpretation of the test results is not yet understood. Intermittent shedding in semen can occur with other viruses and the pattern of Zika virus shedding in semen is unknown. In addition, the detection of Zika virus RNA in semen might not indicate the presence of infectious virus in semen. Studies are underway to better understand the performance of these tests, the persistence of Zika virus in semen, and how best to interpret the results.

What should providers consider when ordering a test for Zika virus infection?

Each clinical scenario is unique, and healthcare providers should consider all available information when ordering a test for Zika virus infection, including patient travel history or possible exposure through sexual contact, history of flavivirus infection, vaccination history, ultrasound findings, and the presence of symptoms. Providers should work with their state, local, and territorial health departments for assistance obtaining and interpreting test results.

What should healthcare personnel do to avoid spreading Zika virus in healthcare settings?

CDC released a [report](#) emphasizing the importance of healthcare personnel following practices, called Standard Precautions, to prevent the spread of infectious diseases such as Zika when caring for all patients, including pregnant patients in labor and delivery settings. Currently, there are no confirmed reports of Zika spreading from an infected patient to a healthcare provider or other patients. However, healthcare personnel are reminded to use Standard Precautions when they might come in contact with high volumes of body fluids. Standard Precautions to minimize contact with body fluids are important to reduce the possibility of spreading infectious diseases such as Zika.